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info@barcelonahair2019.org
Welcome

Hair diseases represent a significant portion of cases seen by dermatologists. In fact, the study of hair disorders has become one of the most important fields of dermatology nowadays. So, it is a great pleasure for us, three dermatologists, to be the organizers of the 11th World Congress of the Hair Research Societies in Barcelona.

During these 4 days we will have the best international hair specialists from all over the world to discuss and deliver the last knowledge on hair diseases.

Biologists, dermatologists, surgeons, and researchers from all areas of expertise will gather together in the greatest scientific event of the Hair Research world. During the last decade, the field of hair disorders has attracted many investigators and young dermatologists involved in clinical or basic research. In particular, molecular analysis of genetic hair disorders is developing rapidly. Trichoscopy has also emerged as an invaluable diagnostic technique for most types of alopecia. New approaches to therapy of common hair disorders have also made this subspecialty more attractive and have changed the tendency that we had at the end of the last century.

Dermatologists are in the enviable situation of being able to study many disorders with non-invasive diagnostic techniques. The hair is easily accessible to examination but, paradoxically, this approach is often disregarded by non-dermatologists.

We believe as organizers of the meeting that these days will be very useful for all attendees in their daily practice. The information delivered during this meeting will hopefully stimulate and encourage the cooperation between physicians and especially with dermatologists experienced in this important field of medicine.

We would like to thank all the support from the companies that have believed in our project and just to remind all of us that without them this would have not been possible.

Finally, we want to show our gratefulness to the scientific committee, the chairs, the speakers and the authors of the free communications. Their hard work was essential to create this abstract book.

The organizers

Prof. Juan Ferrando  
President

Prof. Ramon Grimalt  
President

Dr. Sergio Vañó-Galvan  
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- Change in hair growth-related gene expression profile in human isolated hair follicles induced by the 5-alpha reductase inhibitors, dutasteride and finasteride, in the presence of testosterone
- Hormones, hair growth and FPHL
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- SAHA syndrome 2019

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**HOW TO SUCCESSFULLY RUN A HAIR CLINIC**

The keys to running a successful hair clinic are three fold:

1) Positive patient outcomes with clear cut patient satisfaction: In order to do this, the time you spend with the patient, consistent photographs including trichoscopy with objective quantification of hair density and diameters, as well as a detailed explanation of the treatment plan with risks and benefits. All questions must be answered to make sure patients fully comprehend the diagnosis and management plan specifically customized for them. The patient’s input is pivotal in determining how much risk they are prepared to take. All medical and surgical options must be presented in a tiered approach.

2) Personal growth as a hair specialist: One must be current and adapt to new technologies. It is crucial to collaborate with colleagues as well as enlisting younger dermatologists into your clinics who are always questioning what you are doing. Questions will make you a better physician.

3) Your ability to advance the entire field of trichologic medicine: Participation in clinical research and liaising with basic science research are important. Also passing on the knowledge that you have accumulated over the decades to the next generation. Teaching will ensure a legacy and help advance the field of trichologic medicine to an even greater level as the next generation modernizes your treatments. We will see great changes with the next generation of hair specialists.

**HOW FAR ARE WE FROM CLONING HAIR?**

Forty years ago, we learnt that hair follicle development is induced by signalling in the skin dermis, resulting in a series of well-coordinated interactions between the mesenchyme and epithelium. For decades since, research has tried to exploit this knowledge to promote growth of new hair follicles in non-hairy skin, otherwise referred to as hair cloning. Advances in imaging and sequencing technology has enabled the field to rapidly progress over the past decade, and human hair follicles have now been grown in a laboratory environment. In this presentation, I will discuss the history of hair cloning, and the work currently ongoing in my laboratory looking at epigenetic and genetic changes in the hair follicle dermis as it becomes inductive.
Chairs: Dimitrios Ioannides, Dominique Van Neste, Maria Fernanda Gavazzoni

INTERACTIVE Q&A CLINIC-DERMATOSCOPY-HISTOPATHOLOGY AND TREATMENT

Maria Fernanda Reis Gavazzoni Dias
Universidade Federal Fluminense
Hospital Universitário Antônio Pedro - Niterói - Rio de Janeiro - Brasil

Inflammatory alopecias with scarring (Lichen-planus pilaris, Frontal Fibrosing Alopecia, Fibrosing alopecia in a pattern distribution, Central Centrifugal Cicatricial Alopecia, Folliculitis Decalvans, Dissecting Folliculitis, Miscellanea)

Primary cicatrical alopecia is a group of hair disorders that leads to permanent scalp scarring. The diagnosis always needs a scalp biopsy, interpretation of the histopathological findings and their correlation with the physical exam and the dermatoscopy features. Some extra-scalp clinical features may also suggest important tips to help with the diagnosis.

This presentation will describe the uttermost information, based on the medical literature and personal experience, of how to recognize the different aspects of this group of diseases, to achieve the final correct diagnosis and to choose among the available multiple treatments. The audience will learn about how to recognize the patterns of the disease, make an early diagnosis in different ethnicities and avoid irreversible cicatrical hair loss.

AN INTERACTIVE Q&A CLINIC-DERMATOSCOPY-HISTOPATHOLOGY AND TREATMENT

Maria Fernanda Gavazzoni Dias
Universidade Federal Fluminense
Hospital Universitário Antonio-Pedro Niterói, Rio de Janeiro, Brazil

This 2-hour course session will cover the most common types of scarring and non-scarring alopecia including telogen effluvium, male and female pattern hair loss, alopecia areata, lymphocytic and neutrophilic cicatricial alopecia and some miscellanea interesting secondary alopecia cases.

Primary cicatrical and non-cicatrical alopecia encompasses two groups of hair disorders in which the main difference is whether the hair follicle is reversibly or irreversibly affected during the process. The proper early diagnosis is the main key to prevent a distressful and/or permanent hair loss. In this course, we will discuss the propedeutic and advanced instructions about the most frequent types of scarring and non-scarring alopecia and present tips to a better understanding of the correlation between clinical examination, dermatoscopy findings and, when needed, histopathological features.

As hair loss treatments have evolved during the last few years, an updated guideline of treatment options will be discussed based on personal experience and scientific evidences. Presentation of clinical cases and interaction with the audience will allow an easy and pleasant manner of learning and assimilating the actual concepts in the different types alopecia.

LEARNING OBJECTIVES

Following this course, the attendee should be able to:

• Diagnose the most common types of cicatrical and non-cicatrical alopecia.
• Approach of the hair loss patient in the daily practice (investigation of hair loss causes: blood tests, image, hormones, drugs, etc)
• Learn the pits falls in dermatoscopy of the scalp and other body sites, when related to the alopecia type.
• Learn when and how (theoretically) to perform a scalp biopsy.
• Correlate the clinical features with dermatoscopy and, if indicated, with the histopathological findings.
• Discuss the various alopecia treatments and learn about tips and hot topics with hair experts.
• How to manage the patient long-term follow-up: complications, drug side effects, lab tests.
• Proposal of treatment algorithms to different types of hair loss conditions.
Basic course on diagnosis and treatment of hair disorders

Chairs: Dimitrios Ioannides, Dominique Van Neste, Maria Fernanda Gavazzoni

NON-SCARRING ALOPECIAS (AGA OR MPHL AND CONCOMITANT HAIR LOSS AA, EFFLUVIIUM AND OTHERS)

Van Neste Dominique, MD, PhD
Skinterface Laboratories and Brussels’ Hair Clinic, Brussels, Belgium

The course will integrate as many different points-of-view as possible inasmuch as they apply to the phenomenology of hair growth, dynamics of hair loss and potential for regrowth in non-scarring alopecias. This encompasses information related to physiology and pharmacodynamics. Grey areas including non-science, pseudo-science and pure speculations will be identified whenever possible. During the lecture, each attendee will be invited to fill out his personal «test-your-knowledge». By comparing his personal answers before and after the lecture, she/he will objectively check whether his understanding has changed (preferably improved!) on the occasion of this presentation. After a brief recall of our to-day's understanding of the scalp hair cycle, the lecture will consider scalp biopsies - often referred to as a golden standard - and to put hair cycle dynamics in a clinical perspective.
ARE WE ANY CLOSER TO FINDING THE HAIR FOLLICLE (AUTO) ANTIGEN(S) IN ALOPECIA AREATA?

Desmond J Tobin
The Charles Institute of Dermatology, University College Dublin, Ireland

Current literature has largely concluded that the common immune-mediated hair follicle (HF) disorder Alopecia areata (AA) is ‘auto’ immune in nature. This designation provides limited insight on AA etiology, instead providing a handle for understanding potential patho-mechanism. Despite a current folliculo-centric view of AA, chronic and complex inflammatory diseases exhibit both tissue-specific and systemic responses. The latter are reflected in AA by the induction of both humoral and cellular immune responses. Also, like other ‘auto’-immune diseases, AA is likely to have significant environmental and polygenic components that define susceptibility and severity in the population.

Progress in elucidating the cause and development of therapeutic interventions for this most-commonly self-resolving condition has been frustrating, and after decades of intense research there remains no FDA-approved treatment. Specifically, the identification of the (auto)immunogenic HF targets has also been very slow; though some may view this may not be a requirement for effective and safe treatment discovery.

We and others continue to interrogate the hair follicle for targets of the immune response in AA. We continue to add incremental data, some informed by GWAS findings that suggest AA autoantigen candidates may not appear at the GWAS gene-association level. The finding that AA and celiac disease (CD) have some genetic association has encouraged us to see if antigenic motif sharing between immune-mediated conditions could guide us to target HF antigens in AA. Using combined immunohistochemistry and immuno-blotting approaches, we have some evidence of immunogenic epitopes in the anagen HF on inner root sheath (IRS), specifically for trichohyalin (TCHH). Immuno-reactivity of anti-gliadin antibody with TCHH-rich areas of the HF suggests potential cross-talk between AA and CD. Citrullinated antigenic motifs co-localised in HF where the relevant PAD enzymes are expressed to drive this citullination biotransformation. Human AA sera showed reactivity with α-gliadin itself, while antibodies to citrulinated proteins co-localize with HF TCHH. A new citrulline-specific rhodamine phenylglyoxal probe further confirms citrullination sites in the IRS. As shared TCHH motifs occur also on deimidated α-gliadin peptide in gluten, to which CD patients react, TCHH may be post-translationally implicated in AA. Our challenge will be to determine whether anti-Citrullination immune responses directed against the hair follicle are pathogenic in this condition.

MAINTAINING YOUR MANE: HAIR SHAFT PRODUCTION AND SYNTHESIS IN HEALTH AND DISEASE

T. L. Dawson Jr1,2 and D. P. Harland3

1 Agency for Science, Technology and Research, Skin Research Institute Singapore, and 
2 Department of Drug Discovery, School of Pharmacy, Medical University of South Carolina, Charleston, SC USA 
3 Food and Biobased Products Group, AgResearch, Crown Research Institute, New Zealand

Over the last four decades, research into biological manipulation of hair “quality” has ebbed and waned. Today there is a resurgence, leveraging opportunities presented by new tools, technologies, and techniques. Hair appearance or “quality” is regulated by multiple intervention opportunities - adding more hairs by pushing follicles from Telogen to Anagen or by slowing the transition from Anagen into Telogen; making “more” hair by modulating shaft diameter or shape; or, in principle, by altering the shaft physical properties by changing its synthesis. The vastly most common mechanism of current investigation is to increase hair density. This has obviously proven difficult and, to date, has yielded minimal perceptible benefits. We hypothesize that perceptible benefits may be best achieved by combining multiple opportunity areas - minimizing hair loss and miniaturization, maximizing shaft production, and treating/strengthening existing hairs. As a foundation, we must have better characterization of hair fiber assembly during Anagen.
Basic science course for hair researchers

Chairs: Desmond Tobin, Gill Westgate

Producing full anagen hair follicles and terminal hair shaft is among the most energy intensive processes in human metabolism. Further, it has previously been shown that alteration of follicle metabolism can influence hair shaft diameter. The human hair shaft structure is amazingly complex, consisting of multiple linear and circumferential structures all contributing individually to the various hair shaft physical properties. In the follicle base multiple biologically driven zones can be defined with vastly different processes: proliferation, production, construction and elongation, and maturation. Detailed understanding of the processes occurring in each zone should enable identification of factors necessary for optimum shaft production and identify new intervention opportunities. Recent investigations into the transition from the construction and elongation to the maturation phase reinforces a key developmental threshold, over which hair shaft production rapidly transforms from a primarily biological into a primarily biochemical process. We now name this “The Orwin Threshold”.

CURLY HAIR: JUST ROOTED IN BIOLOGY AND GENETICS?

Dr. Gillian E Westgate
Centre for Skin Sciences, Faculty of Life Sciences, University of Bradford, Bradford, UK

What makes hair curly is a question of biology, genetics and biomechanics - thus to address this most fascinating process we must consider how all the contributing factors come together. Curly hair occurs in many racial groups to greater or lesser extent and evolved twice as a result of environmental adaptive pressure over time. It was the early studies of wool fibre crimp that led to the original hypotheses of how curl is formed, with asymmetry in the distribution and lengths of cortical cell types being a strong morphological clue. However, this is less evident in larger wool and curly human fibres. Mapping of the different types of cortical cells in hair with respect to the arrangement of intermediate filaments has provided greater understanding in this respect for curl, however, is not sufficient to explain it. The follicles producing the curliest of human hairs are retro-curved with a club shaped bulb leading to hypothesis that curly hair originates in the bulb. Observed asymmetric rates of cell proliferation and expression of cortical cell differentiation markers supports a role of the follicle shape. However, the degree of curve in the follicle is generally much less than the fibre suggesting curl is somehow ‘stored’ during fibre formation and released which the fibre emerges. Curly hair is clearly a genetic trait, however, it was the study of genetic disorders in which normally straight hair is curly that pointed to the follicle inner root sheath having a role in hair shape, with keratin 71 and 74 and trichohyalin demonstrating polymorphic variation with hair fibre shape. One of the most difficult concepts to understand is how fibre coil and twist is determined. In this regard, two possible explanations have emerged; firstly that dermal papilla (DP) cell asymmetry has been suggested to explain aspects of axial rotation that generate the coil in curly hair. Secondly, a fibre stress/strain model proposes that a specific zone of stress is exerted in the forming hair by the follicle that translates into mechanical stress/strain that results in curly shape. In conclusion, formation of curly hair remains a fascinating multidisciplinary topic of interest to hair researchers.
LAB BASED APPROACHES FOR STUDYING HAIR FOLLICLE DEVELOPMENT AND CYCLING

Claire A Higgins
Department of Bioengineering, Imperial College London

All hair follicles are formed during embryogenesis, as a result of coordinated interactions between the skin mesenchyme and epithelium. In adult skin, these interactions continue and enable the hair follicle to transition through continuous cycles of growth (anagen), regression (catagen) and rest (telogen). While in murine skin, the signals coordinating these interactions can be studied *in vivo*, in human skin investigations are limited to *in vitro* and ex vivo. In this precongress course, I will discuss lab based approaches for studying hair follicle development and cycling in the human hair follicle.
**EPIGENETIC REGULATORY MECHANISMS AS A DRIVING FORCE OF PHENOTYPIC PLASTICITY AND EVOLUTIONARY ADAPTATION**

In the era of tissue engineering and development of novel approaches for stem cell-driven organ regeneration, it is important to understand how multi-potent stem cells establish distinct programs of gene expression during their differentiation into specialized cell lineages and why these programs are altered during ageing. Lineage-specific gene expression programs are governed by signaling/transcription factor-dependent and epigenetic mechanisms, and understanding how these two key regulatory machineries operate in concert to coordinate expression of lineage-specific genes is highly important for effective modulation of stem cell activity and translation of these data into clinical practice.

Epigenetic mechanisms play an important role in the control of cellular functions in living organisms. Variability in the epigenetic status helps to explain the relationships between an individual genetic background and effects of the environment on susceptibility to different diseases.

Epigenetic regulatory machinery operates at several levels including modulation of covalent DNA/histone modifications, as well as through higher-order chromatin remodeling to establish long-range topological interactions between the genes and their enhancer elements in three-dimensional nuclear space.

Epigenetic regulators exhibit both activating and repressive effects on chromatin states in keratinocytes: some of them promote terminal keratinocyte differentiation, while the others stimulate cell proliferation, as well as inhibit premature activation of terminal differentiation-associated genes. In this lecture, the involvement of different components of epigenetic machinery in the control of hair follicle-specific keratinocyte differentiation and hair growth will be discussed in the context of their interactions with distinct signaling pathways and transcription factors that form a platform for coordination of hair cycle-associated changes in gene expression programs in keratinocyte stem cells and their progenies.

**TET-MEDIATED DNA HYDROXYMETHYLATION IN DERMAL PAPILLA CELLS IS REQUIRED TO ACTIVATE HAIR GROWTH DURING HAIR CYCLE**

The biological characteristics of dermal papilla (DP) cells, including global gene expression profiles and biomarkers for hair-inductive capacity, have been well-studied in both mice and humans. However, a little is known about the functional role of epigenetic mechanisms of gene expression in the regulation of hair inductive properties in the DP. DNA methylation and subsequent oxidation of 5-methylcytosine (5mC) into 5-hydroxymethylcytosine (5hmC) by Ten-eleven-translocation (TET) proteins at the gene regulatory regions, promoters and enhancers, are the key epigenetic events regulating many biological pathways during development and tissue homeostasis. Here, we show that levels of Tet1, Tet2 and Tet3 proteins progressively increase in DP during telogen-to-anagen transition and reach the highest levels in mature anagen hair follicles. The changes in Tet proteins expression directly correlated with the abundance of 5hmC in DP during hair cycle. To study the role of Tet2, we genetically ablated Tet2 gene in DP cells using Prom1-driven cre recombination in mice. Tet2-deficient mice showed a marked delay in telogen-to-anagen transition during the first postnatal hair cycle reaching the late ana-
Epigenetics
Chairs: Elena Ezhkova, Vladimir Botchkarev

During the hair follicle cycle, significant epigenetic changes occur in the follicle epithelium, but much less is known about events in the mesenchyme. We are interested in epigenetic processes potentially undergone by dermal papilla (DP) cells, in two different scenarios: in vivo, over the course of the hair follicle cycle, and in response to their transition to bidimensional in vitro primary culture conditions. As indicators of chromatin remodelling processes, several histone methylation markers, as well as the histone-binding protein CBX5, were analysed by immunofluorescence, together with a number of other markers of cell identity, nuclear architecture, polarity and migration status. Mouse and rat vibrissa follicles, were either cryosectioned for the in vivo analyses or microdissected for DP isolation. The latter were plated onto cover glasses and cultured as explants. Stromal tissue, from mouse corneas, was also grown in explant cultures as a comparative independent mesenchymal cell population. These were obtained by enzymatically separating the stromal layer from the overlying cornea epithelium.

Our results indicate a variation in the histone methylation levels in DP cells depending on the stage of the hair follicle cycle. Thus, higher methylation levels were detected in anagen (growing) than in telogen (resting) phase for all the markers analysed (H4K20me2,3; H3K9me3; H3K27me3; H3K4me3). However, during the transition from in vivo to in vitro culture, we found a drastic difference in the pattern of expression of heterochromatin vs. euchromatin related markers in DP explants. Moreover, heterochromatin related CBX5 protein showed a characteristic pattern of expression in DP compared to cornea stroma explant cultures, suggesting distinctive features of DP cells. Interestingly there is evidence that explanted papilla cells undergo an initial telogen-like condition as a result of the dissection process. A number of cells in early outgrowths also show indications of DNA double-strand breaks. These observations pose the question of whether these chromatin remodelling processes have functional implications, both in the course of the hair follicle cycle in vivo and/or modifying/reprogramming the inductive ability, self-renewal capacity and differentiation potential of DP cells in vitro.

Polycomb repressive complexes (PRCs) 1 and 2 are essential chromatin regulators of cell identity. PRC1, a dominant executor of Polycomb-mediated control, functions as multiple sub-complexes that possess catalytic-dependent H2AK119 mono-ubiquitination (H2AK119ub) and catalytic-independent activities. Here, we show that, despite its well-established repressor
functions, PRC1 binds to both silent and active genes. Through in vivo loss-of-function studies, we show that global PRC1 function is essential for skin development and hair follicle stem cell specification, whereas PRC1 catalytic activity is dispensable. Further dissection demonstrated that both canonical and non-canonical PRC1 complexes bind to repressed genes, marked by H2AK119ub and PRC2-mediated H3K27me3. Interestingly, loss of canonical PRC1, PRC1 catalytic activity, or PRC2 leads to expansion of mechanosensitive Merkel cells in neonatal skin. Non-canonical PRC1 complexes, however, also bind to and promote expression of genes critical for skin development and hair follicle stem cell formation. Together, our findings highlight PRC1’s diverse roles in executing a precise developmental program.

THE SWI/SNF ATP-DEPENDENT CHROMATIN REMODELING COMPLEX DIFFERENTIALLY CONTROLS KERATINOCYTE PROLIFERATION AND MIGRATION IN HUMAN ANAGENE HAIR FOLLICLE AND HEALING CUTANEOUS WOUND

SWI/SNF ATP-dependent chromatin remodeling complexes alter nucleosome structure, positioning and chromatin compaction state resulting in target gene activation or repression. The SWI/SNF complexes contain either BRG1 or BRM as the core ATPase together with other common and variable subunits. BRG1 is required for epidermal terminal differentiation in both mice and human; and for hair follicle stem cell activation during mouse hair regeneration and cutaneous wound healing. However, the role of SWI/SNF complexes in human hair growth and skin wound healing remains unknown.

Here, we demonstrate that genes encoding SWI/SNF complex subunits are expressed in human epidermis and hair follicle, and BRG1 is substantially upregulated in hyper-proliferating and migrating keratinocytes in healing cutaneous wounds. siRNA mediated BRG1 gene suppression leads to the significant increase in the outer root sheath keratinocyte proliferation, but does not affect hair shaft elongation in short term ex vivo hair follicle organ culture. siRNA mediated BRG1 gene suppression leads to the substantial retardation of the wound closure in the full thickness human excision skin tissue culture model and in scratched human primary keratinocyte monolayers. Furthermore, we showed that the retardation in the keratinocyte migration with no changes in cellular proliferation or apoptosis. Micro-array based transcriptome analysis revealed that BRG1 is required for full induction of genes encoding several signaling molecules, transcription factors and structural proteins involved in changes in cellular adhesion and cytoskeletal organization, driving keratinocyte migration during skin wound healing, including the stress cytokeratins 16 and 17.

In summary, our data uncovered an essential role of the BRG1 chromatin remodeler in control of the cell proliferation in the human hair follicle. In contrast, BRG1 controls induction of the transcription programme driving keratinocyte migration, but not affecting their proliferation during skin wound closure and re-epithelisation.
MICRORNAS AS REGULATORS OF HAIR FOLLICLE CYCLING AND IMMUNE PRIVILEGE

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MicroRNA (miRNA)-dependent control of gene expression plays a fundamental role in the balancing and fine-tuning of lineage-specific differentiation programs in many organs including skin and hair. Recent research signified the crucial roles for miRNA regulatory networks in the formation of functional skin and its appendages by orchestrating gene expression programs in a spatiotemporally specific manner. Specifically, the functional significance of individual miRNAs was characterized in key processes underlying hair follicle cycling, such as activation and differentiation of stem cells, keratinocyte proliferation and differentiation during the anagen phase, and activation of apoptosis during catagen. Moreover, recent studies provided evidence for involvement of miRNAs in the pathogenesis of alopecia areata (AA). For example, genome-wide miRNA analysis revealed a role for miR-30b/d in the etiology of AA (J Invest Dermatol. 2018;138:549). Also, miR-486 play a protective role in the pathogenesis of AA. In normal mouse and human anagen skin, miR-486 is expressed in the follicular epithelium, while its expression is dramatically reduced in AA. Furthermore, INF-gamma inhibits miR-486 expression in the hair follicle. Pharmacological inhibition of miR-486 in mouse and human anagen hair follicles promotes anagen-to-catagen transition and alters the expression of the MHC class components and pro-inflammatory genes. These data suggest that miR-486 contribute to the maintenance of hair follicle immune privilege. These findings provide an evidence that modulation of miRNAs activity might be used as novel therapeutic approach for AA management.
ABSTRACT BOOK • 11TH World Congress for Hair Research • SITGES, BARCELONA 2019 • SPAIN

PRE-COURSES

Chair: Lidia Rudnicka

BASIC TRICHOSCOPY STRUCTURES

Michela Starace
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The knowledge of dermatoscopic bases is fundamental for a correct use of the technique itself. Dermatoscopy is a non-invasive tool that has always been used to study pigmented lesions and from some diseases this technique is also applied to diseases of skin appendages. The recognition of elementary lesions of hair diseases helps in the diagnosis and follow-up of the patient.

TRICHOSCOPY OF UNCOMMON OF HAIR LOSS IN CHILDREN

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Trichoscopy is a very useful tool for the diagnosis of hair disorders in children as it is painless and fast and allows to examine not only the scalp but also eyebrows and eyelashes that sometimes are the only sites that present diagnostic features in hair shaft disorders. This presentation will focus on the use of trichoscopy to diagnose uncommon hair disorders in children.

The following conditions will be discussed:
1) Trichorrhexis nodosa due to severe protein deficiency presenting with a patch of alopecia, with clinical features resembling alopecia areata. In this case dermoscopy shows their breakage at the same level in all the affected hair.
2) Keratosis follicularis spinulosa decalvans: dermoscopy shows absence of follicular openings, tufting and peripilar casts, diagnosis is confirmed by presence of eyelash involvement.
3) Pili torti as part of rare congenital syndromes such as Björnstad (sensorineural deafness), Menkes (focal neural degeneration and growth retardation), and Bazex Dupre (hypoidrosis, basal cell carcinomas) or as an acquired localized condition. Dermoscopy shows irregular twisting of the hair shaft, which is diagnostic.
4) Loose anagen hair syndrome, where dermoscopy shows rectangular granular structures on the scalp. It can also be utilized to examine and identify the typical LAH, which is an anagen hair devoid of sheaths.
5) Pili annulati showing alternating white bands that correspond to air filled areas of the shafts
6) Congenital triangular alopecia characterized by presence of a carpet of vellus hair.
7) Sebaceous nevus where dermoscopy shows bright yellow dots not associated to the hair follicles.
8) Pressure alopecia, where dermoscopy shows broken hair and black dots.
9) Friction alopecia characterized by proximal trichorrhexis nodosa.

TRICHOSCOPY IN DIFFERENTIAL DIAGNOSIS OF CICATRICIAL ALOPECIAS

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Trichoscopy allows visualization of morphologic structures that are not readily visible by the naked eye, including perifollicular and interfollicular features, as well as changes to hair shaft thickness and shape. Trichoscopic features have good correlation with pathology, allowing differential diagnoses between most causes of hair loss. In the field of primary scarring hair loss, diseases from the lymphocytic, neutrophilic and mixed groups can be diagnosed or at least
TRICHOSCOPY IN WOMEN WITH DIFFUSE HAIR LOSS

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In the course of life, almost every woman experiences a certain type of hair loss, ranging from an acute telogen effluvium after a physical stress, such as a crush diet, to the common androgenetic alopecia. Other less common hair disorders include alopecia areata and cicatricial alopecia. Beside severity and duration, hair loss always causes severe emotional distress: loss of self-confidence, low self-esteem, and heightened self-consciousness are common complains of patients with hair problems, as well as anxiety and stress.

The first step for a correct management of alopecia is a correct diagnosis. The clinical evaluation is helped by several techniques, in particular pull test and trichoscopy. We can now avoid biopsy in several cases due to the use of these noninvasive technique. A videodermatoscope is the best tool for trichoscopy, but a manual dermatoscope can be utilized as well, since most of the important signs are already seen at 10x magnification. Dermoscopy should be performed in areas affected by hair thinning and in clinically normal area.

Combining the different dermoscopic signs with the clinical history and appearance we are now able to diagnose several types of alopecia, including the 2 most common: telogen effluvium and androgenetic alopecia and we can manage the patient correctly.

HAIR LOSS IN THE FRONTAL HAIR LINE

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Hair loss in the frontal hair line can be caused by many conditions. Both male androgenetic alopecia and frontal fibrosing alopecia are characterized by progressive recession of frontal or frontotemporal hair line. Trichoscopic features diagnostic for androgenetic alopecia are: high percentage of vellus hairs, hair shaft thickness heterogeneity, presence of yellow dots, decrease in percentage of follicular units with three hairs and increase in percentage of follicular units with single hair. Trichoscopic features characteristic for frontal fibrosing alopecia are: perifollicular scaling (peripilar casts), perifollicular erythema, loss of follicular openings, presence of black dots, pili torti and lonely hairs. It was shown that there is a strong correlation between the severity of peripilar casts (assessed in 3 point scale) and the degree of lymphocytic infiltration on trichoscopy-guided biopsies. Early cases of frontal fibrosing alopecia can be diagnosed with trichoscopy by loss of vellus hairs in frontal hair line.

Traction alopecia can be clinically presented as marginal alopecia. A clue to the clinical diagnosis is the preservation of the fringe sign. Trichoscopy can be helpful in the diagnosis and can detect the ongoing traction by the presence of hair casts. In its later stages, the disease may progress into an irreversible scarring alopecia if traumatic hairstyling continues without appropriate intervention.

Alopecia areata sisaipho (ophiasis spelled backward) is uncommon variant of alopecia areata. It consists of scalp loss sparing the temporal and occipital areas, just the opposite the ophiasis. In this cases trichoscopy shows: exclamation-mark hairs, tapered hairs, Pohl-Pinkus constrictions, black dots, broken hairs, numerous yellow dots, circle hairs, vellus hairs and regrowing hairs.

En coup de sabre is a variant of localized sclero-
Trichoscopy

Chair: Lidia Rudnicka

Trichoscopy has become an established method in diagnosing hair and scalp diseases. In some cases trichoscopy - in the hands of the experienced physician - may provide hints for a previously undiagnosed non-dermatological disease. Thus far trichoscopy features, characteristic for such diseases have been described. In systemic sclerosis, dermatomyositis and systemic lupus erythematosus a characteristic feature is the presence of thick (enlarged) capillaries, which in some cases may resemble abnormal capillaries observed in nailbed capillaroscopy. Sarcoidosis presents with orange-colored round or oval areas. Similar findings may be observed in multicentric reticulohistiocytosis. Folliculotropic mycosis fungoides is characterized prominent keratotic plugs on a red background. Various vascular patterns of other clinical types of CTCL have been identified. Thyroid insufficiency may present with prominent avascular areas and hyperparathyroidosis with extensive hair growth. Scalp metastases show a prominent vascular network with a combination of areas with and with no hair follicle opening. Characteristic trichoscopy features of ectodermal dysplasia disorders have been identified. Most importantly, the presence of multiple hypopigmented hair in a dark haired child. It should be pointed out that trichoscopy findings may occasionally initiate a diagnostic process leading to a final diagnosis, but trichoscopy cannot be considered a diagnostic method beyond disorders associated with abnormal function of the hair follicle and scalp skin.

HOW TO PERFORM A TRICHOSCOPY-GUIDED BIOPSY?

Scalp biopsy is an important diagnostic tool in dermatological practice. Histopathology is crucial for diagnostic decisions in different types of cicatricial alopecias and very helpful for differentiating non-cicatricial alopecias. However, incorrect selection of biopsy site may affect the clinico-pathological correlation. In order to avoid multiple biopsies there is a need for tool that could increase diagnostic accuracy of scalp biopsy. Trichoscopy is a simple and noninvasive technique for the diagnosis and follow up of hair and scalp disorders. Although, the use of trichoscopy has considerably decreased the need for invasive methods in the evaluation of hair loss, when a scalp biopsy is necessary to confirm the diagnosis, it may be useful as a guiding device in selecting the most appropriate site to obtain a biopsy specimen. Trichoscopy allows screening large areas to detect features of disease activity. When the site is selected, the area is circled with a marker and biopsy is obtained. The advantage of trichoscopy-guided biopsy is rapid and precise identification of individually affected follicles. The correct site of biopsy increases the rate of accurate pathological assessment. Trichoscopy-guided biopsy allows also for the morphologic characterization of particular follicular structures. This method may be particularly useful if there is a suspicion that patient has more than one hair disorder and trichoscopy helps in selecting biopsy site for a particular pathology.
HAIR TRANSPLANT SURGERY: CURRENT STATE OF THE ART & INDICATIONS FOR TREATMENT

Hair transplant surgery has evolved beyond recognition over the last 60 years or so, from the original 4mm punch grafts (plugs), partial plugs, minigrafts, micrografts and now follicular unit grafts. The current harvesting techniques include Follicular Unit Extraction (FUE, and Strip harvesting (FUT).

The aesthetic appearance of today’s hair transplants should be almost indistinguishable from original hair when performed skillfully and expertly. Importantly, the transplant should age naturally with the patient. To achieve this, emphasis must be placed on correct patient selection, and appropriate hairline design and placement in order to ensure the patient keeps a natural pattern of hair as they age and as hair loss progresses further.

As well as doctors’ skill and experience, technology has also advanced greatly in terms tools, equipment and care of the grafts whilst outside the body. No one method, technique or solution is necessarily right for everyone. The ethical and experienced surgeon will have enough at their disposal to suit the patient’s circumstance. Sometimes the best treatment is not to do a hair transplant!

THE ROLE OF HAIRLINE ADVANCEMENT SURGERY TO TREAT HAIR LOSS

Hairline lowering surgery, also known as forehead reduction surgery or surgical hairline advancement, allows for the lowering of the frontal hairline by 2cm or more in a single procedure. It is unsurpassed in the density it can achieve, and the dramatic results that are near instantaneous. While it is not the mainstay of hair restoration, it has a definite role in treating congenitally high hairlines, assisting with the transition process for male to female transgender patients and also in the late management of certain scarring alopecias.

Appropriate candidates for hairline lowering surgery require a stable frontal hairline without risk of further hair loss progression, a mobile elastic scalp, a motivation to achieve the most dramatic results, and no history of any prior browlifting. Because of these requirements, the great majority of these surgeries are performed on women, most commonly presenting with a naturally high hairline.

Recently we have begun to apply this procedure for patients with frontal fibrosing alopecia (FFA), a primary lymphocytic scarring alopecia in which hair follicles are destroyed and replaced with scar tissue. First-line conventional treatment of FFA is anti-inflammatory medications, which varying degrees of efficacy, and some carry risky side-effects. They also are focused on stopping the progression of hair loss, but not with restoring the lost hairs. Hairline lowering surgery, in the case of dormant/burnt out frontal fibrosing alopecia, permits the removal of the scarred scalp and a lowering of the higher hairline to its native, more aesthetic position.

We are excited to present these early results on frontal fibrosing alopecia, within a presentation on this surgery for treating congenitally high hairlines.
Hair transplant surgery is becoming increasingly popular. There are two methods used to harvest donor hairs - Follicular Unit Excision (FUE) and Strip Follicular Unit Transplantation (Strip FUT). Strip FUT is often referred to as the more traditional method with FUE described as the modern, more sophisticated, less invasive, and less painful technique. There is a bias towards the FUE technique on the internet and most new hair transplant surgeons only offer this technique. However, there are advantages and disadvantages of both techniques and every patient should have these clearly explained to them so that they can make an informed choice. This lecture will clarify the pros and cons of FUE vs Strip FUT so that attendees will have a clear understanding and be able to discuss these with patients seeking to have a hair transplant surgery procedure.
Ethnic hair in those of African ancestry have fragile hair, yet often have the most elaborate hair care practices. The importance of genetics in the development of hair and scalp disorders is just starting to be understood. This talk discusses the most common forms of hair and scalp disorders seen in patients of color. Both the hair shaft and scalp will be discussed. Disorders of the hair shaft including hair breakage and the approaches that are the most successful to improving hair shaft health will be discussed. Hair care treatments that are commonly used and cause hair shaft damage will be discussed and recommendations on less damaging hair care practices will be given. Chemical relaxers, heat, and various forms of braiding the hair will be discussed and protective styles will be noted. The most common forms of scalp conditions seen in darker skin patients will be discussed including central centrifugal cicatricial alopecia, traction alopecia, and seborrheic dermatitis. Traditional approaches to treatment along with more current updated treatments including surgery and PRP will be discussed.
The scalp condition often associates with hair loss. In this session, the management of various scalp problems will be discussed in connection with hair loss by four speakers representing the Society for Hair Science Research (SHSR). SHSR is currently based in Tokyo, which is founded by Prof. Hideoki Ogawa in 1993 and has been working closely with hair societies all over the world. First, the chair of the session (Prof. Manabu Ohyama [Kyorin Univ., Tokyo, Japan]) will present a short lecture entitled “Skin diseases involving the scalp and associated hair loss.” The talk will cover the scalp manifestation of skin/systemic diseases such as pemphigus, collagen diseases and lymphoma and the clinicopathological characteristics of their related hair loss. Needless to say, accurate diagnosis is indispensable for better management of scalp lesions and hair loss. Dr. Misaki Kinoshita-Ise (Toronto Univ. Sunnybrook Health Sciences Centre, Toronto, Canada) will share her pearls in trichoscopic investigation based on her bicontinental experience by her talk entitled as “Trichoscopy in the evaluation of scalp dermatosis and hair loss.” Association between atopic dermatitis and alopecia areata has long been implicated. A. Prof. Taisuke Ito (Hamamatsu Medical Univ., Hamamatsu, Japan), a distinguished expert of hair/skin immunology, will discuss about the management of two subtypes of atopic dermatitis, including those affecting the scalp associated with alopecia areata, and possible therapeutic approaches for managing both conditions under the title of “Scalp involvement of atopic disease and alopecia.” The session will be closed by the lecture by Prof. Yutaka Shimomura (Yamaguchi Univ. Ube, Japan). He is a widely recognized dermatologist/geneticists who have made landmark contributions in the field. The title of his lecture will be “Scalp lesions of congenital hair diseases.” When compared to hair loss disorders, scalp dermatoses are infrequently discussed. We hope this session will enhance opportunity to revisit sometimes disregarded scalp conditions.
2007). Genome-wide association study of AA reveals a significant association between rs20541 (Pcomb = 7.52 x 10^{-10}; odds ratio [OR] = 1.30 [1.23-1.38]) and AA, thus implicating IL-13 as a susceptibility locus for AA (Jagielska et al. J Invest Dermatol 2012). In another study of IL-13 in AA, significant associations are found for rs20541 in both groups of AA patients with AD and AA patients without AD (Chu et al. J Am Acad Dermatol 2011). In our study, the patients with AA with AD show significant increases of the frequency of IFN-γ+CD4+ or IFN-γ+CD8+ T cells compared to AA or healthy subjects in PBMCs. Furthermore, IgE level and the frequency of IFN-γ+CD8+ T cells is negatively correlated in extrinsic AD. These results suggest that contact immunotherapy should avoid to be applied on AA with AD. In summary, cytokine balance of AA is basically Th1 shifted. However, AA with AD has been remained to be clarified, and dupilumab might show some affects on not only AD skin condition but also hair regrowth in patients with AA with AD.

**SCALP LESIONS OF CONGENITAL HAIR DISEASES**

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The mammalian hair follicle (HF) is an active skin appendage which undergoes hair cycles throughout postnatal life. Recent advances in molecular genetics have led to the identification of numerous genes expressed in the HF. Furthermore, mutations in some of these genes have been shown to underlie congenital hair loss disorders in humans. Although methods for genetic analysis have recently been so much developed, clinical diagnosis is still the most important step. Patients with congenital hair loss disorders can show characteristic hair shaft anomalies and conditions of the scalp skin, which enable us to determine the correct clinical diagnosis and choose proper candidate gene(s) to analyze.
**LINEAR EXCISION IN HAIR TRANSPLANTATION (FUT)- IS IT STILL RELEVANT?**

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**Introduction** Hair transplantation is an important treatment modality in advanced stages of androgenetic alopecia and inactive scarring hair loss. The standard harvesting technique has been the linear excision of a strip of hair-bearing skin followed by dissection of FU under the microscope, called Follicular Unit Transplantation (FUT). The growing popularity of directly harvesting each individual FU with micro-punches, called Follicular Unit Excision (FUE), has raised the question whether linear harvesting is still relevant.

**Material and Methods** To demonstrate the different techniques, both harvesting methods were performed in a typical patient. Graft quality was assessed using a Graft Quality Index (GQI) and compared intra-individually. The density of FU in the safe donor area was digitally measured preoperatively. The possible maximum yield of FU grafts as well as the cumulative size of the scar and excision length was estimated for different scenarios of FUT, FUE and a combination of both.

**Results** In this patient, the graft quality index of FUT grafts was higher than in FUE grafts. The maximum graft yield would be highest in FUT combined with a second FUT or FUE and lower in FUE alone. The calculated size of the scar and incision length is lower in linear FUT compared to FUE.

**Discussion** Both harvesting techniques have their specific advantages and disadvantages. In linear FUT, grafts are dissected under the microscope with direct vision. Especially in fine hair, this can reduce transection and grafts can be left with more follicle-surrounding structures and adipose tissue. Therefore, FUT grafts are often more robust. This may potentially lead to better growth and more fullness. As linear FUT harvesting can be done in the safest part of the donor area and does not lead to pin-point scars, it has a higher yield and safety margin in patients with a potentially narrow donor area. With careful surgical technique and trichophytic closure, minimal linear scars are typical. While the hair does not need to be shaved before, a very short hair style is not possible after linear FUT. In FUE, the excision involves a blind incision and forceful extraction, which can lead to transection and denuded vulnerable grafts, especially in fine hair and splaying FU. The development of less traumatic harvesting and placing instruments is directed towards minimizing this specific disadvantage of FUE. Graft yield and the threshold when visible thinning and scarring occurs depend on the individual hair characteristics. For many patients, the graft yield of FUE alone may not be sufficient if the safe zone is respected and overharvesting is avoided.

**Conclusion** Both linear FUT and selective FUE have specific indications. A combination may be best in advanced stages of alopecia. In order to act in the best interest of the patient, the hair surgeon should master both techniques and recommend the most suitable method based on individual criteria.

**HAIR TRANSPLANTATION IN FEMALES**

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In the old day, hair transplantation in women is not widely appreciated. Follicular unit grafts (micro-grafts) have replaced mini-grafts and create natural, undetectable hairlines. Therefore, the demand for hair restoration to create feminine hairlines has steadily been rising in the past few years. From the survey of International Society of Hair Restoration Surgery (ISHRS) in 2017, 14.3% of members performed hair transplantation in women. Indications for hair transplantation in
women include female pattern hair loss (Ludwig/olsen type FPHL: diffuse thinning (loss of hair volume) over the mid-frontal scalp, female hairline correction (Norwood-Hamilton bitemporal recession pattern, high forehead), inactive scarring (cicatricial) alopecia (primary eg. frontal fibrosing alopecia (FFA), pseudopelade (end stage of scarring alopecia), and secondary eg. Burn, surgical scars, cosmetic surgery-induced alopecia and scars, face-lift/surgical scars and traction alopecia.

There are some tips for successful hair transplantation in females; select good candidate, realistic expectation, good hair transplant technique and always combine with medication. Since hair loss in women is complex, complete history & examination to confirm diagnosis is important. Other etiologies that are not indicated for hair transplant should be identified. Hair transplant should be considered for women who have little success with medication and medication such as 5% minoxidil lotion should be encourage for all women undergoing hair transplant. In my opinion, FUT is preferable than FUE in women due to 2 reasons. Firstly, women rarely have very short hair cut/ shaved hair, so the surgical scar will not show in the future. In addition, women have limited donor area due to miniaturization, therefore FUT is preferable to get the best quality graft. Nowadays, female hairline correction is increasingly popular in East Asians, whose faces are flatter, wider, and more brachycephalic. This make the patient’s face small, slim, feminine, younger, balanced facial proportion and more attractive.

Lastly, hair transplant in scarring alopecia, disease must be inactive for several years before HT consider. Inactive stage should be confirmed by dermoscopy or histopathology. Patient should be informed “disease may recur and destroy transplanted hair”. In scar, which has limited vascular supply, lesser graft density of 25-30 FU/cm² is recommended.

DIFFICULT CASES IN HAIR RESTORATION

Hair restoration surgeries in the majority of cases are straightforward procedures usually performed for treatment of androgenetic alopecia. In this study we look at our experience over the last 10 years to identify those cases that we class as difficult or complex. This may be due to a medical or a surgical condition pre-operatively or due to a post-operative complication that needs addressing.

Objective
Our aim was to review the treatment options that we have employed when treating this patient group. We were particularly interested in looking at patient outcomes in order to improve our understanding of patient expectations.

Materials and Methods
A series of patients were looked at spanning a 10-year period restricted to those patients meeting the following criteria:

1. Complex previous surgery (such as skin/flap grafting)
2. Underlying dermatological condition
3. Underlying medical condition
4. Unexpected post-operative complication

Discussion
A variety of different situations have occurred over the years comprising approximately 3% of the patients operated on over a 10-year period. This includes diagnoses such as ulerythema oophryogenes, alopecia areata, LPP, FFA, burns scars, and post operative necrosis. I will present a few of these cases and the surgical dilemmas and outcomes.

Conclusion
Modern hair transplant techniques have enabled us to treat a wider variety of patients but we do still have to be cautious and treat patients on a case by case basis so modifications to our approach must be considered.
Hair Transplantation

SESSIONS Wednesday, April 24th
Chairs: Nilofer Farjo, Alex Ginzburg

FREE COMMUNICATIONS TO THE TOPIC

HAIR TRANSPLANT IN FRONTAL FIBROSING ALOPECIA: A MULTICENTER REVIEW OF 51 PATIENTS

Introduction Frontal fibrosing alopecia (FFA) is a primary lymphocytic scarring alopecia characterized by a progressive and bilateral recession of the fronto-temporal hairline. Some treatments have been described as useful to achieve stabilization, mainly oral antiandrogenic drugs and hydroxychloroquine. The usefulness of hair transplantation (HT) is controversial in these patients. There are very few reports describing the outcome of HT in patients with FFA. The objective of this study was to describe the results of HT in a multicenter series of patients diagnosed with FFA.

Material - Methods A retrospective, multicenter, descriptive and analytical study was designed. A review of the evolution of patients diagnosed with FFA that underwent HT was performed in 6 centers (5 Spanish and one French). Patients with a confirmed diagnosis of FFA and at least 2 years of follow-up after the HT were included. Epidemiological, clinical and therapeutic data were recorded, as well as information regarding the HT. The main outcome of success was the survival of grafts after the HT evaluated clinically and by trichoscopy. The patients were asked about their global satisfaction with the procedure.

Results A total of 51 patients (48 females and 3 males) with a mean age of 54 years and a mean grade of severity of 2.3 out of 5 were included. The HT was done after a mean time of 15 months of stabilization of the disease. The strip technique was performed in 44 patients (86%) and the FUE technique in 7 patients (14%). The mean number of transplanted grafts per surgery was 1345 follicular units. The most frequent site of the HT was the temporal area (30 patients, 59%), followed by the frontal area (22 patients, 44%) and the eyebrows (15 patients, 29%). The patients were followed a mean of 3.2 years after the HT (range 2-10). All the patients received medical therapy for FFA after the HT. The mean grafts’ survival after 1, 2, 3 and 5 years of follow-up was 87% (n=51), 71% (n=51), 60% (n=38) and 41% (n=12), respectively. Of the 51 patients, 42 (82%) were satisfied with the HT.

Conclusion The result of hair transplant in patients with FFA is temporary, despite receiving medical therapy. Although the satisfaction of the patients is high, a careful discussion with the patient about the duration of the results of the HT is highly recommended.

EYEBROW HAIR TRANSPLANTATION IN FRONTAL FIBROSING ALOPECIA: DOES IT WORK?

Introduction Loss of eyebrows occurs in almost 80% of frontal fibrosing alopecia (FFA) patients, and is usually the first reason for consultation causing significant distress to patients due to the change in their facial appearance. For this reason, patients seek treatment options including tattooing, drawing makeup, or the transplantation of hair into the eyebrows. Eyebrow autologous hair transplantation is a very well-accepted cosmetic procedure; however, very little has been published about the outcome of eyebrow transplantation in patients with FFA. Here we present the immediate, short- (6-12 months) and long-term (>2 years) results of eyebrow hair transplantation surgery in FFA patients.

Materials and Methods Ten FFA patients complaining of partial or total loss of the eyebrows came to our hair transplant clinic enquiring about the feasibility of transplanting hairs into their eyebrows. Of these, 9 were female and...
Hair Transplantation  
Chairs: Nilofer Farjo, Alex Ginzburg

only 1 male, with ages ranging between 31 and 63 years. The onset of the disease varied from 1 to 10 years. After explaining other treatment options including eyebrow tattooing or artificial eyebrows, these patients opted to proceed with hair transplantation.

The transplanted hairs were harvested from the occipital scalp from an area clinically not affected by the disease. The harvesting was done either excising a small strip with a scalpel or with a 0.9 mm punch (FUE). With both harvesting techniques, the follicular units were then micro-dissected into single hairs under a stereomicroscope and placed briefly in physiologic saline before implantation into the eyebrow area using implanters.

Results Eight out of 10 patients achieved satisfactory short-term results 6-12 months after transplantation, with the hair growing as expected in any normal eyebrow transplantation (80-100% growth). Seven patients have been followed for more than 2 years; of these, 3 started to lose transplanted hairs after two years and another 3 after 3-4 years. Only 1 patient has maintained the transplanted hairs after more than 4 years of follow-up. One patient could not be evaluated long term because she was treated with chemotherapy for a breast cancer and lost her eyebrows.

Conclusions Outcomes after eyebrow hair transplantation in FFA patients are variable. Around 80% of patients achieve satisfactory short-term results 6-12 months after transplantation. However, in the majority of cases the results are not permanent. The onset of significant hair transplant loss is around 3-4 years post-transplantation according to our series. FFA patients seeking hair transplantation should be advised about the possibility of hair graft loss over time.

TRANSPANTATION OF ANAGEN HAIR FOLLICLES PROMOTES REMODELLING OF STRETCHED SCARS

Introduction The rapid healing of deep cutaneous wounds often leads to the formation of unwanted scars. An estimated one hundred million people per year in the developed world alone suffer from excessive scarring. Despite insights into the biology of scar formation provided by previous studies, to date, there are few clinical treatments for established scars. All scars are characterized by deposition of large amounts of collagen type I and an absence of skin appendages, including hair follicles. As a result, scars lack functional and mechanical properties of healthy skin elicited by its diverse structures. In particular, anagen hair follicles can induce substantial remodelling changes in the surrounding skin, including increased vascularization and collagen remodelling, characteristics sought for treatment of scars.

Methods With the goal of remodelling established scars, in this study we tested whether implantation of anagen hair follicles into scars could induce the same remodelling changes as seen in healthy skin. In a clinical study, hair follicles were grafted into stretched scars formed as a result of strip harvesting for previous hair transplantation surgery. Due to a lack of research on stretched scars, we first characterised them in comparison to healthy skin from the same location. Using Second Harmonic Generation (SHG) imaging to analyse dermal collagen type I, we found a significant increase in the thickness and alignment of fibres in scars. In addition, image analysis of the cellular composition of skin layers revealed decreased epidermal thickness and dermal cell density, and substantially reduced vascularization in scars. Using a global transcriptomic analysis, we identified 200 genes that were differentially expressed between stretched scars and healthy skin. Of these, a high proportion were associated with matricellular proteins linked to the extracellular matrix, including thrombospondins.

After establishing the baseline differences between stretched scars and healthy skin, we investigated whether hair transplantation into scars can induce scar remodelling. Using the same imaging techniques, we assessed scars before the follicle implantation, and then at 2, 4, and 6 months after.
Results We found a shift in structural characteristics, including remodelling of collagen fibres, higher cell numbers, and a significant increase in vascularization in scars after hair transplantation. The structural and cellular changes were accompanied by a shift in the transcriptome of the scar dermis, with 1,785 genes changing their expression after transplantation.

Comment We believe that the substantial changes in scars observed after hair transplantation demonstrate the beneficial role of follicles in scar remodelling. Currently, we are conducting experiments to elucidate the mechanism by which this happens. In the long term, the results of our study will enable identification of therapeutic targets and design of strategies to remodel and reduce established scars.
Alopecia areata (aa) has been a focus of research and treatment development for at least 3500 years. The Ebers papyrus, found between the feet of an Egyptian mummy, provides a list of treatments for many diseases including “bitten hair loss”; most likely AA. Treatments ranged from a red ochre, carob, alabaster and honey mixture to rubbing skin with hedgehog or porcupine hair annealed in oil. The description of AA and treatment for it remained largely unchanged for over 1000 years. Around 30 A.D. Roman translator Cornelius Celsus, probably transcribing the work of Greek physician Menekrates, describes AA in the form of spots and the windings of a snake, and suggests treatment using caustic compounds and scarification. The first modern description of AA came in 1817 from Dr. Thomas Bateman, though treatment approaches still largely focused on skin irritation using caustic agents and other methods. From the mid-19th century onwards, various hypotheses were developed to explain AA, supported by the first AA research experiments. AA was believed to be induced by infectious agents (Gruby 1843), deficient nutrition (Wilson 1847), nerve defects (Von Barensprung 1858), physical trauma (Kinney 1881), psychological stress (Collier 1881), nerve irritation from diseased teeth (Jaquet 1902), toxins (Adamson 1912), and endocrine disorders (Sabouraud 1913). Focal inflammation was first suggested as the primary mediator of AA by Giovannini in 1891, but unfortunately his detailed, insightful histology analysis was largely ignored. It was not until the 1950s that new advances in AA occurred with the first use of corticosteroids for AA published (Dillaha and Rothman 1952). The first suggestion that AA was autoimmune in nature was made by Dr. Stephen Rothman in discussion of a conference paper in 1958. Slowly, the research focus shifted towards examination of auto-antibodies, initially for antinuclear antibodies and similar, later looking for hair follicle-specific antibodies which were eventually identified in 1995 (Tobin and Bystryn). The potential role of t lymphocytes in AA was made implicit with immunohistological analyses in the 1970s-1980s. However, functional research data supporting their role was not published until the development and use of rodent models (McElwee et al, 1996; Gilhar et al. 1998). Genetic studies, particularly genome wide association studies (Petukhova et al 2010), have come to the forefront in recent years and open up a new era of AA research investigating individual gene contributions to the complex inflammatory aa pathway. Today, AA research is active in genetics, the microbiome, dietary modulators, the role of atopy and allergens, immune cell types in AA pathogenesis, primary antigenic target(s), mechanisms by which immune cells influence the hair follicles, and of course new treatment development based on these discoveries. This presentation will provide a brief, albeit biased, view on the progress we have made in AA over 3500 years.
cells, T-cells, classic NK cells, ILC1), all of which can produce large amounts of IFN-γ, may also drive AA pathobiology independent of classical, autoantigen-dependent CD8+ T cell functions. Another important new frontier is the role of regulatory lymphocyte subsets such as Tregs, γδ Tregs, NKT10, as well as perifollicular mast cells in maintaining the physiological HF immune privilege (IP), to which extent these functions are defective in AA patients, and how this IP-protective role can be therapeutically restored in established AA. Broadening our AA research horizon along the lines suggested above promises not only to open the door for innovative and even more effective immunotherapy strategies for AA, but will likely also be relevant for other autoimmune disorders in whose pathobiology ectopic MHC class I expression and IP collapse play an important role.

**TRIGGERS OF HAIR FOLLICLE IMMUNE PRIVILEGE COLLAPSE IN ALOPECIA AREATA REVISITED**

Ralf Paus, MD, FRSB
Professor of Dermatology; Director, Dermatology Medical Science Training Program| Dept. of Dermatology & Cutaneous Surgery; University of Miami Miller School of Medicine; Miami, FL, USA & Professor of Cutaneous Medicine; Director of Research; Centre for Dermatology Research; University of Manchester; Manchester, UK

Current evidence suggests that collapse of the physiological hair follicle immune privilege is a conditio sine qua non for alopecia areata (AA) to develop in any given hair follicle, irrespective of a patient's genetic predisposition to develop AA. Two major trigger factors that can induce this collapse have been identified: interferon-gamma (secreted e.g. by perifollicular NKG2D+ cells like CD8+ T cells, NK cells and gamma/delta T cells) and substance P, most likely secreted by perifollicular sensory nerve fibers under conditions of perceived stress/neurogenic skin inflammation. However, it is also important to dissect and therapeutically target other locally active factors that impact on or even critically control the sensitivity of a given hair follicle in a specific location and genetic setting to undergo immune privilege collapse. Relevant key candidates are discussed briefly.

**TRANSLATIONAL RESEARCH IN ALOPECIA AREATA: PATHWAYS TO CLINIC**

Angela M. Christiano

Our lab has worked extensively on the genetic and immunologic basis of Alopecia Areata (AA), and have identified new therapeutic targets including JAK-STAT pathways. We have used the C3H/HeJ mouse model of AA to test the efficacy of small molecule JAK inhibitors in the treatment of AA in several contexts of both early and late disease. Our findings provided the basis for testing whether JAK inhibitors are effective in treating patients with AA, which has opened new avenues for clinical research in AA. We have conducted similar studies with selective next-generation JAK inhibitors, and we are now working to identify upstream triggers of AA, specifically, environmental factors such as the microbiome.
**NERVES, NEUROPEPTIDES AND ALOPECIA AREATA**

**Introduction and Objectives** Nervous system dysfunction has been implicated in the pathogenesis of alopecia areata (AA) for over a century and patients frequently report increased pain with intralesional injections in the occipital scalp compared to the frontoparietal scalp as well as paresthesia with regrowth or hair loss. We hypothesized there would be a difference in both nerve structure and function in AA scalp when compared to healthy scalp.

**Materials & Methods** We examined nerve and neuropeptide (NP) expression and sensory perception in both normal and AA occipital and frontoparietal scalp using transcutaneous electrical stimulation, we studied Ab, Ad, and unmyelinated C-fibers. Scalp punch biopsies were removed from AA scalp and two normal defined scalp regions and fixed in Zamboni’s solution. Sixty micron sections were cut and immunostained for pan-neuronal antibodies to protein gene product 9.5, type IV collagen, substance P (SP), and calcitonin gene-related peptide (CGRP). Epidermal nerve fibers (ENFs) were traced and counted in adjacent fields of normal scalp confocal images using Neurolucida 5.05.4 (MBF Bioscience). Nerve fibers in the subepidermal nerve plexus that stained for SP, CGRP, and VIP were visually counted using fluorescent microscopy (Nikon Microphot-SA).

**Results** In the normal control specimens, ENF density was much greater in the opiasis region compared to the frontopincipal scalp; CGRP and SP expression was similar in both areas. Mean current intensity thresholds needed to evoke sensation perception measured from AA affected opiasis and control opiasis at 5Hz (C-fibers) were 226 µamps and 116 µamps, respectively, and differences were statistically significant (p = 0.006) suggesting a lower ENF density in affected AA opiasis scalp. Smaller follicles with “collapsed” follicular innervation were seen in AA specimens.

**Conclusions:** Functional differences in C-fiber sensory perception are present when comparing affected and unaffected AA scalp, with more current required to consistently activate C-fibers in affected AA occipital scalp. Whether this is a direct or an indirect result of the AA disease process remains to be determined. The higher ENF density in the control opiasis region may correlate with the observation of greater pain associated with procedures in this region. Future studies should focus on expanding a normative reference database for ENFs and NP expression in healthy and AA scalp and expanding both structural and functional data to include several age groups and Fitzpatrick skin types.
ABSTRACT BOOK • 11TH World Congress for Hair Research • SITGES, BARCELONA 2019 • SPAIN
SESSIONS Wednesday, April 24th

FREE COMMUNICATIONS TO THE TOPIC

MHC RISK HAPLOTYPE SEQUENCING AND ALLELE-SPECIFIC GENOME EDITING BY CRISPR/CAS9 SYSTEM REVEAL CCHCR1 AS SUSCEPTIBILITY GENE FOR ALOPECIA AREATA

(1) Dermatology, Juntendo University, (2) Dermatology and (3) Molecular Life Sciences and (4) Institute of Medical Sciences, Tokai University, Japan

Introduction & Objectives Previous genome-wide association study about Alopecia areata (AA) results have implicated a number of immune and non-immune loci in the aetiology of AA. However, no variants among those have provided experimental evidence for biological functions between alleles and AA pathogenesis. Therefore, we attempted to pinpoint a susceptibility variant within the major histocompatibility complex (MHC) and to confirm the susceptibility variant.

Materials & Methods We performed association and haplotype analysis for the MHC region to identify risk haplotypes using AA patients and controls. Next, we sequenced the risk and control haplotypes to identify AA-susceptibility variants. Next, we engineered mice carrying the human risk allele using allele-specific genome editing with the CRISPR/Cas9 system to reproduce AA phenotype.

Results We sequenced risk and non-risk MHC chromosomal segments. Among the large number of variants there was only one nonsynonymous variant identical in the AA risk haplotype. The variant is located in the coiled-coil alpha-helical rod protein 1 (CCHCR1) gene. Next, mice were generated with the risk allele concordant with the variant of CCHCR1 in humans, then we established mouse strains with risk alleles (AA mice). Half of AA mice displayed patched hair loss until 10 months after birth, thus successfully phenocopying the hair loss phenotype. Over time, the initial area of hair loss expanded in the majority of the AA mice, though constant and recovered hair loss was observed in some of those mice. Their surface displayed black spots, while the hairs appeared to be broken and tapering, similar to the conditions seen in humans with AA and specific for AA-associated hair loss.

Conclusions First, the discovered susceptibility variant is a rare example of a non-mendelian common disease variant that can be phenocopied in a mouse model. Second, our alopecia model mouse provides a novel mechanism for the observed hair loss and potential a venue for developing a drug for AA patients.

ALOPECIA AREATA IS ASSOCIATED WITH ALTERED FREQUENCIES OF CD4+ T CELLS AND A SYSTEMIC INFAMMATORY CYTOKINE SIGNATURE

*University of Glasgow, UK **Respiratory, Inflammation and Autoimmunity IMED Biotech Unit, AstraZeneca, Gothenburg ***Queen Elizabeth University Hospital, Glasgow, UK ****University of Manchester. UK

Alopecia areata (AA) is an autoimmune disease, causing patchy hair loss that can worsen to affect the entire scalp (alopecia totalis) or body (alopecia universalis). Therapies for AA include topical, intralesional and systemic corticosteroids, contact sensitisers and immunosuppressants. However, they lack efficacy, especially for people with severe hair loss. 60% of people with AA develop psychiatric illness, and associated comorbidities include atopic and autoimmune diseases, particularly thyroid, due to shared immunological risk loci. Genetic and functional studies have implicated NKG2D+ CD8+ T cells as central players in driving hair follicle pathogenesis, however the specific mechanisms involved are not fully understood.
**Methods** We sought to characterise the immunophenotype of AA to identify novel pathways central to disease pathogenesis. We established a research clinic at the Queen Elizabeth University Hospital, Glasgow to collect peripheral blood, stool samples and clinical information from consented volunteers with a diagnosis of AA. We assessed frequencies of peripheral blood mononuclear cell (PBMC) subsets using 11-parameter flow cytometry and used multiplex platforms to determine the plasma concentration of inflammatory cytokines.

**Results** Immunophenotyping revealed a significant increase in the frequency of CD4+ T cells expressing CCR6, a surrogate marker for Th17 cells, in the circulation of people with AA compared to age and sex-matched healthy controls. Stratification of AA patients, based on severity of hair loss, revealed that those with patchy (<50%) AA were associated with a significant increase in this subset. Multiplex analysis revealed significant increase in the concentration of type 17 associated cytokines, IL-17A, IL-21 and IL-23. We also observed increases in type 2 associated cytokines IL-31 and IL-17E/25.

**Comment** Our data indicate that AA is associated with an inflammatory signature, dominated by a type 17 response. We hypothesised that this broad dysregulation may be linked to comorbidities associated with AA, such as depression and other inflammatory disease. Based on hospital anxiety and depression scale (HADS) assessment, we identified high levels of depressive symptoms in our cohort. Using linear regression modeling, we identified a significant positive correlation between depression scores and levels of both IL-22 and IL-17E. Using stool samples, we are also investigating whether AA is associated with changes in the intestinal microbiome. AA and inflammatory bowel disease (IBD) share genetic risk loci and we hypothesise that changes in the microbiota may be contributing to the systemic inflammatory signature observed in AA circulation.

**Conclusion** In summary, we have generated the first comprehensive immunophenotype in AA, detailing changes in CD4+ T cell populations and type-17 and -2 associated cytokines, thus broadening the understanding of immunological pathways altered in AA.

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**DYSREGULATION OF AUTOPHAGIC FLUX CONTRIBUTES TO ALOPECIA AREATA ETIOLOGY**

**Introduction & Objectives** Alopecia Areata (AA) is an autoimmune disease that specifically attacks the hair follicles, causing hair loss in well-demarcated skin lesions. The prevalent etiology underlying disease is thought to be the loss of the immune privilege of hair follicles. However, the causative molecular mechanisms that lead to the loss of immune tolerance are not known. Our previous GWAS and meta-analysis uncovered two AA risk genes, STX17 and BIM, which play a role in autophagy. We also found that mRNA expression of the autophagy genes ATG4B and STX17 is downregulated in AA patient skin compared to unaffected controls. Based on these findings, we wanted to understand how autophagy plays a role in skin or hair homeostasis, and whether dysregulation of autophagic flux is involved in AA pathogenesis.

**Materials & Methods** We exploited grafted C3H/HeJ mouse model of AA and monitored autophagy in the skin of these mice using western blotting and immunofluorescence staining.

**Results** We observed that autophagic flux is perturbed as the mice develop skin inflammation and lose hair such that the western blot analysis showed the level of autophagosome LC3-II and SQSTM1 is increased in the skin from AA mice exhibiting hair loss. Further, immunostaining for LC3 is stronger in AA hair follicles compared to normal haired mice and positively correlates with the extent of CD8+ T cell infiltration and induction of ICAM-1. Systemic treatment of mice with the autophagy blocker chloroquine exacerbated the development of hair loss in grafted C3H/HeJ mice.
Conclusions Since chloroquine accelerates the anagen and induces hair associated melanogenesis in normal mice, our experiments suggest that dysregulation of autophagy in hair follicles perturbs the hair cycle and generates melanin related antigens that become accessible to auto-reactive T cells present in a disease-susceptible skin environment. These autophagy-dependent perturbations may contribute to the break in immune privilege and precipitate the autoimmune inflammatory reaction against the hair follicle in AA.
LONG-TERM TREATMENT FOR SEVERE ALOPECIA AREATA WITH ORAL TOFACITINIB CITRATE

Tofacitinib citrate is a janus kinase 1/3 inhibitor that is FDA-approved for the treatment of rheumatoid arthritis and that has recently been shown to effective in treating alopecia areata (AA). The Department of Dermatology performed a retrospective chart review of 31 AA patients presenting from March 2015 to June 2017, including 27 with alopecia totalis or universalis, with a mean pretreatment scalp hair loss of 88.7% calculated the Severity of Alopecia Tool (SALT) score. All other AA therapies were stopped, and patients were started at an initial dose of Tofacitinib citrate 5mg orally twice daily. Doses were increased monthly as tolerated, and maintained after the treating physician noted the first signs of hair regrowth. Labs (CBC, CMP, and lipid panel) were checked monthly, and after maintenance dose was achieved, every 3 to 4 months. Standardized photos were taken with each clinic visit. Statistical analysis of data was then performed using SAS® Software (version 9.4; Cary, NC). SALT scores at follow-up visits were estimated using mixed effect models, and regrowth and nail improvement estimates were performed using Kaplan-Meier analysis to account for patients lost to follow-up. Twenty patients ultimately received treatment, of which 10 patients have taken tofacitinib for 12 or more months. SALT scores decreased over time and scores at 3, 9 and 12 months were significantly lower than baseline. In addition, the mean score at 12 months was lower than 6 months (p=0.015). At 9 and 12 months, the estimated regrowth was 94%. Improvement of nail dystrophy was not as notable, with estimated levels of 23% at 6 months and beyond. In general, lab values were stable over time. There were 6 clinical adverse events (e.g. chest palpitations, herpes zoster, hypertension), and each happened in a different patient. There were 5 patients that experienced an adverse event, and a total of 10 adverse events were observed.

In our patient population, of the 20 patients treated, 47% experienced regrowth of hair by 12 months. However, the extent of regrowth in varied greatly, ranging from only 5% to nearly complete regrowth. Overall the majority of patients experienced regrowth independent of age, disease severity, and disease duration.

### Table 1. SALT Score by Time Point in Treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Time</th>
<th>Mean (95% CI) vs. Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALT</td>
<td>Baseline</td>
<td>88.7 (77.6, 99.8)</td>
</tr>
<tr>
<td></td>
<td>3 Months</td>
<td>67.0 (53.9, 80.1)</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>75.0 (59.1, 90.9)</td>
</tr>
<tr>
<td></td>
<td>9 Months</td>
<td>59.6 (41.8, 77.4)</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>47.0 (27.9, 66.1)</td>
</tr>
</tbody>
</table>

### Table 2. Kaplan Meier estimates of time to Hair Regrowth and Nail Improvement

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Time</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regrowth</td>
<td>3 Months</td>
<td>70.0 (49.9, 90.1)</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>76.0 (56.8, 95.2)</td>
</tr>
<tr>
<td></td>
<td>9 Months</td>
<td>94.0 (82.7, 100)</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>94.0 (82.7, 100)</td>
</tr>
<tr>
<td>Nail Improvement</td>
<td>3 Months</td>
<td>10.0 (0.0, 23.1)</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>22.9 (2.9, 42.8)</td>
</tr>
<tr>
<td></td>
<td>9 Months</td>
<td>22.9 (2.9, 42.8)</td>
</tr>
<tr>
<td></td>
<td>12 Months</td>
<td>22.9 (2.9, 42.8)</td>
</tr>
</tbody>
</table>

PLATELET RICH PLASMA FOR AA

PRP may have the ability to induce a longer disease remission. Patients treated with PRP appeared to regrow pigmented hairs from the beginning of hair regrowth compared with 25% of those treated with triamcinolone injections. Non-standardized treatment protocols and methods for assessing response make it challenging to adequately assess the potential benefit of the treatments.
ALLERGEN DESENSITIZATION TREATMENT DECREASES SEVERITY OF RELAPSE IN ATOPIC PATIENTS WITH ALOPECIA AREATA

Background House dust mite (HDM) allergy was previously reported as a possible facilitating factor in alopecia areata (AA) patients with early onset and extensive hair loss. The underlying immune mechanisms of atopy associated with AA are unknown. As allergen immunotherapy (AIT) against HDM might modify immune status, we hypothesized that AIT might improve long-term prognosis. Objectives To investigate the long term effect of AIT on disease severity at the time of AA relapse in atopic patients with a confirmed HDM allergy. Methods We retrospectively analyzed the efficacy, safety, relapse rate, and severity of AA under standard alopecia treatment (TrAA) plus AIT treatment (TrAA-AIT) and TrAA alone in AA patients with confirmed HDM allergy. Serum total immunoglobulin E (tIgE), HDM specific IgE (sIgE), HDM specific IgG4 (sIgG4) and inflammatory cytokines including IL-4, IL-5, IL-10, IL-12, IL-13, IL-33 and IFN-γ were measured. Results A total of 69 patients were evaluated, among them, 35 were treated with TrAA, and 34 with TrAA-AIT. Although relapse rates were similar in both groups, the TrAA+AIT group showed significantly lower SALT scores than that of the TrAA group after 36 months, especially in those with elevated tIgE levels or in patients with alopecia totalis/ universalis. Throughout AIT in TrAA group, we found out that elevation of tIgE was positively correlated to exacerbation of AA, and we observed an elevation of IL-5 during early AIT treatment stages (3-6 months), a decrease of IL-33 in late stages (>12 months), but no significant change of other cytokines. Conclusions Treatment against specific allergens, concomitant with standard corticosteroid treatments, may benefit atopic AA patients in the long term.
**DEVELOPMENT AND CONTENT VALIDATION OF CLINICALLY MEANINGFUL CLINICIAN-REPORTED OUTCOME (CLINROS) MEASURES FOR EYEBROW, EYELASH AND NAIL ASSESSMENT IN ALOPECIA AREATA**


*Eli Lilly and Company, Indianapolis, IN, USA; **DRG Abacus, Manchester, UK; ***University of California, Irvine, CA, USA; ****Stanford University, CA, USA; *****Yale School of Medicine, Middlebury, CT, USA*

**Introduction & Objectives:** In addition to scalp hair loss, alopecia areata (AA) can affect patient’s facial and body hair, and nails. Comprehensive evaluation of treatments in clinical trials should include assessment of signs/symptoms important to patients. This study explored the non-scalp hair signs/symptoms of AA that are important to patients and developed clinician-reported outcome measures (ClinROs) and accompanying photoguides to aid assessment of these signs/symptoms.

**Materials & Methods:** The ClinROs and photoguides to assess non-scalp hair signs/symptoms were iteratively developed through three rounds of qualitative interviews with: 1) US dermatologists expert in AA, 2) patients in North America with AA and 3) a sub-sample of the expert dermatologists previously interviewed. To evaluate the relevance of the ClinROs, purposive sampling aimed to include patients with eyebrow and/or eyelash involvement. All interviews were semi-structured, transcribed, and thematically analyzed. Data from each round of interviews informed revisions to establish the acceptability and content validity of the final ClinROs and photoguides.

**Results:** All clinicians (n=10) described eyebrow and eyelash loss in the signs of AA; involvement of these sites was unpredictable and concerning for the patients affected. Clinicians noted eyebrow loss could change a patient’s face affecting other people recognition of them, and was difficult to conceal cosmetically. Also, eyelash loss was associated with dust/sweat getting into the eyes, which could cause eye irritation. Clinicians described continuity, symmetry, and fullness as important features in the assessment of eyebrow involvement. Clinicians indicated that the eyebrow ClinRO should include examination of gaps and distribution (related to symmetry), and that the eyelash ClinRO should include examination of gaps and even spacing. All 10 clinicians discussed nail pitting, splitting and/or roughness as a sign of AA. These data informed the development of three single item, 4-point Likert scale assessments of current eyebrow hair loss, eyelash hair loss and nail damage. Patients (n=45, aged 15-72 years, with eyebrow and/or eyelash (78%) and/or nail (31%) involvement) frequently reported eyebrow and eyelash loss in the top three most bothersome AA signs/symptoms and described related physical and social impacts. Most patients queried confirmed the relevance and importance of the ClinROs. Five clinicians informed the accompanying photoguides, and ensured that: 1) the example photos appropriately represented each severity level of the ClinROs and 2) the photoguides would aid standardized ratings.

**Conclusions:** The ClinRO Measure for Eyebrow Hair Loss™, ClinRO Measure of Eyelash Hair Loss™ and ClinRO Measure for Nail Damage™ provide meaningful assessments of critical outcomes important to patients with AA. In addition, the accompanying photoguides provide clear visual instruction to standardize these clinician assessments.
TOFACITINIB IN COMBINATION WITH ORAL MINOXIDIL FOR THE TREATMENT OF SEVERE ALOPECIA AREATA

Introduction & Objectives: The Janus kinase (JAK) inhibitor, tofacitinib, has been shown to be effective for the treatment of alopecia areata (AA), but dose escalation from the standard dose, 5mg twice daily, to 10mg twice daily is necessary to achieve complete or near-complete hair regrowth in a majority of patients. In this study, we investigated the effect of combination tofacitinib and oral minoxidil treatment in patients with severe AA.

Materials & Methods: This is a retrospective study of patients with severe AA treated with tofacitinib, 5mg twice daily, and oral minoxidil, 2.5mg twice daily. Patients with complete or near-complete scalp hair loss of >10 years duration were excluded. Scalp hair loss was assessed using the Severity of Alopecia Tool (SALT), with scores ranging from 0 (no scalp hair loss) to 100 (complete scalp hair loss).

Results: In a total of 11 patients (55% female), ages 19-51 (median 35), 8 patients experienced substantial scalp hair growth and 3 patients were non-responders during 3-6 months of combination treatment. The median baseline SALT score was 100% (interquartile range [IQR] 80-100) and the median final SALT score was 24% (IQR 15-95), p=0.0049.

Comment: The results of this study suggest that combination tofacitinib and oral minoxidil therapy leads to substantial hair growth in patients with severe AA. While JAK inhibitors target the immune response in AA, oral minoxidil stimulates hair growth, in general, via an uncertain mechanism. It may be that there are synergistic effects of combination treatment with JAK inhibitors and oral minoxidil.

Conclusion: While JAK inhibitors are emerging as the mainstay of treatment of severe AA, results of recent randomized, double-blind, placebo-controlled clinical trials suggest that a majority of patients may not achieve complete or near-complete scalp hair regrowth with new JAK inhibitors. Therefore, combination therapies that enhance the efficacy of JAK inhibitors would be welcome. The results of this work suggest that combining oral minoxidil with JAK inhibitors may be one such combination therapy.
SHH SIGNAL IN HAIR FOLLICLE NEOGENESIS

Mammalian wounds typically heal by fibrotic repair without hair follicle (HF) regeneration. Fibrosis and regeneration are currently considered the opposite end of wound healing. This study sought to determine if scar could be remodeled to promote healing with HF regeneration. Here, we identify that activation of the Sonic hedgehog (Shh) pathway reinstalls a regenerative dermal niche, called dermal papilla, which is required and sufficient for HF neogenesis (HFN). Epidermal Shh overexpression or constitutive Smoothened dermal activation results in extensive HFN in wounds that otherwise end in scarring. While long-term Wnt activation is associated with fibrosis, Shh signal activation in Wnt active cells promotes the dermal papilla fate in scarring wounds. These studies demonstrate that mechanisms of scarring and regeneration are not distant from one another and that wound repair can be redirected to promote regeneration following injury by modifying a key dermal signal.

AUTOLOGOUS CELL-BASED THERAPY FOR HAIR LOSS USING DERMAL SHEATH CUP CELLS - BASIC CONCEPT AND CLINICAL APPLICATION

Dermal sheath cup (DSC) cells are the peribulbar component of the hair follicle dermal sheath, and they have been shown to have a hair inducive potential similar to the dermal papilla (DP) (McElwee et al., J. Invest. Dermatol. 2003). A recent study showed that DSC cells behave as precursor cells for DP cells, migrating into the DP region from the dermal sheath during the hair cycle (Rahmani et al., Dev. Cell. 2014). We have characterized the gene expression profiles of intact DSC cells compared with DP cells and upper dermal sheath cells, and have identified several DSC signature genes. One such DSC signature gene, GREM2, known BMP inhibitor, revealed its DSC specific expression pattern in human hair follicles by in situ hybridization (Niiyama et al., Acta Derm. Venereol. 2018).

The injection of DSC cells into reconstituted human hair follicles in an in vivo model revealed that they migrate and localize around hair follicles and that some of them are even incorporated into the DP, presumably becoming part of DP cells.

Since attempts to utilize the DP as a source of cell therapy for hair loss have been less than successful in the past, taken together with the preclinical evidence summarized above, DSC cells have been considered as an alternative source of hair mesenchymal cells for cell therapy.

After a Phase I clinical study with DSC cells in the EU showed no serious adverse events (McElwee et al., JSRM. 2014), we conducted clinical research studies in Japan on autologous cell-based therapy both for 66 male and female patients with AGA (Androgenic Alopecia) using DSC cells. This type of cell therapy is characterized by acting on existing miniaturized hair follicles with a safe and organized procedure. The study is currently ongoing in two medical institutions and no serious adverse effect has been reported.

In this talk, I also would like to introduce a unique registration law for cell therapy in Japan, which enables hospitals and clinics to outsource cell and tissue processing to specialized cell processing facilities (CPC) located outside hospitals. We have introduced a cell manufacturing process for DSC cells in the CPC established in Kobe by ourselves, and I will discuss future prospects for cell-therapy in patients with AGA.
HAIR FOLLICLE GERM FORMATION ON OXYGEN-PERMEABLE MICROWELL ARRAY CHIPS FOR HAIR REGENERATIVE MEDICINE

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Introduction Regenerative medicine has emerged as a promising approach for hair loss, in which autologous follicular stem cells have been transplanted into bald regions to regenerate hairs. Because cells transplanted as a single cell suspension scarcely generate hairs, the engineering of three-dimensional (3D) tissues before transplantation has been explored to improve this approach. Recent studies have shown that transplantation of engineered hair follicle germs (HFGs), which was fabricated by integrating two respective 3D aggregates of epithelial and mesenchymal cells in vitro, led efficient hair regeneration with repeated hair cycles after transplantation onto the back skin of mice. This approach is excellent and may open a new avenue for hair regenerative medicine, but it remains challenging to prepare a large number of HFGs necessary for a human treatment. In this study, we propose a more efficient and scalable culture method using oxygen-permeable microwell array chips for preparation of a large number of HFGs.

Materials and Methods The microwell array chips were fabricated via micro-milling and molding processes. Briefly, the mold configurations (well diameter, 1 mm; well depth, 1 mm; well number, 20-5000 microwells) were custom designed and fabricated using the micro-milling machine. A precursor solution of oxygen-permeable poly-dimethyl siloxane (PDMS) was poured onto the mold and the configurations were transferred to PDMS rubber. Epithelial and mesenchymal cells were suspended in a culture medium and seeded in a fabricated PDMS microwell array chip. As a comparison, the same experiments were conducted using a microwell array chip fabricated with non-oxygen-permeable polymethyl methacrylate. After 3 days of culture, cell aggregates formed on the chips were transplanted into shallow stab wounds prepared on the back of mice under anesthesia. Transplanted sites were observed at 18 days after transplantation, and images of the generated hair were captured using a digital microscope.

Results Epithelial and mesenchymal cells initially formed a randomly-distributed single cell aggregate in each microwell in the PDMS chip but then spatially separated each other and exhibited typical morphological features of an HFG during 3 days of culture. We demonstrated that oxygen supply through the bottom of the PDMS chip was crucial for the spontaneous formation of HFGs and subsequent hair shaft generation. This spontaneous HFG formation facilitated the preparation of a large number of cell aggregates (~5000 aggregates/chip). Further, the HFGs formed hair follicles and hairs generated on mice after 18 days of transplantation. The same results were obtained with dermal papilla cells dissociated from scalp hair follicles.

Conclusion This simple HFG preparation approach may provide a promising strategy for advancing hair regenerative medicine.

THE ROLE OF EXTRA CELLULAR MATRIX IN INDUCING IN VITRO MORPHOGENESIS OF THE FOLLICLE-LIKE STRUCTURES

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Introduction Hair follicle morphogenesis depends on epithelial-mesenchymal interactions. Many researchers have attempted to recapitulate epithelia mesenchymal interaction in vitro using a range of different strategies and approaches. Hair adult stem cells or pluripotent stem cells have been used in skin equivalent models to support the induction of new hair follicle forma-
**Neogenesis and tissue engineering**
*Chairs: Mike Philpott, Sung-Jan Lin*

**SESSIONS Wednesday, April 24th**

**ABSTRACT BOOK • 11TH World Congress for Hair Research • SITGES, BARCELONA 2019 • SPAIN**

Chairs: Mike Philpott, Sung-Jan Lin

**Neogenesis and tissue engineering**

In vitro. Today there is a growing awareness of the fact that the extra cellular matrix (ECM) has a functional importance as a dynamic repository for morphogens, cytokines and growth factors, which in vivo regulate morphogenetic processes. Recently, we established a human skin equivalent by means of a tissue engineering process that induces the full morphogenesis of functional dermal and epidermal compartments. In our skin model the dermal ECM presents laminin, fibronectin, hyaluronic acid, versican, elastin and collagen arranged and organized as in the human counterpart. As proof of the physiological relevance of such tissue environment we demonstrate that without adding mesenchymal stem cells but only using adult human skin cells is possible to generate follicle-like structures in vitro resembling what occurs in vivo in the fetal skin. Immunotypization evidences an inward-oriented differentiation of the follicular-like structures through immunopositivity for epithelial stem cell markers such as p63 and K19. On the contrary, no follicle-like structures morphogenesis was observed when human skin equivalent model was built by using exogenous bovine collagen.

**Methods** To enhance the inductive features of our skin model we added an aggregate of human dermal papilla cells in the phase of epidermal tissue formation.

**Results** We demonstrate the possibility to restore the stemness of dermal papilla cell during 3 weeks in vitro through the immunolocalization of PROM-1 and detection of ALP.

**Conclusion** In conclusion this work shows a novel bioengineering strategy to guide epithelial cells towards the development of follicular like structures in vitro, highlighting the fundamental importance of cell-synthesized ECM in displaying the correct time and space presentation of hair inductive signals.

**HUMAN ADULT SKIN STEM CELLS SELF-ORGANIZE INTO HAIR FOLLICLE GERM IN VITRO**

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**Background** Tissue and organ replacement based on autologous cell application is one of the most promising fields of modern regenerative biology and medicine. Hair loss treatment strategies are concentrated on the development of the therapy for adult and aged people, although most of researches have been conducted using fetal or neonatal cell sources. The current study aimed to investigate the ability of human postnatal skin cells to produce hair follicle-like structures in vitro and to examine the suitability of the produced organoids for transplantation.

**Comment** We showed that human epidermal keratinocytes and hair follicle dermal papilla cells are able to self-organize producing the aggregates with hair follicle germ properties. The folliculogenesis initiation was confirmed by Lef1 upregulation in the epithelial-mesenchymal junction of developing organoids. Dermal papilla cells aggregate in spheroids and maintain specific expression markers: versican and laminin V. Keratinocytes upregulate hair follicle specific markers: p-cadherin, keratin 6, AE13, and downregulate interfollicle keratin 1, 10 and E cadherin. Hyaluronic acid and matrigel support the keratinocytes proliferation and aggregate development in vitro. Subcutaneous transplantation of organoids into nude mice leads to hair follicle-like structure formation.

Adult tissues preserve the stem cells while the aging microenvironment unfortunately depletes the regenerative potential. The investigation of the ability of postnatal stem cells to contribute and support the organogenesis in vivo and in vitro will promote the development of novel patient-specific strategies in modern biotechnology.

We demonstrated that human postnatal skin cells are able to regenerate hair follicle in culture and after transplantation to immunodeficient animals.

**Conclusion** We consider that our approach could be suitable for other human tissues and appendages modeling.

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The histopathology of primary inflammatory cicatricial alopecia is characterized by two main features: folliculocentric inflammation in the permanent zone of the hair follicle (the infundibular region) where the epithelial hair follicle stem cells (eHFSCs) reside in the bulge, and the ultimate replacement of the follicle with fibrous tissue. Several mechanisms have been implicated involving deficient peroxisome proliferator-activated receptor (PPAR) γ followed by destruction of the pilosebaceous unit, CD-8+ T-cell induced apoptosis of the eHFSCs that have lost their immune privilege and epithelial mesenchymal transition (EMT) of the follicular eHFSCs which have survived the massive apoptosis. Dermoscopy (trichoscopy)-guided biopsies are helpful to identify the optimal site for the biopsy by sampling follicles with peripilar casts, compound hairs (tufts), broken hairs and keratotic plugs. Horizontal sections are superior to vertical sections to identify focal follicular involvement in a background of overall preserved follicular architecture. On horizontal sections two clues for the diagnosis on scanning magnification are the "eyes and goggles" sign which refer to compound follicular structures assessed at the level of the isthmus or below that are reminiscent to big owl’s eyes (when the fusion is between the connective tissue sheath of the affected adjacent follicles) or to goggles (when the fusion is between the outer root sheaths of the affected adjacent follicles). Traction alopecia and cicatricial marginal alopecia are an example of irreversible non-inflammatory cicatricial alopecia that shows a different histopathologic pattern characterized by preservation of the sebaceous glands with loss of hair follicles.

In summary, this lecture will discuss the most common histopathologic patterns in primary lymphocytic cicatricial alopecias with special focus on the trichoscopic-pathologic correlation.

Central centrifugal cicatricial alopecia (CCCA) is a form of scarring alopecia which is most commonly seen in women of African ancestry, with few cases reported in males and children. True epidemiologic data regarding CCCA remains limited. CCCA may be transmitted as an autosomal dominant trait and is often but not exclusively triggered by hair-grooming practices, thus explaining its prevalence among females. It is usually asymptomatic, with hair loss advancing in a centrifugal pattern resembling androgenetic alopecia. Histopathological examination shows variable degrees of lymphocytic inflammation, follicular degeneration and fibrosis with dermoscopy showing a perifollicular grayish halo. A number of therapeutic modalities has been used, but none superior, with most authors advocating early diagnosis and prevention of further hair loss. The pathogenesis of CCCA has remained elusive for years and only recently has efforts been made to delineate the molecular basis of the disorder. The recent findings of mutations in peptidylarginine deiminase 3 (PADI3) an enzyme that post-translationally modifies other proteins essential to hair shaft formation has been associated with CCCA, and will be discussed.
Chairs: Wilma Bergfeld, Andrew Messenger

Genetics and inflammatory markers of cicatricial alopecia

The molecular basis of cicatricial alopecias (CA) are largely unknown, although an immune component has been postulated to underlie this rapidly emerging group of scarring and permanent hair loss. CA is a growing family of disorders that also have been postulated to have a significant environmental trigger, potentially from cosmetic or sunscreen ingredients that have been developed over the past approximately 30 years coincident with the rapid rise in cases of CA. While the clinical presentations and the populations affected are somewhat different, the symptoms of CA and histologic findings are surprisingly similar, raising the possibility that they are unified by common underlying pathomechanisms. We conducted an RNAseq study of scalp biopsies from a large number of patients with LPP and FFA, and identified several new molecular pathways associated with the family of CA disorders, which may help to identify new therapeutic approaches for these difficult to treat conditions.

Endpoints in clinical trials for cicatricial alopecia

One of the main challenges in primary cicatricial alopecia (PCA) management is the ability to monitor disease progression over time. Currently, assessments rely on patient reported symptoms, reduction in signs of inflammation and evaluation of the extent of hair loss (e.g. using measurements or photography). However, each criteria has limitations either by the subjective nature of the assessment, uncertainty about whether clinical signs reflect disease activity, difficulty accurately recording the areas of hair loss and the often very slow progression, which makes identification of changes in the short-term challenging. The majority of clinicians would rate extent of hair loss as the most important outcome in PCA. This talk will discuss potential outcome measures in PCA and their limitations.
**IMMUNOHISTOCHEMISTRY PATTERNS IN CICATRICAL ALOPECIAS**

**Introduction** Diagnosing cicatricial alopecias might be challenging due to their broad spectrum of clinical and histopathological characteristics. To avoid diagnostic delays and inaccuracies, adjuvant tools to facilitate diagnosis might be needed. The use of immunohistochemical stains (IHC), has been useful in some entities; though, further comprehension is needed.

**Objective** To analyze some IHC stains in cases clinically compatible with cicatricial alopecias, in order to evaluate differences between cicatricial entities that show overlapping features, and between cicatricial and non-cicatricial alopecias.

**Materials & Methods** We included cases from Hospital Clinic of Barcelona, clinically diagnosed as lichen planopilaris/frontal fibrosing alopecia (LPP/FFA) and lupus erythematosus (LE) during 2015 and 2016, in which histopathology was available. The IHC markers analyzed were CD123 (plasmacytoid dendritic cells), CD1a (Langerhans cells), and CD3 (T-cells). The presence of each marker was evaluated as mild (+), moderate (++) or intense (+++). The distribution pattern was also analyzed.

**Results** Eleven cases of cicatricial alopecia were analyzed: 8 with LPP/FFA and 3 with LE. We used 2 cases of alopecia areata (AA) as controls of non-cicatricial alopecia.

All cases of LPP/FFA were positive for CD1a, mostly in an intrafollicular pattern. Intense positivity (+++) was seen in more acute cases. CD123 was positive +/++ in most cases in a perifollicular pattern. CD3 was positive (++/+++) in all cases with a predominant perifollicular pattern.

In cases with LE, CD1a was mildly positive (+) in an intrafollicular pattern; CD123 was mildly to moderately positive (+/++) in isolated or clustered perifollicular patterns; CD3 was mildly to moderately positive (+/++) in different patterns (perifollicular, interstitial, and superficial dermis). In the 2 cases of AA, there was mild positivity of CD1a and mild positivity of CD3 in interstitial and perivascular patterns. CD123 was negative for one case and mildly positive (+) in another case.

**Conclusions** Presence of CD1a and CD3 in both cicatricial and non-cicatricial alopecias suggests that both share similar initial inflammatory mechanisms, that may diverge at some point of their pathogenesis.

**Comment** We found no significant difference in CD123 patterns of LE and LPP, even though recent literature states that it may be more common to find a cluster distribution in LE and a single interstitial distribution in LPP. According to previous literature there is a decrease of Langerhans cells in LPP, since they play a role as antigen presenting cells, which leads to an increase of CD8+ cytotoxic cells. By contrast, in our study, we found that Langerhans cells were noticeable in more acute cases, which may represent a very initial stage of inflammation.

**Conclusion** Even though this preliminary study needs further analysis, these provisional data highlights the potential role and importance of IHC as a complement for a more accurate diagnosis.
Cicatricial alopecia (Non FFA)

Chairs: Wilma Bergfeld, Andrew Messenger

women and is the most common form of primary scarring alopecia in the African population. The treatment of CCCA is aimed, as a priority, to interrupt the process of follicular loss and to alleviate possible symptoms associated. To date, there have been no published randomized trials of CCCA treatment.

Materials and Methods We selected 15 from 900 records from the Hair Diseases Department of Santa Casa da Misericordia of Rio de Janeiro, which met the following criteria: women with clinical and histopathological diagnosis of CCCA, who were not pre-treated for a minimum period of six months, who did not present other hair diseases and who were treated with triamcinolone infiltrations in monotherapy. We excluded from the analysis pregnant women, infants or patients submitted to hairstyles with traction, prothesis or use of capillary chemistry during the treatment.

The sample had an average age of 60 years and of this, 80% of patients reported having already done some type of chemical smoothing in some period of life, 47% had already done hairstyles and mega hair, and 40% practiced thermal smoothing. All patients were submitted to monthly infusions of triamcinolone at the dilution of 2mg per ml, for a total of a six sessions. The response was obtained by a photographic analysis that was done by four dermatologists who evaluated the observational parameters of follicular density and alopecia plate diameter and rated the response to treatment in good response, clinical stability and worsening clinical.

Results Of the 15 patients, 53% were classified as a good response, 30% were classified as clinical stability and 17% classified as clinical worsening, and it is possible to affirm that there was improvement after treatment (p < 0.005). Seven patients were submitted to new biopsies, in a region adjacent to the scar of the first biopsy and all of them showed a decrease of inflammatory activity and four of them (57%) showed increase in the ratio of terminals: velus hair.

Conclusion In this manuscript injectable corticosteroids have been shown to be effective in the treatment of CCCA. Even the patients who did not show clinical signs of improvement in alopecia plaques have reported increased hair length at the end of treatment, which, according to them, had a great impact on quality of life and self-esteem. Our hypothesis for the improvement of the clinical aspect of CCAA is that this treatment reduced chronic inflammatory activity contributing to increase the number of terminal hairs in the region and increase the growth rate of the remaining thin and short hairs distributed on the alopecia plaque.

Although this study represents a hope for improvement for patients with CCAA, more studies are needed to prove our results.

PPAR-G STIMULATION WITH NAC-GED-0507-LEVO PROTECS FROM CYCLOPHOSPHAMIDE-INDUCED HAIR FOLLICLE CYTOTOXICITY AND BULGE STEM CELL DAMAGE


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Introduction Permanent chemotherapy-induced alopecia (pCIA) has severe psychosocial repercussion on cancer patients, and remains a major unmet medical need in clinical oncology. While it is known that the acute hair follicle (HF) damage in CIA is due to major, but reversible damage of the rapidly hair matrix proliferating keratinocytes, the mechanism leading to pCIA remains to be discerned. We hypothesized that irreversible hair loss in pCIA may result from permanent destruction of HF epithelial stem cells (eSCs), possibly undergoing cell death and epithelial-mesenchymal transition (EMT).

Methods We explored here if this is the case by investigating bulge CK15+ eSCs activities after treatment of full-length HFs ex vivo with 4-Hydroperoxy Cyclophosphamide (4HC- 3µM, and 30µM), which severely induces reversible CIA and sometimes permanent scarring alopecia.
Cicatricial alopecia (Non FFA)

Chairs: Wilma Bergfeld, Andrew Messenger

Given the well-known protective role of PPAR-g signaling in eSCs biology, we also investigated whether the PPAR-g modulator, NAC-GED-0507-Levo (NACGED- 0.01, 0.1 and 1 mM), protects HFs and their bulge CK15+cells from 4HC-induced damage.

**Results** As expected, treatment of full-length HFs ex vivo with 4HC significantly induced HF cytotoxicity, assessed by increased LDH release into the medium, and HF dystrophy (increased number of melanin clumps), and promoted catagen development. 4HC treatment also reduced the number of CK15+ cells in the bulge, and increased their apoptosis. Moreover, 4HC also induced EMT in the bulge, as indicated by decreased expression of E-cadherin and upregulation of fibronectin expression and the appearance of vimentin+ intra-bulge cells.

**Comment** Using this ex vivo surrogate assay for pCIA, HFs pre-treatment with NACGED exerted some preventive effects on 4HC-induced cytotoxicity and dystrophy, including reducing LDH release into the medium and melanin clumping, but not catagen development. NACGED also prevented CIA-induced depletion of bulge eSCs pool by hindering the reduction of CK15+ cell proliferation and protecting them from apoptosis. Finally, pre-treatment with NACGED helped to protect HF eSCs from EMT by hampering the 4HC-induced reduction of E-cadherin expression and by preventing the 4HC-induced increase of vimentin+ cell number.

**Conclusion** Our results suggest that permanent scarring CIA may indeed be caused by apoptosis and/or EMT-mediated destruction of CK15+ eSCs in the bulge. In addition, our data support the hypothesis that promoting PPAR-g signaling may provide an effective CIA-management strategy, and advocate the use of PPAR-g modulators, such as NACGED, as possible therapy for preventing permanent hair loss in chemotherapy-treated cancer patients.
The capacity of the stem cells (SC) to self-renewal and differentiate is tightly orchestrated by signals within the SC niche. In the skin, the hair follicle stem cell niche is the main reservoir of stem cells. Alterations in signaling from the hair follicle SC will affect their niche by changing its fate. Premature senescence of dermal papilla cells has been pointed out as a key player during androgenetic alopecia (AGA). Here we show how after inducing senescence, within the hair follicle SC niche, the SC exit their niche invading the Sebaceous Glands. We have generated novel genetic tools to target DP cells and HFSC niche. Using these genetic tools, we developed an in vivo mouse model to induce senescence in hair follicle stem cell niche. Lineage tracing experiments show that, after inducing senescence, hair follicle stem cells directly contributed to the development of enlarged multi-lobular sebaceous glands. As a consequence of this change of cell fate, the hairs failed to regenerate during the following hair follicle cycle. Preliminary data indicates that this mouse model resembles the human senescence or AGA alopecia phenotypes. We are using novel senescence markers to investigate whether senescence affects different cell types within the hair follicle during hair loss. Finally, to establish causality, we have prospectively isolated senescent cells at the HFSC and analyzed key molecular signals in an effort to understand the mechanistic link between premature senescence and the molecular signaling changes directly associated with AGA in our novel in vivo model.

Our lab recently demonstrated that blockade of JAK-STAT signaling using topical JAK inhibitors was sufficient to induce hair growth (anagen) in resting (telogen) mouse hair follicles, raising the possibility that JAK-STAT signaling is required for maintaining hair follicle stem cells (HFSC) in their quiescent state. Here, we demonstrate that the IL-6 family cytokine Oncostatin M (OSM) is a negative regulator of hair growth that maintains HFSC quiescence via JAK-STAT5 signaling in vivo. Unexpectedly, we identified that the source of OSM is not intrinsic to the HF itself, but rather, emanates from a distinct subset of TREM2+ dermal macrophages that are present in mouse telogen skin. Furthermore, we show that depletion of macrophages using genetic and pharmacological approaches induces hair growth by removing the source of OSM, opening the possibility of treating human hair disorders characterized by arrested telogen follicles by targeting a cell type outside the HF itself.
**BEYOND GOOSEBUMPS: INTERACTIONS BETWEEN THE HAIR FOLLICLE, THE ARRECTOR PILI MUSCLE, AND THE SYMPATHETIC NERVE DURING DEVELOPMENT AND HAIR FOLLICLE REGENERATION**

Piloerection, commonly known as goosebumps, involves three interconnected cell types: the hair follicle, the arrector pili muscle (APM), and the sympathetic nerve. The interactions between these three cell types during development and adult tissue maintenance remains poorly understood. Here, we identify a central role of the developing hair follicle in regulating the formation of APMs, which then attract sympathetic innervation to the hair follicle stem cells. Although dispensable for hair follicle development, impulses from the sympathetic nerves are crucial for regulating hair follicle stem cell activity during hair follicle regeneration. Formation of the APMs requires Sonic Hedgehog secreted from the developing hair follicles. Once developed, APMs do not undergo turnover, providing a stable anchor that maintains sympathetic innervations to the hair follicle stem cells. APM ablation leads to concurrent loss of sympathetic nerve innervation to the hair follicles. Our results uncover a novel function of APM in bridging the body’s sympathetic modulations to influence hair follicle stem cell activity, and illustrate an example for how a developing tissue regulates the establishment of the niche to modulate its regeneration in adulthood.

**A LYMPHATIC VASCULAR NICHE CONTRIBUTES TO THE CYCLIC ACTIVATION OF ADULT HAIR FOLLICLE STEM CELLS**

Lymphatic vessels play fundamental homeostatic functions in the skin, including the balanced transport of fluids and macromolecules, the local coordination of immune responses, as well as immune cell trafficking. Whether lymphatic vessels functionally associate with the cyclic regeneration of hair follicles is not known. Here, we show that lymphatic capillaries connect to individual hair follicles, in a hair follicle stem cell (HFSC) dependent manner. LV emanate at the level of HFSC interconnecting adjacent hair follicles in organized patterns across the skin. Steady and live imaging approaches suggest the existence of coordinated communication between hair follicles at tissue-level. Importantly, the depletion of lymphatic vessels impairs the pharmacological induction of hair follicle regeneration. These results define LV as novel components of the HFSC niche, coordinating the communication between hair follicles at tissue-level and provide insight into their functional connections to HF regeneration.
Introduction Object recognition, texture discrimination and socio-emotional exchange are crucial capabilities in our day-to-day life that are mediated by synergistic interactions between skin epithelium and neural tissue. On the skin, the human hair follicle is a main sensory receptor of tactile stimulation. The axons from somatosensory neurons located on the trigeminal and dorsal root ganglion innervate hair follicles forming a complex neural network that enables the encoding of mechano-tactile stimuli. While the morphology and physiology of specific types of mechanoreceptors that innervate murine hair follicles has been well described, structural differences between murine and human hair follicles make interspecific extrapolation arduous.

Methods In this project, we sought to unravel how the human hair follicle acts as a sensory mechanoreceptor. After obtaining follicular units from occipital scalp and beard locations, we used a combination of whole-mount immunolabelling and confocal microscopy to image whole follicles and their associated axonal networks.

Results This revealed a specialized axonal network in the bulge region positive for specific mechanoreceptor markers such as NFH, Npy2r, CGRP and Th. The afferent region of these axons showed a high myelinization pattern of S100+ Schwann cells. Moreover, specific axonal fibres are organized forming lanceolate complexes with designated circumferential and longitudinal endings. Outer root sheath cells were also isolated from human scalp follicles to perform calcium dynamics experiments. These cells were positive for KRT15, CGRP and Piezo2 and we were able to detect calcium oscillations after mechanical stimulation.

Comment Pharmacological inhibition using non-specific channel blockers suggests the activation of Piezo and TRPC channels as potential mediators of these oscillation. When co-cultured with dorsal root and trigeminal ganglion neurons, the hair follicle cells were also able to signal to and trigger a calcium spike in surrounding neurons. Importantly, these findings indicate that in addition to their involvement in tissue homeostasis and renewal, hair follicle KRT15+ cells can be involved in signalling sensory information.

Conclusion Currently we have shown that the human hair follicle is an exquisitely sensitive organ innervated by different classes of mechanoreceptors. The development of more complex co-culture models between hair follicle stem cells and neurons to perform calcium dynamics, genetic knock-out and patch-clamp electrophysiology will help to identify which molecular components of the human hair follicle trigger and support the signalling of mechano-tactile stimulus. Collectively these approaches will reveal how epithelial-neuronal interactions in the human hair follicle modulate our sense of touch.
Introduction Stem cells are often regulated by short-range signals from the local microenvironment. Whether and how they communicate with the external megaenvironment is unknown. We found that stimulation of animals’ eyes with intense light, especially with blue light, lead to rapid activation of hair follicle stem cells and induced anagen entry. Retinal cone and rod cells were not essential for light-triggered anagen entry. Instead, the light signals were interpreted by M1-type intrinsically photosensitive retinal ganglion cells (ipRGCs), which signaled to the suprachiasmatic nucleus (SCN) via the photoreceptor melanopsin.

Comment Subsequently, efferent sympathetic nerves were immediately activated. Increased norepinephrine release in skin activated hair follicle stem cells by enhancing hedgehog signaling. Therefore, the ipRGC SCN-sympathetic circuit connects the external environment with the local stem cell niche and allows the interpretation of external signals by hair follicle stem cells for regeneration.

Conclusion The results also demonstrate that, in addition to the direct irradiating skin with red light to promote hair growth, hair follicle stem cells can also be activated indirectly by optic light stimulation.

Introduction & Objectives Although human dermal white adipose tissue (DWAT) closely envelops resident scalp hair follicles (HFs), the bidirectional communication between perifollicular adipocytes and human HFs remains to be explored. Recently, we determined that culturing human HFs with surrounding DWAT promoted hair growth and pigmentation ex vivo. The current study aimed to further expand knowledge of the human DWAT-HF axis.

Material & Methods Following proteomic analysis we cultured isolated human HFs for 24hr (n=3) with/without recombinant human hepatocyte growth factor (HGF) and HFs with surrounding DWAT with/without a neutralizing antibody for human HGF. We then profiled cellular proliferation, apoptosis and melanogenesis markers combined with immunohistomorphometry to assess the effect of HGF upon follicular functions. Finally, we utilized multiplex gene expression assays followed by Ingenuity Pathway Analysis (IPA) to identify HGF-induced early and late changes in human HF gene expression.

Results Intriguingly, proteomic analysis identified hepatocyte growth factor (HGF) as the most abundantly-secreted DWAT product within long-term HF+DWAT ex vivo cultures. Therefore, we chose to stimulate HFs with HGF ex vivo. Both HFs cultured with DWAT, or HGF in the absence of DWAT showed a significantly increased pigment content and number of gp100+ melanocyte cells compared to untreated HFs. Both HGF and DWAT maintained higher numbers of melanocytes with three or more dendrites, with a trend towards higher numbers of gp100/Ki-67+ proliferating melanocytes. These
positive effects were partially ablated by a neutralizing HGF antibody added to HF+DWAT. As expected, HGF-treated HFs displayed increased proliferation and decreased apoptosis within matrix keratinocytes, effects mirrored by culturing HFs with surrounding DWAT, indicating a prolonged anagen phase. In addition, preliminary data showed that HGF increased hair shaft elongation between days 2-4 in culture and maintained HFs in anagen phase for longer than control HFs. Transcriptomic analysis of HFs treated with HGF (6hr) revealed that HGF up-regulated PAX3 and SOX10 (pigmentation pathway), as well as VEGFA (angiogenesis) and WNT5B. Gene expression analysis on 24hr cultures coupled with IPA, revealed that key Wnt pathway inhibitors are down-regulated in HFs treated with HGF, whereas Wnt agonists, WNT6 and WNT10B, show an upward trend for HF+HGF and HF+DWAT.

Comment Here we provide the first evidence that human dermal adipocytes communicate with adjacent scalp HFs by secreting HGF, one of the most potent promoters of hair growth and pigmentation. In turn, the human HF epithelium and pigmentary unit express cognate receptors (cMET) and likely respond to HGF signalling by activating early pigmentation pathway members. This study designates human perifollicular adipocytes and HGF-dependent DWAT-HF communication an intriguing novel target for therapeutic intervention in the future management of disorders of hair growth or pigmentation.
BEYOND ANDROGENETIC ALOPECIA
-PATIENT AWARENESS, QUALITY OF LIFE, AND COMORBIDITIES

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When dealing the patients with androgenetic alopecia (AGA), there are things to consider beyond merely treating hair loss. Firstly, although there are many people who have concerns with their baldness, some of them hesitate to visit dermatology clinics for hair loss. Those patients seek non-medical treatments instead, however, they are poorly satisfied in most cases. Therefore, it is important for dermatologists to provide appropriate information about AGA and its treatment, strengthening the rapport between physicians and AGA patients.

Secondly, AGA is not limited to hair loss, but should be considered comprehensively as a systemic condition with hair loss. Significant systemic conditions causing AGA such as polycystic ovarian syndrome and hyperandrogenism should be evaluated. And co-morbidities of AGA such as cardiovascular diseases, metabolic syndrome, prostate diseases and others should be checked. Lastly, AGA negatively affects patients’ perception, body image, thus lowering their quality of lives. In addition to pharmacological treatment, it is necessary to identify and correct the factors that may affect the quality of lives of patients with AGA.

Conclusively, in advance of confining AGA as hair loss, something overlooked in AGA such as the reason why bald people seek non-medical treatment, associated systemic condition, its co-morbidities and patients’ quality of lives should be considered in dermatologic clinics.

STUDYING AGA IN THE LAB

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Androgenetic alopecia (AGA), known as male pattern baldness (MPB) in men and female pattern hair loss (FPHL) in women, results from miniaturization of hair follicles. Hair follicles must cycle in order to miniaturize. Hair follicle stem cells remain relatively intact in MPB, but progenitor cells are decreased. Markers for human hair follicle stem cells include cytokeratin 15 (K15) and, for progenitor cells, CD200. These markers can be used in fluorescent activated cell sorting (FACS) and immunohistochemistry to assess hair follicle stem cells and progenitor cells. Gene expression studies in humans provide candidate genes and pathways that may be important for hair growth. By culturing human hair follicles in explant using the Philpott model, hair growth rate can be assessed after application of compounds. In mice, telogen to anagen transitions can be studied as well as anagen duration. These mouse models are important for screening for hair growth compounds. The combination of mouse and human culture and graft models provides a powerful preclinical approach to assess potential growth promoting approaches.
**Background** We recently presented a clinical study protocol for RNA analysis in plucked hair follicles to identify putative markers of androgenetic alopecia (AGA). Herein, we applied the technique to monitor gene expression in plucked hair follicles during the early phase of minoxidil treatment.

**Methods** In addition to phototrichogram assessment, 20 hair follicles were plucked from AGA-affected vertex and from lower occiput of Hamilton-Norwood IIIv-IV patients (n=12) before, 4 and 8 weeks after topical minoxidil 5% foam treatment. RNA was extracted (RNeasy Kits, Qiagen) quality checked via Agilent 2100 Bioanalyzer and submitted for hybridization (Miltenyi Biotec GmbH, Germany) using the Agilent 60-mer Whole Genome Oligo Microarray protocol. Differential gene expression (combat method, unadjusted Anova and Tukey’s Posthoc test p values) and gene set enrichment analyses (GSEA, CAMERA method, C2 collection, Molecular Signatures Database) were performed.

**Results** Consistent with the expected shedding effect of minoxidil responders, 9/12 individuals experienced a reduction in the anagen/telogen ratio (A/T) at week 4 (4 in a pronounced drop with subsequent recovery, while the others showed a trend of less pronounced but prolonged A/T reduction over 8 weeks). Differential gene expression analyses revealed 412 significantly down-regulated genes at week 4, while 563 were upregulated (approximately half of those remained upregulated over the whole treatment period). GSEA yielded association with 188 pathways, almost all of them predominantly downregulated mostly involving transcription, translation, RNA and protein metabolism. Interestingly however, downregulated rapamycin sensitive genes were among the highly represented pathways, while this same gene set was among the pathways predominantly upregulated in vertex compared to occiput before the beginning of treatment. In comparison, changes in gene expression between week 4 and 8 weeks were less pronounced (42 additionally down- and 58 up-regulated genes). Involved pathways were predominantly upregulated with interferon signature pathways being highly represented, but also stat3 targets and angioproliferation. Interestingly, gene expression changes in the clinically unaffected and untreated occiput area reacted in parallel.

**Conclusion** The data obtained in this set-up give deep insights in the changes, which the epithelial compartments undergo during the early phase of minoxidil treatment, but may also reveal further information on hair cycle regulation in general. The reproducible results obtained by choosing two time points (week 4, week 8) and the comparison of affected and unaffected areas prior to treatment support the validity of our findings.
DOES HAIR FOLLICULAR KAPT CHANNEL GATING BY MINOXIDIL- AND/OR MECHANO-STIMULATION CONTRIBUTE TO HAIR GROWTH IN VIVO?

**Background** Despite topical therapy with minoxidil, a potent hair growth agent, for androgenic alopecia over three decades, details of the mechanism and cell behavior induced by minoxidil on cultured human dermal papilla cells (HDPC) remain unknown.

**Objectives** We examined here the cellular response on the level of KATP channel gating in HDPC with the mechanical stimulation of compression force besides the addition of minoxidil sulfate as the active form of minoxidil. Furthermore, we studied minoxidil- or mechanical compression-induced hair growth in vivo.

**Methods** Opening of K+ channels was evaluated by the use of a fluorescence-based Tl+ flux assay using Thallos. Lateral images during addition of minoxidil sulfate (100 µM) were obtained by confocal microscopy. Shaved backs of C3H/He and C57BL/6 mice were stimulated by 5% minoxidil topical reagent and cyclic compression (10 Hz, 90.6 Pa, 1 hour/day for three consecutive days), respectively. Then, hair re-growth was observed up to 4-5 weeks.

**Results** Addition of minoxidil sulfate and/or cyclic compression from the apical surface significantly stimulated the gating of K+ channels. KATP channel blocker such as U-37883A, glibenclamide, and tolbutamide inhibited compression and/or minoxidil sulfate-induced the Tl+ influx. Particularly, in the presence of U-37883A (10 µM), a selective blocker of the Kir6.1/SUR2B channel, minoxidil sulfate did not evoke the opening of K+ channels. The lateral images when minoxidil sulfate was added revealed cell swelling. U-37883A suppressed this cell swelling. Compared with topical minoxidil treatment, micromechanical force of cyclic compression promoted have substantially more robust hair regrowth in vivo.

**Conclusion** Treatment with minoxidil sulfate might enhance the mechanically induced upstream responses in HDPC. Our data suggests that the combination of cyclic compression and minoxidil sulfate could promote therapeutic potency for hair growth by the amplification of signaling via Kir6.1/SUR2B as KATP channel. Kir6.1/SUR2B activation and microdeformation of cells and tissues may be essential and effective strategy for androgenic alopecia.

SKIN STIFFNESS OF THE SCALP IS ASSOCIATED WITH ANDROGENETIC ALOPECIA

**Introduction** Androgenetic alopecia (AGA) primarily involves the frontal to vertex scalp and spares the temporal and occipital scalp. We hypothesize that the physical property of the scalp, namely the scalp stiffness, may be the determinant for this pattern distribution. The stiffness of the tissue is known to modify the behavior and properties of cells.

**Objectives** This study aimed to map the skin stiffness on the scalp and to investigate the association between skin stiffness and AGA.

**Materials & Methods** Both AGA and non-AGA patients were recruited. The skin stiffness, hair density and hair diameter at 15 designated anatomical points on the scalp was measured. The skin stiffness was measured by Durometer, which quantified the skin stiffness as the number 0-100. The hair density and hair diameter (represented by ratio of terminal/vellus hair numbers) were measured by close up images of the scalp taken by a handheld digital microscope. The severity of AGA was graded according to the Hamilton-Norwood scale.
Androgenic Alopecia Research

Chairs: George Cotsarelis, Annika Vogt

for men and Ludwig classification for women. For statistics, generalized estimating equation (GEE), was used to estimate the correlation between the scalp stiffness and alopecia. T-test was used for the comparison of data between two groups.

Results Total 150 subjects were included for analysis in this study. There were 73 males (including 57 AGA and 16 non-AGA subjects) and 77 females (including 51 AGA and 26 non-AGA subjects). The mean age of the subjects was 34 years (range 20-65 years). Among all scalp areas, the frontal scalp had the highest skin stiffness (32.9) and the occipital scalp had the lowest skin stiffness (9.5). The hair density was in a decreasing trend and hair diameter in an increasing trend along the mid-sagittal axis from the frontal to the occipital scalp.

Comment The skin stiffness of the scalp areas along the mid-sagittal axis was positively correlated with the presence of AGA (p=0.027) and the severity of alopecia (P=0.001) by GEE analysis. Among the 15 scalp areas in males, the vertex scalp of AGA subjects had higher skin stiffness than non-AGA subjects (28.0 vs. 25.0, p=0.044) by t-test. In females, the mid-scalp of AGA subjects had higher skin stiffness than non-AGA subjects (28.6 vs. 26.5, p=0.041). The difference of scalp skin stiffness was even more prominent when comparing the subjects with severe AGA (stage V-VII) and non-AGA subjects.

Conclusion The bald scalp in AGA subjects was correlated with higher skin stiffness. Further investigation was required to elucidate the mechanism.

Introduction and Objectives 5-α reductase (5AR) subtypes I and II are suggested to be involved in the development of androgenetic alopecia (AGA); however, the involvement of type I 5AR in the pathogenesis of AGA and downstream molecular events following androgen receptor inhibition are still poorly understood. We investigated the changes in gene expression levels of growth factors and related molecules responsible for hair growth, such as enzymes and transcription factors, using the bulbar portions of plucked human hair follicles, and evaluated the involvement of type I 5AR in human hair growth.

Materials and Methods Anagen hairs were plucked from male donors with AGA and cultured in medium containing dihydrotestosterone (DHT) or testosterone in the presence or absence of the 5AR inhibitors, dutasteride or finasteride. Total RNA extracted from the bulbar portions of hair follicles was subjected to quantitative reverse transcriptase polymerase chain reaction analysis to assess gene expression levels of growth factors and other related molecules.

Results DHT stimulation resulted in a trend to decrease the expression of genes encoding fibroblast growth factor 7 (FGF7; p=0.52), insulin-like growth factor 1 (IGF1; p=0.85) and WNT family member 5A (WNT5a; p=0.08). Subsequently, testosterone stimulation led to a decreased expression of genes encoding FGF7 (p=0.53), IGF1 (p=0.93) and WNT5a (p=0.51), which was reversed by dutasteride or finasteride treatment. Gene expression levels of FGF7, IGF1 and WNT5a with dutasteride or finasteride under testosterone stimulation showed a consistent trend of re-increasing. The fold change (mean ± standard error of the mean) in FGF7 expression compared with the 0.1% (v/v) dimethyl sulfoxide control ranged from 1.00 ± 0.25 to 1.53 ± 0.04 (P=0.10) with finasteride and 0.93 ± 0.36 to 1.22...
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± 0.10 (P=0.23) with dutasteride. Similarly, IGF1 expression ranged from 0.56 ± 0.78 to 4.34 ± 2.71 (P=0.72) under finasteride treatment and 1.70 ± 0.78 to 2.73 ± 1.24 (P=0.61) under dutasteride treatment. WNT5a expression ranged from 1.03 ± 0.99 to 1.14 ± 0.10 (P=0.26) and 1.08 ± 0.25 to 1.21 ± 0.20 (P=0.65) under finasteride and dutasteride treatment respectively.

Conclusion Among the assessed growth factors and other molecules related to hair growth, the expression levels of FGF7, IGF1 and WNT5a were reversed by 5AR inhibitors under testosterone stimulation. Our data suggest this assay may be useful to deeper dissect the effect of 5AR on human hair follicles and supports the previously unreported involvement of type I 5AR in hair growth.
The name “SAHA syndrome” was proposed in 1982 by Orfanos to define the presence in women of androgen-dependent cutaneous signs. This syndrome is an exacerbation of the “constitutinal hyperandrogenism” that must not be confused with hyperandrogenism developed as a consequence of disorders from the ovaries, adrenal glands, hypophysis, liver and others. There are five forms of SAHA Syndrome in relation with the procedence of the androgens:

1. Constitutional or familial SAHA. Young girls with seborrhoea, facial papulopustular acne, slight hirsutism and hair loss of female pattern with all the hormonal parameters absolutely normal.

2. Ovarian SAHA Syndrome (Overproduction ovarian androgen syndrome): Young girls with pustular and nodule-cystic acne, mammary and lateral beard hirsutism under 2 degrees, severe seborrhoea, FAGA, slight obesity and frequent, painless menstruations of short cycles. It is possible to observe slightly high levels of androstenedione, free testosterone and 3-á-androstanediol glucuronide, and low levels of SHBG.

3. SAHA syndrome in HAIRAN. It is the most recent admitted form. Obese women, habitually diabetics with insulin resistance, acanthosis nigricans and all the other signs of ovarian SAHA. As in ovarian SAHA, there are slightly high levels of androstenedione, free testosterone and 3-á-androstanediol glucuronide, glucose and insulin, and low levels of SHBG.

4. Adrenal SAHA Syndrome (Adrenarche persistence syndrome): Women present severe seborrhoea, nodule-cystic acne with scars on the face and back, FAGA.I-II or with male pattern I-II (FAGA.M.I-II), slight to moderate central hirsutism that can join the pubic triangle with the chin, and palmar hyperhydrosis. The patients are thin, stressed and their menses are of long cycles including oligoamenorrhea with important pain on the first day. It is possible to observe slight elevations of DHEA-S and androstenedione.

5. Hyperprolactinic SAHA: The clinical features are similar to adrenal SAHA Syndrome. The hormone levels in serum show high quantity of prolactin.

Treatment is similar to that of the cases with organ failure: Ovarian SAHA: ethinilestradiol and antiandrogens. SAHA syndrome in HAIRAN with the same that ovarian SAHA plus metformine. Adrenal SAHA: corticosteroids during six months and antiandrogens with a tricyclic anovulatory during nine months to two years. Hyperprolactinic SAHA: bromocriptine until prolactine levels were normal.

F.M. Camacho
SAHA syndrome: Female androgenetic alopecia and hirsutism. Experimental Dermatology 1999; 8:304-5 (FI 2,183).

F.M. Camacho


F.M. Camacho
FEMALE PATTERN HAIR LOSS 2019

Female Pattern Hair Loss (FPHL), a non-scarring alopecia with progressive miniaturization of hair follicles typically in the frontal and central areas may present clinically with onset of puberty or in young adulthood or only become visible in premenopausal or postmenopausal period with variable progression in the rapidity and final degree of hair loss. In general, women present with normal hormonal levels but there is a subset of women with FPHL and associated hormonal dysregulation.

The androgen dependence and the hereditary nature of this miniaturization process in affected women is not as obvious as it is in affected men, thus the term female androgenetic alopecia coined by Ludwig in 1977 has been continuously abandoned with new findings from experimental and clinical research. Androgen-mediated mechanisms are probably involved in FPHL in some women but the evidence is less strong than in men with AGA. Genome-wide association studies have identified several genetic loci for male androgenetic alopecia and have provided in AGA better insight into the underlying biology. However, recently published studies could not clearly identify any susceptibility locus/gene for FPHL, thus suggesting that the etiology differs substantially from that of male pattern baldness. The attempt to investigate the candidate genes of the sex steroid hormone pathway failed to demonstrate significant association with FPHL (Redler et al 2017). So other non-hormonal pathways, including environmental influences, may contribute to the etiology. Investigation of miniaturized hair follicles in female pattern hair loss have shown e.g. overexpression of the aryl hydrocarbon receptor (AHR) which can be activated by environmental pollutants leading to alterations in the cell cycle, inflammation, and apoptosis, findings which suggest the activation and migration of AHR to the nucleus in miniaturized FPHL follicles. However, the mechanisms through which AHR is involved in miniaturization are not clear (Müller Ramos et al 2015).

Other research groups focused on investigations aiming to analyze the role of 5α-reductase and aromatase in plucked anagen hair follicles and were able to demonstrate that aromatase mRNA levels were significantly lower in women with FPHL than in controls, suggesting a reduction in estrogen levels and an increase in the androgen/oestrogen ratio in hair (Sánchez et al 2018).

Improved understanding of etiology and pathomechanism in FPHL is imperative to develop new therapeutic approaches being able to develop a targeted approach to prevent the miniaturization process. Albeit we do have currently good evidence based recommendation for managing FPHL, the clinical outcome could clearly be improved in a large number of concerned women with significant impact on their quality of life.

HIRSUTISM 2019

Hirsutism is defined as the presence in woman of terminal hair in the proper locations of male. There are multiple classifications, for us the most appropriate is Ferriman and Gallwey classification.

When reviewing the literature, there are very few bibliography in this regard, and the majority in non-dermatological journals.

We will discuss the novelties in its pathogenesis (mainly associated with polycystic ovarian syndrome and constitutional hirsutism), about its diagnosis, and treatment. Also the importance and relationship to insulin resistance, and efficacy of antiandrogens such as finasteride, and metformin.
**FREE COMMUNICATIONS TO THE TOPIC**

**A NEW CLASSIFICATION OF EARLY FEMALE PATTERN HAIR LOSS**

**Background** Global photographs (GPs) have been widely used to grade the severity in female pattern hair loss (FPHL). However, existing classifications for FPHL are not useful in the evaluation of early FPHL. Because despite variations in early FPHL, even to a mild degree, those are categorized into just one by existing classifications. Therefore, the authors have devised a grading system for early FPHL with five levels focusing on the changes revealed by the surface reflected light of flash generated on GPs.

**Aims** To examine the possibility of evaluating the treatment course of early FPHL using the grading system based on changes in hair surface reflection patterns.

**Subjects and Methods** Retrospective chart review of 114 early FPHL patients was performed. GPs of these patients were classified into five grades. Photographs of the lowest and the highest grades of each patient were selected and paired. Based on that, we examined two issues, relevance with existing evaluation methods and utility of this new classification in course evaluation. Regarding relevance with existing evaluation methods, we analyzed the relevance between the value of female pattern hair loss-severity index (FPHL-SI) and grades of all the selected photos. In addition, we examined the scope findings of the same period of each photo. In terms of utility, three volunteers graded the paired photographs and chose the milder degree, and then the concordance rate among author’s and volunteers’ evaluations was analyzed.

**Results** Value of FPHL-SI and hair diameter diversity tended to rise along with increasing of GP grade. Concordance rate of grading among author and more than two volunteers was 57%. Concordance rate of course evaluation between author and two volunteers was 97%.

**Conclusion** The new classification can finely classify the grade of early FPHL and can be used for treatment course evaluation.
Post-finasteride syndrome (PFS) is a term recently coined to characterize a constellation of reported undesirable side effects described in post-marketing reports and small uncontrolled studies that developed during or after stopping finasteride treatment, and persisted after drug discontinuation. Symptoms included decreased libido, erectile dysfunction, sexual anhedonia, decreased sperm count, gynecomastia, skin changes, cognitive impairment, fatigue, anxiety, depression and suicidal ideation.

The Post-Finasteride Syndrome Foundation (PFS), which was created to raise awareness about post-finasteride syndrome, recently sent an email to dermatologists practicing in the United States and in Europe to inform them about the syndrome and its inclusion into the National Institute of Health’s Genetic and Rare Diseases (GARD) Information Center even though inclusion in the GARD is not an official recognition of post-finasteride syndrome by the NIH as explained in the web site disclaimer. The NIH is currently founding a study on epidemiology of adverse events of 5-alpha-reductase inhibitors (5αRIs) specifically focused on persistent side effects.

According to information from the website for the PFS, the PFS is also funding research projects seeking to elucidate the nature of the condition including hormonal, genetic and epigenetic causes. The foundation website lists a number of physicians that collaborate with them including urologists, endocrinologists, psychiatrists and psychologists, but no dermatologists. The aim of this talk is to review the existing medical literature for evidence based research of permanent sexual dysfunction and mood changes during treatment with 5αRIs including finasteride and dutasteride. During our talk we shall also discuss about the alternatives in front in patients that believe they might suffer from the PFS and will also deal about discriminating in what type of patient is better not to start with oral 5αRIs.
MINOXIDIL 1 MG ORALLY VERSUS MINOXIDIL 5% SOLUTION TOPICALLY FOR TREATMENT OF FEMALE PATTERN HAIR LOSS: A RANDOMIZED CLINICAL TRIAL

Introduction Topical minoxidil is the only FDA approved drug for female pattern hair loss (FPHL). Many patients discontinue treatment prematurely due to lack of efficacy, intolerance or altered hair texture.

Objective To compare the efficacy, safety and tolerability of once daily minoxidil 1 mg orally versus once daily minoxidil 5% solution applied topically in FPHL.

Material & Methods A 24-week, prospective, randomized, open-label, parallel, two-arm comparative, evaluator-blinded study conducted in a single center from January of 2017 through March of 2018 including 52 women (18-65 years old) with FPHL. Patients with FPHL were randomly assigned, in a 1:1 ratio, to receive once daily minoxidil 1 mg orally or once a day minoxidil 5% solution applied topically. The primary endpoint was change from baseline in hair density from a target area at week 24. Secondary endpoints were terminal hair density, global photographic assessment by three group-blinded evaluators, hair shedding score, and the Women’s Androgenetic Alopecia Quality of Life Questionnaire (WAA-QoL).

Results Fifty-two women with FPHL with a mean (sd) age: 44 (12) years-old, were enrolled and randomly assigned to receive once daily minoxidil 1 mg orally (26 patients) or daily minoxidil 5% solution applied topically (26 patients). Participants of both groups had improvement of hair density in the target area (p<0.01), without difference between the groups (p=0.10): oral 12% (CI95% 8.0-16.1%) and topical 7.2% (CI95% 1.5-12.9%). There was improvement on terminal hair density, on the evaluation of global photographic assessment and on the WAA-Qol score with no difference between the groups (p>0.08). The reduction on the hair shedding score was more intense in the oral group (p<0.01). Hypertrichosis was more prevalent in the oral group (27%) than the topical (4%). Heart rate increased 10% in the oral group (p<0.01), without tachycardia. There was no difference on the variation on the blood pressure between the groups (p=0.51).

Conclusions Oral 1mg minoxidil was safe and well tolerated in the treatment of FPHL. Its efficacy did not differ from topical 5% minoxidil solution. It can be an option for patients with poor compliance to topical therapy.
with FPHL who were treated with various treatment modalities. Global photography, target area hair counts using the trichoscope (FotoFinder Systems), hair mass index and adverse events were assessed.

Results Sixty women (mean aged 58.05 (25-70)) with mean duration of 9.07 (1-36) years were evaluated. Each treatment was given to patients for 24 weeks; 15 women treated with 3% minoxidil solution twice a day, 15 women with 5% minoxidil solution twice a day, 10 women with LLLT (home-used, helmet type device, 655nm, 5mW) 25 min/day, every other day and 14 women were received 3 sessions of fractional thulium laser plus PRP injection at 1-month interval. All groups have significant increases at weeks 12 and 24, and there are small non-significant difference in the groups versus the 3% minoxidil. At 24 weeks of treatment, the terminal hair count increased in the highest number in 5% minoxidil treated group, (22.86%) followed by LLLT (19%), PRP (17.29%) and 3% minoxidil (15.47%), respectively. HMI also increased in highest value in 5% minoxidil solution. In the photographic assessment, the number of patients with moderate (+41-70%) to mark improvement (+71-100%) was highest in LLLT treated group (80%), followed by 5% minoxidil (57%), 3% minoxidil (40%), and PRP (36%), respectively.

Conclusion All methods are safe and effective for treating mild to moderate FPHL with no group is significantly better. However, 5% minoxidil appears to be the most effective followed by LLLT, PRP treatment and 3% minoxidil respectively.

RETINOIC ACID ENHANCES MINOXIDIL RESPONSE IN ANDROGENETIC ALOPECIA PATIENTS BY UP-REGULATING FOLLICULAR SULFOTRANSFERASE ENZYMES: A CROSS-SECTIONAL STUDY IN AN INDIAN COHORT

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Introduction Topical minoxidil is the only US FDA approved topical drug for the treatment of androgenetic alopecia. Unfortunately, the clinical response to topical minoxidil remains low, i.e., 30%-40%. Several studies have suggested that combining topical minoxidil with a topical retinoid may increase minoxidil response. The studies primarily rely on work demonstrating enhanced minoxidil absorption, when combined with a retinoid. Several groups proposed that the mechanism of action is via reduction in skin barrier function due to the application of the topical retinoid; however, this explanation is unlikely as retinoids tend to increase dermal thickness. In our previous work, we have demonstrated that the enzymatic activity of the sulfotransferase enzymes in hair follicles predicts minoxidil response. Minoxidil ‘non-responders’ were defined as subjects with an Optical Density (OD) < 0.4 Arbitrary Units (AUs), of follicular outer root sheath (ORS) sulfotransferase.

Methods In this study, we further build on our findings to demonstrate the topical retinoid application up-regulates follicular sulfotransferase enzymes and hence increases minoxidil response.

Results Interestingly, increased follicular sulfonation would likely produce an increase in detectable minoxidil in the blood, as minoxidil sulfate is more water soluble than minoxidil. This would explain previous reports, albeit, would not support the conclusion that retinoids decrease the barrier function of the skin. Of clinical significance, in this cohort of 20 patients, 60% of subjects (n=12) initially predicted to be non-responders (to topical minoxidil were converted to responders following 5 days of topical retinoid application.

Conclusion To our knowledge, this is the first study to elucidate the interaction between topical minoxidil and retinoids and thus provides a pathway for development of future alopecia treatments.
**PHASE II STUDY TO EVALUATE EFFICACY AND SAFETY OF PYRROLIDINYL DIAMINOPYRIMIDINE OXIDE (PDPO) TOPICAL SOLUTION FOR MILD TO MODERATE ANDROGENIC ALOPECIA**

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**Introduction** Androgenic alopecia (AGA) is a multifactorial disorder. Optimal treatment in AGA should target different pathways for synergistic effects. The topical solution, investigated in this study, was formulated with 9 active ingredients-PDPO, Azelaic Acid, Lysophosphatidic acid, Copper tripeptide-1, Myristoyl Pentapeptide-17, Adenosine, Piracetone olamine, Retinol and Caffeine—which have shown individually to stimulate hair growth, reduce scalp inflammation and improve efficacy of minoxidil when used in combination. Nanosomal encapsulation and delivery system, enhances stability, penetration and accumulation of active ingredients in hair follicles. The key novel molecule of this topical solution is PDPO, a potassium channel opener with a molecular structure that is similar to minoxidil but with higher activity on potassium channels and lower molecular weight.

**Methods** Twenty-seven patients (8 women and 19 men) aging 21 to 60 years with hair shedding and moderate hair thinning were included. Exclusion criteria were hair shaft or scalp diseases other than AGA, previous hair transplant and use of minoxidil, finasteride or other hair growth treatments during last 6 months. Participants applied treatment the solution twice a day on clean and dry scalp. Study duration is of 6 months but we present here interim analysis at 3-months for 14 subjects (8 men and 6 women). Total hair count, hair density and terminal hair density (n/cm²) were measured at the beginning and at 3-month using TrichoScan. Target area (~0.9 cm²) on scalp was shaved; after 3 days, hairs were dyed to obtain digital images at 20X. Dermaloscopic analysis of target area was performed to evaluate degree of inflammation. This was evaluated by percentage of scalp showing arborizing vessels and/or scales under 20X magnification: Grade 5 - 100 %, 4 - 75%; 3 - 50%; 2 - 25%; 1 - 25% to 10%; and, 0 - less than 10%. A paired t-test was used to compare TrichoScan data. Inflammation scores were compared using Wilcoxon signed rank test. p value of <0.001 was considered statistically significant.

**Results & Discussion** After 3-month treatment the total target area hair count increased from 193.4±58.06 to 198.18±50.05 and the hair density increased from 214.17±64.27 to 219.39±55.4 per cm². Anagen percentage also increased from 75.22% to 77.15%, while that of telogen hair reduced from 24.78% to 22.85%. Dermaloscopic data revealed very significant improvement in inflammation scores after 3-month of treatment in comparison to baseline (Wilcoxon test α <0.001). Treatment was well-tolerated.

**Conclusion** This interim 3-month data suggest that the treatment improves hair counts and hair density and reduces scalp inflammation. Although a large-scale trial is warranted, this preliminary study provides encouraging results of safety and efficacy of PDPO in the treatment of AGA.
Hair follicles undergo cycles of growth (anagen), regression (catagen), rest (telogen) and re-growth that depend on hair follicle epithelial stem cells (HFSCs) residing in the permanent, bulge region of the follicle. A specialized population of mesenchymal cells, known as the dermal papilla, provides an essential niche for HFSCs. HFSCs also respond to signals from nerves, immune cells, and adipose tissue, allowing them to adapt to changes in their environment. Delin-eating the controls of HFSC function is critical for understanding the basis of hair loss diseases. Research using genetic mouse models has revealed many of these mechanisms. Comparative studies show that regulators involved in murine hair growth control are also expressed in human hair follicles, and mutations in many of these are associated with abnormal hair growth in patients. Thus, the murine hair follicle is an excel-lent model for delineating the basic mechanisms that control activity of HFSCs and their niches. Bulge HFSCs remain dormant though much of adult life, and are normally dedicated to the hair follicle. However, following skin wounding, bulge HFSCs exit their niche and contribute to healing of the epidermis. Mutations that cause loss of HFSC quiescence ultimately lead to HFSC depletion, suggesting that the quiescent state is necessary to retain long-term functionality. A battery of transcription factors, including SOX9, LHX2 and TCF3/4, is required to maintain quiescence. Wnt/β-catenin signaling is a key regula-tor of hair follicle cycling: during telogen TCF3/4 transcription factors directly repress Wnt/β-catenin target genes; towards the end of telogen Wnt signals and BMP inhibitory factors increase in secondary hair germ cells at the base of the bulge, and LEF1/β-catenin complexes displace TCF3/4, activate Wnt targets, and promote sec-ondary hair germ proliferation, resulting in forma-tion of a transient amplifying hair matrix popula-tion. Wnt-activated stem cells contribute to all of the epithelial lineages of the hair follicles, and inhibition of this pathway prevents anagen. Predicted loss of function mutations in human WNT10A are associated with adult-onset defects in hair growth, and a WNT10A variant with lower expression levels is associated in GWAS with androgenetic alopecia. Using genetic mouse models, we found that inducible deletion of epithelial Wnt10a causes reduced Wnt/β-catenin signaling, decreased proliferation of hair follicle progenitor cells, and reduced hair growth. As mutant mice age, their hair follicles retain stem cell populations, but miniaturize and develop enlarged se-baceous glands, similar to hair follicles in balding human scalp. These results identify WNT10A as a critical ligand controlling adult epithelial prolifera-tion and suggest downstream β-catenin pathway activation as a possible approach to ameliorate hair growth defects in patients with WNT10A variant isoforms or mutations.

The secondary hair germ (SHG) - a transitory structure in the lower portion of the mouse telo-gen hair follicle (HF) - is a key player in anagen induction and HF regrowth. Therefore, the in-sight into SHG functions and its ontogenetic rela-tions with other HF parts represents one of the key objectives of hair biology. Yet, many aspects of its functioning remain unclear or a subject of controversy. Thorough analysis of recently acquired data revealed that in contrast to previous bulge-centric views, the SHG is a primary target of papilla-de-rived anagen-inducing signaling and a source of both the outer root sheath (ORS) and ascend-
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ing HF layers during the initial (morphogenetic) anagen sub-phase. Furthermore, the effective separation of the bulge and the FP by SHG, but not bulge/FP intercommunication (as thought before), is the crucial prerequisite for bulge stem cell niche integrity and maintenance of HF cycling pattern. The bulge appears to stay quiescent during initial anagen and serves just as a reserve stem cell population.

The SHG is comprised of two functionally distinct cell populations. Its lower portion (originating from lower HF cells that survived catagen) forms all ascending HF layers, while the upper SHG (formed by bulge-derived cells during catagen-telogen transition) builds up the ORS during the M-anagen phase of the cycle.

The strong predetermination of SHG cells to a specific morphogenetic fate contradicts their attribution to the “stem cell” category and supports SHG designation as a “germinative” or a “founder” cell population. The mechanisms of this predetermination, which drives the transition of the SHG from “refractory” to the “competent” state during the telogen remain poorly defined.

In contrast to mouse SHG, the existence of SHG (or a population of SHG-like cells) in human HF is still questionable. So far, there is neither morphological, nor expressional data providing a sufficient ground for drawing parallels between the mouse SHGs and the putative SHGs in human terminal HFs. Nevertheless, human vellus HFs, being comparable to mouse telogen follicles in size, may form a SHG-like structure.

Considering all of the above, we assume that the formation of SHG in mouse HFs is a prerequisite for efficient “pre-commitment” of these cells and provides for easier sensing and a faster response to anagen-inducing signals. Furthermore, the SHG provides a barrier, which protects the quiescent bulge stem cell niche from the extensive follicular papilla/SHG signaling milieu in a small-size mouse HF. In general, the formation of the SHG represents an evolutionary adaptation, which has allowed the ancestors of modern Muridae to acquire a specific, highly synchronized pattern of hair cycling.

SCARRING ALOPECIAS AS MODEL HUMAN STEM CELL DISEASES: FROM IMMUNE PRIVILEGE COLLAPSE TO EPITHELIAL-MESENCHYMAL TRANSITION (EMT)

Pathobiologically, lymphocytic primary cicatrical alopecias such as lichen planopilaris (LPP) and frontal fibrosing alopecia (FFA) are best viewed as model human stem cell diseases. In these, one can study exemplarily and in situ how adult human epithelial stem cells are physiologically protected from immune attack by the bulge immune privilege, and how they respond to immunologically mediated damage that compromises this immune privilege. While we do not really understand yet what exactly incites and attracts immune-mediated bulge damage (plausible hypotheses are discussed), we do know that bulge stem cells undergo irreversible damage through apoptosis, abnormal proliferation, and/or epithelial-mesenchymal transition (EMT). This leads to irreversible bulge damage through exhaustion of the hair follicle’s stem cell pool (and thereby its regenerative capacity) and contributes to the scarring phenotype. Therefore, these stem cell responses are key targets for therapeutic intervention. On this background, it is discussed why PPARg modulators and therapeutic restoration of the bulge immune privilege are particularly promising approaches in future scarring alopecia management.
MECHANICAL STRETCH INDUCES HAIR REGENERATION THROUGH THE ALTERNATIVE ACTIVATION OF MACROPHAGES

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Introduction Stem cells are fascinating because of their potential in regenerative medicine. The homeostasis of stem cells has been thought to be mainly regulated by signals from their adjacent micro-environment named the stem cell niche. However, more and more studies reveal that there can be multiple layers of environmental controls which allowing stem cells to adapt to a larger changing environment and physiological needs. Our previous work which demonstrated topological hair plucking can induce a ‘quorum sensing’ like efficient regeneration response suggests that mechanical force elicited by plucking may play an important role in regeneration process. In fact, tissues and cells in organism are continuously exposed to a complicated set of mechanical cues from the environment.

Methods Furthermore, mechanical stimulations affect cell proliferation, differentiation, migration, and determine tissue homeostasis as well as repair. By using a specially designed skin-stretching device, we discover hair stem cells activate in response to stretch and hair regeneration occurs only when proper strain and duration were delivered.

Results Counterbalance between WNT and BMP-2 followed by a two-step mechanism was identified through molecular and genetic analyses. Macrophages were first recruited by chemokines elicited by stretch and polarized to M2 phenotype. Growth factors such as hepatocyte growth factor (HGF) and insulin-like growth factor 1 (IGF-1) released by M2 macrophages then activated hair stem cells and facilitate hair regeneration. Collectively, a hierarchical control from mechanics, chemical signals, cell behaviors, to tissue responses was revealed.

Conclusion This novel finding shed new light on regenerative medicine and disease control since one can manipulate cellular processes through simple mechanical stimulation.
Trichoscopy, or hair and scalp dermoscopy, is an important diagnostic tool and for many dermatologists has become an essential part of the dermatological consultation. As a new method, many nomenclatures and new descriptions arise with every new publication. However, trichoscopy is not about memorizing names, but correlating features with our understanding of disease pathogenesis, in order to make a diagnosis. In addition, trichoscopy is only part of a bigger picture: the patient. Correlation with other clinical information is central. In this lecture, important considerations and a few tips to learn how to use trichoscopy will be discussed.

**TRICHOSCOPY WHAT IS IMPORTANT TO KNOW**

The dermoscopic examination of the hair and scalp is known as trichoscopy. This is a very useful technique to differentiate non-scarring from scarring alopecia, diagnose early androgenetic alopecia, distinguish alopecia areata from other patchy alopecia as well as to provide fast diagnosis of tinea capitis. It also allows very rapid diagnosis of hair shaft disorders and permit to select optimal site for biopsy. Trichoscopy is a non invasive technique that does not require expensive instruments and is very well accepted by patients. It definitely improve the quality of care of patients with alopecia and reduce the necessity of taking scalp biopsies.

For scalp examination, dermatologists can use a manual dermoscope (x10 magnification) or a videodermoscope equipped with various lenses (from x20 to x1000 magnification). Dermoscopy findings include vascular patterns, follicular and perifollicular signs and hair shaft characteristics. Examination of the normal scalp can show simple fine red loops that represent capillary loops in the dermal papilla. In dark skinned individuals, a perifollicular pigmented network (honeycomb pattern) is well appreciated.

In scalp psoriasis, within the typical scaly plaques, twisted red loops are observed. Twisted loops are also seen to a limited extent in unaffected psoriatic scalp as well as in newly treated psoriatic scalp. In seborrhoeic dermatitis, arborizing red lines, which have a wider caliber than the loops, can be observed.

In alopecia areata, yellow dots are very characteristic. These dots represent follicular openings filled with keratinous debris mixed with sebum. They are often associated with classic findings of active disease as dystrophic hair, exclamation mark hairs and cadaverized hairs. Dermoscopy findings are important to differentiate alopecia areata from trichotillomania where hairs are broken at different distances from the scalp and longitudinal splitting of hair shafts can also be seen.

Androgenetic alopecia is characterized by hair diameter diversity due to miniaturization of the hair follicles. Variability in hair shafts diameter of more than 20% is diagnostic of this condition.

**HOW TO CHOOSE THE BEST INSTRUMENT FOR YOUR NEEDS?**

Once you have decided that your wish is to dedicate your practice to hair disease patients, you need proper instruments to have a full perspective of the trichoscopic universe. As a principle we should be familiarized with basic trichoscopic structures, because understand-
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ing of trichoscopic signs as a dynamic phe-

nomenon, will enable the clinician to under-

stand the dependency of trichoscopy to the

mechanisms of the disease rather than pathog-

nomonic and unchanging. For this purposes

a hand held dermoscope could be enough to

visualize basic trichoscopic structures. Before

examining with other device is important to
take a first look with the handheld option, in
order to decide which method will be needed
for further visualization. According the diag-
nostic needs increase, the next step could be a
digital dermoscope, those devices permit to vi-

visualize and document at higher definition, also
giving the opportunity to record the images,
allowing you to analyze trichoscopic struc-
tures retrospectively and evaluate treatment
response. Once the pathway of trichologic
practice advance, the requirement of diagnos-
tic details increase, videodermoscopy technol-

ogy allows to visualize from 20 to 140 x, with

the opportunity of a polarized lens for better
visualization of the peripilar cast , or increased
magnification for vascular structures, skipping
the need of a biopsy, helping to diagnose very
early stages of many pathologies. Recently
confocal microscope has proved their valu-
able use in trichology, it allows you to observe
trichology at cellular level, evaluating fibrotic
changes, inflammatory infiltrate, perifollicular
fibrosis, epidermal thickness, loss of dermal
papilla, to the point that you may not need a
biopsy. Also there are other valuable options,
like teletrichoscopy, in this platform the user
can send the pictures taken without shaving
and obtain all the measures either for patient
retro alimentation or for research purposes.
This platform also offers an expert for evalua-
tion of trichoscopic pictures to have accurate
diagnosis in difficult cases. Future trichoscopic
technologies, will allow us to visualize tricho-
copy from a cellular point of view.

TRICHOSCOPY: WHAT’S NEW

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New trichoscopy signs are periodically discov-
ered, and trichoscopy features of different hair
diseases are continuously described, in order to
help the clinician in the diagnosis. Recently described trichoscopy signs include for
example Pohl-Pinkus hair constrictions.

Diseases whose trichoscopy features have been
recently detailed include wholly hair, scalp my-
cosis fungoides, eyebrow signs of alopecia are-
ta and frontal fibrosing alopecia, and other in-
flammatary and infective disorders.
A review of the recent literature will be provided.

TRICHOSCOPY: WHAT I FORESEE
FOR THE FUTURE

Lidia Rudnicka
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Trichoscopy has become an established meth-

od in diagnosing hair and scalp diseases. I see
multiple major fields for the developments of
trichoscopy. First, trichoscopy may be of ma-

jor significance in examining treatment efficacy.
We currently use the benefit of trichoscopy for
monitoring purposes, however clear monitoring
criteria are still missing. Second, trichoscopy has
the potential of serving as a prognostic tool for

hair regrowth and potential treatment efficacy
in hair and scalp diseases. Third, I believe that
trichoscopy should become a sine qua non tool
for clinical trials in hair diseases, and maybe for
validation of cosmetic products, which are de-
signed to improve hair regrowth. Fourth, in ge-
netic hair shaft disorders it should be possible
in future to identify the abnormal function of a
specific gene on the basis of trichoscopy. Fifth,
some diseases beyond hair and scalp, may be suspected on the basis of trichoscopy. In my opinion especially the easy visibility of horizontally located capillaries on the scalp may provide a basis for further research in disorders affecting the smallest blood vessels. In conclusion, In my opinion trichoscopy is a new method with high potential in many clinical applications and areas of research.

**PHYSIOCHEMICAL HAIR ANALYSIS IDENTIFYING TITANIUM IN FRONTAL FIBROSING ALOPECIA**

Frontal fibrosing alopecia (FFA) has increased markedly in incidence over the past 20 years. Daily, year-round use of facial moisturizers and sunscreen has been implicated in good studies. Nanoparticle titanium dioxide, a common ingredient, has significant photocatalytic activity which could result in inflammation, perhaps a precursor to FFA. Zinc dioxide has a lower level of photocatalytic activity. The photocatalytic activity in titanium and zinc dioxide is significant enough that most products use titanium and zinc dioxide that has been coated with a nonreactive chemical. Nanoparticles, having a particle size of only 40 nanometers can enter skin cells, the impact of which on cellular function is unknown.

Hair shafts from 16 women with FFA were plucked from the frontal hairline after the patients were asked to not wear products on the day of sampling. Titanium was identified in all 16 women using scanning electron microscopy with an energy-dispersive X-ray spectroscopy (SEM/EDX). Titanium was also identified on the hair shaft of 3 female control patients who had no evidence of FFA. A single male control with no evidence of FFA who reported no use of facial moisturizer, sunscreen or hair dye was negative.

The identification of titanium in all 16 FFA samples and 3 of the negative controls demonstrates the difficulty of assessing whether titanium dioxide is causative. Assessing the level of exposure (i.e. concentration in products) could be helpful. Likewise, assessing the composition and source of the titanium dioxide, such as nanoparticle size and the presence or absence of an insert coating, may be helpful.

In summary, the findings of this small study demonstrate the ubiquity of titanium dioxide, being found on the hair of patients with and without FFA. It remains unknown whether titanium dioxide is causative of FFA. Perhaps final proof of causation can only come from observing the incidence of the disease falling after removal of suspect ingredients from products.

**OPTICAL COHERENCE TOMOGRAPHY (OCT) IN SCALP DISORDERS**

**Introduction**

OCT is a non-invasive imaging modality using optics to acquire real-time, cross-sectional and en face images of tissue up to 2 mm below the skin surface, allowing visualization of scalp architecture. Dynamic OCT (D-OCT) can capture blood vessels and their distribution. Also, blood flow may be calculated.

**Objective**

To describe the structural and vascular findings in normal scalp and different scalp disorders using D-OCT.

**Methods**

This was an observational study aimed to evaluate the characteristic features in the normal
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scalp and scalp disorders in D-OCT. Psoriasis, lupus erythematosus, contact dermatitis, seborrheic dermatitis and frontal fibrosing alopecia were evaluated.

Results
Normal scalp vessels have an interfollicular granular pattern, more intense at deeper plexus. In Psoriasis, superficial plexus showed spindle like scattered vascular dilations, more evident at deeper levels and on cross-sectional view (CSV) spiral network of vessels at dermal papilla. Seborrheic dermatitis showed a network of arborizing vessels, more dilated and ramified at deeper levels. Contact dermatitis has a dilated network of vessels at deeper levels and a diffuse pattern of enlarged vessels present along all dermis on CSV.
In Lupus at the inflammatory areas with alopecia, were almost absent on the superficial plexus and at deeper levels giant dilated serpiginous capillaries. On CSV, showed clusters of capillaries around the hairs, while in cicatrical areas dilated vessels were prominent and distributed homogenously. Frontal Fibrosing alopecia presents with increased epidermal thickness in inflammatory and decreased in cicatrical skin. In the initial inflammatory stages, collagen distribution is irregular and in advanced cicatrical stages, a concentric hyperreflectant “onion shape” pattern is observed. Inflammatory tissue is consistently more vascular at all levels. Vascular flow in the superficial levels in cicatrical skin is decreased compared to inflammatory and normal skin, but increased at deeper levels. Vessels in the deeper plexus form a perifollicular “crown-like” pattern and presence of perforating vasculature communicates both the superficial an deep plexus.

Conclusion.
OCT is a powerful non-invasive tool in the diagnosis and follow-up of patients with scalp disorders.

REFLECTANCE CONFOCAL MICROSCOPY IN HAIR DISORDERS

Clinical management of alopecia represents one of the major issues in dermatology. Management of scarring and non-scarring alopecia can be challenging for the esthetical and social implications derived from hair loss. A prompt diagnosis, even better if supported by histopathology examination, is highly recommended for an early and adequate treatment to avoid irreversible hair loss. However, scalp biopsies are not easily accepted because of the high bleeding and sensitive anatomical area. Furthermore, samples are often too shallow because deeper incisions cause profuse bleeding due to high vascularization of the scalp. For these reasons non-invasive imaging is an excellent alternative for early diagnosis and further management of alopecia.
Dermoscopic examination of hair and scalp, also named “trichoscopy,” is routinely used for diagnosis of alopecia and is currently considered as an essential tool for the diagnosis and management of hair and scalp diseases providing proved advantages compared to clinical examination with the naked eye. The success of this non-invasive method is related to the reduction of the needing of skin biopsies. Nevertheless in several cases thrichoscopy lack to provide sufficient information on the status of the disease. In vivo reflectance confocal microscopy (RCM) offers to clinicians the possibility of a real-time, non-invasive microscopic examination of the tissue that has been widely reported for the assessment of neoplastic and inflammatory skin diseases. Outlines of cells and their architecture are imaged and may be analyzed both horizon-tally and vertically to the skin surface. Recently, RCM demonstrated its usefulness for the evaluation of several inflammatory skin condition and preliminary reports about alopecia have been proposed in the literature. Infact RCM is able to study the hair follicle structure and the perifollicular area as well as the hair shaft. Is useful for the diagnosis, together with tricoscopy, and also to monitoring hair diseases activity during treatment.
TRICHOSCOPIC DYNAMIC REFLECTANCE MICROSCOPY IN ATRICHA WITH PAPULAR LESIONS

Background Atrichia with papules is an uncommon autosomal recessive disease characterized by hair loss after birth with scarring alopecia and the presence of keratin cysts over the body appearing around the age of 2 years; without hearing, teeth and nails involvement. The complete pathogenesis is unclear, but some authors associated it with a mutation of the human hairless gene located on chromosome 8p21.2, which encodes zinc-finger transcription factor protein that may regulate the catagen remodeling in hair cycle. Some authors proposed criteria for the diagnosis includes: family history, physical examination, and skin biopsy showing few vellus follicles in the mid-dermis, with absence of terminal hairs, cyst filled with cornified material and the lack of therapeutic response.

Objectives Correlate the findings of reflectance confocal microscopy with the known histology of atrichia with papules.

Methods Descriptive, and observational study. Patients with previous diagnosis of atrichia with papules were submitted for scalp high definition trichoscopy, which was followed by Reflectance Confocal Microscopy examination of the same areas, with the use of Vivascope 3000.

Results Two patients were included, 1 male and 1 female, with previous diagnosis of atrichia with papules. We found in the scanning of the scalp with in vivo reflectance microscopy, disarranged pattern of the honeycomb, mild spongiosis, and the presence of inflammatory cells in the epidermis; no edge no ringed papilas, sparse perifollicular infiltrate and number of follicles were reduced; with follicular cysts surrounded by fibrosis and diffuse fibrotic changes.

Comment It is interesting to mention that in the transition areas were one of the patients still has hair, we observed owl eyes like cystic structures, which are probably remnants of the previous fusion of the connective tissue sheaths of 2 adjacent follicles during the degenerating process of hair int his patients.

Conclusion Reflectance confocal microscopy may be useful un patients with atrichia with papules.

A VALIDATED TRICHOSCOPIC ACTIVITY SCALE FOR FOLLICULITIS DECALVANS

Introduction & Objectives Folliculitis decalvans (FD) is a cicatricial alopecia with inflammatory flare-ups and progressive destruction of the hair follicles. Early detection is essential to start prompt treatment and stop hair loss. The aim of the study is to design an activity scale for FD based on trichoscopy.

Material & Methods A cross-sectional multicentric study was designed. Patients were enrolled in the first consultation and follow-up visits. Clinical information was taken by anamnesis, physical examination and trichoscopy. Dry trichoscopy was performed using either FotoFinder medicam 1000® or Heine iC1® attached to an iPhone 7. Immersion fluid was used to evaluate vascular findings. Clinicians provided a subjective evaluation of the activity with the Investigator General Assessment (IGA) index from 1 to 10 (1-3: severe inflammation, 4-5: moderate inflammation, 6-7: mild inflammation, 8-10: complete remission). Recruitment of data...
from consecutive visits was encouraged. Three dermatologists (DSC, RRB, OMMA) evaluated trichoscopy images independently. All analyses were performed using SPSS 21.0 statistical software package (IBM SPSS Statistics for Macintosh, Version 21.0, released 2012; IBM Corp., Armonk, NY, USA). To describe categorical variables frequency and percentage were used, and significant relationship between them was determined with the chi2 test. Those trichoscopy findings associated with the activity of the disease were assessed by the Spearman Rho test to find the grade of correlation. All tests were 2-sided and statistical significance was considered with P < 0.05.

**Results** A total 193 lesions from 38 patients (26 female, 12 male) were retrieved. Mean time of the disease was 5 years. Data from consecutive visits was obtained from 15 patients (40%). Previous medical treatment was topical steroids (36, 94.7%), triamcinolone injections (25, 65.8%) and oral antibiotics (31, 81.6%). The trichoscopic findings associated with disease activity were extent perifollicular erythema (14.8%, -0.19, P=0.003), perifollicular pustules (36.3%, -0.47, P=0.000), perifollicular hemorrhage (17.6%, -0.22, P=0.000), yellow tubular scaling (28.6%, -0.29, P=0.000), yellow crusts (27.5%, -0.27, P=0.003), yellow interfollicular scales (12.7%, -0.20, P=0.003) and thin arborizing vessels (21.4%, +0.20, P=0.003; the only one as positive prognostic factor). According to the statistical analysis we assigned a score to each trichoscopic feature (+2 points: perifollicular pustules; +1 point: yellowish structures - yellow tubular scaling, crusts and interfollicular scales - and red structures - perifollicular erythema and hemorrhages; - 1 point: thin arborizing vessels). The scale showed significant correlation to the clinical assessment of disease activity and passed the internal and external validation process.

**Conclusion** We designed and validated a trichoscopic activity scale for FD that can be used in clinical practice and future research.

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**PSORIASIFORM ECZEMA-LIKE AND HAIR LOSS IN WOMEN UNDERGOING STRAIGHTEN HAIR: CLINICAL AND DERMOSCOPIC FINDINGS OF 13 CASES**

**Introduction & Objectives** Different treatments for straight hair are available in the market, most of them contain formaldehyde or derivatives. Also known as Brazilian Keratin Treatment (BKT), they have been reported as unsafe due to the potential risk of skin reactions with eczema-like lesions days after BKT. Our objective is to communicate the clinical and dermoscopic findings of patients who presented symptoms related to the BKT straightening.

**Material & Methods** A retrospective study was conducted, using the clinical files of “Centro de Restauración Capilar”. We included patients of any gender and age who had consulted by hair loss and worsening, or onset of eczema-like psoriasiform on the scalp and have a history of straightening treatment hair. Hair loss evolution, time since last BKT, number of treatments, erythema and scales on clinical evaluation were recorded and pull test was performed. The dermoscopic patterns using light polarized (Dermlite DL3N) are described. Descriptive and inferential statistics was used for data analysis.

**Results** We found 13 patients female, median age were 32 years (range 20 to 61 years), the median evolution time of symptoms was 12 months (range 2 to 48 months). All received at least one treatment for hair straightening (range 1 to 4), the median time between the last treatment of BKT and the onset of symptoms was 12 months (range 4 to 60 months). The symptoms included scales on 13 (100%), erythema on 7 (53.8%) and pull test positive on 11 (84.6%). We do not found relationship between positive pull test and time of evolution <6 months (75%) vs. >6 months (87.5%, p > 0.05, Fisher’s exact test). Dermoscopic patterns were as follows: red dots and globules 4 (30.8%), twisted red loops
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4 (30.8%), glomerular vessels 3 (23.1%), arborizing 5 (38.5%), atypical vessels 7 (53.8%) and red patches 11 (84.6%).

Discussion Eczema-Like Psoriasiform Skin Reaction occurring days after BKT was first described in 2016 by Gavazzone et al, in Brazil. Our patients did not presented skin reactions days after the BKT, but worried about hair loss months after and scaly or seborrheic scalp that worsen or started after the first BKT. We found positive pull test, scales and red patches on most patients; as well as dermoscopic patterns described for psoriasis (red dots and globules, twisted red loops and glomerular vessels); and for seborrheic dermatitis (arborizing and atypical vessels). We hypothesize that there is a relation between BKT, chronic eczema on scalp, and hair loss. Skin biopsies were not performed in any of our patients, representing a limitation of the study.

Conclusions We consider important that physicians become familiar with the clinical and dermoscopic features of these patients, especially on the background of straightening with BKT, and advice about this entity to patients.
THE MULTIPLE FACES OF CUTANEOUS MELANOCYTES - HARLEQUINS AND CHAMELEONS

As social beings, humans communicate significantly via our physical appearance, with skin and hair color contributing disproportionately. Brown-black (or eumelanic) pigmentation type is the default human skin and hair coloration, and this environmentally-friendly pigment type predominates in >90% of the world’s human population. The remaining 10% of the world’s population (mostly those with a north-western Europe geographic origin) exhibit cutaneous pigmentation genotypes/phenotypes that provide for an array of colors often with strong pheomelanin contribution. For hair these range from white blonde, yellow blonde, auburn to red, to dark brown and raven black, while for skin pale white, pinkish, freckled, to olive and cafe-au-lait colors. It is the latter branch of the global human family that appears less well-adapted to solar irradiation on planet earth, as pigmentation lesions including melanoma feature disproportionately. The power laboratory mouse genetics has appealed to the researcher community and as their preferred vehicle has driven much of our current understanding of human pigmentation. This is rather paradoxical however as most human ‘skin’ pigmentation knowledge derives from the intensive study of mouse ‘hair’ color. We are reminded however, that functional epidermal-melanin units and follicular-melanin units each co-exist anatomically in human skin, while mouse pelage epidermis strikingly lacks functional melanocytes. It is also striking that the principle melanogenic enzymes show important regional variations in regulation and function in human haired skin. For example, the expression and activities of both dopachrome tautomerase (DCT) and tyrosinase-related protein 1 (TRP1) show distinct regional variations in skin versus hair follicle melanocytes in humans, and against between human and mouse skin. We are learning more also about other cutaneous melanocyte populations for example in the sebaceous gland, the eccrine gland (at least in human volar skin), and of course in the dermis where these may be the forerunners of nevi or even melanomas. Thus, a greater understanding of the life histories of the cutaneous melanocyte(s) will be important for discovery of cellular and molecular pathways that underpin pigmentation defects in human aging and disease.

ROLE OF SENESCENCE DURING HAIR GREYING

Hair pigmentation is a complex process tightly regulated by the signaling within the melanocyte stem cell niche. The hair follicle stem cell niche is the only described source for melanocyte stem cells within the skin. Melanocyte stem cells are located within the bulge and ORS hair follicle compartments, and they are mostly undifferentiated and amelanotic. Whereas the mature melanocytes, producing and transferring pigment to hair shaft-differentiating keratinocytes, are located at the bulb of the hair follicle. Patients suffering from premature ageing syndromes such as Werner syndrome or Hutchinson-Gilford Progeria exhibit premature hair greying. Thus, here we study a possible role of premature senescence during hair greying. We have analyzed hair scalp biopsies, from donors undergoing different stages of hair greying, finding 1) accumulation of senescent cells and 2) loss of self-renewal and ectopic pigmentation at the hair follicle melanocyte stem cell compartment. To study the mechanistic link between senescence and pigmentation, we have developed an in vitro melanocyte-keratinocyte co-culture model in which we can conditionally induce senescence. Our preliminary data reflects that senescent co-cultures upregulated both melanogenesis and pigment transfer in our human in vitro model.
Hair pigmentation/Hair graying

Identifying the mechanisms resulting in hair depigmentation during ageing will allow for the development of translational programs targeting pathways and molecules with large therapeutic and commercial interest.

UNDER-INVESTIGATED MAJOR REGULATORS OF THE HUMAN HAIR FOLLICLE PIGMENTARY UNIT

Even though differentiated, melanogenically active epidermal and hair follicle melanocytes represent quite distinct cell populations, it is often erroneously assumed that the controls of epidermal and hair follicle pigmentation follow the same principles. Here, we first delineate controls of melanin synthesis and other activities that the melanocytes of the human hair follicle pigmen-
tary unit share with epidermal melanocytes, and then emphasize distinct controls. We highlight the importance of under-investigated, “non-conventional” controls such as CRH, β-endorphin, TRH, P-cadherin-mediated signaling and peripheral clock gene activity, also in the context of disorders of hair follicle pigmentation and as future targets for therapeutic intervention.

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A BIOMIMETIC PEPTIDE USE TO COUNTERACT THE APPEARANCE OF GREY HAIR

Introduction & Objectives Hair greying (i.e., canities) is an inherent component of chronological aging and occurs regardless of gender or ethnicity. Premature canities and progressive loss of hair pigmentation are phenomenon directly linked to a melanin lack in the hair bulb as well as an increase in oxidative stress in the hair follicle and shaft. To promote hair pigmentation and counteract the hair greying process, an α-MSH biomimetic peptide (palmitoyl tetrapeptide-20; PTP20) was developed. The aim of this study was to describe the effects of PTP-20 on hair greying.

Materials & Methods The anti-oxidant potential of the peptide, its effects on the catalase activity and on the production of H2O2 by HFDP cells were evaluated. Moreover, its influence on the melanogenesis process was documented through its actions on the expression of melanocortin receptor-1 (MC1-R) in transfected HEK cells, the production of melanin in NHEM cells. Additionally, SIRT1 activity in tubo, and ex vivo hair repigmentation of microdissected human hair follicles were also performed. All these investigations were confirmed by a clinical study on 15 human male volunteers suffering from premature canities (> 20% of white hairs). Hair color changes upon treatment for 3 months with PTP20 was evaluated by chromametry and photography.

Results In tubo, PTP20 stimulated catalase activity by +7.5% over control and decreased by -30% the intracellular level of H2O2 in follicle cells. In transfected HEK cells maximum activation (+137%) of the MC1-R receptor was obtained with 10 μM of the peptide. PTP20 also stimulated melanin synthesis by +19% in melanocytes and increased SIRT1 activity by +16% in tubo. Ex vivo, the peptide stimulated hair repigmentation by +66% over control. In fact, an increase in the production of melanin was shown to be correlated with elevated expression of MC1-R, the regulation of SIRT1 and the decrease in the oxidative stress in the hair follicle. These data were confirmed clinically. Indeed, the daily application of a lotion containing 10 ppm of the biomimetic peptide for 3 months resulted in a significant decrease in brightness L* factor by 5.3% compared to the based level. Interestingly, this finding stays in line with the decrease in the density of white hair (30%) after 3 months of peptide application.

Conclusions The current findings demonstrate the effectiveness of a biomimetic peptide to preserve the function of follicular melanocytes. These results suggest potential cosmetic application of this newly designed analog of α-MSH to promote hair repigmentation and counteract the hair greying process.

DEVELOPMENT OF A MODEL OF AGED DERMAL PAPILLA CELLS FOR THE STUDY OF MIRNAS ASSOCIATED WITH HAIR AGING

Introduction & Objectives The hair follicle is a mini-organ which grows in a cyclic pattern during the whole life. With age, this hair cycle becomes altered, hair is thinner, more fragile and it grows slower. These alterations are due to many internal and external factors that contribute to the change of expression level of several markers and leading to cell senescence. To study the hair aging process, we performed a bioinformatic analysis associated with a thorough bibliographic research, to identify potential microRNAs related to this phenomenon. The
microRNAs, regulators of the major cellular and physiological processes are poorly described in human hair physiology. MicroRNAs are about 20-25 nucleotides and target-specific mRNAs inducing their degradation or inhibiting their translation into proteins. After this combined research, we highlighted the predictive involvement of a microRNA (miR-ac) in human hair cycle and in skin aging.

**Methods** Then, we developed *in vitro* models with induced aging in human dermal papilla cell cultures by chemical treatment or siRNA silencing. Dermal papilla cells are a good support to study hair cycle; indeed, they belong to the compartment that controls the entrance and the duration of the growth phase of the hair cycle. Using a model of aged dermal papilla cells, miR-ac level was evaluated in cells to determine its implication in hair aging. Moreover, we assessed the senescent state of the cells by evaluating the mRNA level of p21 and SA-beta-galactosidase activity.

**Results** The study showed that miR-ac level was increased in aged dermal papilla cells. The senescent state of the treated cells was also confirmed using the SA-beta-galactosidase staining and p21 mRNA level evaluation by qPCR.

**Conclusion** The bioinformatics and bibliographic analysis allowed us to identify potential microRNAs involved in hair aging. This microRNA prediction studied *in vitro* in aged dermal papilla cells demonstrated for the first time the correlation between the increase of miR-ac level and hair aging.

**AN EQTL IN SYNTAXIN17 (STX17) LEADS TO DISRUPTED MELANOGENESIS IN ALOPECIA AREATA**

**Introduction & Objectives** Previous observations in the field together with our work in antigen discovery led to the hypothesis that HF melanocyte-specific antigens play a key role in AA disease onset. Recently, several essential autophagy proteins were shown to have pleiotropic roles in the regulation of melanin production and melanosomal formation in the melanogenesis pathway. Our previous GWAS and meta-analysis uncovered two AA risk genes, STX17 and BIM, which play a role in autophagy. STX17 is involved in hair pigmentation of Lipizzaner horses, in which an intronic mutation in a MITF binding site in STX17 leads to the premature loss of pigmentation. In order to investigate the role of STX17 in AA, we found that STX17 exhibits a 1.5-fold reduction in expression in AA patient skin compared to unaffected controls. Moreover, we identified the most significantly associated SNP in the STX17 region, rs10760706, as a potential eQTL due to the finding that individuals with risk allele C expressed significantly reduced levels of STX17 (P=0.0152).

**Comment** Follow-up genome analysis replicated the finding of significant enrichment of rs10760706 C allele frequency in 36% AA cases compared to 21% in controls (P=1.75E-30). Functional studies revealed that not only is STX17 expressed in hair follicle melanocytes, but also that the subcellular localization of STX17 changes in response to melanogenesis stimulation, during which STX17 appears to migrate distally towards the dendritic tips. Furthermore, in the absence of STX17, melanocytes showed aberrant perinuclear localization. Knockdown of STX17 led to inhibition of melanin production and accumulation of the melanosomal markers, MART1 and Tyrosinase, two melanosomal membrane antigens capable of eliciting T-cell responses in human patients with vitiligo and AA.

**Conclusion** Take together, our findings suggest that STX17 plays a role in melanogenesis and that disruption of this pathway may increase immune activation, serving as a catalyst for AA autoimmune attack on the HF in genetically susceptible individuals.
**ADHERENCE TO TREATMENT FURTHER ENHANCES EFFECTIVENESS OF A NUTRACEUTICAL FOR TELOGEN EFFLUVIUM**

**Introduction & Objectives** Telogen effluvium is the most common cause of hair loss in women. Knowing that nutrition plays a determinant role, supplementation with nutraceuticals is widely recommended in order to cover possible nutritional deficiencies, preventing hair loss and enhancing hair recovery.

One of the objectives of this study was to determine the effect of adherence on the effectiveness of a food supplement in participants with Telogen Effluvium.

**Methods** The therapy consisted in an intensive treatment with Pilopeptan®Intensive sachets during one month followed by a maintenance treatment with Pilopeptan®Woman tablets for 3 months.

**Results** A total of 160 women were included in the study, with a mean (SD) age of 45.5 (18.81), and a BMI (SD) of 23.56 (3.8). An 88.8% of patients showed Fitzpatrick phototypes II and III and 20.6% showed nail damage. Significant improvements were observed after 1 month in hair density (p < 0.001), hair shine (p < 0.001), and nail involvement (p < 0.003). All variables analyzed (anagen phase, telogen phase, anagen/telogen ratio, hair density, hair shine and nail involvement) significantly improved (p < 0.01) from baseline to final visit (at 16 weeks). These changes had effect sizes from Cohen’s d = 0.51 (hair density) to d=2.37 (anagen phase improvement). When effectiveness analyses were adjusted by adherence, compliant patients showed a higher improvement in all analyzed variables, with Odds Ratios of 4.87 for anagen phase improvement, 3.28 for telogen phase reduction, 4.5 for anagen/telogen ratio, 1.6 for hair density, 4.8 for hair shine and 3 for nail involvement.

**Conclusions** The use of the combined treatment of Pilopeptan®Intensive and Pilopeptan®Woman showed a significant improvement in all measured parameters with effect sizes considered large to very large.

**HAIR LOSS PATTERNS IN WOMEN WITH TELOGEN EFFLUVIUM**

**Introduction** Telogen Effluvium is a non-scarring type of hair loss that is caused by physical, emotional stress and drugs. Physical stress includes: systemic lupus erythematosus, severe infections, HIV disease, thyroid disease, anemia, cancer, dermatomyositis, chronic renal failure and Vitamin D deficiency. Drugs which can cause TE include the following: isotretinoin, acitretin, discontinuation of contraceptives, paroxetine, lamotrigine, lithium, valproic acid, phenytoin, carbamazepine, terbinafime, omeprazole, amitriptyline, heparin, dopamine, alpha 2b interferon, beta blockers (propranolol, propylthiouracil), methimazole among others. Both males and females can be affected, although females are most commonly affected, at any age. Is reported worldwide, it represents from 7% to 84% percent of the hair loss consults.

To date, there are no specific clinical patterns of Telogen Effluvium reported in the literature. It is a controversial subject among published articles. Some authors have stated that is a diffuse type of hair loss and some authors reported that it has non- specific features. Telogen Effluvium patients could loose up to three hundred hairs per day. Also patients complain of having trichodynia. In Dermoscopy, it has been reported only short regrowing hairs, it does not show any specific features. All hairs have the same hair diameters. Scalp skin is normal.
Histology indicates a normal total number of hairs, a normal number of terminal hairs, an increase in the telogen count to >20% (>15% is suggestive), and an absence of inflammation and scarring.

Methods We evaluated one hundred female patients; clinical history and a physical exam were performed; also macro and microphotographs were taken. Also, professional art work was created in order to make it easier to identify these three clinical patterns.

Results We observed three specific clinical patterns of Telogen Effluvium.

Conclusions Identification of these different hair patterns will allow us to diagnose more easily our patients and to give them multidisciplinary treatment.

REVIEW OF MEDICATIONS IMPLICATED IN TELOGEN EFFLUVIIUM

Introduction & Objectives Telogen effluvium (TE) is a type of nonscarring alopecia characterized by diffuse shedding of telogen hairs approximately three to four months after an inciting event. A number of potential triggers for TE have been identified, including but not limited to febrile illnesses, nutritional deficiencies, and extreme physical or emotional stress, such as loss of a loved one or a major surgery. Certain drugs and medications-oral retinoids, oral contraceptives, beta blockers, and selective serotonin reuptake inhibitors (SSRI)- have also been implicated as potential TE triggers. However, our understanding of the frequency and classification of medications that induce TE is limited. In this review, we aim to better understand the prevalence of TE secondary to medications.

Materials & Methods A retrospective review of new patient intake forms from a specialty alopecia clinic was performed. Data was collected between August 2016 and December 2018. Intake forms included questions regarding potential triggers for TE, such as recent pregnancy, illness, hospitalizations and surgeries, substantial weight loss, new medications, and emotional stress. This study was conducted under Institutional Review Board approval.

Results Of 1019 patients, 24% were given a diagnosis of TE. In 12% of cases, TE was attributed to a medication. Patients in this subset were almost exclusively female (93%) and Caucasian (79%) with a mean age of 40 years old. The highest percentage of TE attributed to a medication was associated with the starting, discontinuing, or switching of an oral contraceptive pill (OCP) (38%), followed by selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors (SNRI) (24%). Changes to thyroid medication dosing or formulation and chemotherapy medications were also noted in a few cases.

Conclusion This study highlights the frequency of medications as a trigger for TE in our patient population. Medications were implicated in 12% of TE cases, highlighting the importance of collecting a detailed history of potential TE causes. As 38% of patients in this study experienced TE after starting, discontinuing, or switching an OCP, educating patients about this possibility is recommended to prevent undue patient concern regarding this self-limiting form of hair loss.
VITAMIN D LEVELS IN MEXICAN PATIENTS WITH TELogen EFFLUVIUM: CASE SERIES

Introduction & Objectives Telogen effluvium (TE) is one of the leading causes of diffuse hair loss and it is classified within the group of non-scarring alopecia. It could be triggered by physical or emotional stress, diseases or drugs, and recently has been associated with vitamin D deficiency, because is well known role in maintaining the hair follicle cycle. However, the results in this respect are scarce and controversial, and we found no reports in Mexican patients. For this reason, the aim of the study was to evaluate the vitamin D levels in patients with TE and if this is related to the severity of the condition.

Material & Methods A retrospective study was conducted. The source of information were the files of “Centro de Restauración Capilar”. Included patients were all born in Mexico, 18 years of age or older, of either sex, with a clinical diagnosis of TE acute or chronic. Patients with history of nutritional diseases, autoimmune or metabolic disease were ruled out. Vitamin D serum levels were measured by chemiluminescence method and divided into two groups: normal (>30ng/ml) and abnormal (<30ng/ml). The activity of disease was evaluated with pull test, which was considered positive when >10% of hair taken falls. For the analysis of the data we use descriptive and inferential statistics.

Results A total of 43 patients were included, 42 women (98%) and 1 man (2%), the mean age of the population was 46 + 15 years-old. The pull test was positive in 33 (77%) cases. The mean level of vitamin D was 26.6 + 14.2ng/ml (range 7.6 to 70ng/ml). Decreased levels of vitamin D were found in 31 (72%) and normal only in 12 (28%) patients. Of the 33 patients with pull test positive, 24 (73%) had decreased serum levels of vitamin D, meanwhile in the group of 9 patients with negative pull test we found low levels in 6 (66%) patients (p = 0.69, Fisher’s exact test).

Conclusions A high proportion of patients with TE showed low levels of vitamin D. This finding is important because it could be decisive in the treatment that patients should receive. However, the pull test was not significantly related in patients with low values. To our knowledge this is the first report in Mexican population regarding vitamin D levels in TE. Studies with a larger number of patients and control group is needed in order to corroborate our results.
THE LATEST HAIR TRANSPLANT SURGERY RESEARCH

Introduction
The hair loss diagnosis, prognosis and the capacity of the donor area can be evaluated by using the multifactorial classification and the digital phototrichogram. Combining procedures of hair restoration should be tailored to the individual’s needs and the wideness of each alopecia.

Objective
Combining the strip follicular unit long hair transplants (FUL long hair) and follicular unit extraction manual FUE or automatic FUE or robotic FUE are all good methods for the correction of various alopecia.

Materials & methods
With the multifactorial classification, the digital phototrichogram (trichoscale®) and the digital trichoscopy (Tricholab®): various parameters are evaluated and allow to predict precisely the evolution of the alopecia and calculate the remaining capacity of the donor area for the future.

Schematically 6 procedures of hair transplantation can be selected:
- The Follicular Unit Long Hair (FUL)
- or follicular unit transplantation (FUT): the scalp is not previously shaved. Long hairs grafts are harvested with a strip of 30 cms x 1,5 cm, followed by a closure leading to an undetectable linear scar. Usually 4000-5000 hairs are implanted in one session. For the surgeon, it is easier to find the best angle and orientation and choose each hair according to their calibers and colors.
- The Follicular Unit Extraction (FUE): the scalp is previously shaved or unshaved. Hairs are harvested manually 0,7 to 0,9 mm punchs. 2000-4000 hairs are implanted in one session according to the donor area density.
- The automatic Safer® FUE
- The robotic Artas® FUE
- The choï implanter

Results
Patterned hair loss is the most common male or female alopecia complaint. Each hair transplant procedure is selected according to the hair and scalp parameters such as caliber, density, shape, colour, the age, the ethnic specificity, the baldness evolution and the esthetic wishes.

The other indications are cicatricial alopecia (burns, post-radiotherapy), eyebrows, beard and moustache.

Conclusion
The modern methods of hair transplantation known as the strip technique (FUT or FUL) and the follicular unit extraction (FUE) manual, automatic or robotic have been refined. This kind of treatments is now a good solution for an aesthetic and definitive correction of various alopecia. The goal for each surgeon is to select precisely one or several hair transplant procedures for each patient.

SCALP HAIR RECONSTRUCTION BY PARTIAL LONGITUDINAL FOLLICULAR UNIT TRANSPLANTATION (PL-FUT) IN SCARRED TISSUE

Introduction
We use human follicular stem cells to implant in cicatricial alopecia in order promote hair growth. In each scenario we need to make a plan with the patient to outline the steps and mark the areas which needs the most attention. In complex cases preferably together with a specialised surgeon from a burn unit. We aim to reconstruct nature as closely as possible in order to avoid the need of artificial hair or tattooing.

Method
The donor site preferably needs to be a non-scarring high density zone on the scalp. Especially in men we need to consider the risk of (future) Androgenetic Alopecia (AGA). PL-FUT is preferred because of its minimum invasive character to harvest follicular units out of a do-
nor site. Partial regeneration in the donor site is expected. Recipient area is marked based on the following parameters: number of grafts, clients goals for the result, aesthetic rules and potential amount of treatments. The recipient area is prepared with a curved needle, this determines the direction of the hair growth. Grafts are immediately implanted.

Results One week after PL-FUT, we see that the superficial healing process is in an advanced stage. After nine months, the final result is established. We see hairs of various lengths. The recipient area seems more flexible and sometimes better perfused then before PL-FUT. Hairs are growing in the implanted direction and sometimes seems a bit coarse. Donor area shows no visible scars, has regenerated and ready for a desirable next treatment.

Discussion Despite the fact that initially there is no hair growth on the scars, it is possible to initiate this through implantation of autologous follicular stem cells. Further attention should be paid at how to get density as high as possible. In case of a limited donor area we noticed a limitation in possibilities. Collaboration with surgeons in a burn units is essential in order to get the best possible result in complex cases.

Conclusion We have shown that hair growth is possible in cicatricial alopecia. Even features of the scar changed after treatment with PL-FUT, for example perfusion improved. Features of the implanted hairs were similar to those in the donor site.

HAIR TRANSPLANTATION AND STROMAL VASCULAR FRACTION

Introduction In recent years there is an increasing need for hair regrowth both in Ukraine and globally. Various methods have been used from massage, mesotherapy to hair transplantation and stem cells therapy. The last two methods have proven to be the most effective. Stromal vascular fraction (SVF) cells have the ability to self-renew, proliferating, form one stem, and one specialized body cells. Stem cells have enormous regenerative potential. A well-known source for obtaining them from an adult is red bone marrow. However, obtaining postnatal stem cells from the red bone marrow is associated with certain difficulties. Therefore, the search for alternative sources is relevant.

Methods Our center provides SVF adipose tissue method to improve hair growth. The content of MSC in adipose tissue of a person is 8 more than in the bone marrow. (Zuk, 2001, Yamamoto, 2007, Bieback, 2008, Fraser, 2008, Bailey, 2010). The content of MSCs in 4x micrographs (follicular compounds) is 90,000-140,000 cells (L.Trovato, J. Cell. Physiol, 230: 2299-2303, 2015.) To obtain SVF concentrate of adipose tissue, we performed aspiration of adipose tissue, de-struction, and double purification. The resulting preparation was injected into the region of the scalp by microinjection. To get hair growth gain it is necessary to carry out from 3 to 6 sessions. To obtain SVF of follicular compounds, micrografts were removed with a punch-knife with a diameter of 2.5 mm, and the material was processed using the Regenera method. The administration of the obtained preparation was carried out by microinjections in the area of the scalp. Also, to improve the quality of the skin and hair growth in the scalp area, the method of autolipographing with PRP, nano-lipographing and lipographing enriched SVF (Kersystem) is used. We use seamless method of hair transplantation.

Conclusion Each presented method is aimed at improving the quality of hair growth. The main component is the content and active regenerative property of SVF cells. But, as before, hair growth in zones of baldness can only be restored by performing hair transplantation. According to our observations SVF is recommended for those patients whose hair thinning corresponds to 1st, 2nd and initial 3rd degree of baldness according to Norwood-Hamilton and...
COMBINING AUTOLOGOUS MICRO-GRRAFTING & PLATELET RICH PLASMA WITH HAIR TRANSPLANTATION FOR THE TREATMENT OF FEMALE PATTERN HAIR LOSS

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Introduction Female pattern hair loss is an ongoing process. Genetic hair loss in females is usually more complex than in males. The number of FDA approved treatments for female pattern hair loss are limited and come with side effects. The other issue is patient compliance with these treatments. Also, many females have hair miniaturization involving the donor area, limiting the option of having a hair transplant surgery. With that, comes the importance of treating the pre-existing hair with adjuvant treatments, which are safe and effective for patients with female pattern hair loss seeking hair transplantation.

Objective To outline an approach to treating female pattern hair loss using autologous micro-grafting and platelet-rich plasma for patients seeking hair transplantation.

Methods To discuss the importance of patient assessment in the treatment of females seeking hair transplantation. I will also discuss my approach using the combination of autologous dermis micro-grafting and platelet-rich plasma during the 6 months before and after hair restoration surgery.

Results/Discussion Combining non-surgical therapies before hair transplantation improves the final outcome and could eliminate the need to perform hair restoration in some females with female pattern hair loss by treating the pre-existing hair. This combination treatment is highly safe and effective for the treatment of female pattern hair loss.

Conclusion As hair loss in females is more complex than in males, a combination of treatments should be used to treat female pattern hair loss in order to provide a synergetic effect. Combining therapies before and after hair restoration will improve the final treatment outcome and increase patient satisfaction. It could also eliminate the need of hair transplantation in many cases.

FOLLICULAR UNIT EXCISION-WHERE WE ARE TODAY

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Background The fastest growing technique in hair restoration is follicular unit excision (FUE), due both to its main advantages (avoidance of a linear donor site scar, need for few technicians, obtaining natural result, less recovery time) and the marketing of newly available devices for assisting with the harvesting of grafts. The technique involves a different approach to obtaining grafts than with traditional Follicular Unit Transplantation (Strip or FUG), excising individual follicular unit grafts one at a time from the donor area using tiny punches, instead of dissected from a linear strip.

Comment These two methods can also be successfully combined in a procedure called the Hybrid procedure where strip is excised first, followed by FUE under and above the incision, as well on the temporal areas. This approach allows harvesting of greater number of grafts, without extending the incision on the side where it is...
at risk to be noticeable. Follicular Unit Excision was done first with manual punches but since it was too time-consuming, and not efficient automated devices started to come out on the market which speeded-up the procedure but had some limitations as well. The device that is used for graft extraction defines critical things of a procedure such as: time, quality of grafts, tissue damage, recovery of the patient and tiredness of a surgeon. Since the concept of the FUE was introduced for the first time in 2002 by Drs. Rassman and Bernstein, many things have changes from types of devices, types and sizes of the punches, depth of the excision, manners of excising grafts, but also process after grafts extraction-graft storage, and implantation techniques as well as post-hair transplant care.

**Conclusion** The goal of this presentation is to review how FUE evolved through years and to introduce the latest surgical method used. Given its popularity with patients and surgeons, the FUE procedure will continue to evolve as more physicians learn about this procedure, gain experience with it in their practices and offer major improvements to the technique. Nineteen years later this method still gets to be improved closely supported by development of technology.
Hair dysplasia represents a significant portion of cases seen by paediatric dermatologists although hair has always been a secondary aspect for paediatricians and dermatologists, due to the erroneous basis that there is not much information extractable from it. But the hair is easily accessible to examination and can bring a lot of information.

Clinical observation and microscopy investigation of hair shaft are the clues for the diagnosis of hair dysplasias. For example, the association of congenital hypotrichosis with ichthyosis should bring us to think in Netherton or Conradi-Hünermann-Happle syndromes or in trichothiodystrophy; specific hair shaft changes in: monilethrix (alternating periodical beading) versus keratosis follicularis declavans (Siemens syndrome) or pseudomonilethrix (scarce and irregular flat nodules); proximal trichorrhexis nodosa versus trichorrhexis invaginata -bamboo hair- (arginosuccinuria or trichohepathoentheric syndrome/Netherton’s syndrome) or thichonodosis (simple, double or complex true knot), pili torti (braided hair with regular periodic angles) versus kinky hair -polydysplastic hair- (Beare/Menkes syndromes). In some specific conditions X-ray microanalysis and chromatography of hair aminoacids may also help (trichothiodystrophy: sulphur content lower than 50%), as well as polarized light microscopy (tiger-tail pattern of the hair shaft). Sometimes SEM is necessary to confirm some diagnosis (pseudomonilethrix, pili canaliculi versus woolly hair).

In the field of congenital hypotrichosis and ectodermal dysplasias only the unsppecific aspect of “brand of dry wood” at SEM is noticeable as well as some phenotypic aspects (trichorhinophalangeal syndrome).

The alopecic pattern sometimes helps in the diagnostic procedure (sutural alopecia: Hallermann-Streiff syndrome; patchy cicatricial alopecia: condrodysplasia punctata, alopecia with milia; non cicatricial patchy alopecia: congenital triangular alopecia.

Trichoscopy has also proven to be very useful as a fast diagnostic procedure of hair disorders (hair dysplasias, lose anagen hair versus short anagen syndrome, bubble hair, etc…).

Concerning some therapeutic perls we can say that topical minoxidil, at different concentration from 1-3%, depending on the age of the child, always helps in congenital alopecia and hair dysplasia; keratolytic agents improve keratosis follicularis declavans; N-acetylcysteine therapy improves trichotillomania and D-penicillamine-based shampoo, among others, solves green hair.

Reference:
deficient brittle hair, which they recognized as a marker for this complex disease and designated it as a “neuroectodermal symptom complex.” Trichothiodystrophy may be accompanied by a variety of other manifestations, sometimes called PIBIDS (Photosensitivity, Ichthyosis, Brittle hair, Intellectual impairment, Decreased fertility, and Short stature) or without photosensitivity termed IBIDS, and without ichthyosis, BIDS. Many patients have recurrent infections, and abnormalities of the bone and teeth may also occur. Rodney Howell identified C7orf11, as the first disease gene for nonphotosensitive trichothiodystrophy (TTD). C7orf11 maps to chromosome 7p14, and the disease locus has been designated “TTDN1” (TTD nonphotosensitive 1). Trichothiodystrophy, Xeroderma pigmentosum, Cockayne syndrome, Bloom syndrome and Rothmund Thomson syndrome are a very disorders due to genomic instability, they are named Genetic Photodermatosis. During the lecture we will discuss about the clinical findings and molecular abnormalities in our Mexican patients.

CHILDHOOD ALOPECIA AREATA: UPDATE ON TREATMENT

Alopecia areata (AA) is a common hair loss condition that can occur at any age. However, 60% of the patients experience the first episode of hair loss before the age of 20, and 20% during infancy. Indeed, AA is the third-most-common dermatosis in children, and can lead to major psychological implications, such as depression and anxiety. Therefore, the children and their parents often seek a quick and effective treatment for their disease. Unfortunately, there is limited information on the efficacy and safety of the different treatments being used today for AA in general, and even less data is available about the management of AA in children. Some of the treatments, such as intralesional injections of steroids, are not feasible in children, and some of the medications used in adults carry a higher risk of side effects in the pediatric population. The aim of this talk would be to review the available information on the different treatment modalities in children, with special emphasis on JAK inhibitors. There is a growing line of evidence showing the effectiveness of this group of drugs for adults with AA, and preliminary results show promise for this treatment also in pre-adolescent and adolescent patients with moderate-to-severe AA, providing hope that in the near future there will be an approved drug for the treatment of children with AA.
FREE COMMUNICATIONS TO THE TOPIC

PREVALENCE OF COMORBIDITIES AMONG PEDIATRIC PATIENTS WITH ALOPECIA AREATA

Introduction & Objectives Alopecia areata (AA) is a common autoimmune disease which may present with non-scarring patches to complete scalp and body hair loss. Comorbidities in AA have been examined in various adult populations; however data regarding comorbidities in children are limited. The aim of this study was to examine the prevalence of comorbidities in pediatric AA using a large de-identified composite patient database.

Methods & Materials The Explorys electronic, aggregate database was used to identify pediatric (<18 years) patients with AA using the SNOMED-CT term “alopecia areata” (n=3,520). Pediatric patients without alopecia areata were used as controls (n=8,347,260). Logistic regression was used for comparisons.

Results Atopic dermatitis was the most common comorbidity among pediatric patients, presenting in 17% of AA patients and 2.2% of controls (OR 9.33, 95%CI 8.55-10.18, p<0.001). Other autoimmune diseases including vitiligo (1.42% AA vs. 0.05% controls, OR 31.81, 95%CI 24.01-42.1, p<0.001), psoriasis (1.42% AA vs. 0.07% controls, OR 20.58, 95%CI 15.55-27.2, p<0.001), celiac disease (0.57% AA vs. 0.08% controls, OR 7.66, 95%CI 4.93-11.9, p<0.001), ulcerative colitis (0.28% AA vs. 0.02% controls, OR 18.01, 95%CI 9.66-33.6, p<0.001), systemic lupus erythematosus (0.3% AA vs. 0.02% controls, OR 18.15, 95%CI 9.73-33.84 p<0.001), juvenile idiopathic arthritis (0.28% AA vs. 0.008% controls, OR 35.49, 95%CI 18.99-66.3, p<0.001), and juvenile rheumatoid arthritis (0.28% AA vs. 0.04% controls, OR 7.34, 95%CI 3.94-13.66, p<0.001) were more common among pediatric AA patients. Metabolic disorders such as obesity (5.68% AA vs. 1.08% controls, OR 5.5, 95%CI 4.76-6.34, p<0.001), hyperlipidemia (1.42% AA vs. 0.25% controls, OR 5.82, 95%CI 4.4-7.7, p<0.001), diabetes mellitus (0.85% AA vs. 0.55% controls, OR 1.56, 95%CI 1.09-2.23, p<0.001) and metabolic syndrome (0.28% AA vs. 0.04% controls, OR 6.41, 95%CI 3.44-11.93, p<0.001) were more common among pediatric AA patients. Other common conditions among pediatric AA patients were anemia (7.7% AA vs. 2.3% controls, OR 3.47, 95%CI 3.06-3.92, p<0.001), vitamin D deficiency (5.4% AA vs. 0.36% controls, OR 15.64, 95%CI 13.5-18.1, p<0.001), hypothyroidism (2.84% AA vs. 0.22% controls, OR 13.1, 95%CI 10.73-15.9, p<0.001), hypertension (0.85% AA vs. 0.22% controls, OR 3.87, 95%CI 2.7-5.55, p<0.001), and depression (1.14% AA vs. 0.17% controls, OR 6.92, 95%CI 5.09-9.45, p<0.001).

Conclusions Pediatric AA patients have higher rates of autoimmune and metabolic disorders. Physicians should be aware of this increased risk and consider further workup if autoimmune or metabolic disorders are suspected.

CONGENITAL TRICHOSSERTIC NODOSA: CASE REPORT AND DERMOSCOPIC FINDINGS

Introduction Trichorrhexis nodosa is a hair shaft disorder that presents with grayish nodes along hair shaft. It is represented microscopically with a hair shaft fracture producing an appearance suggestive of the ends of two brushes aligned in opposition and pushed together (1,2). Trichorrhexis nodosa (TN) is a common hair shaft disorder. The term trichorrhexis nodosa is derived from the Greek word trichos, meaning hair; the Latin rhexis, meaning rupture; and nodosa as nodule, and refers to hair that breaks easily with nodular structures along the hairs (3). This condition can either be associated with other clinical features or present as an isolated congenital abnormality.

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As a sole finding; TN it is observed in only 5.6% of children (4). The condition can also be seen in association with ectodermal defects, genetic syndromes and metabolic disorders.

**Case Report** We report a case of a generalized form of congenital trichorrhexis nodosa of a 10 y-o female.

**Results** A 10 y-o girl was brought for consultation with complaints of unusual rough texture, fragile hair that never grew beyond 1 -2 cm, leaving areas of apparently diffuse alopecia since early childhood. She had no history of related parents, familial genetic syndromes, nor any symptoms suggestive of physical, mental delay or abnormality. She had received previous treatment with antifungal medications with no response. On examination of the scalp, the hair showed different lengths from 0.5 to 1.5 cm with hair shafts that were rough, dry, and brittle with scaling on the scalp. The eyebrows and the rest of her body showed sparse hairs and of the same nature as the scalp hair. The trichoscopy in our patient showed keratotic follicular plugs, broken hairs, irregular coiled hairs (hook hairs), and zig zag hairs. Systemic evaluation was normal. Based on the clinical presentation and excluding genetic syndromes, the patient was diagnosed with congenital trichorrhexis nodosa. She received treatment with Biotin along with other essential micronutrients, daily for 6 months, as well as hair conditioner and was able to obtain a partial response.

**Conclusions** Congenital trichorrhexis nodosa as a sole entity is very rare (5). Very few cases have been reported in the literature (4,6). Trichoscopic findings in our patient were interesting and rarely described. There was partial response to general measures and vitamin supplementation.

**References:**

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**PILI ANNULATI COMPLICATED WITH TRICHORRHEXIS NODOSA: A REPORT OF A CHINESE FAMILY**

**Introduction** Pili annulati (PA) is an autosomal inherited hereditary disorder characterized by the banded or speckled appearance of the hair shaft and has been classified into hair shaft abnormalities without increase of fragility. Clinical examinations of PA patients usually show shiny white spots or bands on the hair shaft, which can be seen as alternating light and dark bands. Though the causative gene of the disease remains unknown, a locus for pili annulati was mapped to a 2.9-Mb interval on chromosome 12q24. 33.

**Case report** A 23-year-old woman visited our department with a complaint of easy-broken scalp hair for eight years. Her mother, half-brother by her mother, and the daughter of her half-brother also suffered from similar scalp hair problems, and her half-brother had the same symptom on his eyebrows. A physical examination revealed multiple small white spots shining on her scalp hair shafts, though the hair on the rest of her body were normal. Under trichoscopy, hair shafts show alternating light and dark bands. The white-colored structure covers nearly the width of a hair with unclear borders. The fraying of cortical fibers can also be recognized on “normal black bands” of hair shafts, resulting in “thrust paint brushes” appearance of trichorrhexis nodosa. Bright swollen nodes can be recognized in the scanning electron microscopy of the “light band”, indicating damage of both cuticle and cortex. The same result was found in the physical and trichoscopy examination of her brother’s both scalp and eyebrows.

**Conclusion** To the best of our knowledge, this is the first case report of PA in Chinese population. The shiny spots on the hair shaft been demonstrated as air-filled cavities within the cortex of
the hair shaft by scanning and transmission electron microscopy. Although PA is not generally related to increased hair fragility, seven cases of PA with fragile hair have been published before, and one of them showed the feature of trichorrhexis nodosa. Acquired trichorrhexis nodosa is mainly caused by repeated physical trauma of the hair. It usually presents as minor nodules on the hair clinically and shows “thrust paint brushes” appearance by trichoscopy, as if two brushes are thrust into each other. Our case also indicates the swollen nodes caused by PA can finally lead to the increased fragility and break when physical damage occurs. Pathological cavities within hair shafts may cause the increased fragility of PA patients’ hair, which may lead to acquired trichorrhexis nodosa as a result of increased sensitivity to weathering.
CONTROL AND TIMING OF DERMAL CONDENSATE FATE SPECIFICATION

Specification of hair placodes and dermal condensates is essential for hair follicle morphogenesis, but the precise timing and sequence of molecular events during skin development are still not fully understood. Here, we identify with 3D microscopy and 4D live imaging the precursors of dermal condensates (DC), signaling niches for placode progenitors, before any signs of cluster formation. With population-based and single-cell transcriptomics, we define a molecular time-lapse from pre-DC fate specification through DC formation and establish the developmental trajectory as the DC lineage emerges from fibroblasts. Co-expression of downregulated fibroblast and upregulated DC genes in DC precursors reveals a transitory molecular state following a proliferation shutdown. Waves of transcription factor and signaling molecule expression then coincide with DC formation. Finally, ablation of epidermal Wnt signaling and placode-derived FGF20 demonstrates their requirement for pre-DC specification. These findings uncover a progenitor-dependent niche precursor fate and the transitory molecular events controlling niche formation and function.

ROLE OF TISSUE NON-SPECIFIC ALKALINE PHOSPHATASE IN TRICHOGENIC ACTIVITY OF 3D-CULTURED HUMAN DERMAL PAPILLA CELLS

The dermal papilla (DP) regulates the overlying epithelial cells and plays a key role in the regulation of hair growth and regeneration. However, unlike the intact DP, two-dimensional (2D)-cultured DP cells lack hair-inductive capacity (trichogenicity). Recent studies showed that sphere formation enhances the ability of 2D-cultured DP cells to induce new hair follicles and alkaline phosphatase (ALP) activity is known to be correlated with the hair-inducing capacity of DP cells and expression of tissue non-specific alkaline phosphatase (ALPL) transcript is restored in DP spheres. To investigate whether restoration of ALPL expression by sphere formation plays a critical role in hair-inducing capacity of DP spheres and, if so, to investigate the mechanism, we employed expression vector-mediated ALPL overexpression and ALPL siRNA-mediated gene knockdown in combination with a hair reconstitution assay. We observed that ALPL plays a critical role in the hair-inductive capacity of human DP spheres by regulating Wnt/β-catenin signaling and maintaining the characteristics of the DP. Since potent dermal cells are necessary for the possibility of cell-based treatment of hair loss, our finding of ALPL involvement in hair-inductive capacity of human DP spheres will provide a rationale for preparing competent DP cells by augmentation of ALPL expression in DP spheres.
MODELLING EPIGENETIC CHANGES
REGULATING HAIR FOLLICLE
INDUCTION

During hair follicle morphogenesis clusters of
dermal cells, known as condensations, signal to
the overlying epithelial cells to induce forma-
tion of various structures of the hair follicle. This
dermal condensation eventually forms the der-
mal papilla (DP), a small structure at the base
of the adult hair follicle which controls differ-
etiation patterns and hair cycle progression.
Moreover, the DP, effectively a condensation of
adult dermal cells, will induce new hair follicle
growth complete with stem cells, if excised from
an adult hair follicle and re-implanted elsewhere
in the skin.

It’s been shown that when grown in 2D culture
conditions DP cells lose their ability to induce
new follicle growth. We previously showed that
promoting 3D spheroid formation in DP cells
through hanging drop culture, recreates an in-
vivo transcriptome, and in turn restores the in-
structive capacity of DP cells. Furthermore, we
found that interfolllicular fibroblasts (Fbs), which
arise from the same progenitor as DP, were un-
able to induce new hair growth in either 2D or
3D cultures, signifying that DP cells hold intrinsic
capabilities that become activated in spheroids,
and affirming their importance in hair follicle in-
duction.

Here, we hypothesise that specific changes oc-
cur in DP cells, but not Fbs, when cultured in
spheroids that restores an inductive mesenchy-
mal niche. To understand the molecular changes
underpinning this phenomenon, we performed
RNA-seq in combination with ATAC-seq, en-
abling us to look at differential gene expression
and associated changes in chromatin arrange-
ment within the nucleus which can regulate
gene expression. DP and Fbs cells in both 2D and
3D culture conditions were sequenced, giving us
4 comparisons allowing for the identification of
both cell-specific and culture induced changes.
Differentially expressed genes (DEGs) (P<0.01
& FDR < 0.05) were first gathered comparing
across cell type then culture condition. We found
that culture conditions play a huge role in deter-
mining gene expression; DP cells and Fbs show
similar profiles in 2D with only 81 DEGs, while
when cultured in 3D, >2,000 DEGs can be seen
between DP and Fbs indicating that each cell
responds uniquely to the altered environment.
By integrating chromatin level information from
ATAC-seq and looking in regions where chroma-
tin undergoes dynamic changes, we have been
able to pick several target transcription factors
potentially with regulatory roles in inductiv-
ity. By combining overexpression and knock-
out techniques in-vitro and developing in-vivo
reconstitution assays, we aim to reprogramme
non-inductive human 2D DP cells or Fbs into an
inductive state. Lastly, using conditional knock-
out models we aim to assess the role of these
transcription factors during hair follicle morpho-
genesis.

DERMAL PAPILLA TUNING TO
PROMOTE HUMAN SCALP HAIR
GROWTH: PRINCIPLES, COMMON
MISCONCEPTIONS, AND THE KEY
ROLE OF SFRP1

The past two decades of hair research have seen
major advances in understanding the biology and
pathology of epithelial hair follicle stem cells. This
has led many investigators to believe that these
stem cells are the main targets for therapeutic in-
tervention in the ongoing quest to develop more
effective strategies for managing the most com-
mon human hair growth disorders, i.e. androge-
netic alopecia (AGA) and telogen effluvium (TE).
Here, we argue that this likely is a misguided con-
cept and that, instead, therapeutic “tuning” of
dermal papilla (DP) secretory activities that con-
Dermal Papilla

Chairs: Michael Rendl, Young Kwan Sung

control Wnt signaling activity in the human anagen hair matrix and the secondary hair germ may well hold the key to the development of breakthrough therapeutics for AGA and TE. Since recent insights into how the potent, hypertrichosis-inducing immunosuppressant, cyclosporine A, promotes human scalp hair follicle growth ex vivo provide intriguing, generally relevant pointers in this respect, these are exemplarily discussed here, with emphasis on the Wnt inhibitor, SFRP1.
SOX2 IN THE DERMAL PAPILLA REGULATES HAIR FOLLICLE PIGMENTATION

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Introduction: The processes and regulation involved in hair follicle pigmentation encompasses the crosstalk between the epithelial-mesenchymal niches. Within the hair follicle niche, Dermal Papilla (DP) cells are well known for the hair induction capacity. Interestingly, DP cell signalling has been also linked to the regulation of the hair follicle pigmentation, however the mechanisms involved in this regulation are still largely unknown. Here we describe how Sox2 in the DP is a key regulator of melanocyte signalling, resulting in a phenotypic switch in hair colour.

Methods To study the unknown regulatory role DP has on hair pigmentation, we first utilized a novel genetic tool, Leptin receptor (LepR) Cre, to target the DP. Data from our novel in-vivo mouse model exhibited the relationship between LepR and DP cells which interestingly remained consistent throughout the various stages of hair follicle morphogenesis and cycling.

Results Isolation of LepR+ cells from hair follicles demonstrated the same genetic expression as DP cells, further proving the suitability of LepR as a cell surface marker to isolate DP cells. We then use LepR Cre to ablate Sox2 in the DP, generating Sox2 KO mice. We quantify the phenotypic switch in hair colour by plucking the hair, separating into its different hair types and the ratio of pheomelanin to eumelanin band measured. We also isolated DP cells and melanocytes to be used as a quantitative analysis of DP and melanocyte gene expression.

Sox2 ablation in the DP results in a phenotypic switch from eumelanin to pheomelanin. Additionally, we found that Sox2-null DPs increases not only the number of guard and awl hairs with pheomelanin band, but also the length of pheomelanin band as well, resulting in a lighter coat seen. Subsequently, we demonstrated that ablating Sox2 in the DP does not affect normal pigment production, but identified upregulated BMP signalling which plays a role in pigment production and transfer, as previous research has established. Interestingly, we have also identified a temporal upregulation of agouti and downregulation of MC1R gene transcripts during the hair follicle cycle of a Sox2 KO mice.

Conclusions From this study, we identified that LepR is a good genetic tool to label the DP, Sox2-null DPs promote pigment switch of eumelanin to pheomelanin, and that Sox2 has the potential to regulate genes involved in melanogenesis and BMP signalling which would contribute to hair follicle pigmentation. Collectively, our data identify Sox2 as a key regulator of hair follicle pigmentation via DP-melanocyte crosstalk. As pigmentation disorders are commonly seen across cultures and can have considerable negative psychosocial impact because of alteration of appearance, the preliminary data obtained here would therefore help better understand the crosstalk between DP and melanocytes. Such knowledge gained would offer the possibility of novel avenues for therapeutics in pigmentation disorders to help treat and improve the quality of life of patients.
Introduction & Objectives Migration of epithelial keratinocytes across a wound bed is a key step in wound repair, and a delay here leads to the formation of chronic wounds. In skin homeostasis, dermal fibroblasts are responsible for coordinating the migration and differentiation of keratinocytes in the overlying epithelium. As fibroblasts within the skin are highly heterogeneous we posited that different fibroblast subtypes might be able to differentially influence reepithelialisation after wounding. Specifically, given previous studies showing that hairy skin heals faster than non-hairy skin, we hypothesised that hair follicle fibroblasts would promote faster epithelial closure than interfollicular fibroblasts.

Methods & Results To test this hypothesis we collected conditioned media from three fibroblast sub-types; dermal papilla, reticular and papillary fibroblasts, and used this in a keratinocyte scratch assay to represent re-epithelialisation of a skin wound in vitro. We found that conditioned media from follicular dermal papilla cells produced 1.9-fold more re-epithelialisation by 9 hours, compared to other fibroblast sub-types and controls (p<0.001, DPfi vs Epilife). In an attempt to understand what components of the dermal papilla conditioned media are responsible for this accelerated migration, we used a cytokine array to identify cytokines released into the media by the three fibroblast sub-types. Differential analysis of the cytokine profiles in each conditioned media enabled us to identify two which are present at significantly higher levels in the dermal papilla cell conditioned media; sAXL and CCL19. Using these cytokines both individually and in combination with one another, we found that similarly to the dermal papilla conditioned media, sAXL and CCL19 could significantly accelerate scratch wound closure. We next used an ex vivo human skin wound assay to assess the effect of fibroblast conditioned media and specific cytokines on wound closure. Here, we observed similar results to the scratch wound assay, with dermal papilla conditioned media, and dermal papilla specific cytokines accelerating closure. We next performed an unbiased transcriptional profiling to determine how dermal papilla cytokines accelerate healing, identifying Ephrin family members as key players mediated by dermal papilla signalling.

Conclusions Our data suggests that the biochemical properties of dermal papilla cells could be harnessed and used to accelerate healing. sAXL and CCL19 cytokines are promising targets for further investigation regarding their ability to accelerate wound healing.
**PLATELET RICH PLASMA**

Platelet rich plasma (PRP) is an autologous biological product defined as that portion of the plasma blood fraction that contains a platelet concentration above the baseline. It is obtained after centrifugation of a small blood volume of each patient. PRP is used in different areas of medicine and recently there has been an increased interest in its application in the area of Dermatology, namely in tissue regeneration, skin ulcers, scar revision, facial rejuvenation and alopecia. In the area of trichology, several papers have been published on the administration of PRP in androgenetic alopecia (AGA) and alopecia area-ta (AA). Currently available treatments sometimes have limited efficacy and platelet rich plasma has been postulated as a novel therapy in this type of alopecia. Based on my experience and clinical trials, PRP had a positive effect on the treatment of androgenetic alopecia, with no relevant side effects. Knowledge of the biology, mechanism of action and classification of PRP allows a better understanding of this new therapy in order to easily classify and interpret the available PRP data in the literature.

**MICRONEEDLING IN ANDROGENETIC ALOPECIA**

Androgenetic alopecia (AGA), is the most common type of alopecia in men, which is an androgen mediated event. Finasteride and minoxidil, which show cosmetically acceptable new hair growth in modest percentage of patients.

**Materials and Method**

Hundred cases of AGA were recruited into weekly microneedling treatment with twice daily 5% minoxidil lotion (Microneedling group); other group was given only 5 % minoxidil lotion. The 3 primary efficacy parameters assessed were: hair count, patient assessment and 7- point evaluation scale. A stereotactic positioning device was used assess global response.

**Microneedling Procedure**

A dermaroller of 1.5 mm sized needles was rolled over the affected areas of the scalp till mild erythema was noted. All patients were instructed not to apply minoxidil on the day of procedure.

**Results**

1. **Hair counts**

The mean change in hair count at week 12 was significantly greater for the Microneedling group compared to the Minoxidil group $P< 0.05$

2. **Investigator evaluation**

Forty patients in Microneedling group had $+2$ to $+3$ response on -point visual analogue scale, while none showed the same response in the Minoxidil group.

3. **Patient evaluation**

In the Microneedling group, $41 (82\%)$ patients reported more than 50% improvement versus only $2 (4.5\%)$ patients in the Minoxidil group. Unsatisfied patients to conventional therapy for AGA got good response with Microneedling treatment.

**Other notable findings during the study period were**

Initiation of new hair growth was noticeable by around 6 weeks in Microneedling group and by 10 weeks in Minoxidil group.

Rapid growth in the existing hair was seen at week 1 in the Microneedling group than Minoxidil group.

**Conclusion**

Dermaroller along with Minoxidil treated group was statistically superior to Minoxidil treated group in promoting hair growth in men with
Mechanical (Physical) therapy for hair diseases

Chairs: Bianca M Piraccini, Rubina Alves

AGA for all 3 primary efficacy measures of hair growth. Microneedling is a safe and a promising tool in hair stimulation and also it is useful to treat hair loss refractory to Minoxidil therapy. This is the first study of use of microneedling in male androgenetic alopecia.

LOW-LEVEL LASER THERAPY FOR THE TREATMENT OF HAIR LOSS DISORDERS

Hair loss is a common dermatologic complaint for patients leading to severe psychological and social impact in both men and women. Whereas low-level laser therapy (LLLT) has been known to stimulate cellular activity, there is considerable skepticism from the dermatology community on its use to promote hair growth due to lack of controlled studies comparing LLLT to other standard treatments, limited understanding of mechanisms, and inadequately defined treatment parameters. For this reason, we examined published clinical trials to clarify uncertainties and determine whether the breadth of evidence supports low-level laser therapy for hair loss disorders. A literature search was conducted through PubMed, Embase, Scopus, and Cochrane Trials to identify original articles that evaluate hair regrowth upon LLLT. Only controlled studies with wavelength of 600-1100 nm, greater than 16 weeks of treatment, and objective evaluation of hair regrowth were included. A total of 11 high-quality studies (9 RCTs) were found, 10 studies on pattern hair loss and 1 study on alopecia areata. The nine RCTs comparing LLLT to a sham device demonstrated significantly improved hair thickness or hair density (p < 0.01) in patients with pattern hair loss. And for alopecia areata, there was no statistical difference in the final mean hair count at treated patches when compared to control patches. LLLT is a useful treatment modality for pattern hair loss but not for alopecia areata possibly due to the need of higher energy to induce apoptosis of T cells. The data acquired for pattern hair loss used different devices, laser parameters and regimens, and evaluation methods. Therefore, future comparison of LLLT to other treatment modalities such as minoxidil and 5α-reductase inhibitor and comparison of different laser setting and regimens are essential for dermatologists to implement a more standardized treatment for patients with pattern hair loss for maximum efficacy.

HOW TO COMBINE PHYSICAL THERAPIES WITH HAIR TRANSPLANT

By physical therapies we consider physical agents (ex: Laser) and invasive treatments (ex: microneedling).

The literature about this subject is scarce. This is probably due to the difficulty in measuring the difference between the final result with hair transplant alone and hair transplant combined. The reason is that while a hair transplant determines an evident clinical difference before/after, in contrast, the differences before/after physical therapies are mild (or inexistent) or only detected by changes in hair thickness/density with phototrichogram.

We may consider physical therapies before, during the hair transplant, and after the procedure. They may be used in the donor area, in the receptor area, and in other parts of the scalp. Those methods may also be useful to improve the viability of the follicles while they are not in the scalp (in the operation table). Low Level Lasers, Platelet-Rich Plasma, microneedling and mesotherapy with finasteride or dutasteride (in patients that are not medicated with this drugs) are good methods to improve
both donor and receptor area before the hair transplant. In my practice, in some patients with a poor donor area, some improvement may be obtained, especially in hair thickness, in the 6 months before the procedure. Another way of improving donor and receptor areas is the use of pluripotential cells. The improvement of hair density may be as much as 5-15% in the injected area. There are three major ways to do it:

- harvesting follicular and papillary pluripotential cells by biopsy punch, mechanical treatment for selection and injection in the scalp (hundreds of pluripotential cells).
- harvesting pluripotential cells from adipose tissue or from bone marrow, mechanical treatment for selection and injection (thousands of pluripotential cells).
- harvesting follicular and papillary pluripotential cells by biopsy punch, and after isolation multiply them in vitro in order to have a huge amount of cells (no limit of number of cells). This is a very promising method but without efficacy in humans by now. Two therapies are prone to combine with hair transplant in the procedure day:

- PRP, that may be used in three ways: to improve the viability of the follicles while they are not in the scalp (in the operation table), to improve the implants while already placed in the scalp, and to treat areas affected by AGA but not implanted in that session.
- microneedling is useful to treat non implanted areas affected by AGA. The effect of even a slight improvement in other areas than the receptor one may be very interesting in the final result and may reduce the effect of physiological telogen effluvium after the procedure.

The need and the effect of mechanical therapies in the months/years after the procedure is difficult to determine. Probably, in addition to AGA medical treatment, it will help to prevent miniaturization of non transplanted remained follicles in both implanted and non-implanted areas affected by AGA. Some beneficial effect over transplanted follicles may also exist. Low Level Lasers, Platelet-Rich Plasma, microneedling, mesotherapy with finasteride or dutasteride and injection of pluripotential cells are valid methods to slightly improve hair density in the months after a hair transplant but we are not sure about the long term efficacy of such procedures.

A plethora of mechanical therapies for hair diseases is in the market, ranging from lasers or light devices, to invasive therapies such as microneedling and PRP. Several papers have been published, reporting different protocols of treatment, different indications and results. What is the real effectiveness of these therapies? What the best indication?
CONGENITAL HYPOTROTRICHOSIS: GENOTYPIC AND PHENOTYPIC CORRELATION

Congenital hypotrichosis refers to marked thinning of the hair present since birth or soon after birth. It can be present as an isolated defect without any signs and symptoms related to other organ systems and is referred to as non-syndromic congenital hypotrichosis or can be associated with abnormalities in other organs, referred to as syndromic congenital hypotrichosis. It is a cause of great agony and cosmetic concern to both the patients and their parents. Awareness of various presentations of congenital hypotrichosis and its associations can help the clinicians to suspect the clinical diagnosis and to provide an appropriate available care. Last two decades have seen a boom in the molecular genetics and candidate genes have been identified for most of these disorders. The aim of this presentation is provide an overview of phenotypic-genotypic correlation of congenital hypotrichosis based of the available literature till date and a personal experience with such cases seen in a tertiary care genodermatoses clinic over a span of 18 years and to provide a step-wise schematic approach to delineate the diagnosis in these cases.

KERATIN-SPECIFIC HAIR DISORDERS: NEW FINDINGS AND TREATMENT STRATEGIES

Keratins form a large group of 54 proteins that combine in the cytoplasm of epithelial cells to form a network of intermediate filaments. They have a critical role in human skin, and they are of special importance in the normal function and growth of hairs, as half of the keratins are trichocyte keratins, expressed specifically in the hair. Mutations in several of these keratins have been linked to genetic disorders, including monilethrix, hypotrichosis/woolly hair, pure hair and nail ectodermal dysplasia and pseudofolliculitis barbae. These genotrichoses expand our understanding of the functional role of each layer of the hair follicle and may thus offer directed therapeutic interventions. In this talk, the recent findings on the keratin-specific hair disorders will be discussed, and possible treatment strategies for these conditions will be reviewed.

HOW TRICHOSCOPY CAN HELP IDENTIFYING GENOTRICHOSES

Trichoscopy is a helpful method in identifying hair shaft abnormalities. However, studies which link trichoscopy features directly to specific mutations are still missing. Trichoscopy allows identification of such hair shaft abnormalities as monilethrix, trichorrhexis nodosa, trichorrhexis invaginata, pili torti or pili annulati. The structures observed by trichoscopy correspond to features observed earlier by light microscopy. However the benefit of trichoscopy is that multiple hair shafts may be observed during one non-invasive examination without the need of (repeated) hair pulling for light microscopy examination. It has to be also kept in mind that trichoscopy has to be performed with high care of details. Monilethrix may be easily confused with Pohl-Pinkus constrictions (i.e. in the course of alopecia areata), bamboo hairs in trichorrhexis invaginata may be confused with a hair shaft projecting into a black dot or an artifact, in pili annulati it is
Genotrichosis

Chairs: Regina Betz, Arti Nanda

important to not confuse the image with interrupted hair shaft medulla. Trichothiodystrophy may be difficult to identify with regular trichoscopy, but may be easily identified with polarized light trichoscopy. In conclusion, trichoscopy currently allows identification of genetic hair shaft abnormalities, however it does not replace detailed genetic testing.

WHAT’S NEW IN HYPOTRICHOSIS RESEARCH? – LSS AS NOVEL DISEASE GENE FOR AUTOSOMAL RECESSIVE HYPOTRICHOSIS SIMPLEX

Hypotrichosis simplex (HS) is a rare form of hereditary alopecia characterized by childhood-onset of diffuse and progressive scalp and body hair loss. Although research has identified a number of causal genes, genetic etiology in about 50% of HS cases remains unknown. The present report describes the identification via whole exome sequencing of five different mutations in the gene LSS in three unrelated families with unexplained, potentially autosomal recessive HS. Affected individuals showed sparse to absent, lanugo-like scalp hair, sparse and brittle eyebrows, sparse eyelashes and body hair. The LSS gene encodes lanosterol synthase (LSS), which is a key enzyme in the cholesterol biosynthetic pathway. This pathway plays an important role in hair follicle biology. After localizing LSS protein expression in the hair shaft and bulb of the hair follicle, the impact of the mutations on keratinocytes was analyzed using immunoblotting and immunofluorescence. Interestingly, wild-type LSS was localized in the endoplasmic reticulum (ER), whereas mutant LSS proteins were localized in part outside of the ER. A plausible hypothesis is that this mislocalization has potential deleterious implications for hair follicle cells. Immunoblotting revealed no differences in the overall level of wild-type and mutant protein. Analyses of blood cholesterol levels revealed no decrease in cholesterol or cholesterol intermediates, thus supporting the previously proposed hypothesis of an alternative cholesterol pathway. The identification of LSS as causal gene for autosomal recessive HS highlights the importance of the cholesterol pathway in hair follicle biology, and may facilitate novel therapeutic approaches for hair loss disorders in general.
FREE COMMUNICATIONS TO THE TOPIC

ORAL MINOXIDIL – A NOVEL AND PROMISING TREATMENT IN THE MANAGEMENT OF MONILETHRIX

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Introduction: In fragile hair conditions such as monilethrix, the application of topical minoxidil can cause dry and tangled hair exacerbating hair breakage. The use of oral minoxidil to treat children with this condition has not previously been reported.

Case Report: An 11-year-old girl was referred with short, fragile and brittle hair noticed from 2 years of age. Her paternal aunt and cousins had similar hair to her. On examination, she had variable hair growth across the scalp with mid-length hair growth at the frontal and right parietal scalp. Fragile, short brittle hair was noted particularly on the left parietal and occipital scalp. There was a generalised rough texture to her hair. A beaded appearance was seen on dermoscopy. This beaded appearance was also seen on light microscopy with areas of hair breakage at the points where the hair was narrowest. This was in keeping with a diagnosis of monilethrix.

Topical 2% Minoxidil was started and clinically this seemed to show some improvement in the density of her hair. However, her mother struggled to fund this treatment and so oral minoxidil was introduced at a dose of 0.625mg PO OD. On review 6 months later, improvement was objectively noted in relation to the general density of the hair. A reduction in hair shedding was reported. There have been no side effects of the treatment.

Comment: Monilethrix is a genetic disorder caused by autosomal dominant mutations in keratin genes (KRT81, KRT83, KRT86) and autosomal recessive mutations in the desmoglein 4 gene (DSG4). Hair is normal at birth and then becomes short and brittle within the first year of life. Sparse hair is noted all over, but accentuation of low-density hair is present on the occipital scalp. Eyebrows and eyelashes may also be affected. Perifollicular hyperkeratosis is a consistent feature. Nails may exhibit koilonychia. Minoxidil is a piperidinopyrimidine derivative and potent vasodilator that is licensed in the management of hypertension. The mechanism of action of topical minoxidil in hair growth is not fully understood. It may relate to vasodilation and opening of potassium channels in the skin and hair follicle. This results in lengthening the anagen hair growth phase and shortening the transition from telogen back into anagen; producing longer thicker hair.

Conclusion: Oral minoxidil offers a promising effective alternative treatment in the management of monilethrix.

HYPOTRICHOSIS WITH JUVENILE MACULAR DYSTROPHY: A CASE REPORT

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Introduction: Hypotrichosis with juvenile macular dystrophy (HJMD) is a rare autosomal recessive disease, characterized by hypotrichosis and progressive macular degeneration, leading to blindness in the first three decades of life. It is associated with mutations in the cadherin 3 (CDH3) gene, resulting in abnormal expression of P-cadherin.

Clinical case: A 4-year-old female patient was referred to our department due to abnormally short scalp hair that never had a haircut. Physical examination revealed short sparse scalp hair, fine in texture, with low overall density. The maximum hair length on the parietal scalp was 2 cm. Eyelashes, eyebrows and body hair were normal. Clinical examination did not reveal any abnormalities of the skin, teeth, nails and limbs. Trichoscopy showed short, thin and vellus hairs and rare yellow dots (figure 1B). Optical and
Genotrichosis

Chairs: Regina Betz, Arti Nanda

scanning electron microscopy examination revealed normal hair shafts and neither ruffled cuticles nor hockey stick-shaped bulbs were found. Structural analysis of the hair shafts using X-Ray spectroscopy showed bioelement values similar to those of normal controls. A systemic examination, serum and urine analysis, including vitamins and amino acids measurement and biotinidase activity, did not reveal other anomalies.

As we proceed with investigations, the girl complained about photophobia and was referred to Ophthalmology. At ophthalmological consultation, best-corrected visual acuity was 5/10 in both eyes. Fundus examination revealed pigmented alterations in the fovea bilaterally. Optical coherence tomography (OCT) demonstrated irregularity of the photoreceptor layer and intraretinal cysts.

Clinical findings suggested the diagnosis of HJMD and a genetic study was performed, revealing a c.830delG homozygous mutation in the CDH3 gene. Our clinical suspicious was supported and the girl's parents were referred to genetic counseling.

Conclusions: HJMD is a genodermatosis reported in approximately 50 cases worldwide and all share mutations in CDH3 on 16q21. CDH3 encodes P-cadherin, a calcium dependent cell-cell adhesion molecule that is strongly expressed in both the hair follicle and the retinal pigment epithelium. Symptom severity varies for each individual, but all share common features of retinal degeneration and short sparse scalp hair from birth, with limited growth throughout life. The most severe complication of HJMD is visual deterioration that culminates in blindness.

Conclusions: HJMD is a rare genetic disease, which makes it difficult to diagnose. It is important to maintain a high level of suspicion in cases of hypotrichosis, allowing the early diagnosis of this genodermatosis, in order to provide a multidisciplinary follow-up, especially by ophthalmology.

Given the advances in stem cell and genetic therapies for retinal diseases, reporting these cases is valuable to acknowledge phenotypic and genetic characteristics of this entity and to select patients for future treatments.

ALOPECIA AREATA AND NAIL DYSTROPHY IN A PATIENT WITH AUTOIMMUNE POLYENDOCRINOPATHY CANDIDIASIS ECTODERMAL DYSTROPHY (APECED) SYNDROME

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Case report: A 17-year-old gentleman presented to Dermatology Outpatients with a history of increased nail breakage and fragility. He also described a history of gradually increasing patchy hair loss over the past 3 years, with the sudden development of new patches of hair loss over the right lateral scalp causing cosmetic concerns. Although he has not had full pubertal hair growth to date, he denied any hair loss from the rest of his body.

He attends Paediatric Endocrinology with a background of Type 1 Autoimmune Polyendocrinopathy, Addison’s disease, hypoparathyroidism, hypothyroidism, pubertal delay and short stature, muco-cutaneous and oesophageal candidiasis and Grade 4 Nephrocalcinosis. Nail examination showed dystrophy of all fingernails. Scalp examination was in keeping with multiple oval smooth patches of hair loss affecting 30% of the scalp and exclamation mark hairs noted in some areas. His eyebrows and eyelashes were normal. Nail scrapings on three occasions showed positive microscopy for hyphae and arthrospores with negative culture.

Initial management of his scalp included treatment with potent topical steroid for three months, with no benefit. He had treatment with pulsed Itraconazole 200mg twice daily for 1 week, repeated after 21 days in October 2016, with no benefit. He had trialled treatment with Amorolfin nail lacquer in 2015, but discontinued this due to side effects of stinging.
**Genotrichosis**

**Chairs: Regina Betz, Arti Nanda**

**Comment:** APECED syndrome or Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dystrophy is a rare autosomal recessive disorder which classically presents with a ‘triad’ of major features, including hypoparathyroidism, primary adrenal insufficiency and chronic mucocutaneous candidiasis. Our patient presents with all three major features, and additional minor features include both hypothyroidism and alopecia. Nail dystrophy and candidiasis is typically a chronic feature; amorolfine nail lacquer and pulsed intraconazole are first line treatment options noted in a 2009 review of APECED syndrome management (1). Diagnosis of APECED syndrome is clinical, but can be further confirmed by genetic testing for mutations of the autoimmune regulator or ‘AIRE’ gene. Specific testing can also be undertaken for auto-antibodies against Interferon (2). Our patient was positive for a common mutation in AIRE-1 gene in 2005, and was homozygous for c. 964del13 (a 13bp deletion in exon 8).

**Conclusion:** We present this complex case to illustrate the challenges of management of alopecia areata and nail dystrophy in APECED syndrome.

**OPTIMISATION OF PLATELET RICH PLASMA SEPARATION METHOD BY PRELIMINARY SEDIMENTATION**

**Introduction:** The proportion of blood components such as RBCs, WBCs, platelets, plasma varies in every individual. In centrifugation, the cells are separated on the basis of mass, size, density and viscosity of plasma. Application of same centrifugation force in all individuals with different blood composition may not be conducive for favourable outcome. Increasing the duration or speed of centrifugation beyond certain point may affect platelet integrity while decreasing the same may affect platelet recovery. Since centrifugation is based on the principle of augmenting the effect of gravity by several times, we have considered sedimentation of blood under the effect of gravity as a preliminary step to guide the duration of centrifugation.

**Objectives:** This study aims to highlight the importance of blood composition and sedimentation for optimising centrifugation steps for PRP separation by double spin method.

**Materials & Methods:** Blood samples were collected from 20 healthy donors in 4 vacutainer tubes of 8.5 ml each containing 1.5 ml of acid citrate dextrose. These tubes allowed to stand for 2 hrs in controlled temperature to allow separation of plasma. At the end of 2 hrs, separation of plasma was different in all tubes. Separation was faster in those individuals with low hematocrit compared to those with high hematocrit. Colour of the plasma also varied from light yellow to amber. The separation of plasma was divided into 3 categories as the proportion of blood volume as <1/3rd, 1/3rd, >1/3rd, RCF of 900G corresponding to 2380 rpm was applied for 5mins, 3 mins, 1mins respectively, which resulted in nearly uniform separation of plasma in all the tubes. For second spin, RCF of 900G (2380 rpm) for 3 mins in all the samples resulted in formation of erythrocyte-platelet pellet at the bottom of the tube. The tubes were shaken to resuspend the platelet plug in 1-2 ml of supernatant plasma, rest of the plasma was discarded. Increasing the duration of second spin beyond 3 mins resulted in formation of platelet plug that failed to dissolve, indicating platelet activation.

**Results:** The mean platelet count was 10.5±2 lakhs/ml. The size of platelet plug correlated with the baseline platelet count in all individuals. The amount of plasma for resuspending the pellet depended on the size of platelet plug obtained. Erythrocytes remained undissolved at the bottom of the tube even after shaking, thus improving the overall quality of PRP.

**Conclusion:** Our study shows that, preliminary sedimentation is relevant for deciding duration of first spin of centrifugation to improve the quality of PRP by double spin method.

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**BEYOND “PLATELET RICH PLASMAS”. AUTOLOGOUS BLOOD BIOMATERIALS AND ANDROGENETIC ALOPECIA, A TEN-YEAR EXPERIENCE**

**Introduction & Objectives:** from their preparation to different delivery methods, several options exist in administering this cell and biologic treatment. We show here the results gathered in more than 700 treated cases and the lessons we are still learning actively following our already peer reviewed series of 232 cases.

**Materials & Methods:** we are following patients submitted to blood-derivatives based therapies in the largest Italian Dermatologic Hospital and research center since 2010. The generic term “platelet-rich plasma” (PRP) was used from the beginning to describe all protocols and harvesting methods, ignoring that several different bio-
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materials can be obtained from human blood. In order to assess types and amounts of blood cells and biologically active molecules in our concentrated plasmas we first and foremost tested a 16-patient sample where platelets numbers, leukocytes (both lymphocytes and granulocytes) and fibrinogen values in the injected enriched plasma were compared to the same patient whole blood baseline. We found a 4,5 times average increase in platelets concentration and an almost 2 and 4,5 time improvement in granulocytes and lymphocytes figures. Fibrinogen showed a five-fold increase when we filtered the ppp layer after a soft spin centrifugation. We assume that similar increased values are equally to be expected in all proteins heavier than the 5kdalton representing our filter cut-off. The significant increase in cells numbers (leucocytes), platelets and fibrinogen values led us to the actual definition of “injectable leucocyte-platelets rich fibrin” or il-prf, the l-prf acronym being applied until now to define only gel, not injectable enriched plasmas. Using this technique AGA affected patients were submitted to a 2-stage procedures within a 3-6 months interval when 7 to 9 ml of i-LPRF were intradermally delivered into the scalp thinning areas. At the same time i-LPRF has been extensively injected as an adjunctive procedures to all hair transplant surgeries.

Results: A total of 232 patients were enrolled in two peer-reviewed studies. Last clinical controls, through a dedicated global photograph protocol, confirm that injecting i-LPRF in AGA patient scalps as a standalone procedure ensures a good degree of clinical efficacy, while biologically enhancing hair transplantation through i-LPRF injections resulted in an improved hair density in the non-transplanted prone-to-baldness areas surrounding the graft receiving sites.

Conclusion: The induction of a minimal local trauma on the scalp, followed by injections of a filtered plasma made of a strongly concentrated platelet fraction, a robust white cells presence, and the inclusion of concentrated fibrinogen and other plasma proteins, yielded positive clinical results as a standalone procedure in androgenetic alopecia and showed a clinically significant improvement when used in different phases of any hair transplantation procedure.

THE EFFICACY OF COMBINATION THERAPY WITH LOW-LEVEL LIGHT THERAPY PLUS MINOXIDIL 5% SOLUTION VERSUS MINOXIDIL 5% SOLUTION MONOTHERAPY IN THE TREATMENT OF ANDROGENETIC ALOPECIA

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Introduction: Despite the current treatment options for different types of alopecia, there is a need for more effective management options. Low-level laser therapy (LLLT) is currently in use to stimulate hair growth and is quickly gaining in popularity due to the ease of use and absence of side effects. This study aimed at evaluating the efficacy of adding LLLT to minoxidil topical solution in the treatment of androgenetic alopecia (AGA).

Methods: This study was a 24-week, randomized, self-comparison clinical trial that enrolled 66 patients with AGA. The patients were randomly divided into two groups. The first group received the topical minoxidil 5% solution twice per day, and the other group received LLLT 3 times weekly for 30 minutes each plus topical minoxidil 5% solution twice per day. Global scalp photography, phototrichogram assessment, the investigator’s global assessment (IGA) of hair regrowth, and the subject’s assessment of the treatment satisfaction were used for evaluation.

Results: The efficacy and safety of both modalities were highlighted with comparable results in all parameters. The percentage of recovery from androgenetic alopecia and the patients’ satisfaction with their treatment were significantly improved. The IGA of hair regrowth was significantly higher in the combination therapy group compared to the minoxidil group, and the subject’s assessment of treatment satisfaction also showed a significant improvement in the combination therapy group.
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higher in the second group compared to the first group. A significantly greater improvement from baseline in hair thickness, hair count, hair coverage, and IGA were also observed in the combination therapy group than in the minoxidil 5% group at the 12- and 24-week visit. No serious adverse events were observed.

Conclusion: Combination treatments with minoxidil, and LLLT may act synergistic to enhance efficacy. Further research is required to establish the true efficacy of these devices and combination therapy for hair growth in comparison to existing alternative therapies.

HAIR FOLLICLE REGROWTH IN ALOPECIA PATIENTS AFTER FRACTIONAL PHOTOTHERMOLYSIS - A PILOT STUDY

Introduction & Objectives: Fractional photothermolysis causes microthermal injury and subsequent wound healing stimulating dermal papillae, accelerating telogen to anagen change, as well as transforming vellus to terminal hairs. The use of fractional photothermolysis for hair regrowth is controversial. Current studies using non-ablative and ablative wavelengths demonstrate 20% to 60% increase in hair density after 5 to 24 treatment sessions, one to six weeks apart. The objective of this pilot study is to demonstrate hair regrowth in varying types of alopecia after non-ablative, fractional photothermolysis.

Materials & Methods: Five patients with non-scarring and scarring alopecias received non-ablative fractional photothermolysis (1550 nm erbium glass) six times over a period of three months. Patients were then followed for two months after laser treatment was complete to determine if hair regrowth was maintained. Hair regrowth was measured quantitatively using a novel, non-invasive imaging system called optical coherence tomography (OCT), and qualitatively using serial photography, dermoscopy, as well as physician and patient-reported scales.

Results: All patients demonstrated significant (p<0.05) quantitative hair density increases during treatment as measured by OCT. Physicians and patients report hair growth is “improved” to “very improved” on a 5-point quantitative Likert scale from “worse” to “very much improved”. Adjuvant topical finasteride causes transformation from vellus to terminal hair clinically. After laser therapy discontinuation, all patients experience a quantitative, non-significant hair density decrease.

Conclusion: Non-ablative fractional photothermolysis stimulates scalp hair follicle regrowth in non-scarring and scarring alopecia. Treatment using low-energy and high-density protocols are effective. Future directions include optimization of spacing of treatments, required number of treatment sessions and techniques to maintain hair regrowth after discontinuation of laser therapy.

TEASER SERIES: MINOXIDIL AND DUTASTERIDE DRUG TATTOOING FOR ANDROGENIC ALOPECIA

Introduction: A significant percentage of patients with androgenic alopecia, despite years of adhesion to standard treatment with 5-alpha-reductase inhibitors and topical minoxidil, still present severe alopecia or low density of hair.

Drug-delivery is one of the hot topics for dermatology in the past decade and many methods have been described as alternatives to injections or microinjections, and may increase scalp dermal concentration of drugs when compared to
oral or topical therapy. Tattooing is a millenary technique which is effective to deliver large solid and ink particles to the superficial dermis, by means of fast wet needle strokes. Although tattoo artists have used pigments to camouflage alopecia for decades, the same technique can be used to deliver active drugs to the dermis. This technique promotes hair growth by associating benefits of microneedling (prostaglandins and growth factors production), with the known pharmacologic action of the drugs which are delivered to the dermis.

Methods: Technique: The scalp is prepared with 70% isopropyl alcohol, Becton Dickinson and company (BD) alcohol swabs, which is allowed to dry for 2 minutes. A sterile ink cup is filled with a mixture of sterile injectable solutions of dutasteride 0.1% (1mL) and minoxidil 0.5% (2mL) - (Pineda Laboratories). A rotatory professional machine equipped with a disposable, sterile 27-Magnum needle cartridge. For comfort, thinnest needles (called “Bug-pin”) with soft edges (lateral shorter needles) are used, Cheyenne 27MG-SE-BP. A regional frontal nerve block may be performed. Occipital and temporal nerve blocks are unnecessary due to mild pain levels in those areas. The frequency of the motor is set to 150Hz, which gives 4.050 microperforations per second. The needle has a range of up to 4mm, but 1mm is enough to achieve superficial dermis. The drug solution is absorbed by capillarity from the ink cup to needle cartridge if the needles are in motion, and this procedure is repeated each time the needles become dry. Each treatment takes from 1-20 min, depending on the surface area involvement. Optionally, 0.3mL of 1% methylene blue may be added ensure proper coverage of the treatment area. The patient is instructed to avoid hair wash for at least 12h.

Results: We present 10 cases that underwent from 2 to 6 treatment sessions. Overall, 80% presented significant hair regrowth. The improvement of hair density is a direct effect of terminal hair growth and results clearly depend on previous density of vellus or intermediate hair in the area. Patients with solar damage and sparse vellus hair had no significant regrowth with up to 6 sessions.

Goals: Explore the rationale of different modalities of drug-delivery versus the standard tattooing with professional machinery. Demonstrate in a case series of 10 patients the successful reversal of hair miniaturization. Split-scalp studies are necessary to demonstrate the superiority of drug tattooing versus mechanical needling only.

Conclusion: Minoxidil and dutasteride drug tattooing may be useful for patients with androgenetic alopecia.

THE EFFECT OF DAILY ASPIRIN USE ON TOPICAL MINOXIDIL TREATMENT FOR PATTER HAIR LOSS

Topical minoxidil is the only US FDA topical drug for the treatment of pattern hair loss. Millions of patients worldwide use minoxidil daily. Minoxidil is a pro-drug converted into its active form, minoxidil sulfate, by the sulfotransferase enzymes in the outer root sheath of hair follicles. In human liver, the phase II metabolism of xenobiotics by sulfotransferase is significantly inhibited by salicylic acid. Due to the widespread practice of daily aspirin use as a prophylactic treatment for heart conditions, it is important to determine if prolonged aspirin use affects sulfotransferase activity in hair follicles. In this study, we utilized the sulfotransferase activity assay previously reported by Goren et. al to determine sulfotransferase enzyme activity in hair follicles before and after 4 weeks of low dosage aspirin treatment. To the best of our knowledge, this is the first study to explore the relationship between long term aspirin use and its effect on topical minoxidil treatment.
PROPHYLACTIC TREATMENT WITH A SMALL MOLECULE PROTECTS BREAST CANCER PATIENTS FROM THE DEVELOPMENT OF CHEMOTHERAPY INDUCED ALOPECIA

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Introduction: Chemotherapy induced alopecia remains one of the most difficult treatment emergent adverse events faced by cancer patients. Among women, approximately 8% refuse life savings treatment in order to avoid chemotherapy induced alopecia. To date, the only FDA approved treatment modality for chemotherapy induced alopecia is a scalp cooling device.

Comment: The device induces scalp vasoconstriction and reduces metabolism in rapidly dividing keratinocytes. The device, while effective, suffers from several shortcomings including: prolonging of chemotherapy sessions, high cost, and discomfort associated with scalp cooling. As an alternate, a novel topical solution, containing a novel small molecule, was developed. In an in-vitro study, the small molecule temporarily reduced cellular metabolic activity without effecting the motility of the cells; therefore, we hypothesized that applying the topical solution prior to chemotherapy sessions could protect cancer patients from developing chemotherapy induced alopecia.

Conclusion: In this communication, we present the results from the first double-blinded placebo controlled study demonstrating the safety and effectiveness of the small molecule in protecting breast cancer patients treated with taxanes from the development of chemotherapy induced alopecia.

CHEMOTHERAPY-INDUCED IRREVERSIBLE ALOPECIA IN PATIENTS WITH BREAST CANCER - A COMPARISON OF THE LITERATURE WITH OWN CASES

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Introduction: Hair loss caused by chemotherapy in treatment of breast cancer is an incisive and psychologically stressful event for many women. In previous studies, more than 75% of the patients with cancer cited alopecia as their most feared side effect of treatment, with as many as 10% considering treatment refusal. Though in most cases, hair regrows completely after chemotherapy, there are also cases of permanent alopecia. These patients with permanent alopecia, especially, require psychological support along with all therapeutic options which are known to improve hair growth. While moderate chemotherapy treatments enable complete hair regrowth within 6 months, chemotherapy-induced alopecia (CIIA) exists at least 6 months after completion of chemotherapy. Previous studies showed that the type and combination of the drugs have a decisive influence on the irreversible damage of the hair follicles. In particular, Taxane, used for neoadjuvant or adjuvant chemotherapy, appears to be particularly damaging.

Methods: In the present study, the chemotherapy regimens of patients with breast cancer and irreversible alopecia were analyzed for their potential to damage hair growth irreversibly. The individual data were compared with the data from the literature to elucidate those chemotherapies which are especially dangerous for the hair follicle. Furthermore, the activity and the type of effluvium were evaluated by linear pluck trichogram investigations. Other causes of diffuse hair loss were excluded.

Results: Long term therapy with Minoxidil 2%
solution led partially to good hair regrowth, supported by systemic supplementation of iron or zinc if necessary.

**Conclusion:** The efficacies of the therapies to improve hair regrowth have been demonstrated by individual clinical courses. Regarding the chemotherapy regimens, it should be clarified before initiation of treatment whether Taxane and its derivatives are absolutely necessary, to avoid serious damage of the hair follicles. The potential for regeneration of the hair follicles cannot be estimated or predicted in advance. Therefore in all cases, long term treatment to restore hair growth is necessary.

**CAPILLARY REACTIONS OF NEW TARGETED THERAPIES DIRECTED AGAINST CANCER**

**Introduction & Objectives:** New immunologic targeted therapies against cancer have been an actual revolution of the treatment and prognosis of these diseases. These treatments act in a more specific way against physiopathogenesis of each disease. This fact suppose an important change in patient’s management and potential side effects to face. Many of these side effects can affect the hair in its cycle, form, color and immunology. Since they are very new treatments, no review of all these hair disorders have been written so far.

**Material & Methods:** We did an exhaustive bibliographic review to better characterize these trichological effects and put them all together. No statistical study has been performed.

**Results:** We identified 16 different drug families classified by its therapeutic targets. The research has been very rich and most of those drugs can induce capillary changes. Most relevant findings include tricomegaly, inflammatory alopecia and scalp follicular reaction due to EGFR inhibitors. Other significant findings are the color changes of immunotherapy with PD-1/PD-L1 and KIT inhibitors. Nilotinib also can induce a very particular kind of alopecia called nilotinib-induced alopecia. Depigmentation can be also seen in patients under VEGF/VEGFR inhibitors. BRAF inhibitors can induce RASopathic alopecia, something avoidable when combined therapy with MEK inhibitors is used. The Hedgehog inhibitors are the group with most incidence of alopecia. Alopecia areata can be induced due to several drugs but is mainly seen with CD52 inhibitors.

**Conclusion:** Capillary changes due the new targeted therapies directed against cancer are frequent and are family-related in most of the cases. Like with cutaneous toxicity, we think the knowledge for the dermatologist of all these possible capillary reactions is capital in order to offer an optimal handling of these patients.

**PERSISTENT POST-CHEMOTHERAPY ALOPECIA: CLINICAL CHARACTERIZATION, IMPACT ON QUALITY OF LIFE AND TREATMENT OUTCOMES**

**Introduction:** Persistent alopecia occurs in a subset of patients undergoing chemotherapy, yet the impact on quality of life and response to therapy has not been described in a large patient cohort. In this study, we characterized the clinical presentation, impact on quality of life (QoL), and therapy outcomes in persistent chemotherapy-induced alopecia (pCIA) and endocrine therapy-
induced alopecia after chemotherapy (EIAC).

**Material & Methods:** A retrospective multicenter cohort of cancer patients treated with cytotoxic agents who were clinically diagnosed with persistent alopecia between January 2009 to July 2017 was analyzed. Data including demographics, chemotherapy regimens, severity, clinical patterns, and response to hair-growth promoting agents were assessed. Data from the Hairdex Questionnaire was used to assess alopecia impact on patients QoL. A total of 192 female cancer patients were included, then categorized into one of two groups: 98 with pCIA, and 94 with EIAC as comparators. The clinical features, response to dermatologic therapy, and impact on QoL of pCIA were assessed and compared to EIAC.

**Results:** A total of 98 patients with pCIA (median age [range], 56.5 [18-83]) and 94 patients with EIAC (median age [range], 56 [29-84]) were included. The most common agents related to pCIA were taxanes in 80 patients (82%), and aromatase inhibitors in 58 EIAC patients (62%). pCIA showed a significant predominance of diffuse alopecia (31 of 75 pCIA [41%] vs 23 of 92 EIAC [25%]; P = .04) with greater severity (29 of 75 pCIA [39%] vs 12 of 92 EIAC [13%]; P <.001). A negative emotional impact on QoL was reported by both groups. After treatment with topical minoxidil or spironolactone, moderate to significant improvement was observed in 36 of 54 pCIA patients (67%) and in 32 of 42 EIAC patients (76%).

**Conclusion:** pCIA is frequently more severe and diffuse when compared to EIAC, and both groups showed a negative impact on QoL. A modest benefit was observed with dermatologic therapy. Additional studies are warranted to develop effective strategies for pCIA and EIAC prevention and effective therapy.

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**THE LXR AGONIST T0901317 PROTECTS HAIR FOLLICLE KERATINOCYTES FROM CHEMOTHERAPY INDUCED DAMAGE**

**Introduction:** There are currently no pharmacological interventions available for chemotherapy-induced alopecia (CIA). There is therefore an urgent need to identify new targets for therapy in order to prevent this distressing side effect of cancer treatment. We have previously hypothesized that increasing drug efflux transport out of the hair follicle we could render human scalp HFs more resistant to chemotherapy.

**Methods:** Here we have examined outer root sheath keratinocytes (ORSKs) as a HF relevant primary cell model to screen for ABC transporter inducing compounds. ABC transporters efflux a wide variety of anti-cancer agents and are associated with the development of multi-drug resistant cancer and therefore, by increasing their expression this novel mechanism would create a ‘multidrug resistant’ HF to prevent chemotherapy induced damage. We cultured ORSKs for 72 hours with putative protective agents and identified six compounds that increased ABC transporter expression/activity. We then examined the response of ORSKs treated with these compounds to Doxorubicin (DOX) a hair loss causing chemotherapeutic. T0901317 (LXR agonist), lopinavir (protease inhibitor) and dexamethasone (glucocorticoid receptor agonist) significantly decreased LDH release (p<0.01, n=5) and Caspase-3 activity (p<0.001, p<0.05, p<0.05, n=4) following incubation with 5µM DOX.

**Results:** Cell survival decreased to 22% following DOX exposure and this was ameliorated by T0901317 where 69% of the cells survived DOX exposure (p<0.01, n=6). DOX also caused a significant increase in γH2AX in ORS keratinocytes (28.5 fold increase, p<0.05, n=3), which was reduced to just 2.6 fold following T0901317 pre-incubation (p<0.05, n=3). These results indicate that T0901317 protects ORSKs from DOX induced damage. We next found ABCG2 transporter expression increased following incubation with T0901317 for 24 hours
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Chairs: Rubina Alves, David Saceda

(p<0.05, n=3), but the protective effect could not be modified by inhibition of ABCG2 transporter activity (p>0.05, n=5). Therefore, RNAseq analysis was performed following TO and Dox treatment in ORSKs. Initial pathways analysis has indicated significant perturbation/changes in lipid homeostasis and steroid biosynthesis.

Conclusion: This could highlight previously unrecognised roles for these processes in protection against cytotoxic injury. Further analysis will focus on these pathways to understand the protective benefits bestowed through their activation.
Frontal Fibrosing Alopecia

Chairs: Sergio Vaño-Galván, Rui Oliveira

WHAT’S NEW IN ETIOPATHOGENESIS

Frontal fibrosing alopecia (FFA), a clinical variant of follicular lichen planus, is a highly distressing inflammatory and scarring dermatosis of unknown pathobiology that affects almost exclusively women of post-menopausal age. Since FFA was first identified by Kossard in 1994, there has been rapid increase in reported incidence, culminating in speculation about likely environmental triggers. Nevertheless, there is substantial evidence for an inherited component in the aetiology of FFA, as demonstrated by familial cases following autosomal dominant transmission and higher concordance among monozygotic twins. We undertook genome-wide association studies in females from a UK cohort, comprising 844 cases and 3,760 controls, a Spanish cohort of 172 cases and 385 controls, and performed statistical meta-analysis. To delineate the molecular signature of the disease at tissue level and correlate this with genomic findings, 14 skin biopsy samples obtained from 7 cases and 7 matched controls were subjected to transcriptomic analysis. A global, untargeted, case-control metabolomic study was also performed to pursue a genome-wide significant signal implicating xenobiotic processing in disease pathogenesis. We observed genome-wide significant association with FFA at four genomic loci. Fine-mapping and co-localisation analysis have identified causal variants, the functional relevance of which was interrogated and will be discussed. Transcriptomic analysis of affected scalp tissue highlighted overrepresentation of transcripts encoding components of innate and adaptive immune response pathways. These findings provide insight into disease pathogenesis and characterise FFA as a genetically predisposed immuno-inflammatory disorder.

THE ROLE OF SUNSCREENS AND OTHER ENVIRONMENTAL FACTORS IN FFA

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Since frontal fibrosing alopecia (FFA) was first described in 1994 in six postmenopausal women, the incidence has increased dramatically worldwide. The direct pathophysiology remains unclear, but genetic, hormonal, autoimmune and inflammatory processes have been postulated. The epidemiology of the condition suggests a contribution of environmental factors. Aldoori et al reported a possible association between FFA and leave-on facial skin care products and sunscreen. To further investigate the association between the use and frequency of sunscreen and facial skin-care products and FFA we performed a case control questionnaire study in 130 women with FFA and 130 control subjects. The use of a dedicated sunscreen in the FFA group was over double that of the controls, with 92% of women with FFA reporting regular use (P < 0.0001). Subjects with FFA reported more frequent use of sunscreen-containing products, with 88% reporting daily use year-round, compared with 29% in the control group (P < 0.001). The high frequency of sunscreen use among women with FFA supports the hypothesis that sunscreen use on the forehead may cause FFA. Extended patch testing will improve the understanding of the role of sunscreen and facial skin care products in the pathophysiology of this increasingly common condition.
FRONTAL FIBROSING ALOPECIA: WHAT’S NEW IN CLINICAL PRESENTATION

Frontal fibrosing alopecia (FFA) is a lymphocytic primary scarring alopecia. It has an increasing incidence. FFA is currently the most frequent cicatricial alopecia. A total of 95% are women, mostly postmenopausal. The clinical presentation is typical: cicatricial alopecia located on the frontal and temporal areas + eyebrow alopecia +/- body hair loss +/- facial papules. During the lecture, we will review the latest papers about the clinical presentation and associated diseases of FFA.

A recent Spanish study has described three clinical patterns of presentation of FFA, with different prognosis: linear (pattern I), diffuse (pattern II) and pseudo-fringe (pattern III). The linear pattern is the band of uniform frontal hairline recession in the absence of loss of hair density behind the hairline. The diffuse zig-zag pattern is the same as linear but with at least 50% decreased hair density. Pseudo-fringe hairline recession was defined as an FFA presenting with a frontal or temporal unaffected primitive hairline. Patients with the diffuse pattern have the worst prognosis, while patients with the pseudo-fringe pattern have the best prognosis.

Another Italian study has described three unusual clinical patterns of presentation of FFA: “AGA-like” pattern (marked and symmetric recession of frontotemporal hairlines, with a peculiar sparing of the paramedian frontal hairline, mimicking the male pattern androgenetic alopecia), “cockade-like” pattern (bilateral oval patches of alopecia in the temporal regions, with peculiar sparing of a band of temporal hairlines, in addition to typical recession of frontal hairline) and “ophiasis-like” pattern (continuous involvement of the hairline from frontal to occipital regions).

FFA affects not only the scalp, but also the skin: facial papules, facial erythema, hypo or hyperpigmented macules, and the prominence or depression of the facial veins have also been described in patients with FFA. Recently, extrafacial red dots/erythema have also been described as localized in the hip and upper chest of female patients with FFA.

Regarding associated conditions, rosacea and hypothyroidism have a remarkably high prevalence in patients with FFA. Lichen planopilaris in other scalp areas or other body areas, as well as lichen planus pigmentosus, may coexist. Cases of concomitant discoid lupus erythematosus with FFA have also been reported.

Finally, we will discuss the potential clinical prognostic factors: the diffuse pattern, the presence of facial papules and the involvement of eyelashes or body hair are associated with more severe cases. The pseudo-fringe sign pattern is associated with a better prognosis.

WHAT’S NEW IN DIAGNOSIS (TRICHOSCOPY, DIAGNOSTIC CRITERIA, SCALES)

Frontal fibrosing alopecia (FFA), a type of lichen planopilaris, is a primary lymphocytic cicatricial alopecia characterized by progressive recession of frontal or frontotemporal hair line. Trichoscopy is used to confirm the diagnosis of frontal fibrosing alopecia and seem to be crucial in diagnosis of early cases, showing loss of velvus hairs in frontal hair line. Other trichoscopic FFA features are: perifollicular scaling (peripilar casts), perifollicular erythema, loss of follicular openings, presence of black dots, pili torti and lonely hairs. It was shown that there is a strong correlation between the severity of peripilar casts (assessed in 3 point scale) and the degree of lymphocytic infiltration on trichoscopy-guided biopsies.

Partial or complete eyebrow loss is observed in 39% to 100% of patients with frontal fibrosing alopecia and is thought to precede scalp alopecia in majority of cases.
Frontal Fibrosing Alopecia

Chairs: Sergio Vañó-Galván, Rui Oliveira

Dystrophic hairs, whitish areas with absence of follicular openings and eyebrow regrowth in distinct directions are the most characteristic dermatoscopic findings for eyebrow loss in FFA and may be considered as negative prognostic factor for eyebrow regrowth. On the contrary, the presence of empty follicular openings, vellus hairs and upright regrowing hairs may be considered as favorable prognostic factors.

Majority of patients diagnosed with FFA complain not only on recession of hairline but also on hair loss in mid-frontal scalp. Clinical examination may suggest that FFA frequently coexist with female pattern hair loss (FPHL). Trichoscopy in this area can show two different trichoscopic patterns of hair loss: fibrosing alopecia pattern (disturbance in normal follicular arrangement with small areas lacking follicular units and yellow dots, predominance of follicular units with one or two hairs, no features of follicular miniaturization and presence of mild perifollicular scaling) or androgenetic alopecia pattern (hair shaft thickness diversity, vellus hairs in percentage higher than 10, presence of yellow dots, increase in percentage of follicular units with 1 hair and decrease in percentage of follicular units with 3 hairs).

It is hypothesized, that in some patients with FFA the lymphocytic inflammatory infiltrate affect intermediate and vellus hair follicles, not only at the border of the frontal area, but also in whole androgen-dependent scalp region. It is considered that patients with androgenetic alopecia pattern in mid-frontal scalp may improve with antiandrogenic treatment, whereas in patients with fibrotic alopecia pattern only inhibition of disease activity may be achieved.

In recent years Frontal Fibrosing Alopecia Severity Index (FFASI) and Frontal Fibrosing Alopecia Severity Score (FFASS) were developed.

WHAT’S NEW IN TREATMENT

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Frontal fibrosing alopecia (FFA) is a chronic condition and patients may need long-term treatment. Currently, there is no gold standard therapy for this condition. After its initial description in 1994, the spectrum of clinical manifestations of FFA has expanded and it may now be regarded as a generalized skin condition. Available drugs may focus on the reduction of inflammatory signs/symptoms and halting progression of hair loss; and/or on the treatment of associated features such as facial papules and lichen planus pigmentosus. In this lecture, there will be an overview of local and systemic treatments commonly prescribed by physicians and discussion of recently published literature regarding management of FFA patients, as well as ongoing clinical trials.
Background: Since its first description, frontal fibrosing alopecia (FFA) has become increasingly common worldwide. Environmental factors may be involved in the etiology, and several epidemiologic studies performed on hundreds of FFA patients suggest an association between FFA and leave-on facial products, including anti-aging moisturizers and sunscreens. The time course of sunscreen and anti-aging moisturizers use by the population does seem to parallel the apparent increase in the incidence of FFA, and to some extent the predominant distribution of FFA matches the usual sites of moisturizer and sunscreen application. Taking into consideration the potential causative role of these products and given that some patients with FFA also present with facial inflammation (clinically diagnosed as facial papules and rosacea), we suspected that frontal fibrosing alopecia could be a new clinical presentation of allergic contact dermatitis (ACD), as all these manifestations can be explained by a type IV cutaneous reaction to an external factor in predisposed patients.

Objectives: To determine if contact allergy is involved in the pathophysiology of FFA.

Materials & Methods: Patients were recruited prospectively during May 2018 and November 2018 in the Hair Unit of the Department of Dermatology, Hospital Clinic and University of Barcelona, Spain. Eighteen patients diagnosed with FFA were patch tested according to the European Society of Contact Dermatitis (ESCD) guidelines.

Results: All patients were females aged between 54 and 75 years (mean age 64.94 years). The mean age of FFA onset was 58.83 years (range 45-73), and the vast majority were postmenopausal (78%). All patients confirmed the daily use of multiple leave-on cosmetics both on the face and body. Of the 18 patients tested, 12 (66.6%) showed positive on at least one patch test and nine gave more than one positive reaction. The majority of positive reactions were due to fragrances and metals. Products used in the fragrance industry to dilute materials and compounds used in hair coloring also showed positive results.

Conclusion: Patch-test positivity in FFA patients was high in our population, suggesting that contact allergy may be involved in these patients. Based on our results, we recommend that once FFA is suspected, patients should be patch-tested and advised to avoid applying leave-on cosmetics on the frontal hair line as part of their treatment.
be up-regulated in microarray analyses of affected and unaffected skin of LPP. This xenobiotic receptor in response to dioxin-like substances, is known to suppress PPAR-γ (Peroxisome proliferator-activated receptor-γ), related to the lipid metabolism in the sebaceous glands. The aim of this project was to study the AhR, its nuclear translocator (ARNT) and interleukin (IL)-17 in affected and unaffected scalp skin from patients with LPP and FFA.

Materials & Methods: Patients with biopsy-proven LPP (n=10) and FFA (n=26) at the Department of Dermatology - University of Sao Paulo were included in the study after IRB approval and signed informed consent. Biopsy samples from affected and unaffected scalp skin were obtained and placed in 10% formalin. Clinical and demographic data were gathered from medical charts. Skin samples from 10 matched healthy/control subjects were also obtained from similar scalp areas. The anti-aryl hydrocarbon receptor antibody - AhR (Abcamâ), aryl hydrocarbon receptor nuclear translocator - ARNT (Novus Biologicalsâ) and anti- IL17 (R&D Systemsâ) were applied following standard methodology and validated protocols. Descriptive statistics including either numerical or graphic representations to summarize the data were used. The expression of AhR, ARNT and IL17 in AFF, LPP and control groups was compared by nonparametric Kruskal Wallis test. Results: No significant differences were found in AhR, ARNT and IL17 results in scalp biopsies of affected skin from LPP and FFA groups compared to control subjects.

Conclusions: Despite previous hypothesis concerning the role of AhR and dioxins in the pathogenesis of LPP and FFA, ongoing research needs to continue so as to identify potential environmental agents other than AhR and dioxins involved in the pathogenesis of these scarring alopecias.
COMMENT ON THE SCIENCE OF HAIR AGING

In contrast to the skin, aging of the hair has seemingly only recently found the attention of dermatological meetings, mainly promoted by the cosmetic industry for marketing purposes. In fact, basic scientists interested in the biology of hair growth and pigmentation have for some time already exposed the hair follicle as a highly accessible model with unique opportunities for the study of age-related effects. As a result, the science of hair aging focuses on two main streams of interest: the aesthetic problem of aging hair and its management, in terms of age-related effects on hair color, quantity, and quality; and the biological problem of aging hair, in terms of microscopic, biochemical, and molecular changes underlying the aging process. Ultimately, the aim of hair anti-aging is to delay, lessen or reverse the effects of aging on hair. According to the complex nature of the aging process, the treatment for lifetime scalp and hair health has to be holistic to include the multitude of contributing factors in a polyhedral and patient-specific manner. It comprises both medical treatments and hair cosmetics. Accordingly, the discovery of pharmacological targets and the development of safe and effective drugs for treatment of hair loss indicate strategies of the drug industry for maintenance of hair growth and quantity, while the hair care industry has become capable of delivering active compounds directed toward meeting the consumer demand for maintenance of hair cosmesis and quality.

HAIR PHOTOAGING AND INTEGRAL HAIR LIPID

Hair aging is manifested as various deteriorated phenotypes such as decrease of hair production, loss of hair color and altered structural integrity of hair fiber itself. Bio-physiological aging of hair follicles cause senescent alopecia and androgenetic alopecia (AGA). It also causes hair graying from pigmentary change. On the other hand, mechano-physical aging of hair fiber causes various surface changes and structural fragility of hair shaft collectively termed as hair weathering or “Hair shaft aging”. Among the various extrinsic causes, ultraviolet light is the most important damaging factor to hair fiber and results in unavoidable hair photoaging. Although main body of hair fiber is mainly consisted of hair keratin-specialized hair protein, integral hair lipid (IHL) which cement and connect various layers within hair cuticle and hair cortex is crucial element to keep structural integrity of hair fiber. Anti-hair photoaging strategy should be focused on this area of hair shaft. So, key manifestations of hair photoaging and importance of IHL in maintenance of surface property and mechanical integrity of hair fiber, and practical strategy to overcome hair photoaging, at least partly, will also be covered in this presentation.
Hair thinning (senile alopecia) is a typical aging phenotypes in mammals. Hair follicles miniaturize by aging and some other causes for alopecia. Our previous study with analysis of hair follicle stem cells (HFSCs) revealed that mouse hair follicles age through the defective maintenance of HFSCs. In vivo fate analysis of aged HFSCs revealed that they differentiate into epidermal keratinocytes through the proteolysis of hemidesmosomal transmembrane collagen COL17A1, thereby causing their depletion and the resultant typical hair aging phenotypes in a stepwise manner. To further understand the hair follicle aging program, we focused on stem cell division types and found that hair follicle aging is driven by a distinct cell division program of HFSCs. We found that the age-associated instability of hemidesmosomes that anchor HFSCs to the basement membrane provokes “senescent-type” asymmetric cell divisions. Those asymmetric cell divisions directly generate strings of aberrantly differentiating epidermal keratinocytes by repetitive asymmetric cell divisions and repress symmetric cell divisions. That program efficiently eradicates aged stem cells thereby causing organ aging. Conversely, the forced stabilization of hemidesmosomes rescued organ aging through recovery of regular cell division program. These results demonstrate that a stem cell division program orchestrates tissue/organ aging.
Introduction: With age, female scalp hair volume and density are reduced, accompanied by a change in the fibre texture. We hypothesize that these external aesthetics originate from alterations within the scalp dermal hair follicle environment and drive changes within the many components of the hair follicle. Therefore, we have compared age-related changes associated with the extracellular matrix (ECM) of scalp derived primary cultures of dermal fibroblasts (DFs) and hair follicle dermal sheath cells (DSCs) from female donors (19-81 yrs) and determined whether these are reflected in changes in-situ.

Materials & Methods: Primary cultured DFs and DSCs were established from female scalp (19-81 yrs, n=16) and those from women <40yrs directly compared with those from women >40 yrs to assess age-related changes in mRNA expression of ECM markers: hyaluronic acid synthase 2 (HAS2), matrix metalloproteinase-1 (MMP-1), protease nexin 1 (SERPINE2), collagen XVI (COL16A1), versican (VCAN) and cartilage oligomeric matrix protein (COMP) using qRT-PCR. Expression of 67 proteins associated with protease activity were studied using a profiler array (R&D systems, cat# ARY025) using cell lysates from DFs and DSCs. To assess whether the same age-related changes occurred in situ, immunohistochemistry of cryo-sectioned scalp tissue from women aged 19-81 yrs (n=16) was also performed.

Results: DF mRNA expression of COMP remained unchanged, though SIRT-1, HAS2, COL16A1, SERPINE2, and VCAN were significantly (p<0.05) reduced with age, while MMP-1 mRNA was increased (p<0.05). In contrast expression of these genes did not change with age in DSCs, apart from SERPINE2 which was reduced. In both DFs and DSCs in vitro, there was a >2-fold increase in the expression of MMP-3 protein with age, furthermore, DSCs showed an increase in the expression of cathepsin L, cathepsin S, CD26, MMP-2, CD10, and urokinase proteases. In situ, expression of the papillary dermis marker podoplanin was reduced in women >60 yrs. While HAS2 was highly expressed throughout the scalp, there was no change with age. In women >40 yrs MMP-1 was increased in the dermal papilla (DP), DS and reticular dermis, while SERPINE2 increased in the DP and DS.

Conclusion: Significant changes associated with remodelling of the ECM were identified in both interfollicular DFs and follicular DSCs from female scalp with increasing age. A significant increase in proteases in DSCs with age may contribute to the aged hair follicle phenotype.
Hair follicle aging

Chairs: Won Soo Lee, Kevin McElwee

Chair: Won Soo Lee, Kevin McElwee

Hair follicle aging

Gen, glucose polymer, the main energy storage site in the human body. Surplus lactate can be converted to glucose and glycogen through gluconeogenesis. The aim of this study was to investigate the functional role of glycogen metabolism and the possibility of internal Cori cycle operating in HF.

Methods: We performed analysis of glycogen and its metabolism enzymes in anagen and catagen hair follicles and tested the impact of manipulating glycogen synthesis and breakdown in outer root sheath (ORS) keratinocytes and whole hair follicles on glycogen and protein levels.

Results: Glycogen occurred abundantly in the ORS and the cuticle of anagen HF and was significantly decreased in catagen and absent in telogen HF.

Comment: Essential glycogen metabolism enzymes showed distinctive expression patterns: glycogen phosphorylase (PYGL) in the ORS, phosphoglucomutase (PGM1) was expressed in the basal ORS, cuticle and hair matrix, whereas glycogen synthase 1 (GYS1) was mainly expressed in the basal ORS and the IRS (Inner Root Sheath). Glucose uptake in whole HF using a fluorescent glucose derivative after 30 min showed accumulation in the ORS, precortex and hair cuticle and after 24h in the ORS with clear glycogen accumulation. Treatment of primary ORS keratinocytes with PYGL inhibitor showed that ORS keratinocytes actively synthesise and metabolise glycogen. In whole HF, inhibition of PYGL increased hair elongation in vitro, maintained ORS glycogen and delayed the anagen to catagen transition. We have previously shown HF can synthesise glycogen from glucose. We now show that an essential enzyme for gluconeogenesis, phosphoenolpyruvate carboxykinase (PCK1) is present in the ORS and that ORS keratinocytes incubated with lactate show a significant increase in GYS1 and glycogen levels suggesting that the ORS is able to synthesise glucose and subsequently glycogen from lactate and hence engages in both gluconeogenesis and glycogen synthesis.

Conclusion: We show human HF have the capability to synthesise glycogen from lactic acid implying an internal HF Cori cycle. These data provide insights into the glycogen metabolism and we suggest that glycogen may be an osmotically neutral mechanism of HF glucose storage. Further we also propose that the human HF engages in a glycogen shunt which allows the HF to maintain glycolytic intermediates and ATP during large shifts in glucose supply or demand.

HYPOXIA, HIF1A AND HAIR FOLLICLE METABOLISM

Introduction: HIF1A is considered the master transcriptional regulator of cellular response to hypoxia. Hair follicles (HF) are reported to express markers of hypoxia and also preferentially engage in aerobic glycolysis which is the preferential metabolism of glucose to lactate despite the presence of oxygen. HIF1A regulates glucose metabolism promoting glycolysis and increases the expression of angiogenic factors. Compounds such as iron chelators are routinely used to enhance HIF1A accumulation. HIF activity induces the expression of VEGF, a gene that is known to be associated with improved hair growth.

Methods: In this study, we have investigated the localisation of HIF family members in human skin and HF and the impact of HIF1A stabilisation on glycolysis.

Results: HIF1A, HIF1B and HIF2A expression was observed within the epidermis, sebaceous glands and HF. HIF1B, a non-oxygen dependent protein, showed the strongest staining within the HF and epidermis. Staining of isolated HF shows strong positive nuclear staining for HIF1A, HIF1B and HIF2A in the outer root sheath (ORS) and this increased in follicles treated with iron chelators (HIF stabilizers). WaferGen analysis confirms hypoxia mimetics used in the study
Hair follicle aging

Chairs: Won Soo Lee, Kevin McElwee

drive VEGF induction in ORS keratinocytes. Validation with nuclear lysates for HIF target genes confirmed HIF activity within this compartment of the HF.

Comment: To study the functional role, metabolic analysis using a Seahorse metabolic analyser showed ORS cells from a balding scalp engage in more under mitochondrial respiration than ORS of non-balding HFs. We have previously shown that balding DP cells in vitro are more sensitive to oxidative stress and ROS than non-balding and undergo premature senescence.

Conclusion: HIF1A stabilisation by promoting glycolysis over oxidative phosphorylation may reduce oxidative stress and promote hair growth.
Illness impact on HrQoL has been widely studied in hair loss-affected patients, yet no study has addressed whether individual differences modulate HrQoL in patients with alopecia areata (AA), androgenetic alopecia (AGA) and telogen effluvium (TE). To identify the personality dimensions most predictive of the impact of disease on HrQoL. A single-site cross-sectional study was carried out in the Dermatology Unit of Sant’Orsola-Malpighi Hospital, Bologna between September 2016 and September 2017. The study included 143 patients (105 females, ages 18-60 years) diagnosed with AA (n = 27), AGA (n = 80) and TE (n = 36). Illness severity, alopecia type, age, gender, education and civil status were documented. Health-related quality of life (HrQoL), personality traits, trait anxiety, emotional intelligence, social anxiety and social phobia were also measured. AA, AGA and TE groups differed significantly for illness severity with most severe patients falling in AA type. For HrQoL, Gender 9 Group interaction resulted significant with AGA females reporting a higher impact of hair loss on quality of life than males, while TE males were more impacted by hair loss than AA and AGA males. Lower scores were obtained by AGA females than males on emotional intelligence while no significant differences were evidenced on other groups. A significant Gender 9 Group interaction was also found for trait anxiety, social phobia and social anxiety: consistently, AGA females reported higher scores than AGA males in all three measures. Finally, discriminant analysis evidenced that anxiety-related traits can contribute to reliably predict hair loss impact on HrQoL, regardless of illness severity and alopecia type. We recommend that gender and individual differences in anxiety-related dimensions be considered as key factors in gaining a deeper understanding of hair loss impact on quality of life as well as in reducing the burden of illness in alopecia-affected patients.

Currently available reports in the literature suggest that male pattern baldness can be associated with significant impact on quality of life, often with very serious psychological problems. Negative effects have been reported, which include lower self-esteem, perception of physical unattractiveness, depression, emotional distress, greater self-consciousness, anxiety and psychosocial maladjustment. In addition, dissatisfaction with appearance, preoccupation with hair loss, worry about others reactions, and fear of social teasing. Further studies suggest that people’s initial impression of men with male pattern baldness is generally less favorable that in men without hair loss. Balding men are viewed as less desirable in a physical, personal and social sense. On the other hand, some authors suggest that the presence of a preexisting personality disorder, may determine whether a person has a psychological problem with alopecia. The same degree of alopecia will be tolerated differently depending on the preexisting personality or psychological disorder of the balding man. So, the question that arises in front of a patient with male pattern baldness is: Will he be better treated and consequently more satisfied if he receives effective anti alopecia agents or will he get more benefit if evaluated and treated for his psychological disorder?
AUTO-INDUCED HAIR LOSS

Dermatologists are often the first physician patients seek regarding alopecia of various causes. “Auto-induced hair loss” is a wide spanning term that one may construe to encompass those conditions that are self-induced psychotropicological disorders and traction alopecia. A sharp recognition of some clinical subtleties, knowing how to read specific dermatoscopy findings how to properly exclude the differential diagnoses, and finally an adequate referral are all essential tasks in the evaluation of these patients. An incorrect diagnosis lets the condition progress and delays proper treatment initiation, which is nevertheless frequently challenging and guided by insufficient scientific data, so far. This talk will show that there are clinical and dermatoscopy clues that are shared between the rarer and commoner conditions, under this term. A series of brief clinical cases will be presented as guide to the talk with a narrative review of literature regarding the main diagnoses.
ADAPTIVE AND MALADAPTIVE BEHAVIOR IN ALOPECIA PATIENTS: HOW CLINICIANS CAN INFLUENCE BOTH

**Introduction:** The dermatologist, the trichologist or the family doctor are the first health care professionals that patient with alopecia will come to visit. The first and further meetings can make a significant contribution to the choices of alopecia patients for their strategy of adaptation with their baldness.

**Method:** The two studies aimed to gather appropriate data and to discuss the following question: how and to what extent the clinician’s emotional reaction to the patient’s condition and the way of information about the prognosis and possible treatment has led to more adaptive or maladaptive behavior of a patient.

Two studies: the qualitative and quantitative were conducted involving (6 + 56) alopecia patients from the alopecia community in Lithuania.

- The qualitative research: The data of the qualitative study was gathered using the method of non-structured interview, and the analysis of the phenomenological approach of P. Colaizzi was used. Four women and two men with varying degrees of alopecia areata and one with androgynous alopecia were interviewed.

- The quantitative research: The online survey was conducted and 56 volunteers diagnosed with alopecia took participation. The two questions related to the aim with an option to write the individual answer were asked: “How the doctor informed you about the diagnosis?”; “Are you satisfied with the information provided by the doctor and treatment?”.

**Results:** The qualitative study shows that patients with alopecia use complex strategies to deal with the hair loss challenge: a) avoiding any publicity b) exploring the reason for the disease and trying to cure in any possible way c) mindset changing: from rationalization to self and public awareness d) searching for the psychosocial help.

**Discussion:** Both studies are not showing straight roads from doctors reaction to the choice of a better or worse adaptation of alopecia patient. There are a much more significant amount of variables influencing further behavior. But still, we can see some tendencies in patients reported reactions after the visit to the doctor which can lead them to better or worse adaptation for years.

SUFFERING IN WOMEN WITH FRONTAL FIBROSING ALOPECIA

**Introduction & Objectives:** Frontal Fibrosing Alopecia (FFA) is a primary scarring alopecia that was described in 1994. It predominantly affects women, most often in menopause. Studies show that alopecias, in general, may have stress as a triggering factor. Regarding cicatricial alopecias, especially the FFA, the relevance of this causal factor was little studied.

Based on analytical psychology, this study aimed to evaluate the role of suffering (considered a stressful factor) in the biography of women with FFA before and after the onset of the disease.

**Material & Methods:** The study included 12 women with a diagnosis of AFF performed clinically and confirmed by biopsy. The sociodemographic questionnaire, the quality of life inventory in dermatology (DQLI) and a semi-structured interview with a mean duration of 2 hours were used for the research. The interview was recorded and transcribed for analysis of its content.
Results: The patients had a mean age of 54.7 years and a mean monthly income of 2000 US dollars. Among the patients, five had autoimmune disease, two with Hashimoto’s syndrome and three with arthritis. The thematic analysis of the interviews about the period before the emergence of the AFF found intense reports of frustrations, impotence in the face of life, insecurity, loss, shame and loneliness.

Discussion: DQLI demonstrated that AFF had an impact on patients’ quality of life. The information obtained by the interview about suffering after the appearance of AFF pointed to sadness, loss of identity, fear, insecurity, concern about people’s opinions about AFF and impotence in the face of life. Suffering as a stressor was present in the biography before and after the appearance of AFF. Analytic psychology suggests that stressful events such as suffering may promote the emergence of clinical manifestations of a psychoneuroimmunoendocrinologica character such as those suggested as causes of AFF. The data obtained by DQLI were reinforced by the themes that emerged in the interview, suggesting that patients with FFA have a high level of suffering caused by the disease. The use of the interview as a tool to collect information allowed a better understanding of the themes related to the most frequent causes of suffering for each patient in the period of life prior to the FFA, as well as reinforced the information of the DQLI allowing a clearer understanding of the suffering caused by the FFA. Clinical psychology evaluation methods, such as interviews, can help to identify more clearly the stressful issues in patients’ lives by collaborating with a better understanding of how stress can act as an epigenetic agent as well as which feelings a disease like frontal fibrosing alopecia can trigger.

PATIENT REPORTED STRESS CAUSED BY SCALP ALOPECIA IN TRANSPEOPLE

Introduction & Objectives:
Body, facial, and scalp hair represent critical components of gender identity. For transgender and gender-nonbinary patients, the impact of scalp hair loss may be particularly distressing, especially for transwomen who may develop male pattern hair loss. In transmen, use of testosterone leads to androgenetic alopecia in up to one-third of patients. While some transmen may embrace hair loss as masculine, others may find new hair loss bothersome and seek treatment similar to some cisgender men. In this study, we thus aimed to understand the emotional impact of scalp alopecia in transgender patients.

Material & Methods:
This study used a secure, web-based software to distribute an online survey through transgender-focused groups on social media in fall 2018. Inclusion criteria required respondents to be at least 18 years old, identify with the transgender community, and live in the United States. The survey included a dual visual analogue scale and numeric rating scale (NRS), asking patients to report the number (0-100) that best indicated the degree of stress their hair loss was causing them (0, no stress; 100, worst stress imaginable). The Partners Healthcare Institutional Review Board granted an exemption from review.

Results:
In total, 991 people responded to the survey with a 77% completion rate. The mean age of participants was 32 years old (range 18 to 77), and most identified as transmen (62%), transwomen (26%), and gender-nonbinary (11%). Over 88% of respondents had medical insurance and reported use of gender-affirming hormones. Of those reporting scalp hair loss and thinning, the median NRS score was 66 (mean 61, range 0 to 100). Transwomen identified a significantly higher NRS score (mean 75) of stress related to scalp hair loss/thinning than both transmen (mean 49, p < 0.001) and gender-nonbinary people (mean 63, p = 0.023). Respondents who self-reported higher alopecia severity scores on the Hamilton-Norwood and Sinclair scales (greater than severity 2 on each scale) identified a significantly
Psychological aspects of hair disease

Chairs: Ramon Grimalt, Michela Starace

higher NRS score (mean 75) than respondents who self-reported more mild alopecia severity (mean 56, p < 0.001). There was no significant association between patient reported NRS scores and use of gender affirming hormones or medical insurance status.

Conclusions:
As demonstrated by patient-reported stress using the dual visual analogue and numeric rating scale, scalp hair loss and thinning represent substantial stressors in the gender expansive population, especially among transwomen. Severity of scalp alopecia was further associated with higher reported stress. Recognizing the limitations of this non-validated survey and convenience sample, it is critical that clinicians appreciate the social, psychological, and medical impact of alopecia in transgender and gender-nonbinary patients.
How developmental programs are reactivated in regeneration is a fundamental question in biology. We addressed this question through the study of Wound Induced Hair follicle Neogenesis (WIHN), a model where stem cells regenerate entirely new hair follicles de novo in adults following deep wounding. The exact mechanism and human applicability of WIHN is uncertain. Here we show that noncoding dsRNA activates the anti-viral receptor TLR3 to induce intrinsic retinoic acid (RA) synthesis and new hair follicle formation after wounding. Transcriptome and proteome analysis revealed an unexpected dramatic overlap of upregulated genes after dsRNA or RA treatment to keratinocytes, many of which inhibit differentiation. Given the role of RA in patterning appendage embryonic development, we hypothesized dsRNA induces RA in adults to promote WIHN. dsRNA stimulates ALDH1A3 transcription to robustly increase RA synthesis in normal mice but not in TLR3-deficient mice, which have lower baseline RA levels. In adult mouse wounds, a dsRNA induced RA morphogen gradient predicts areas of future regeneration. Importantly, the RA receptor RARα is required for WIHN under homeostatic conditions and for exogenous dsRNA induction of stem cell markers and WIHN. Exogenous RA rescues the impaired regeneration in TLR3-deficient mice. Finally, in human subjects, rejuvenating laser treatment similarly induces endogenous RA synthesis. These results demonstrate a novel mechanism of reactivating developmental pathways in adult regeneration and imply a linkage between dsRNA sensing and RA in their broad functions.

Intermediate human hair follicles, midway in size between terminal and vellus follicles, have been morphometrically characterised and established as being a more clinically relevant model for hair growth investigations. Furthermore, they have recently been demonstrated as the first human organ involving multiple cell types that responds appropriately to hormones (testosterone) in prolonged culture, mirroring natural behaviour. Since the prostamide F\(_2\alpha\) (bimatoprost) stimulates terminal hair growth and is licensed for the treatment of eyelash hypotrichosis, we aimed to determine whether the natural prostaglandin F\(_2\alpha\) (PGF\(_2\alpha\)), would affect the growth of the more clinically-relevant intermediate facial hair follicles in organ culture. Matched terminal and intermediate pre-auricular hair follicles from 6 adult women were grown in organ culture with, or without, PGF\(_2\alpha\) or PGF\(_2\alpha\) + PGF\(_{2\alpha}\) receptor antagonist. RT-PCR and immunohistochemistry were undertaken to confirm gene expression and the location of the PGF\(_{2\alpha}\) receptor within both hair follicle types. Intermediate follicles grew less quickly than terminal follicles under control conditions, as assessed by daily observations and length
measurements, resulting in the synthesis of significantly less hair. PGF$_{2\alpha}$ stimulated both terminal (T) and intermediate (I) follicles to synthesise more hair (T $p=0.016$, I $p<0.001$), increase the percentage of follicles remaining in anagen (T $p<0.01$, I $p<0.001$) and their rate of growth (T $p=0.014$, I $p<0.01$). Interestingly, PGF$_{2\alpha}$-treated intermediate follicles synthesised similar amounts of hair ($p=0.708$) and increased the percentage of follicles in anagen (T $p=0.055$) to that of terminal follicles in control medium. Adding the PGF$_{2\alpha}$ receptor antagonist significantly reduced the amount of hair produced, the rate of growth and percentage of follicles in anagen by both terminal and intermediate hair follicles. This first demonstration of increased hair growth in intermediate hair follicles in response to prostaglandin stimulation via the PGF$_{2\alpha}$ receptor has potential clinical significance including extended application during surgical reconstruction of hair-bearing areas, alopecia, or in men with insufficient beard growth.

**PROGENITORS, PROLIFERATION AND PROSTAGLANDINS: HETEROGENEITY OF THE HUMAN ANAGEN HAIR FOLLICLE OUTER ROOT SHEATH**

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Human scalp hair follicles (HFs) remain in anagen and sustain continuous hair growth for years at a time. The outer root sheath (ORS) is a fundamental constituent of the terminal anagen VI scalp HF, spanning from the isthmus to the outermost hair bulb epithelium, where it is contiguous with the lower proximal cup. The human anagen ORS is highly heterogeneous in its compartmental organisation and is not just home to quiescent bulge epithelial stem cells but also to keratinocyte sub-populations that exhibit dynamic behaviours. Residing within and across morphologically and functionally distinct zones, the ORS contains multiple epithelial stem and progenitor cell populations that can be demarcated by their differential expression of key stem cell markers (e.g. KRT15, KRT19, CD200, CD34, NFATC1, SOX9, LHX2). Whilst relatively slow cycling compared to the hair matrix, patterns of ORS proliferation within distinct progenitor-cell demarcated zones of the anagen HF also show marked inter-compartmental differences, as well as intra-compartmental differences in situ i.e. between basal epithelial progenitors and their immediately adjacent suprabasal progeny. Emphasising the functional heterogeneity of the ORS, unique stem/progenitor cell populations show differential cell cycle responsiveness to hair growth-inhibitory prostaglandins i.e. prostaglandin D2 (PGD2) and 15-deoxy-Delta(12,14)-prostaglandin J2(15-d-PGJ2). It has previously been reported that hair growth-inhibitory prostaglandins act through GPR44 signalling. Notably, in situ protein expression analyses in the human HF reveal that anti-GPR44 immunoreactivity localises most prominently to the ORS rather than the hair matrix, with a staining pattern that suggests a link between GPR44 receptor localisation and compartment-specific cell cycle responses to PGD2 and 15-d-PGJ2. Together these observations build a more complete picture of the characteristics of the human ORS that promote investigation into stem/progenitor compartment-specific biological roles and responses in the context of clinical, basic and cosmetic human HF research.
**COMBINED DIFFUSE AND PATCHY HAIR HETEROCROMIA WITH BLASCHKOID DISTRIBUTION**

**Introduction.** Hair heterochromia is characterized by the presence of hair of at least two different colors in the same person. Symmetric distribution of heterochromic hair can be physiologic or caused by systemic diseases or medications, and asymmetric distribution indicates a pigmentation disorder. Three types of heterochromia have been previously described according with the pattern of distribution: focal (patchy), segmental and diffuse. Patchy heterochromia is characterized by a well-circumscribed tuft of hair with a different color, segmental - by alternating bands of different color in individual hairs, and diffuse - by hair with two different colors evenly distributed in the entire scalp. We present a 13-year-old boy with combined diffuse and patchy hair heterochromia with Blaschkoid distribution.

**Case report.** A 13-years-old boy with light-brown hair presented with a patch of dark-brown hair in the posterior vertex. The rest of the hair on his scalp were light brown. The differently colored hair had been present since infancy and expanded gradually with the growth of the skull. His medical history was unremarkable. There were no similar findings in other family members. On exam there was well-demarcated tuft of dark-brown hair at the vertex and additional tufts in parietal and nuchal areas, with arrangement respecting the Blaschko lines. Under dermoscopy the heterochromatic hairs were consistent in color along the hair shaft. In addition to demarcated patches of heterochromia diffuse heterochromia was observed all over the scalp. Scalp skin underlying the differently colored hair did not show any abnormality. Skin examination of the body and extremities as well as general examination were normal. There were no ocular abnormalities, hearing or neurocognitive impairment. Laboratory investigation, including CBC, biochemistry, total iron binding capacity, ferritin, copper, magnesium and zink levels was normal. An examination of the hair under a light microscope revealed a homogenous distribution of pigment along the hair length and did not show any structural abnormalities. A diagnosis of combined patchy and diffuse scalp hair heterochromia was made.

**Discussion.** Rare cases of heterochromia of scalp hair following Blaschko lines have been reported and classified as patchy (focal) heterochromia. It was hypothesized that the isolated heterochromia of sporadic occurrence can be expression of somatic mosaicism of genes affecting pigmentation. Pigmentary mosaicism represents a heterogeneous group of disorders that share the common feature of areas of hyper and hypopigmentation. These areas are usually are have a specific pattern of distribution following lines of Blaschko. The specific genetic alterations that give rise to mosaicism are extremely heterogeneous. Here we report what to our knowledge is the first case of patchy heterochromia in a Blaschkoid distribution in conjunction with diffuse heterochromia of scalp hair.

**SCARING ALOPECIA IN PSORIASIS**

**Background.** Psoriasis is a common skin disorder with typical presentation on a scalp skin. In the vast majority of cases scalp psoriasis does not lead to alopecia. However there were some ceses of scarring alopecia in a psoriatic patient published in which there was no other disease which could lead to alopecia besides psoriasis. Thus scarring alopecia in psoriasis remains the matter of debates.

**Clinical case.** We describe a 33 y.o. female patient who was...
Clinical Cases from Eastern Europe

Chairs: Julya Ovcharenko, Tatiana Siliuk, Nino Lortkipanidze

sessions saturday, april 27th

Chairs: Julya Ovcharenko, Tatiana Siliuk, Nino Lortkipanidze

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Diagnosed scalp psoriasis 8 years ago. Lesions were limited to scalp skin only and never involved other areas. During that time her condition was poorly controlled and it has progressed with formation of scarring alopecia. She has no family history of psoriasis or scarring alopecia. Clinical examination revealed a big area of scarring alopecia in fronto parietal area, surrounding areas showed marked inflammatory changes of the skin with yellowish crusty scaling. Trichoscopy showed perifollicular scaling, and elongated twisted red loops in a peripilar arrangement, and in the central area lack of follicular openings and other signs of scarring alopecia. Blood tests (general, biochemical) were normal. The only change in hormones was elevated DHT (1170...2600pg/ml, normal range up to 368pg/ml). MRI did not reveal any tumor that could be associated with the elevation of DHT. Bacteriologic tests returned Staph. aureus 10^5, mycological test has shown C. albicans growth. Patient improved on itraconasole and doxycycline in terms of reduction of the crusts but hair did not regrow. Patient diagnosed folliculitis decalvans clinically and was biopsied. Histological examination revealed psoriasiform changes of the epidermis and signs of scarring alopecia. These changes were considered psoriatic scarring alopecia by pathologist.

Discussion
Psoriasiform changes of epidermis in folliculitis decalvans were recently described. Our patient shows similar changes and confirms observations. But the nature and role of elevated DHT remains unclear. Pathophysiologic mechanisms of influence of psoriasis or psoriasiform dermatoses and scarring alopecia as well as the mechanism of psoriasiform changes in folliculitis decalvans are still to be studied. Recent studies suggest that these disorders may share some pathophysiologic mechanisms and may have more in common than it was previously considered.

References

Alopecia Areata: Clinical and Therapy

Alopecia Areata (AA) is a genetically determined chronic inflammatory disease of hair follicles. Mechanisms of AA development are based on cell-mediated local immune reactions connected with T-lymphocytes (CD8+ and CD4+) and changes of cytokine profile, which leads to the formation of non-specific autoimmune inflammation under conditions of violation of immune tolerance of hair follicle. Search of triggers which lead to the immune imbalance and hair loss in AA is of current interest. The study of comorbidity is a priority for modern medicine. Suggesting a causal relationship between various diseases in AA, an analysis of comorbid diseases can provide important etiological information; it focuses on the clinical prognosis and possible additional triggers. The different degrees of ‘interaction’ of AA and associated diseases should be taken into account. It is known that patients with AA are susceptible to an increased incidence of the development of immune-inflammatory pathology, including autoimmune diseases, atopy, and mental disorders. Several papers have described the combination of AA with malignant diseases. Single reports on the risk of developing oncological pathology in patients with AA are published. A case of the development of a total form of AA in a 62-year-old female patient in combination with primary non-Hodgkin’s lymphoma of the stomach (MALT lymphoma) is presented clinically. Lymphoma was diagnosed 4 months af-
ter the start of AA. It can be assumed that the clonal proliferation of lymphocytes observed in lymphoma leads to an immune imbalance and the spread of an immune attack on the hair follicle with a violation of the immune privilege. At the same time, genetic aberrations that violate cell proliferation and apoptosis processes are involved. It is possible that lymphoproliferative processes in lymphoma are one of the potential triggers of AA.

It should be taken into consideration that the severity of AA during the first appearance in older patients is usually mild, and more than half of adult patients with AA have less than 10% of the scalp lesion. Consideration of AA as paraneoplastic dermatosis in patients with debut and rapidly progressive course of the disease at the age of 50 years and older is relevant.

**HAIR LOSS DISORDERS SIMULATING ANDROGENETIC ALOPECIA**

Androgenetic alopecia (AGA) is the most common hair loss disorder, affecting both men and women. Androgenetic Alopecia is the cause of more than 95% of all cases of pattern hair loss, including baldness in men and thinning hair in women. Diagnosing Androgenetic Alopecia, is not a complicated process, as we know classification of AGA, the signs of MPHL and FPHL, their diagnostic algorithms, the required laboratory tests, etc. However, diagnostic errors are not so rare, not only between AGA and Telogen Effluvium or Frontal Fibrosing Alopecia, but also between AGA and Trichotillomania.

We suggest using trichoscopy to prevent these diagnostic errors, for all types of hair loss, in the future.

**PSORIASIS AND CONCOMITANT HAIR LOSS**

Psoriasis is a chronic, inflammatory, immune-mediated dermatosis affecting 1-3% of the general population. Psoriasis is characterized by formation of well-demarcated plaques with silver scales. The clinical presentation ranges from mild disease to more severe forms, involving large areas of skin and/or joints. Scalp is one of the most common affected area of the disease and almost 80 % of psoriasis patients usually present with it. Occasionally, scalp psoriasis may be associated with either increased hair density or psoriatic alopecia. Hair loss is demonstrated on the areas affected by psoriatic lesions. In most cases, there is a regrowth of hair, but sometimes it can cause scarring alopecia. It is not rare when psoriasis is in combination with other diseases such as alopecia areata, telogen effluvium, but there is a rare combination, such as psoriasis and trichoteiromania.

**PEDIATRIC CASES**

The causes of alopecia often found in adults (e.g., androgenetic alopecia) are rare in children and, by contrast, the conditions that occurs in children are rarely diagnosed in adults (e.g., loose anagen hair syndrome, tinea capitis). The diagnosis of alopecia in children is a clinical chal-
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lenge. The examination should be as noninvasive as possible. Trichoscopy as an easy and non-invasive method can be easily applied to diagnose hair loss during childhood. First of all, trichoscopy enables to diagnose a particular genetic syndrome (monilethrix, pili torti, trichorhexitis invaginata). The majority of alopecia in children is presented as patchy alopecia, which is most commonly diagnosed as alopecia areata. However, other causes of patchy alopecia such as tinea capitis, trichotillomania, temporal triangular alopecia, and aplasia cutis congenita can be missed. Trichoscopy can easily confirm alopecia areata due to its particular trichoscopic features: exclamation mark hairs, yellow and black dots, and caudability hairs. The prevalence of regrowing hairs in alopecia areata patches in children (upright regrowing hairs, circle hairs and vellus hairs seems to be slightly higher than in adults. The differential diagnosis of diffuse alopecia in children includes telogen effluvium, congenital hair shaft abnormalities, diffuse alopecia areata and loose anagen hair syndrome (LAHS).

**OUR EXPERIENCE OF TREATMENT DISSECTING CELLULITIS OF THE SCALP WITH COMBINATION OF HIDRADENITIS SUPPURATIVA/ACNE INVERSA**

Hidradenitis suppurativa/acne inversa (HS) is characterized as a chronic, inflammatory, recurrent, debilitating skin disease of the hair follicle. The definition of the disease was formulated at the 1st International Conference on Hidradenitis suppurativa/Acne inversa (2006). In a clinical practice HS is found as a skin disease involving inverse regions of the body. We can see display of the disease in such areas as in the axillae, inguinal and anogenital without inflammation on the scalp. It can also be found in combination with Dissecting cellulitis (Perifolliculitis Capitis). According to our experience we noticed that the different involvement of the skin areas is correlated with efficacy of isotretinoin treatment. 8 male and 1 female patients with HS were examined. The age of males was 19 to 43 years; the female was 23 years old. The clinical picture of the patients: two male patients had the rash localized in the axillae, inguinal and anogenital regions, on the faces there was acne conglobata and the scalp was also involved as Dissecting cellulitis (Perifolliculitis Capitis). On the tailbone we discovered pilonidal sinus. In the dermatology publications this clinical picture is also called Follicular occlusion tetra. The clinical manifestations of 3 male patients were only in the form of acne conglobata on the faces and Dissecting cellulitis on the scalp and last 3 male patients had inflammations in the axillae, inguinal and anogenital regions, and pilonidal sinus without lesions of the scalp skin. The female had inflamed lesions in the axillae, inguinal and anogenital regions, infra-mammary area and on the back. There was also pilonidal sinus, however the skin on the scalp wasn’t involved. All the patients had the same clinical pictures regarding nodules (inflamed or non-inflamed), sinus tracts (inflamed or non-inflamed), abscesses, scarring. According to severity classification proposed by Hurley all the patients were diagnosed with the Stage II. All the patients had a long period of treatment with antibiotics, but all of them concluded that the treatment was effective for several months, eventually relapsing. Following up the Guideline on Hidradenitis suppurativa, the Isotretinoin isn’t recommended in the first line of the therapy. However, in this case, we treated the patients retrospectively, against the background of ongoing or complete therapy. Patients had been taking Isotretinoin 0,5mg/kg for period of 9-15 months. Due to the therapy, a satisfactory result (absence of inflammation and new lesions) was observed only in patients with a pathological process on the scalp and the effectiveness was noted not only on the scalp, but also in other parts of the body. If the lesions were localized on the body without damaging on the scalp, Isotretinoin treatment was ineffective, we noticed new foci of inflammation during the all period of treatment. Undoubtedly, this observation requires further analysis and final conclusions are still early to be made.
Frontal fibrosing alopecia (FFA) is a primary lymphocytic cicatricial alopecia. The incidence of FFA appears to be increasing, but its ethology is still unknown. FFA has a typical clinical picture of fronto-temporal scarring hair loss, follicular hyperkeratosis, absence of vellus and intermediate hair and variable perifollicular erythema. Eyebrow involvement is common with occasional involvement of body hair loss.

The condition is extremely challenging to manage with an often limited treatment response. A wide variety of topical and systemic pharmacological modalities have been reported in the literature.

This is the case of a 48-year-old woman who presented with a 1-year history of recession of the frontal hairline, associated with eyebrow loss. The patient was generally healthy person, didn’t present any allergic reactions or wrong habits. Patient had passed through a kidney surgery because of tumour 16 years ago, she had only one normally functioning kidney. Her grandfather had psoriasis. Her mother had tick, healthy hair, her father had androgenetic alopecia.

On examination, there was scarring alopecia and hair recession at the frontal and both temporal areas with perifollicular erythema at the affected hairline and almost complete loss of eyebrows. The clinical appearances were in keeping with FFA.

Full blood count of the patient did not show any significant abnormal deviations. Cholesterol was elevated, vitamin D level low. Autoimmune antibody titers, TPHA titers were negative. Erythrocyte sedimentation rate, Haemoglobin, TSH, Androsenedione, Ferritin all were in normal ranges. Trichogramma showed increased amount of dysplastic hair. On microscopy only small amount of oval spores and and Gram-positive bacteria were found which often is part of normal micro flora of the skin.

Patient received local therapy with corticoids, Minoxidil, local and systemic antiandrogens, herbal remedies, and vitamins (including vitamin D) and food supplements with zinc. After some period of treatment, no considerable improvement has been reached, so the decision was done to continue with triamcinolone acetonide (Kenalog®) injections on affected area. To increase the regenerative potential PRP was added. However, there is little experience about the outcome of PRP therapy in patients with FFA. In this case improvement in progression of disease and considerable decrease in inflammation were observed after the procedure.

When doing injections in scalp skin I usually use anesthesia with nitrous oxide (N2O) - laughing gas. It makes much easier for patient to withstand pain and stress related to injections. It is very easy to implement this technique in doctors practice. In my experience this approach helps to stabilize condition considerably faster, so it could be a useful option in treatment of FFA patients. Treatment still remains a challenge.

Three Cases of Scleroderma. Trichoscopic Features in the Early Stages

Introduction & Objectives: Scleroderma is a rare connective tissue disease manifested by cutaneous sclerosis and variable systemic involvement. It is known to be broadly separated into two major groups: systemic sclerosis which is characterized by sclerosis of the skin and visceral involvement, and localized scleroderma or morphea which classically presents benign and self-limited evolution, involving the skin and the subcutaneous tissue. Localized scleroderma is a rare disease of unknown etiology. Recent studies show that the localized form may affect internal organs and have variable morbidity. Because of its high morbidity treatment should be started as early as
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SESSIONS Saturday, April 27th

possible before complications occur. So, an early diagnosis is of great importance. We suggest the presence of such trichoscopic features as Pili torti may help in the early diagnosis of the disease.

Materials & Methods: We consider 3 cases of scleroderma localized on the skin of the scalp. A description of the detected trichoscopic features is given.

Results: We present 3 middle-aged women with scleroderma on the scalp. On examination, except for some other trichoscopic signs a large number of Pili Porti were also observed in a diffuse distribution. This feature is not so expressed with other cicatricial alopecia.

Conclusions: Our observations indicate that Pili torti can be regarded as a reliable sign, which may indicate scleroderma, especially in the early stages, in the absence of a clear picture formed.

ALOPECIA AREATA – MPHL LIKE PATTERN

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Introduction & Objectives: There are a number of different types of alopecia areata (AA). One of them is sisapeho, first described by Camacho and Muñoz in 1996. In addition, there are single reports of cases of AA with a type androgenetic alopecia (AGA) pattern.

Materials & Methods: We describe the case of diffuse form AA with a type androgenetic alopecia coexisting with Male Pattern Hair Loss (MPHL)

Results: We present a patient, male, 30 years old, who was diagnosed three years ago with androgenetic alopecia and had been treated with topical minoxidil 5% b.i.d. and oral finasteride 1 mg q.d. for one year with no obvious signs of improvement. The patient was presented with a clinically classic Hamilton-Norwood V, but trichoscopically we found not only signs of MPHL but also signs of AA distributed diffusely in the androgen dependent area of his scalp. These features include giant yellow dots with regular distribution, combining in groups according follicular unit, what distinguishes them from yellow dots for AGA. Also we found black dots, broken hairs. Trichoscopic examination of the occipital and lower temporal areas revealed no pathological features. The diagnosis MPHL + AA was made and to treatment were added topical clobetasol propionate 6 times a week and intralesional injections of triamcinolone acetonide 3 times a month. He responded with significant improvement and disappearance of trichoscopic signs of AA.

Conclusions: In this case we would like to show the importance of trichoscopy even with clinically clear diagnoses.

LPP AND HAIR TRANSPLANTATION: DO THEY GROW? TRICHOSCOPIC VIEW

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Introduction&Objectives: Hair transplantation (HT) is used in patients with inactive Lichen planopilaris (LPP). It has specific features at the stage of planning and follow-up. There are currently only few trichoscopic descriptions of hair regrowth from transplanted grafts in clinical studies and cases.

Materials&Methods: We describe a 18 months trichoscopic follow-up of two cases of HT with inactive LPP.
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Results: We present two patients, female, 36 years old and male, 35 years old with LPP hair transplant for 18 months post-op. Both patients showed no visible signs of inflammation for two years before HT. However, they had received medical treatment 6 months before and 6 months after HT to minimize the risk of reactivation. The patient female underwent FUT 1925 grafts and the patient underwent FUE 2500 grafts. The both of them have visible improvement of their hair and no signs of LPP reactivation. We observed the regrowth of new hair with a sharp tip at 3-5 months post-op and also uninterrupted hair growth of some transplanted grafts (the hair cycle did not stop and they continued to grow).

But the trichoscopic studies done at 6, 12, and 18 months post-op showed that some transplanted grafts retain short and shaved hair shafts. We suppose these are the same shafts that were in grafts on the day of HT. They did not fall out, but they did not grow either. We remove a couple of these shafts with forceps and found the terminal anagen roots with loss of the root sheaths. In our opinion these follicles are obviously dead (in this place where we remove hair shaft we did not find any trichoscopic indications of the follicle ostia after some time). But they keep their shafts because of underlying fibrosis due LPP. Even frequent washing and use of minoxidil for 18 months did not lead to their loss.

Conclusions: The trichoscopic studies done at 3,5,6,12, and 18 months post-op showed the regrowth of new hair with a sharp tip, uninterrupted hair growth and short shaved shafts. In these two cases we see partial growth and maybe the visible result here would be more successful if we did Long Hair (Unshaven) HT.
SKIN, A SYMPHONY OF SINGLE CELLS

The mouse skin with its hair follicles constitutes an excellent model system for studying tissue maintenance and repair. Recent advances in single-cell transcriptomics have enabled unprecedented analyses of organs by simultaneously revealing all cell types that form an organ together with their cell-type specific gene expression programs. Using single-cell transcriptomics and lineage-tracing mouse models, my lab explores the cellular heterogeneity, lineage specification and adaptability of skin cells during homeostasis and wound repair. As a first step, we molecularly profiled the full repertoire of epithelial cells (i.e. epidermis and hair follicles during telogen), and described spatiotemporal gene expression patterns and the heterogeneity of stem and progenitor cells. Next, we elucidated how skin stem cells from different niches respond to injury. To that end, we traced Lgr6+ stem cells from the interfollicular epidermis, and Lgr5+ stem cells residing in the hair follicle bulge niche. Subsequently, we FAC-sorted these populations at multiple time points after tissue injury - while both Lgr5 and Lgr6 progeny migrate to the wound front - and profiled them. The single-cell transcriptomics analysis revealed that Lgr5 and Lgr6 progeny molecularly converge during wound healing as wound healing activates in Lgr5 progeny an IFE-like signature and downregulates bulge genes. Interestingly, major transcriptional adaptations in Lgr5+ cells occur already within their original niche, which in consequence permits interactions with the wound environment, an ability that the Lgr6+ cells already possess before wounding. Finally, in our most recent work we analyzed the complete mouse skin, including both epithelial and stromal cells during hair growth (anagen) and rest (telogen). We identified more than 50 different subpopulations of cells including new cell types and cell states in the stromal part of the skin, and we modeled the cellular differentiation of anagen hair follicle lineage specification at unprecedented resolution. In summary, using single-cell RNA-sequencing, we could define new transcriptional cell types and states in homeostatic skin, and shed light on the cellular adaptability during wound repair.


EPITHELIAL STEM CELL HETEROGENEITY AND ITS FUNCTIONAL CONSEQUENCES

Human epidermis is a richly diverse organ system composed of basal stem cells that divide to produce a highly connected spinous layer rich in cell-cell communication, a granular layer that provides strength to the organ, and a dead stratum corneum layer that caps the water-tight organ. Morphologically, human interfollicular epidermis classically displays three living keratinocyte subpopulations with melanocytes and Langerhans cells dispersed throughout the organ. However, the homogeneity of interfollicular epidermis has been called into question with recent single-cell RNA-seq (scRNA-seq) data from mouse and human epidermis. Here we used scRNA-seq of human epidermis and patient basal cell carcinoma samples to profile nearly 80,000 single cell transcriptomes to reveal unbiased clustering of epithelial cells and the skin tumor microenvironment. Surprisingly, we observe four main Keratin 14 high subpop-
Next generation sequencing approaches

Chair: Maria Kasper, Michael Rendl

Next generation sequencing approaches: two basal stem cell subpopulations and two basal transit subpopulations each with spatially distinct immunostaining patterns. Basal cell carcinoma, the most common skin cancer, derives from only one epithelial stem cell subpopulation, suggesting functionally distinct microenvironments can either promote or suppress tumor growth. Our scRNA-seq data comprehensively reconstructs the complexity of human interfollicular epidermis and basal cell carcinoma, revealing spatial and pseudotemporal differences between transcriptional programs at the single cell level and unexpected heterogeneity.

RNA VELOCITY OF SINGLE CELLS - PREDICTING DIFFERENTIATION FROM DIFFERENTIATION

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Single-cell RNA sequencing is a powerful method designed to characterize the cell heterogeneity of tissues and organs. The technique can be used for the more ambitious goal of describing the dynamical cellular processes such as differentiation and transcriptional activation. The main limit in this direction is the destructive nature of the measurements: cells need to be lysed and multiple readouts cannot be collected from the same cells. Furthermore, since cells differentiate asynchronously, sampling at different time points does not immediately reveal the dynamics of single cells. The most commonly used strategy to face this limitation has been “pseudotemporal analysis,” an algorithmic approach that orders transcriptomes by similarity. However, the determination of the differentiation directionality was impossible with this method without prior knowledge available. To overcome this fundamental limit, we developed a method capable of estimating “RNA velocity,” the time derivative of gene expression. The technique exploits the fact that the time scale of developmental and reactive processes in mammals matches the one of RNA metabolism. Therefore, by measuring the abundance of both unspliced and spliced RNA in the same cell, it is possible to estimate the rate of change of gene expression and predict the future expression levels of a single cell. We illustrate the behavior of our method under different scenarios and we detail various ways in which RNA velocity can be estimated and visualized. The analysis framework was applied to multiple murine datasets and used to study lineages in the human embryo. RNA velocity holds promise to unveil dynamics from static RNA-seq data in various systems including the skin and the hair follicle.
BACTERIAL MICROBIOME EXTENDS BELOW THE INFUNDIBULUM OF HEALTHY SCALP FOLLICLES – FINDING OF A POTENTIAL RELEVANCE FOR HAIR PHYSIOLOGY AND SCALP DISEASES

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Introduction & Objectives: The skin microbiome remains in a constant dialogue with the local immune system, fosters the defense against pathogens and maintenance of skin homeostasis. Although the skin surface microbiome and its role in skin diseases have received increasing attention over the past years, little is known about the microbiome of hair follicles. Herein, we aimed to study penetration depth and composition of bacterial microbiome in scalp hair follicles of healthy individuals and possible correlations with the expression of immunoregulatory molecules.

Materials & Methods: We performed immunohistochemical staining (anti-CD3, -CD4, -CD8, -Foxp3, -IL17a, -hBD1 and hBD2 antibodies) gram, giemsa and PAS staining on tissue sections from healthy individuals. Following up on those screening investigations, we confirmed marked presence of IL-17a- and hBD2 in infrainfundibular compartments by ELISA analyses of plucked hair follicles cut at the level of the outer root sheath (frontal and occipital sites of healthy volunteers). 16s rRNA sequencing on microbial DNA extracted from infrainfundibular tissue and bulb as well as fluorescence in situ hybridization (FISH) were applied to investigate for deeper penetration of microbial material below the infundibulum level.

Results: Gram-positive cocci and rod-shaped bacteria were found numerously in the infundibulum, which was also characterized by high presence of T cells within the tissue. Interestingly, however, structures of similar morphology were also identified below the infundibulum, i.e. in suprabulbar and bulbular tissue. FISH not only revealed biofilm formation in the infundibulum and along hair shafts, but also pointed towards Cutibacterium acnes penetration between the inner root sheath and hair shaft below the infundibulum. Overall, microbial DNA could be extracted from all plucked hair follicles (suprabulbar material and to a significantly lesser extent bulbs) with Lawsonella clevelandensis, Staphylococcus capitis and Staphylococcus epidermidis as most abundant species with mean relative abundances of 64.3% and 43%, 16.7% and 12.9%, 8.8% and 5.6% respectively.

Conclusions: We found first evidence, that bacterial microbiome extends below the infundibulum, in proximity to structures of the immune privileged status, essential for hair cycle. Expression of IL-17a and hBD2 both within the infundibulum and lower portion of the scalp hair follicle may be correlated with the presence of microbiota in these areas. Further studies are ongoing to evaluate the impact of those findings for onset and maintenance of inflammatory scalp diseases.
Hair cosmetics are important tools to help dermatologists to enhance the patient’s adherence to hair loss treatments. Over processed frizzed, dry brittle hair is a main issue in patients complaining of hair problem. Keeping a beautiful and healthy hair, regardless of the many topical treatments that are part of the doctor’s prescriptions, is possible when the correct hair care products and hair care practices are scientifically explained and recommended to the patient.

Learning objectives
Following this presentation, the attendee should be able to:
• Learn about the hair shaft composition and chemical behavior.
• Learn about the importance of the 18-methyleneleicosanoic acid for the healthy hair shaft.
• Learn about different types of shampoos and conditioning agents.
• Learn how to neutralize hair frizz and keep the hair cuticles sealed by choosing the correct shampoo and conditioner according to the hair type.
• Learn about the hazards and side-effects of performing hair-straightening procedures with formaldehyde-releasers.

Increasing globalisation has resulted in heightened awareness of the different and specific hair care needs of different cultures and ethnicities, with emergence of products aimed specifically to address such needs. The environmental impact of pollutants and UV damage on hair is recognised, with ranges designed to combat the damage caused by such factors on the hair fiber. Consumer trends focussing on the environmental impact of products and packaging results in emergence of several environmentally friendly hair products and ranges focussing on avoiding animal cruelty and compatibility with vegan values.

Hair care, color and style play an important role in people’s physical appearance and self-perception. With today’s increasing life-expectations, the desire to look youthful plays a bigger role than ever. The hair care industry has become aware of this and is delivering active products directed towards meeting this consumer demand. Hair cosmetic agents are preparations intended for placing in contact with the hair and scalp, with the purpose of cleansing, promoting attractiveness, altering appearance, and/or protecting them in order to maintain them in good condition. Currently, hair cosmetics for the aging hair include conditioners, hair styling aids, and hair dyes. Current shampoo formulations are tailored to the variations associated with age, gender, hair quality, hair care habit, and problems relating to the superficial condition of the scalp. Much effort is invested in the development of conditioning agents, which impart luster, smoothness, volume
Hair cosmetics news and views

Chairs: Maria Fernanda Gavazzoni, José Cucchia

and buoyancy. Traditionally, the medical focus has been either on hair loss, or on the condition of the scalp in terms of specific dermatological diseases. The proximate structural arrangement of the scalp and hair leads to an interdependent relationship between the two. Oxidative stress is prevalent in many skin conditions, including normal skin aging. On the scalp, the hair appears to be impacted prior to emergence, and oxidative stress to play a role in hair loss. The scalp commensal organism Malassezia has been recognized to be a source of oxidative damage. Therefore, hair care products, specifically shampoos with active Malassezia inhibitory agents, may reduce premature hair loss, besides the known benefits in treating specific dermatologic scalp pathologies, and therefore should represent an integral part of every treatment regimen for hair loss, even in individuals not showing symptoms of scalp pathologies.
Introduction: Chemical and physical procedures are constantly carried out by women or men, intended to increase the quality of life and personal well-being, such as dyeing, bleaching, and straightening, in order to achieve certain standards of beauty. However, such treatments can damage the integrity of the outermost layer of the hair shaft, ie, the cuticle, impairing sensory characteristics. The cortex, responsible for the mechanical resistance and natural color of the shaft also can be affected, to a lesser extent, because it is protected by the cuticles scales since this layer is intact. In addition to these deliberate damages, hair is exposed to environmental damage, such as solar radiation and pollution. Knowledge of chemical and physical treatments and their negative consequences to hair shaft is fundamental to guide hair care development.

Material & Methods: Caucasian and Afro-ethnic virgin hair tresses from DeMeo Brothers® (New York) were used. Caucasian hair was classified according to the curl patterns, ranging from straight to curly, and natural color, in straight dark brown, straight blond, wavy dark brown and curly dark brown. They were submitted to physical and chemical treatments, such as: bleaching and dyeing, artificial solar radiation, hair straightening brush and flat iron. Tresses had the following parameters evaluated after chemical and physical procedures: dry combing and mechanical properties using Dia-stron® MTT 175. The tensile strength was obtained by the ratio between the cross-sectional area and the break load. Color changes after procedures were measured, protein loss using bixinconininc acid, tryptophan content and pictures with scanning electron microscopy were taken. Possible significant differences in the results among treatments were analyzed with statistical analysys using two- sample t-test (α = 0.05) using the Origin® Software 2016.

Results & Comment: All procedures studied led to modifications in the properties of the hair shaft.
- Discoloration / tincture: caused significant loss of protein in all types of hair (average of 5.7mg/g), especially in straight hair. It provoked a significant increase (115%) in the work for combing Afro-Ethnic hair, and an increase (19.5%) in its breaking strength.
- Thermal heat: caused significant loss of protein in all hair types (mean of 2.4mg/g), being higher in the ethnic (3.43 mg/g).
- U.V. radiation: significant protein loss for straight hair dark brown, straightened blonde and wavy dark brown (average loss of 2.13 mg/g protein).
- Hair straightening: greater color difference for all types of hair, except for blond straight hair, in which the greatest color difference occurred after UV radiation.
- Loss of protein: greater for discolored / dyed hair, regardless of hair type when compared to virgins. The use of thioglycollate did not cause statistically significant protein loss(1.18 mg/g).
**TRANSEPIDERMAL UVA+UVB RADIATION OF HUMAN SCALP SKIN INDUCES EXTENSIVE HAIR FOLLICLE DAMAGE, WHICH IS ALLEVIATED BY TOPICAL CAFFEINE TREATMENT**

**Introduction:** We have previously shown that ultraviolet radiation (UVR), namely UVB, induces massive damage, and catagen development in human microdissected HFs cultured ex vivo. However, it remained unexplored whether such HF responses are also triggered when UVR irradiates the skin surface.

**Methods:** Here, we investigated the effects of UVA+UVB on HF by irradiating human scalp skin transepidermally ex vivo with solar spectrum UVR. In addition, we investigated whether any detrimental effects can be mitigated by a widely used cosmetic and dietary ingredient, caffeine, which has been shown to protect HF from premature catagen development.

**Results:** In addition to replicating the well-recognized skin cytotoxicity and epidermal damage, transepidermal low (10J/cm²UVA+20mJ/cm²UVB) or high (50J/cm²UVA+50mJ/cm²UVB) UVR treatment also increased the number of melanin clumps, and the expression of 8-OHdG in hair matrix (HM) and outer root sheath (ORS) keratinocytes. Therefore, UVR exposure of the skin surface stimulated HF cytotoxicity and oxidative DNA damage. In addition, UVR decreased proliferation and promoted apoptosis in HF keratinocytes in the distal, central, and proximal ORS, and in the HM. UVA+UVB down-regulated the expression of insulin like growth factor (IGF)-1, up-regulated the expression of transforming growth factor (TGFβ)-2, throughout the whole ORS, and stimulated catagen development. In addition, UVR induced perifollicular mast cell degranulation. UVR-mediated HF damage was more severe after high-dose UVR and reached deeper HF compartments. Topical 0.1% caffeine itself did not induce HF cytotoxicity, stimulated IGF-1 protein expression in the proximal ORS, but it also promoted keratinocyte apoptosis in selected HF compartments under these ex vivo conditions. Importantly, caffeine provided protection towards UVR (40J/cm²UVA+40mJ/cm²UVB)-induced HF cytotoxicity, HF keratinocyte apoptosis, and increase of intrafollicular TGFβ2 expression.

**Conclusion:** Our study presents a simple, instructive, and clinically relevant ex vivo assay for the transepidermal solar UV irradiation of human scalp skin, and provides the first evidence that transepidermal UVR profoundly negatively affects important human HF functions. Our results suggest the potential benefit for inclusion of agents that can act as HF photoprotectants, such as caffeine, into sun-protective cosmeceutical formulations as a prophylactic strategy to protect HFs from UVR-mediated damage.

**DELETERIOUS EFFECTS OF AIR POLLUTION ON SCALP AND HAIR**

**Introduction:** Urban life and daily exposure to air pollution affect scalp and hair follicle health. The scalp feels dry and itchy, hair appears heavy, flat, dull and fragile. The oxidation of the scalp sebum participates in the chronic inflammation of the scalp and in the fragility of the epidermal barrier. Moreover, pollutants impact the hair cycle biology and consequently hair growth and quality. A botanical extract from a fruit seed was tested for its natural detox properties to protect scalp and hair physiology against the deleterious effects of pollutants.

**Methods:** The oxidation of the sebum in pres-
ence of exhaust gas pollution and UV, was quantified in tubo by the malondialdehyde level. A 3D cellular model of pseudo-dermal papilla was used to evaluate the impact of pollutants on the hair follicle health. Dermal papilla fibroblasts isolated from hair bulb were cultivated in aggregates and exposed to benzo[a]pyrene at 10 µM. After 5 days of culture, the levels of ATP and cellular apoptosis were respectively evaluated by bioluminescence and flow cytometry. The anti-pollution properties of an aqueous extract of Rambutan seeds were also tested in these models. Finally, the botanical extract was formulated in a shampoo and conditioner to assess in vivo its scalp and hair benefits.

Results: The exhaust gas induced the oxidation of lipids contained in the sebum, while the treatment with the Rambutan seed extract decreased this oxidation. The chemical pollutant benzo[a]pyrene significantly increased the cellular apoptosis and decrease the production of ATP in the dermal papillae aggregates compared to the unpolluted condition. The botanical extract significantly decreased the cellular apoptosis and increased the ATP level in the pseudo-dermal papilla. In vivo, the treatment with the botanical product improved significantly the scalp moisture and the hair appears and feels visibly healthier and shinier after 28 days.

Conclusion: The scalp and hair follicle need to be protected from the harmful effect of air pollution and UV to produce a healthy hair fiber. A botanical seed extract from the Rambutan fruit exhibited anti-pollution properties and health-promoting effects on scalp and hair and gives a natural protective solution for hair care.
LESSONS LEARNED FROM BIOPSIES OF FRONTAL FIBROSING ALOPECIA: WHAT’S NEW?

Frontal Fibrosing Alopecia (FFA) is an irreversible scarring alopecia with unknown etiology and no cure. The classical histopathologic features are consistent with those of lymphocytic cicatricial alopecia and involve follicular dropout, perifollicular concentric fibrosis with lichenoid lymphocytic infiltrate and atrophy of the sebaceous glands. A biopsy is rarely necessary for the diagnosis in cases of classic frontotemporal hair line recession resulting in a smooth atrophic band of hairless skin. Nowadays, the goal is to make the diagnosis at the earliest possible stage prior to developing visible changes of skin atrophy and loss of follicular openings. Biopsies should be obtained by using dermoscopy to select the best site. In such early cases the biopsies often fail to demonstrate concentric perifollicular fibrosis but show a common new recognizable pattern for the diagnosis of early FFA in horizontal sections characterized by inflammatory involvement of the vellus follicles by perifollicular lichenoid layered or patchy infiltrate and the atrophy of the sebaceous glands.

Other new histologic findings in FFA involve the presence of adipose tissue in the dermis, involving the arrector pili muscle, and dermal displacement of eccrine sweat coils. It is possible that the close interaction of the hair follicles and the arrector pili muscle with the adipose tissue may play a role in arrector pili muscle degeneration and in epithelial mesenchymal transition.

In summary, the lecture will discuss some new histopathologic observations in biopsies from early cases of Frontal Fibrosing Alopecia, as well as new morphologic features with possible implication to translation research, histopathology of facial papules and extrafacial body sites.

CHALLENGING HAIR CASES WITH CLÍNICO-PATHOLOGICAL CORRELATION

The cases presented herein demonstrate, that the correct diagnosis is often only achieved after clinical-pathological correlation. Complex disorders, some of them with multiple diagnoses are subject of the lecture.

TEASING IT OUT: PEARLS IN THE HISTOPATHOLOGY OF TRACTION ALOPECIA

Timing and location are two critical components to consider when evaluating the histopathology of traction alopecia (TA). Because of the unique biphasic nature of TA, histologic changes in TA are variable and depend on the stage of disease. Further variability arises based on the clinician’s selection of biopsy location. Clinicopathologic correlations are thus critical in rendering an accurate diagnosis. Reports of histopathologic evaluations in TA are likely skewed toward late disease however, there is as yet no published data on the histopathologic spectrum of clinically graded mild to severe disease.

Timing: In early TA, the histopathology can show trichomalacia, increased numbers of telogen and catagen hairs, a normal number of terminal follicles, and preserved sebaceous glands. Though TA is typically thought of as a non-in-
flammatory alopecia, early disease or ongoing traction can be associated with a mild folliculitis. In later stages, there may be “follicular drop-out” of the terminal hairs where the follicles seem to have disappeared. Along with this decrease in the number of terminal follicles, one may note fibrotic fibrous tracts as well as vellus-sized or miniaturized hairs. The characteristic finding of retained but diminutive/smaller-caliber hairs along the frontal and/or temporal hairline (so-called fringe sign) may correlate with the vellus hairs seen on histology. Even in longstanding TA, sebaceous glands are retained which can help distinguish the late stage of the disease where fibrosis is present from a primary scarring alopecia. Transverse sections may further offer advantages over vertical sections in distinguishing between primary scarring alopecias and TA. Specifically, a diagnosis of TA should be considered if there is a low-power pattern of miniaturization and follicular dropout with retained sebaceous glands. In primary scarring alopecias, the sebaceous glands, are absent in early-stage disease and even in clinically unaffected areas.

**Location:** A biopsy from the center of the area of hair loss and one from the “leading edge” where the density may still be close to normal can paint significantly different histopathologic pictures. In early or active traction, the leading edge may show evidence of inflammation and trichomalacia whereas in late stage traction, the leading edge may significantly underestimate the amount of follicular damage. Conversely, a biopsy from the center of hair loss in early stage/active traction may underestimate the degree of inflammation whereas in late stage alopecia it can confirm the presence and extent of follicular damage by highlighting the decreased density and fibrosis. Detailing the clinical stage of disease (early vs late) as well as the location of the biopsy (leading margin vs central) can help in providing an accurate histopathologic determination in traction alopecia.

**References:**

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**LESSONS LEARNED FROM HAIR PATHOLOGY CONSULTS**

This session will cover pitfalls in the histopathologic diagnosis of alopecia. Using a case-based approach clinical and histopathologic findings will be correlated, highlighting what features to focus on to properly manage the patient.
LICHEN PLANOPILARIS VERSUS FRONTAL FIBROSING ALOPECIA: HISTOPATHOLOGICALLY DISTINCT DISEASES OR NOT?

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Introduction & Objectives: Because of their similar histopathological features, most hair authors consider frontal fibrosing alopecia (FFA) as a clinical variant of lichen planopilaris (LPP). However, FFA has a unique clinical pattern, is more common in postmenopausal women, and some environmental triggers may have a role in its etiopathogenesis. Therefore, whether FFA can be accepted as a form of LPP just because they resemble each other histopathologically is questionable. Only a few studies compared the histopathology of LPP and FFA. However, they either included a small number of specimens or evaluated only the transverse sections. We compared the histopathologic findings of LPP and FFA in a large number of patients by thoroughly examining both transverse and vertical sections in order to determine if these two diseases can be regarded in the same disease spectrum or represent distinct entities.

Materials & Methods: Forty-two cases with LPP and 19 cases with FFA were enrolled in the study. The hair pathologist who was blinded to the diagnoses re-evaluated the transverse and vertical sections of scalp biopsy specimens and recorded the findings to the checklist recommended by North American Hair Research Society. Additional findings and the localization of inflammation were also noted. We compared the frequency of each finding in LPP with that in FFA, and statistically analyzed the differences using χ² and Fisher’s exact tests. Values of p<0.05 were considered as significant.

Results: All patients with FFA were females (mean age, 55.6 years). The LPP group included 27 females and 15 males (mean age, 47.4 years). Epidermal changes were more common in LPP cases (81%) compared to FFA cases (52.6%) (p=0.032). Of those, epidermal lichenoid change was present in 33% of LPP cases, while it was not observed in FFA cases (p=0.003). Also, epidermal vacuolar change was more frequent in LPP cases (28.6%) compared to FFA cases (5.3%) (p=0.047). Interfollicular interstitial lymphocytic infiltration was noted in 28.6% of LPP cases whereas in none of the FFA cases (p=0.012). Miniaturization of terminal follicles was more frequent in FFA cases (57.9%) compared to LLP cases (31%) (p=0.044). Terminal and vellus follicle density, features of follicular unit and adnexial structures, follicular changes and their localizations, the density and localization of lymphocytic inflammation (besides interstitial localization), elastic fiber pattern, the presence of interfollicular mucin, the presence and type of perifollicular fibrosis and follicular tract did not differ between two diseases.

Conclusions: LPP is characterized by a lymphocytic infiltrate which involves the whole epidermis and dermis, while FFA by a more follicle-centered lymphocytic inflammation. We propose that LPP and FFA may represent distinct diseases which exhibit a similar pattern of lymphocyte-mediated follicular reaction, albeit with a different extent of epidermal and interfollicular dermal involvement.
FRONTAL FIBROSING ALOPECIA. A VARIANT OF LICHEN PLANUS PILARIS, OR AN INDEPENDENT ENTITY? CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL STUDY OF 73 CASES

Introduction: Frontal Fibrosing Alopecia (FFA) is a type of cicatricial alopecia, with a very characteristic presentation in the form of recession of the frontal hair line with loss of sideburns and very frequently eyebrows. Even though its incidence is growing there are still many unknowns which complicate its treatment. Histopathological studies in the literature are scarce. With this study we sought to create a more detailed description of the pathology of FFA.

Material and methods: A retrospective and descriptive study of histopathological findings of 73 cases of Frontal Fibrosing Alopecia was undergone. We reviewed biopsies from patients with a diagnosis of FFA and Lichen Planus Pilaris made at the Fundación Jiménez Díaz in Madrid between January 2015 and March 2017. Cases were then separated between those clinically considered Frontal Fibrosing Alopecia and those considered Lichen Planus Pilaris. Details were reviewed following a checklist established by the group. This was completed with immunohistochemical study.

Results: Seventy-three cases of FFA were included. 38% of the cases presented a lymphocytic inflammatory infiltrate of low intensity. 41% of the biopsies included sebaceous lobules. 56% of them had presence of eosinophils. For the comparison with LPP, 27 cases of it were included. Only 11% of them had a low intensity inflammatory infiltrate, the rest at least moderate, with 26% of them showing persistence of sebaceous lobules. 33% showed eosinophils in a much lower quantity. Immunohistochemical studies of hormonal receptor on both diseases showed negativity.

Conclusions: Histopathological findings associated to the clinical differences give weight to the idea that FFA and LPP are independent entities which share the same inflammatory pattern. We consider hence, that the studies investigating the pathogenesis should separate them as individual entities.

A HISTOPATHOLOGICAL STUDY OF SEBACEOUS GLANDS IN ANDROGENETIC PATIENTS - INSPIRED BY IN VIVO MULTIPHOTON MICROSCOPY FINDINGS OF SUPERFICIAL SEBACEOUS GLANDS

Sebaceous glands are an integral part of the folliculo-sebaceous unit and are connected to the junctional zone of the hair follicle. The location of the sebaceous glands may vary depending on physiological or pathological reasons; they are usually localized to the upper permanent part of the hair follicle in close proximity to the infundibulum. After surveying scalp skin with multiphoton microscopy in patients with non-scarring alopecia, sebaceous lobules appeared to be larger when compared with the miniaturized hair follicles and as superficial as 5 microns deep. Since these findings have not been found in histopathological surveys of androgenetic alopecia we collected all biopsy-proven androgenetic alopecia histology records from our medical center to investigate sebaceous gland depth. Controls were collected from scalp excisions that contained normal epidermis and folliculo-sebaceous units. We compared sebaceous gland features and depths between the two groups.
Introduction
Currently, there is no ideal treatment for severe AA. There are several case reports of patients treated with oral tofacitinib, the Results are mostly successful and with minimal adverse events, however, in Mexico there are no published studies. We present five patients with severe alopecia areata treated with oral tofacitinib.

Case report
Five patients were studied: 2 men and 3 woman, ages 13 - 46 years, with the diagnosis of severe AA (three of them with AA totalis) for more than 6 years. Previous treatment included topical steroids, systemic steroids, cyclosporine and methotrexate without clinical improvement.
Treatment with oral tofacitinib at 5 mg twice daily for 6 months led to 80%, 60% and 30% improvement in SALT score from baseline, and no adverse event were reported in the patients with totalis AA.
The cases with severe AA have better response.
Currently, patients continue with the same tofacitinib regimen, and we added high potency topical steroid.

Discussion
Alopecia Areata is a frequent cause of dermatological consultation in Mexico, the prognosis is unpredictable and severe cases usually have a poor response to the treatments described in the literature.
Tofacitinib is known to effectively treat rheumatoid arthritis by modulating the IFN response inflammatory pathway by inhibition of JAK1/JAK3, and AA and rheumatoid arthritis share the same IFN response pathway. In preclinical trials in mice, tofacitinib successfully prevented AA development and reversed established disease. In humans, it was reported for the first time hair regrowth with JAK inhibitors in a patient with universal alopecia and psoriasis by Craiglow and King, in 2014.
Key role played by cytotoxic T lymphocytes in AA and the potential for JAK inhibition is currently being investigated.

Conclusions
Tofacitinib may be a therapeutic option for treatment of patients with severe AA who do not improve with first-line treatment.
In our experience clinical response was achieved with no adverse events, however, further information is needed to elucidate optimal treatment strategies for maintenance of response and minimization of risks.
ELUCIDATION OF DEMOGRAPHIC, CLINICAL, AND TRICHOSONIC FEATURES FACILITATING THE EARLY DIAGNOSIS OF SELF-HEALING ACUTE DIFFUSE AND TOTAL ALOPECIA

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Introduction & Objectives
Acute diffuse and total alopecia (ADTA) has been recognized as a rapidly-progressive and severe subtype of alopecia areata (RP-AA) with short-time recovery and favorable prognosis regardless of corticosteroid administration. A subpopulation of ADTA has been reported to recover spontaneously and can be categorized as self-healing ADTA (sADTA). As interventions are not necessary for sADTA cases, differentiation between sADTA from classic RP-AA requiring appropriate remedies is of clinical importance.

Material & Methods
To elucidate demographic, clinical, and trichoscopic features facilitating the early diagnosis of sADTA, a retrospective clinical and trichoscopic analysis of 19 sADTA cases accumulated in our institute was conducted.

Results
Among those cases, 8 cases were referred to our institute for the sake of intravenous corticosteroid pulse therapy. The average duration from the onset to the first visit was 2.6 1.8 months. All cases were female and the average age was 39.5 16.5. Four cases had pollinosis and two cases had atopic dermatitis accompanied by alopecia areata (AA) respectively. The frequencies of these comorbidities were lower than those observed in common AA. Five cases had familial histories of AA. All cases demonstrated increase in pluckable anagen hairs in gentle hair pull test on the whole scalp. The eyebrows, eyelashes, and body hairs were unaffected. In trichoscopic examination, AA signs including broken hairs and black dots, could be observed and, most characteristically, grouped short vellus hairs with increase in of vacant follicular ostia were noted all over the scalp on the first visit in all cases. Chronological clinical photo image analyses revealed that all sADTA shared the same clinical course. The progression of hair loss areas peaked at 3.7 1.5 months, and the complete hair regrowth was achieved without any therapeutic approaches in 7.9 3.0 months. Despite the observations supported the spread of disease activity to be whole scalp, visual total hair loss was recorded in 4 out of 19 cases, suggesting the simultaneous disease progression and recovery.

Conclusion
These findings suggested that sADTA is a distinct clinical entity which can be distinguishable from RP-AA. Close follow-up without intervention up to 4 months can be a possible option for the management of severe and progressive AA cases manifesting the findings identified in this study.
Introduction
Alopecia areata (AA) is a common inflammatory condition affecting hair, but epidemiologic study on the disease, especially in Asia, is rare and offers inconsistent results from one study to another. Objective: To investigate the prevalence and incidence of AA, including alopecia totalis (AT) and alopecia universalis (AU), and to clarify their demographic distribution.

Methods
We analyzed a nationwide representative sample cohort of over one million South Koreans using data from the National Health Insurance Service-National Sample Cohort from 2002 to 2013.

Results
Overall incidence and prevalence during the study period was 98.5 (95% confidence interval (CI), 96.6-104.4) and 154.6 (95% CI, 134.9-174.3), respectively. Overall increases were seen in both of these measures during the period. The mean prevalence of AT per 100,000 persons was 3.7 (95% CI, 3.5-3.9), and the prevalence rate of AT per 100 AA patients was 2.4 (95% CI, 2.2-2.7). The mean prevalence of AU per 100,000 persons was 0.9 (95% CI, 0.7-1.1) and the prevalence rate of AU per 100 AA patients was 0.6 (95% CI, 0.5-0.7). More men were newly registered as AA, while more women were newly registered as AU or AT. The age distribution resembled a bell shaped curve peaking at ages from 30 to 39 for both the AA and AU or AT combined.

Conclusion
This is the first nationwide population-based, epidemiologic study of AA in the Asian population. Our result demonstrates an increase in the frequency especially in milder forms of AA in South Korea, contributing to a greater appreciation of the disease burden.
ASSOCIATION BETWEEN ALOPECIA AREATA AND AUTOIMMUNE THYROID DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Instruction & objectives
Alopecia areata (AA) is a common hair disorder related to idiopathic autoimmune processes. The association between alopecia areata (AA) and autoimmune thyroid diseases (AITD) has been suggested, however, the exact prevalence of thyroid antibodies in AA patients is unclear and the relationship between AA and AITD remains elusive.

The purpose of the study is to assess the association between AA and AITD involving the prevalence of thyroid antibodies by performing a systematic review and meta-analysis.

Methods
A systematic review and meta-analysis were performed by searching articles between Jan. 1990 and Oct. 2018 through two electronic databases: Medline and Embase. Case-control, cohort, and cross-sectional studies were included. Meta-analysis of studies eligible for quantitative synthesis was performed to estimate pooled odds ratios (ORs) of thyroid antibodies; peroxidase antibody (TPO-Ab) and thyroglobulin antibody (TG-Ab), diagnosed thyroid diseases and serological thyroid dysfunctions.

Results
490 research papers were identified and 17 studies with 262,581 patients and 1,302,655 control subjects were included for meta-analysis. AA was significantly associated with both TPO-Ab and TG-Ab. In comparison, there was no significant association between AA and diagnosed hypothyroidism or hyperthyroidism and serological hypothyroidism or hyperthyroidism.

Conclusions
AA is significantly associated with the existence of thyroid antibodies rather than with clinical or laboratory thyroid abnormality. Lack of long-term follow up data is a limitation of the existing literature. Our findings do not support routine screening for thyroid disease in asymptomatic AA patients but highlight the potential future risk of AITD particularly in severe and refractory AAs.
Introduction
The frequency of facial involvement in alopecia areata (AA) is 32%. Effective treatment available for this phenotype is limited.

Objective
To determine the evidence for treatment efficacy and safety on treatment options for facial AA.

Methods
A literature search was carried out through PubMed, Medline, Scopus and the Cochrane Library. Articles published between 2006 and 2017 were reviewed, analysed and graded according to the American College of Physicians outcome study grading system. Ten articles which involved 226 patients were included in this study.

Results
a) Treatment efficacy
Eyebrow AA was discussed in three articles (46 patients). DPCP combined with anthralin showed the highest rate of regrowth. Superficial cryotherapy and pulsed infrared diode laser were described in lower grade studies with variable response. Eyelash AA was discussed in five articles (100 patients). Among grade 2 studies, patients who applied DPCP on the affected scalp and anthralin on the eyebrow achieved the highest rate of regrowth. Prostaglandin analogue did not yield consistent results across studies with similar or lower level of evidence. Moustache AA treated with infrared diode laser was discussed in one low grade study which resulted in partial response. Beard AA was discussed in five articles (78 patients). The biggest study described patients with good response topical (30.3%), oral (40%) and intrallesional (44.4%) corticosteroids. However, DPCP and anthralin treated patients had a higher rate of complete regrowth (85.7%). Minoxidil (5%), calcineurin inhibitor, photodynamic therapy and laser were discussed in lower grade studies with suboptimal response.

b) Treatment safety:
The majority of adverse effects reported by patients were transient and tolerable.

Conclusion
Combined treatment with DPCP and anthralin provided the best overall result for the level of evidence and treatment response for AA of the eyelashes, eyebrows and beard. Patients also experienced early regrowth and had longer remission compared to areas treated with DPCP alone. Given the potential adverse effects, good education and supervision are necessary to ensure the safe use of this treatment.

References
**P 006**

**CTP-543, A JAK1/JAK2 INHIBITOR, ACHIEVES PRIMARY ENDPOINT IN INTERIM ANALYSIS OF PHASE 2 TRIAL IN ALOPECIA AREATA**

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**Introduction**

There is growing evidence that Janus kinase (JAK) signaling contributes to the pathophysiology in alopecia areata (AA). The mechanism of hair loss in AA is believed to involve cytotoxic T cell attack of the hair follicle after loss of immune privilege, regulated by upstream JAK signaling. CTP-543 selectively inhibits JAK1 and JAK2.

A Phase 2a dose-escalating trial was conducted to evaluate the efficacy and safety of CTP-543 in adults with moderate-to-severe AA. Results from the completed 4 and 8 mg BID cohorts are reported.

The trial is ongoing and dosing in the final cohort, 12 mg BID, is underway.

**Methods**

In this randomized, double-blind, placebo-controlled Phase 2a trial, adult AA patients (18-65 years) having at least 50% hair loss were sequentially randomized to receive CTP-543 or placebo BID for 24 weeks.

For this interim analysis subjects received either placebo, 4, or 8 mg BID. Hair loss was measured by Severity of Alopecia Tool (SALT). The primary endpoint was the percentage of patients achieving at least a 50% relative reduction in SALT between Week 24 and baseline. Safety was assessed by adverse event reporting, physical examination, and clinical laboratory assessments.

**Results**

For this analysis, a total of 104 patients were randomly assigned to receive either 4 mg BID CTP-543 (N = 30), 8 mg BID CTP-543 (N = 38) or placebo BID (N = 36).

At Week 24, 47% of patients treated with 8 mg BID of CTP-543 achieved a ≥ 50% reduction in their overall SALT score compared to 8.6% for placebo (p < 0.001). 21% of patients treated with 4 mg BID of CTP-543 achieved a ≥ 50% reduction in their overall SALT score compared to 8.6% for placebo (NS). The 8 mg BID dose group was significantly different from the 4 mg BID dose group (p < 0.05).

The percentage of patients achieving the primary endpoint continued to increase at Week 24. The most commonly reported adverse events were headache, upper respiratory tract infection, cough, acne and nausea.

No significant laboratory abnormalities were noted. No serious adverse events were reported.

**Conclusions**

Treatment with 8 mg BID of CTP-543 for 24 weeks resulted in significant hair regrowth in patients with AA, with an acceptable safety profile.
PHOTOTHERAPY AS SUCCESSFUL TREATMENT FOR DIFFUSE ALOPECIA AREATA

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Background
Phototherapy is an indicated treatment for alopecia areata, but it is not frequently used, it can be used as a single therapy or combinated treatment, it can help for partial or complete hair restoration.

Objective
Measure the utility of phototherapy as a treatment for disusse alopecia areata.

Case report
Male patient, 5 years old. As an important fact of his clinical history is that he suffers atopic dermatitis controlled with moisturizer creams. He presented a localized dermatosis, affecting head, predominating over the scalp in frontal and parietal areas in both sides, it was also affecting some places in the right temporal and left occipital areas. Constituted by alopecic patches of different sizes, confluent among them, irregular and produced extensive hairless patches. To palpation, the scalp had a soft consistency and some areas were completely smooth. He began with hair loss 3 months before the first dermatological visit. He was asymptomatic, terminal hair easily removable, weak and brightness. Trichoscopy: initially it showed broken hairs, some of them with thinner bottom than the superior (exclamation mark), also black dots and yellow dots, flakes were not present. Treatment: Topical steroids were the first primary treatment as well as oral immunostimulants (Pidotimod). With topical treatment he presented adverse effects: erythema, papules and itching, treatment had to be suspended. Treatment with Pitimod, was not completed.

We decided to start treatment only with phototherapy with UVB NB lamp, which has a component that averages a range of release between 290 and 311 nm. One or two sessions were applied every week. We started with 40 seconds and increased 10 seconds every 4 sessions until reaching 2 minutes and 20 seconds as maximum.

Results
A total of 40 sessions were given getting almost completely repopulation of the scalp. During the time he received phototherapy we did not observe erythema and the patient was asymptomatic. Trichoscopy also presented positive changes presenting gradual increase of terminal hair. Until now, he is 4 months without relapse.

Comment
Phototherapy is an option of physical therapy used in many of different dermatological diseases. The mechanism of action is complex and it is explained through one combined action: the reduction in the epidermic proliferation, an anti-inflammatory action and also immunomodulator mechanism. Alopecia areata can become a challenge when it does not respond with the first line of therapy. In this cases, phototherapy, can be an important support tool. Always explaining to the patient that therapy is not short and a good attachment is necessary. When observing positive Results, it is more factible to continue until desired improvement.
THE BENEFITS AND HARMS OF 308-NM EXCIMER LASER TREATMENT FOR ALOPECIA AREATA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background
Although it has been reported that the excimer laser (EL) treatment is effective for alopecia areata (AA), there has been no comprehensive systematic review of its efficacy and safety.

Objective
This study aimed to systematically review the benefits and harms of EL treatment in AA patients.

Methods
A comprehensive database search of MEDLINE, EMBASE, Web of Science and the Cochrane library databases from inception to December 31, 2018, was performed for all prospective studies.

Of 22 studies initially identified, the full texts of 11 studies were assessed for eligibility, and 5 were finally included in the analysis. Two reviewers independently extracted the following data: study design, number and characteristics of the participants, treatment protocol, and rate of hair regrowth based on the quartile scale.

The primary outcome was the proportion of treatment success, defined as cosmetically acceptable hair regrowth or at least 75% regrowth of each designated patch or whole lesions in a patient. Random-effects meta-analyses were performed.

Results
We analyzed 5 randomized controlled trials comprising a total of 87 AA patches/patients. The EL treatment showed a significantly higher treatment success rate than the untreated control group (risk difference [RD] 50.3%; 95% confidence interval [CI] 21.1-79.5%; number needed to treat 2).

No special harm was found related to the use of EL. In a subgroup analysis excluding cases with alopecia totalis or universalis, the EL treatment had a superior result (RD 59.1%; 95% CI 25.1-93.1%) as well.

Conclusions
This systematic review revealed the significant benefit of EL in the treatment of AA. Given that EL treatment is noninvasive, as opposed to intraleisional corticosteroid injection, the use of EL should be encouraged for AA patients.
Introduction
Dermatosis neglecta is a dirt-associated condition caused by the failure of washing. Cases have been reported as complications of trauma, radiotherapy and even schizophrenia, but no case associated with alopecia areata has been published in the literature before.

Case report
A 30-year-old male presented with patches of hair loss with a dirt-adherent lesion on the frontal scalp for four months. He was diagnosed as alopecia areata for the initial two patches of hair loss and treated with topical 5% minoxidil, which was withdrawn after three days because of erythema and itching. He then strictly avoided washing the hair loss patches, where finally developed asymptomatic, yellowish-brown plaques with a verrucous surface and adherent crust and scales. The center of the lesion was removed easily when rubbed with 70% alcohol during the physical examination. Dermoscopy showed broken hairs, “black dots” and exclamation-mark hairs, which consisted of alopecia areata, and cornflake-like scales. Fluorescence staining of adherent scales showed numerous spores, indicating the infection of Pityrosporum orbiculare. The final diagnosis was dermatosis neglecta complicated with alopecia areata. All the scales and crust were rubbed off, and he was encouraged to wash his hair with shampoo every day. After two weeks of oral itraconazole and two sessions of intralesional triamcinolone acetonide injection, the hair regrew completely without recurrence of dermatosis neglecta.

Comment
As a disorder caused by the washing failure, dermatosis neglecta shows a feature of hyperkeratosis and hyperpigmentation with adherent crust and scales. It may accompany with Pityrosporum orbiculare as a result of a suitable environment for overgrowth, and soap water can easily remove the lesion. Psychological factors including anxiety and depression play a significant role in both alopecia areata and dermatosis neglecta. Rubbing with soap water or alcohol can remove the dirt-adherent lesion easily, but it is much more important to treat the primary diseases. Consulting with the patient and encouraging him/her to maintain personal hygiene would be helpful.
**Introduction**

Oral Janus kinase (JAK) inhibitors are currently being investigated in phase II and phase III clinical trials for several inflammatory skin diseases including alopecia areata (AA).

Topical JAK inhibitors have been investigated in atopic dermatitis, psoriasis, and AA. While a number of case series using topical JAK inhibitors in AA have been published, to date there have been no placebo-controlled, double blind studies examining hair regrowth with topical JAK inhibitors in patients with AA universalis.

**Objective**

To determine the efficacy of topical JAK inhibitors in the treatment of AA.

**Methods**

We conducted a phase I, 28 week prospective, placebo-controlled, double-blind study in patients with alopecia universalis investigating hair regrowth with two topical JAK inhibitors, 2% tofacitinib and 1% ruxolitinib.

Topical clobetasol dipropionate 0.005% was the active comparator while vehicle was used as the placebo control. Sixteen patients were recruited for the study.

**Results**

Six patients demonstrated partial hair regrowth in areas treated with 2% tofacitinib ointment applied twice daily.

Five patients demonstrated partial hair regrowth in the areas treated with 1% ruxolitinib ointment. Ten patients demonstrated partial hair regrowth in the areas treated with clobetasol dipropionate 0.05% ointment.

No regrowth was observed in the placebo treated area. Interestingly, generalized hair regrowth was observed in two patients. One patient had 100% regrowth over his entire scalp and eyebrows by week 24 but relapsed after 12 weeks. A second patient also experienced generalized scalp regrowth and significant eyebrow growth and continued to maintain growth 14 weeks later.

**Conclusion**

Our findings suggest that topical JAK inhibitors could be developed as a potential new treatment for AA and alternative to clobetasol dipropionate 0.05% ointment.
Introduction & Objectives
Minoxidil is an effective off-label adjunct therapy for alopecia areata (AA). Though application of 2% and 5% topical minoxidil is believed to be safe, pediatric patients may be at higher risk of inadvertent secondary side effects. We present two cases of minoxidil-induced hypertrichosis in children with alopecia areata. This report aims to raise awareness of hypertrichosis as a marker for systemic absorption of topical minoxidil in the pediatric population.

Materials & Methods
An otherwise healthy 3-year-old and 8-year-old female presented for treatment of alopecia areata. On exam, alopecic patches were well demarcated with centrally located fine white hairs and exclamation point hairs on dermoscopy. Both were treated with topical clobetasol 0.05% cream twice a day and 5% minoxidil foam once a day on the affected area.

At two and four months, respectively, the patients presented with marked hair alopecic patch regrowth as well as increased and thickened hair growth on the nape of the neck, back, arms, legs, and face. The patients denied chest pain, palpitations, numbness, tingling, or vision changes.

Results
Both patients were recommended to discontinue minoxidil after one week taper and to taper clobetasol to twice a week over the next eight weeks. Locations of hypertrichosis slowly resolved to normal three months after complete discontinuation of minoxidil.

Conclusion
These cases heighten awareness of systemic absorption of topical medications in children and is particularly important with regards to minoxidil use in youth afflicted with alopecia areata. We conclude that clinicians should take caution in treating pediatric alopecia areata patients with topical minoxidil when hypertrichosis is observed.

Further research is needed to elucidate appropriate indications and dosing guidelines for pediatric topical minoxidil use.
ETIOPATHOGENETIC FACTORS OF DEVELOPMENT OF ALOPECIA AREATA

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Introduction
Nowadays, due to fundamental research in the field of cytogenetics and biochemistry, the ideas about the morphology and physiology of the hair follicle have significantly expanded. However, the location and type of inducers and inhibitors of the anagen phase has not yet been studied. Fibroblast growth factor and insulin-like growth factor are interesting and promising in terms of the study of the anagen inducer of the hair follicle cycle. bFGF is able to act intracellularly as an activator of proliferation. In studies of scientists Li and Panchaprateep (2014), it was proved that exogenous IGF-1 prolongs the anagen phase and increases the number of hair follicles in the experiment in natural conditions. Therefore, the targeted study of the effect of IGF-1 on the hair follicle cycle in alopecia will open up new pathogenetic pathways for the development of the disease.

Objective
To establish the role of insulin-like growth factor in nesting alopecia.

Materials & Methods
Under observation there were 56 patients with various forms of alopecia areata, aged 19 to 38 years. The majority of patients was with the local form, among which there were 20 (36.2%) patients with the focal form, 16 (29.7%) with poly-focal form, and 1 (1.9%) with a ribbon-like form. Patients with subtotal form of alopecia areata were 9 (16.1%), total - 3 (4.5%), universal - 7 (11.6%). The largest proportion of patients suffered from alopecia areata for up to 1 year - 43.8% and from 1 to 5 years - 38.7%. Longer periods of the disease were observed in 1/5 of the patients (17.5%). The control group consisted of 20 healthy people, representatives of the same gender and age. All patients underwent a video trichoscopy with an Aramo SG camera (Korea) with X60 and X200 lenses, and the Trichoscience diagnostic program to determine the presence of pathological hair and the degree of atrophy of hair follicles. A study of insulin-like growth factor (IGF-1) and fibroblast growth factor (bFGF) in the blood was performed on a Humareader Single by an automated enzyme immunoassay.

Results
In patients with alopecia areata, there was a significant decrease in insulin-like growth factor (IGF-1) and fibroblast growth factor (bFGF) compared with control group, which was correlated with the severity of the disease.

Conclusion
The obtained Results prove the undoubted role of these growth factors in the cycling of the hair follicle and the decrease in the mitotic activity of the hair follicle cells, and are promising in terms of developing new pathogenetic methods for treating alopecia areata.
P 013

TREATMENT OF BEARD ALOPECIA AREATA USING MICROINFUSION OF MINOXIDIL

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Introduction

Alopecia areata of the beard is rarely mentioned in the literature (as Beard AA - (BAA) or AA barbae, when this symptom limits itself exclusively to the beard. Its prevalence ranges between 1-2%. It is one of the clinical forms of Alopecia areata, an autoimmune manifestation mediated by T cells. It affects middle-aged men mostly in plates along the chin.
This poster shows long-term clinical presentation exclusive to the beard that did not respond to topical nor corticosteroid infiltrations. This patient was submitted to microinfusion of medication into the skin (MMP®) to which the patient responded and improved atrophy caused by preceding therapies.

Case Report

Forty-six year old male, mechanic, from the City of Taubaté, Brazil. Patient referred hair loss since childhood and beard loss during adult phase. In 2014, he referred beard loss for 2 years, during which period he was submitted to topical and infiltration treatments, with worsening of skin texture and of hair loss. Patient also referred "sunken" skin.

Dermatological examination

Presence of slightly atrophic alopecia plaques in the right mandibular region. Trichoscopy: presence of yellow and black dots.
Treatment consisted of injecting Minoxidil using microinfusion of medication into the skin (MMP®), first described by Dr. Samir Arbache for treatment of keloid scars and idiopathic guttate hypomelanosis (IGH) in which a Cheyenne tattoo machine was used with a Magnum 17 cartridge to microinfuse the drugs in situ, thus creating a greater effect at the treatment site with less side effects. After one session were excellent with a decrease in atrophy and onset of repilation.

Conclusion

Microinfusion of medication into the skin (MMP®) is a safe technique that has been effective in repilation of alopecia areas presenting skin atrophy that are resistant to conventional treatment, with no signs of local side effects.
THE CURRENT COSTS OF TREATING ALOPECIA AREATA IN A UK SECONDARY CARE SETTING

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Introduction & Objectives
Alopecia areata (AA) is a common autoimmune disorder characterized by non-scarring alopecia. With a lifetime risk of 1.7%, it is the most prevalent autoimmune condition and the second most prevalent alopecia. The condition has a significant psychological impact, as reflected by quality of life scoring.

To date, treatment options have been limited and of low efficacy. The financial costs of current management have not been assessed and, with the prospect of effective new drugs on the horizon, it is important to understand these and how they compare with the potential costs of newer treatments.

The aim of this study was to review the costs of AA treatments in secondary care, in a large tertiary referral centre in Glasgow, UK and to compare these with the potential costs of newer systemic treatments, such as JAK inhibitors.

Materials and Methods
The costs of treatments offered for AA patients in NHS GG&C were analysed. Data were collected from NHS Scotland National Procurement, NHS GG&C wig database, as well as departmental and pharmacy financial reports.

Results
Wigs account for the greatest expenditure in AA management. NHS Scotland spent nearly £6M on wigs over the last 3 years over all specialties and conditions. The wig expenditure for NHS GG&C Dermatology is approximately £450-500K per year with approximately 40% of this (£180K) for AA patients. Based on an average of 3 manmade wigs p.a., the annual cost of wigs per patient is approximately £400-1200. Current BAD guidelines recommend Diphencyprone (DCP), for extensive patchy AA, alopecia totalis or universalis. In NHS GG&C, approximately 30 patients attend the DCP clinic at any time: 35% attend weekly and 65% attend monthly.

The total annual expenditure is approximately £23K including pharmacy and nursing expenses, or £570 per patient.

Conclusion
The current costs to secondary care of treating extensive AA relate largely to wigs and DCP treatment. For a patient with severe AA requiring a prescription for wigs and treatment with DCP, the annual cost of treatment is estimated at £1500. It is likely that new drugs approved for AA will be expensive. Patients with extensive or refractory AA are those most likely to be considered for treatment.

Increasing numbers of uncontrolled trials have reported treatment success with JAK inhibitors (30-75% patients with >50% regrowth), although optimal duration of treatment, as well as the long-term efficacy, remains unclear and further high quality clinical trials are needed.

The current annual cost to the NHS for the JAKI tofacitinib (5 mg BD) is approximately £4900. While the current costs of treating AA are not insignificant, it will be important that novel drugs for severe AA are affordable, to ensure that these treatments can be prescribed for the AA patients who need them.
Introduction
Alopecia areata is characterized by non-scarring hair loss having an autoimmune origin and affects both children and adults. Despite no association with mortality, it presents high morbidity due to its psychological effects. In more diffuse cases, it is resistant to treatment and therefore difficult to address. Even when repilation occurs recurrence rates are high. Its autoimmune origin encouraged us to use cyclosporine microinfusion into the scalp to leverage treatment and prevent drug side effects, since treatment occurred at the target site. The goal of this case is to report this novel technique for cases refractory to conventional treatment.

This method was initially described by Dr. Samir Arbache for keloid and idiopathic guttate hypomelanosis treatment using a tattoo machine to microinfuse 5-FU, a method registered under the trademark MMP®.

Materials & Methods
Two patients with diffuse onset of alopecia areata, one presenting a universal pattern and the other an ophiasis pattern with hair loss throughout the body, received 3 sessions of 50 mg/ml cyclosporine microinfusion on the scalp using the MMP® (microinfusion of medications into the skin) tattoo machine technique.

Results
Repilation initially occurred in body regions presenting alopecia and afterwards in the scalp after 3 sessions with 50 mg/ml of cyclosporine. Cyclosporine was undetectable in both patient’s bloodstream and no side effects were observed. Laboratory exams remained unaltered.

Conclusion
The cyclosporine microinfusion technique using a tattoo machine (MMP® technique) has proven to be effective in persistent alopecia areata cases refractory to other treatments, with remote repilation being observed. Further studies are needed with a greater number of patients as well as a better understanding of the remote immunosuppression observed using this technique in order to include it as a therapeutic option in more severe cases of alopecia areata.
Background
Alopecia areata (AA) is an autoimmune skin disorder causing hair loss and has a large impact on patients’ quality of life. Laser treatment including 308-nm excimer laser has an advantage in treating AA in a targeted manner. Recently, a gain-switched 311-nm Titanium: Sapphire laser (TSL) was developed and demonstrated similar therapeutic efficacy to excimer laser in the treatment of vitiligo.

Objective
We evaluated the effectiveness and safety of the 311-nm TSL in the treatment of AA.

Methods
We conducted an open trial and enrolled 16 AA patients between June 2017 and December 2018. A 311-nm TSL laser treatment was conducted once or twice a week. The dose started at 300 mJ/cm² and increased by 50 mJ/cm² in each subsequent session until post-treatment erythema occurred. In some patients, prior medical treatments were not discontinued to maintain the existing therapeutic effect.

Results
Among the 16 enrolled AA patients, three had alopecia totalis (AT). The patients received a median of 12 sessions (range 4-35 sessions) of TSL treatment. Eleven patients (68.8%) showed excellent to complete (≥75%) hair regrowth after medians of 11 (range 6–35) treatments for 4 (range 2-12) months. Of the remaining 5 patients, 3 patients had good (50-74%, n = 1) or moderate (25-49%, n = 2) hair regrowth. The other 2 patients who had AT showed no hair regrowth. There were no serious adverse events to stop the treatment.

Conclusions
The 311-nm TSL treatment has several advantages over conventional AA treatments such as intraleisonal corticosteroid injection and topical corticosteroids. It provides non-invasive, pain-free treatment to AA patients, without any risk of adverse drug reaction. In particular, TSL treatment has great benefits for children who worried about painful treatment.
NAIL ABNORMALITIES ARE ASSOCIATED WITH DISEASE SEVERITY IN ALOPECIA AREATA

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Introduction

Alopecia areata (AA) is an autoimmune non-scarring hair loss disorder which ranges in appearance from single delimited patches of hair loss to total loss of scalp and body hair. Nail abnormalities are reported in 7-66% of AA patients. Prior studies reported higher frequency of nail abnormalities in severe disease, although this association may be more prevalent among pediatric patients. However, few studies regarding frequency of nail involvement in AA included data from a U.S. population. The aim of this study was to characterize the prevalence and variation of nail involvement and evaluate its association with disease severity and onset among AA patients.

Methods

Patients diagnosed with AA evaluated at the Cleveland Clinic Department of Dermatology between January 2004 and May 2015 were identified after approval from the Institutional Review Board (n=587). Patients were categorized into those with mild scalp involvement (focal patchy or ophiasis), severe scalp involvement (diffuse patchy or totalis) and severe scalp and body involvement (extensive patchy or universalis). Data regarding clinical history, hair and nail examinations were extracted. T-test, chi-square test, Mann-Whitney U test or logistic regression were performed with statistical significance defined as p<0.05.

Results

Nail examinations were completed in 347 (59.1%) patients. Positive nail findings were present in 41.8% (n=145), with 7.8% (n=27) having multiple abnormalities. Pitting (57.8%), onychorrhexis (15.4%), and onychomycosis (8.7%) were the most common (Table 1). Nail abnormalities were associated with earlier disease onset (mean age 26.5 vs 31.9 controls, p=0.01) and male gender (p=0.04). Patients with nail abnormalities had 3 times greater odds (OR 3.14, 95%CI 2.07-4.77, p<0.001) of severe disease relative to controls after adjustment for patient or family history of autoimmune disease and family history of AA. Patients with comorbid autoimmune diseases had more severe disease (OR 1.65, 95%CI 1.05-2.57, p=0.029).

Conclusion

In conclusion, nail abnormalities cluster in AA patients with more severe patterns of hair loss and/or an earlier onset of disease. Nail examination can provide important prognostic information to aid clinicians in the management of AA and should be part of a standardized evaluation protocol in AA.
Introduction
Alopecia areata (AA) is a polygenic, patchy non-scarring hair loss that presents on the scalp and body. New therapeutic options emerged in recent years, however there is limited data regarding safety and efficacy of AA treatment in the pediatric population. This study aimed to provide an evidence-based analysis of current treatment efficacy for pediatric AA.

Methods
Using PRISMA guidelines, PubMed and Cochrane electronic libraries were searched for articles published in English with no time restrictions. Data regarding AA treatment regimen and efficacy in pediatric patients only were extracted. Studies that reported data on patients above the age of 18 were excluded. Grading was based on the American College of Physicians Grading System with grade 1 being the highest level of evidence and grade 4 the lowest.

Results
In total, 975 records were identified from the electronic search, with 149 eligible for full review. Twenty three studies involving 250 pediatric patients (57% female, 43% male) fulfilled selection criteria. The highest level of evidence were four Grade 2 studies, involving 91 patients. One Grade 2 study examined the effects of high potency topical steroid in comparison to low potency steroids and found significantly improved hair regrowth without additional side effects. Another Grade 2 study found 1% anthralin ointment used for at least 9 months to be effective in 70% of their patients, with no adverse effects. Other articles with grade 2 level of evidence included using 308-nm excimer laser, and combination of zinc aspartate, biotin, and clobetasol propionate. There were also 12 grade 3 studies, examining use of tofacitinib, methotrexate, oral corticosteroid pulses, DPCP, prostaglandin drops and sildenafil cream, and 6 grade 4 studies examining minoxidil, latonoprost, topical steroids, and hydroxychloroquine. These studies had small sample size, lacked control groups, and randomization.

Conclusion
High potency topical steroids were the most commonly used and had the highest level of evidence supporting its efficacy in grade 2 studies. However, larger clinical trials are needed to further investigate newer treatments for pediatric AA, including JAK inhibitors, diphenylcyclopropenone, minoxidil, and laser based therapies.
Introduction
Alopecia areata (AA) is a common autoimmune patchy hair loss. Autoimmune diseases have been previously associated with increased risk of cardiac and metabolic diseases; however limited information exists regarding AA. The aim of this study is to examine the prevalence of comorbidities in alopecia areata using a large de-identified composite patient database.

Methods
The Explorys electronic, aggregate database was used to identify patients with AA using the SNOMED-CT term “alopecia areata” (n=33,130). Patients without alopecia areata were used as controls (n=57,246,350). Logistic regression was used for comparisons.

Results
Essential hypertension was the most common condition, present in 28% of patients with AA and in 17.5% of controls (OR 1.84, 95%CI 1.80-1.88, p<0.001). Next were hyperlipidemia in 19.8% of AA patients and 6.6% of controls (OR 3.52, 95%CI 3.43-3.62, p<0.001) and obesity in 18.1% of AA patients and 3% of controls (OR 7.1, 95%CI 6.9-7.3, p<0.001). Diabetes Mellitus was present in 11.4% of AA patients and 7.4% of controls (OR 1.61, 95%CI 1.56-1.67, p<0.001) while metabolic syndrome was noted in 1.4% of AA patients and 0.3% of controls (OR 4.97, 95%CI 4.53-5.44, p<0.001).

Cardiac disorders more likely to occur among AA patients were coronary artery disease (5.5% AA vs. 1.8% controls, OR 3.13, 95%CI 2.98-3.28, p<0.001), atrial fibrillation (1.7% AA vs. 1.2% controls, OR 1.4, 95%CI 1.3-1.5, p<0.001) and stroke (1.7% AA vs. 1.2% controls, OR 1.45, 95%CI 1.2-1.7, p<0.001). Prevalence of myocardial infarction did not differ between the two groups (2.2% vs. 2.1%, OR 1.04, 95%CI 0.97-1.12).

Conclusions
Prevalence of cardiac and metabolic disorders except for myocardial infarction is higher among patients with AA. Patients with a high risk of cardiovascular events should be advised to follow up with a cardiologist.

Future studies should examine if treatment of AA reduces the rate of cardiac comorbidities.
Efficacy and Safety of Diphenylcyclopropenone (DPCP) and Anthralin Combination vs DPCP Alone in the Treatment of Chronic Patchy Alopecia Areata

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Introduction
DPCP (Diphenylcyclopropenone) and Anthralin, both have been used for the treatment of chronic refractory alopecia areata. The reported response of DPCP in chronic refractory Alopecia areata (AA) is varying from 25% to 75% in different studies. Therefore we combined DPCP and anthralin to study the possible synergistic effect of contact immunotherapy and irritant therapy.

Objectives
To study efficacy and safety of DPCP and Anthralin combination vs DPCP alone in treatment of chronic alopecia areata.

Methodology
In randomized interventional study, 70 patients of clinically diagnosed AA of more than 6 months duration were divided into two groups; Group A and B was given combination therapy and DPCP alone therapy respectively. In both groups, sensitization with 2% DPCP was done. After 2 weeks, DPCP application was done every week starting from 0.01% concentration increased gradually every 3rd visit until the appearance of mild eczema or pruritis, for a period of 6 months. In group A, patients have been given Dithranol also for 1-10 minutes for 5 days a week. All patients were explained post-application precaution of not to apply water for 48 hours and avoid sun exposure. The response in terms of percentage change in SALT score (Severity of Alopecia Tool Score) and the number of adverse events was evaluated at 3 and 6 months.

Results
At the end of 6 months, moderate to good response was seen in 76.2% of the cases among Group A and 85.2% of the cases among Group B (p=0.380), which is not statistically significant. Side effects observed were pruritus, enlarged lymph nodes, hyperpigmentation, depigmentation, urticaria and fever; but higher in the combination group. (p=0.012733)

Conclusion
Combination therapy with DPCP and anthralin is not better than DPCP alone but have a significantly higher rate of side effects.
NUCAL NEVUS FLAMMEUS AND ALOPECIA AREATA: WHEN SIZE MATTERS

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Introduction

Background
Alopecia areata (AA) is a high-prevalence immune-mediated hair loss disorder. Extra follicular affections, including nail and ocular abnormalities, are classically related to a worse prognosis of the disease, and previous studies have suggested that the presence of a persistent nuchal nevus flammeus (NNF) also indicates a greater severity and duration of the disease. The association between AA and persistent NNF was first described by Hatzis et al in 1988, who demonstrated that the relation was statistically evident and not due to a simple observer bias.

Objectives
To determine and compare the presence/absence and size of the NNF in 80 individuals (40 patients diagnosed with AA and 40 controls).

Material & Methods
Examination of all cases and controls was performed by the same two experienced clinicians. The diagnosis of NNF was based on the presence of a congenital pink patch on the nape or in the occipital area and exclusion of other possible causes. Statistical analyses were performed using SPSS v.25.0 (IBM Corp., Armonk, NY, USA). Pearson’s c2 test was used to compare categorical variables and Man Whitney test was used to compare continuous variables not normally distributed. P-values <0.05 were considered statistically significant.

Results
We found that the prevalence of NNF was higher in patients diagnosed with severe forms of AA than in patients diagnosed with a milder form of AA. Moreover, we also observed that the size of the NNF was also directly associated with the severity of AA, having a larger birthmark those diagnosed with multifocal AA, AA totalis and AA universalis. We believe, that this observation could be a useful marker of widespread and chronic disease.

Conclusions
The size of the NNF in AA patients might be a useful marker of widespread and chronic disease. Further studies with a greater number of patients are necessary to validate this association and determine which molecular pathways or genetic markers are involved in order to elucidate the link between both.
GUT MICROBIOTA ANALYSIS IN ALOPECIA AREATA PATIENTS


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Introduction & Objectives
Gut microbiota has been revealed as a key modulator of systemic immunity and may play a role in the etiopathogenesis of alopecia areata. The aim of this study was to determine if patients affected by alopecia universalis present differences in gut bacteria composition compared to healthy controls and investigate bacterial biomarkers of the disease.

Materials & Methods
We conducted a cross-sectional study that involved 15 patients and 15 controls. Alpha biodiversity and beta biodiversity of gut microbiome of the study subjects were analyzed by sequencing the 16S rRNA of stool samples. We searched for bacterial biomarkers of alopecia universalis using the linear discriminant analysis effect size (LEFse) tool. The linear discriminant analysis (LDA) effect size (LEFSe) method was applied at the genus and species taxonomic levels to identify taxonomic biomarkers, combining Kruskal-Wallis and pairwise Wilcoxon tests for statistical significance and feature selection. We fixed an \( \alpha \) value < 0.05. The bacterial taxa with significant differences between samples were used to build the LDA model and to estimate its effect as a discriminant feature among them. The threshold used to consider a discriminative feature for the logarithmic LDA score was set to >2.

Results
In total, 30 study subjects (46.6% female; mean [SD] age, 40.1 [9.8] years) were enrolled. Neither alpha (Shannon diversity index 5.31 ± 0.43 vs. 5.03 ± 0.43, \( p = 0.1 \)) or beta diversity (ADONIS \( p \) value: 0.35) of gut microbiota showed statistically significant differences between cases and controls. In patients affected with alopecia, we found an enriched presence (LDA SCORE >2) of Holdemania filiformis, Erysipelotrichacea, Lachnospiraceae, Parabacteroides johnsonii, Clostridiales vadin BB60 group, Bacteroides eggerthii and Parabacteroides distasonis.

A predictive model based on the number of bacterial counts of Parabacteroides distasonis and Clostridiales vadin BB60 group correctly predicted disease status in 80% of patients (AUC 0.804 (0.633 – 0.976), \( p = 0.004 \)).

Conclusions
Alopecia universalis does not seem to affect broadly gut microbiota structure. Bacterial biomarkers found associated with the disease could be involved in pathophysiology or be used as diagnostic tools.
ALOPECIA AREATA IS ASSOCIATED WITH ELEVATED EXPRESSION OF TH1, TH2, TH17, AND MACROPHAGE ASSOCIATED CYTOKINES IN PERIPHERAL BLOOD PLASMA

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Background
Alopecia areata (AA) is known as a lymphocyte mediated autoimmune disease. While the activity of CD4+ and CD8+ lymphocytes in AA pathogenesis is understood, little is known about the relative contributions of different immune cell types and CD4+ T helper (Th) cell subsets in disease. Th1 cytokines (IFN-γ, IL-12) are typically associated with tissue destruction, while classic Th2 (IL-4, IL-5, IL-10) cytokines attenuate Th1 cell activity and are generally associated with atopy and humoral immune responses. Beyond the Th1/Th2 model, Th17 (IL-6, IL-17) cells are a subset with pro-inflammatory properties often associated with cell mediated autoimmune disease. CD4+ Treg and Tr1 (TGFb, IL-10) cytokines exhibit suppressive effects on inflammation.

Objectives
To investigate the expression profiles of cytokines specific to different cell types and subsets in AA.

Methods
Blood plasma samples from 26 AA patients and 12 controls were examined for expression of 22 cytokines using a commercial standard multiplex assay system. Statistical significance was evaluated by two-tail T-test assuming unequal variances for each factor.

Results
Th1 cytokines (IFNg, IL-12) were elevated in AA, though only IL-12 reached statistical significance (P=0.033). Th2 cytokines were increased in expression; IL-4 (P=0.032), and IL-5 (P=0.033). Further, Th17 cytokines IL-6 (P=0.007) and IL-17 (P=0.008) were both higher in AA plasma. Treg/Th2 cytokine IL-10 was strongly increased (P=0.001) in AA. As well as cytokines mainly produced by lymphocytes, IL-15, typically produced by macrophages, was also raised (P=0.031). TNFa (P=0.009) can be produced by macrophages as well as other immune cells and was increased in AA plasma. In addition, hematopoietic growth factors and chemoattractants made by both immune and non-immune cells were significantly increased in AA including IL-7 (P=0.057), GMCSF (P=0.0008), MIG (P=0.026), MIP1b (P=0.002), and sIL-2r (P=0.044). Other cytokines/chemokines examined did not exhibit significant differences between AA and control plasma (IL-2, IL-13, Eotaxin, IFNa, IP-10, MCP1, MIP1a, sIL-1Ra).

Conclusions
While evidence based on plasma cytokine expression alone is not conclusive, the data suggest Th1, Th2, Th17, and macrophage cells may be active in AA.
P 024

THE STUDY OF CHARACTERISTICS OF ACUTE DIFFUSE AND TOTAL ALOPECIA: HISTOPATHOLOGIC AND DERMOSCOPIC FINDINGS AND CYTOKINE PROFILE

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Introduction
Acute diffuse and total alopecia (ADTA) is a type of alopecia areata (AA) and it is characterized by rapid hair loss and rapid recovery unlike alopecia totalis (AT). AA is an organ-specific autoimmune disease characterized by T-cell infiltrates and cytokine production around hair follicles. T-helper 17 (Th17) cells and T regulatory (Treg) cells are crucially involved in the pathogenesis of AA, however, these cytokine profile of ADTA has not been studied yet. And histopathologic examination may be necessary because it can be confused with other sudden hair loss disease, such as acute telogen effluvium. Although a number of studies have been reported on dermoscopic finding of AA, studies on ADTA are extremely limited. If a non-invasive method, dermoscopy, can identify ADTA, clinicians will be able to diagnose ADTA faster. To determine the characteristics of Th17 and Treg cytokines, and to evaluate the characteristic dermoscopic and histopathologic findings of ADTA.

Methods
Scalp skin and serum of ADTA patients were obtained for real-time quantitative PCR and ELISA for IFN-γ, TNF-α, TGF-β, IL-1, IL-2, IL-4, IL-10, IL-12A, IL-13, IL-17, IL-22 and IL-23. The biopsy specimens were taken from the scalp in areas of recent, active hair loss or marginal areas and the specimens were sectioned by Tyler technique. The scalp skin were examined by dermoscopy (Dermlite DL3N) and photographed.

Results
The lesional and serum IL-17 and IL-22 levels were significantly increased in AA than control group, and lower in ADTA than in other types of AA. Peribulbar lymphocytic infiltration was shown in all cases of ADTA, eosinophilic infiltration and pigment incontinence around dermal papilla were prominent in ADTA than in others. The decreased number of hair follicles and less than 1 of anagen/telogen ratio were not observed in ADTA. Yellow dots and black dots were observed in 73.3% and 76.1%, respectively. Broken hairs and short vellus hairs were seen in 63.3% and 56.1%, respectively. Tapering hair appeared in 23.8%. Yellow dots, black dots, broken hairs, short vellus hairs and tapering hairs were observed in ADTA as well as the previously reported AA studies. However, these findings were observed at a higher rate than other types of AA, especially in the findings of broken hair, black dot, and short vellus hair.

Conclusion
Although we failed to find any typical significant cytokine profile of ADTA, it is meaningful finding that Th17 cytokine levels were decreased in ADTA compared to other types of AA. In particular, according to these findings and clinical course, ADTA has a certainly good prognosis. And we demonstrate the characteristic histopathologic features and dermoscopic findings that the simultaneous increase in the number of broken hairs and black dots, suggesting sudden hair loss, and short vellus hairs, suggesting regrowth of hairs. These Results could be a helpful to understand the immunologic pathogenesis and course of AA and diagnose ADTA.
Introduction & Objectives
Alopecia areata (AA) is an autoimmune form of hair loss affecting up to 2% of the population. AA is associated with a high level of disease burden and patient morbidity. The pathogenesis of AA is not well-defined and includes derangements in innate immunity, environmental exposures and genetic predisposition. Human microbiome dysbiosis has been implicated as a contributing factor in a variety of inflammatory conditions ranging from inflammatory bowel disease to atopic dermatitis. Recent cases demonstrate that the gut microbiome plays a role in AA development. This pilot study was designed to characterize the local (scalp) and global (gut) microbiome of AA patients, and compare these results to healthy individuals to determine significant differences.

Materials & Methods
At a single, academic center in Southern California, 25 patients with AA and 25 healthy controls, with no active gastrointestinal disease, were enrolled. Patients were age, gender and race-matched to controls. Scalp swabs and stool samples were obtained from each subject. Bacterial and fungal taxonomy were identified using operational taxonomic units and appropriate databases. Comparison of the AA and control microbiomes was completed using multi-variant statistical analysis.

Results
Demographic data (mean age, distribution of races/ethnicities) did not differ significantly between AA and control groups. AA patients reported a higher prevalence of atopy, thyroid disease, gastrointestinal disease and psychological comorbidity. Both the bacterial and fungal, AA scalp and gut microbiomes demonstrated significant dysbiosis when compared to healthy microbiome samples.

Conclusions
Our preliminary data demonstrates significant changes in both the bacterial and fungal, scalp and gut microbiomes of AA patients compared to healthy subjects. Dysbiosis can cause systemic inflammation and possibly autoimmune alopecia in predisposed patients. In the future, we hope to characterize microbiome changes as related to disease severity, predict clinical response to both topical and systemic therapies, and define the possible impact of dietary practices on AA disease pathogenesis.
P 026

PREGNANCY OUTCOMES IN TOFACITINIB AND THE APPLICATION TO ALOPECIA AREATA

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Introduction

Alopecia areata (AA) is an autoimmune condition that most commonly presents as patchy areas of non-scarring hair loss. The course of AA may be unpredictable and while many effective treatments exist, response varies greatly among individuals. For patients with recalcitrant AA, oral Janus associated kinase (JAK) inhibitors (e.g. tofacitinib) have been shown to be effective and well-tolerated. While not currently FDA-approved for AA, tofacitinib (pregnancy risk category C) is an immune modulating small molecule used in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ulcerative colitis (UC). It preferentially inhibits cytokine signaling receptors for JAK 3 and JAK 1 pathways, blocking production of IL-15 and IL-6.

As tofacitinib represents a new medication first approved in the US in 2012, its safety in pregnancy is not known. Accordingly, all randomized controlled trials established pregnancy as an exclusion and discontinuation criterion due to the unknown effects of maternal tofacitinib exposure on child. This review thus aims to assess known pregnancy outcomes of females on tofacitinib during the gestational period.

Methods

Safety database reports from randomized controlled trials of tofacitinib for the treatment of RA, PsA, psoriasis and UC were reviewed for pregnancy outcomes. Outcomes were categorized as healthy newborn, spontaneous abortion, medical termination, congenital malformation, fetal death or lost to follow up.

Results

Sixty-one cases of maternal exposure to tofacitinib were reported. The median age of women who reported maternal exposure during pregnancy was 31 (range 19-43). Overall, 9 (15%) cases of spontaneous abortion and 10 (16%) cases of medical termination were reported. One (2%) congenital malformation was seen (pulmonary valve stenosis) in a child born to a 32-year old mother who had RA and hypertension. The remaining 32 (52%) pregnancies ended in healthy newborn deliveries and 9 (15%) were lost to follow up with no fetal deaths reported.

Additionally, 13 women received a combination of tofacitinib and methotrexate, a well-known teratogen. In this subset, there were 3 spontaneous abortions (23%), 3 medical terminations (23%), 2 lost to follow up (15%) and 5 healthy live births (38%).

Conclusion

The incidence of congenital heart disease and spontaneous abortion in the reported cases are consistent with those seen in the general population. Due to a lack of controlled clinical trials assessing the effect of tofacitinib in pregnant women, definitive conclusions cannot be made regarding the effect of tofacitinib on pregnancy outcomes. Compared to other diseases treated with tofacitinib, patients with AA typically have an earlier onset of disease presentation and a decreased incidence of concomitant systemic inflammatory disease. As use of tofacitinib increases for the treatment of AA, the need for more robust evidence of the impact of tofacitinib on fetal outcomes is critical.
**Introduction**

Alopecia areata (AA) is an autoimmune disease characterized by non-scarring hair loss on the scalp and/or body. Currently patient management and clinical trials in AA are complicated by a dearth of reliable clinical indicators of more severe and refractory variants. Multiple studies demonstrated increased prevalence of atopy among AA patients; however the utility of atopy as a predictor of hair loss has not been evaluated. Similarly, peribulbar eosinophilic infiltrate and elevated serum IgE levels have also been reported in AA patients with unclear prognostic usefulness. The objective of this study was to investigate the prevalence of atopy and eosinophilia in AA and evaluate their relationship with disease severity.

**Methods**

Patients with AA seen in the Cleveland Clinic Department of dermatology from 2004-2014 were identified (n=205). Atopy was defined as current or past diagnosis of asthma, allergic rhinitis, atopic dermatitis or hyper IgE syndrome (n=92). Eosinophilia was defined as those with 2 or more consecutive elevated serum eosinophil counts or a current or past diagnosis of eosinophilic disease (n=38). Controls were patients without atopy or eosinophilia (n=75). Patients were categorized into having mild (focal patchy or ophiasis) or severe hair loss (diffuse or extensive patchy, alopecia totalis, alopecia universalis)

**Results**

Patients were predominately female across all 3 groups, with 71% of eosinophilic patients, 76% of atopic and 81% of controls being female. Average age at diagnosis was 30.1 ± 3.7 for eosinophilic, 30.5 ± 2.0 for atopic and 31.2 ± 2.3 for control patients. After adjusting for personal and family history of autoimmune disease, and family history of AA, patients with eosinophilia had 3.45 greater odds (OR 3.45, 95%CI 1.59-7.47, p<0.002) of developing severe AA when compared to controls. Similarly, patients with atopy had 2.31 greater odds (OR 2.31, 95%CI 1.25-4.27, p=0.008) of developing severe AA compared to controls. There were no differences in AA severity between eosinophilic and atopic patients (OR 1.49, 95%CI 0.72-3.07, p=0.28).

**Conclusion**

Concomitant atopy and eosinophilia were associated with more severe patterns of hair loss in AA patients. Further research is required to determine whether this represents an etiopathologic mechanism in severe AA or merely a concomitant phenomenon.
Background
In recent years, dermatologists have observed an increase in the incidence of male androgenetic alopecia (AGA). This phenomenon has no apparent explanation. Due to the strong genetic component of AGA, a social or environmental factor that favors inheritance of genes associated with an increased risk for AGA is suspected.

Observation
There are many genes associated with the development of AGA. To date, the strongest predictor of AGA in men has been the length of the CAG repeat located on the androgen receptor gene (AR gene). The same genetic variant in women is associated with a phenotype of ovulation at a later age. Additionally, the gene is associated with higher antral follicle count and lower risk for premature ovarian failure. This led us to theorize that due to social pressure to conceive later in life, women carriers of the short CAG repeat in the AR gene would have a selective advantage because they are more aptly suited to conceive later in life. As such, an older child bearing population would favor offspring with AGA.

Key Message
In the past three decades, women in first world societies are delaying parenthood to a later age. Attempting to conceive at a later age is associated with childlessness due to declined fertility and increased risk of fetal death. Thus, social selection to reproduce later in life favors females that have a higher chance of late-age conception. Female carriers of a short CAG repeat allele in the AR gene have phenotypes that are beneficial to late age conception. Consequently, we put forth the theory that social selection for later conception favors offspring prone to the development of AGA.

SOCIAL SELECTION FAVORS OFFSPRING PRONE TO THE DEVELOPMENT OF ANDROGENETIC ALOPECIA
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P 029

EXPRESSION AND CLINICAL SIGNIFICANCE OF 5α-REDUCTASE ISOENZYME MRNA IN HAIR FOLLICLES OF MALE ANDROGENETIC ALOPECIA

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Objective
To investigate the expression and clinical significance of 5α-reductase mRNA in the hair follicles of male androgenetic alopecia.

Methods
Total RNA from hair follicles of 63 male androgenetic alopecia patients and 30 healthy controls was extracted, followed by reverse transcription.

Expression levels of 5α-reductase isoform mRNA [I-type 5α-reduced (SRD5A1), II-type 5α-reductase (SRD5A2), III-type 5α-reductase (SRD5A3)] were assessed by fluorescence quantitative polymerase chain reaction (PCR).

Therapeutic efficacy was evaluated following treatments with finasteride (1 mg daily) for 6 months.

Results
The expression levels of these three types of 5α-reductase mRNA were comparable in hair follicles obtained by pulling hair out and by follicular unit extraction (FUE) (P>0.05).

Expression levels of SRD5A3 mRNA were higher than that of SRD5A1 and SRD5A2 mRNA. Expression levels of these three mRNA correlated positively with each other (P<0.05).

Conclusions
Expression of 5α-reductase mRNA can be detected in hair follicles obtained by pulling hair out. SRD5A3 is present in the inner and outer root sheaths of hair follicles, and its expression levels are higher than that of SRD5A1 and SRD5A2. Expression levels of these three SRD5A mRNA correlate positively.

Key words
5α-reductase; mRNA; androgenetic alopecia; finasteride; hair follicle
Introduction
Topical minoxidil is the only topical drug approved by the US FDA for the treatment of androgenetic alopecia (AGA). Clinical studies have demonstrated that the majority (>60%) of AGA patients fail to respond to topical minoxidil therapy. Minoxidil is a pro-drug converted to its active metabolite, minoxidil sulfate, via sulfotransferase enzymes located in the outer root sheath (ORS) of hair follicles. Previously, we have demonstrated that follicular sulfotransferase activity predicts minoxidil response in AGA patients.

Objective
The sulfotransferase family of enzymes (SULTs) lack a TATA response element and thus are not easily inducible. However, other pathways have been suggested that can influence the expression of sulfotransferase. Here, we report a novel topical formulation that up-regulates sulfotransferase expression and would be expected to increase minoxidil clinical efficacy.

Methods
Subjects with AGA were recruited to study. Plucked hair samples were collected at the initial visit and analyzed using the sulfotransferase activity assay previously reported by Goren et al. Subjects were provided with the novel topical formula (a shampoo) and instructed to use it daily. After 7 days of using the topical formula, plucked hair samples were collected and analyzed using the sulfotransferase activity assay.

Results
Of the subjects that completed the study, approximately 60% demonstrated up-regulation of sulfotransferase enzymatic activity.

Conclusion
Minoxidil efficacy in the treatment of AGA is limited by the sulfotransferase enzymes activity in the ORS of hair follicles. The novel formula described here up-regulates sulfotransferase in the ORS. As such, we predict that a combination therapy of the new topical formula and minoxidil will lead to better clinical Results for AGA. We are currently studying the clinical Results of the new combination therapy versus traditional topical minoxidil.
STUDY ON USING SULFOTRANSFERASE TO PREDICT MINOXIDIL EFFICACY FOR ANDROGENETIC ALOPECIA

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Objective
To determine whether the sulfotransferase activity and its mRNA expression levels can serve as biomarkers for predicting the therapeutic efficacy of minoxidil for androgenic alopecia (AGA).

Methods
1. 135 AGA patients treated with minoxidil (minoxidil group) and 10 surgically treated AGA (operation group) were enrolled in this study. In the minoxidil group, hairs at anagen phase were pulled out, and sulfotransferase activity was measured (a value of absorbance). 2% of minoxidil was applied to the alopecia area for 6 months. Global photography assessment was conducted at initial visit and sixth months of treatment. According to the changes in the affected area and extent of hair loss following the treatment, therapeutic efficacy was graded as improved (98), under control (23) and ineffective groups (14);
2. In operation group, hairs at anagen phase were also pulled out, but hair follicles were obtained using the drill punch method. Hair follicles at anagen phase were also obtained from 47 patients in minoxidil group. Expression levels of sulfotransferase mRNA were assessed by real-time fluorescence quantitative polymerase chain reaction (qPCR).

Results
1. In minoxidil group, sulfotransferase activity differed significantly among improved, under control and the ineffective groups (P=0.000, P=0.000, P=0.036);
2. The best threshold of sulfotransferase activity in predicting efficacy of 2% minoxidil was 0.430, with sensitivity of 83%, and the specificity of 95%
3. Expression levels of sulfotransferase mRNA in hair follicles and hairs correlated positively (r=0.703, n=10, P=0.023). Expression levels of sulfotransferase mRNA correlated positively with the severity of hair loss prior to the treatment (r=0.320, n=47, P=0.028). But there was no association among expression levels of sulfotransferase mRNA, cumulative scores of efficacy and sulfotransferase activity (r=0.038; n=29; P=0.846; r=-1.515; n=47, P=0.311).

Conclusions
1. Sulfotransferase activity can be used to assess the efficacy of 2% minoxidil for AGA
2. The noninvasive method of pulling hair can substitute for the traditional invasive drill punch method to measure expression levels of sulfotransferase mRNA
3. Sulfotransferase mRNA may regulate sulfotransferase activity at post-transcriptional, translational and post-translational levels.
IDENTIFICATION OF THE SULFOTRANSFERASE PRIMARILY RESPONSIBLE FOR THE BIO-ACTIVATION OF TOPICAL MINOXIDIL

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Introduction
Topical minoxidil is a pro-drug converted to its active form, minoxidil sulfate, via sulfotransferase enzymes located on the outer root sheath of hair follicles. There are currently eight members of the SULT1 family known to exhibit substrate specificity toward minoxidil. Of these, three are known to be present in the scalp; SULT1A1, SULT1A3, and SULT1E1.

Objective
To improve topical drug development for androgenetic alopecia, it is important to elucidate the isoform of sulfotransferase responsible for the bio-activation of minoxidil in hair follicles. In this communication, we report the minoxidil sulfonation capacity of the various SULT1 isoenzymes.

Methods
Purified recombinant SULT1A1, SULT1A3, and SULT1E1 were studied kinetically with a sulfotransferase activity assay utilizing minoxidil as a substrate. In addition, plucked hair was collected from several human subjects and reacted with the sulfotransferase activity assay over 24 hours.

Results
Kinetic data from the pooled human subjects was compared to the data obtained from each of the SULT1 isoforms studied. Human samples did not correlate with the kinetic data obtained from recombinant SULT1A3 or SULT1E1. The human data closely correlated with the kinetic data obtained from recombinant SULT1A1 (correlation coefficient = 0.9712, p<0.001).

Conclusion
SULT1A1 is the most likely SULT1 isoenzyme responsible for the sulfonation of minoxidil in hair follicles.
THE EVALUATION OF LONG-TERM EFFICACY OF FINASTERIDE IN KOREAN MEN WITH ANDROGENETIC ALOPECIA USING THE BASIC AND SPECIFIC CLASSIFICATION SYSTEM

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Introduction
Finasteride 1 mg is considered to be the standard treatment method for male androgenetic alopecia (AGA). However, there have only been a few studies investigating its long-term efficacy. Moreover, its effect on various types of AGA remains unknown.

Methods
In this study, the authors investigated the 5-year efficacy of finasteride 1 mg in Korean men with AGA and analyzed the changes in hair growth according to the distribution of hair loss. The medical records of male AGA patients who were treated with oral finasteride for a period of at least 5 years at two university hospitals were retrospectively reviewed. Patients’ photographs were evaluated using the Basic and Specific (BASP) classification and investigator’s global assessment.

Results
Of the total 126 patients, 108 patients (85.7%) showed improvement after 5 years of treatment. According to the BASP classification, hair loss of the anterior hair line (Basic type), vertex (V type), and frontal area (F type) was improved in 44.4%, 89.7%, and 61.2% of patients, respectively. The V type showed a more rapid and steady improvement compared with the other types. Progression of alopecia after peak improvement was seen in 10.3% of cases in the V type, 16.2% in the F type, and zero percent in the Basic type.

Conclusion
Finasteride 1 mg showed a sustainable effect for at least 5 years in Korean male AGA patients. The exact time points showing signs of first clinical improvement and sustainability were different depending on the type of alopecia.
FUNCTION OF GPRC6A-DUOX1 SIGNALING CASCADE IN ANDROGENIC ALOPECIA

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Background
Testosterone is well-known as a steroid hormone that regulates the various functions of skin biology, such as hair growth, skin barrier homeostasis, and wound healing.

Here, we show that testosterone stimulates GPRC6A and then induces intracellular calcium mobilization and H2O2 generation leading to apoptosis of hair follicle cells. Primary keratinocytes from GPRC6A KO mice failed to calcium mobilization and Duox1-dependent H2O2 generation in response to testosterone compared to wild type (WT) keratinocytes. Duox1-dependent H2O2 generation induced to apoptosis of keratinocytes and hair follicle cells.

Comment
Moreover, application of testosterone into backskin of Duox1 KO and GPRC6A KO mice resulted in delayed anagen to catagen transition compared to that of WT mice. These results provide a molecular mechanism in which testosterone induces apoptosis of hair follicle cells through the activation of GPRC6A-Duox1 cascade and a therapeutic insight into androgenic alopecia.
Introduction & Background
Androgenetic alopecia, commonly known as male pattern baldness, is the most common type of progressive hair loss in men and one the main reason for dermatological consultation.

The treatments available for this purpose are minoxidil topical solution and oral treatment with 5α-reductase inhibitors (finasteride, dutasteride), the outcomes are observed in a long-term period but they depend on the patient’s attachment and often tend to be discontinued.

That is the reason why research must now aim developing treatments with better results. The efficacy of dutasteride in mesotherapy has been studied since 2008, nevertheless, despite it has demonstrated excellent outcomes, there is no uniformity of the application protocols.

Up to now, no trials have ever been done in Mexico nor Latin America. The aim of this work is to evaluate the efficacy and safety of mesotherapy using dutasteride in treatment of androgenetic alopecia in Mexican male patients.

Material & Methods
We report five Mexican patients treated with dutasteride in mesotherapy; each one of them received three doses that were injected every three months. The evaluation of the response was done with self-assessment, photography and clinical evaluation with Norwood-Hamilton scale.

Results
Regarding the self-assessment, every patient improved, when it comes to digital photos, they were taken in the scalp before and at every session of therapy, the grading was evaluated by two blinded dermatologists, and photographic improvement was evident.

In clinical evaluation, according to the Norwood-Hamilton scale every patient improved to a lesser degree and none of them reported side effects.

Conclusion
According to the present trial, the use of dutasteride in mesotherapy in Mexican patients was effective, tolerable and with promising outcomes in the treatment of androgenetic alopecia.
**P 036**

**Efficacy and Safety of Topical Finasteride in a “New” Delivery System.**

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**Introduction & Objectives**

Patients with male pattern hair loss (MPHL) may be reluctant to utilize oral finasteride for the fear of side effects including sexual dysfunctions and mood changes. Different studies show that topical finasteride is effective, but concentration and optimal vehicle to prevent absorption are still not established.

In this study, we utilized 2.5% topical finasteride carried in a silicone gel with liposomes vehicle. The finasteride permeation profiles of this vehicle were evaluated in vitro and established as optimal by comparison with other vehicles providing a possible systemic absorption much inferior to 1 mg oral finasteride.

**Materials & Methods**

This retrospective study evaluated twenty-eight male patients (aged 16-48 years, median age 26.7 years old) affected by MPHL who had been treated for 6 months with 2.5% topical finasteride in liposomal gel at the dosage of 1 ml three times a week.

In twenty-four patients (85.7%) MPHL involved the frontotemporal and vertex region with a score from 2 to 5 according to the Norwood-Hamilton scale. Four patients had diffuse thinning of the crown and retention of the frontal hairline, resembling the female pattern hair loss (Ludwig type).

Efficacy assessment included global photographs using a 7-point evaluation scale of global hair density and videodermoscopy.

**Results**

At 6 months, 11 patients (39.2%) showed a moderate improvement of global photography, 14 patients (50%) had a minimal improvement and 3 patients (10.7%) showed no changes. Treatment was well tolerated and considered easy to use by the patients.

**Conclusions**

Our Results confirm the efficacy of topical finasteride in the treatment of male MPHL. The silicone gel liposomal offers the advantage of a controlled release.

Liposome technology in fact prolongs drug delivery and prevents systemic absorption.

With this delivery system treatment can be used only three times a week, instead of daily, which is an important advantage for the patient.
THE EFFICACY AND SAFETY OF 5α-REDUCTASE INHIBITORS IN 487 MEN OVER 50 YEARS OF AGE WITH ANDROGENETIC ALOPECIA

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Introduction
Finasteride and dutasteride, inhibitors of 5α-reductase (5ARI), were used for the treatments of androgenetic alopecia (AGA). Until now, many studies have been reported on the efficacy and side effects of 5ARI, but most of them were conducted on young men under 50 years of age. Therefore, we studied the efficacy and safety of 5ARI in men over 50 years of age.

Methods
We studied on the efficacy and side effects of 5ARI in men aged 50 to 70 years who visited Kyung Hee University hospital at Gang-dong for the first time from 2006 to 2017 who were treated with finasteride (1 mg/day) or dutasteride (0.5 mg/day) on the diagnosis of AGA. AGA was classified according to the modified Norwood-Hamilton scale (N-H scale). We compared the photographs taken at the first visit with the photographs after taking the 5AR for 6 months or more, and described the degree of improvement as seven-point scale. (-3: greatly decreased, -2: moderately decrease, -1: slightly decreased, 0: no change, 1: slightly increased, 2: moderately increased, 3: greatly increased).

Results
Of the 487 patients, characteristics of all patients evaluated for treatment efficacy are as follows: mean age at start of treatment, 55.02 years; and values of each N-H scale II/III/IV/V/VI/VII/F1/F2 were 24/170/102/79/14/0/61/37, respectively. Compared with baseline, seven-point scores increased significantly after treatments as determined by Wilcoxon signed-rank test. (mean=1.62, p<0.001). Proportions of patients with improvement (seven-point score ≥1) and prevention of disease progression (seven-point score ≤0) were 94.05% (458/487) and 99.18% (483/487). Also, 50% of the patients (242/487) had taken finasteride, and 49% (241/487) taken dutasteride, and 1% (4/487) had changed from finasteride to dutasteride, and there was no difference in the efficacy between patients with finasteride and patients with dutasteride. In addition, there was no statistically significant difference in the degree of treatment response between the age groups at the 5-year intervals. Side effects of sexual dysfunction were observed on 2.26% (11/487), which is similar to the previous report of patients less than 50 years of age (2.1% to 3.8%); five patients with libido reduction, four patients with erection dysfunction, and two patients with reduction of the ejaculated semen amount. According to study by Yoshitake, et al., it showed similar improvements in the relatively younger patients (37.9±10.8 years) after one year from the treatments with 5ARI (mgPA mean score=5.64, 1: significant disease progression, 2: moderate disease progression, 3: slight disease progression, 4: no change, 5: slight improvement, 6: moderate improvement, and 7: significant improvement).

Conclusion
Although 5ARI had been studied in patients under 50 years of age, this study proved efficacy and safety of 5ARI for patients over 50 years of age.
Introduction
Clipping, a typical human intervention during scalp preparation for hair growth analysis, is supposed to be set at a precise stubble length. It follows that length measurement on images captured 2 or 3 days later and length evaluation on a single image has been proposed as a surrogate for the phototrichogram1 as a surrogate for more sophisticated imaging protocols like contrast-enhanced phototrichogram-with-exogen-collection (CE-PTG-EC further PTG). This includes hair-per-hair measurements of length immediately after clipping (t0) and 48h later (t2) and measurement of growth rates hair by hair by dividing length increase by the exact duration between the 2 images.
As a consequence, various systems have been proposed for clinical use with an automated analysis of a single image (t2 only) for discrimination between anagen and telogen i.e. growing from non-growing hair follicles.

Methods
During a PTG study in males [controls and patterned hair loss (MPHL)], the measurement of 4750 stubbles identified immediately after clipping (t0) was 388 ± m (St.Dev. 188 µm).

Results
However, analysis of variance (ANOVA) revealed that the mean stubble length at t0 varied statistically significantly if images were taken from healthy male controls or from MPHL sufferers (P<.001). It also appeared that diameter (P<.001) and growth stage of the hair follicle (P<.001) were associated factors affecting statistically significantly stubble length after clipping.

Error exceeding the preset threshold in commercially available systems affected telogen hair in MPHL (respectively 4.7% of vellus and 7.1% of terminal hair) as compared with 1.8% of vellus and 2.1% of terminal telogen hair from male controls. Shorter stubbles - found equally in MPHL and in controls (24% <250 m) - may also interfere with ‘hair visibility’.

Conclusion
During a multicenter clinical trial (1) problems arose during dot-mapping of ‘visible hair counts’ as length significantly affected hair counts after dot-mapping. The present data demonstrate that extreme stubble lengths (too long or too short) - especially in telogen fibers in MPHL- may lead to an overestimation of anagen counts and % with USA-born ‘visible hair count’ method including automated PTG-Methods (2).

In the future, technologies that seem appropriate in control subjects should also be checked before application on patients (MPHL) where biophysical factors may confound investigational procedures like diameter and hair growth stage. In practice computer assisted Methods imply known or ignored human interventions, technologies with errors between 4% and 7% might interfere with the measurement of efficacy of hair growth promoters and should be rejected.

CLINICAL STUDY ON THE EFFECTIVENESS AND TOLERABILITY OF PREFORMED GROWTH FACTORS VEHICULATED THROUGH IONOPHORESIS ON PATIENTS WITH ANDROGENETIC ALOPECIA

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Introduction
Androgenetic alopecia is characterized by a progressive miniaturization of hair follicles usually occurring in a pattern distribution in genetically predisposed individuals.
The main Objectives of treatments are prevention or improvement of the hair miniaturization and prolongation of the anagen phase, in order to normalize the follicular cycle.
Recent studies have shown that the different cellular components that compose the hair bulb undergo to an apoptosis process induced by the alteration of cellular control mechanisms, especially triggered by the caspases cascade within the DNA of the dermal papillae.
It is also described how stimulation of the microcirculation and local blood circulation increases hair growth or delays the atrophy of the hair bulb.

Objective
Evaluation of the efficacy and tolerability of a combined therapy: preformed growth factors vehiculated through iontophoresis in the treatment of androgenetic alopecia.

Materials & Methods
We performed the treatment on 20 patients with androgenetic alopecia. The total number of sessions was 4 every 3 weeks. Researcher clinical evaluation, global photography and trichoscopy with measurement of the Density / cm² ratio by Tricho-scanner® were collected at every session of therapy. All patients filled out a brief questionnaire for self-assessment.

Results
Results of our study were very promising, with improvement in most of patients seen with both global photography and trichoscopy. All patients defined the treatment as “painless and pleasant” and all were satisfied of the clinical result.

Conclusions
The use of growth factors associated with ionophoresis technique is a useful treatment for treating and preventing androgenetic alopecia, through a cold / hot thermal stress that stimulates the blood microcirculation, improving the tropism of the hair bulb.
Introduction
Odd theories resist the test of time on a long term and refrain progress of science in the field of hair growth measurement.

Methods
The author explains how belief based on biased observations employing un-appropriate technology may turn into dogmatic thinking.

Results
1  XVIIth Century: anatomy for doctors and students.
Based on interpretation at his time, Bartholyn’s textbook (1) explained hair growth in correlation with menstruation.
After puberty, males grow beards but in the absence of menstruation. Elderly women grow beards after disappearance of menstruations. Accordingly, hair growth was interpreted as an excretion process that evacuates ‘old blood’.

2  XXth Century: published papers promoting FDA-approved technology.
After serious criticism, in vivo counting of hair was replaced by photography measuring ‘visible hair’ without actual characterizing ‘visible hair’. Indirect support came from histologic measurements: counting vellus-like (≤30 µm diameter) and terminal (≥40 µm) hair follicles on scalp biopsies taken before and after treatment with either minoxidil or finasteride documented statistically significant hair cycle changes reported as ‘ratio between vellus and terminal hair’ (2).
Accordingly vellus-like follicles would be ‘turned on’ to produce terminal hair while in fact absolute numbers of vellus hair remained unchanged over time (3).

3  XXIst Century: non-invasive technology for measuring hair dynamics.
From 13 males with MPHL, 1 after 2 years oral intake of finasteride (Propecia, MSD, 1 mg/d, compliance 98%) was rated as having a moderate clinical response with +2 points on a 7 point scale (from -3 greatly decreased to +3 greatly increased).
Employing a validated non invasive imaging technology with a resolution equal to horizontal sectioning of a scalp biopsy, the responder showed 43 extra growing terminal hair (diameters ≥ 40 µm) that re-grew from follicles already present at baseline but resting or empty i.e. telogen stage or post-exogen dormancy. Openings of 79 out of the initial 113 vellus hair follicles (diameters ≤ 30 µm) at baseline still showed a vellus hair after 2 years on finasteride while no-hair was seen at the other dots except for an “uncertainty” with 2 terminal hairs: a rare event, if any event at all.

Conclusion
We demonstrated that a good clinical response after 24 months intake of oral finasteride (1 mg/d) was not due to reversal of the vellus hair identified at baseline but from turning resting or empty terminal follicles into long-lived anagen follicles while cycling of miniaturized follicles was not improved by finasteride as 30% of the initial vellus hair follicles became un-productive at month 24.

References
1 Bartholyn Thomas: Anatomia. 1656 ; Book III, Ch I, p. 242
EFFECTIVENESS AND SAFETY OF LOW-DOSE ORAL MINOXIDIL FOR MALE ANDROGENETIC ALOPECIA

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Introduction & Objectives
Oral minoxidil is an antihypertensive with potential side effects at standard doses (10-40 mg daily), which discourage its prescription for hair loss. Low-dose oral minoxidil (0.25-1 mg daily) has been successfully used in female androgenetic alopecia (AGA). The objective of our study was to evaluate the effectiveness and safety of low-dose oral minoxidil (2.5-5 mg daily) in male patients diagnosed with AGA.

Material & Methods
A prospective study was performed in male patients diagnosed with AGA grades I-IV of modified Norwood-Hamilton scale. Oral minoxidil was administered daily at a dosage of 2.5 or 5 mg for a minimum of 6 months. From the group of patients receiving other concomitant therapies, only those with no changes in the last 12 months were included. Therapeutic response was assessed by the comparison of pre and post-treatment clinical images by 3 independent hair experts (worsening, stabilization, mild improvement or marked improvement). An improvement in one grade or more of the Norwood-Hamilton scale was defined as marked improvement.

Results
A total of 41 men with a mean age of 33.3 years (range 20-55) were included in the study. AGA grade I, II, III and IV was present in 5 (12.2%), 12 (29.3%), 16 (39%) and 8 (19.5%) patients, respectively. The mean dosage of oral minoxidil used was 4.4 mg daily, ranging from 2.5 (10 patients) to 5 mg (31 patients). 25 patients (61%) had previously undergone other therapies for a mean of 18 months (range 12-48), mainly oral dutasteride 0.5 mg (18 patients), followed by mesotherapy with dutasteride (9 patients), oral finasteride (3 patients), topical minoxidil (2 patients), and topical finasteride (1 patient). A total of 16 (39%) patients received oral minoxidil in monotherapy. Clinical improvement was observed in 37 (90.2%) patients, with 11 (26.8%) of these patients presenting a marked improvement. Only 4 (9.8%) patients did not present clinical improvement, and no patients worsened. Of the subgroup of 16 patients receiving oral minoxidil in monotherapy, all of them presented clinical improvement, with 6 (37.5%) patients showing marked improvement.

Adverse effects were detected in 12 (29.3%) patients: hypertrichosis in 10 (24.3%) patients, lower limb edema in 2 (4.8%) patient, and intense shedding in 1 (2.4%) patient. All of them were mild and well tolerated. Only 1 patient discontinued the treatment, due to pedal edema.

Conclusion
Oral minoxidil at a dosage between 2.5-5 mg daily was effective and generally well tolerated in our cohort of male patients with AGA. Therefore, low-dose oral minoxidil could be a potential therapeutic alternative in selected males with AGA. Further investigations are needed to objectively assess long-term effectiveness and safety.
**Background**
Growth factor cocktail (GFC) in combination with microneedling is an effective and safe treatment for patients with androgenetic alopecia (AGA).

However, there is a lack of studies on the absorption effect of the GFC in the scalp through iontophoresis.

**Objective**
This study aimed to evaluate the effect of iontophoresis with GFC including Fibroblast growth factor 5-short (FGF5s) on hair growth in patients with AGA.

**Methods**
The study was performed on patients with AGA who were treated with topical GFC including FGF5s using iontophoresis headset once in a day for 12 weeks.

The scalp was divided into right and left sides, and treated with GFC including FGF5s (right side) and normal saline (left side). The effect of the iontophoresis by head set was applied to the scalp every 15 minutes a day.

A total of 20 patients (9 males and 11 females) were enrolled. Treatment efficacy was evaluated through phototrichogram and digital photograph analyses every 4 weeks for 12 weeks.

**Results**
Phototrichogram images showed that 12 weeks of treatment with GFC including FGF5s through iontophoresis increased hair density from 165.5±21.0/cm² to 169.7±21.1/cm² and diameter from 54.7±10.7 μm to 56.7±10.9 μm.

These results were statistically significant in difference (p < 0.05). The phototrichogram images of the region treated with saline after 12 weeks showed that hair density from 165.7±23.3/cm² to 164.9±22.6/cm² and diameter from 53.4±10.9 μm to 53.9±11.0 μm.

The results treated with saline after 12 weeks were not significant in difference from baseline in both hair density and diameter.

**Conclusion**
Absorption of GFC including FGF5s through iontophoresis showed its effect for patients with AGA in the time frame of 12 weeks. However, further study is needed on the long term efficacy of absorption of GFC through iontophoresis.

**Key words**
Androgenetic alopecia, Iontophoresis, Growth factor cocktail, Fibroblast growth factor 5-short.
HAIR GROWTH EFFICACY OF FERMENTED SOYBEAN MILK LIQUID

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Introduction & Objective
Androgenetic alopecia (AGA) is characterized by the structural miniaturization of androgen-sensitive hair follicles in susceptible individuals and is anatomically defined within a given pattern of the scalp. Biochemically, one contributing factor of this disorder is the conversion of testosterone (T) to dihydrotestosterone (DHT) via the enzyme 5α-reductase. Here, we report the hair growth efficacy of botanical substance, which is fermented soybean milk liquid by a placebo-controlled, double blind study. The goal of this study was to examine 5α-reductase inhibitory activity and to evaluate the hair growth efficacy of fermented soybean milk liquid.

Materials & Methods
In vitro study was carried out the inhibition of the activity of 5α-reductase type 1, which is present in rat liver by HPLC. In vivo study was conducted on a total of 46 healthy male subjects aged between 20-55 years (inclusive of both the ages) for a period of approximately 3 months for each subjects. The hair growth efficacy of fermented soybean milk liquid was evaluated hair density, hair growth rate, hair thickness, vellus count and terminal count by Phototrichogram.

Results
In vitro study, fermented soybean milk liquid showed 5α-reductase inhibitory activity. In vivo study, fermented soybean milk liquid showed significant improvement in hair density and hair growth rate at 3 month in comparison to placebo. Fermented soybean milk liquid showed significantly improvement in hair thickness at 1 month and 2 month when compared with placebo. The mean value of fermented soybean milk liquid was noted to higher than placebo implying that fermented soybean milk liquid was effective rendering improvement in terminal hair with placebo at 2 month and 3 month.

Conclusions
The fermented soybean milk liquid safely and effectively promoted hair growth in healthy male. Accordingly, the fermented soybean milk liquid may play a role to the treatment of AGA.
Background
Many studies have investigated the epidemiology and clinical features of female pattern hair loss (FPHL) but there are few studies for long term study.

Objective
The purpose of this study was to evaluate a large number of long-term period FPHL patients and to compare them with short term ones from other studies.

Methods
A retrospective chart review was conducted at the Alopecia Clinic, Department of Dermatology, Myongji Hospital with FPHL patients during a ten-year period from March, 2007 to February, 2017.

Results
Among 3,549 alopecia patients, there were 2,346 androgenetic alopecia patients and 986 were FPHL patients (27.7%).

The most frequent age group was in the thirties (24.5%) followed by the twenties (21.7%), forties (20.3%), fifties (13.8%), and teenagers (9.2%). And the youngest patient was thirteen years old. There were 301 FPHL patients (30.5%) with a paternal familial predisposition, 136 (13.7%) with a maternal familial predisposition, and 70 (7.0%) with both familial predispositions.

FPHL was classified according to the Ludwig classification: type 1 (62.7%), type 2 (33.2%), and type 3 (3.9%).

The most common co-morbidity was seborrheic dermatitis (34.7%), followed by hypertension (10.4%), hyperlipidemia (6.3%), thyroid diseases (5.2%), diabetes mellitus (3.5%), polycystic ovary syndrome (3.1%) and anemia (2.2%).

Conclusion
The period of FPHL diagnosis becomes earlier, which may be due to early puberty in teenagers. With FPHL patients increasingly concerned about the appearance of their hair, milder FPHL type is increasing.
MULTIPLE APPLICATION OF INTRAMUSCULAR COMPOUND BETAMETHASONE IS EFFECTIVE IN THE TREATMENT OF ALOPECIA AREATA

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Introduction and Objectives
Corticosteroid has been known as one of the efficient therapies in alopecia areata (AA) management, with various ways of applications. Here we introduce a systematic application of corticosteroids with satisfactory efficacy and fewer side effects for the treatment of AA.

Materials and Methods
A total of 67 patients of AA were allocated into 3 groups to accept different regimens, i.e., A. compound Glycyrrhizin group (CGT group, 13 patients, 150 mg/d for 14 weeks); B and C. intramuscular injection of Compound betamethasone with an interval of 2-week group or 3-week group for 4 times (median) (23 patients of CB 2-week group and 31 patients of CB 3-week group).

The treatment effect was judged by Oslen’s SALT equivalent, side effects and relapse were recorded.

Results
The patients of three groups were matched with sex, age, disease duration, alopecia types and alopecia area before treatment. After treatment, in two CB groups, 94.4% patients were responsive, whereas efficacy rate of CGT group was 76.9%. When compared with two CB groups, significantly larger hair loss area and lower effective assessment score were found in CGT group (P<0.05). Within the two CB groups, unwanted side effects were presented without significant differences on prevalence and occurring time (P>0.05).

During the follow-up, patients of the two CB groups with longer disease duration had a higher relapse rate than those with short duration (P=0.001). Besides, the relapse rate in CB 2-weeks group was significantly higher than in CB 3-weeks group (P=0.020).

Conclusions
Multiple intramuscular injection of CB is a worthy therapeutic attempt to treat AA. With a better response, less relapse rate and fewer side effects, a maximal of 4 intramuscular injections of CB with 3-week interval is our recommendation.
P 046

ANDROGENETIC ALOPECIA
AND NANOFAT

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Introduction
The study and scope of androgenetic alopecia is, nowadays, a latent problem which demands significant effort and money, both for the patient and for the labs. The latter’s quest to find solutions to the problem derives in requests for enormous amounts of money.

Regarding available treatments for this ailment, one can find some of a non-invasive nature through the use of different varieties of topical agents, some oral medical therapies, as well as invasive ones such as a hair transplant.

All these treatment attempts are not exempt from minor or major complications in all cases, and can be costly. In recent years this problem has been tackled through the use of stem cells obtained from patient tissue. A solution which has yielded very positive Results but still lacks protocol consensus.

Androgenic alopecia & Stem cells: In recent years studies have endorsed the efficiency of stem cells derived from fat tissue, thus proving that Adipose-Derived Stem Cells (ADSCS) are effective in hair regeneration and growth. This has mostly been observed in patients who do not require or indeed wish treatment involving a hair transplant. This also proves that applicable trichogram checks after adipocyte-derived stem cell injections, cultivated in hypoxic conditions, highlight significant hair growth, compared to those patients who only received a placebo treatment.

Methodology & Materials
This prospective study used 10 males and one female between the ages of 30 and 60. All had been diagnosed with androgenetic alopecia and did not present important comorbidities, infections, autoimmune diseases, etc. Blood tests and trichoscopic studies were carried out prior to the treatment and at the end of month six. Within the protocol guidelines, patients were asked to sign the informed consent form.

The mesotherapy with nanofat procedure in the alopecia area was carried out systematically in theatre for elective liposuction and hair mesotherapy.

Conclusions
A mesoplasty in hair biostimulation using nanofat is a safe, simple and practically side-effect-free procedure; able to be associated with other non-invasive treatments.
CHARACTERISTIC FINDINGS OF SCALP HAIR IN KOREAN MEN USING PHOTOTRICHOGRAHM


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Introduction & Objectives
Male pattern hair loss is diagnosed by clinical features. It is helpful to use a phototrichogram additionally. However, phototrichogram analysis of Korean men is not well characterized. Furthermore, the role of phototrichogram in the diagnosis of male pattern hair loss is limited. Our aim was to investigate the characteristic findings of scalp hair in Korean men using phototrichogram and how to apply phototrichogram to diagnose male pattern hair loss and measure the severity.

Methods
We enrolled 299 men between the ages of 4 and 69 including 97 men who had male pattern hair loss. Hair density and thickness were measured by phototrichogram. Five scalp sites including frontal, both temporal, occipital and vertex area were measured.

Results
The range of hair thickness from 5 scalp sites were 64 ± 43µm to 69 ± 55µm. Hair from occipital area showed highest density and thickness. The density difference between occipital area and frontal area was 2.3% and that between occipital area and vertex area was 2.0%. The density of hair tended to decrease from 60s except occipital area. The density difference between occipital area and frontal area was 16.3% and that between occipital area and vertex area was 11.1%. The thickness of hair tended to decrease from 30s.

Conclusion
As in the previous study, it was confirmed that the hair density and thickness of the occipital area were maintained well compared with other areas as age increases. When male pattern hair loss became worse, the ratio between the occipital area and frontal area or vertex area tended to increase. Checking these ratios may be helpful to diagnose and measure severity of male pattern hair loss.

Hair thinning appeared after approximately 30s of age. It is advisable to take a phototrichogram for hair thinning even if patient do not show clinical signs of male hair loss in his 30s or older.
**Introduction**

Androgenetic alopecia is a frequent cause of hair loss in both men and women. It is characterized by the progressive, non-scarring miniaturization of hair follicles and presents gender-specific distribution patterns. Although androgenetic alopecia has a high prevalence, treatments still offer limited results.

This poster presents a type of treatment in which recovery of alopecia-affected areas can be observed with an important improvement in follicle density in both macro and microscopic images.

**Materials & Methods**

Dutasteride was microinfused into the scalp using a Cheyenne tattoo machine with a Magnum 27 cartridge in patients without a history of comorbidities and that had not been submitted to any other prior treatment.

Patients were submitted to 3 monthly sessions using 1 mg/ml of injectable Dutasteride. A total of 2 ml was used to treat the entire scalp. This type of application uniformly infuses microdoses of the medication over the entire alopecia site directly into the scalp, thus leveraging its action at the target location and minimizing or even eliminating systemic side effects.

**Results**

Macroscopic images show coverage improvement in the grade IV alopecia area and microscopic trichoscopy images reveal follicle density increase, with an important reduction in miniaturization.

**Conclusion**

This technique of microinfusing medication into the skin (MMP®) was first described by Dr. Samir Arbache for treatment of keloid scars and later for idiopathic guttate hypomelanosis (IGH). The purpose of this method is to directly treat the target site (as opposed to systemic treatment) to improve therapeutic outcomes with less or no observed side effects.

This technique is easy to perform and enables nonsurgical follicle regeneration.

Patients refer little or no pain during treatment.

Further studies of this technique are required to better establish the protocol and prove its efficacy.
Introduction & Objectives
Androgenic alopecia (AGA) is a common disorder characterized by the gradual hair loss from the scalp. AGA affects roughly 50% of men and perhaps as many women over 40. Although several treatments have been developed to treat alopecia, there are still limitations.

Adipocyte-derived stem cell conditioned media (SCM2®-Black) contains several growth factors such as extracellular matrix and cytokines. Hence, it induces cell proliferation, tissue reproduction, and anti-apoptotic effect.

We conducted this research to evaluate AGA improvement and safety of stem cell conditioned media in AGA patients.

Materials & Methods
A total of 20 patients with AGA were enrolled in this study. AGA area of each patients were separated into left and right side which are defined as the control side and test side. Each side had an area of 1 cm² of hair cut and marked with tattoos for testing. The control side and test side were each applied with normal saline and stem cell conditioned media. Microneedle stamp was practiced immediately and the same amount of each substance applied again on each side. Patients were treated with both substances on each side while visiting every week until the first month and every two weeks up to 3 months. All patients took phototrichogram in 1cm² area of each hair cut site to count the number of hair every two weeks.

Results
The test site show a statistically significant increase in the number of hair on the test side compared to the control site (normal saline) (p = 0.024). The number of hair in the test site increased from 133.45 to 151.05 (total number of increased hair: 17.6), however, the control site showed increase from 133.05 to 142.60 (total number of increased hair: 9.55). No patients had adverse effects during this study.

Conclusion
In this study, we demonstrated that adipocyte-derived stem cell conditioned is effective in increasing the number of hair and is also a safe treatment for AGA. Stem cell derived agents can be an alternative treatment for the patients with recalcitrant AGA.
FOL-005 - MODULATION OF HAIR GROWTH IN CLINICAL STUDIES

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Introduction & Objective

FOL-005 is a well-characterized osteopontin-derived peptide that binds specifically to hair follicles (HFs).

Osteopontin, a multifunctional immunomodulatory glycoprotein has been shown to exert multiple roles in skin physiology and pathology (Kothari et al., 2016; Scatena et al., 2007; Wei et al., 2017; Ganzetti, 2015) and is significantly expressed in human HFs (Chang et al., 2008) while rat hair HFs reportedly express it only during catagen (Yang and Xiang, 2000; Yu et al., 2001).

New pharmacological treatment strategies that offers safe and effective agents for the treatment of hair-loss need to be developed. The hypothesis that osteopontin-derived peptides modulate human hair growth, has been tested and FOL-005 was shown to give rise to an increased hair growth in an experimental mice model.

In addition, FOL-005 has undergone a battery of toxicological tests without signs of any overt toxicity and a first-in-man clinical study with FOL-005, “Investigation of FOL-005 on Clinical Safety and Effect on Hair Growth”, was conducted which showed no safety concerns.

In addition it showed a significant increase in hair density at one of the doses. Recently a Phase IIa study, “A randomised, double-blind, placebo-controlled phase 2 trial of FOL-005 to investigate efficacy on hair growth on scalp skin in healthy volunteers”, was completed.

Materials & Methods

The Phase II trial was a randomized, double-blind, placebo-controlled safety and efficacy trial. FOL-005 was administered as intradermal injections to minizones on the scalp of men with androgenic alopecia of grade 3V to 4/4a according to Norwood/Hamilton.

Two minizones on the scalp of each subject were identified and each one of the separate areas were treated with either one of four different active concentrations or placebo. The subjects were treated three times a week and were monitored continuously for safety signals during the study. The hair growth potential was assessed by using TrichoScan® software according to a standardized procedure.

Results

There were no safety concerns in the Phase II study. FOL-005 was well tolerated at all doses, no differences from placebo were noted. After 12 weeks of treatment the change in the primary endpoint, change in total hair density from baseline, was 7 hairs per cm² at the highest dose. This change however was not statistically significant (p=0.078, mixed effects model). Further studies should investigate the dose, dosing frequency and hair growth parameters.

Conclusions

From the Results of this Phase II clinical study with FOL-005 it was concluded that the compound was very well tolerated and further studies are needed to investigate hair growth promotion capacities using a newly developed topical formulation in a proof of concept.
Introduction & Objectives
Female pattern hair loss (FPHL) is a diffuse, chronic and progressive hair miniaturization affecting approximately 12% of women up to 30 years old. Topical minoxidil has already been established as an effective treatment in clinical trials. In Brazil, topical alpha-estradiol is authorized for the treatment of FPHL, despite little scientific evidence. The purpose of the study is to evaluate the effectiveness of topical minoxidil 2% and topical alpha-estradiol 0.025% when used alone and together.

Materials & Methods
This is a double-blind randomized clinical trial with 102 patients. Inclusion criteria were age greater than 18 years, presence of FPHL and signature of consent form. The exclusion criteria were the presence of other alopecias, the use of contraceptives with anti-androgenic action, any treatment for FPHL, surgery or weight loss in the last six months, pregnancy in the last year, any alteration in the laboratory tests for the evaluation of hyperandrogenism and telogen effluvium and chemical hair treatments during the study. Participants were randomized into 3 treatment groups: minoxidil 2%, -estradiol 0.025% + minoxidil 2% and -estradiol 0.025%; and 84 patients concluded the study. The patients were followed for 6 months. Each one received 2 amber bottles each month with 50 ml of medication and/or vehicle.

The medication (1ml) was used on the scalp in the morning and in the evening for 6 months. In months 0 and 6 macroscopic photos and digital trichogram were taken. The photos of the patients were evaluated by three blind observers and classified as outcome A (“improvement and” stabilization”) or outcome B ("worsening"). A questionnaire about satisfaction were answered in the end of the study.

Results
The minoxidil and minoxidil + alpha-estradiol groups showed no difference in any of the evaluated parameters (p> 0.05) in the trichogram before and after 6 months of treatment and achieved greater satisfaction with the treatment. The group who exclusively used alpha estradiol had a statistically significant (p<0.05) worsening in total hair count and hair density and terminal hair density. This group had a lower satisfaction. The evaluation of the macroscopic photos showed excellent agreement among the observers, but there was no significant difference in the outcomes between the groups.

Conclusions
FPHL is a chronic and progressive disease in which stabilization is already considered a therapeutic outcome. Topical minoxidil can stabilize FPHL and increase the total count of hair and the density and count of terminal hair. Although authorized and widely prescribed in Brazil, alpha-estradiol was not able to increase hair density nor to stabilize FPHL when used alone and didn’t improve the performance of minoxidil when used in combination. Thus, we must rethink the cost and necessity of adding another topical medication in the treatment of FPHL besides minoxidil has already proved effective.
Background
Currently, topical minoxidil is the only FDA approved treatment for FPHL. Oral finasteride 1 mg per day taken for one year fail to increase hair growth or slow the progression of hair thinning in postmenopausal women with FPHL. The efficacy of oral finasteride at higher doses of 2.5 to 5 mg daily has been reported. However, a randomized controlled study of oral finasteride for FHPL is limited and controversial.

Objective
To evaluate the efficacy and safety of a combination of 5 mg oral finasteride (Proscar) and 5% minoxidil solution in postmenopausal women with FHPL compared to using 5% minoxidil solution alone.

Material and Method
Forty postmenopausal women with FPHL Ludwig I-4, II-1, II-2 and frontal type were randomized to receive a combination of 5 mg oral finasteride plus 5% minoxidil solution or 5% minoxidil solution monotherapy for 24 weeks. Efficacy was evaluated by a total hair count and non-vellus hair count, hair mass index, global photograph assessment, and patient’s satisfaction at baseline, 12 and 24 weeks.

Result
A total of 40 patients with a mean age of 59.4 years (range 45-70) completed the study. There were 19 patients receiving a combination of oral finasteride plus topical minoxidil and 21 patients were using topical minoxidil alone. At the end of 24 weeks of treatment, the change in hair count and hair mass index significantly increased in both groups compared to baseline. In oral finasteride plus topical minoxidil group showed superior Results in terms of total hair count and terminal hair count (p=0.030 and p=0.027, respectively). In oral finasteride plus topical minoxidil group, total hair count increased from baseline by 30% (108.4 to 139.5 = +31.1 hairs, p=0.000), while topical minoxidil alone showed 18.1% increase (128.6 to 150 = +21.4 hairs, p=0.000). The global photography showed moderate (+2) to great improvement (+3) in 89.5% of patients in a combined group and 57.2% in the topical minoxidil group. Seven patients (37%) in a combined group and 3 patients (14.3%) in topical minoxidil group reported adverse events including increased body hair growth (6/40), breast enlarge (1/40), breast tender (1/40), and mood swing (2/40).

Conclusion
In postmenopausal women with FPHL, oral finasteride at a dose of 5 mg/day plus 5%minoxidil solution was clearly superior to 5% minoxidil solution monotherapy in increasing total and terminal hair count, and global photographic assessment at week 24.
LOW-DOSE ORAL MINOXIDIL FOR THE TREATMENT OF FEMALE PATTERN HAIR LOSS


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Introduction
Currently, only the use of topical minoxidil and cyproterone acetate is FDA approved for the treatment of female pattern hair loss (FPHL), despite the widespread use of 5-alpha reductase inhibitors, or other antiandrogens. Chronic treatment is required given the progressive nature of the alopecia.

Topical minoxidil was approved for the treatment of FPHL in 1992, with good tolerance but with possible side effects such as mild hypertrichosis and contact eczema.

On the other hand, the need to perform a chronic and frequent application, along with the cosmeticity of the minoxidil formulation, are factors that limit patient adherence to treatment.

Material & Methods
In order to determine the efficacy and tolerance of low dose oral minoxidil, during a minimum period of 4 months, we performed a retrospective, uncontrolled and observational study in women with FPHL.

The improvement response was evaluated by comparing global digital photographs pre and post-treatment, assessed by 3 independent trichologists (worsening, stabilization, mild improvement and significant improvement). A significant improvement was defined as improvement in one grade or more on the Ludwing scale.

Results
A total of 148 women, with a mean age of 47.2 years (range 17-85 years) were included in this study. The patients presented a grade I, II and III on the Ludwing scale of 67.6%, 25.6% and 6.8%, respectively.

Doses between 0.25 and 2 mg of minoxidil were used daily, for a period of time between 4 and 27 months. 15.5% of the patients received oral minoxidil as monotherapy, while 84.5% were with other concomitant therapies. 20.3% of the patients presented stabilization of their alopecia, while 79.7% presented clinical improvement. Of these, 64.2% represented a slight improvement and 15.5% a significant improvement. The clinical improvement was more marked in more advanced stages of the alopecia (p=0.026). Overall, treatment was well tolerated and only 29 patients (19.6%) reported mild side effects (hypertrichosis, tachycardia, oedema, general malaise and increased liver enzymes), which required suspending treatment in only 10.3% of those patients.

Conclusion
Treatment with low dose oral Minoxidil seems to be an effective treatment in FPHL, with a higher degree of response in more advanced stages, both in monotherapy and in combined treatment regimens, with good tolerance and safety profile. Placebo controlled studies are needed to confirm these Results.
OPTIMIZING PRODUCTIVITY OF VIABLE TERMINAL SCALP HAIR FOLLICLES IS EXPLANATORY FOR THE THERAPEUTIC BENEFIT OF FINASTERIDE IN MEN WITH MPHL.

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Introduction
In the absence of any hard evidence, the “reversal hypothesis” claimed conversion of vellus-like hair follicles into terminal follicles as a mechanism for the clinical improvement FDA-approved drugs for female and male pattern hair loss (MPHL) (1). While hypothesis became a generally admitted theory, we demonstrated in 2005 (EHRS meeting, Zurich) that the productivity of vellus hair in a male subject with MPHL was not improved by finasteride while some “viable” terminal hair follicles were re-initiated and augmented their productivity (2). The same volunteer mentioned in this seminal peer-reviewed paper maintained clinically acceptable hair growth during a period of 10 years. Monitoring went on employing the same validated non-invasive method at regular intervals. In the region of interest (ROI) and at the end of the finasteride treatment period, 192 terminal hair (diameter ≥40 µm of which 83% were anagen hair) were identified. From those only 22 remained 30 months after treatment representing a severe 77% loss in a short period of time. This was much a higher rate than expected from the natural loss process predicted 10 years earlier. If not exactly of the same nature, this rapid and severe hair loss mimics a kind of “rebound phenomenon” that has not been properly quantified during the phase III clinical trials. From a pharmacodynamic perspective, this is further proof that the individual had incipient MPHL at the beginning of the finasteride intake i.e. 10 years ago, that the maintained terminal follicles were “finasteride dependent”. The rather great performance under treatment from the phenotypical perspective could probably not prevent the genetically programmed regression in the predisposed follicles. Indeed, while less than 5 nanohair were present in the ROI at the end of the finasteride period, 58 nanohair were detected after the 30 months weaning.

Comment
In short, our data indicate maintenance of terminal hair follicle productivity during long term finasteride treatment. Our experimental evidence, together with the detailed evaluation of the best responder out of our 13 subject study (presented at this meeting) keep in line with more statistical data (3) supports our view that the ‘reversal hypothesis’ is a misunderstanding on the mechanism of action of medical drug treatments in MPHL.

Conclusion
Our assumption based on hard evidence with oral intake of finasteride might lead to the formal rejection of the ‘reversal hypothesis’ – and this claim for drug efficiency should no longer be maintained. More work will be required for raising the same concerns with so-far unsubstantiated claims in relation with the mechanism of action of topical minoxidil formulations and providing hard evidence.

References
EFFICACY AND SAFETY OF ADIPOCYTE-DERIVED STEM CELL CONDITIONED MEDIA IN THE TREATMENT OF ANDROGENIC ALOPECIA

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Introduction & Objectives
Androgenic alopecia (AGA) is a common disorder and characterized by the gradual hair loss from the scalp. AGA affects roughly 50% of men and perhaps as many women older than 40 years. Although several treatments have been developed to treat alopecia, there are still limitations. Adipocyte-derived stem cell conditioned media (SCM2®-Black) contains several growth factors, extracellular matrix, and cytokines, therefore it induce cell proliferation, tissue reproduction, and anti-apoptotic effect. We conducted this research to evaluate AGA improvement and safety of stem cell conditioned media in AGA patients.

Materials & Methods
A total 20 patients with AGA were enrolled in this study. AGA area of each patients were separated into left and right side which are defined as the control side and test side. Each side had the hair cut in 1 cm² area and perform tattoos for marking. Control side and test side had been applied normal saline and stem cell conditioned media respectively. Patients had been applied both materials on each side while visiting every week until the first month and every two weeks up to 3 months. All patients took phototrichogram in 1 cm² area of each hair cut site to count the number of hair at every two weeks visit.

Results
The test site show statistically significant increase the number of hair compare with the control site (normal saline) (p = 0.024). The number of hair in the test site increased from 133.45 to 151.05 (total number of increased hair: 17.6), however, the control site showed increase from 133.05 to 142.60 (total number of increased hair: 9.55). No patients had adverse effects during this study.

Conclusion
In this study, we demonstrated that adipocyte-derived stem cell conditioned media have efficacy in increase of the number of hair and safety as a treatment for AGA. Stem cell derived agents can be an alternative treatment for the patients with recalcitrant AGA.
TRANSCRIPTOME ANALYSIS OF HAIR FOLLICLE DERMAL FIBROBLASTS FROM THE FRONTAL AND OCCIPITAL SCALP REVEALS INHERENT DIFFERENTIAL GENE EXPRESSION

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Androgenetic alopecia (AGA), more commonly known as male-pattern baldness, is an androgen-dependent genetic condition affecting almost 50% of males by the time they reach 50 years old.

In AGA, hair follicles undergo miniaturisation in a defined pattern from the sides of the head and the frontal scalp; however, the hairs on the occipital scalp are spared.

During miniaturisation, the hair shaft transitions from a terminal to a vellus state, while there is an associated decrease in the volume of dermal papilla (DP). It remains to be determined if this is due to an intrinsic change in the DP, or an inability of dermal sheath (DS) cells to replenish DP cell numbers in early anagen.

To better understand the role of the DP and DS in AGA, we isolated DP and DS from matched occipital and frontal follicles from 4 male patients undergoing hair transplantation for AGA. RNA was isolated and used for unbiased transcriptome profiling. A comparative analysis of this transcriptome data enabled identification of genes specifically upregulated in just one of the four cell types; 60 in frontal DP, 181 in frontal DS, 16 in occipital DP and 84 in occipital DS.

For example, USP47 is expressed at highest levels in frontal DS while BLCAP is expressed at high levels in occipital DP. Expression of genes associated with cell adhesion in occipital DP suggest a loss in aggregative properties in the frontal scalp DP and DS may influence miniaturisation.

In addition, we are also assessing transcription factor expression, to identify master regulators of miniaturisation. This study will help us to develop our understanding on how inherent gene expression in the DP and DS cells influences miniaturisation of frontal scalp follicles in AGA, while occipital follicles remain resistant to this process.
L-\((+)-\)TARTARIC ACID SUPPORTS HUMAN HAIR FOLLICLE CELL GROWTH FACTOR PRODUCTION AND PROLIFERATION IN VITRO

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Background
L-(+)-tartaric acid (LTA) is a white crystalline dicarboxylic acid found in various plants. LTA is a member of alpha-hydroxy acids (AHAs), which have been used as an additive of hair care products, however, the influence of AHAs, especially that of LTA, on the biological behavior of hair follicle (HF) cells has been ill understood.

Objectives
To investigate the biological effect of LTA on HF cells in vitro, especially focusing on growth factor production in human HF dermal cell populations and proliferation of HF keratinocytes (KCs).

Methods
Human HF connective tissue sheath cells (HFCTSCs) and dermal papilla cells (DPCs), which have been shown to play central roles in HF homeostasis and regeneration, were individually exposed to LTA and the expression levels of representative HF growth factor genes were assessed.

Results
When compared to non-treated counterparts, up-regulation of FGF7, WNT5A, HGF, and PDGFA in HFCTSCs and VEGFA, FGF7, WNT5A, HGF and FGF2 in DPCs were detected 24 to 48 hours after LTA-treatment. Indeed, LTA-treated HFCTSCs or DPCs respectively exhibited dose-dependent increase in FGF7 or VEGFA secretion in the culture supernatant as detected by enzyme-linked immunosorbent assay (ELISA), which were shown to be statistically significant (p<0.05).

Addition of LTA alone to the culture medium did not ameliorate human HFKCs proliferation in culture. Importantly, the supplementation of LTA-treated HFCTSCs or DPCs culture supernatant to cultured HFKCs promoted the proliferation of HFKCs compared to those exposed to LTA-non-treated DPCs culture supernatant by the fold of 1.26±0.061 (p<0.01) without affecting morphological features.

Conclusions
These findings implied that L-(+)-tartaric acid may positively influence human HF cells to maintain or promote hair growth via up-regulating the secretion of hair growth factors.
EFFECTIVENESS AND SAFETY OF DUTASTERIDE VERSUS FINASTERIDE IN ADULT MEN WITH ANDROGENETIC ALOPECIA IN SOUTH KOREA: RESULTS FROM A REAL-WORLD PILOT CHART REVIEW STUDY


Introduction & Objectives

Real-world evidence (RWE) comparing the long-term effectiveness and safety of dutasteride and finasteride in men with androgenetic alopecia (AGA) is lacking. A pilot study was conducted to inform the design of a large observational study aiming to collect RWE in South Korea, where dutasteride was first approved for AGA in 2009.

Materials & Methods

A pilot chart review form (informed by investigator responses to a 19-item feasibility survey) was administered in the setting of 5 specialist dermatology clinics in large tertiary hospitals in South Korea. Medical charts (Jan 2010–Dec 2016) of 50 male patients (10/clinic) ≥18 years of age, with an AGA diagnosis, undergoing ≥6 months dutasteride/finasteride therapy were abstracted. Patients with a history of surgical correction of scalp hair loss or malignancy were excluded. The observation period spanned from the first dutasteride/finasteride prescription (index date) to loss to follow-up, or data cut-off (whichever was earliest). Demographic and clinical characteristics, treatment patterns, effectiveness measures and adverse events (AEs) were evaluated.

Results

Of the 50 patients with data abstracted, 23 received dutasteride and 27 finasteride. In the dutasteride group, mean age (standard deviation [SD]) was 39.0 (11.4) years, with 52.2% (12/23) reporting a family history of AGA. In the finasteride group, mean age was 36.8 (9.6) years with 59.3% (16/27) reporting a family history of AGA. Mean (SD) duration of follow-up was 470.5 (506.6) days for the dutasteride group and 367.4 (346.1) days for the finasteride group; 13.0% (3/23) dutasteride patients and 3.7% (1/27) finasteride patient had ≥3 years follow-up. Modified global photographic assessment score was the most commonly used effectiveness measure -dutasteride: 43.5% (10/23) patients had ≥1 assessment for vertex and 39.1% (9/23) for frontal view; finasteride: 70.4% (19/27) patients had ≥1 assessment for both vertex and frontal. Mean (SD) change in hair loss on a 7-point scale from index to Month 12 for vertex and frontal improved by 2.3 (0.5) and 2.3 (0.5) points for dutasteride versus 1.7 (0.8) and 0.8 (0.8) points for finasteride. AEs were reported by 21.7% (5/23) dutasteride and 29.6% (8/27) finasteride patients (no serious AEs or death). Decreased libido was reported by one patient in each group.

Conclusion

The pilot study provided key data to inform the full study design. Due to availability and relative completeness of modified global photographic assessments, this outcome will be used as the primary effectiveness measure in the full study. Some sites selected patients with short follow-up due to resource constraints; therefore, follow-up (both groups) was shorter than expected. Based on pilot findings, a minimum duration of ≥3 years follow-up is planned for the full study to investigate long-term real-world effectiveness and safety of dutasteride versus finasteride.
CYSTINE MAY PLAY ROLE TO HAIR GROWTH AND HAIR GROWTH EFFECT WITH MINOXIDIL

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**Introduction & Objective**

Approximately 85% of hair component is constituted by keratin. Cystine is the highest amino acid of the hair keratin. It is unknown whether cystine is just component of keratin or it correlates with hair growth.

The goal of this study was to explore the relationship between cystine and hair growth. We examined that cystine is high components of hair keratin, correlate with hair matrix cell proliferation. Furthermore, we hypothesized that cystine is related to hair growth effect with minoxidil. We also explored the relationship between cystine and hair growth effect with minoxidil.

**Materials & Methods**

Hair matrix cells were cultured separately in usual hair matrix cell culture medium and cystine free medium.

In immunohistochemistry, fluorescence intensity of amino acids in cells was evaluated and cell proliferation rate in each medium was analyzed. In addition, hair matrix cells were cultured separately in usual culture medium, cystine free medium, usual culture medium with FGF-7 and cystine free medium with FGF-7. Cell proliferation rate in each medium was analyzed.

**Results**

In immunohistochemistry, hair matrix cells cultured in usual hair matrix cell culture medium showed significantly higher amino acid compared with cells cultured in amino acid free medium.

Cells cultured in cystine free medium showed significantly lower cell proliferation rate compared with cells cultured in usual hair matrix cell culture medium.

Moreover, cells cultured in cystine free medium with FGF-7 also showed significantly lower cell proliferation rate compared with cells cultured in usual hair matrix cell culture medium.

**Conclusions**

Cystine correlates with hair matrix cells proliferation. Accordingly, cystine may play a role to hair growth and hair growth effect with minoxidil.
JAPANESE GENTIAN ENHANCES THE EFFECTS OF MINOXIDIL THROUGH THE INCREASE IN THE EXPRESSION AND ACTIVITIES OF MINOXIDIL-SULFATING SULFOTRANSFERASES IN NORMAL HUMAN EPIDERMAL KERATINOCYTES

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Objective
Increase in the expression and activities of minoxidil-activating sulfotransferases (SULTs) in human keratinocytes is assumed to improve effects of minoxidil for treatment of androgenetic alopecia. In the present study, we attempt to increase expressions of various SULTs and minoxidil-sulfating activities in normal human epidermal keratinocytes exposed to two products containing natural substances, Japanese gentian and Kakkonto, a Japanese Kampo medicine.

Methods
Normal human epidermal keratinocytes (105 to 106 NHEK cells, Kurabo) were cultured for 2 days, and for additional 2 days after the addition of either 0.02-0.04% Gentian (powders, the Japanese Pharmacopoeia), or 0.02-0.04% Kakkonto (a traditional Kampo medicine, Tsumura & Co., Tokyo, Japan). Levels of mRNA encoding SULT1A1, SULT2A1, SULT2B1a, and SULT2B1b were determined by real-time reverse-transcriptase polymerase chain reactions. Minoxidil-sulfating activities, mainly attributed to SULT1A1, were determined in the substance-treated NHEK by a colorimetric assay method reported by Frame et al. (Drug Metab. Dispos. 28: 1063, 2000).

Results
In the present experimental conditions, SULT2A1 expression was below limit of detection in the NHEK cells. Gentian (powders, 0.02-0.04%) increased SULT1A1 mRNA levels with statistical significance. Minoxidil-sulfating SULT1A1 activities were 4.0 nmol/min/ mg protein in Gentian-treated NHEK (vs. 1.1 nmol/min/ mg protein in vehicle-control). We will also present data on the SULT1A1 mRNAs and SULT1A1-dependent minoxidil-sulfating activities in the NHEK cells by the Kakkonto.

Conclusions
The SULT inductions and the enhancement of minoxidil-sulfating SULT activities by Gentian may be useful for development of Methods for enhancing the minoxidil effect on hair growth in combination with application of prospective remedies to the human scalp.
PLATELET-RICH PLASMA INTRADERMAL INJECTIONS INCREASE THE AREA OF EXPRESSION OF CD34 AND β-CATENIN IN MALES WITH ANDROGENETIC ALOPECIA

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Introduction
Intradermal injections of platelet-rich plasma (PRP) is proposed to be an effective treatment for androgenetic alopecia (AGA). The mechanisms by which PRP affects the hair follicle (HF) are still not well understood. The aim of the study was to evaluate the effect of PRP on the microcirculation and proliferative activity of hair follicle cells in males with AGA.

Materials & Method
The study included 25 men aged from 20 to 43 years. AGA degree II-IV on the Hamilton-Norwood scale was diagnosed in 23 (92%) patients and degree I in 2 patients. All patients received intradermal injections of PRP.
To obtain PRP, blood samples (18 ml) were collected from each patient by venipuncture into 2 tubes with an anticoagulant (3.8% sodium citrate). Centrifugation was carried out twice. An official calcium chloride solution was used as an activator.
The course of treatment consisted of 4 procedures with an interval of 4 weeks between each procedure. The clinical efficacy of the therapy was evaluated by the dynamics of morphometric indicators of hair growth.

Biopsies of skin were obtained from 8 patients. Immunohistochemical examination was performed on vertical paraffin sections. Used monoclonal antibodies to CD34 and β-catenin. In each slice, the total area of the preparation, the total area of protein expression, the relative area of expression were estimated.
All studies were performed before and after 4 months after treatment using a digital camera and the software.

Results
Against the background of treatment with PRP, all hair growth indicators underwent significant changes: hair density increased by 12% (p = 0.000067), average hair diameter by 12% (p = 0.001947), the share of vellus hair decreased by 17% (0.002225), and the proportion of telogen hair by 16% (p = 0.02836).
Significant positive changes were absolute and relative values of CD 34 expression area (Δ287%, p = 0.0001 and 325%, p = 0.0003 respectively), as well as the absolute and relative values of the expression area of β-catenin (Δ165%, p = 0.0306 and Δ96%, p = 0.0018, respectively).

Conclusions
The accumulated world experience in the use of PRP-therapy in the treatment of AGA is mainly clinical. Only scarce data are available on the immunohistochemistry analysis from biopsy of skin, investigated the level of proliferative activity of HF cells and the number of vessels per mm2 using antibodies to Ki67 and CD31.
In our study an increase in the expression area CD34 reflects an improvement in the microcirculation and proliferation of HF cells during anagen, know that anagen-associated angiogenesis promotes hair growth and increases follicle size. An increase in the β-catenin protein level and an increase in its transcriptional activity shows activation of the Wnt / β-catenin signaling pathway and is also associated with increased cell proliferation, which was clinically manifested in a decrease in the proportion of telogen and vellus hair and an increase in the density and diameter of hair.
P 063

A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLINDED PILOT STUDY TO EVALUATE SUBLINGUAL MINOXIDIL IN ANDROGENETIC ALOPECIA: AN INTERIM ANALYSIS.

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Introduction
Androgenetic Alopecia (AGA) is the most common cause of hair loss in both men and women. AGA is produced by androgen-mediated hair follicle miniaturization in genetically susceptible individuals. Topical minoxidil is FDA, EMA and TGA-approved for the treatment of AGA and is generally available without prescription in most countries. Twice daily application of 5% minoxidil lotion produces a 9% average increase in hair count. Oral minoxidil is FDA, EMA and TGA-approved up to 100 mg daily for treatment of hypertension.

Objectives
To conduct a 32-week, double blind randomized placebo controlled trial to evaluate the efficacy and safety of sublingual minoxidil 0.45 mg once daily in men and women with AGA.

The primary endpoint is the change in hair count at week 24 from baseline as assessed by phototrichogram. Secondary endpoints are standardized global photographs of the frontal and vertex scalp by a blinded panel of 3 independent experts and patient satisfaction.

Methods
A sample size of 40 men and women with AGA, 20 in each arm, is sufficient to detect a difference in hair count of 20% between minoxidil 0.45 mg and placebo groups using a two-tailed z-test of proportions between two groups with 80% power and a 5% level of significance. Patients with scalp hair loss due to other conditions, a history of hair restoration surgery or using concomitant scalp hair growth medications or products during the study or within 12 weeks prior to commencing study were excluded. Dot ink tattoos were used to determine areas on the frontal and vertex scalp for macrophotography. The area measured for hair density was 1.7 cm². Photographs were uploaded onto a secure server and submitted to TrichoLAB for analysis and quantification. Novel hair-to-hair matching technology provided accurate quantification of new hair growth.

Results
Twenty nine men and 11 women were enrolled. Interim Results from the first 12 patients to complete the study are presented. Five were on minoxidil, 7 on placebo. The mean baseline hair density in the active group was 161.3 hairs per square centimetre (hair/cm²) and the placebo group was 202 hair/cm². At week 24, the mean hair density was 190.9 hair/cm² in the minoxidil group and 177.9 hair/cm² in the placebo group. Four out of 5 patients on minoxidil achieved an increase in hair count while six out of 7 patients in the placebo group had a decrease in hair density. The mean increase in the minoxidil group was 18.4% while the mean decrease in the placebo group was 12.3%. The difference between the 2 groups was 30.7%.

Conclusions
The interim analysis suggests that sublingual minoxidil 0.45 mg daily may promote new hair growth at 24 weeks. Continuation of the trial is warranted. This is the first report of the use of sublingual minoxidil for the treatment of AGA.
YUFA PROMOTES HAIR GROWTH AND PROLONGS ANAGEN HAIR CYCLE: IN VIVO AND IN VITRO EVALUATION

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The key feature of androgenetic alopecia (AGA) is a progressive shortening of the anagen duration and resultant progressive miniaturization of terminal hairs to vellus-like hairs. Therefore, promote or prolong anagen duration of hair follicle is a key to develop remedies for treatment and prevention of hair loss. Minoxidil and finasteride have been approved to treat hair loss by the Food and Drug Administration. However, some of side effects of those substances had been issues for curing hair loss problems. YUFA is a natural plant essence which contains Gynostemma pentaphyllum, Swertia japonica, Polygonum multiflorum, Panax ginseng and Angelica sinensis.

This study evaluated the effect of YUFA on hair growth by using in vivo and in vitro models. Topical YUFA administration for hair regeneration was investigated using an in vivo model with C57BL/6 mice. Effects of YUFA on human hair growth were investigated using an in vitro hair follicle organ culture model.

As Results, YUFA-treated mice showed remarkable promotion of hair growth after 14 days of application. Hematoxylin and eosin staining was performed for investigation of progression of the hair cycle. At day 7, hair follicles for both YUFA and minoxidil-treated mice had progressed to the anagen phase, whereas hair follicles in control mice remained in the telogen phase.

At day 14, hair follicles in control mice had progressed to the anagen phase, whereas YUFA and minoxidil treated mice showed markedly increased depth and size of hair follicles, compared with control mice. At day 28, most hair follicles in mice of each treatment group were in the anagen VI stage.

Thus, YUFA induced an earlier telogen-to-anagen conversion and prolonged the mature anagen phase in C57BL/6 mice. When human hair follicles were cultured in the presence of YUFA for 8 days, YUFA significantly promoted the hair growth and prolonged anagen duration by reducing apoptosis and inducing proliferation of hair follicle cells in the bulb region.

YUFA exert a hair growth promotion effect and, therefore, can be used as a therapeutic agent for prevention of hair loss.
EFFECTS OF OVEREXPRESSION OF LRRC15 ON HUMAN DERMAL PAPILLA CELLS

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Introduction
A number of studies showed that the balding frontal and non-balding occipital hair follicles of androgenetic alopecia patients have different characteristics. This is at least partly due to the difference of dermal papilla (DP) in those follicles. In this study, we analyzed RNA transcripts obtained from three-dimensionally (3D)-cultured frontal DP cells and occipital DP cells. Many genes were found to be differentially expressed between two kinds of DP spheres.

Methods
Of the genes upregulated in frontal DP spheres, we focused on the role of LRRC15. LRRC15 is a type I transmembrane protein 15-leucine-rich repeat containing membrane protein, and is also a kind of the LRR superfamily. LRR superfamily is known to be associated with protein-protein interactions and signal transduction, but its role in hair biology has not been reported. Assuming that increased expression of LRRC15 in frontal DP spheres may contribute to the characteristics of balding hair follicles, we first assessed the effects of overexpression of LRRC15 on DP cells.

Results
We observed that overexpression of LRRC15 in occipital DP cells inhibited the viability of cells as examined by MTT assay. We also observed that H2O2-mediated inhibition of cell growth is further exacerbated by overexpression of LRRC15 in occipital DP cells. Since the resistance to ROS is decreased in LRRC15 overexpression, we next examined expression of COX2, a target gene of ROS-induced NF-κB signaling pathway.

Comment
We found that the level of COX2 transcript is increased by LRRC15 overexpression. In addition, COX2 transcript was further increased by H2O2 treatment in LRRC15 overexpressed occipital DP cells.

Conclusion
Our data suggest that increased expression of LRRC15 in frontal DP cells makes these cells more vulnerable to ROS and may contribute to the characteristics of balding hair follicles.
ROLES OF MATURE ADIPOCYTES IN HUMAN HAIR GROWTH

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Introduction

Human hair follicles are buried deeply in adipose tissue during anagen phase and must be strongly interacting with adipocytes. Recently, the functions of premature adipocytes and adipose derived stem cells in hair follicle regeneration were elucidated, but the functions of mature adipocytes in hair growth have not been fully understood.

Objective

In this study, we investigated the role of mature adipocytes (differentiated adipocytes: difAD) compared to preadipocytes in the gene expression of dermal papilla cells by using co-culture system and conditioned medium of adipocytes.

Comment

Gene expression profiling revealed that matrix metalloproteinase 1 (MMP1) was strongly suppressed by difAD, while type I collagen which is a substrate of MMP1 was slightly upregulated. During transition from anagen to telogen, dermal papilla rapidly shrinks with degradation of extracellular matrix components. Since it was observed that type I collagen was abundantly present in dermal papilla during anagen phase, it was possible that mature adipocytes may contribute to maintaining extracellular matrix composition of dermal papilla by suppressing collagen degradation. Moreover, difAD enhanced the expression of fibroblast growth factor 7 (FGF7) and some other factors which have hair growth promoting effect in dermal papilla cells. Additionally, difAD themselves strongly expressed insulin-like growth factor 1 (IGF1).

These functions of mature adipocytes might be essential for maintenance of anagen hair follicles. To clarify the direct involvement of difAD in hair growth, single isolated human hair follicles were cultured with conditioned medium of adipocytes, resulting that difAD could inhibit anagen-catagen transition.

Conclusion

Thus, our study suggests that mature adipocytes are involved in human hair growth and play distinct roles from immature adipocytes.
DO HUMAN DERMAL ADIPOCYTES SHIFT FROM LIPOGENESIS TO LIPOPHAGY AND LIPOLYSIS DURING ANAGEN-CATAGEN TRANSITION?

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Introduction

A previously underappreciated skin depot, dermal white adipose tissue (DWAT) undergoes well-documented fluctuations in size across the murine hair cycle. In contrast, changes in function, size, and metabolism of dermal adipocytes (DAs) during the human scalp hair cycle remain unexplored. Therefore, we aimed to investigate key changes in human DAs adjacent to scalp anagen versus catagen HFs at the ultrastructural level.

Methods

Transmission electron microscopy was conducted on uncultured anagen VI versus early catagen HFs enveloped in DWAT.

Results

Interestingly, DAs surrounding catagen HFs displayed well-defined circular vacuoles within their lipid droplets (LDs) compared to DAs adjacent to the LDs of anagen HFs, a feature that is reminiscent of autophagy in certain yeast studies. These Results suggest that human DAs utilize autophagy to undergo lipophagy within their LDs during anagen-catagen transition.

To confirm this hypothesis, we carried out whole-mount staining of hair follicles (HFs) and surrounding DWAT for the autophagy marker LC3B; preliminary Results confirmed the increased presence of LC3B+ LDs adjacent to catagen HFs. Furthermore, DWAT around catagen HFs engaged in greater glycerol and free cholesterol release compared to DWAT surrounding anagen HFs, a feature that suggests increased lipolysis.

Conclusions

Thus, we hypothesize that human DAs switch from lipogenesis during anagen to lipophagy and lipolysis together with release of free glycerol and cholesterol during catagen. Given the preliminary nature of our Results, we propose various experiments to further prove our hypothesis, and discuss the potential effect that DWAT-derived free cholesterol may have upon HF cycling. Overall, we believe that these Results represent an encouraging start towards characterizing the functions of human DWAT.
TREATING PRIMARY AND SECONDARY SCARRING ALOPECIAS WITH ADIPOSE TISSUE PRIOR TO HAIR TRANSPLANTATION: A 5 YEAR EXPERIENCE

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Introduction
Scarring (cicatricial) alopecia results from follicular damage that is sufficient to cause the destruction and replacement of pilosebaceous structures by scar tissue. The surgical management of any progressive scarring alopecia imposes risk of reactivation of disease.

Scars in hair bearing areas are a very common indication for a hair transplant procedure and they can be a result of multiple etiologies including physical, thermal, chemical or surgical injury. While transplanting grafts into larger scars or scarring alopecia there is an increase risk of tissue necrosis especially in the central zone of the scar due to poor or compromised vascularization.

Adipose tissue injection can minimize the risk of these complications and contribute to achieving better result.

Objective
The aim of this presentation is to show benefits of pretreating primary and secondary scarring alopecias with autologous adipose tissue prior to performing a hair transplant procedure. It is authors’ belief that pretreatment can maximize regrowth of transplanted hair grafts.

Material and methods
Autologous adipose tissue is harvested from the donor area by mini-liposuction. The surgical procedure is performed under local anesthesia with the abdomen being the preferable donor site for adipose tissue harvesting. Selected area is infiltrated with tumescence. 3 mm diameter, 15 cm long 3-hole distal opening blunt tipped cannula (Tulip, San Diego, CA) attached to a 10 cc syringe is used to harvest adipose tissue. Fat is filtrated by Puregraft®, closed membrane filtration system that removes tumescent fluid, oil, blood cells and debris leaving purified fat. The use of Puregraft closed system was important due to longer viability of fat processed by this system. PRP (Platelet Rich Plasma) can be added into adipose tissue in order to improve graft survival and further soft tissue restoration.

Purified adipose tissue with PRP is then put in 1cc Luer-lock syringe connected to a 21-gauge blunt cannula, and then injected into subcutaneous layer of scalp while creating multiple tunnels running in different directions. This technique was also helpful in releasing scar adhesions to deeper tissue. Three months later, after assessing the survival of the fat graft, hair transplantation procedure can be performed. This period is critical to ensure the graft survival as well as for neoangiogenesis to take place.

Hair grafts are harvested either by strip of FUE method and implanted into areas affected by scarring alopecia.

Conclusion
The outcome of hair transplantation procedure in patients with scarring alopecia varies because of the suspected systemic autoimmune nature of this disease. Adipose tissue grafting prior to hair grafting showed improvement in skin texture, vascularity and outcome of hair transplant procedure.
Erosive Pustular Dermatosis of the Scalp, A Case Series

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Introduction
Erosive pustular dermatosis of the scalp is an inflammatory, chronic and relapsing disease of the scalp and less frequently the legs. It predominates in the elderly with a history of actinic damage, physical or mechanical trauma. It affects the frontal region and vertex and is characterized by plaques of erythema, pustules and yellowish crust of oily appearance that when detached leave eroded areas. When they resolve, they tend to atrophy and cicatricial alopecia. There is no curative treatment for this disease. Case series have been published in Europe, so we could not find publications in Latin American population.

Methods
A retrospective review of the patients diagnosed with erosive pustular dermatosis was performed. Clinical and trichoscopic findings, as well as therapeutic choices, were recorded.

Results
We report 5 patients with erosive pustular dermatitis of the scalp, evaluated from January 2017 to November 2018 in a dermatological center in Mexico City. Two men and three women, with an average age of 77.6 years (range of 54-96 years). The five cases had some associated risk factor: antecedent of resection of squamous cell carcinoma, two cases with a history of cryotherapy for actinic keratosis, one resection of a basal cell carcinoma, and another referred repetition trauma with the edge of his litter. The evolution was from 6 months to 4 years, with periods of exacerbation and partial improvement. The clinical presentation observed in all cases corresponded to erythematous plaques, hematic, and yellowish crusts of oily appearance, in addition to superficial erosions. Pustules were documented in three patients. A dermatoscopy showed severe cutaneous atrophy with absence of follicular openings, yellow and yellowish crust, telangiectasia, and pustules. All the patients showed different degrees of cicatricial alopecia. The five patients were treated with 0.05% betamethasone cream once a day for 10 days and then pimecrolimus 1% cream twice a day for 3 months, with resolution of the pustules and erythema, with residual atrophy, with free periods of disease from 4 to 8 months.

Conclusion
Erosive pustular dermatosis of the scalp is rare and is considered a diagnosis of exclusion. A high index of suspicion is required, since it is usually confused with other entities such as actinic damage and actinic keratosis, squamous cell carcinoma and bacterial diseases that do not respond to conventional treatments or patients undergo numerous biopsies to rule out skin cancer or they are over treated with cryotherapy. There is no established treatment, the use of high-potency steroids is controversial because of the risk of atrophy in patients with perioral atrophic skin due to advanced age and previous photodamage. Other authors have described the use of 0.1% tacrolimus in ointment, however, in our experience caused irritation and burning so severe that patients discontinued their use after 1 to 3 days, so we suggest the initial use of a medium steroid potency and subsequently an inhibitor of calcineurin such as pimecrolimus or tacrolimus.
Background
Folliculitis decalvans (FD) is a type of scarring alopecia characterized by follicularly based pustules and crusting that is often associated with bacterial infection. It has been reported that the preponderance of patients have staphylococcal (staph) infections. In this study we aimed to evaluate rates of non-staphylococcal infections in patients with FD.

Methods
Retrospective chart review of patients seen at a hair referral center at Kaiser Permanente Northern California.

Results
Thirty-nine patients with biopsy proven FD were identified for inclusion in the study. The majority of patients were male (77%). Average age was 46 with a range of 26-70 years. Race was self-reported as white (41%), black (28%), Hispanic (18%), Asian (8%), unknown (5%). Five patients did not have cultures. Of the remaining 34 patients, 97 bacterial cultures were done. The majority of cultures showed staph: S. aureus (15), methicillin-resistant S. aureus (15), S. lugdunensis (4). Eleven patients (32%) had gram-negative rod infections: Escherichia coli (7), Enterobacter aerogenes (6), Klebsiella pneumoniae (6), enteric gram-negative rods (5), Pseudomonas aeruginosa (2), Enterobacter cloacae (1), Klebsiella oxytoca (1), Proteus mirabilis (1), Citrobacter koseri (1), Serratia marcescens (1).

Conclusions
In this cohort, the rate of gram-negative rod infections was high and likely represents a referral bias of patients who did not respond to standard treatment. Potential causes for these infections includes long-term antibiotic use as well as nosocomial/environmental exposure and disruption of the normal epidermal barrier due to ongoing inflammation.

We conclude that regular bacterial cultures should be considered in patients who have ongoing/active disease to evaluate for the presence of non-staph bacterial infections. Additionally, alternative treatments including appropriate antibiotics, eradication of the potential source of the infection, topical or systemic retinoids, and re-establishment of the epidermal barrier may be necessary for disease control.
FOLLICULITIS DECALVANS OF THE FACE
A RARE CLINICAL MANIFESTATION

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Introduction

Folliculitis decalvans (FD) is a rare neutrophilic cicatricial alopecia, predominantly observed on the vertex and the occipital area of the scalp. FD is characterized by follicular pustules, crusts, “tufted hairs” and perifollicular hyperkeratosis with development of scarring alopecic patches as outcome.

Case report

We report on a 73-year old male patient with folliculitis decalvans faciei with predominant manifestation in the beard and eyebrows region. For differential diagnosis tinea faciei, lichen planopilaris, lupus erythematoses and primary cicatrical alopecia were considered. Finally, pathomorphological examination proved to be the diagnostic clue for the diagnosis. Two months prior to first presentation to our department the patient started to develop pustules on the beard region and erythema with pustules on the upper lip. Simultaneously with mentioned above lesions patchy hair loss along with erythema and edema were present on eyebrows.

The patient underwent a treatment with systemic clindamycin 600 mg/daily and topical steroids (prednisolone pivalat) without any change. All routine laboratory analyses including differential blood cell count, liver enzymes, bilirubin, creatinin and urea proved to be normal. ANA and Anti/ds- DNA-antibodies were negative. Repeated microscopic and cultural bacterial and mycological examinations were all negative. Due to clinical findings initially antimycotic treatment with itraconazol 200 mg for 7 days combined with topical clindamycin 1% and benzoyl peroxide 5% gel was administered, which led to reduction of pustules and erythema on upper lip. Methylprednisolone aceponat 0,1% crème was prescribed topically on eyebrows region for symptomatic treatment. Histological examination from the chin and facial skin presented perifolliculitis accompanied by granulomatous inflammatory reaction consisting of lymphocytes, giant cells and neutrophilic granulocytes in the dermis. Perifollicular fibrosis was illustrated. PAS-staining was negative for fungi. Folliculitis decalvans of the beard with partly destroyed hair follicles was diagnosed. Oral clindamycin 300 mg twice daily and fusidic acid cream were prescribed for longtime treatment.

Comment

FD is a rare chronic inflammatory scarring alopecia affecting young adults presenting usually as papules, pustules and abscesses characterized by granulomatous cell infiltrate and perifollicular fibrosis. Only few individual cases have been reported with manifestation of FD in the beard. Differential diagnosis of the clinical manifestation in our patient comprised a wide range of inflammatory alopecia while histopathology was a crucial key in the final diagnosis.
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CENTRAL CENTRIFUGAL CICATRICIAL ALOPECIA FOLLOWING A PATCHY PATTERN: A NEW FORM OF CLINICAL PRESENTATION AND A CHALLENGING DIAGNOSIS FOR THE DERMATOLOGIST.


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Introduction
Central centrifugal cicatricial alopecia (CCCA) is included among the primary lymphocytic cicatricial alopecias. Its current term of CCCA was established in reference to its clinical pattern of presentation, which begins in the central area of the scalp and has a progressive centrifuge evolution. However, a new clinical variety of CCCA presenting with patches of hair loss affecting the lateral and posterior scalp has been recently described.

Case report
A 50-year-old woman from Ghana with previous history of hair straightening using chemical products as well as hair styling that involved important traction of the hair in her youth referred hair loss for more than 10 years.

Results
In the physical exam a central alopecic patch on the vertex and numerous interconnected alopecic patches in the occipital and both parietal areas were visible.

The trichoscopy revealed a honeycomb network, pinpoint white dots in an irregular distribution, variations in hair shaft diameters, white patches and peripilar grey-white halos.

A biopsy was performed on one of the parietal patches and confirmed CCCA diagnosis, with the presence of premature desquamation of the inner root sheath, broken hair shafts and and compound follicular structures with perifollicular fibrosis forming goggles.

Conclusion
The current nomenclature of CCCA suggested by the North American Hair Research Society (NAHRS) refers to the traditional clinical presentation pattern of this type of alopecia. In the majority of patients with a clinical and/or histopathological diagnosis for this kind of alopecia this pattern is also described. However, some exceptions should be highlighted; like some cases presented by the groups of Nicholson, Khumalo or Olsen and finally the description by Miteva et al of a CCCA with a patchy pattern, manifesting with alopecic patches in the parietal or occipital areas in addition to the traditional central affection. This new patchy presentation of CCCA has a difficult differential diagnosis with other alopecias that have patches as their presentation such as alopecia areata, lichen planopilaris, discoid lupus erythematosus, tinea capitis or traction alopecia. The characteristic trichoscopy findings of the CCCA such as the peripilar grey-white halos, the irregular interfollicular white dots over a honeycomb network or the cicatricial white areas and, at a histological level, the inflammation and compound follicular structures with perifollicular fibrosis or the destruction of sebaceous glands will allow the correct diagnosis.

Here we report a new case of CCCA presenting with a patchy pattern. Knowing the existence of this new presentation of the CCCA is essential to perform an accurate diagnosis that will allow a directed treatment and avoid an unfortunate prognosis. Both the trichoscopy and the histopathology are essential for confirmation. We suggest a reflexion regarding the current CCCA terminology, due to the fact it does not comprise all the cases of this pathology.
SURGICAL CORRECTION POSSIBILITIES OF SCALP PATCHES IN PATIENTS WITH WIDESPREAD FORM OF LICHEN PLANOPILARIS

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Introduction
Lichen planus is a chronic inflammatory disease of the skin and mucous membranes, skin appendages, the main typical elements of which are papules. Follicular form of lichen planus - Lichen planopilaris (LPP), is characterized by development of cicatricial alopecia (the group of primary cicatricial alopecia). Late stages of lichen planopilaris often have extensive patches of cicatricial hair loss.

Therapeutic Methods of treatment do not allow hair growth in the patches of alopecia, surgical Methods of correction (reduction, hair transplant) can be used to close the defective patches. The purpose of the demonstration of a clinical case in a person with extended patches of hair loss, because of deprived hair loss, is to show the possibility of closing the patches of cicatricial alopecia with hair transplantation.

Methods
Several FUE hair transplants were performed, a histological examination and a hair transplant were performed earlier. It was also tested for hair transplantation from alternative donor areas (chest and beard).

Results
The Results of surgical correction had a positive effect on the closure of missing hair areas, visual perception of defective patches formed as a result of the scar process. Activation of the disease after surgical treatment was not observed. Subsequent hair transplant sessions are planned, including the use of hair from alternative donor areas (chest and beard) with maximum exhaustion of the normal donor area.

Conclusion
Surgical correction of stable stages of lichen planopilaris (LPP) can have a positive result, giving the opportunity to cover areas of no hair, if it is impossible to obtain the effect of therapeutic treatment. For optimal Results it is necessary to follow the rules for this method in patients with flat hair on the nose in stable stages.
TRICHOSCOPIC AND HISTOPATHOLOGICAL CHARACTERISTICS OF CENTRAL CENTRIFUGAL CICATRICIAL ALOPECIA IN A PHOTOTYPE III PATIENT.

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Introduction
Central centrifugal cicatricial alopecia (CCCA) is the most common form of scarring alopecia in African-American high phototype female patients.

Case report
We report a 56-year-old caucasian woman, phototype III, with no other personal history of interest, with a five-year history of progressive alopecia associating isolated episodes of pruritus and hair sensitivity. Visual inspection showed a blonde, curly hair with diffuse alopecia predominantly in vertex. Pull-test and tug-test were negative. Trichoscopy showed decreased follicular density with loss of follicular orifices and pronounced follicular hyperkeratosis with slight perifollicular erythema at the infundibulum. Remarkable findings were the presence of an accompanying whitish perifollicular halo and the presence of hyperpigmentation with a honeycomb pattern in the interfollicular spaces. The hair shafts showed no alterations nor signs of miniaturization. Suspecting CCCA, a cutaneous biopsy was performed. It showed a superficial perifollicular and perivascular lymphocytic infiltrate, perifollicular concentric laminar fibrosis in onion layers and a decrease in the number of sebaceous glands. The follicular epithelium of some follicles was fused at the level of the outer radicular sheath.

Discussion
The estimated prevalence of CCCA in African-American women is around 3%. It was first recognized in woman of this group population with traction-inducing hairstyling practices such as tight braids; weaves; and use of chemical relaxers. Currently CCCA does not affect only woman with tractional hairstyling practices, several factors, including mechanical factors specific to the follicle, heredity, and Methods of hair grooming, contribute to this predisposition. Clinical features of CCCA consist on a chronic and progressive central scalp hair loss which expands centrifugally. Follicular papules and polytrichia can be present. Advanced cases show a smooth and shiny scalp with impressive follicular dropout.

Discussion
There is typically no overt evidence of inflammation. The most common trichoscopic features are:
1) Peripilar white halo;
2) Honeycomb-pigmented network;
3) Pinpoint white dots; and
4) Hair shaft variability.

Histology shows common features with other lymphocytic cicatricial alopecias. In active stages there is a follicular lichenoid inflammation that progresses into follicular fibrosis.

Main diagnostic keys are:
1) Reduced follicular density with altered follicular architecture due to areas of follicular dropout;
2) Absent or only focally preserved sebaceous glands;
3) Premature desquamation of the inner root sheath and
4) Individual or compound follicular structures surrounded by perifollicular fibrosis (google-like structures).

Conclusion
We report a case of CCCA in a patient with fair skin type. This is the first report of CCCA in a woman with this characteristics. Trichoscopic and histologic findings were the same that had been previously described in dark skin types.
CLINICAL CASE OF SCALP METASTASIS FROM BREAST CANCER

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Introduction & objectives
Cutaneous metastases have been associated with lung, gastric, and breast cancers in the late stages. Breast cancer is the most common tumor among women.
Scalp metastases are rare and a few cases have been described as the only sign of progression or widespread metastatic disease.

Case report
The patient is a 65-year-old female with concerns of a firm, painless, immobile, hardened, skin-colored mass fixed to the underlying tissues, alopecia-like patches.
She had a history of breast cancer 20 years prior. She noticed the lesions one year ago and was treated with topical glucocorticosteroids and antimicotics for a short period of time (1-2 months).
The lesions measured 1 to 3 cm on the scalp frontal and occipitalis without regional or distant lymphadenopathy. In late stage (about 8 months) lesions became depressed and erythematous.

Results
Suspected lesions on the scalp were observed under trichoscopy and showed such vascular structures as: extravasation, aborizing vessels, dotted vessels, milky red globules.

A biopsy of the scalp lesion with a diameter of 1 cm was obtained. Histological examination of biopsied tissues showed: epidermis of irregular thickness, insignificant hyperkeratosis, acanthosis. The dermis is strongly fibrosing, anaplastic cells with large hyperchromic nuclei are seen between the collagen fibers, forming chains and primitive glandular structures. Pathology test Results showed metastasis from breast cancer.
The patient was referred to oncology service and now is at a process of examination.

Conclusions
Given that the clinical characteristics of cutaneous metastases are not significantly specific, elderly individuals presenting with multiple or solitary, painless, cutaneous nodules or non-typical alopecia should be examined and investigated carefully to rule out metastatic diseases.
Metastasis to the skin is often a preterminal event that heralds poor prognosis.
Introduction
Erosive pustular dermatosis of the scalp is a chronic eruption that leads to scarring alopecia.

Material & Methods
We performed an international open multicenter clinical study including patients with a diagnosis of erosive pustular dermatosis in order to describe the epidemiology, clinical presentation, diagnostic findings and therapeutic choices of this disease. In all, 56 patients (29 women and 27 males) were included, with a mean age of 62.7 years.

Results
The vertex was the most common location (44 patients), followed by the frontal and parietal areas (respectively 17 and 5 patients). The disease mean onset time was 26 months, ranging from 3 to 144. Mechanical and/or chemical trauma was reported in 16 patients, actinic damage in 14 patients, a previous infection in 6 patients and a previous cryotherapy in 3 patients. Androgenetic alopecia was present in 27 patients, 5 of whom had previously treated it with topical minoxidil. Trichoscopy showed an absence of follicular ostia with skin atrophy, associated with tufted and broken hair. In active cases, crusts, a serous exudate, enlarged and dilated vessels, perifollicular pustules and hyperkeratosis were also present. Histopathology revealed 3 different features, depending on the disease duration.

The most prescribed therapy was topical steroids (35 patients), followed by the association between topical steroids and topical tacrolimus (5 patients) or systemic steroids (4 patients); topical tacrolimus 0.1% alone was prescribed only in 3 patients. A reduction of inflammatory signs was observed in 28 patients treated with topical steroids and in all 3 patients treated only with topical tacrolimus 0.1%.

Conclusion
The relatively high number of patients allowed us to identify a better diagnostic approach, using trichoscopy, and a more effective therapeutic strategy, with high-potency steroids or tacrolimus, which should be considered as first-line treatment.
DERMOSCOPIC FEATURES OF FOLLICULITIS DECALVANS: A STUDY OF 42 CASES AND THEIR CLINICO-PATHOLOGICAL CORRELATIONS

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Introduction & Objective
Folliculitis decalvans (FD) is an uncommon form of primary cicatricial alopecia, which causes centrifugally progressive permanent hair loss accompanied by inflammation of the scalp lesions. The objective of this study was to describe the dermoscopic features of FD and to describe the clinico-pathological correlations.

Material & Methods
Dermoscopic images and histopathological specimens were obtained from the scalp lesions of 42 patients with FD, and clinical courses were reviewed retrospectively.

Results
Dermoscopy of the affected sites in all the patients revealed the histological finding of absent follicular ostia, which indicated the loss of follicles and sebaceous glands.
Most of the patients presented tufted hairs (dolly hairs) emerging from a common dilated follicular ostium, which histologically corresponded to fused infundibula with numerous hair shaft clusters as well as white to milky-red areas correlating with dermal fibrosis and a dense infiltration of inflammatory cells.
Serous or hemorrhagic crusts and follicular pustules were observed in the inflamed areas where Staphylococcus aureus was frequently identified by bacterial culture and associated with the disease activity. Thickened perifollicular and interfollicular, keloid-like areas showing the histological features of epidermal hyperplasia and dermal fibrosis were noticed in the early stages of the lesions. Perifollicular scales with follicular and epidermal hyperkeratosis, perifollicular erythema corresponding to intrafollicular and perifollicular inflammatory cell infiltration, and keratotic infundibular plugs due to hyperkeratosis tended to remain even after the inflammation of the scalp lesions decreased.

Conclusions
Dermoscopy is useful for the diagnosis and the disease activity of FD.
CICATRICIAL ALOPECIA AS AN OUTCOME OF CHRONIC MUCOCUTANEUS CANDIDIASIS

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Cicatricial alopecia is a destructive immune-mediated hair loss that develops as a result of perifollicular fibrosis associated with a wide range of autoimmune diseases and other comorbidities. We report on a 10 year clinical observation of the male patient diagnosed with APECED syndrome presented in this case with chronic recurrent mucocutaneous candidiasis and secondary cicatricial alopecia of the scalp.

In 2008, the 6 years old patient was hospitalized with horn-like formations of yellow-brownish color – adhered to the underlying skin accompanied by itching. Regarding the anamnesis, recurring candidiasis episodes on the oral mucosa were detected in the newborn period.

At the age of 1 year systemic antibiotic treatment and erythromycin ointment were prescribed because of pyoderma lesions on the face. Few weeks afterwards, the growth of tumor-like formations and horns, which periodically fell off and grew back, was noticed on the scalp and face region. The child was observed by a dermatologist and an oncologist and diagnosed with hyperkeratosis of unknown etiology.

Routine laboratory analyses as differential blood cell count, liver enzymes, HIV-test, serum hormones (TSH, T3, T4, STG, and cortisol), cultural mycological and pathomorphological examinations were performed. Blood count test revealed anemia, leukopenia, lymphopenia, increased eosinophils and ESR. Liver exams showed increased levels of AST, ALT and alkaline phosphatase. Hormones - reduced cortisol. Ascaris lumbricoides eggs were detected in coprogram.

Cultural examination revealed an excessive growth of Candida albicans.

Based on the obtained data, the clinical diagnosis of chronic mucocutaneous candidiasis, ascariasis, iron-deficiency anemia, hypocorticotoidism was carried out. Oral fluconazole (50 mg) daily for 14 days, mebendazole (200 mg) daily for 3 days, vitamins were prescribed. Externally, 5% salicylic in mixture with clotrimazole ointments used.

From the 7th day until 17th day of therapy all the horn formations fall off. Due to a chronic inflammation, secondary cicatricial alopecia developed on the scalp. Trichoscopic findings diagnosed perifollicular fibrosis, telangiectasia, and post-inflammatory hyperpigmentation.

In May 2018, the patient was readmitted again with verrucous growths and crusts, mainly on the face. This relapse lasted for 3 months and was related to prolonged episode of coughing.

Based on the findings, the patient was diagnosed with the type 1 autoimmune polyglandular syndrome (APECED) - a rare inherited autosomal recessive disease caused by mutations in the AIRE gene involved in the regulation of the autoimmune response.

The clinical picture of APECED syndrome is associated with autoimmune damage to the organs of the endocrine and other systems. The main symptoms of the disease are the chronic mucocutaneous candidiasis, hypoparathyroidism and chronic primary adrenal insufficiency accompanied with minor clinical features.
FOLLICULITIS DECALVANS IN ASSOCIATION WITH CROHN’S DISEASE: CASE REPORT

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Introduction
Crohn’s disease is a chronic inflammatory bowel disease often associated with distinctive mucocutaneous manifestations, including, in particular, erythema nodosum, pyoderma gangrenosum, Sweet’s syndrome, and oral aphthous ulcers.

There have also been reported cases of hair loss in patients with inflammatory bowel disease, mostly involving chronic diffuse hair loss and alopecia areata.

Folliculitis decalvans is a neutrophilic cicatricial alopecia, the pathogenesis of which remains unclear. We present a case of a patient who was diagnosed with folliculitis decalvans and soon after with Crohn’s disease.

Case report
A 30-year-old male patient was referred to our department of dermatology in March 2018 for the clinical evaluation of recidivating painful inflammatory lesions on his scalp vertex, which were healing with scarring.

The first skin manifestations were noticed in 2015. In 2016, he also began experiencing recurrent perirectal abscesses. In 2016 and 2017, he underwent two colonoscopies, a CT scan of the abdomen, and a PET CT scan. Despite the positive ASCA serology test, all of these imaging studies failed to prove any significant pathology. During these three years, the patient underwent several surgical procedures.

In March 2018, he visited our department, and we performed a skin biopsy on the vertex of the scalp, confirming the diagnosis of folliculitis decalvans.

Laboratory tests including complete blood cell count, liver and kidney function tests, C-reactive protein, thyroid gland function tests, syphilis, and ANA screening showed no pathology. A bacterial culture of purulent exudate identified Staphylococcus epidermidis. We prescribed a combination therapy consisting of prednisone 40 mg as an initial dose and clindamycin 300 mg. The patient also received betamethasone/gentamicin cream as a topical treatment. During this treatment regimen, no folliculitis decalvans outbreaks happened.

Unfortunately, relapses did occur when the prednisone dosage was lower than 20 mg.

During this time, the patient underwent more gastroenterological checkups, leading to the diagnosis of Crohn’s disease. In November 2018, adalimumab treatment was initiated. Soon after, we gradually lowered the prednisone dosage to 15 mg/day, and no folliculitis decalvans relapses occurred during the next two months of follow-up.

Comment
To the best of our knowledge, this is the first report of Crohn’s disease and concomitant folliculitis decalvans.
A RARE CASE OF A MAN WITH FIBROSGING ALOPECIA IN A PATTERN DISTRIBUTION

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Introduction
Fibrosing Alopecia in a Pattern Distribution (FAPD) is a recently discovered form of cicatricial patterned alopecia described in 2000 by Zinkernagel and Trüeb as a possible variant of lymphocytic primary cicatricial alopecia.
FAPD clinically presents as a male or female pattern alopecia, featuring with hair rarefaction, miniaturized hairs and anisotrichia on the crown area of the scalp associated with perifollicular fibrosis and loss of follicular ostia.
Histopathology is similar to what is seen in patients with lichen planopilaris associated with androgenetic features. Based on literature data, it seems that FAPD is much more prevalent in women, since there are only nine cases reported so far in male patients.

Case Report
The authors hereby describe a 53-year-old man with a history of eight months of diffuse and progressive hair loss, mainly noted in the vertex region, who was diagnosed as having FAPD. A global photographic assessment showed reduced hair density in the crown area and dermoscopic examination of the scalp revealed anisotrichia, perifollicular erythema and scaling and absence of follicular ostia, suggesting the existence of an inflammatory process admixed with fibrosis.

Three scalp biopsies were taken. The histopathology revealed increased number of miniaturized hair follicles, the presence of lymphocytic inflammatory infiltrates, perifollicular lichenoid folliculitis with fibrosis and vacuolar degeneration of the follicular basal layer. FAPD represents a unique entity that is, by definition, related to AGA, but with a perifollicular lichenoid inflammatory infiltrate which finally turns into lamellar fibrosis. Genetic, environmental, and hormonal factors may explain the clinical pattern and reported efficacy of anti-androgens in addition to the anti-inflammatory modalities for treatment of this distinctive disease.

Conclusion
The hallmark of this type of alopecia is the combination of clinical and histopathological features of lichen planopilaris and androgenetic alopecia.
Introduction
Lichen planopilaris (LPP) is considered as a follicular variant of lichen planus. The main clinical manifestations of LPP include classic form, frontal fibrosing alopecia (FFA), and Graham-Little-Piccardi-Lassueur syndrome (GLPLS). GLPLS is a relatively rare lichenoid dermatosis composed of progressive cicatricial alopecia of the scalp, the non-cicatricial loss of pubic and axillary hair and follicular keratosis lesions of body.

We report a case of middle-aged Chinese patient presenting as a GLPLS with massive hair casts and normal pubic and axillary hair.

Case Report
A 35-year-old female complained of multiple patchy hair loss with itching on her scalp and dandruff-like things on her scalp hair for about two years. Physical examination reveals multifocal bean-sized scarring alopecia of her scalp, dandruff-like hair casts and perifollicular erythema throughout the head except occipital area, as well as keratotic papules and hair loss over the trunk and the extremities. Light microscopy examination for head lice was negative. Trichoscopy showed preservation of perifollicular erythema and small blood vessels with silver-white perifollicular scaling and hair casts distributed along the hair shafts.

Histopathology of vertical section of scalp punch biopsy showed a lichenoid inflammation limited to the upper portions of the hair follicles. The final diagnosis was GLPLS, and to the best of our knowledge, this is the first Case report of GLPLS in Chinese population.

Comment
Reported initially in 1913, GLPLS predominantly affects middle-aged females. The exact pathogenetic mechanism is still obscure, but it might be similar to LPP which was an immune-mediated inflammatory reaction induced by lymphohistiocytic infiltration of upper half of the pilosebaceous unit. Axillary and pubic hairs were involved in most previously reported GLPLS cases, however, in the present case axillary and pubic hairs were spared even trunk and extremities are extensive involved, which was rare in GLPLS.

Hair casts (peripilar keratin casts) are firm, white, freely movable tubular masses that encircle the hair shafts, which could be a feature for active LPP and visualized best on dry trichoscopy. Differential diagnoses for tons of white hair casts on the scalp include pili annulati, pediculosis capitis, pityriasis capitis (dandruff), tinea capitis and trichorrhexis nodosa.

In pili annulati, alternating light and dark bands could be seen in the hair shaft on trichoscopy, and the white bands are nearly the width of a hair and their borders are not clear-cut. In pediculosis capitis, the nits fixed to the side of hair shaft but not warp it.

Treatment of GLPLS is difficult for the scarring alopecia and the follicular keratotic eruption. The aim is halting the progression or improving the symptoms. Treatments with topical and intraleisional corticosteroids, hydroxychloroquine, doxycycline, cyclosporine, thalidomide and prednisone have been reported, however, their effectiveness is still controversial.
**PICCARDI-LASSUEUR-GRAHAM-LITTLE SYNDROME CASE REPORT.**

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**Introduction**
Piccardi-Lassueur-Graham-Little Syndrome (PLGLS) is a rare lichenoid dermatosis characterized by the triad of scarring alopecia of the scalp, keratotic papules on hairless skin, and non-cicatricial alopecia of the axillary and pubic regions. The alopecia of the scalp may precede the other clinical conditions from a few months to even years. Affects adults between 30 and 60 years old, being 4 times more frequent in women. The present Case reports a PLGLS, relevant due to its infrequent presentation and difficult treatment.

**Case Report**
A 58 year old woman consulted due to diffuse hair loss primarily in the frontal region, eyebrows, armpit and genitals; that began 6 years earlier. No relevant medical history.
In the clinical evaluation we found a chronic disseminated dermatosis to the frontal region of the scalp, trunk and armpits characterized by perifollicular keratosic papules.
In addition, to the recession of frontotemporal line, an alopecic patch in the crown area with diffuse hair loss in eyebrows, armpit and pubis.

**Scalp Biopsy:** Superficial reticular dermis with inflammatory infiltrate by lymphocytes. Terminal hair follicles surrounded by lymphocytes and multiple necrotic cells.

**Axillary Biopsy:** Epidermis with ortho-hyperkeratosis. Reticular dermis shows an interstitial inflammatory infiltrate due to lymphocytes and absence of hair follicles. Clinical-pathological features diagnose a Piccardi-Lassueur-Graham-Little syndrome.

Treatment is started with Prednisone 20 mg / day for 5 days, Triamcinolone Acetonide 0.05% Lotion, Minoxidil 2%; with partial improvement. Subsequently, intralesional Triamcinolone 10% was indicated without clinical improvement, so it was decided to start therapy with platelet-rich plasma monthly for 3 months.
Due to poor response to treatment it is considered to start treatment with Hydroxychloroquine.

**Conclusion**
Graham Little first described this entity in 1915. Its exact etiology remains obscure and there is no underlying systemic disorder except for one report of its association with androgen insensitivity syndrome. Histopathology shows follicular plugging with perifollicular infiltrate.
Eventually, epidermis becomes atrophic with follicular and dermal scarring. The treatment of this condition is a challenge with variable therapeutic response. First line high-potency Topical Steroids and infiltrations with triamcinolone Acetonide.
The use of topical tacrolimus, systemic steroids, hydroxychloroquine, methotrexate, cyclosporine, thalidomide, PUVA and doxycycline has also been reported with controversial Results. In our patient there was no improvement with the topical and intralesional treatment established, so we opted for systemic treatment.

A better understanding of the etiopathogenesis could be beneficial for future treatments.
Introduction & Objectives
Dissecting cellulitis is a chronic, relapsing, cicatricial alopecia that belongs to the follicular occlusion triad, which prognostic relies on an early clinical, trichoscopic and histopathological diagnoses. Usually described on the scalp, we report a male patient with an abscessed lesion in the neck, an unclear history of folliculitis in the area of the beard, with progressive dysphagia which diagnoses was very confused at the beginning. Clinical findings and diagnostic studies including trichoscopy suggested a dissecting cellulitis in the beard area, an atypical location in the clinical presentation of this type of primary cicatricial alopecia.

Case Report
A 27-year-old man, presented with a two-week history of a growing progressive neck mass associated to dysphagia with a similar history two years before that required drainage by surgery and a diagnosis of folliculitis was made. He received multiple cycles of antibiotics, including clindamycin, rifampicin and isotretinoin 20 mg/day 3 times per week, during three months without response.

Results
A complete workup was made, including infectious panel (VIH-RPR) and blood and secretion cultures were negative. A CT scan revealed a large abscess in the neck. A cervicotomy was made by head and neck surgery service. A dermatology consultation was requested finding at the physical exam a male with Fitzpatrick phototype III, nodules, pustules and alopecic patches of cicatricial appearance in the area of the beard, compromising the jaw, and also a large soft mass of approximately 5 cm, very painful to palpation in the left neck. Trichoscopy showed perifollicular pustules, yellow 3D dots, violaceous areas and areas with loss of the follicular ostium. With these findings, skin biopsy guided by trichoscopy was performed.

The histopathology showed a cicatricial alopecia mediated by neutrophil polymorphonuclear cells, with the presence of follicular tamponade, decreased hair follicles, foreign body giant cells, granulation tissue, fibrotic areas and hemorrhage foci. The patient completed a 7 days treatment with Ceftaroline and it was proposed to continue oral isotretinoin at higher doses than previously received, with a close follow up.

Conclusion
We report a male patient with clinical diagnosis, confirmed by trichoscopy and histopathology, of dissecting cellulitis in the beard area, atypical localization for this entity, commonly described in the scalp of patients with darker phototypes. Trichoscopy is highlighted as a tool of great diagnostic utility for the correct approach of primary scarring alopecias.
ABSTRACT BOOK • 11TH World Congress for Hair Research • SITGES, BARCELONA 2019 • SPAIN
POSTERS

CICATRICIAL ALOPECIA

THE GREAT MIMICKER: A CASE OF SCALP SARCOIDOSIS MIMICKING DISCOID LUPUS ERYTHEMATOSUS

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Introduction
Termed ‘the great mimicker,’ sarcoidosis is a complex, multi-system granulomatous disorder with diverse clinical presentations. Approximately 15-25% of patients with sarcoidosis will have cutaneous manifestations (Haimovic, 2012). Although scalp sarcoidosis has been described in the literature, it is rare and clinical presentations are varied. Both scarring and nonscarring forms of alopecia secondary to cutaneous sarcoidosis have been described. Included in the differential of scarring alopecia is discoid lupus erythematosus (DLE). Both DLE and sarcoidosis present with atrophy, crusting, scaling, and erythematous plaques, as well as local or diffuse scalp alopecia (Katta, 2000). On trichoscopy, perifollicular or follicular orange spots with prominent telangiectasias can help differentiate scalp sarcoidosis from DLE (Torres, 2011). Recognition of scalp involvement in sarcoidosis is paramount as it is a clinical clue for additional cutaneous and systemic involvement (Haimovic, 2012). Several cases demonstrate significant overlap in morphology, distribution, and scalp involvement between scalp sarcoidosis and DLE, thus necessitating histopathology for diagnosis (Dash, 2007).

Case Report
We present a 60 year-old female with known pulmonary sarcoidosis who presented to New York University Connective Tissue Disease Clinic for alopecia. For over 7 years, the patient had scattered erythematous and hyperpigmented atrophic plaques on the extremities that improved with topical and intralesional glucocorticoids, and were biopsy-proven as cutaneous sarcoidosis. During this period, she developed multiple alopecic areas on her scalp vertex, causing significant pruritus. Physical exam revealed multiple atrophic, erythematous and hyperpigmented plaques of the vertex scalp, with some scale noted. Trichoscopy revealed perifollicular orange spots with prominent telangiectasias. Features of atrophy and pigmentary alteration with scale prompted histopathologic evaluation for scalp sarcoidosis or concurrent discoid lupus erythematosus. A punch biopsy of the vertex scalp demonstrated granulomatous dermatitis with nodular aggregates of mono- and multinucleated epithelioid histiocytes with a thin rim of lymphocytes suggestive of sarcoidosis.

Conclusion
Sarcoidosis is varied in its cutaneous presentations. Although this patient had a known history of cutaneous and pulmonary sarcoidosis, this case highlights the overlap in morphology between scalp sarcoidosis and DLE, including changes in pigmentation, erythema, scale and atrophy. For non-scarring presentations of alopecia, sarcoidosis various morphologies may be presumed as alopecia areata and thereby delay diagnosis and systemic evaluation. Thus, in light of the potential for concurrent systemic involvement, the need for early and optimal immunosuppressive therapy supports a low threshold for biopsy of alopecic scalp patches to obtain histopathologic correlation and confirm the diagnosis.
Introduction & Objectives
This is the case of a male patient with a history of an occupational accident involving fuel, with multiple burns on the body surface, including the scalp. After months, he developed itching and pain in one of the scars in the scalp and a diagnosis of Folliculitis decalvans on a scar in the scalp was made. A diagnostic and therapeutic challenge that requires the dermatologist’s ability to recognize clinical findings and to propose an effective treatment to prevent progression.

Material & Methods
A 38 years old man arrives at our dermatology service one year after suffering multiple burns that compromised 38% of the total body surface, including scalp and face. He complained about the presence of nodular lesions in the right parieto-occipital region, painful on palpation with associated secretion. At the physical examination, Fitzpatrick III, presence of an alopecic patch of 4x3 cms, with red and yellowish crusts, erythema and perifollicular hyperkeratosis, hair casts and tufted hairs. Clinical impression of FD was made, so a skin biopsy was decided to confirm the diagnosis.

Results
Histopathology reports normal epidermis, intra and perifollicular mixed inflammatory infiltrate, composed of neutrophilic granulocytes, lymphocytes and plasma cells, some group of hair follicles, with destruction of the follicular epithelium, and periadnexal fibrosis.

Numerous hair follicles surrounded by lamellae, with infundibular dilation and fused in number of 3 and 4. In the dermis an interstitial mononuclear inflammatory infiltrate. Compatible with the diagnosis of folliculitis decalvans. An antimicrobial regimen with clindamycin and rifampicin was proposed associated to topical corticosteroids but due to different difficulties, the patient could not receive adequate treatment on time, later he presented an adverse reaction with the antibiotic regimen, so it was decided to continue with intralesional corticosteroids, topical therapy with corticosteroids and antibiotic every day and gluconate of zinc orally with partial response. Oral isotretinoin could not be started due to associated transaminitis.

Conclusions
We report the case of a male patient with Folliculitis decalvans developed on a scar after a burn in the scalp due to an occupational accident, highlighting the importance of clinical findings and diagnostic suspicion to make the appropriate diagnostic and therapeutic approach. Given the lack of specific protocols, multiple approaches are proposed for the management of this patient focused on controlling flares and preventing progression of the alopecia.
Introduction
Trichodynia or scalp dysesthesia is defined as a painful sensation within scalp. Patients that suffer from Trichodynia are significantly more sensitive to scalp touch. When combing, they complain about their “painful hairs” all scalp long or circumscribed (“spotty”) in a region. This sensation is uncomfortable and it has been many times related to alopecia. In Literature, it has been described that 1/3 of female patients with diffuse alopecia (Ludwig Alopecia Grade I) complain about this phenomenon while other authors reported that 14% of their diffuse alopecia patients suffer from trichodynia.

The cause of trichodynia is not known, but it is suggested to be of multifactorial origin. The activity of neuropeptides as substance P (SP) around the hair follicles may be responsible for pain sensation.

Case report
We present a case of a young male, 30 years of age, good socioeconomic status and work position, with very good hair density, normal standard biochemistry blood tests, with no other illness background, whose only complain was trichodynia in vertex zone. First physician didn’t give much importance but psychological (stress) because of final exams for doctorate. Three month later, burning feeling, itching, redness started. Topic Cortisone and ketoconazole shampoo was prescribed.

On the 5th month, he started losing hair in vertex. He came to our interdisciplinary group six month after trichodynia started, with an alopecia dot in vertex-zone expressed. It was important the interaction between dermatologist and trichologist technician. Tufted folliculitis was seen. Trichoscopy showed several hairs that grew out of the same ostium. Cicatricial Alopecia caused by Folliculitis Decalvans was diagnosed. Allopathic and relief treatment to ease symptoms based on antibacterials and gentle scalp touch was prescribed.

Conclusion
Trichodynia symptoms are of great relevance because:
1) Patients feel pain
2) It could be of significance for detection of an early stage of this Cicatricial Alopecia (Folliculitis Decalvans).

Interdisciplinary treatment is necessary. Trichodynia anamnesis place the hair expert (Trichology Technician and Dermatologist specialized in Trichology) in a challenging diagnostic and therapeutic situation.

As Trichodynia patients exhibited cranial-mechanical-hyperesthesia and cranial-hyperalgesia, it is important to support physician allopathic treatment providing some gentle scalp maintenance to ensure some relief and to give other relaxation techniques such as gentle and scalp-planes-precise-movements so as to help in reducing symptoms.
Introduction

Folliculitis decalvans is classified as a primary neutrophilic scarring alopecia occurring mainly in middle-aged adults. Strong bacterial colonization and deficient immune response of the host have an important role in the pathophysiology of this scalp disease.

This recurring condition is usually difficult to control, causing pustular lesions, erythema and local edema with the presence of follicular constrictions resulting in tuft formations, which worsens clinical conditions.

The presence of erosion and bleeding brings the sensation of important local pain and results in bad odor and a disfiguring aspect. In such cases there is an increased quantity of Staphylococcus aureus and in some cases fungal colonization, which may cause a clinical condition compatible with Kerion of Celsius.

Case Report

Thirty-five 35-year-old male patient, farmer, presenting inflammatory processes in the scalp for more than 5 years. Patient referred increased local inflammation starting 5 months ago with foul odor, pustules and erosions, which resulted in scarring alopecia plates in the scalp.

Three antibiotic sessions were performed with little improvement. Bacterial and fungi culture tests were conducted which showed the presence of gran positive and negative cocci and spores.

We then opted for 3 monthly sessions of amphotericin B and triamcinolone microinfusion treatment using the MMP® technique with a Cheyenne Tattoo machine.

Complete patient recovery can be observed with the patient now being stable for six months.

Conclusion

In this case of difficult treatment, microinfusion of medication into the skin was used with potent anti fungal and anti inflammatory drugs with an excellent response and no side effects.

Local treatment using microdoses allows for important improvement of the pathology and can be used as a mode of treatment for difficult response cases.

Since this is a novel mode of treatment further studies of this technique are required.
Background
Lichen planopilaris (LPP) is a difficult-to-treat, inflammatory scarring alopecia characterised by loss of bulge immune privilege (IP) associated with immune cell infiltration, epithelial-mesenchymal transition (EMT) and eventual destruction of the hair follicles (HFs) epithelial stem cells. Gaining a better understanding of what leads to bulge IP collapse will facilitate the development of novel and more effective treatment LPP intervention strategies before hair loss becomes permanent. Following pilot electron microscopy data showing that mitochondria are deformed and mitochondrial dysfunction in lesional LPP skin being highlighted by pathway analysis by Karnick et al.

Comment
We investigated whether mitochondrial damage could contribute to IP collapse. By quantitative immunohistomorphometry, Mitochondrial transcription factor A (TFAM), essential for mitochondrial transcription and intact energy metabolism, was down-regulated in in lesional LPP skin compared to non-lesional. Interestingly, however, mitochondrial proteins MTCO1 (cytochorome c oxidase I) and VDAC1 (Voltage-dependent anion-selective channel) were upregulated in the bulge, suggesting that although mitochondria in LPP HFs may be defective, they are in fact over-active.

Conclusion
As ATP-over production and excessive reactive oxygen species production can lead to damage associated molecular pattern production (DAMPs), which induce chronic inflammation. Indeed, TLR4 protein expression, a key DAMP receptor that activates immune cells, was increased by 1.5-fold in the bulge of lesional HFs compared to non-lesional. Moreover, RNA for DAMPs S100 and heat shock proteins were substantially upregulated (30-fold increase and 7-fold respectively) suggesting that dysfunctional mitochondria produce excessive DAMPs leading to increased TLR4 expression in the bulge stem cells.

FRONTIERS IN LPP PATHOBIOLOGY: DOES DEFECTIVE MITOCHONDRIAL FUNCTION PROMOTE HAIR FOLLICLE INFLAMMATION BY UP-REGULATING DAMAGE ASSOCIATED MOLECULAR PATTERNS (DAMPS) IN THE BULGE?

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**Posters**

**Introduction**

Keratosis follicularis spinulosa decalvans (KFSD) is a rare condition characterized by keratosis pilaris and scarring alopecia of scalp and eyebrows (1). Genetic heterogeneity has been observed among affected families. It has a chronic and progressive course and treatment is often disappointing (2). Herein, we report 2 cases of KFSP, an under suspected entity that may cause permanent hair loss.

**Case Report**

A 59-year-old male patient with no history of comorbidities or medications consulted for longstanding progressive alopecia. Physical examination revealed extensive vertex and occipital alopecia with loss of follicular openings, hair tufting and acne keloidalis was seen at the nape. He also presented with keratosis pilaris in eyebrows, arms and forearms.

Dermatoscopy revealed extensive hair tufting and peripilar casts. Biopsy showed perifollicular and interfollicular fibrosis with lymphocytic inflammatory infiltrate around the follicle, mild presence of neutrophils and giant cells around the hair shafts, compatible with folliculitis decalvans.

We began treatment with isotretinoin 30 mg/day and topical clobetasol every other day for 8 weeks. Treatment continued for another 6 months without significant halting of the disease. Follow-up showed refractoriness and even worsening of the condition. Treatment with 1 g/day of mycophenolate mofetil was initiated, after 8 months we did not see any improvement. During control, the patient’s son also referred to have alopecia and extensive keratosis pilaris.

At physical exam, he presented with extensive keratosis pilaris and diffuse occipital alopecia. Perifollicular casts, erythema and mild tufting were seen under dermatoscopy.

New histologic exam on both patients showed concentric perifollicular fibrosis at the level of follicular infundibulum and isthmus with a mild superficial and deep lymphocytic inflammatory infiltrate around the dermis.

The inner root sheath showed focalized thinning without premature desquamation, compatible with keratosis follicularis spinulosa decalvans. Both patients recently initiated acitretin 25 mg/day.

**Discussion**

KFSD is an uncommon cause of cicatricial alopecia, is accompanied by extensive keratosis pilaris of trunk and extremities. Scarring alopecia of the scalp occurs in childhood or early adolescence. Concomitant acne keloidalis nuchae have been reported (1).

Topical and intralesional corticosteroids may produce transient control of erythema. Oral etretinate, isotretinoin and dapsone have been used. Unfortunately, no treatment has produced uniformly successful Results (1,2).

**References.**


Introduction & Objective
Lichen planopilaris (LPP) is a rare, autoimmune carring hair loss occurring primarily on the scalp. Patients with autoimmune disease, including lichen planus, have increased risk for cardiac and metabolic diseases; however this topic has been largely unexplored for LPP. The aim of this study is to examine the prevalence of cardiac and metabolic disease among patients with lichen planopilaris using a large de-identified composite patient database.

Methods & Materials
The Explorys electronic, aggregate database was used to identify patients with LPP using the SNOMED-CT term “lichen planopilaris”(n=3,170). Patients without LPP were used as controls (n=63,442,000). Logistic regression was used for comparisons.

Results
LPP patients were predominantly female (89%), while 54% of controls were female. Hyperlipidemia was the most common condition, present in 52% of patients with LPP and in 14.6% of controls (OR 6.43, 95%CI 6.00-6.89, p<0.001). Next were hypertension in 47% of LPP and 18% of controls (OR 3.93, 95%CI 3.67-4.22, p<0.001) and obesity in 27% of LPP patients and 6.6% of controls (OR 5.23, 95%CI 4.83-5.66, p<0.001).

Diabetes mellitus was present in 17% of LPP patients and 7.5% of controls (OR 2.61, 95%CI 2.38-2.86, p<0.001) while metabolic syndrome was noted in 3% of LPP patients and 0.3% of controls (OR 10.11, 95%CI 8.2-12.47, p<0.001).

Cardiac disorders more likely to occur among LPP patients were coronary artery disease (7.6% LPP vs. 4.7% controls, OR 1.65, 95%CI 1.45-1.88, p<0.001), atrial fibrillation (4.4% LPP vs. 2.9% controls, OR 1.6, 95%CI 1.33-1.86, p<0.001) and myocardial infarction (3.2% vs. 2.1%, OR 1.51, 95%CI 1.24-1.84, p<0.001).

Conclusions
Similarly to other autoimmune diseases, prevalence of cardiac and metabolic disorders is higher among patients with LPP.
Older patients, those with a personal or family history of cardiac disease, or those with other autoimmune diseases should be advised to follow up with a cardiologist.
Future studies should examine if treatment of LPP can reduce the rate of cardiac and metabolic co-morbidities.
Introduction & Objectives

Human dermal papilla cells (hDPCs) are special mesenchymal part of hair follicle (HF) that have crucial role in hair follicle development and regeneration. This particular compartment, dermal papilla cells release many different factors and these are associated with hair cycle regulation.

One of various factors, Wnt/β-catenin signaling is essential for hair growth phase (anagen) maintenance. Autophagy is intracellular recycling system for cellular homeostasis. Recent studies indicate that autophagy is more active in matrix cells at the anagen phase and inhibition of autophagy accelerate hair regression phase (categen).

However, mechanism of hair cycle regulation and function of autophagy in dermal papilla cells are not revealed. In this study, we explored role of autophagy in human dermal papilla cells during anagen phase using autophagy inhibitor 3-methyladenin (3-MA) and effect of ginseng extract on autophagy.

Materials & Methods

Human dermal papilla cells and human hair follicles are used for experiments. The autophagy inhibition by 3-methyladenin in dermal papilla cells was confirmed by immunoblotting and autophagy detection kit. Wnt activity was investigated by three ways.

First, expression of Wnt associated genes in dermal papilla cells was examined by qRT-PCR. Second, β-catenin translocation was checked by immunoblotting. Cell based luciferase assay was performed in Wnt reporter cell line. Hair cycle and hair shaft elongation were checked using hair follicle organ culture. All experiments were repeated three times.

Results

Autophagy inhibition through 3-methyladenin was confirmed by reduction of LC3-± and autophagic vacuoles. The expression of Axin2, Lef1, known as the Wnt target genes and the amount of β-catenin translocated to the nucleus were decreased in 3-methyladenin treated human dermal papilla cells. The ginseng extract simulates autophagy in dermal papilla cells. Also, treatment of 3-methyladenin with the ginseng extract alleviates the catagen phase development in human hair follicle organ culture.

Conclusions

Here, we showed that autophagy inhibition promote down-regulation of Wnt/β-catenin signaling in human dermal papilla cells. And this down-regulation cause catagen phase development. In addition, ginseng extract would help maintaining hair growth phase by autophagy enhancement.
Introduction & Objective
Ambient particulate matter (PM) represents an environmental threat to which millions of humans worldwide are exposed. Particle pollution includes: PM10 inhalable particles, with diameters that are generally 10 micrometers and smaller; PM2.5 fine inhalable particles, with diameters that are generally 2.5 micrometers and smaller. The average human hair is about 70 micrometers in diameter – making it 30 times larger than the largest fine particle. The adverse effects of PM on human health are currently a serious concern, and they have been shown to increase the risk of cancer, and pulmonary and cardiovascular diseases. The effects of ambient PM exposure on human skin in general, and on hair in particular, have not been widely studied. In this study, we investigated the effect of fine PM in human dermal papilla cells.

Methods
In this study, we used two sources of pollutants, fine dust (PM10-like) and diesel particulate extract. Human follicle dermal papilla cells were treated with various concentrations of fine dust and diesel particulate and subsequently incubated for 24 h. cell proliferation was assessed by the MTT and WST-1 assays. To investigate the expression of Wnt/β-catenin and cell cycle genes, we performed western blotting.

Results
We found that fine dust and diesel particulate did not affect the cell proliferation of human dermal papilla cells. However, fine dust and diesel particulate decreased Wnt/β-catenin pathway, important role in hair growth and phosphorylation of extracellular signal-regulated kinases (ERKs) and Akt in a dose-dependent manner. Moreover, fine dust and diesel particulate induced cell-cycle arrest by decreasing the level cyclin D1, cyclin E and cyclin-dependent kinase 2.

Conclusion
These Results provide that particulate matter could shorten the duration of the hair growth cycle by inducing cell-cycle arrest, downregulating the β-catenin level.
Introduction
Chemotherapy or radiation therapy, which targets rapidly dividing cancer cells, often leads to the most visibly distressing side effects such as hair loss. Depending on anti-cancer drugs, chemotherapy-induced alopecia (CIA) is mild to severe, which often causes refusing chemotherapy. Understanding follicular cell damages by chemotherapy might ameliorate CIA.

Hair follicles continuously cycle through anagen (growth), catagen (regression) and telogen (resting) stages, and shortening of anagen induces hair loss.

Dermal papilla cells (DPCs) are the key dermal component of the hair follicle and directly regulate hair cycle via the interaction with epithelial components. 5-Fluorouracil (5-FU), an antimetabolite anti-cancer drug, is widely used for the treatment of gastrointestinal cancers, breast, gynecological as well as head and neck tumors.

Methods
In the study, to improve CIA, we thus investigated in vitro and in vivo follicular damages by 5-FU and the mechanism of 5-FU on the shortening of anagen in DPCs. 5-FU significantly inhibited proliferation of DPCs (IC50: 9.8 M) in vitro.

Results
In vivo study showed that 5-FU delayed anagen initiation compared to untreated controls. When investigated how 5-FU delayed anagen initiation in DPCs, we found that 5-FU induced cell cycle arrest and increased the Bax/Bcl-2 ratio, which was followed by apoptosis of DPCs.

Moreover, 5-FU decreased the nuclear translocation of β-catenin, a mediator of anagen activation and the level of cyclin D1, target gene of β-catenin. 5-FU also decreased the mRNA levels of fibroblast growth factor-7 (FGF-7) and FGF-10, which are positive regulator of hair growth.

Conclusion
These findings indicate that 5-FU induces delayed anagen initiation by the inhibition of DPCs proliferation through the decrease of nuclear β-catenin and FGF-7/-10 levels.

Acknowledgement
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Introduction
Hair follicles continuously cycle through anagen (growth), catagen (regression) and telogen (resting) stages and hair growth is directly proportional to duration of anagen. Hair growth is regulated by remodeling of both dermal and epithelial components in hair follicle. In particular, dermal papilla cells (DPCs) are the key dermal component of the hair follicle and directly regulate anagen initiation via the interaction with hair germ cells. During progression of the hair cycle, the Wnt/β-catenin pathway has a crucial role in the hair growth. On the other hand, mackerel-derived fermented fish oil (FFO) extract was reported to have effects of skin anti-aging and anti-apoptotic cell death by scavenging intracellular reactive oxygen species (ROS) in human HaCaT keratinocytes.

Methods
In the study, we investigated whether FFO extract and the principal have hair growth-promoting effect and then mechanisms of FFO extract and the principal on hair growth.

Results
FFO extract and docosahexaenoic acid (DHA), a main component of FFO extract, result in increased the DPC proliferation by progression of the cell cycle. In addition, in vivo effect of FFO and DHA on the hair growth were determined using the dotmatrix planimetry method. The skin color changes of FFO extract- and DHA-treated mice from telogen (pink) to anagen (black) accelerated than that of control group. Moreover, when investigated Wnt/β-catenin pathway in DPCs, we found that FFO and DHA inactivated glycogen synthase kinase 3β by increased phosphorylation. FFO extract and DHA activated β-catenin by the increased phosphorylation at serine 552 and serine 675, which was followed by the translocation and accumulation of activated β-catenin into the nucleus.

Conclusion
Taken together, these Results indicate that FFO extract and DHA stimulate hair growth via the Wnt/ -catenin pathway activation and cell-cycle progression in DPCs.

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INTRODUCTION

Dermal papilla (DP) displays a pivotal role in hair follicle (HF) morphogenesis and cycling through epithelial-mesenchymal interactions. Some factors from the macro-environment are crucial in HF development such as fibroblast growth factors (bFGF) or platelet derived growth factor (PDGF). The aim of this study is to investigate the dialogue between HF and its macro-environment through secretion of extracellular vesicles (EVs) and their potential to activate dermal papilla cells (DPC) and stimulate HF growth.

MATERIAL & METHODS

For this purpose, primary human dermal fibroblasts (DF) were maintained in culture and stimulated by both bFGF and PDGF-AA (2GF) to mimic the HF macro-environment. Secreted EVs were isolated from DF conditioned medium stimulated by 2GF (2GF-EVs) or not (ctrl-EVs). Then, DPC or HF cultivated ex vivo were stimulated by ctrl-EVs or 2GF-EVs and cell proliferation as well as hair growth were quantified respectively.

RESULTS

We demonstrate that 2GF-EVs significantly stimulate the DPC proliferation (P<0.05) whereas ctrl-EVs has no effect on cell proliferation. Very interestingly, ex vivo experiments revealed that the HF growth was significantly increased by 2GF-EVs compared to ctrl-EVs (P<0.01). Moreover, the direct stimulation of HF ex vivo with 2GF did not affect the hair growth.

A transcriptomic study revealed the expression of an activator of the Wnt/β-catenin pathway, in DPCs after stimulation by 2GF-EVs. Western blot analyses revealed an increase of the synthesis and secretion of this activator by DPCs after 2GF-EVs stimulation compared to ctrl-EVs.

CONCLUSION

This study demonstrates for the first time a communication system between dermal fibroblasts and hair follicle mediated by extracellular vesicles. These Results reveal the importance of the macro-environment (2GF stimulation) on the extracellular vesicles action since ctrl-EVs display no effect whereas 2GF-EVs stimulate hair growth. Hence, extracellular vesicles could be a modulator of dermal papilla cells activation and a valuable tool to maintain and restore dermal papilla cells activity and hair follicle cycling.
Introduction

Hair regenerative medicine has been investigated as a promising approach for the treatment of hair loss. Recent studies reported that transplantation of follicular stem cells resulted in regeneration of hair follicles and hairs. However, a challenge is that the hair induction ability of dermal papilla cells (DPCs) is gradually lost after isolation from in vivo tissues and during expansion culture. In this research, we propose an electrical stimulation culture to maintain and recover the hair induction ability of DPCs.

Material & Methods

A culture device for electrical stimulation was fabricated by electrochemically synthesizing conductive polypyrrole (PPy) on a slide grass and placing a four-well chamber on it. DPCs at passage 4 were seeded at $1 \times 10^4$ cells/well into the chambers and applied electrical stimulation under several different stimulation conditions. Gene expressions associated with hair follicle morphogenesis were evaluated at d of culture.

To investigate hair generation ability, the cells were collected after electrical stimulation and mixed with embryonic epidermal cells, and let them form spherical aggregates in a commercial non-cell-adhesive round-bottom 96 well plate (1). The aggregates were then transplanted into shallow stab wounds prepared on the back of mice. Hair shaft generation at the transplanted site was evaluated for up to 3 weeks.

Results & Discussion

DPCs attached and proliferated on the PPy-coated culture device during 3 days of culture. The application of electrical stimulation significantly promoted alkaline phosphatase gene expression in DPCs. The most optimum condition was alternate current *****.

The electrical stimulated DPCs formed an aggregate in a U-shaped microwell. The two types of cells were initially randomly distributed in a single cell aggregate but in the following culture they spatially separated each other and exhibited typical morphological features of hair follicle germ in three days of culture. On intracutaneous transplantation into the backs of nude mice, the hair follicle germs prepared with the electrical stimulation efficiently generated hair follicles and shafts compared to those without electrical stimulation.

Conclusions

Electrical stimulation upregulated trichogenic gene expressions of DPCs and improved hair generation when the cells were mixed with epidermal cells and transplanted into mice as hair follicle germs. These Results suggest that electrical stimulation can be used to maintain and recover the hair induction ability of DPCs in expansion culture and thus can be adopted for hair regenerative medicine.
EXOSOMES DERIVED FROM DERMAL PAPILLA CELLS
PROMOTE HAIR GROWTH IN CULTURED HUMAN HAIR FOLLICLES
AND REGULATE HAIR CYCLING IN MICE


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Introduction & Objective
Exosomes (Exos), 30–150nm extracellular vesicles, are a newly identified mechanism for cell-to-cell communication. They are important for the transfer of mRNAs, microRNAs, and proteins to target cells, thereby altering the gene and protein levels of recipient cells to regulate their function. Recent studies have reported that Exos secreted by stem cells, including mesenchymal stem cells (MSCs), are promising for tissue regeneration. Dermal papillae (DP) play key roles in hair growth and regeneration by regulating follicular cell activity. To investigate whether DP-derived exosomes (Exos), especially those from three-dimensional (3D)-cultured DP cells, affect hair growth, cycling, and regeneration.

Materials & Methods
Proliferation and expression of growth factors and hair differentiation markers in cultured DP cells and outer root sheath (ORS) keratinocytes in the presence of Exos was examined by MTT assay and real-time PCR, respectively. Hair shaft elongation was measured after cultivation for 6 days in the presence of various concentrations of Exos. Hair cycle scoring was performed after injection of Exos into back skin of C57BL/6 mice. The effects of Exos on the hair-inducing activity of human DP cells were assessed using a hair reconstitution assay.

Results
Exos derived from 3D DP (3D DP-Exos) promoted the proliferation of DP cells and ORS cells and increased the expression of growth factors (IGF-1, KGF, and HGF) and differentiation markers (K6, K16, K17, and K75) in DP cells and ORS cells, respectively. 3D DP-Exo treatment increased hair shaft elongation in cultured human hair follicles. Local injections of 3D DP-Exos induced anagen from telogen and also prolonged anagen in mice. Exo treatment in human DP spheres augmented hair follicle neogenesis.

Conclusion
Collectively, our data strongly suggest that Exos derived from DP cells promote hair growth and hair regeneration by regulating the activity of follicular dermal and epidermal cells; accordingly, these findings have implications for the development of therapeutic strategies for hair loss.
CHARACTERISATION OF IMMORTALISED HUMAN BALDING AND NON-BALDING DERMAL PAPILLA CELLS

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Introduction

Androgenetic alopecia (AGA) is a hereditary disorder that involves the progressive thinning of hair in a defined pattern and is driven by androgens. The hair follicle dermal papilla (DP) expresses androgen receptors (AR) and plays an important role in the control of normal hair growth. In AGA it has been proposed that the inhibitory actions of androgens are mediated via the DP although the molecular nature of these interactions is poorly understood.

Methods

To investigate mechanisms of AGA we have generated immortalized DP cells (DPC) from balding (BDPC) and non-balding (NB-DPC) scalp by retroviral expression of the catalytic subunit if human telomerase (hTERT). These immortalised cells have been molecularly characterized for known DP markers.

Results

We report that both NB-DP and B-DP cells express established signature genes versican, LEF1, ALPL. Furthermore, signaling ligands associated with DPC such as WNTs, BMP4 and FGF were also identified as being expressed. Additionally, co-culture models of the immortalised dermal papilla cells alongside keratinocyte cell lines exhibit ‘switching on’ of hair specific keratins; demonstrating the immortalised DPC inductive capability to activate expression of hair specific keratins such as KRT31.

Comment

Gene expression has also been explored; showing that this co-culture model increases expression of inductivity related genes in DPC. Furthermore, we have investigated the gene signature change of these cells when put into 3D spheroid culture. We have determined that upon 3D culture NB-DPC cells have an increased gene expression in inductivity related genes in comparison to B-DPC.

Conclusions

We therefore suggest that immortalised DPC represent a useful model with which to investigate AGA and will help identify pathways that could lead to novel therapeutic strategies for treatment of AGA.
DIFFERENTIAL MOLECULAR SIGNATURE OF DERMAL PAPILLA CELLS (DPCs) FROM BALDING AND NON BALDING SCALP IN 2D, 3D CULTURE AND CO-CULTURE WITH ADIPOSE-DERIVED STEM CELLS (ASCs).

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Background
Androgenic alopecia affects hair follicles from frontal and vertex area. Hair inductive properties of DPCs are lost in bi-dimentional (2D) culture. In a recent study three dimentional (3D) structure of cultured DPCs was able to recapitulate 22% of molecular signature of the intact dermal papilla. The aim of this study is to compare gene expression differences between DPCs from balding scalp and non balding scalp (occipital area) and their changes in 2D and 3D cultures. Two immortalized dermal papilla cell lines from male non balding (NB-DPC) and balding (B-DPC) hair follicles previously established by our group expressed respectively 75% and 65% of DP signature genes.

Methods
We investigated whether three-dimentional structure of these immortalized cells and their co-culture with ASCs could increase the expression of hair inductivity markers. 2D culture from early primary DPCs (P3-DPCs), 2D culture and spheroids from B-DPCs and NB-DPCs and also co culture of immortalized DPCs with ASCs were established, followed by analysis of gene expression. RNA sequencing -Anova analysis with14 million reads/ sample and 98% alignment to the genome-then gene clustering by using David gene software were performed.

Results
Both immortalized DPCs in 2D culture showed a significant decrease of expression of WNT5A compared respectively to spheroidal immortalized DPCs. However, the decrease of expression of WNT5A was more important in 2D B-DPCs compared to spheroidal B-DPCs in co-culture with ASCs. NB spheroidal DPCs in co-culture with ASC showed a high expression of LEF1 compared to 3D NB-DPCs alone. P3-DPCs in 2D expressed considerably alkaline phosphatase compared to both immortalized cells lines. The differential expression level was slightly higher in P3-DPCs versus B-DPCs.

Comment
In 2D P3-DPCs LEF1 was upregulated and DKK1 (inhibitor of Wnt signaling pathway) downregulated compared to 2D NB-DPCs. DDK1 is also strongly upregulated in 2D NB-DPCs compared to spheroidal NB-DPCs. It was previously reported that androgens upregulate DDK1 gene expression in DPCs(3) and recently spheroid DPCs lowered the expression of DDK1 and enhanced Wnt agonists expression. Our result confirms this latter finding. In this study 3D structure in both immortalized cells promote expression of some hair inductivity markers such as Wnt5A. By contrast 2D immortalized DPCs show a strong decrease of hair inductivity markers such as Alkaline phosphatase and LEF1 compared to P3-DPCs. Also 2D culture promote expression of an inhibitory factor of Wnt signaling pathway such as DDK1 in NB-DPCs.

Conclusion
In our study, the spheroidal immortalized DPCs seem to have a more inductive profile than 2D immortalized DPCs. 3D structure seem to restore some hair induction features present in P3-DPC in immortalized DPCs, as 3D structure was able to partially restore molecular signature of cultured DPCs compared to the intact DPCs.
Introduction & Objectives

The dermal papilla cells (DPCs), differentiated from mesenchymal cells and located in the base of hair follicle, play important roles in the regulation of hair growth.

In androgenic alopecia, commonly known as male pattern baldness, hair follicle undergoes a process of miniaturization in which the hair shaft becomes thinner and shorter.

This reduction in hair shaft is closely related to the reduced hair follicle volume which in turn determined by the volume of dermal papilla. In this study the effects of Cnidium officinale (CO), Polygonum multiflorum (PM) and Hottuynia cordata (HC) extracts, which are oriental herbal medicinal plants widely used in complex prescriptions for alopecia treatment, on dermal papilla cells grown in 3 dimensional culture.

Materials & Methods

DPCs (2x10^5 cells/well) were seeded in 24well Hydrocell plate (Nunc, Roskilde, Denmark), which had chemically coated surface to prevent attachment of cells to plate surface, resulting in spheroid formation.

Cells were incubated for 72hr to generate spheroids with/without natural plant extract.

The changes in size distribution of resulting spheroids by dihydrotestosterone (DHT) and natural plant extract were measured.

The expression of Bcl-2 protein, thought to be important for maintaining anagen phase, was evaluated by immunocytochemical method in cryo-sectioned spheroids.

Results

Treatment of DHT at 10nM concentration resulted in reduced size of spheroids formed.

Treatment of CO, PM and HC extract, however, fully abrogated the inhibitory effect of DHT on spheroid formation and recovered the size of spheroids.

The expression of Bcl2 protein was increased by CO, PM and HC extract with varying extent. Because we found that the expression of androgen receptor (AR) was increased by DHT treatment and this increment was down-regulated by CO, PM and HC extract, the effects of natural plant extracts are exerted at least in part through the regulation of AR.

Conclusions

It has been reported that thinning and shortening of hair in androgenic alopecia are coupled with a process known as miniaturization and shorted anagen phase, respectively.

The miniaturization of hair follicle is caused by reduced dermal papilla volume.

Our data demonstrate the possibility that the natural herbal extracts, CO, PM and HC, could promote hair growth by preventing the androgen induced miniaturization of hair follicles and prolonging the anagen phase.
FRONTAL FIBROSING ALOPECIA

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FRONTAL FIBROSING ALOPECIA IN 18 MEN

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Introduction

Frontal fibrosing alopecia (FFA) is included in the area of acquired primary lymphocytic cicatricial alopecias and have been described by Steven Kossard in 1994. In the last decade there has been a large increase in the incidence of FFA worldwide, as well as occurrence in both premenopausal women and men. The etiopathogenesis of FFA is still unknown. It is characterized by a progressive symmetric recession of the frontotemporal hairline, loss of the eyebrows, as well as eyelash loss and body hair loss. The diagnosis is based on the distinctive clinical picture, trichoscopy and, in case of doubt, histological examination. In the majority of patients, the therapy is difficult and sometimes disappointing, due to the unpredictable nature of the disease. Because of it causes irreversible alopecia, the main therapeutic concern is to prevent its evolution.

Material & Method

The purpose of the present study was to research and document men diagnosed with FFA, the last five years, at “Andreas Syggros” hospital, Athens, Greece. The diagnosis was based on the typical clinical findings. A questionnaire was used in order to record both individual and family history data. The findings were evaluated and the Results recorded and statistically studied.

Results

The age of men ranged between 20-74 years. The average age was 45.55 years and the duration of the disease varied from 0.5 to 15 years. The severity score was type I for 16 patients (80%) and type II for 4 patients (20%). In 13 patients (65%) the disease seemed to be active with perifollicular erythema and follicular hyperkeratosis. Recession of the frontal hairline was observed in 19 patients (95%), temporal recession in 16 (80%) and parietal recession in 2 (10%).

7 patients (35%) had multifocal scalp alopecia, 5 (25%) beard alopecia. 4 patients (20%) suffered from eyebrow alopecia, 4 (20%) from eyebrow dilution and only 1 (5%) from eyelash dilution. Hair loss from the upper extremities was observed in 2 patients (10%) and from the lower extremities in 5 (25%). 1(5%) had axillary and 1 (5%) had genital hair loss. The lonely hair sign was observed in 6 (30%) and facial papules in 5 patients (25%).

Pale skin and atrophy had 10 men (50%) and loss of follicular openings was observed in all men (100%). Regarding the symptoms, 3 patent mentioned trichodynia, 3 burning sensation and 9 pruritus. Coexistence with AGA (androgenetic alopecia) was observed in 8 patients (40%) and with LPP (lichen planopilaris) in 11 patients (55%).

Although FFA was considered a female disease, it is also observed in men. Predominant androgenetic alopecia may lead to subdiagnosis of the disease. Loss and thinning of the eyebrows, hair loss from other sides, typical porcelain-like atrophy facilitates the differential diagnosis of the disease from androgenetic alopecia seen in men. This study includes the most number of men diagnosed with FFA, compared with previous studies and the findings seem to be similar with them. Men with frontal fibrosing alopecia show the disease at a younger age than women and there appear to be differences in the clinical picture between male and female patients.
FRONTAL FIBROSING ALOPECIA

FRONTAL FIBROSING ALOPECIA: EFFECTIVENESS AND SAFETY OF ORAL DUTASTERIDE IN ROUTINE CLINICAL PRACTICE

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Introduction
Frontal fibrosing alopecia (FFA) is a primary lymphocytic scarring alopecia characterized by a progressive and bilateral recession of the fronto-temporal hairline. As its pathogenesis is still unknown, there are no molecularly targeted treatments. The characteristic localization and the predominance of postmenopausal women suggest that a hormonal imbalance may play a pathogenic role. Among all the therapeutic options, the 5-alpha reductase inhibitors (finasteride and dutasteride) have shown the greatest evidence in stopping the progression of the disease.

Objectives
The aim of this study was to describe the effectiveness and safety of the treatment with oral dutasteride in patients with FFA in routine clinical practice. The secondary objective was to assess the most effective dose of oral dutasteride.

Material & Methods
A retrospective, descriptive and observational study was designed. A review of the medical histories of the patients cataloged as “AFF” from January 2011 to December 2018 was performed. Sociodemographic variables, treatments, physical examination and adverse effects were collected. The measurement of the recession of the frontal hair line was the main variable used to assess the effectiveness of the different therapeutic options. Oral dutasteride was compared with the other therapeutic modalities. The effectiveness was also compared according to the weekly dose of dutasteride.

Results
A total of 287 histories of patients with FFA were collected. One hundred histories were discarded due to absence of a minimum follow-up of 6 months. There were 186 women (99.5%), with mean age of 61.94 years (range 34-85). The initial glabellar-frontal distance ranged between 4.5 and 17.5 cm (mean, 7.7 cm). The oral therapeutic modality was dutasteride in 77.78% of the patients (from 1 to 7 capsules per week). The mean annual frontal increase in patients without dutasteride was 0.71 cm, with one or two capsules a week of dutasteride was 0.67 and with three or more capsules of dutasteride was 0.31 cm, with statistically significant Results.

Comment
Three or more capsules per week of dutasteride seems the most effective treatment for FFA.
Introduction
Frontal fibrosing alopecia (FFA) has a chronic and progressive nature, thus necessitates an effective treatment. The main and currently available agents include oral finasteride/dutasteride, topical/intralésional/systemic steroids, topical minoxidil, topical tacrolimus and oral hydroxychloroquine, however, there is no optimal and definitely efficacious treatment option.
Platelet rich plasma (PRP) is an autologous product rich in several growth factors, chemokines and cytokines that is manufactured by centrifugation from patients own venous blood. It can promote hair growth and follicle survival by stimulating the stem cells located in the bulge region which in turn can activate the proliferative phase of the hair cycle and also by its anti-inflammatory effects. Recently, a number of reports have been published showing encouraging Results regarding the use of PRP for the treatment of alopecias, particularly androgenetic alopecia and alopecia areata, however, its efficacy in FFA is unknown.

Case report
A 44-year-old female presented with itching and widening of her forehead with hair loss on the eyebrows, arms and legs. Dermatological examination revealed a 4 cm recession of the frontotemporal hairline, perifollicular erythema, scaling and lichenoid papules on the frontal and temporal scalp, lonely hair sign, fringe sign and loss of hair of eyebrows and extremities. Perifollicular erythema and scaling were noted on trichoscopy. Histopathological examination of transverse sections of lesional scalp biopsy specimens disclosed a reduced number of terminal follicles, fibrovascular scars, vacuolar change which affects the isthmus of some follicles and sparse necrotic keratinocytes. Vascular degeneration along the dermoepidermal junction, perifollicular band-like lymphocytic infiltration and fibrosis were observed on the vertical sections. The patient was diagnosed with FFA and started on 0.05% clobetasol propionate lotion (scalp) and 0.125% prednisolone cream (eyebrows) (twice daily for 10 days, 4 treatments with 1 week interval). After 2 months, the itching was partially subsided, however as all the clinical signs were persisting, oral hydroxychloroquine (400 mg/d), topical 5% minoxidil lotion (twice daily) for the scalp was initiated and continued for 9 months. Additionally, intralesional triamcinolone acetonide injections was applied to the eyebrows (2.5 mg/ml) and frontotemporal hairline (5 mg/ml) (6 treatments with 1 month interval).
On follow-up, due to further recession of the frontotemporal hairline, no hair regrowth on the eyebrows and persistence of clinical signs, we started on PRP injections (5 treatments with 1 month interval) to the frontotemporal hairline and eyebrows. After 1 month, perifollicular erythema, scaling and lichenoid papules improved and after 5 months no further hair loss was noted.

Conclusion
PRP can be preferred as a well-tolerated, easy to apply and a promising treatment modality in cases of FFA recalcitrant to other therapies.
Introduction & Objectives
Frontal fibrosing alopecia (FFA), a clinical variant of lichen planopilaris, is characterized by progressive, scarring hair loss of the frontal hairline and eyebrows. The prevalence of FFA is increasing worldwide and it is considered a dermatologic emergency.

FFA pathogenesis is currently unknown. The purpose of this study is to determine if an association exists between facial procedures and the development of FFA.

Material & Methods
A cross-sectional study was conducted comparing FFA patients with age and race-matched androgenetic alopecia (AGA) patients at a single, tertiary medical center in Southern California.

Information regarding patient demographics, onset of alopecia, concomitant diseases, and previous facial procedures (including but not limited to medically necessary reconstructive surgeries, rhytidectomy, blepharoplasty, or head trauma). Statistical analysis comparing the FFA and AGA survey Results was completed.

Results
Fifty FFA patients (48 Females, 2 Males) were compared to an equal number of age and race-matched AGA controls. Analysis of demographic data did not reveal statistical differences in the mean age or race/ethnic distribution between the FFA and AGA groups (mean age: FFA: 63.52 years old, AGA: 60.98 years old). 48% of FFA patients reported prior facial procedures which was significantly increased compared to 10% of AGA patients (p=0.001).

The average years in between the facial procedures and hair loss was 8.9 years. No significant difference was observed between the two groups for sunscreen use on the face, frequency of wearing hair in a ponytail or tight bun, precancerous lesions treated on forehead or scalp at the same time as hair recession, progressive neurologic disease, cerebrovascular accident, or migraines.

Comment
These data demonstrate that there is an association between facial procedures and development of FFA.

Future directions include collection and analysis of cross-sectional data from multiple academic centers, and cohort studies to determine a causal relationship between facial procedures and FFA.
FRONTAL FIBROSING ALOPECIA

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FRONTAL FIBROSING ALOPECIA: IS THERE A LINK IN RELATIVES?

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Introduction

Frontal fibrosing alopecia (FFA) is a scarring alopecia that causes progressive recession of the frontotemporal hairline. Some authors consider it a variant of lichen planopilaris due to their histological similarities. Its prevalence is increasing worldwide. Early diagnosis and prompt treatment are necessary to prevent definitive scarring and permanent hair loss. The pathogenesis remains unknown. Genetic, environmental, hormonal, and autoimmune related factors might play a role in the development of this condition; however, information regarding familial cases of FFA is scarce.

Methods

We conducted a retrospective cohort study of familial frontal fibrosing alopecia (F-FFA) cases diagnosed at the University Hospital “Dr. José E. González” between 2013 and 2018. Six patients belonging to three different families were included. The diagnosis was confirmed by histological examination.

Allergy Patch Testing was performed in all patients. Clinical and dermoscopic features were analyzed. A review of all cases of F-FFA reported in the literature was made.

Results

All patients included in this study were female. Two of the three families were composed of mother and daughter; the third family included two sisters. Mean age was 60.6 years. Usually the disease started 34.6 months (range 8-60) prior to diagnosis. 83% of patients demonstrated some degree of eyebrow alopecia. The same percentage had body hair loss, with limbs being most commonly affected. Fifty-percent of cases had eyelash involvement. Four of six patients had a family history of autoimmune disease in first-degree relatives, and 66% of them had a personal history of autoimmune disease. The Allergy Patch Testing was positive in 66% of patients, with the most common positive allergen being propolis.

Comment

Twenty-five families with F-FFA, including our 3 families, have been reported in the literature since Kossard first described the disease in 1994. Of all patients described, only 6.25% were male. Regarding the other published cases; we found a total of 48 patients in whom no relevant characteristics of the disease are mentioned other than scarce body hair (on extremities) and eyebrows. Of the 48 patients 11 were younger than 45 years of age and 37 were older.

Five patients within 3 families described in our study were postmenopausal at the time of diagnosis.

The 3 families reported in this cohort study, plus the personal and family history of autoimmune disease support the hypothesis of this disease being genetic. However, exposure to environmental triggers may also play a role in the pathogenesis.

The Allergy Patch test is a tool that can help us clarify whether a causative role for facial leave-on products exist, as suggested by Aldoori et al. It is important to consider studying this entity since few data exists regarding familiar cases and this might give us insight towards its pathogenesis.
Introduction
Effective treatment for eyebrow alopecia in frontal fibrosing alopecia (FFA) is limited with disease progression specific to eyebrows is common despite stabilization of disease on the scalp.

Case report
A 48-year old premenopausal woman presented with thinning of her eyebrows for one year. She also had progressive scalp alopecia which occurred for six months.
Examination revealed bilateral loss of eyebrows and recession of her anterior hairline which was associated with perifollicular erythema and scale. Histopathology from scalp biopsy revealed perifollicular lichenoid lymphocytic inflammation consistent with FFA. Her thyroid function was normal and FFA severity index score was 11/100.
She was treated with hydroxychloroquine 200 mg twice daily, clobetasol propionate 0.05% lotion once daily and tacrolimus ointment (0.1%) once daily which stabilised her scalp alopecia. Her eyebrows did not improve after 8 months of treatment.
She was commenced on twice daily application of prostaglandin analogue solution to her eyebrows which resulted in significant regrowth after six months of treatment.
It is uncommon for eyebrow alopecia to improve with systemic treatment alone. Intralesional corticosteroid has been reported to improve eyebrow alopecia in FFA but at a risk of developing skin atrophy (1,2).
Prostaglandin analogue (PA) induces the anagen phase in hair follicles which increases the number, thickness and length of hair. Its use to treat eyebrow alopecia has been reported to be ineffective in alopecia areata but it had demonstrated some response with hair regrowth when used on the scalp in patients with androgenetic alopecia.
There have been anecdotal reports on its use with some benefit in patients with vitiligo due to its proposed action in stimulating melanogenesis (3). Its application in FFA has not been described. It is possible that eyebrow alopecia in our patient had responded to topical PA from its anti-inflammatory and anagen stimulating properties which halted the inflammatory process and stimulated hair regrowth.
It is a safer treatment option for this cohort with eyebrow alopecia as it allows application for longer duration to maintain disease stability.

Larger studies incorporating the use of PA for FFA on the scalp and eyebrows would confirm its therapeutic benefits for this subtype of cicatricial alopecia.

Reference
Introduction

Frontal fibrosing alopecia (FFA) is a cicatricial lymphoproliferative disorder which incidence is increasing worldwide. The risk factors for this phenomena are a matter of intensive research in order to explore its etiology. To date, there is no such investigation in a Brazilian miscegenated population.

Objective

To evaluate clinical and demographic profile in a sample of Brazilian patients with FFA, besides to compare exposition factors with patients with non-scarring alopecia.

Materials and Methods

Multicenter case-control study involving 223 FFA patients and 115 controls. Clinical patterns and demographics of FFA patients were summarized, 28 exposition variables were explored in FFA and controls. The associations were assessed by logistic regression.

Results

Women accounted by 95% of FFA patients, the mean (SD) age of onset was 50 (12) years. Classical frontal alopecia was present in 92% of cases, 76% lost eyebrows, 42% had facial papules, 5% referred a first degree familiar with FFA, and non-scalp alopecia was perceived in 44% of the patients.

FFA patients differed from controls regarding greater BMI (OR=1.07), greater frequency of curly hairs (OR=4.9), reported less exposure to computer light (OR=0.51), but greater daily sun exposure (OR=1.02), and ever lived in a rural area (OR=12.0), greater use of OTC bar soaps for facial cleansing (OR=9.22), also for OTC shampoos (OR=5.84) but less anti-residual ones (OR=0.31) and greater report of procedures for hair straightening (OR=1.61); as well as the report of living a severe stressful event (OR=3.33). Sunscreens, anti-aging creams, facial moisturizers, common allergens and nutritional aspects were not associated to FFA in this sample.

Comment

We characterized clinical and demographic profiles from Brazilian patients with FFA. There was preliminary evidence that those FFA patients have been exposed to some environmental stimuli, facial and scalp cleansing, hair cosmetic procedures as well as stressful events; what can subside hypothesis on pathophysiologic models.
Introduction
Facial anthropometry and aesthetic medicine usually divide the face into 3 parts: forehead segment (from glabella to hairline), nasal segment (from subnasale to glabella), and lower segment (from menton to subnasale). Folk knowledge describes the ideal forehead length as four fingerbreadths; a longer forehead is less aesthetically pleasing, and associated with receding hairline or advanced age. It is essential to define “normal” forehead length, as deviations may be an early indicator of hairline recession and can be used as a marker of hair loss severity in alopecia subtypes involving frontal hairline recession.

Methods
In this single-center, cross-sectional pilot study, the authors aim to define forehead length for healthy individuals across age groups, sexes and race/ethnicities. Forehead length was defined as the distance between glabella and hairline and was measured using tape measure. Demographic data for each participant was also collected. Statistical analysis comparing forehead length over age, gender and race/ethnicity was completed.

Results
Two hundred fifteen participants without hair loss were enrolled using a quota sampling method in Southern California. Statistical analysis demonstrates that men have a significantly longer forehead than women (7.22 cm vs 6.41 cm, p<0.0001) and Asian foreheads are significantly longer than those of Hispanic/Latino (6.98 cm vs 6.37 cm, p=0.0107) populations. There is a positive correlation between age and forehead length, with length increasing by 0.2003 cm per year increment of age from the second to seventh decade (p=0.0034).

Discussion
Larger scale, multi-center, multi-national studies will be necessary to establish a definition for typical forehead length across ages, sexes and races. Further studies can also be done to analyze forehead length and forehead-to-face ratio among alopecia patients and elucidate their role in terms of hair loss initiation and severity in alopecia subtypes involving frontal hairline recession.
Introduction & Objectives
Frontal fibrosing alopecia (FFA) is a lymphocytic scarring alopecia with a rising prevalence in Dermatologic clinics. Available therapies are not greatly effective in order to interrupt disease progression and symptoms are difficult to treat. Furthermore there are not any randomized controlled trials involving this disease. Low level-light therapy (LLLT) has demonstrated its effectiveness in androgenetic alopecia and it may even play some positive role in scarring alopecias such as lichen planopilaris. In patients with FFA we evaluated the anti-inflammatory, antifibrotic efficacy of domiciliary LLLT to control disease and symptomatology.

Methods
We designed a single-centre, double-blinded, and randomized clinical trial. Helmet-shaped devices composed by 246 high-powered red LEDs at a wavelength of 630 nm were given to patients and used 15 minutes daily for 6 months. Each device had a sham side and an active side, and the latter was masked and randomized for all 37 patients. The active side emitted at a fluence of 4.5 J/cm² whereas sham side was 10 times weaker at a fluence of 0.45 J/cm². Patients were evaluated at baseline and each 12 weeks for a total duration of 6 months.

The primary endpoint was the effect of LLLT in the disease, assessed with frontal regression and cicatricial band (in centimetres). Other primary endpoints included improvement in inflammatory clinical-trichoscopic (erythema, hyperkeratosis) and symptom-related variables in a qualitative scale (none/moderate/severe). Secondary endpoints included improvement in terminal and general hair thickness, assessed in each visit by a digital videodermatoscope with a trichoscopic software tool. We also evaluated the improvement in FFA severity scale (FFASS) and in its inflammation item. Patients underwent a patient global assessment (PGA) survey in each visit from 1 to 5.

Results
We herein report preliminary data of LLLT effectiveness after 6 months of therapy without comparing to placebo. Thirty-five patients completed treatment. Mean age was 63.26 years (range 49-81). After 6 months of LLLT there were global statistical differences with a worsening in mean frontal regression (8.68 cm at baseline versus 9.03 cm; p<0.001), with no differences in the cicatricial band (p=0.882).

There were significative decreases in pruritus (p=0.002), burning (p=0.013) and erythema (p<0.001) with no differences in hyperkeratosis after 6 months of therapy (p=0.827).

Overall, there was a significant thickening of terminal hairs (p=0.048) but not a general hair thickening. There was not a significant reduction in FFASS global scale whereas the inflammation item showed a reduction after 6 months of therapy (p<0.001). There were not differences in PGA score after therapy.

Conclusion
LLLT could be an effective therapy for symptom control and inflammation in FFA. Final comparative Results will be presented in this congress.
Background
Fibrosing Frontal Alopecia (FFA) is a progressive cicatricial alopecia, with predilection for the frontotemporal hairline, included in the context of dermatological emergency as cicatricial alopecias. Currently being classified as variant of the lichen plan pillar once they are histologically indistinguishable evidencing lichenoid infiltrate (LI). FFA occurs mostly in postmenopausal women. The number of reported cases are increasing, although the origin remains uncertain.

Objectives
To discuss the diagnosis and treatment of FFA and warn that precocity in diagnosis and the combination of appropriate topical and systemic therapies are important factors for therapeutic success.

Case report
Forty-four year-old premenopausal female, with one year history of progressive hairline recession over frontotemporal area. Previous history does not include other pathology. The clinical examination presented a shiny affected area, incomplete hair loss, and subtle loss of follicular ostia visible in frontotemporal. Follicular hyperkeratosis and focal minimal perifollicular erythema were found at the hairline. Eyebrow presented symmetrical thinning of the hair, but all other body hair appeared normal. Laboratory tests, including routine biochemistry tests, hemogram, thyroid function, antinuclear antibodies, hepatitis C, VDRL test, sex hormones showed no abnormalities. Histologically, we observed scanty lymphocytic infiltrate and fibrosis around hair follicles, especially the isthmus and infundibulum portion, without lichenoid inflammation in the papillary dermis and normal basal membrane. It is consistent with a case of FFA with typical clinical presentation and supporting histologic features. After the biopsy, the patient reported the use of Minoxidil (M) (5%) and topical steroids (twice a day) for one year when she came to our service. In this occasion it was prescribed: Oral therapy (T) with finasteride 5 mg per day; Topical T with cloebetasol ointment and 5% M, both twice a day; Intradermotherapy: 12 sessions so far that included Platelet Rich Plasma (PRP) associated with triamcinolone (9 sessions) and Dutasteride + M + vitamin complex also associated with triamcinolone (3 sessions) with total repilation of the affected area.

Comment
The knowledge of this condition helps to achieve early diagnosis and appropriate treatment. It is aimed at blocking and preventing the evolutionary process of fibrosis, increasing the chance of repilation and success therapeutic (not satisfactory in most cases), besides obtaining improvement of the self-esteem and consequently of the quality of life of these patients. The use of the intradermal combination of PRP associated with triamcinolone in combination with the use of M, high potency steroids and oral finasteride proved extremely effective in this case of early diagnosis, showing that it could be an effective treatment protocol for this condition.
Introduction
Frontal fibrosing alopecia (FFA) is a form of progressive primary lymphocytic scarring alopecia generally involving the frontotemporal hairline and eyebrows. Hair loss on other areas of the body has also been reported. Since its initial description by Kossard in 1994 as a variant of lichen planopilaris affecting postmenopausal women ("postmenopausal frontal fibrosing alopecia"), premenopausal patients as well as male patients have been described, thus the term "postmenopausal" has been dropped. The cause of this emotionally devastating disease remains unclear, despite the fact the number of cases has achieved epidemic proportions.

Material & Methods
We chose to study the demographic characteristics of patients with frontal fibrosing alopecia with disease onset under the age of 50. Data on all new patients seen at the Hair Clinic of Boston Medical Center between 2005 and 2017 who were diagnosed with FFA and under the age of 50, who had participated in an IRB approved data repository, were collected.

Results
The total number of new patients with clinically diagnostic FFA during this period of time was 187. Of these, 31 patients (17%) were under the age of 50, and of these, 26 (84%) were female and 5 (16%) were male. The age of disease onset ranged from 19 to 48 years.
Of the 26 women, 23 (88%) were premenopausal, 1 (4%) was perimenopausal, and 2 (8%) were postmenopausal. Self-reported ethnicities include Caucasian (68%), African American (6%), Asian (10%), Hispanic (6%), Moroccan (3%), and Iranian (3%). In 3% ethnicity was not recorded. There was a family history of androgenetic alopecia in 61% of patients; none reported a family history of FFA or lichen planopilaris. Seven patients (22%) had a history of at least one autoimmune disorder including Hashimoto’s thyroiditis (5), lichen planus pigmentosus (2), and discoid lupus erythematosus (1).

Comment
The percentage of our premenopausal female patients, 23 of 181 or 13%, is on the lower end of what has been reported in the literature, which ranges from 13% to 34%. Because we chose to look at patients under 50 years of age, it is possible that we omitted patients with premenopausal onset of symptoms who presented late with long duration of disease. It is interesting that 5 of our 6 male patients (83%) with FFA during the time period studied had disease onset under the age of 50, compared to 14% of women. This younger age of onset in men has not, to our knowledge, been previously reported. Some have suggested that FFA has an earlier onset and is more severe in different ethnic groups. However, all 5 of the men with FFA in our study were Caucasian.

Conclusion
The finding that men with FFA may have a younger onset than women needs to be further investigated, as this could potentially offer a clue as to the elusive pathogenesis of this disease.
Background

Frontal fibrosing alopecia (FFA) is a rare primary lymphocytic cicatricial alopecia, thought to be a variant of lichen planopilaris, resulting in permanent inflammation-induced hair loss. We present an unusual case of a man diagnosed with FFA following previous facial trauma and hair transplantation.

FFA is characterised by frontotemporal recession with perifollicular erythema, follicular hyperkeratosis and scarring. FFA was first described in 1994 in postmenopausal women and is rarely reported in men. Histology shows perifollicular lichenoid inflammatory infiltrate of the isthmus and infundibulum progressing to perifollicular fibrosis. The pathogenesis of FFA remains unknown and there is lack of consensus on its aetiology. Proposed causative factors include hormonal triggers, cosmetic allergy, genetic predisposition and trauma such as cosmetic surgery. The underlying mechanism for the latter may be due to several factors including koebnerization, autoimmunity and collapse of hair follicle immunoprivilege.

Case report

A 30 year old man presented with a left zygoma fracture following an assault. He underwent left eyebrow incision to periostium and the fracture was reduced and fixed (4 hole 1.5mm plate, 4 screws). After a prolonged recovery he was discharged from clinic with minor residual infraorbital paraesthesia. Over the next 9 years he noticed gradual left eyebrow loss followed by recession of his frontal hair line and hair loss elsewhere (right eyebrow, temporal areas, face and limbs) and associated pruritus. He went on to undergo hair transplantation to the eyebrows and temporal scalp from posterior scalp donor sites. His transplant surgeon referred him to the specialist hair clinic for an opinion given the unusual pattern of hair loss. Past medical history includes polymorphic light eruption, rosacea and hayfever, taking finasteride, fexofenadine, topical metronidazole and ketoconazole shampoo. There was no family history of hair loss. Examination showed frontal hair line recession with thinning at transplant sites (bitemporal scalp/eyebrows) and arms. Dermoscopy showed perifollicular plugging at the mid-frontal hairline and lack of follicular ostia in-keeping with scarring in the temporal areas, face and arms.

Full blood count, thyroid studies and sex hormone profile were normal. A 4mm punch biopsy of the frontal hair line demonstrated patchy lymphocytic inflammation around the upper segments of hair follicles associated with lichenoid damage and perifollicular fibrous scarring. Treatment with topical betacap lotion and lymecycline led to reduced pruritus and stabilised hair loss. He remains under close follow up.

Comment

The exact cause of FFA remains unclear and the pathogenesis may be multifactorial. This unusual case supports a possible association between trauma and FFA, whereby an immune response may be triggered by previous local trauma/surgery (Chiang et al. 2011). Further studies of aetiology of this elusive condition are needed.
EVIDENCE FOR LYMPHOCYTIC INFLAMMATION IN UNAFFECTED SCALP OF PATIENTS WITH FOLLICULITIS DECALVANS: A HISTOLOGICAL STUDY OF AFFECTED AND UNAFFECTED SCALP BIOPSY FROM 25 PATIENTS

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Introduction & Objectives
Folliculitis decalvans is considered to be a predominantly neutrophilic scarring alopecia that leads to chronic inflammation and permanent hair loss. Key clinical features include the presence of one or more confluent areas of scarring alopecia on the scalp and pustules and papules primarily at the periphery of areas of alopecia. The cause of folliculitis decalvans is unknown. Evaluation of scalp biopsies can help to confirm the diagnosis and lead to a better understanding of the pathologic process. This project aimed to study the histopathological findings of affected and unaffected scalp areas from patients with folliculitis decalvans.

Materials & Methods
Twenty-five patients seen between 2016 and 2018 with biopsy-proven folliculitis decalvans (18 males, between 22 to 72 years and 7 females, between 17 to 60 years) from the Department of Dermatology – University of Sao Paulo were included in the study after IRB approval and signed informed consent.

Results
In the male group, 38% of the patients showed inflammation exclusively in the affected area compared to 14% of the patients in the female group. Sixty one % of the male patients showed inflammation in both affected and unaffected scalp areas, compared to 85% of the female patients. The most common findings in the affected areas were: diffuse fibrosis, and perifollicular inflammation mostly around the isthmus, with lymphocytes, histiocytes, plasma cells and neutrophils. Perivascular inflammation, granuloma formation with giant cells, follicular destruction, and naked hair shafts were also seen. In the unaffected areas the specimens showed perifollicular fibrosis, and inflammatory infiltrate with lymphocytes, histiocytes and plasma cells around the isthmus, sebaceous glands and eccrine ducts.

Comment
The presence of inflammation and fibrosis in 68% of the patients in the absence of clinical lesions points to a more generalized inflammatory process. The lack of neutrophils in unaffected areas may suggest that early or subtle stages of folliculitis decalvans could possibly start with a lymphocytic inflammation. In the future, new approaches focused at addressing both neutrophilic and lymphocytic inflammation may be beneficial to patients with folliculitis decalvans.
Background
Since its first description, frontal fibrosing alopecia (FFA) has become increasingly common worldwide. Environmental factors may be involved in the etiology, and several epidemiologic studies performed on hundreds of FFA patients suggest an association between FFA and leave-on facial products, including anti-aging moisturizers and sunscreens.

The time course of sunscreen and anti-aging moisturizers use by the population does seem to parallel the apparent increase in the incidence of FFA, and to some extent the predominant distribution of FFA matches the usual sites of moisturizer and sunscreen application. One Case report showed the presence of titanium species on the hair shaft of a patient diagnosed with FFA, suggesting that titanium dioxide could have a potential role (1) and a recent study confirm this feature (2).

Objectives
To determine the presence of titanium nanoparticles (Ti NP) in the hair shaft of FFA patients.

Materials & Methods
Patients were recruited prospectively during May 2018 and November 2018 in the Hair Unit of the Department of Dermatology, Hospital Clinic and University of Barcelona, Barcelona, Spain. The composition of each hair was carefully analyzed.

A scanning electron microscope (SEM) JEOL FE-SEM J-7100 was used to obtain amplified images of samples in order to study their shape and structure, and the presence of micro and nanoparticles attached to the hair shaft and the hair root. For more detail, X-ray microanalysis was performed with an EDS Oxford Inca to study the elemental composition of the studied samples.

In order to confirm the presence of titanium and other micro and nanoparticles, topographic and chemical contrast tests were performed, and composition was confirmed by energy dispersive x-ray microanalysis spectrometry (EDS) microanalysis.

Results
We evaluated 11 samples of independent patients diagnosed with FFA (9 hair shafts and 2 hair roots) and 4 samples of individuals without scalp or hair disease (two hair shafts and 2 hair roots).

We found Ti NP in 7 out of 9 hair shafts of the patients diagnosed with FFA (77.7%). However, Ti NP were not found in any hair root. Regarding controls, none of them presented TiNP (neither in the hair shaft, nor in the hair root).

Conclusion
We demonstrate the ubiquity of titanium NP, being found on the hair shaft of patients diagnosed with FFA. However, its causative role is still to be elucidated, as Ti NP were not found in the hair root. Further studies must be performed in order to determine the exact cause of the disease.

Lichen planus pigmentosus (LPP) is an infrequent variant of LP characterized by insidious onset of ill-defined, dark brown or slate gray macules, primarily appearing over sun-exposed areas and flexures. LPP and frontal fibrosing alopecia (FFA) may co-exist and some authors consider them as part of the same spectrum. We present a case of a woman with LPP who developed FFA and had a good response to treatment with isotretinoin.

Case report
A 58-year-old Caucasian woman presented with a one-year evolution hyperpigmented macules on both axillae and eyelids that were occasionally pruritic. On examination, hyperpigmented macules with slight areas of erythema were observed in axillae and upper and lower eyelids, together with lateral eyebrow loss and loss of axillary hair. During her follow-up she also developed a slight recession of her left temporal hair line, compatible with cicatricial alopecia. No facial papules, oral lesions or other signs were present. Biopsy showed histological findings compatible with LPP. Treatment with topical corticoids and topical tacrolimus were ineffective, so 2 years after the starting of her clinical signs, treatment with Isotretinoin 20 mg/day was initiated. After 4 months of treatment she presented improvement mostly in the hyperpigmentation of eyelids, but also noted stabilization of alopecia. Dose was tapered then to 10 mg/day and she maintains this dose after one year follow up with good Results.

Discussion
Coexistence of FFA and LPP was first reported by Dlova in 2013 in African patients. In more recent series of 37 patients with FFA and LPP, 81% were postmenopausal women, 97% had eyebrow involvement and in 51% LPP preceded FFA presentation, as in our patient.

In a multicenter case–control study the presence of LPP was found to be a risk factor for developing of FFA (OR=5.14). Hyperpigmentation of the upper eyelid is considered by some authors an important clue to the diagnosis of LPP that helps differentiating it from other common photodermatoses such as melasma, thus avoiding unnecessary biopsies. Oral retinoids had shown to be effective in some cases of lichen planus, especially in oral and erosive variants.

There is one single clinical trial studying the efficacy of them in LPP. It showed that isotretinoin is a promising treatment modality in stabilizing and decreasing the pigmentation particularly in early and limited disease.

Concerning the role of retinoids in FFA, a recent study reported an arrest of disease progression without progression after discontinuation of treatment in the majority of patients using oral isotretinoin 20 mg/day and in those treated with acitretin 20 mg/day; Results were superior to the control group treated with finasteride 5 mg/day.

Conclusion
We report a woman with LPP as an early sign of a FFA, in which treatment with isotretinoin was effective, improving the eyelid hyperpigmentation and stabilizing the alopecia.
Introduction
Ultrasound imaging of the skin is becoming more and more useful. Skin ultrasound is a non-invasive, fast and accessible dermatological diagnostic imaging examination is increasingly used in skin cancer and inflammatory conditions as well as in cosmetic dermatology. However, little is known when it comes to evaluate and determine the response to treatment in scarring alopecia, specifically in frontal fibrosing alopecia (FFA).

Objective
To determine the ultrasonographic characteristics of FFA patients by comparing healthy area, atrophic area and inflamed area; and to correlate the data with clinical and trichoscopic findings.

Materials & Methods
Fifteen cases of FFA were evaluated with the ESAOTE My Lab Class C (22 MhZ for eco-doppler and follicle evaluation, and 13/18 MhZ for dermis-hypodermis assessment), with a PRF of 750 and a gain of 26%. Four zones were evaluated and compared (Zone 1: healthy frontal skin, Zone 2: frontal atrophic skin, Zone 3: frontal affected recession line, Zone 4: healthy parietal skin).

Results
In the patients with active clinic findings such as erythema and hyperkeratosis, intense inflammation was detected in the recession line. The presence of a hypoechoic band was also detected in the affected area, a finding that was not found neither in the atrophic frontal zone nor in the healthy area. Atrophy was observed in the dermis of the recession zone, a finding that became more evident when compared with adjacent healthy skin. The hair follicles were located more superficial and were thinner in the inflamed area than in healthy scalp.

Conclusion
Since skin ultrasound allows us
1) to detect presence/absence of hair follicle,
2) to differentiate anagen/telogen/catagen follicle cycle,
3) to assess inflammation, and
4) to diagnose atrophy; this imaging technique could play a role in the monitoring of scarring alopecia, specifically in FFA.
INTRODUCTION
Lichen Planopilaris (LPP), a rare variant of lichen planus (LP), is a scarring alopecia that carries a significant morbidity. The clinical presentation of LPP is diverse, with the condition itself being divided into several subtypes: classic LPP, frontal fibrosing alopecia (FFA) and Graham Little syndrome. There are a number of different treatment options put forward for the management of LPP, however there is a distinct lack of a global consensus on the best therapeutic approach to this condition. Systemic treatment options include tetracyclines, hydroxychloroquine and immunosuppressants such as steroids, ciclosporin and mycophenolate mofetil. In addition, pioglitazone and naltrexone have recently been suggested as having some benefit in the management of LPP.

The scarring nature of LPP necessitates rapid diagnosis and effective treatment. However the lack of guidelines for the management of this disease threatens this aim. A 2018 systematic review by Errichetti et al suggested that for extensive LPP, the first step should be hydroxychloroquine monotherapy (1).

OBJECTIVE
The aim of this retrospective review was to examine the outcome of initial treatment options for patients with extensive LPP, for whom treatment with an oral systemic agent was deemed appropriate.

RESULTS
The initial treatment approach was overwhelming with monotherapy (predominantly hydroxychloroquine). Of the 45 patients, only 4 showed an adequate response to monotherapy at initial review. The remaining patients generally progressed to combination therapy, with the exclusion of a small number of patients who decided not to proceed further with medical treatment.

Combination therapies yielded improved clinical results, with 16 of the remaining patients showing a good response (i.e. static progression). The outcomes of patients with ongoing uncontrolled disease following this included initiating immunosuppressive treatment (e.g. with mycophenolate mofetil), trialing triamcinolone injections and cover-up techniques i.e wigs.

COMMENT
Despite being a small, retrospective review these findings suggest that treatment with monotherapy rarely yields adequate results for those with advanced LPP. It is therefore suggested that the initial therapeutic approach for those with advanced LPP could include combination therapy. There are other important factors to consider, including adverse drug effects.

CONCLUSION
However, in view of the need for rapid control of this scarring alopecia, the conduction of larger cohort clinical studies to assess the response to initial combination therapy is recommended.

Background
Since its first description, frontal fibrosing alopecia (FFA) has become increasingly common worldwide. Environmental factors may be involved in the etiology, and several epidemiologic studies performed on hundreds of FFA patients suggest an association between FFA and leave-on facial products, including anti-aging moisturizers and sunscreens.

The time course of sunscreen and anti-aging moisturizers use by the population does seem to parallel the apparent increase in the incidence of FFA, and to some extent the predominant distribution of FFA matches the usual sites of moisturizer and sunscreen application.

Even if some authors believe that a causative role for leave-on facial products is not able to explain the frequency of hair loss on the limbs and occipital hairline seen in some men and women, we know that people tend to apply leave on cosmetics also in these areas.

Case report
We present the case of a woman in her sixties with hypothyroidism who presented to our dermatology department complaining of hair loss in the occipital area during the last four years.

At examination, the eyebrows and the frontal hair line were present, however, she had lost all the hair in the occipital area. Trichoscopy showed perifollicular hyperkeratosis, without erythema (the patient had been treated with topical clobetasol propionate 0.05% for 5 months prior to our diagnosis), and absence of follicular openings in the alopecic area suggesting a cicatricial alopecia pattern.

The patient denied the use of leave on cosmetics on the face, however, she had been applying hair lacquer on the occipital area for more than six years. A skin biopsy of the affected area was performed, and the patient was patch tested with the standard series according to the European Society of Contact Dermatitis (ESCD) guidelines and the hair lacquer.

Discussion
This case suggests that fibrosing alopecia might be due to leave-on products.

In this case, the patient denied the use of leave on cosmetics on the face (which is in accordance with the fact that her eyebrows and frontal line were not involved), but she applied a considerable amount of hair lacquer on the occipital area everyday (the site in which fibrosing alopecia was diagnosed).

Conclusion
Based on our Results, we recommend that once FFA is suspected, patients should be advised to avoid applying leave-on cosmetics on the recession hair line as part of their treatment.
**LOW SEBUM EXCRETION - A RISK FACTOR FOR FRONTAL FIBROSING ALOPECIA?**

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**Introduction**

Frontal fibrosing alopecia (FFA) is an increasingly common form of scarring alopecia that mainly affects postmenopausal women. The epidemiology strongly suggests an environmental cause and there is some evidence implicating leave-on cosmetics in the aetiology.

We hypothesise that cosmetic ingredients introduced within the last 20-30 years (there are several candidates) enter the upper part of the hair follicle and initiate an inflammatory reaction that ultimately results in follicular destruction. In this study we have explored the idea that sebum has a flushing role in removing exogenous substances from the pilosebaceous duct and, consequently, that low sebum excretion may be a risk factor for the development of FFA.

**Method**

The sebum excretion rate (SER) was measured on the mid-forehead, below the zone of scarring hair loss, in 25 women with FFA and in 22 control subjects. All subjects were postmenopausal. The casual sebum level was measured using a Sebometer® at baseline and then 1 hour after cleansing the forehead with an alcohol wipe.

**Results**

We observed a substantially and significantly lower SER in subjects with FFA than in controls (FFA mean 12.5±g/cm²/h 18.2 SD, Controls 64.9±52.6, p<0.0001).

**Comment**

Our Results are in keeping with the hypothesis that low sebum excretion is a risk factor for FFA. Previous studies have shown that sebum excretion declines following the menopause in women, whereas it does not fall until after the age of 70 in men, and this may partly explain why FFA is much more common in postmenopausal women than in younger women and men.


The alternative interpretation is that FFA damages or destroys sebaceous follicles. This was not clinically evident at the sample sites in any of our subjects but, at present, cannot be ruled out.

There could be therapeutic implications if the first of these two possible explanations proves correct.
FRONTAL FIBROSING ALOPECIA

INTRODUCTION & OBJECTIVES
The prevalence of fibrosing frontal alopecia is increasing rapidly throughout the world. However, there are few Case reports from Latin America, and some have suggested the presence of special characteristics in this population.
We aimed to describe the clinical and epidemiological characteristics of patients with fibrosing frontal alopecia in two private dermatology practices from Colombia.

MATERIALS & METHODS
We reviewed the medical records of patients with a diagnosis of fibrosing frontal alopecia who consulted between January 1, 2016 and January 31, 2019, and their clinical and epidemiological characteristics were recorded.

RESULTS
Seventy-four patients of Hispanic origin with a new or previous diagnosis of frontal fibrosing alopecia were included; of these, two patients were men (2.7%). The average age was 60 years. Among women, 16.9% (12/71) were premenopausal. These patients were phototypes from II to VI, being phototypes III (58%) and IV (25%) predominant. 40% (29/73) of the patients presented lichen planus pigmentosus, of which 41% were phototype IV, 38% were phototype III and 21% phototypes V and VI.
Clinical pattern I was the most common (60%), followed by pattern II (19%). Most of the patients (79%) presented affectation of the eyebrows, facial papules (58%) and loss of body hair (57%). 40% of patients had facial veins atrophy (29/73).

COMMENT
The patients of this case series from Colombia present characteristics similar to other case series reported in the world, however, the high frequency of patients with associated lichen pigmentosus, even in phototype III, suggests that apart from the phototype, could there be other factors that may have relevance in the pathogenesis of lichen planus pigmentosum in the context of frontal fibrosing alopecia.
Genotrichosis are genetic defects of hair growth, cycling, or morphogenesis. New genome sequencing technology such as exome sequencing has facilitated the identification of mutated genes. So far, over 250 human genes have been identified to be involved in hair diseases. Currently there is no classification for genotrichoses.

The criteria for classification should be simple, logical, and practical for clinicians and researchers alike.

We suggest the following criteria:
1) Hair amount, (atrichia, hipoatriachia and Hypertrichosis)
2) Distribution (generalized vs. localized),
3) Isolated vs. syndromic hair disease,
4) Hair morphology, and
5) Occurrence and inheritance pattern.

**Generalized atrichia**: alopecia universalis congenital or atrichia with papular lesions and vitamin D-resistant rickets type IIA (VDRR).

Localized alopecias would include linear nevus sebaceous syndrome (LNSS) and congenital triangular alopecia.

True hypotrichoses would include three isolated hair diseases: hypotrichosis simplex, hypotrichosis with juvenile macular disease and hypotrichosis Marie Unna.

Hair shaft dysplasias include monilethrix and woolly hair disease and some others. The Ectodermal dysplasias represent part of this group too.

Hypertrichosis may be localized such as anterior neck, cubital or trichomegaly of the eyelashes, or generalized. The latter is most often syndromic, Cantu syndrome, Coffin-Siris syndrome, and Zimmermann-Laband syndrome.
Introduction & Objectives
Autoimmune PolyEndocrinopathy Candidiasis Ectodermal Dystrophy (APECED) syndrome or Autoimmune Polyendocrinopathy Syndrome type 1 (APS1) is a rare disease with recessive autosomal inheritance. Clinically, APECED syndrome manifests with triad chronic mucocutaneous candidiasis, hypoparathyroidism and Addison’s disease. Our objective is to describe a Case report of a man diagnosed with APECED syndrome in his adulthood.

Materials & Methods
Here we present the case of one patient diagnosed with APECED syndrome. We will report his medical history and we will describe all his dermatologic manifestations.

Results
We present a 47-year-old man with history of cutaneous lesions and 20 nails onychopathy diagnosed as psoriasis since he was 7-year-old with no response to topical corticosteroids. Moreover, since he was 10-year-old he presents repeated oral candidiasis successfully treated with systemic antifungal agents but with multiples relapses after finishing treatment. His parents and son do not have any cutaneous manifestation, but his sister presented repeated mucous candidiasis since infancy and hypoparathyroidism, so APECED syndrome was suspected and confirmed with genetic test.

Three years ago, our patient consults in our Department of Dermatology because of alopecia areata universalis, ungueal dystrophy and multiple erythematodesquamative pruritic plaques in arms, legs, hands and feet. Nail and skin KOH-mycology tests were positive to T. rubrum and candida, so antifungal treatment was initiated, being necessary maintenance treatment with fluconazole until today. With all this information, our patient achieve clinical diagnosis of APECED syndrome, subsequently confirmed with detection of AIRE gene mutation.

Comment
We report a new case of APECED syndrome, a rare monogenic disease. Clinically, our patient presents chronic mucocutaneous candidiasis and alopecia areata. Family history is important. We have to think in APECED if a patient with alopecia areata or vitiligo presents chronic candidiasis that relapse when finishing treatment.

Is very important to follow up these patients because they can develop serious autoimmune diseases.
HR007 is a high-purity (> 95%) mixture of non-crosslinked glycosaminoglycans. We have previously demonstrated that a HR007 1.5% induces proliferation and motility of human primary fibroblasts and keratinocytes.

Objective
In a step further, the aim of this study was to evaluate and characterize the effects of HR007 on human resting hair follicles grown in ex vivo cultures.

Methods
Individual human resting (telogen) hair follicles were obtained as remnants of hair transplant and routinely grown in Williams E medium. For morphological analysis, 6-10 um histological sections were stained with H & E. The expression and localization of the cell proliferation marker Ki67, the stem cell marker CK15 (Cytokeratin 15) and the Wnt/b-catenin gene target CCND1 (Cyclin D1) was analyzed by immunofluorescence/imunohistochemistry and evaluated by confocal microscopy. The gene expression of components/targets of BMP/Smad and Wnt/b-catenin signaling pathways and of different telogen-anagen transition factors was quantified by qRT-PCR.

Comment
Here we report that treatment of hair follicles with HR007 promotes a rapid thickening of the dermal papilla/hair bulb region and of the outer and inner root sheaths. This stimulatory effect is associated with the induction of Ki67 all along the hair follicle, with a strong increase in the number of CK15 positive cells and with the activation of Wnt/b-catenin signaling (induction of CCND1 target and repression of the inhibitors/antagonists GSK3β and DKK1). Significantly, the activation of Wnt/b-catenin signaling occurs even when BMP2/BMP4 signaling, essential to maintain the telogen phase is still active. Interestingly, HR007 positively modulates the expression of TGFb2, a factor involved in the telogen/anagen transition, but not of FGF7. As a whole, these Results indicate that HR007 1.5% promotes very efficiently the entry of human resting hair follicles grown ex vivo into the growing phase through the activation of Wnt/b-catenin signaling.
Introduction & Objectives
Biotin has sustained a substantial social media and marketing presence in support of its use for hair and nail growth. In rare instances of biotin deficiency and several specific pathologies (e.g. brittle nail syndrome), biotin supplementation may offer some benefit; however, several recent systematic reviews have demonstrated that biotin use in otherwise healthy individuals offers no benefit to improve hair growth and quality. Conversely, routine consumption of biotin supplements may be detrimental in some patients as biotin interferes with several common immunoassays for troponin, thyroid function, and certain tumor markers. Given the limited efficacy of biotin for hair growth and its potential interference with critical lab markers, we sought to identify the prevalence of biotin supplementation in patients presenting for hair loss.

Materials & Methods
A retrospective review of new intake forms for patients presenting to a specialty alopecia clinic from July 2017 to January 2019 was performed. Intake forms included questions regarding all previous and current treatments for hair loss and use of herbs, vitamins, and supplements. The Partners Healthcare Institutional Review Board granted approval to maintain a database of information collected from the new patient intake forms and for a subsequent retrospective review.

Results
In total, 1019 patients were included in the analysis. The mean age was 46 years old with most patients identifying as female (81%) and Caucasian (81%). Over 58% of patients (n=598) reported previous or current use of treatments for their hair loss. Of the patients reporting hair loss treatments, the most commonly indicated treatments included topical minoxidil (n=348, 58%) followed by biotin supplementation (n=247, 41%).

Additionally, 52% of patients (n=528) reported use of herbs, vitamins, and/or supplements in general, not necessarily for their hair loss. Of the patients reporting vitamin or supplement use for any reason, biotin (n=247, 47%), vitamin D (n=212, 40%), and multivitamin (n=207, 39%) were most frequently indicated.

Comment
This retrospective review is the first to our knowledge to quantify the frequency of biotin supplementation in patients with hair loss. While less frequent than topical minoxidil which remains one of the strongest evidence-based treatments for male and female pattern hair loss, biotin supplementation represented the second most common patient-reported treatment for hair loss in individuals presenting for an alopecia consultation. Biotin use was also more frequently reported than any other vitamin or supplement in general in our patient cohort.

As more than half of respondents indicated that they consumed vitamins and supplements, it is critical that clinicians routinely inquire about their use. Additionally, clinicians should continue to counsel patients on the limited efficacy of biotin and its potential interference with critical lab tests.
Today, many people suffer from scalp and hair disorders for various reasons, such as excessive stress, changing in climate, bad eating habits, and so forth. The main symptoms of these disorders are itching, dandruff (flaking), and greasy hair.

For the improvement of these symptoms, people use anti-dandruff shampoo containing powerful antifungal agents (zinc pyrithione, climbazole and so on), and silicone free shampoo for greasy hair. This study is aimed to formulate an advanced scalp-care shampoo, having not only good conditioning effect with lower build-up on the surface of the scalp, but also anti-itching effect on the scalp.

With the combination of cationic polymer, amphoteric surfactant, conditioning oil and viscosity increasing ingredients, the formulated shampoo showed not only good conditioning effect on the hair, but also low build-up on the scalp.

In the panel test (sensory evaluation), the shampoo showed significant improvement (questionnaire) of itching.
Introduction
Shampoos and conditioners are considered among safest cosmetic products as their contact with the skin is limited and they diluted with water during use. However, consumers often complain of adverse effects after use of hair care products, including skin irritation and allergy, hair damage and even hair loss. For this reason, it is very important for hair care products to be tested for safety regarding irritation, allergy and damage to the hair fiber.

Objective
The aim of this study was to evaluate the safety of MonatR shampoos and conditioners on the skin and on the hair shaft.

Materials & Methods
The following tests were performed to evaluate potential skin irritation /allergy with final products and/or single ingredient/ingredient mix. The following products and ingredients were tested:
- Shampoos (Balance Renew, Revive, Black 2 in1, Intense Repair Treatment)
- Conditioners (Balance Restore, Intense Repair Treatment, Volume Revitalize).

Repeated insult patch tests (RIPT) on 50 volunteers for 45 days. (final products and 9 selected ingredient/ingredient mix)
Safety in real condition of use (SRCU) in 60 volunteers including subjects with normal skin, sensitive skin and subjects with history of psoriasis. (final products)

Videodermoscopy to detect scalp deposits (Rejuveniqe hair oil blend, Intense Repair Treatment final products). The following tests were performed to evaluate safety of final products on the hair shaft.
Wet combability and tensile strength using the EMIC DL-500 test equipped with a dynamometer.
SEM analysis of hair structure using the Scion® for Windows software program that detects damage to the hair fiber surface (e.g. raised cuticles, fragments) as lighter colored areas.

Results
RIPT and SRCU gave negative Results for all tested products.
The Results of the tensile tests showed that the tested hair products improved hair combability and did not reduce the mechanical resistance of hair. In particular they did not cause hair breakage or loss of hair flexibility even when utilized on bleached damaged hair.
SEM analysis showed that the tested products did not change the superficial structure of normal virgin hair and improved the superficial structure of damaged bleached/dyed hair.

Comment
Safety tests are very important to show that hair care products do not irritate the skin, do not contain strong contact allergen and do not damage the hair fiber. Results of this study shows that Monat R tested products are not irritant for the skin and actually improve hair shaft quality.
Introduction
About 50% of general adult population worldwide are affected by dandruff. In addition to the physical discomfort elicited by itching and greasy appearance of the hair, it also causes social discomfort given by an impaired self-image, often compromising the psychosocial functioning. The purpose of the present study was to assess the pre-clinical efficacy on erythema, discomfort relief and itching relief in an in vitro model of human keratinocytes culture and greasy control in human fibroblasts culture of a shampoo containing 0.5% climbazole, 1% salicylic acid, 2% niacinamide, 1% Tamarindus indica extract.

Material & Methods
Human keratinocytes were stimulated with LPS (20 ng/ml) and treated with the investigated product for further quantification of TRPV-1, IL-1, histamine and prostaglandin E (PGE). In parallel, human fibroblasts were pretreated with the investigated product for 48 hours and after stimulated with testosterone and re-treated with the product. After 24 hours the supernatant was collected for quantification of dihydrotestosterone (DHT) and 5α-reductase.

Results
LPS stimulation significantly increased IL-1, histamine, TRPV-1 and PGE production relative to baseline control. Treatment with the product significantly reduced the overproduction of all evaluated cytokines compared to the LPS-stimulated group. 1) IL-1: reduction of 48.46% at concentrations of 0.01 mg/mL; 2) Histamine: reduction of 58.19%, 56.46% and 38.27% at concentrations of 0.01; 0.00316 and 0.001 mg/ml; 3) TRPV-1: reduction of 66.19%, 66.24% and 31.86% at the concentrations of 0.01; 0.00316 and 0.001 mg/ml; 4) PGE: reduction of 53.49% in the concentration of 0.01 mg/ml.

The stimulation with testosterone produced a significant increase in DHT production relative to the basal control, contributing to the process of sebum secretion. The investigated product was able to prevent the increase of DHT secretion induced by testosterone in 24.18% at the concentration of 0.01 mg/mL.

Similarly, 5α-reductase production was stimulated in the presence of testosterone but treatment with the product did not reduce production of this mediator.

Discussion
These Results demonstrated the potential of the investigated product in the improvement of erythema, itching and redness through the modulation of important inflammatory mediators. The prevent of excessive secretion of DHT production in cells stimulated with testosterone also demonstrated the ability of the product to prevent and control capillary oiliness.
Introduction
During the last few years, airborne pollution has become a major concern for environment and health, especially in large metropolitan areas. The exposure of hair and scalp to air pollutants has been associated with a pro-oxidant effect, increased AhR (Aryl hydrocarbon Receptor) signaling and inflammation status, reduced microvasculature in the dermal papilla, decreased melanin synthesis in the hair bulb, as well as increased sebum secretion and scalp sensitivity.

Methods
First, different in vitro and ex vivo models were used to investigate the effect of pollution, including cultures of keratinocytes from scalp skin, 3D spheres of human dermal papilla cells or ex vivo scalp biopsies, that were exposed to PM2.5 or cigarette smoke, respectively. A combination of botanical extracts obtained from Pisum sativum and Salvia hispanica was evaluated for their potential effect to mitigate the negative effects of pollution exposure stress on the hair and scalp. When the combination of extracts was applied on cells or scalp biopsies that had been exposed to these pollutants, a decrease in CYP1A1 (AhR signaling), a reduced level of IL1R1 (receptor for interleukin-1), and an increased level of VEGFA were observed.

Then, a clinical study was conducted in two parts. The first part was a short-term study with 5-hour application of the combination of extracts on scalp that had been stressed by cigarette smoke exposure. The second part was a long-term study with 42 days of application of a hair serum (containing either the combination of extracts or a placebo) on the scalp of 40 volunteers living in a large urban area.

Results
The short-term study showed that oxidative damage on scalp stratum corneum was decreased after application of the combination of extracts. For the long-term study, evaluations were performed on scalp health and scalp soothing, and revealed that this combination of extracts helped to re-balance the scalp’s oiliness, improve the scalp’s hydration and scalp barrier, and decrease scalp irritation and flaking.

To focus on the effects of airborne pollution on hair and scalp, this study included both in vitro and ex vivo models, followed by a clinical study.

Conclusion
Taken together, the Results showed a mitigating effect of a combination of botanical extracts on the negative effects of exposure to certain types of pollutants on hair and scalp.
Introduction

Hairs are daily exposed to situations that can cause damage to its structure. A good appearance is related to a health, shiny and smooth hair. Therefore, it is important to develop new hair care products.

Methods

The cosmetic market has abundantly launched products for the treatment of damaged hair and nanotechnology have been an ally in this process. Nanotechnology refers to the research and technological development of the material within nanometric scale (smaller than 1 m, usually in the range of 1 - 100 nm), with new functionality and properties, allowing new applications. Nanoparticles can be differentiated by the morphology, size, surface charge, solubility in the biological environment and by their supramolecular composition and these characteristics affect the biological effects of them.

Results

Lipid nanoparticles are the most studied and among these are nanoemulsions, liposomes, solid lipid nanoparticles and nanostructured lipid carriers. Polymeric nanoparticles are carrier systems which, according to the structural organization, are called nanocapsules or nanospheres. Once the hair shaft is covered by molecules of fatty acids, the majority of which is 18-methyl eicosanoic acid, lipid nanoparticles may have more affinity with it. In addition to surface distribution (adsorption), the nanoparticles can be absorbed by the transcellular pathway (via cuticular cells, through high and low cross-linking proteins) and, by intercellular diffusion (between cuticle cells, through of the cell membrane complex and the endocutícula). For nanoparticles, the intercellular diffusion would be the most plausible, since inter-scale cement occupies a space between 200 and 300 nm.

Comment

In conclusion, nanotechnology-based hair care products should be further studied regarding hair shaft attributes, as shine, moisture content and elasticity.
Introduction

We report a case with the aim to highlight the life-threatening side effects of hair dyes that are frequently used in people’s ordinary grooming. PPD must be taken into account as a potentially causative agent for the development of eyelid angioedema, a skin disorder that can lead to severe impairment in quality of life.

Background

Angioedema is a deep swelling and erythema that involves skin or mucoses that usually lasts longer than wheals and may be painful rather than itchy. It is IgE (Immunoglobulin E) mediated and causes mast cell activation and degranulation, with release of histamine and bradykinin, which causes vasodilatation and increased vascular permeability. Plasma complement C4 levels drop, because it is consumed, but the levels of C1 and C3 are usually normal.

Beard dyes and Hair dyes contain PPD (para-Phenylenediamine) as ingredient. P-Phenylenediamine, or which is the same 1,4 di-amino-bencene, is an aromatic amine which derives from Para-Nitro-Aniline. PPD has potential toxicity, which includes acute toxicity such as allergic contact dermatitis and subacute toxicity.

Eighty percent of dye allergies point PPD as responsible and due to its very high PPD concentration, dark dyes increase the allergy risk. Through years, PPD molecule is well recognized as an allergen because of its low PM (Molecular Weight) considering it as an haptene or pro-haptene. The immuno-stimulatory effects of PPD have been proposed to be induced by Bandrowski’s base (BB), a cutaneous secondary oxidation product. However, elevated levels of BB were described either in PPD-allergic and PPD-tolerant individuals, so the presence of BB does not necessarily trigger immune response in the PPD-tolerant individuals.

Case report

We present a 70 years old glaucoma patient who developed eyelid swelling (angioedema) after his usual beard dye (previously well tolerated) just following a family member death. He was deemed to have an immunoglobulin E (IgE)- mediated hypersensitivity to PPD.

Conclusion

In this case we will focus on the main difference in this dye application: the psychological factor. This stressor triggers the Cortico - Limbic - Hipotalamus pathway (and Hipotalamus Pituitary Adrenal - HPA axis) to the releasing of ICAM and IL4 which activates Linfocites B and eosinofiles, ending in an IgE excessive release, activating mastocites which release histamine, the responsible of oedema.
Introduction & Objectives
Essential oils have been widely proposed for the treatment of some skin and hair disorders, including androgenetic alopecia and seborrheic dermatitis. This study aims to evaluate the proliferative potential of these one on the human fibroblasts (CCD-1072Sk; ATCC).

Materials & Methods
Essential oils of rosemary, tea tree and lavender were evaluated through trypan blue technique and MTT reduction to formazan. In addition, we quantified the total collagen synthesized by test of Sirius red.

Results
By the trypan blue technique, the Results obtained suggest that among the essential oils tested, only the essential oil of melaleuca was not capable of inducing the proliferation of fibroblasts so clearly, when compared to control cells (untreated cells). In the same sense, the MTT reduction technique was performed with the intention of confirming the proliferative activity of the evaluated essential oils. Similarly, to the trypan blue test, the MTT test indicated that lavender and rosemary oils presented greater capacity of cellular proliferation in relation to melaleuca oil and control cells. The quantification of collagen produced by CCD-1072SK fibroblasts was performed by the test of Sirius Red. The Results showed that the lavender and rosemary oils, as might be expected, were the ones that stimulated the fibroblasts the most to produce collagen during the 24 hours.

Comment
In these preliminary tests we observed that lavender and rosemary oils were able to induce proliferation of fibroblasts and collagen synthesis. Fibroblasts are found in the dermal papilla of the hair follicles and are strongly implicated in the regulation of hair growth through the ability to modulate gene expression by activating the neogenous phase of the capillary growth cycle and the activation of the signal transduction pathways cell and mitogenic survival. Further evaluations should be performed to confirm the action of essential oils of rosemary and lavender on regulating the hair growth cycle.
Introduction
Nowadays many women suffer from eyelash hypotrichosis, which comprises either eyelash loss and/or thinning. It can have multifactorial etiologies. Due the cosmetic and psychological consequences specially in women, those patients look for alternatives (extensions, masks, permanent dye), in order to increase the length, volume and thickness perception of their eyelashes, however most of these alternatives cause adverse reactions like chronic contact dermatitis or inflammatory processes which can cause permanent loss of the eyelashes.

The topical solution, investigated in this study, was formulated with Hydrolyzed Soy Protein, Adenosine, Myristoyl Pentapeptide-17, Magnesium Ascorbyl Phosphate, Lysophosphatidic acid and safflower oil, which have shown individually to stimulate eyelash growth. Nanosomal encapsulation and delivery system, enhances stability, penetration and accumulation of active ingredients in hair follicles.

The Objectives of this study were to evaluate the capacity of Spectralash solution of improving hair growth in relation to length, volume and thickness, and identify possible signs of ocular adverse local reactions related to the application.

Methods
An open-label, prospective study was performed in healthy women during a daily administration period of 3 months.

Results
The thickness and length of hair was determined taking trichoscopic images at 20x with Fotofinder® medicam-800-HD at the beginning and after 3 months treatment. A total of 40 images were taken and visual assessment of length, volume and diameter has been blinded and performed by 6 independent trichological software technicians.

For evaluation a metric of 1 was assigned for cases with volume, length, diameter increase, -1 for cases with volume, length, diameter decrease and 0 for indecisive respectively. Average value and standard deviation was calculated for the assigned metrics for the assessed parameters.

The result obtained for length was 0.93 +/-0.37 - over 2σ statistically significant increase, for volume was 0.93 +/-0.38 - over 2σ statistically significant increase. For the diameters was 0.47 +/-0.90 - inconsistent.

Comment
The solution was capable of improving growth of eyelashes by increasing hair length and volume without causing local adverse effects, with an excellent profile for security and efficacy.
LAMIN B1 AS NOVEL BIOMARKER FOR SENESCENCE IN HUMAN HAIR FOLLICLES?

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Introduction & Objectives

The thinning of hair and loss of pigmentation due to aging can be classed as ‘senescent’ or involution alopecia. However, the underlying mechanisms and changes leading to these aging-associated phenotypes, and how they contribute towards them, are still largely unknown. It has been previously demonstrated that the loss of lamin B1, a major structural component of the nucleus, can be used as a biomarker to quantify cellular senescence in chronologically aged and photoaged skin. Therefore, we sought to determine whether lamin B1 is also expressed in human hair follicles (HFs) and thus a potential biomarker of human hair ‘senescence.’

Materials & Methods

Fresh frozen human HFs obtained after routine hair transplant surgery were utilized to establish and determine the expression of lamin B1. Using confocal and light sheet microscopy we investigated the expression of lamin B1 protein in situ.

Results

We found that the lamin B1 is indeed expressed in terminal anagen VI human HFs from scalp skin, with prominent expression in the nuclear membrane, namely in the keratinocytes of the hair matrix and the outer root sheath. Although to a lesser extent than the HF epithelium, lamin B1 expression was also seen in the fibroblasts of the mesenchymal ‘command centre’ the dermal papilla.

Comment

This pilot study demonstrates lamin B1 protein is expressed in both the epithelium and mesenchyme of human HFs. Ongoing investigations will determine whether expression of lamin B1 is altered between HFs of young and old donors, and thus define whether lamin B1 may serve as a novel biomarker of senescence. This will help to further delineate the underlying causes of age-associated phenomena seen in human hair growth, which remain largely undiscovered.
Background Changes in hair with aging, such as hair thinning, concern even healthy individuals. The causes of age-related hair thinning and other hair changes are complex and multifactorial, including influences such as hormonal changes, genetic susceptibility, and environmental insults.

There is growing evidence that the build-up of hydrogen peroxide (H2O2) within the hair follicle plays a role in cellular damage and leads to a disruption of homeostasis.

With age, the body is less able to defend against this naturally occurring metabolite, with reductions in detoxification enzymes, including catalase. Additionally, previous studies have shown that dermal papilla cells (DPC) from balding hair follicles were more likely to enter senescence after exposure to oxidative stress and growth inhibition by androgens than DPC from non-balding hair follicles. Therefore, we developed a high-throughput screening method to screen study the potential protective effect of both plant extracts and naturally occurring molecules as a step toward helping maintain the optimal state of the hair follicle over time.

Methods & Results A 96-well plate, screening assay using low (150 M), repeat (4x) dosing of H2O2 to induce senescence in human DPC was developed.

Over 100 compounds and plants used traditionally, for health promotion and skin and hair, along with those with known biological activity with potentially relevant activities, such as antioxidant, nrf2 agonist, and anti-inflammatory activities, were chosen for testing.

Conclusion Two of the most highly protective molecules against this senescent phenotype were the stilbenoid, resveratrol, and the flavonoid, luteolin. Both of these molecules have a number of reported anti-aging activities and are found in foods, beverages, and medicinal plants.
Introduction & Objectives

Particulate matters (PM), a mixture of particles in suspended in air. The major components consist with metals, organic compounds, materials of biological origin, ions, and particle carbon core, which is known to be associated with increased risks of cancer, pulmonary and cardiovascular diseases including skin diseases possibly by stimulating the production of reactive oxygen species (ROS) and inflammatory mediators.

A recent study found that keratinocyte cytotoxicity increased in a dose-dependent manner by PM treatment. IL-8(Interleukin 8) and MMP-1 (Matrix metalloproteinase-1) mRNA expression and protein levels were significantly increased compared to control by qPCR and ELISA, respectively. Moreover, collected PM from urban area was observed in hair follicles in both intact and barrier-disrupted mouse dorsal skin in vivo. These findings suggest that PMs might penetrate into hair follicles via transfollicular and transdermal routes depend on the barrier state of skin. Thus, we investigated the effects of PM on human hair follicular cells.

Materials & Methods

Primary cultured dermal papilla (DP) cells and outer root sheath (ORS) cells from human occipital scalp hair follicles were exposed to suspension of PM 10 (fine particles, ≤ 10 um; Sigma). Cell viability was measured by MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay. Expression levels of proinflammatory cytokines such as TNF-α (Tumor Necrosis Factor-α), IL-1α, IL-1β, IL-6 and IL-8 in the presence of PM 10 were quantitated.

Results

PM 10 treatment decreased the viability of both DP cells and ORS cells in a dose dependent manner. PM10 treatment of DP cells markedly upregulated the expression of IL-6 and IL-8 in a dose dependent manner. PM 10 treatment also increased IL-1α, IL-1β, IL-6 and IL-8 expression in ORS cells.

Comment

This study suggest that particulate matters can aggravate hair loss.
Background
The etiology of hair color changes has been documented to be caused by systemic diseases, medications and several external agents. Different drugs can affect the hair, however out of types of various drug-induced hair changes, color change is a rare phenomenon which is less reported in the literature. Hair color changes include hair lightening, whitening or returning to the original color and even change to a new color. Hair shaft discoloration can range from blue, green, red-brown, purple, mahogany to yellow. We report a patient presenting with hair yellowing (xanthotrichia) due to topical treatment with minoxidil solution.

Case report
A 56-year old white male presented with complaint of gradual yellowing of previously white scalp hair under topical minoxidil treatment for male pattern baldness.

Discussion
Xanthotrichia can occur secondary to a diversity of etiologic factors including environmental, occupational exposures, systemic disease or medications. Pathogenetic mechanisms of hair discoloration include deposition of pigmented compounds in hair shaft, chemical alteration of hair shafts components and alteration in melanin synthesis and toxic effect on melanocytes. Deposition of pigmented compounds was suggested as a cause of xanthotrichia in an environmental exposure to several agents and also due to the iatrogenic cause with use of several topical medications including anthralin, tar shampoo, selenium sulfide and minoxidil.

Chemical alteration of hair shaft may result from oxidative damage to melanin, melanosomes and photo-oxidation of keratin. Systemic disease and medications can alter by altering of melanin synthesis. In the patient presented there was no difference in chemical composition between white and yellow areas. Therefore we suggest that the effect of minoxidil is associated with chemical alteration of hair shaft. A detailed medical and occupational history is essential to elucidate the etiology of hair discoloration.

Conclusion
Patients with grayish to white hair should be educated on possible hair discoloration when using topical minoxidil.
Case report
A 50-year-old patient with a medical history of hypertension, hyperuricemia and attention deficit hyperactivity disorder (ADHD) that were controlled with enalapril, allopurinol and lisdexamfetamine, consulted for presenting a dark brown hair zone in the occipital area for 2 years and for 1 month another one on the centre of the moustache. The patient presents white white-grey hair for the last 8 years and says that before he had blond hair. Physical examination showed two plaques of darker brown hair in the occipital area and in the midpoint of the moustache. The rest of the hair was white-grey. There was some scaling erythema on the scalp under the dark hair in the occipital area. A biopsy sample was taken from the occipital area and showed a psoriasiform pattern with acanthosis and mild spongiosis. We also observed parakeratosis and hypogranulosis with exocytosis of neutrophils and focal neutrophilic abscesses. Melan A showed neither atypia nor increased number of melanocytes. Grocott’s GMS stain did not show fungal structures.

Discussion
The hair of our patient had been completely white-grey before he noticed the two localized dark brown plaques. As only skin alteration there was a scaling dermatitis on the scalp of the occipital area compatible with a seborrheic dermatitis that caused itching.

We did not find any pigmented lesion on the scalp or on the lip where we observed the repigmentation of the hair.

It has not been published any case of localized repigmentation of hair in patients under treatment with enalapril, or allopurinol neither with lisdexamfetamine therefore although there are drugs that may be the cause of repigmentation as cyclosporine, defibrotide, corticosteroids, etretinate, L-thyroxine, verapamil, levodopa, tamoxifen, cisplatin and cyanocobalamine, among others.

Localized spontaneous hair repigmentation in white-haired individuals has been reported with melanoma or lentigo maligna of the scalp. In our patient these causes were ruled out.

Conclusion
We hypothesized that the repigmentation in our patient may be due to chronic inflammation or as spontaneous event.


Introduction
Thirty years after the original article published in PIEL in 1986, “Hair Micrografting”, we have the opportunity to write about the novelties and the changes that have arisen in this field of dermatological surgery: the hair transplant. Much has changed the hair transplantation techniques in 30 years, with an exponential increase in the number of patients operated in Spain and around the world as well as the increase of medical doctors dedicated to this field of the skin surgery. The increase of this activity is a direct consequence of the simplification of the process and the advances in the surgical technique, which offers exceptional results together with the almost absence of complications for the patient.

All this interesting process takes a significant turn in 1995 with the Introduction of the concept of the “follicular unit” (FU) by doctors Bernstein and Rassman, and the use of stereoscopic microscopes by Dr. Limmer. Then, the transplantation of macro and mini-grafts is definitively replaced by micrografts, and then smaller FU micrografts that perfect the naturalness of the results.

Comment
The micrografts are based on the minimum transplantable FU without negatively affecting their survival, composed of basic anatomical structures. This supposes a revolution in this field, with natural Results and similar to the aspect of the hair not transplanted, in contrast with the larger grafts, which the so notorious aspect that they came to be called “doll hair” due to their similarity with this, due to the high number of grafted hair in the same incision and the large space that was left between them.

Each FU is independent of the others anatomically and physiologically, with a unique direction and angle, which allows its separation from the surrounding tissue in the donor area individually, both with follicular unit extraction (FUE) and with the Strip, also known by the English acronyms of FUT (follicular unit transplant) or FUSS (follicular unit strip surgery).

In the receptor area, FUs are implanted individually in any technique used in the extraction, Strip or FUE. Each FU have one to 4 terminal hairs, which we distribute by implanting with a single terminal hair on the anterior line of frontal area, that is mandatory to achieve the naturalness of the frontal hairline, and progressively placing FU from lower to higher number of terminal hairs (from 2 to 4) as we move to the neighbors areas of the scalp. Frontal and vertex tufts being the areas where we need a higher density.

Conclusion
The FUE technique requires less surgical training of the doctor and that has led to an invasion by doctors of non-surgical specialties who nowadays perform hair transplantation.
Introduction & Objective
The frontal hairline delimits and frames the face. It is determined by ethnicity and genetics, this characterized the thickness, density, shape of the hair fiber, and the angle and direction of the hair implantation. Throughout life suffers modifications caused by hormonal and environmental factors, styles and practices of combing, scarring inflammatory diseases, aesthetic surgeries, among others.

There are reports of frontal hairline patterns in American, Asian, Caucasian and Turkish population. In Mexico and Latin America there is no information about this topic. The objective of this work, was to identify the most frequent patterns of frontal hairline in Mexican women and men aged 15 to 25 years.

Material & Methods
This is a observational, descriptive, prospective and transversal study. Women and men between 15 and 25 years of age were evaluated by two dermatologist. We recorded the gender, age and classified the hairline of the forehead in 5 patterns: rectangular, M, round, triangular and bell. Measuring the height of the forehead, width of the forehead and distance orbiculo temporal (DOT).

Results
Ninety seven men and 67 women were included (167 in total). The patterns found in men were: rectangular 47.4%, in M 41.2%, triangular 6.1%, round 5.1%.
Average forehead width of 13.7 ± 1.9 cm, average forehead height 6.1 ± 0.7 cm, average DOT 4.6 ± 0.7 cm. In women the rectangular pattern in 38.8%, in M 20.8%, round 19.4%, triangular 14.9% and in bell 5.9%. Average forehead width of 13.5 ± 1.3 cm, average forehead height 6.1 ± 0.8 cm, average DOT 4.6 ± 0.4 cm.

Comment
Knowing the characteristics of shape and measures of the implantation line as well as their differences between men and women is important for an adequate design of correction of alopecias by means of hair transplants.

In our study the most frequently pattern of hairline was the rectangular shape.
The rapid healing of deep cutaneous wounds often leads to the formation of unwanted scars. An estimated one hundred million people per year in the developed world alone suffer from excessive scarring. Despite insights into the biology of scar formation provided by previous studies, to date, there are few clinical treatments for established scars. All scars are characterized by deposition of large amounts of collagen type I and an absence of skin appendages, including hair follicles. As a result, scars lack functional and mechanical properties of healthy skin elicited by its diverse structures. In particular, anagen hair follicles can induce substantial remodelling changes in the surrounding skin, including increased vascularization and collagen remodelling, characteristics sought for treatment of scars.

With the goal of remodelling established scars, in this study we tested whether implantation of anagen hair follicles into scars could induce the same remodelling changes as seen in healthy skin. In a clinical study, hair follicles were grafted into stretched scars formed as a result of strip harvesting for previous hair transplantation surgery.

Due to a lack of research on stretched scars, we first characterised them in comparison to healthy skin from the same location. Using Second Harmonic Generation (SHG) imaging to analyse dermal collagen type I, we found a significant increase in the thickness and alignment of fibres in scars. In addition, image analysis of the cellular composition of skin layers revealed decreased epidermal thickness and dermal cell density, and substantially reduced vascularization in scars. Using a global transcriptomic analysis, we identified 200 genes that were differentially expressed between stretched scars and healthy skin. Of these, a high proportion were associated with matricellular proteins linked to the extracellular matrix, including thrombospondins.

After establishing the baseline differences between stretched scars and healthy skin, we investigated whether hair transplantation into scars can induce scar remodelling. Using the same imaging techniques, we assessed scars before the follicle implantation, and then at 2, 4, and 6 months after.

We found a shift in structural characteristics, including remodelling of collagen fibres, higher cell numbers, and a significant increase in vascularization in scars after hair transplantation. The structural and cellular changes were accompanied by a shift in the transcriptome of the scar dermis, with 1,785 genes changing their expression after transplantation.

We believe that the substantial changes in scars observed after hair transplantation demonstrate the beneficial role of follicles in scar remodelling. Currently, we are conducting experiments to elucidate the mechanism by which this happens. In the long term, the Results of our study will enable identification of therapeutic targets and design of strategies to remodel and reduce established scars.
Introduction & Objectives
Appropriate storage of human hair follicle (HF) grafts during Follicular Unit Excision (FUE) procedure is crucial towards successful hair shaft implantation. It is thus of utmost importance to consider storage conditions that ensure ex vivo maintenance of follicular grafts.
Several commercial storage solutions with different biochemical compositions are currently used for ex vivo maintenance of follicular grafts viability and trichogenicity. Some studies have attempted to determine the effects of storage temperature, nutrients, or biochemical components on graft viability. However, quantitative experimental evidence demonstrating molecular changes in hair follicle cells associated with the usage of different storage conditions is largely missing. Therefore, we aim to identify gene expression changes in hair micrografts preserved ex vivo under different preservation conditions of temperature and biochemical environment.

Materials & Methods
A dermal papilla–centric analysis of hair bulbs isolated from human hair follicles to dissect the main signaling pathways being altered after exposing hair micrografts to different temperatures and holding solutions.

Results
We found chilled vs. room temperature to prevent inflammatory cytokine signaling. Under chilled conditions, all solutions tested, except ATPv-supplemented saline, compromised the expression of the trichogenic genes HEY1 and LEF1. Thus, ATPv-supplemented saline is the best condition to preserve hair follicle grafts.

Comment
Our data disclose DP gene expression analysis as a useful methodology to ascertain the efficacy of preserving solutions and elucidate about the best currently available option for FUE clinical practice.
Introduction & Objectives
Alopecia is one of the most common adverse events caused by numerous anticancer agents. Although alopecia in cancer patients is not a life-threatening event, it has a significantly negative psychological and social impact. Although it has been well documented in chemotherapy and radiotherapy, the incidence of alopecia in patients treated with targeted therapies or endocrine therapy is not anecdotal. Some cases were reported assessing the efficacy of Minoxidil in endocrine-therapy induced alopecia. However, the long term efficacy in this indication is unknown. In addition, the side effects and the application twice daily limit its use for a long term period. The aim of this study was to assess the efficacy and safety of hair transplantation in the treatment of endocrine-therapy induced alopecia.

Materials & Methods
Women with breast cancer, suffering from endocrine-therapy induced alopecia, have been grafted with “follicular unit long hair” technique. With this technique a strip of non-shaved hair is harvested from the donor area, segmented into follicular units under stereomicroscope and transplanted into the recipient area. The efficacy on global hair coverage was assessed by both investigator and patient themselves. In addition, hair density, thickness and growth rate were assessed with a digitalized phototrichogram on the donor area (FotoFinder™).

Results
Twelve patients, ranged from 42 to 72 years old, presented male pattern hair loss, emphasizing the hormonal role of endocrine therapy in this type of alopecia. Hair coverage assessed either by the investigator or by the patient was improved by 50 to 70%. The long term follow-up, up to 3 years, showed the lasting efficacy of hair transplantation. Neither transplantation failure nor side effect, except frontal oedema during the 3-4 days after surgery, has been reported.

Comment
Endocrine-therapy induced alopecia is not rare. Its clinical pattern is similar to androgenetic alopecia. Hair transplantation has demonstrated its efficacy for the long term treatment of alopecia induced by endocrine therapy. Since no shaving is needed with “follicular unit long hair” technique, this is particularly recommended in women. The advantages of hair transplantation are the long-lasting effect, the poor side effects and the absence of compliance issue.
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A COMPARATIVE STUDY BETWEEN TOTALLY PRESERVED GRAFT AND EPIDERMIS TRIMMED GRAFTS IN POST TRANSPLANT PROGRESSION

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Introduction
FUE is one of the most popular procedure in hair transplant surgery. More than 75 percent of surgeons from worldwide are trying to perform FUE through their career. In FUE, the debate of survival rate has been a topic of controversy over the past and various efforts have been made for better results beyond FUSS. The main concern of FUE is about the quality of graft.

For better graft the dumbell and the trumpet type punch were introduced by surgeons. Easy punching, extraction and minimal injury to graft are the goal of FUE punching. Next issue is about how to implant graft. Forcep delivery to premade slit and Choi implanter are used.

However, forcep method is not so useful due to characteristics of minimal perifollicular tissue in asian people and have shown various result according to surgical assistants’ technique. So, the usage of the implanter are increasingly used worldwide. In using implanter it is difficult to load grafts into implanter especially in case of chubby FUE graft.

Therefore sometimes graft preparation is needed for loading of graft. And preparation make various trauma to grafts essentially. According to types of trauma of grafts, there are differences in progression of transplanted like hair cycling abnormalities, unngrowing, and thinned hair.

Methods
In this study I investigated how to progress following implantation according to the condition of graft preparation. The difference in post-implant progression between completely preserved grafts including sebaceous gland and epidermis trimming for easy insertion into slit of the implanter were evaluated.

Results
As a result, there were differences between the two groups, but they were not significant.

Comment
Totally preserved graft showed minimal postoperative shedding of transplanted grafts. However, the survival rate is not different significantly.
**A TRICHOSCOPIC STUDY OF THE CHARACTERISTICS OF TRANSITIONAL ZONE A STEP TOWARDS CREATING NATURAL HAIRLINE**

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**Introduction**

Understanding about a natural hairline is one of the most important elements of a successful hair transplant. Simply using single hair grafts in irregular fashion while creating frontal hairline does not guarantee naturalness.

A study of the components of the hairlines would help hair restoration surgeons to get better equipped to create a natural hairline which meet high expectation of patients.

**Method**

Frontal hairlines of 30 male healthy volunteers aged 24-30 years were studied with regards to transition zone (TZ), defined zone (DZ), frontal tuft (FT), temporal points, lateral lump etc. Close observation of normal TZ was done with the help of a trichoscope.

Characteristics of TZ like sentinel hair, micro-irregularities, macro- irregularities were plotted on transparent sheets.

**Results**

Transition zone in all men consisted of multiple rows of a single hair of 0.5 to 1 cm of the hairline. Small intermittent clusters of hair in ill-defined triangles of various sizes formed micro-irregularity was seen between two micro-irregularities. The density of micro-irregularity decreased in fronto-temporal angles.

A few isolated (sentinel) hairs were found in front of the TZ. Frontal tuft was not present in all the volunteers. The calibre of a single hair in TZ and DZ were equal in diameter. However, the calibre of sentinel hair was thinner.

**Conclusion**

This study highlights the principles of hairline design & will help the surgeons create hairlines with a high degree of naturalness.
PERIFOLLICULAR REPIGMENTATION IN LUPUS HAIR TRANSPLANT: AN INITIAL SIGN FOR HAIR REGROWTH?

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Introduction

Chronic discoid lupus (CDL) is a frequent disease in primary cicatricial alopecias (PCA) that may lead to permanent hair loss. Hair transplant is one of the surgical options after disease stabilization is achieved.

Skin repigmentation is a well-known sign and the final goal in surgical management of vitiligo, but undivulged in hair transplant surgery.

Herein, we present two cases of CDL treated with hair transplant surgery using the follicular unit extraction (FUE), whom presented with perifollicular repigmentation before hair regrowth.

Cases Report

Nº1. A 64-year-old woman with a history of hypertension consulted for longstanding progressive alopecia with trichodynia and pruritus. Physical examination revealed, extensive cicatricial alopecia with atrophy and hypopigmentation. Loss of follicular openings, enlarged dilated vessels and keratotic plugs were seen under dermatoscopy. Biopsy showed follicular fusion, mild perifollicular fibrosis and mild perifollicular lymphocytic inflammatory infiltrate, compatible with active discoid lupus. We began treatment with Mycophenolate mofetil 1 g/day and intralesional corticosteroids. After 18 months halting of progression was achieved.

We performed a test transplant with 50 follicular units of 2-3 hairs, using the FUE technique with good regrowth after 6 months. Consecutively, she received multiple (250-300 follicular unit) hair transplants, with progressive repigmentation and subsequent hair regrowth.

Nº2. A 65-year-old woman with no history of comorbidities consulted for progressive alopecia with pruritus during the last 10 years. Physical examination showed central scalp cicatricial alopecia with atrophy and hypopigmentation. Loss of follicular openings, hemorrhagic crusts and keratotic plugs were seen under dermatoscopy. Biopsy highlighted loss of sebaceous glands, interstitial dermal mucin, perifollicular fibrosis and mild perifollicular lymphocytic inflammatory infiltrate, suggestive of active discoid lupus.

Treatment with Mycophenolate mofetil 1 g/day and intralesional corticosteroids every 8 weeks was initiated. After 15 months disease progression stopped. A test transplant of 100 follicular units of 2-3 hairs, using the FUE technique was made. After 3 months repigmentation began and after one year marked hair regrowth was noticed.

Conclusion

Skin repigmentation is a well-known sign and the final goal in surgical management of vitiligo, but undivulged in hair transplant surgery. Persistent hair repigmentation have been rarely described following hair transplant. CDL can usually present with skin hypopigmentation or depigmentation.

In our patients, perifollicular repigmentation preceded hair regrowth in every transplant event. Skin repigmentation is related to a healthy follicle and maybe can predict a good response in hair transplant surgery.
USEFUL PROTOCOL FOR SKIN PREPARATION PRIOR TO THE HAIR IMPLANTATION IN SCARRING ALOPECIA

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Introduction
Being the hair transplantation is an alternative therapy and can be considered as a definitive solution to treat scarring alopecia in selected cases, and since scarring injuries show diminution of vascularity and elasticity, it is important to prepare the tissue prior to the implantation to enhance the implanted grafts growth and survival.

Objective
The article tries to define an easy protocol using the combination of three therapeutic techniques with the aim of improving and revitalization of scarring alopecia tissue.

Method
Eighteen patients with non-active scarring alopecia were selected from an original group of 20 (two patients were excluded have shown active signs of scarring alopecia in the pathological anatomy analysis during the study). Three cycles of weekly sessions were carried out during 3 months as the following order:
1. Microneedling using Dermapen 2.5 mm depth  
2. Mesotherapy with Hyaluronic acid, polypeptides and vitamins complex  
3. Diathermy using selective capacitive monopolar system 1.8 Mhz/100W, cutaneous temperature achieved at dermis (55 - 60°C) using the reference scale of temperature in epidermis (38 - 42°C)  

We describe it as the DMD Protocol: Dermapen (Preparation) -> Mesotherapy (Infiltration) -> Diathermy (Activation)  
The scarring areas were divided into two marked parts; one of them received the click of the treatments mentioned previously. Dermis enhancing were measurements by weekly recorded dermatoscopy and monthly ecography.

Results
On the treated areas the elasticity was improved by the 43% and vascularization by 68 % compared to the non treated areas.

Conclusion
It is necessary to condition the cutaneous tissue before performing hair implantation in lesions with decreased vascularity and elasticity. Elasticity and capillarity are both the main two critical factors to treat in scarring lesion before performing graft implantation.
Consider steroids treatment for cases with active scarring alopecia.
Waiting for a period of at least 6 months without lesion activity before performing the transplantation.
Periodic dermatoscopic control with record of photographs to evaluate the clinical improvements.
In this study the selected number of sessions were 3 cycles, moreover, this depends on the clinical improvement of each case.
No side effects were observed, only one case of herpes zoster rash in a patient with previous episodes. 
The selected is not limited as other combination of treatments can be considered.
Such combination of treatments might be useful prior hair implantation in healthy skin, more studies are required.
This protocol was described with a small number of cases; however, more studies are required to define clinical and therapeutic evidences.
Introduction
In the interesting world of trichology, we come across a few cases which baffle us. Such cases open our minds to a whole new possibility. We have put together a cases series of such interesting cases which help us in broadening our horizons.

Case report
Case 1 - A 15 year old female presented with a single swelling over scalp since 5 years. It was a well defined skin coloured to bluish white swelling of size 0.5cm x 0.5cm. Clinical differentials were pilomatricoma, hidrocystoma and sebaceous cyst. The histopathology revealed a nodule in deep dermis consisting of monomorphic cells with central dark staining nuclei with multiple blood vessels. This clinched the unique diagnosis of Glomus tumour on a rare site-scalp.

Case 2 - A 28 year old female presented with asymptomatic raised lesions over the chest, abdomen since 6 months. Multiple, discrete, smooth, dome shaped flesh colored papules 1-5 mm in size were present. Differential diagnosis was steatocystoma multiplex, trichilemmal cysts or eruptive syringomas. The biopsy demonstrated a mid dermal cyst lined by squamous epithelium with cross sections of vellus hair. There was laminated keratinous material. This was suggestive of eruptive vellus hair cysts.

Case 3 & Case 4 - These 2 cases presented to us separately with complains of sparseness of hair on scalp and spiny papules with photophobia. There was no scarring. Systemic evaluation revealed borderline intelligence and growth retardation with squamous blepharitis in the second case. The biopsy showed pilosebaceous hypoplasia. The diagnosis of a rare syndrome- Ichthyosis Follicularis Alopecia Photophobia (IFAP) syndrome was made for these cases.

Conclusion
Intriguing Cases like these help us to think beyond the usual and histopathology aids the diagnosis of such cases.
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SEBACEOMA
SIMULATING MELANOCYTIC MALIGNANT CUTANEOUS NEOPLASIA

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Introduction
The correct identification of pigmented lesions on the scalp is often challenging. Despite the importance of clinical patterns and dermoscopy, an important adjuvant tool that is usually helpful, their interpretation sometimes is not clear cut. In this paper, we discuss a case of sebaceoma mimicking a malignant pigmented neoplasia, with conclusive histopathology.

Case report
An 80-year-old female patient, Fitzpatrick phototype II, with a history of endometrial cancer, developed a black, nodular and asymptomatic lesion with erythematous base and central crust on the scalp vertex. Dermoscopy showed a yellowish erythematous area, yellow globules, hematic crust, a red-milky area and polymorphic vessels, suggesting seborrheic keratosis, an adnexal tumor or traumatized melanocytic nevus. The presence of whitish veil, a bright white area, asymmetric follicular openings and rhomboidal structures did not allow exclusion of cutaneous melanoma. An excisional biopsy was performed and histopathological examination evidenced a circumscribed proliferation of large basaloid cell masses and sebaceous cells, with the diagnostic conclusion of sebaceoma.

Discussion
Sebaceoma has been called sebomatrixoma or sebaceous epithelioma, with the term epithelioma suggesting malignancy. Classified by Troy and Ackerman in 1984 as a benign neoplasm with sebaceous differentiation, it affects more often women, with predominance in the eighth decade of life. Clinically, it appears as a yellowish or orange, solitary or rarely multiple hemispheric exophytic tumor located in the seborrheic areas of the body, especially on the scalp. Dermoscopy of sebaceoma may present an amorphous yellowish-erythematous area with or without ulcerations, arboriform vessels centripetally branched. The amorphous yellowish-erythematous area may be an important finding suggesting the sebaceous nature of the lesion. Sebaceomas are constituted by cells masses located in the dermis, connected or not to the epidermis, with histological architecture that suggests benignity: rounded contours, greater vertical axis and symmetry, different from the sebaceous carcinomas, despite the possible presence of mitosis. They are composed of undifferentiated cells and cells with different degrees of sebaceous differentiation. The absence of peripheral palisade and clefts between the aggregates and the stroma distinguish them from basal cell carcinomas with sebaceous differentiation.

Conclusion
The diagnosis of pigmented nodular lesions of the scalp is challenging. Dermoscopy is an excellent tool for the definition of these cases, having well-established standards for the diagnosis of neoplasms, pigmented or not. However, it does not replace the histopathological study that was fundamental for the characterization of the sebaceous nature of this neoplasia.
Background
A scalp biopsy is useful to identify women with early FPHL who present with increased scalp hair shedding, but little or no reduction in hair volume. Scalp biopsy is also useful in identifying women with fibrosing alopecia in a pattern distribution that can mimic advanced FPHL. Sinclair et al. reported triple horizontal scalp biopsies better than single horizontal biopsy, the accurate diagnosis was achieved in 98% of versus 79% of women respectively.

Objective
To evaluate the reliability of a single horizontal sectioned scalp biopsy in diagnosis of FPHL versus triple scalp biopsies.

Methods
Patients with diffuse hair loss >6 months duration consenting for scalp biopsy were enrolled. Nineteen women with chronic diffuse hair loss had three 4-mm punch biopsies taken from the midscalp. All 3 biopsy specimens were sectioned horizontally. Findings were compared with 23 patients of diffuse hair loss who underwent single horizontal biopsy.

Results
Among the 23 patients with a single horizontal scalp biopsy, 7 were diagnosed as AGA/FPHL (T:V<4:1), 1 have CTE, 6 have indeterminate hair loss (T:V = 5:1, 6:1, 7:1) & in 9 patients biopsy was inconclusive (poor sectioned). Among 57 horizontally biopsy specimens were assessed from 19 patients, 15 were diagnosed to have FPHL, 2 have CTE & 2 having indeterminate hair loss. Among these women, 11 were assessed clinically having stage 1 & 2 hair loss (Sinclair grading), of these 9 were diagnosed to have FPHL & 2 having CTE.

Conclusion
An accurate diagnostic definition was achieved in 17/19 (89.47%) of women with triple biopsies versus 8/23 (34%) with single horizontal biopsy. Patients without increase hair parting could have FPHL or CTE.
Lichen simplex chronicus (LSC) is characterized by lichenification of the skin because of primary excessive scratching. LSC on the scalp is uncommon and usually, go undiagnosed or confused with trichotillomania, prurigo nodularis or psoriasis etc. Here, we show a useful tool to diagnose LSC from trichoscopic and histopathological findings.

**Case report**

A 23 years old man presented with localized paroxysmal severely itchy lesion over scalp since 3 years with no history of hair pulling or stress. On examination, there was a hyperpigmented plaque, approximately 1 x 1.5 cm in dimensions, with mild scaling noted at the occipital area. Hairs on the lesion were broken.

Dermatoscopic examination (Heine NC1® polarised light), revealed hair shafts with the distal split of the hair tips into two or three tiny hair endings, described as ‘broom hair fibers’. Also, there was present mild perifollicular scaling with hyperpigmentation.

On histopathological examination, at the level of the infundibulum and isthmus in horizontal sections, the outer root sheath formed jagged acanthotic projections, which resembled a ‘gear wheel’. The infundibular ostium showed hyperkeratosis with hair shafts split in two (the hamburger sign). The sebaceous glands were diminished in size and number.

The patient was given intralesional triamcinolone 40 mg/ml injection every 3 weeks along with sedative antihistaminics. After three months, we observed a significant improvement.

**Conclusion**

Broom hair fibres on dermoscopy and the hamburger sign and the gear wheel sign on histopathology is helpful in the diagnosis of LSC in the scalp.
Introduction
Epidermolysis bullosa (EB) is a clinically and genetically heterogeneous skin fragility disorder characterized by trauma-induced skin dissociation and the development of painful wounds. There are a few papers describing the alopecia in EB patients, these included, diffuse alopecia, scarring alopecia and lichen planus pilaris. The gradual onset of scarring alopecia due to traction in areas with traumatism due to rubbing and blistering in patients with Epidermolysis Bullosa (EB) is frequent.

Objective
The purpose of the study is to show the histological characteristics of alopecia in patients with EB.

Methods
An observational and invasive (skin biopsy) cross-sectional study was conducted with a sample of 25 patients with Recessive Dystrophic EB (RDEB). The study was approved by the ethics committee of the Universidad De Monterrey. The inclusion criteria: RDEB confirmation by a skin sample, routine histology, immunofluorescence of antigen, or electron microscopy and DNA analysis was available. Finally, 4 mm-wide punch biopsies were obtained in areas with alopecia and and from clinically unaffected. Each piece was subjected to routine paraffin embedding with hematoxylin-eosin sectioning and staining. Two certified dermopathologist analyzed and made the diagnoses of the 50 skin samples (two each patient).

Comment
The alopecia in female patients with RDEB is worst than males and has worse prognosis than in men regardless of age. Regardless the mutation in EB patients with the same genotype, the clinical expression is different. The severity of alopecia is not correlated with the type of mutation, sex, age or gender. In all this RDEB patients the collagen fibers in the reticular dermis have a horizontal orientation with the epidermis. The majority of the skin biopsies from the RDEB patients presented histological findings of cicatricial alopecia, and the presence of syringoma-like and dilatations of eccrine gland-like structures. The horsetail-style was commonly observed in female patients and looks like the traction is the mechanism as the main etiology as the fragility of the skin.

Conclusion
This data should allow us to give a better management of patients with alopecia with EB and provide useful tools for the pathological interpretation of hair.

References
Introduction
Vismodegib is a hedgehog pathway antagonist used to treat locally advanced and metastatic basal cell carcinoma (BCC). The most frequent adverse events include muscle spasm (66%), non-scarring diffuse alopecia (62%) and dysgeusia (55%). Herein we report an adverse event not reported previously to Vismodegib.

Case Report
An 85-year-old male with an inoperable multifocal BCC on the scalp attended our skin cancer unit. He had been treated surgically and with topical imiquimod, but BCC relapsed. Physical examination showed a 12x13cm partially pigmented patch with undefined borders in frontoparietal region. Dermoscopically arborizing vessels, and blue ovoid nests and globules were visualized. Oral Vismodegib 150mg daily was started. Progressively, he developed tolerable fatigue and mild muscle spasms and decrease in global hair growth, while he noticed moustache hair thickening and hardening.

Trichoscopy revealed the presence of hair shaft thickness heterogeneity, with a unique enlarged hair per follicle opening. On cheeks, these hair changes were not observed. Moreover, non-scarring diffuse moderate alopecia was seen on scalp. Body hair was not affected.

A skin biopsy from moustache showed terminal anagen enlarged channel and hair shaft, without accompanying inflammatory reaction. He achieved complete response of the BCC in the 22nd week of treatment and Vismodegib was stopped.

Comment
Acquired trichomegaly has been reported located on eyelashes associated with topical prostaglandin analogues. Other less common causes include EGFR inhibitors (erlotinib, cetuximab), tacrolimus, cyclosporine, zidovudine, topiramate and AIDS. Hedgehog pathway antagonists, such as Vismodegib, interfere with hair growth. It is known that they prevent anagen phase to start after hair shedding. This mechanism explains the common non-scarring alopecia. However, hair shaft enlargement cannot be explained. Interestingly, Richey et al. reported a patient who developed perioral erythematous, pruritic, papules with white spicules after 3 months of vismodegib treatment. Biopsy specimen showed abnormally large trichohyalin granules within inner root sheath epithelium, and the patient was diagnosed with trichodysplasia spinulosa. However, neither electronic microscopy nor polymerase chain reaction for poliomavirus were performed to prove the presence of trichodysplasia spinulosa.

Conclusion
The present case shows just enlarged hair shaft and openings, without any other signs or symptoms what supports that he developed an acquired trichomegaly limited to the perioral area probably induced by Vismodegib. Follow-up after drug withdrawal and electronic microscopy will shed some light on the underlying mechanism.

Introduction
MicroRNA, a small non-coding non-messenger RNA, is one of the major biological regulators which inhibits gene activity. Previous studies showed that microRNA (miR92) could regulate bio-functions of stem cells, and played important roles in modulating development of tissues and organs. Recently, one research unveil that miR92a is selectively expressed within the follicular epithelial cell compartments during early follicular morphogenesis by microarray and in situ hybridization.

Objective
To establish a model of hair follicle (HF) outer root sheath cell (ORSC) with high expression of MicroRNA92a and explore the effect of MicroRNA92a on Wnt/-catenin signaling pathway as well as the proliferation function of ORSC.

Material & Methods
Scalp samples from normal healthy people were obtained, and the outer root sheath cells of the hair follicle were isolated and cultured in primary culture. Using liposome transfection to obtain the outer root sheath cells which highly express MicroRNA92a. MTS method was used to study the proliferation function of outer root sheath cells, mRNAs were extracted from the cells and detected by reverse transcription polymerase chain reaction.

Results
Reverse transcription polymerase chain reaction showed that the expression of microRNA92a in transfected outer root sheath cells was significantly higher than the control (P<0.01). According to the MTS Results, the proliferation of miR92a-treated ORSCs was higher than control group (P<0.05). Reverse transcription polymerase chain reaction Results revealed that miR92a overexpression up-regulated mRNA expression of catenin (P<0.05).

Conclusion
MiR92a can promote the proliferation capacity of outer root sheath cell and regulate the Wnt/catenin pathway.
Background
The hair growth cycle includes three phases: a growth phase (anagen), regression phase (catagen), and quiescence phase (telogen). Androgenic alopecia is a major kind of hair loss, characterized by a shorter anagen phase and miniaturization of hair follicles. Current therapies for alopecia are thus mainly based on extending the anagen phase and enlarging the hair bulb. However, existing drug therapies have some limitations. Kartogenin is a heterocyclic compound able to promote the proliferation, migration, and differentiation of various cell types and induce cartilage-like tissue regeneration. However, the role of kartogenin in hair follicles, which undergo a growth cycle involving telogen, anagen, and catagen phases, remains unknown. We therefore investigated the effects of kartogenin on the regulation of hair growth and hair growth cycle transition.

Methods
The effects of kartogenin on the proliferation, cell cycle status, and migration of primary human outer root sheath cells were evaluated by A 3-(4,5-di-methylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay, flow cytometry, and Transwell® assays, respectively. We exposed human outer root sheath cells to kartogenin and determined changes in mRNA and protein levels of transforming growth factor-beta2/Smad signaling molecules by reverse transcription polymerase chain reaction, western blotting, and immunofluorescence. We also examined the effects of kartogenin on HF s in mice by histology following cutaneous injection.

Results
Kartogenin enhanced the proliferation and migration of human outer root sheath cells in a dose-dependent manner, and downregulated the mRNA and protein expressions of transforming growth factor-beta2/Smad signaling molecules in vitro. Injection of kartogenin delayed catagen in hair follicles in mice in vivo.

Comment
Kartogenin may modulate hair follicles growth and regulate the hair growth cycle via the TGF-beta2/Smad signaling pathway, providing a potential new approach for the treatment of hair loss.
Background
The management of female diffuse hair loss is often difficult because its pathophysiology remains elusive, thereby limiting treatment options that are supported by clear evidence. Considering that the prevalence of female diffuse hair loss increases in the fifties and that its period is consistent with menopause, we hypothesized and studied the relationship between female hormones and hair physiology.
In our previous study, we identified the possibility of estradiol affecting the hair cycle and some other properties in vitro; however, its direct effect on human hair remains to be ascertained.

Objective
To clarify the effect of female hormones on human hair physiology.

Methods
For female patients undergoing hormone replacement therapy (HRT), hair growth (i.e., appearance of vertex and hairline, phototrichogram, and analysis of plucked hair), blood tests (i.e., biochemical, hematological, hormonal, and hair-related factors), and a questionnaire were assessed at three points (before HRT initiation and at 3 and 6 months following treatment). This study was approved by the institutional review board of Lion Corporation and Haginaka Clinic.

Results
A total of 11 female patients were assessed (mean age, 51.4 ± 2.8 years; awareness of hair loss, feel = 2, feel somewhat = 3, and do not feel = 6). The effect of HRT was confirmed from blood test results and questionnaire evaluation. The objective evaluation of appearance revealed improvement in the hair loss score at the hairline after 6 months (1.24 points) compared with that before HRT initiation (1.91 points) (in four grades, P < 0.01, Wilcoxon test). The hair plucking test revealed increasing extraction force of plucking after 6 months (63.6 gF) compared with that before HRT initiation (49.7 gF; P < 0.05, paired t-test).

Conclusion
We determined that female hormones affect the appearance and the plucking strength of human hair. These novel findings may contribute to the identification of the mechanism of the onset of female hair loss and development of therapeutic methods.
Background
Sildenafil, a phosphodiesterase 5 (PDE5) inhibitor, increases the intracellular level of cyclic guanosine monophosphate (cGMP) to cause vasodilation. Stimulating the skin blood flow of the human scalp promotes microcirculation in the surrounding hair follicles and can eventually lead to the promotion of hair growth. However, the effect of sildenafil on human hair follicles (hHFs) is unknown.

Objective
The purpose of this study was to determine a novel role of sildenafil on hair growth.

Methods
We investigated the expression of PDE5 in human dermal papilla cells (hDPCs) and hHFs. The effects of sildenafil on hDPC proliferation were evaluated using BrdU assays. The mRNA expression of growth factors and extracellular signal-regulated kinase (ERK) phosphorylation was investigated by using real-time PCR and western blotting, respectively. Additionally, anagen induction and perifollicular vessel formation were evaluated in vivo mouse model.

Results
We confirmed high expression of PDE5 in hDPCs and hHFs. Sildenafil not only enhances the proliferation of hDPCs but also up-regulates the mRNA expression of vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF), which are responsible for hair growth. Furthermore, sildenafil time-dependently up-regulated the levels of phosphorylated ERK. Sildenafil accelerates anagen induction by stimulating perifollicular vessel formation after topical application in mice. Also, increase in perifollicular vessel size and the number of MECA32-positive vessels was observed in the sildenafil-treated group.

Conclusion
Our Results demonstrate that sildenafil significantly stimulates hair growth both in vitro and in vivo. It enhances proliferation of hDPCs and accelerates the anagen hair cycle by promoting perifollicular vessel formation. Thus, sildenafil may function as an additional therapeutic agent for alopecia.
Introduction

Dihydrotestosterone (DHT), a steroid hormone, is synthesized by specific cells of androgen-dependent tissue including prostrate, skin and hair follicles. DHT play an important role in the progression of androgen-dependent diseases such as prostate cancer, benign prostatic hyperplasia and hair loss. Hair loss, also known as baldness or alopecia, is a distressing disorder, and the most frequent hair loss is androgenetic alopecia.

Androgenetic alopecia is characterized by thinning of hair on the head, and this process accompanies with the death of cells within the hair follicles. DHT induces androgenic alopecia by targeting androgen receptor in dermal papilla cells, but the mechanism of action of DHT on keratinocytes is unclear.

Methods

Here, we describe the involvement of DHT-mediated Smad2/3 upregulation on keratinocytes death.

Results

We found that DHT decreased the proliferation of immortalized human keratinocytes (HaCaT). Treatment of HaCaT with DHT resulted in cell cycle arrest, which was accompanied by the decreases of cyclin D1, E2F transcription factor-1 (E2F-1), and phospho-retinoblastoma protein (pRB) levels, whereas the p21 level increased.

We could also observe the apoptotic characteristics such as increase of the cleaved caspase-3, cleaved poly (ADP-ribose) polymerase (PARP), annexin V-positive cells, and the production of apoptotic bodies. To elucidate the action mechanism of DHT on the cell cycle arrest and apoptosis induction, we investigated the activation of canonical transforming growth factor beta (TGF-β) signaling in HaCaT cells. DHT increased level of Smad2/3 protein, which was followed by nuclear translocation of Samd2/3, proteins of TGF-β signaling.

Conclusion

These finding suggest an essential role of TGF-β/Smad signaling in DHT-mediated keratinocyte death.

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Introduction
Rapid market expansion related to the hair loss disorders demands for biologically relevant, reliable and well-defined human cell based three-dimensional (3D) in vitro model. Furthermore, hair follicle (HF) morphogenesis requires large number of physiologically active human dermal papilla (HDP) cell based 3D spheroids. Many research works of HDP spheroids have been reported including hanging drop method, and culturing on poly (ethylene-co-vinyl alcohol) plates. However, size and physiological property of generated HDP spheroids were not consistent and amount of the spheroids was not enough to apply in vitro systems.

Material & Methods
We developed new culture plates possible to generate large number of HDP 3D spheroids with consistent in cell population and size of the spheroid. Furthermore, this plate allowed to generate spheroids with predetermined alignment and density on the surface. This plate was prepared with the particle array film fabrication technology, which was internationally patented and fully commercialized in the display industry recently. For this study, the plates were fabricated with 700 nm silica particles layer on cyclic olefin polymer films which were optically transparent and fluorescence free substrate. The surface of the plate was divided to cell adhesive regions and passivated regions to induce co-cultured HDP and human outer root sheath (HORS) cells aggregation only on pre-designed area. In this study, 96-well plates were used with hexagonally arranged 400 diameter cell adhesive regions with 200 space between patterns while rest of surface was passivated.

Results
From one 96-well plate, it was possible to produce ca. 9,700 HDP-HORS spheroids of 185 ± 15 diameter, which meant a little more than 100 spheroids on each well of the plate. By changing the size and density of the pattern, we could generate spheroids in the range of 100-300 diameter.

Discussion
If one T175 plate is employed, about 56,000 spheroids can be generated, which is more than enough for a transplantation. Generated HDP-HORS spheroids kept their stability on the plate more than a week while maintaining their physiological activity and spherical structure. Immunofluorescence analysis indicated that HDP were surrounded by HORS. Although HORS were located entire of outer region of the spheroids, they were consistently located with higher density at certain area of the spheroid.

Conclusion
This large scale production of size specific HDP-HORS spheroids may be useful as in vitro HDP organoid models for drug development of hair loss disorders and serve as a platform technology for HF regeneration.
Introduction
The human hair follicle is a complex micro-organ, which switches between growth, degeneration and rest phase. These cycles are controlled by complex crosstalk between epithelial, mesenchymal and ectodermal cells. Involving several pathways (e.g. Wnt, BMP, Shh), these interactions contribute to the homeostasis of the hair cycle and pigmentation.

Multiple factors can cause disruption of this balance (e.g. genetic, environmental, hormonal or immunological factors) and can lead to progressive baldness or hair greying.

In vitro 2D-culture cannot properly reflect these in vivo mechanisms and crosstalk between all these cells. Indeed, 2D-culture of one of the key structures of hair, Dermal Papilla cells, cause a loss of their trichogenic profile. To mimic and study hair follicles, it is necessary to build a 3D-model, combine the key elements of hair follicles and restore the epithelial-mesenchymal interaction.

Material & Methods
We already developed a 3D-hair model based on three different hair cell types derived from primary cells: Outer Root Sheath keratinocytes, melanocytes and dermal papilla. The hair keratinocytes are responsible for the hair shaft production; melanocytes produce pigmentation while dermal papilla cells among other things control proliferation and final differentiation of these both cell types. We now develop an identical autologous model based on induced Pluripotent Stem Cell-derived model to respond to the need of a suitable model for high-throughput screening with high specificity and reproducibility.

Results
We have successfully optimized the differentiation protocols for these three cell types from the same donor and validated specific marker expression. The iPSC-derived keratinocytes expressed specific markers as cytokeratins 14 and 19 but also CD200, ITGA6 and TP63. We validate melanogenesis efficiency in our iPSC-derived melanocytes by qPCR (MITF, OCA2, TYR, TYRP1, DCT), IF (Melan-A, TYRP1, Sox10, PMEL17) but also by the melanin production. Concerning the iPSC-derived dermal papilla cells, we confirmed expression of versican and alkaline phosphatase after spheroid formation.

Conclusion
The next step will be the iPSC-derived microfollicle formation by association of this three cell types. The evaluation of hair cytokeratin expression, melanin transfer to keratinocytes and restoration of the signalling pathways should validate our in vitro model.
Background
Despite advances in the development of in vitro tissue models such as reconstructed human skin, the questions in hair research, which can be addressed with these models, are limited. Indeed, the most of the existing bioengineered human skin equivalent available at present are simplistic and devoid of a functional dermis that in vivo has the fundamental role to provide permissive and instructive morphogenetic signals. In this perspective we established a tissue engineering approach in which fibroblasts are guided in producing and assembling their own ECM, resulting at the end of the process in the formation of thick, endogenous and functional human dermis model (Endo-HDE). Unlike exogenous human skin equivalent (Exo-HDE), Endo-HDE represents an intricate complex of cells and cell-synthesized matrix, which resembles the structure and the physiology of its in vivo counterpart.

Comment
We assessed the presence of some fundamental components of the dermal ECM, demonstrating that Endo-HDE resembles the morphological and ultrastructural organization of the native dermis presenting its major components, such as elastin, hyaluronic acid, versican, fibronectin, laminin and collagen assembled and organized in the typical interwoven network. In addition, we found a spot signal of versican in the ECM of Endo-HSE while observed only an intracellular and pericellular signal in fibroblasts of the Exo-HSE, demonstrating the inability of dermal cells to assemble this instructive signal in an exogenous collagen matrix. As proof of the physiological and morphogenetic relevance of such environment we demonstrate that exogenous human hair elongation occurred for 17 days in Endo-HDE compared to Exo-HDE. Just after two days of culture few microns of external shaft are visible, and a consistent elongation persisted for 17 days in the Endo-HDE. Histology showed that the exogenous hair was ECM surrounded and dermal papilla cells of the hair bulbs were well visible in immune-staining for versican signal. The inner and outer sheaths made of keratinocytes layers were preserved during the experiments. Since versican has a fundamental role as inductive factor for the hair follicle morphogenesis we strongly believe that its presence and correct organization in our Endo-HDE can be correlated with the growth ability of the exogenous hair shaft.

This result encourages further investigations on the role of tissue environment in in vitro hair follicle growth and regeneration.
Introduction
Decorin is a prototypical member of the small leucine-rich proteoglycan (SLRP) family, which is involved in multifaceted biological processes. Our previous research found that decorin expression was highly enhanced in mouse dorsal hair follicles (HFs) during the anagen phase and the local injection of rhDecorin into the hypodermis of depilated C57BL/6 mice prolonged hair anagen. However, the exact role of decorin in hair follicular cycling has not been elucidated.

In this study, to further clarify the effects of decorin in the postnatal follicular cycling, K14Cre-Decorin transgenic mice were used to investigate the effects of decorin overexpression in hair epithelium.

Comment
Decorin overexpression significantly arrested hair follicles in catagen during the first postnatal catagen-telogen transition, as demonstrated by the assessment of the following parameters: (i) hair shaft length, (ii) follicular bulbar diameter, (iii) hair follicle cycling score and (iv) follicular phase percentage. Moreover, decorin overexpression upregulated the expression levels of β-catenin and downregulated the TGF-β2 expression than that were observed in wild-type mice by imaging and histological analyses. Our whole genome sequencing analysis of decorin over-expressed dorsal skin revealed that multiple kinds of keratins involved in the follicular changes, which involved in the terminal differentiation of inner root sheath, outer root sheath and cortex. KEGG analysis of our whole genome sequencing revealed PPAR signaling and MAPK signaling involved in decorin-induced follicular morphogenesis.

Conclusion
This study reveals the significant role of decorin in postnatal hair morphogenesis-cycling transition and provides new insight into the molecular control mechanisms governing postnatal hair follicular cycle change.
Introduction
Trichoscopy allows various hair shaft structure abnormalities to be evaluated and distinguished. Hair shaft fractures are observed in a range of hair disorders most commonly in Alopecia Areata (AA) and Trichotillomania (TTM).
Despite the fact that AA and TTM have distinctive macroscopic clinical features, there are cases, especially in children and adolescent where clinical picture could be interpreted wrongly. In our practice we met cases of TTM previously misdiagnosed and treated as AA. Careful examination and trichoscopic observation in these cases could contribute for right diagnosis. We aimed to find trichoscopic differences in the pictures of AA and TTM.

Material & Method
We observed two patient groups with AA and TTM for a period from March 2016 to January 2019. In the first group were included 12 patients with AA from 6 to 11 years of age. In the second group with TTM we followed 10 patients from 9 to 14 years. Patients of the both groups had similar macroscopic pattern of hair loss. We used trichoscopic camera ARAMO SG diagnosis system and software Trichoscience Pro with medical image storage and comparison capability for trichoscopy of the children from both groups.

Results
In a group of patient with AA we observed the following trichoscopic characteristics of the scalp hair: Trichoclasis (a transverse fracture across the hair shaft), Exclamation marks (refers to short hairs that are thin and hypopigmented at the proximal end and thicker and darker at the distal end), Tapered hairs (thin at the proximal end present a long exclamation mark).
In a group of patients with TTM we saw the following tricosopic changes: Broken hairs with different length, Tulip hairs (present as a light-colored hair shafts with dark distal ends), Exclamation mark hairs, Re-growing pigmented hairs. Due to extraction of the hairs, in infundibular areas blood was observed.

Conclusion
As a result of our observations, we came to the conclusion that in AA patients the broken hairs are at the same level, unlike broken hairs in patients with TTM that are broken down at different levels above the scalp. Presence of Exclamation mark hairs commonly believed to be pathognomonic for AA, in children with TTM may lead to misdiagnosis. Re-growing hairs in TTM are always pigmented in contrast to AA. We interpreted tapered hairs observed in AA patients as a sign of decreasing of the disease activity.
**Introduction & Objectives**

Hypotrichosis of the scalp is a rare condition that affects hair growth. It may occur as an isolated event or as part of a syndrome. The aim of the study was to describe the association of hypotrichosis with extracutaneous manifestations in a 6-year-old boy.

**Materials & Methods**

We report a case of a 6-year-old boy referred to the dermatology clinic at Hospital Universitário de Santa Catarina with hypotrichosis, strabism, brachyonychia, autism and tall stature. The patient underwent a clinical and laboratory examination, radiography of the hands, and brain CT scan. Hair pull test, trichogram, scalp biopsy and electron microscopy were performed in order to investigate the cause of hypotrichosis.

**Results**

On physical examination, his hair was light blond, with fine texture, and sparse, but it adequately covered the scalp.

He had sparse eyelashes and eyebrows. He presented with strabism and freckles on face. Teeth were normal. He had brachyonychia in both middle finger nails and flat feet.

Laboratory examination and brain CT scan revealed no abnormality. The wrists and hands showed delayed bone age, however he had tall stature for his age. The patient hair was pulled out easily and painlessly by the root, and was positive for telogen and anagen hairs. Hairs were not fragile.

Trichogram revealed predominance of anagen hairs, some anagen hairs showed distortion of the hair bulb as well as ruffling of the cuticle and absence of the external root sheat. Scalp biopsy was non-diagnostic.

Scanning electron microscopy showed that a little proportion of the hair shafts had an abnormal shape with grooves, ridges and twisting and other shaft disorders.

**Comment**

A wide range of conditions can present hypotrichosis. Making a diagnosis for a genetic or rare disease can often be challenging.

In this case several differential diagnoses had been suspected as Alopecia Areata, Loose Anagen Hair syndrome, Short Anagen Hair syndrome and Clouston’s syndrome.

None of them fulfilled the required criteria.

An integrated approach that involve the dermatologist, clinical geneticist is crucial for diagnostic definition.
Introduction & Objectives
The Uncombable Hair Syndrome is a genodermatosis that compromises only the hair. This abnormality is noticed in the child, around 3 years of age, when the hair becomes rebellious (with frizz) and resistant to all forms of alignment with brushing, always remaining with beaded appearance.

The objective of this work is to report the case of a girl with this diagnosis, to present the clinical images obtained, as well as the images of the alterations by optical and electronic microscopy, and to review the literature.

Case report
Female, 5 years old, white, phototype 3, referred for medical consultation due to the complaint of armed hair. Her mother referred unruly hair that was difficult to comb and, even with the use of hair conditioners and moisturizers, never are aligned and have a “broom” appearance since the age of two.

Patient had normal neuropsychomotor development and no associated comorbidities. Her mother also reported that she had this alteration in her hair as a child, and her condition improved when she was an adult. Hair samples were collected and the evaluation was performed by optical and electronic microscopy, confirming the clinical suspicion of Uncombable Hair Syndrome.

Discussion
The Uncombable Hair Syndrome, also known by Spun-Glass Hair and pili trianguli et canaliculi is an autosomal dominant genodermatosis restricted to the hair.

This abnormality is noticed in the child around 3 year-old, when the hair becomes rebellious (with frizz) and resistant to all forms of alignment. These hairs are abundant and bulky, dry and armed, with rough texture and have normal growth. The pathognomonic characteristic is that 50% of the hairs have a triangular or kidney-like shape in the shaft cross section. These shafts have a longitudinal groove along almost their entire length. There is no specific treatment to reverse this hair alteration and, evolutionarily, these tend to improve spontaneously after puberty.

Conclusion
Hair shaft disorders, as described in this case, can cause problems with the child’s self-esteem and parents’ concern in relation to the possibility of other organs involvement. The knowledge of the clinical, tricoscopic and/or microscopic aspects of this disease are fundamental to diagnosis and also assists in the orientation regarding its benignity and prognosis.
CLINICAL CASE OF TRIHOTILLOMANIA FLOW IN THE PUBERTY PATIENT

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Case report

Twelve years old female Patient of normostenic physique, a resident of Kiev, applied to the clinic. She complained about local thinning of hair covering a large part of temporal and parietal zone, rounded, oval-shaped, merging words of the patient not disturbing subjectively. Locally reduced sensitivity. Prior to the visit to the clinic, were not treated only once to a dermatologist. Treatment took place diagnosed with alopecia areata (L 63.2). The patient was examined: the laboratory and instrumental examinations.

The Results were within reference values. Bacteriological seeding on pathogenic flora and fungi tests are negative. From the words of the mother of the patient, hair falling out, a year ago. Hair on the pillow, in the bathroom, on clothes is not observed.

Comment

Psycho-emotional status burdened: frequent mood swings, by nature timid, introverted, vulnerable. Trichotillomania (TTM)-chronically leaking disease, flexible as a result of persistent state, in consequence of which the patient cannot resist the pull and pull out their own hair on head, body. In health professional literature first described case of TTM in 1989 g. F. A. Hallopeau, is observed at neurotic States, schizophrenia, organic brain diseases. Among both sexes with TTM prevails female gender with 10 years to 16 years. In adulthood TTM occurs in 2-3 times more often than males.

Very important is the fact the innervation of a dense network of efferent and afferent sensory, autonomic nerve fibers of the skin and hair follicles (appendages of the skin) in the pathogenesis of self-fulfilling liquidity dermatosis, format, removing mental stress through self-harm self-harm and its derivatives.

Visual: oval and rounded pockets with jagged edges merging among themselves in the form of “flames”, peeling, crust. In the middle of the hearth visually, clearly defines the difference between hair length, hair frayed on the periphery of the zone no.

When inspecting the trihology on camera “Aramo under the x 200 and x 60 increased: on the structure of hair pigment is present, there are no signs dermatoskopy. Alopecia signs:” yellow, white dots”, exclamation points, splitting, trichorrexis. Hair bulbs without features.

Based on the clinical picture of the patient’s complaints, anamnestic data, special inspection trihology, trihology diagnosis equipment: Trichotillomania (TTM).

The patient has not denied pulling out hair. The girl’s mother said that daughter loves touch hair especially when immersed in myself, while watching tv or during a strong tensions, concentration.

In parallel with the dermatological treatment is directed to a therapist.

In the course of treatment and active surveillance, photo control, dynamics within 9 months has changed for the better.
Introduction & Objectives

Hair shaft defects are common and can result in growing disturbances, fragility and hair loss. These alterations may be congenital, hereditary or acquired (by mechanical or chemical damage) and can be systemic or restricted to the hair. Numerous structural abnormalities of the hair shaft were identified, some can be seen without lens and others only by using trichoscope, optical microscope and or electron microscope.

Hairs with abnormal presentation, growing disturbances and/or fragility, are markers of many diseases with many gravity degrees, with neurological and sistemic envolvement. Anomalies in the hair may be present on over 300 genetic conditions and identify them by trichoscopy or optical microscopy can help on the diagnosis. This study intend to determine hair shaft disorders diagnosed in children attended in a Pediatric Dermatology Service, of an Federal Hospital in Brazil, in the last 22 years, and also make a review of these disorders.

Materials & Methods

Cross-sectional, observational, retrospective and descriptive study, composed by 88 hair samples of patients attended in a Pediatric Dermatology Service, between the years 1996 and 2018. All the samples were collected from patients who, due to their alterations in the clinical examination, like hair color, resistance, growth and texture, required the evaluation of the hair shaft as a diagnostic aid method. From 88 samples collected in 22 years, 45 were excluded due to the structural normality on optical microscopy and 43 were selected, due to presenting any morphological hair shaft alterations.

Results

From 43 samples, 33 presented hair shaft disorders (many samples with more than one alteration): 10 trichorrhexis nodosa, 3 monilethrix, 4 pili trianguli et canaliculi (Uncombable Hair Syndrome), 3 pili torti (Menkes Disease), 2 pseudo-monilethrix, 2 trichorrhexis invaginata (Netherton Syndrome), 2 woolly hair (Wooly Hair Nevus), 2 loose anagen, 2 pili annulati, 2 trichoptilosis and 1 trichonodosis. Alterations out of hair shafts were also found: 3 white piedra, 2 nits, 3 pigmentary alterations (gray hair) and 2 hair casts.

Conclusion

Identifying alterations in hair shafts, found in several diseases, can help in it’s diagnosis. It is a marker for both mild and aggressive disorders, with localized or systemic involvement. The adequate training in the visualization of the hairs, by trichoscopy or optical microscopy, are non-invasive, fast and low cost examination. The early and continuous monitoring of the patients with changes in hair growth or resistance is important, by collection of hair samples at the time of initial suspicion and serial. The evaluation of the hair shafts allows diagnosis, the necessary counseling for parents and treatment options.
INHIBITORS OF PROSTAGLANDIN D2 SYNTHASE (PTGDS) ACTIVITY AS A SOLUTION FOR ANTI-HAIR LOSS

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Introduction

Prostaglandin D2 synthase (PTGDS) catalyzes the conversion of prostaglandin H2 (PGH2) to prostaglandin D2 (PGD2). PTGDS and PGD2 have been studied as markers for hair loss. In androgenetic alopecia (AGA), PTGDS was elevated in the bald scalp areas compared to haired scalp areas. In addition, PGD2 inhibits hair growth through PGD2 receptor G protein (heterotrimeric guanine nucleotide) – coupled receptor 44 (GPR44) (Garza et al., 2012).

Method

Here we studied another way to prevent hair loss caused by PGD2. We tested enzyme activity of PTGDS in cell-free system to find inhibitors which target PTGDS exactly. First of all, it was conducted to set the protocol for testing PTGDS enzyme activity such as concentration of reactants, reaction time and positive control. PGH2, substrate of the reaction, was incubated with inhibitors before the PTGDS enzyme reaction occurred. For positive control, AT-56 which is known as an inhibitor of lipocalin-type PTGDS was used. Enzyme activity of PTGDS was determined by the amount of PGD2 production using PGD2 ELISA.

Inhibitor candidates were selected from the result of in silico modeling study. According to the reference study, specific herbal constituents could bind to the active site of PTGDS and act as inhibitors (Fong et al., 2015).

We tested the PTGDS inhibitory activity of the constituents in the cell-free system and several candidate materials inhibited PGD2 production to less than 50 %.

Comment

These inhibitors are expected to prevent PGD2-induced hair loss by suppressing the enzyme activity of PTGDS. Moreover, this cell-free system for testing PTGDS activity would be effective to screening PGD2 inhibitors for the purpose of anti-hair loss. For more accurate efficacy of anti-hair loss, it is necessary to verify the effects of these inhibitors in hair follicles in further studies.
**PROSTAGLANDINS AND HAIR FOLLICLE REGULATION**

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**THE INFLUENCE OF PROSTAGLANDIN D2 IN ANDROGENETIC ALOPECIA**

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**Introduction & Objectives**

Androgenetic alopecia (AGA) affects genetically susceptible men and women with onset at puberty and progressive prevalence. Around 80% of men will be affected at age 70.

AGA is characterized by miniaturization of the hair follicles, decrease of hair density, diminution of anagen phase and hyperplasia of the sebaceous glands. Recently prostaglandins have revealed great interest of hair researchers from all over the world. Recent studies demonstrate that prostaglandins regulate hair growth.

Prostaglandin D2 (PGD2) inhibits hair growth in humans, in contrast, prostaglandin E2 (PGE2) and prostaglandin F2a (PGF2a) enhance hair growth. Some Chinese herbs as ricinoleic acid, acteoside, amentoflavone, quercetin-3-Orutinoside and hinokiflavone were predicted to be PGD2 indirect inhibitors (Prostaglandin D2 synthase). The objective of this study is review the international scientific literature about the influence of prostaglandin D2 in androgenetic alopecia.

**Methods**

**Search strategy.** The PubMed database was searched for articles published. Search terms included (“prostaglandin d2”[MeSH Terms] OR (“prostaglandin”[All Fields] AND “d2”[All Fields]) AND (“hair”[MeSH Terms] OR “hair”[All Fields]) OR “prostaglandin d2”[All Fields]) AND (“alopecia”[MeSH Terms] OR “alopecia”[All Fields]).

References from articles were searched for additional articles.

A manual search was also conducted based on citations in the published literature.

**Results**

Search Results were 20 articles, which 3 were excluded not corresponding to subject. 1 article was included from references.

**Conclusion**

A perspective is emerging for a key role of prostaglandins in hair control function. Scientific evidence suggests PGD2 have an inhibitory effect on hair growth in AGA and suggest PGD2-GPR44 pathway as a possible treatment. A balance between PGE2 and PGD2 controls hair growth and should focus on enhancing PGE2 and inhibiting PGD2 signaling. The inhibition of PGD2 production or GPR44 signaling will promote hair follicle regeneration. PGD2 levels inversely correlate with WIHN. Inhibiting PGD2 may prevent AGA advance.

DP1 could be the main PGD2 receptor involved in the process or repair and wound healing.

No genetic support for a contribution of prostaglandins to the etiology of AGA.

PGD2 directly stimulates the expression of androgen target genes, AKT and its downstream substrates are involved in mediating these effects. Although ROS and oxidative stress suggests negatively regulate hair growth, treatment with exogenous antioxidants or compounds that enhance cells antioxidants functions, may be useful in AGA treatments.

PGD2 directly stimulates the expression of androgen target genes, AKT and downstream substrates are related in mediate these effects. The activity of AR could be regulated not only with DHT, but also with signaling by PGD2 in hDPCs.
Background
Alopecia areata (AA) is thought to be associated with psychiatric disorders. However, a causal relationship between these diseases and the effect of disease severity and duration are not well known.

Objective
To assess the risk of psychiatric disorders in AA patients and investigate the risk in relation to disease severity and duration.

Method
A retrospective cohort study of 7,706 AA patients and 30,824 1:4 matched control subjects was performed from 2004 to 2013, using the National Health Insurance Service data. We defined severe AA patients as those having alopecia totalis, alopecia universalis, or ophiasis, and long-standing AA patients as with over a year of disease duration.

Results
The risk for overall psychiatric disorder in the AA group was significantly higher when compared with the control group (adjusted HR 1.38; 95% CI 1.21-1.56). There was a significant difference in cumulative incidence of psychiatric disorders between the two groups (log-rank P<0.001). In the case of patients with more severe AA or over a year of disease duration, the adjusted HR for psychiatric disorders was higher when compared with overall AA patients.

Conclusion
AA is a risk factor for psychiatric disorders, and disease severity and duration are also important factors in a causal relationship between these diseases.
**TRICHOTILLOMANIA: CLINICAL VARIABILITY**

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**Introduction & Objectives**

There are some evidences of trichotillomania (TTM) clinical heterogeneity. There are several subtypes of TTM indicating it’s complex clinical structure and mainly dichotomous differentiation (focused vs automatic, early vs late pulling). Objective is to analyse the differences in TTM clinical presentations and to distinguish TTM subtypes based on trichological and psychopathological features.

**Materials & Methods**

The study sample comprise 18 dermatological outpatients (15 female; mean age 26.3 years) diagnosed with TTM. The diagnosis was verified by trichologist, and all patients underwent psychiatric assessment.

**Results**

Two clinical pattern of scalp alopecia were identified by the trichologist: diffuse hypotrichosis with decrease of hair density without precise borders (diffuse pattern, n=10) and localized hypotrichosis with legible borders (focal pattern, n=8). Three subtypes of TTM were distinguished by the psychiatrist: with predominate compulsive (n=10; 55.6%), impulsive (n=6; 33.3%) or dissociative (n=2; 11.1%) hair pulling.

The statistically significant relation between the clinical pattern presentation and TTM subtype was found (p<0.05). The diffuse pattern predominated in impulsive TTM (n=5 out of 6), and the localized pattern was more common in compulsive TTM (n=7 out of 10) with no consistent pattern for dissociative TTM subtype.

**Comment**

In impulsive TTM, sensory phenomena, triggering hair pulling, had a penetrating pattern and a projection on hair follicles. Patients described skin sensations metaphorically “like needles dig in skin”. Chaotic pulling of hair (predominating diffuse pattern) was accompanied with generalized vital drive, often compared to hunger or thirst. “Irresistible impulse” was associated with irritation/dysphoric affect. Relief occurred after pulling and was accompanied with a feeling of satisfaction and pleasure.

In compulsive TTM, sensory phenomena, triggering hair pulling, had a protruding pattern and a projection on hair shafts. Patients tactilely perceived some hair as “different from the others”, “wrong’ (cranked, rough, scratchy), which undergo selective compulsive pulling often at the same scalp sigths. Attempts to resist the urge were associated with anxiety increase that ceased right after the pulling.

In dissociative TTM, there were no sensory phenomena, triggering hair pulling (automatic pulling). Patients pulled their hair imperceptibly for themselves: being busy with something (reading, watching TV etc.) in detached mild dissociative state (“meditativeness”) or subwaking. Pathological act happened quasi “automatically” with alienation of actions and local dissociative amnesia of a pulling act.

**Comment**

TTM subtypes seem to be distinguished not just dichotomously (focused vs automatic) but more dimensions, including trichological, psychological, emotional and behavior factors, could be established.
Hair follicle-associated-pluripotent (HAP) stem cells are located in the bulge area of the hair follicle, express the neural stem-cell marker nestin. HAP stem cells have been shown to differentiate to neurons, glial cells, keratinocytes, smooth muscle cells, melanocytes and beaters cardiac muscle cells.

Implanted HAP stem cells promoted the recovery of peripheral nerve and spinal cord injuries and have the potential for heart regeneration as well. GFP-expressing HAP stem-cell colonies, captured on polyvinylidene fluoride membranes (PFM), were implanted in the severed thoracic spinal cord of nude mice. HAP stem cells differentiated into neurons and glial cells by 7 weeks after implantation and rejoined the thoracic spinal cord. The rejoined spinal cord was also shown by H&E staining.

Quantitative motor function analysis by Basso Mouse Scale for Locomotion (BMS) score showed a significant difference between the implanted mice and non-implanted mice with a severed spinal cord. HAP stem cells are readily accessible from everyone, do not form tumors, and can be cryopreserved without loss of differentiation potential.

Demonstrations HAP stem cells have greater potential than iPS or ES cells for regenerative medicine.
EXOSOME FOR HAIR REGENERATION: FROM BENCH TO BEDSIDE

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Introduction
Exosome, a relatively recently founded 30 to 150nm sized extracellular vesicle, is secreted from most cells and acts as a communicator between them.

Objective
We would like to explore whether exosomes from mesenchymal stem cells (MSCs) could be used as a novel therapeutic option for hair loss.

Materials & Methods
Several in vitro experiments have tried to evaluate the function of exosome on hair follicle cells. Then, we conducted a pilot study to prove the efficacy of exosome for the treatment of male and female pattern hair loss.

Results
With laboratory experiments, we found exosome can stimulate the proliferation of hair follicle, accelerate the telogen-anagen transition, and protect hair follicle cells against ROS and androgen.

Twenty patients (41.9 ± 13.4 years old) were enrolled for in vivo study. Hair density increased from 105.4 to 122.7 counts/cm² (P<0.001), while mean hair thickness increased from 57.5 to 64.0 mm (P<0.001), after 12 weeks of treatment. None of the patients reported serious adverse reactions.

Conclusion
Exosomes can be an effective and safe alternative therapeutic strategy for hair loss.
**Introduction**

Adipose and adipose derived regenerative cells (ADRCs) play an increasing role in the understanding of androgenetic alopecia. The objective of this clinical study (STYLE) is to evaluate the safety and feasibility of autologous fat grafts enriched with ADRCs in the treatment of early alopecia.

**Materials & Methods**

A total of 71 subjects were randomized and treated accordingly: 16 with Puregraft fat + 1.0 x 10⁶ ADRCs/cm² scalp; 22 with Puregraft fat + 0.5 x 10⁶ ADRC/cm² scalp; 24 with Puregraft fat alone; and 9 saline control.

Treatments were delivered in the adipose layers of the scalp via injections: the first a subcutaneous injection of either 0.1ml/cm² scalp of adipose or saline followed by a second intradermal injection of ADRCs or saline in each square centimeter of scalp. In each subject, 40 sq. cm of scalp was treated and hair count and width were obtained at baseline, 6-weeks, and 24 weeks.

**Results**

There were zero unanticipated adverse events associated with STYLE. At 24 weeks, there were no statistical differences between any of the treatment groups with respect to terminal or vellus hair counts or width when evaluating all subjects. When evaluating males with early stage hair loss (Norwood-Hamilton 3), a statistically significant increase in terminal hair count (p<0.05) was observed in patients receiving Puregraft Fat + Low Dose ADRCs compared to the Control Population at 24 weeks (mITT; n=29).

This population also showed a trended increase in terminal hair width (p=0.065) compared to controls.

In the Norwood-Hamilton 3 Per Protocol populations (n=22), terminal hair counts remained statistically significant (p<0.05) in the Puregraft Fat + Low Dose ADRCs versus controls and the terminal hair width also remained statistically trended (p=0.056) versus controls.

**Conclusion**

Fat + ADRCs is safe and tolerable. In early male hair loss, this therapy demonstrated a statistically significant increase in terminal hair counts relative to the matching control population at 24 weeks and represents a promising new approach for the treatment of early androgenetic alopecia.
The present disclosure relates to a bioengineering process to derive hair follicles in vitro from the in vitro disposition and differentiation of pluripotent stem cells and dermal papilla stem cells. The present disclosure also relates to bioengineering of hair follicles and hair follicle containing sheets with asymmetric disposition of hair shafts.

The present disclosure also relates to a bioengineering process to derive hair follicle containing sheets in vitro from a biodegradable supportive grid and said in vitro derived hair follicles.

The present disclosure also relates to the controlled asymmetry of the hair shaft on said hair follicle containing sheets.

The present disclosure also relates to the field of cosmetic materials and method for reconstructing hair follicle containing materials in vitro.

The present application describes a method for deriving hair follicles and sheets containing hair follicles using autogenous sources, and can be implemented in good manufacturing procedures pipelines and xeno free conditions.

Furthermore, using as source biodegradable grids containing and carrying said hair follicles, facilitates the downstream surgical process by augmenting the hair follicle count used and handled per surgical step.

What is Claimed Is:
1. A bioengineered hair follicle comprising: one or more bioengineered dermal papillae stem cell derived hair follicles, and containing hair bulge, hair shaft, and protruding hair filament, also a cell composed cortex containing stem cell derived synthetic interfollicular epidermis, and intertwining extracellular matrix.

2. The dermal papillae stem cell of claim 1, wherein the cell is preferably a dermal papillae stem cell or a dermal papillae stem cell line, and said cell is preferably genetically modified for unlimited expansion, or immortalized, or engineered to overexpress extracellular matrix proteins or attachment proteins, or combinations of the above.
Introduction
The therapeutic use of autologous stem cells has great advantages such as minimizing the need for systemic immunosuppression while reducing ethical and regulatory issues.

In an earlier study we revealed that plucked hair follicles as well as follicles from skin biopsies expressed CK19 and Bcl-2 in cells from the upper to the lower third of the follicle. Cells positive for Bcl-2 and CK 19, but Ki-67 and Bax negative, is a strong indication that they represent stem cells in the hair follicle. These characteristics may be of great use in the development of an autologous cell-based therapy for a broad range of (degenerative) diseases. Rationally, the use of plucked hair follicles will increase the practical application of follicular stem cells.

Materials & Methods
Plucked hairs were derived from the scalps of healthy volunteers. Stem cells were allowed to migrate out of the plucked hairs and examined immunocytoplogically. Viability of the cells was tested after cryopreservation and subsequent transplantation circumstances, i.e., syringe needle flow stress. After expansion and cryopreservation, neural and glial differentiation capacity was established.

Results
The yield of stem cells is, on average, 3x 10^4 cells/follicle 1 month after the start of the culture. The protein profile was similar to Neural Crest Stem cells (NCSC) Cell viability after cryopreservation and syringe-mediated disaggregation (30 Gauge, 0.5 L/min.) was more than 80%. Neural differentiation is achieved within 3 weeks after neural induction. Glial differentiation yielded positive cells after 2 weeks of induction.

Discussion
Stem cells derived from human plucked hairs can easily be cultivated and possess a NCSC immunological profile. These cells can be expanded efficiently and subsequently kept frozen until needed. After cryopreservation the cells are viable and displayed neural and glial differentiation potential. Therefore, these stem cells allow practical use towards (neural) regenerative therapies and cosmetic procedures like hair restoration.
Introduction

Hair follicle stem cells play important roles in hair growth and inducing anagen phase. It is known that the activated hair follicle stem cells are differentiated to hair progenitor cells which present some specific markers such as CD200 and ITGA6 (Garza LA et al, 2011).

However, it has been less studied about the materials activating hair follicle stem cells for new hair growth because of the limitation of hair follicle stem cell isolation and culture technique. In this study, we obtained human hair follicle stem cells and optimized the culture and stem cell activating conditions.

In addition, we evaluated the effect of AP-flavone-01 on re-activating hair follicle stem cells in DHT-treated alopecia-mimic condition by stimulating wnt/β-catenin signaling in hair follicle organs.

Methods

First, we characterized the commercially obtained human hair follicle stem cells by measuring the expression of hair follicle stem markers. Then we optimized the culture and activating conditions of hair follicle stem cells by treating dermal papilla conditioned media.

Also, we analyzed the specific markers, such as CD200 and ITGA6, which represent the hair follicle stem cell activation and differentiation by using fluorescently activated cell sorting (FACS) method. DHT treated-dermal papilla conditioned media was prepared for alopecia-mimic condition as a negative control. Then we evaluated the stem cell activating effect of AP-flavone-01 which is a well-known component found in diverse plants, for example, celery, grapefruits and bean leaf. Firstly the effect of AP-flavone-01 on wnt/β-catenin signaling was determined, then it was applied to the prepared hair follicle stem cell activating experiment model.

Results

We found that the commercially obtained human hair follicle stem cells had the proper characters, and they could be used by activation with the dermal papilla conditioned media.

And we could measure the hair follicle stem cell activation by analyzing the expression of CD200 and ITGA6 using FACS successfully. AP-flavone-01 showed significant effects on stimulating the wnt/β-catenin signaling and enhanced the expressions of the wnt target genes such as LEF-1, AXIN2 and CCND1 in human hair follicle organs. Moreover, AP-flavone-01 recovered the hair follicle stem cell activation which was down-regulated by DHT-treated dermal papilla conditioned media.

Conclusion

This study showed that the newly discovered AP-flavone-01 had significant effects on activation and differentiation of hair follicle stem cells by stimulating the wnt/β-catenin signaling. We suggest that the AP-flavone-01 can be used as a new agent for improving the hair growth by recovering the hair follicle stem cell activities to the normal state.

Further studies about the clinical evaluation of the effect of hair follicle stem cell activation are expected to prove the value of AP-flavone-01 for hair loss treatment more obviously.
INTRODUCTION

Many hair loss disorders chiefly result from a disturbance of physiological hair follicle cycling, indicated by an increased telogen/anagen ratio. While the molecular signals that induce anagen (hair growth) in “quiescent” telogen hair follicles (HFs) are well-described in mice, they are unknown in the human HF. Identifying these signals provides crucial information for developing anagen-promoting or -suppressing agents for hair growth disorders.

METHODS

Recognising the central role of Wnt signalling in hair biology, we sought to qualitatively and quantitatively delineate the differential expression of key agonists, antagonists and target genes of this essential pathway during the telogen-to-anagen transformation of human scalp HFs by in situ hybridisation as a first step towards charting the “molecular morphology” of human HF cycling. First, we analysed the differential expression of Wnt/β-catenin signalling in the secondary hair germ (SHG) and dermal papilla (DP).

RESULTS

As indicated by up-regulated mRNA expression of the Wnt target genes, AXIN2 and LEF1, β-catenin activity is elevated in both the SHG and DP upon anagen induction. This is associated and likely reflects an increase in Wnt ligand activity as the gene required for Wnt ligand secretion, WLS, is elevated in both the SHG and DP. In addition, of the 7 Wnt ligands we probed for, we detected a significant increase in specific Wnt ligands (WNT3, WNT4 and WNT10B) within the SHG, whereas WNT1 and WNT2 were negative and WNT10A demonstrated no differential expression upon anagen induction in the SHG. Also, this increase in Wnt ligand expression is accompanied by a reduction in the secreted Wnt ligand inhibitor SFRP1 in the SHG and DP. Conversely in the bulge epithelial hair follicle stem cells (eHFSCs), we could detect β-catenin activity (AXIN2) in telogen, early-anagen and anagen VI HFs; this is also complemented by the expression of WLS and SFRP1 suggesting that eHFSCs can self-regulate Wnt activity. While Wnt1 and Wnt4 are responsible for this activity in mice during telogen eHFSCs, we could not detect these ligands in the human telogen bulge. However, upon anagen induction eHFSCs induce the expression of WNT4 and WNT10A, suggesting that these ligands are necessary for eHFSC activation.

CONCLUSION

Our study provides the first evidence that key changes in Wnt/β-catenin activity understood to drive murine anagen induction also apply to human scalp HFs, but also shows important differences in Wnt ligand expression (e.g., WNT1, WNT4 and WNT10A). This provides an essential basis for the development of experimentally testable working hypotheses on the functional role of individual Wnt signalling players in human hair cycle control. Moreover, therapeutically manipulating these key Wnt signalling molecules and activity during human anagen induction invites more targeted interventions to counter excessive hair loss by promoting anagen induction, and undesired hair growth (hirsutism) by arresting hair follicles in telogen.
INTRODUCTION

Taxane regimens are a leading cause of severe and potentially permanent chemotherapy induced-alopecia (CIA), a major psychosocial burden for cancer patients. Therefore, greater efforts are required to elucidate the as yet ill-understood pathobiology of taxane-CIA and develop effective treatments. However, a clinically relevant human model of taxane-CIA has been unavailable.

METHODS

Here, we report such a model, using microdissected organ-cultured human scalp hair follicles (HFs), and novel findings on how paclitaxel, a prototypic microtubule stabilizing taxane frequently used in cancer chemotherapy, damages the human HF epithelium.

RESULTS

We show that paclitaxel induces a massive accumulation of mitotic aberrations within cycling anagen HF matrix keratinocytes (MKs), as evidenced by profoundly increased phospho-histone H3 (pH3) immunoreactivity and micronuclei formation. Furthermore, paclitaxel treatment increased matrix cleaved caspase 3 (CC3) expression and induced transcriptional arrest specifically within MKs undergoing aberrant mitosis. Interestingly, we also provide the first evidence that paclitaxel can cause major damage to Krt15+ bulge stem cells (SCs) and the HF lower outer root sheath, as evidenced by increased CC3+ expression in these compartments. Subsequently, we explored whether the controlled induction of cell cycle arrest can protect against cell cycle-dependent paclitaxel cytotoxicity in the HF.

COMMENT

In summary, using a new, clinically relevant human model of taxane-CIA, we establish key characteristics of taxane HF toxicology and provide a first proof-of-principle that CDK4/6 inhibitor-based therapeutic strategies have the potential to protect human anagen MKs and eSCs/progenitors from chemotherapy.
The high prevalence of skin pigmentation disorders affects 1 out of 3 people worldwide and it frequently imposes serious psychological burden. However, current treatment strategies have varying efficacy among patients, thus magnifying the importance of developing novel treatment approaches. Hair follicle pigmentation is a complex process known to encompass the interplay between various populations of cells in the hair follicle and these mechanisms are essential in both the process of skin pigmentation and hair cycle. Overall, there is still a lack of knowledge in the mechanisms involved in skin pigmentation and a better understanding of the regulation of skin pigmentation is essential.

Bone Morphogenetic Protein (BMP) signaling is a major regulator of the hair follicle stem cell niche and here we are describing its role in regulating melanogenesis, pigment transfer and melanocyte migration. Using human skin biopsies, we have identified the presence of active BMP signaling in the mature and stem cell melanocyte compartments of the hair follicle and epidermis. Interestingly, data from human keratinocyte and melanocyte co-cultures shows that BMP signaling can regulate melanogenesis and melanin transfer. Moreover, we have adapted our in vitro co-cultures to study melanocyte migration at a functional level and our novel data indicates that BMP signaling significantly modulates migration of melanocytes and keratinocytes.

Finally, and to probe deeper, novel genetic tools are developed to construct an in-vivo model for the study by targeting the non-active amelanotic melanocytes in the stem cell niche compartment. Together with the reporter gene, melanocytes were specifically isolated out with live cell sorting for further downstream analysis. Similar to the in-vitro part, our in-vivo data has demonstrated that BMP signaling is involved in the regulation of melanocyte migration in-vivo. In addition, our recent in-vivo data suggests that BMP signaling is involved in regulating skin pigmentation too.

With the aid of this study, it will bring us closer to the goal of developing novel therapy strategies against skin pigmentation disorders like vitiligo by inducing a faster migration and more pigmentation produced by melanocytes.
Introduction
The number of women looking for treatment for Female Pattern Hair Loss has been rising in the last decade, as well as therapeutic options and Methods to evaluate its treatment efficacy. Twenty-one century: increase in the number of patients with hair loss (Telogen Effluvium / Androgenetic Alopecia): increased incidence x increased search x new medical treatments? According to the Brazilian Dermatology of Society: hair loss is the 6th most common reason for visiting a dermatologist. In this context, the development of simple and objective Methods to quantitatively evaluate the effectiveness of hair treatment is necessary. Usual Methods, such as: Trichoscopy / Phototrichoscopy, Trichogram, Trichometer: hair weight and Phototrichogram (Trichoscan®) cover just a small area.

Aim
To validate a quantitative method to evaluate the effectiveness of hair loss treatments. Our suggested method is: Q, simple, painless and non-invasive method, with greater adherence to clinical protocols. Standardized Images are obtained before and after treatments and treated by a specific imaging analysis and editing a software (Image Pro Premier), that allows evaluation of the effectiveness of hair loss/regrowth treatments. We use exposure correction in order to enhance contrast. Analysis: automatic calculation of the balding area (pixel²), from the contrast between clear (bald area) and dark (hairy area), so we can estimate the area (pixel²) of the scalp that does not have hair coverage.

Methods
The standardized photos, obtained before and after the treatments, were analyzed using the software Image Pro Premier®. The analysis performed by the software consists of the automatic calculation of the area of, in square pixels, from the contrast between light (hair loss region) and dark (region with normal amount of hair), making it possible to estimate the scalp area that does not present hair coverage and thus, quantify the effectiveness of the treatments, comparing photographs obtained before and after the treatments.

Results
The method is effective for assessing the area affected by hair loss in patients with initial grade (Savin I-4 scale) and in patients with more advanced hair loss.

Comment
The proposed method allows the rapid, simple and inexpensive evaluation of the effectiveness of different types of treatments for Telogen Effluvium and Androgenetic Alopecia.
Introduction & Objectives
Several trichoscopic patterns related to alopecias have already been well established in the literature. However, there are few data on non-disease findings that mimic typical signs of alopecias. We aim to didactically illustrate artifacts and pitfalls in trichoscopy, comparing them to clinically relevant trichoscopic signs, demonstrating how to distinguish them and also how to avoid the presence of artifacts during scalp examination.

Materials & Methods
We retrieved trichoscopy images from our patients’ database. As artifacts, we included dirty dots, trimmed hair shafts, residues of hair dyes and cosmetic hair fibers in order to compare them with true black, red, and yellow dots as well as broken and miniaturized hairs. The images are compared to illustrate their similarities and differences.

Results
Dirty dots are environmental residues physiologically found in children and the elderly and can simulate clinically relevant black dots. Trimmed shafts from patients with short hair recently cut can resemble broken hairs. Residues of hair dyes may be confused with clinically relevant red or yellow dots. Cosmetic hair fibers may be similar short regrowing or miniaturized hairs.

Comment
Artifacts in trichoscopy are more common than imagined and represent possible pitfalls during scalp examination that may lead to incorrect diagnoses and perhaps unnecessary treatments.

We illustrate four of these findings, comparing them with real clinical relevant trichoscopic signs. It is important that dermatologists are aware of the existence of these artifacts and are able to recognize possible trichoscopic pitfalls, minimizing diagnostic misinterpretations.

Furthermore, a well-done anamnesis and correct orientations to the patient are the key to avoiding the appearance of these artifacts during trichoscopic examination.
Introduction & Objective
Using highly magnified images of the scalp to compare the visibility of trichoscopic signs with different dermoscopic imaging devices.

Materials & Methods
Dermoscopic images were compared from 2 different imaging systems from patients with various hair disorders including, lichen planopilaris, frontal fibrosing alopecia, fibrosing alopecia in a pattern distribution, alopecia areata, seborrheic dermatitis and monilethrix.

Images were obtained from the same scalp area using Fotofinder Leviacam and Fotofinder Medicam 800 HD.

Results
1. The pictures taken by Leviacam showed brighter images than the pictures taken by the Medicam.
2. Subtle peripilar casts were better detected by Leviacam.
3. Dilated arborizing blood vessels were easily detectable in the images from the Leviacam device.
4. Grey-white hair shafts are more visible when using the Leviacam.
5. The Medicam enhanced zoom makes certain features more visible than in the Leviacam images.

Comment
As imaging and computer technology have advanced, dermoscopy has become an essential tool in the dermatologist’s arsenal for increasing diagnostic accuracy. With certain dermoscopic devices, some trichoscopic signs may be more visible. The Leviacam produces brighter images with certain features such as peripilar casts and arborizing blood vessels more noticeable compared to the images from the Medicam 800HD, which can aid in the diagnosis of scarring alopecias such as lichen planopilaris and frontal fibrosing alopecia.

However, the Medicam 800HD has increased zoom levels and may enable it to produce images with microscopic signs that would be invisible with the Leviacam.

It is important for a clinician to know the strengths and limitations of their dermoscopic devices in order to ensure diagnoses are not missed.
Introduction & Objectives
The use of superficial non-ablative fractional Erbium: Glass lasers 1550nm (NAFL) for treatment of alopecia has becoming a more popular intervention in hair clinics.

We present a case of imprints from laser-grid as a pitfall from trichoscopy, which to our knowledge none trichoscopy patterns related to NAFL has been describe since now.

Case report
A 37-year-old male patient had submitted to superficial non-ablative fractional Erbium: Glass lasers 1550nm for treatment of androgenetic alopecia. We observe between 5 until 10 days after the procedure, we have on scalp dermoscopy imprints from laser-grid.

They appear as homogeneous brown-black structures, in a regular intervals on the scalp, unrelated to follicular openings. The others dermoscopy patterns were discrete and transient erythema and hyperpigmentation.

Conclusion
We know that trichoscopic are very important for the differential diagnosis of alopecias. We show that these imprints from laser-grid are a pitfall for black dots and dirty dots. Black dots are broken hairs, related to follicular openings and they are observed in active alopecia areata, after quimioterapy and tinea capitis, for example. They indicate active diseases and cannot be removed after shampooing. Dirty dots are irregular structures unrelated to follicular openings and can be removed after shampooing. Usually we see in patients skin type III or more who tend to develop more pigmented burn scars and are at an increased risk of developing post-inflammatory hyperpigmentation after resurfacing treatments. To reduce the risk of post-inflammatory hyperpigmentation and other treatment adverse events the literature recommend using lower fluences, reduced treatment densities, fewer treatment passes and strict sun avoidance pre- and post-procedure.
Introduction & Objectives
The term trichoscopy has been used in trichology since 2006, when Rudnicka L. and co-workers began to use the standard dermatoscopy to determine the diseases of the scalp. Currently, it is one of the leading methods in differential diagnosis of alopecia, including early androgenetic alopecia. The Objectives of the study was to evaluate the frequency of main trichoscopic features in androgenetic alopecia (AGA), the presence of these features depending on sex, grade of AGA and its activity.

Materials & Methods
The study included 270 patients with AGA: 67 men and 203 women, 18-59 years old. The trichoscopic features were observed in 4 fields of view with magnification 60 and in 1 field of view with magnification 20 in the frontoparietal area, with and without immersion fluid. The images were taken at a 20- and 60-fold magnification (Dermlite DL3, Heine Delta 20 Plus and FotoFinder medicam 1000) at standard points - in the central part of the frontal area in women, in the parietal area in men. The following signs were assessed: anisotrichosis (A)-hair heterogeneity in diameter, % vellus hairs (VH - less 30 μm thick), yellow dots (YD), single follicular units (SFU), peripilar sign (PS).

Results
The following trichoscopic signs were observed:
1. Anisotrichosis >20% was presented in 94.4% of cases (20X magnification), and was comparable in men and women (95.5% and 94.1%). Anisotrichosis was not observed in severe cases of male AGA (grade V, Norwood-Hamilton classification) due to the transformation of all terminal hairs into VH. Anisotrichosis was not typical in advanced female AGA (scale Ludwig, III grade), due to the loss of VH in androgen-dependent follicles as a result of fibrosis.
2. The VH number was increased both in men and women, in 83.6% and 70.9% respectively (60x magnification in 4 fields of view). In the early stages of AGA, the percentage of VH was 20%; in intermediate stages of AGA VH was 35% in women and 51% in men. VH decreased to 14% in advanced female AGA (Ludwig III); in advanced stages of male AGA (grade V, Norwood-Hamilton) VH was more than 60%.
3. Four and more YD were presented in 4 fields of view in 61.1% of female AGA, more often in 1-II Ludwig grades (60x magnification). In male AGA this sign was less specific and appeared in 41.8% cases.
4. SFU more than 30% were detected in 4 view fields in 25.4% cases of male AGA and in 40.4% of female AGA, more often in advanced AGA (60X magnification).
5. Brown PS occurred in 34.8% (magnification 20X), mostly in women with complaints of trichodynia, severe hair loss and a rapid progression of thinning. It is possible that the presence of brown PS indicates the AGA process activity.

Comment
Trichoscopy is a noninvasive method of examining hair and scalp. It allows differential diagnosis of hair loss in most cases, it is effective in early progressive AGA in men and women.
Introduction
Hair loss disorders afflict people of all subtypes, are often difficult to treat, and extremely disruptive to the psychological well being of patients. Unfortunately, clinicians are often limited in optimally addressing alopecia by imperfect diagnostic and monitoring methodologies, currently hinged on the gold standard of scalp biopsies and hair follicle histology. Researchers are currently investigating the potential and practicality of non-invasive imaging in order to enhance general alopecia care.

Objective
The aim of this study was to evaluate the ability of non-invasive in-vivo imaging to aid clinicians in diagnosing, characterizing, and monitoring various types of alopecia.

Methods
Optical coherence tomography (OCT) was used to capture quantitative scalp measurements including hair density and epidermal thickness. These measurements were recorded for several separate 5x7mm scalp locations commonly effected by alopecia on 20 subject scalps before and after respective treatment and five control subjects.

Results
Preliminary Results show significant variation in measurements of control subjects based on ethnicity and hair type. No significant differences exist between alopecia subjects and controls in unaffected scalp locations. Epidermal thickness is significantly larger in scarring alopecia subjects compared to non-scarring and control subjects. Scarring patients exhibit higher proportions of doublets and triplets than non-scarring control subjects.

Conclusion
Findings of this study show that OCT has significant potential for clinical relevance in addressing alopecia. The process of image analysis elucidates the importance of developing systematic Methods of characterizing the sub-epidermal qualities of hair. This imaging modality potentiates the tracking of follicular units over an alopecia course that is unattainable by and safer than scalp biopsy.
Introduction
Lipedematous alopecia (LA) is a rare, non-scarring acquired alopecia, that characterizes by an increasing in scalp thickness and that typically appears in women around the fourth decade. Its origin is still unknown. No trichoscopic features have been described in the literature.

Case report
We present a 33-year old man who presented with many years of progressive hair loss. He had a mild mental retardation associated with epilepsy and he was treated with fluvoxamine and aripiprazole. He denied any history of trauma or surgery in the scalp. Physical examination revealed a diffusely thickened, boggy scalp, mainly localized in the occipital area, with no clinical signs of inflammation. Androgenetic alopecia was associated with miniaturized hairs in the interparietal area. Trichoscopy revealed areas with big yellow dots and five or more hairs emerging from a single follicle orifice similar to tufted follicles, measuring less than 2 cm long. Hair pull test was negative. Scalp biopsy showed normal epidermis and dermis, with reduced anagen tufted hair follicles and a mild chronic perifollicular inflammation. No signs of fibrosis, dermal edema, mucin deposition, panniculitis or alterations in collagen bundles or elastic fibers were seen. Magnetic resonance imaging and ultrasounds of the scalp, showed an important difference in the thickness between the vertex and the occipital area, with the latter measuring more than 25 mm. After explaining to the patient the nature of his disease, he declined any treatments.

Comment
LA and lipedematous scalp, are two rare conditions of unknown etiology that are thought to correspond to the same spectrum of a single scalp disorder. Magnetic resonance imaging was one of the best imaging diagnostic Methods and, as far as we know, ultrasounds have only been used once by Martin et al. for assessing LA. Regular mean thickness of scalp is considered to be 5 to 8 mm. Both imaging tools may reveal a 9 to 19 increase in scalp thickness in LA. Cutis verticis gyrate, that is the main differential diagnosis, could be ruled out with this imaging techniques because this entity is characterized for an increased thickness of the scalp dermis with furrows or convolutions with a cerebriform resemblance. No trichoscopic findings have been reported in the literature.

We found bundles of tufted hairs made up of more than 5 hairs arising from single preserved hair follicles. Tufted hairs are the manifestation of a fibrosis-induced gathering of adjacent follicular structures, as well as a follicular retention of telogen phase hairs over multiple cycles. In this case, we think that the pressure on the hair follicles from thickening of the subcutaneous fat layer, might induce the fusion of the follicular structures.

Conclusion
We present a case of LA with distinct trichoscopic findings and we would like to remark the usefulness of ultrasounds in an outpatient department as a handy imaging tool in assessing and following-up of LA.
Introduction

Discoid lupus erythematosus (DLE) is a cause of cicatricular alopecia on the scalp. Trichoscopy allows us to recognize characteristic features of DLE and to make differential diagnosis between different types of alopecia. It also provides a more precise follow-up, and it may be used to identify an adequate biopsy site.

Objective

The main objective of our study is to describe systematically the trichoscopic findings in a group of patients with DLE on the scalp.

Methods

We designed an observational cross-sectional study. Patients from the Trichology Unit of the Dermatology Department of the Ramón y Cajal University Hospital with DLE alopecia on the scalp were included from June 2018 to February 2019. Diagnosis was confirmed by skin biopsy and clinical correlation. Epidemiological (age, gender, personal history, previous autoimmune diseases), clinical (duration of the disease, clinical presentation of previous and current lesions) and therapeutical data (previous and current therapies and treatment response) were collected. Clinical and trichoscopic images were taken. Dry trichoscopy was performed using FotoFinder medicam 1000®. Immersion fluid was used to evaluate vascular findings.

Three independent trichologists made the analysis of the trichoscopic images. All analyses were performed using SPSS 23.0 statistical software.

Thirty-three lesions from 17 patients with DLE were included in the study. A total of 16 patients were women (94.1%). The mean age was 52.8 years (range 29-90), and none of the patients associated systemic lupus erythematosus. Duration of the disease was 7.9 years (range 0.2-16 years), the mean duration of the lesions was 6.8 years (range 0.2-15 years). The treatments received were topical corticoids 10 (45.4%), intralesional triamcinolone 7 (31.8%) and oral hydroxychloroquine 5 (22.7%). Two patients (12.5%) received three treatment schemes simultaneously (topical, intralesional and systemic) and 8 received only one treatment scheme (47%).

Results

The most frequent trichoscopic findings were: loss of follicular openings 31 (96.9%), white scarring areas 30 (93.8%), perifollicular scaling 30 (93.8%), white dots 29 (90.6%), milky-red areas 23 (71.8%), scattered brown discoloration 19 (59.4%), well-defined thin arborizing vessels 14 (43.7%), chrysalides 13 (40.6%), follicular keratotic plugs 12 (37.5%) and rosettes 10 (31.2%).

Association between trichoscopic features and clinical data was analysed. Patients with personal history of autoimmune comorbidities had more red dots (P=0.003) and incontinentia pigmenti features (scattered brown discoloration, P=0.021; blue-gray dots, P=0.015). No statistically significant associations were found with the rest of the variables.

Comment

Patches of alopecia due to DLE may show chrysalides and rosettes. They are trichoscopic features not previously described in this condition. Red dots and pigmented incontinence patterns are important findings related to autoimmune comorbidities.
Introduction & Objectives
Hair has the characteristic that the moisture content inside changes due to external humidity change similar to wool or other fibers. The change in the internal moisture content of these hair affects the physical characteristics of the hair itself, it is known to appear differently depending on the damage or condition of the hair.

Materials & Methods
In this study, we examined whether damage caused by aging or various cosmetic procedures affects the change of hair moisture due to relative humidity in human hair, and measured the physical characteristics of hair related to the change of hair moisture.

We also tested the efficacy of hair care cosmetics that can improve surface lipids and protein structure changes expected to cause these hair moisture changes.

Results
The moisture content inside the hair increased or decreased due to the relative humidity change, and the amount and speed of water changed according to the degree of aging or damage of the hair. Depending on the moisture content of the hair, the physical characteristics such as the tensile strength and diameter of the hair decreased or increased, and the change of moisture and physical characteristics in the damaged hair such as dyeing were faster and greater.

In addition, it has been confirmed that the characteristics of moisture absorption change are improved when hair-improving cosmetics that improve lipid supply or protein structure are used for damaged hair.

Comment
These absorption of hair moisture can be greatly changed by aging of hair and various damage, and it is expected that it will be caused by changes in lipid composition and protein binding structure on the surface of hair because it is changed by the use of hair care products.

Therefore, the evaluation method of change of moisture absorption characteristics of hair can be used to evaluate the damage of hair and the efficacy of hair care products.
EFFICIENCY OF HAIR DETECTION IN HAIR TO HAIR MATCHED TRICHOGRAPHY

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Introduction
Precise evaluation of changes in hair count are crucial for monitoring of hair condition progression and hair treatment effects. One may use automated software tools, manually corrected analysis or hair-to-hair matching technique to statistically process trichoscopy images of the test spots.

Methods
In this study the following options for before/after hair count evaluation have been compared:
• Automatic phototrichogram evaluation with TrichoScan,
• Manually corrected analysis of single phototrichogram and trichoscopy images,
• Hair-to-hair matched analysis of phototrichogram and trichoscopy images.

All these examinations have been performed on exactly the same test spots in few patients allowing for direct comparison of the Results.

To determine the Results reproducibility the examinations have been subsequently repeated on the same spot where no change of hair condition occurred.
To determine sensitivity of different measurement techniques to hair count change the controlled hair extraction was performed.

Results
The Results indicate that the techniques under study provide quite different levels of precision implying also different applicability areas.

Conclusion
Hair detection in hair to hair matched trichoscopy is precise and may have several applications in trichology.
Introduction
Oxidative stress and scalp inflammation cause telogen effluvium, affect the health of the follicle and could trigger androgenetic alopecia. Scalp inflammation is commonly associated with scalp psoriasis or seborrheic dermatitis. Patients are often symptomatic and complain of itching and burning. Trichoscopy has been used to diagnose and grade severity of inflammatory changes in these conditions. In scalp psoriasis trichoscopy shows red dots and twisted/glomerular capillary loops. In seborrheic dermatitis it shows an increased number of arborizing vessels.

A severity scale was developed to assess inflammation as a % of scalp showing glomerular, arborizing vessels or scales under 20x magnification (Grade 5:100%; Grade 4:75%; Grade 3:50%; Grade 2: 25%; Grade 1: between 10% and 25%, Grade 0: - 10%).

Objective
The aim of this study was to evaluate the efficacy of poly N-Acetyl Glucosamine (pGlcNAc) in the treatment of scalp inflammation due to mild/moderate scalp psoriasis or seborrheic dermatitis. pGlcNAc is a natural polymer derived from microalgae.

Methods
The evaluation involved a 14-day randomized placebo-controlled study in 20 Subjects (11 females / 9 males, ages 18-60) presenting with mild to moderate scalp psoriasis or seborrheic dermatitis complaining of itching and burning. Subjects with scores in the itching/burning scale (1 to 10) and dermoscopic scalp inflammation score of 2 were given the opportunity to participate in the study. Each subject was randomly assigned to either the Active Ingredient (pGlcNAc) or Placebo (USP Water) and instructed to apply on the affected scalp daily. Clinical evaluation at Day 0-7 and 14 included: 1) Dermoscopy (twisted/glomerular or arborizing vessels involving > 50% of field at 20X magnification, 5 level scale), 2) itching/burning sensation 1 to 10 subjective scale, 3) degree of erythema/scaling and 4) tolerability and patient`s satisfaction.

Results
At day 14, Subjects in the Active Ingredient had a statistically significant reduction in clinical and dermoscopic signs of inflammation (twisted capillary 58%, scales 64%, erythema 69%) compared to Placebo Subjects (twisted capillary 0%, scales 0%, erythema -10%). Significant reductions in itching and burning were also reported (Active Ingredient: itching 70%, burning 78%. Placebo: itching 3%, burning 10%). pGlcNAc was very well tolerated and none of the subjects complained of side effects.

Comment
Our preliminary data show that topical poly N Acetyl Glucosamine has important anti-inflammatory action and can be an effective treatment option in patients with hair loss associated with scalp inflammation. The subjects tolerated the treatment very well and reported a healthy rejuvenated scalp.
Introduction & Objectives

Human hair follicles (HFs) express the olfactory receptor OR2AT4, whose specific stimulation ex vivo (in organ hair culture) by the synthetic sandalwood-like odorant, Sandalore®, prolongs anagen, and suppresses apoptosis by up-regulating intra-follicular IGF-1 mediated signalling.

To study whether this effect of Sandalore® is clinically relevant, we conducted a randomized, double-blinded, placebo-controlled, prospective clinical trial involving 60 female volunteers affected by telogen effluvium with a defined, substantial degree of hair shedding.

Material and Methods

Thirty patients clinically diagnosed as telogen effluvium were randomly assigned to a verum group applying once daily a solution containing 1% Sandalore®, and 30 patients with telogen effluvium were included in a placebo group that applied a solution containing natural sandalwood oil (placebo), which has the same odor as Sandalore® but does not stimulate OR2AT4. The trial period consisted of 24 weeks. The main study read-out parameters were the degree of hair shedding, hair density, anagen/catagen-telogen ratio (phototrichogram), hair mass index (cross sectioned trichometry), hair thickness, patient self-assessment questionnaire and clinical evaluation.

Results

Sandalore® 1% ameliorated clinical signs of telogen effluvium, namely it reduced hair shedding, increased hair volume and increased the percentage of anagen HFs over time significantly more than placebo, and showed a trend towards increasing the ratio of terminal/vellus hairs.

Hair shaft thickness and density were not affected. Most of the anti-hair shedding effects were seen already after 8 weeks and maintained at week 24. Subjectively, individuals in the treatment group were more satisfied than in the placebo group regarding hair appearance and overall Results.

Conclusion

This clinical trial confirmed the anagen-maintaining effects of Sandalore® seen ex vivo and provides the first evidence that a cosmetic odorant can positively impact on human hair growth in vivo, encouraging the use of topical olfactotherapy with Sandalore® as adjunct therapy of hair disorders characterized by excessive hair shedding.
Background

Primary cutaneous follicle center lymphoma (PCF-CL) usually presents with erythematous nodules and plaques on the head, neck, or back. We report a case of PCFCL presenting with unusual clinical manifestations.

Case report

A 64-year-old female with a history of PCFCL grade 1-2 followed by hematology/oncology presented to our dermatology clinic for a well-defined 3x3cm sized atrophic patch of hair loss on the central scalp. She stated that 3 years ago she had a large subcutaneous nodule due to the lymphoma in the region of the patch, and that the nodule regressed after treatment with rituximab, leaving the alopecic area. She states that she had many other subcutaneous nodules that regressed with treatment without causing alopecia. She refused a biopsy from the alopecic patch.

In 2016, a biopsy taken from one of the subcutaneous nodules for routine histopathology and immunohistochemistry was diagnostic for cutaneous B cell lymphoma. Staging included laboratory analyses, PET/CT scan, lymph node ultrasonography, bone marrow aspirate and biopsy, all of which were negative. The final diagnosis was consistent with primary cutaneous follicle center lymphoma stage 1-2 with disease recurrence. At time of our visit she also had a 3x2cm subcutaneous nodule on her right temporal area.

Dermoscopy of the alopecic patch showed preserved follicular openings with vellus and miniaturized hair over an erythematous background, with red dots and arborizing blood vessels. Dermoscopy of the right temporal area overlying the nodule showed miniaturized hair follicles in a background of serpentine, arborizing blood vessels.

Conclusion

We were able to find a case of PCFCL in the literature presenting with scarring alopecia, where the lesion was biopsied and showed PCFCL in a background of androgenetic alopecia. However in our patient, dermoscopy showed non-scarring alopecia. We hypothesize the alopecic patch could have been caused by pressure, but it is unclear why it only developed in one of the nodular lesions.
Background
Bee venom has been used in traditional medicine to treat inflammatory diseases. Several studies have reported its anti-inflammatory, anti-cancer, and antifungal activities. Malassezia species are part of normal skin flora, and also lipid dependent yeasts that inhabit more often on the scalp, and are a major component of the skin microbiome. The Malassezia species are frequently associated with many dermatologic disorders, including seborrheic dermatitis on the scalp.

Objective
Bee venom is consisted with many different components, including peptides, including melittin apamin, adolapin, enzymes, and also unknown chemicals. Many studies to figure out bee venom’s effects have reported that there are anti-inflammatory, anti-arthritis, and also antifungal effects. Previous studies about antifungal effect of bee venom showed whole bee venom have antifungal effect against T. rubrum and Candida species. The purpose of this study was to evaluate the in vitro antifungal effect of bee venom component, melittin and apamin on the Malassezia species.

Materials & Methods
Minimal inhibitory concentrations (MICs) were determined with 10 Malassezia species, which are Malassezia restricta CBS 7877, KCTC 27524 and KCTC27527, M. globosa CBS 7966, KCTC 27511 and KCTC 27520, M. sympodialis CBS 7222, M slooffiae KCTC 27517, M. furfur CBS 1878 and M. pachydermatis CBS 1879, grown in Leeming and Notman medium, using bee venom and its components, and Zinc pyrithione was used as a reference antifungal drug.

Results
Bee venom and its components were not effective as antifungal agent against Malassezia species.

Conclusion
Although bee venom and its component, mellitin and apamin were not effective on Malassezia species, according to former studies, bee venom has antifungal effect against strains of fungi. Regarding former studies, hair product using bee venom could be helpful to reduce scalp inflammation and other fungi related diseases. Further studies should focus on understanding the antifungal mechanisms of bee venom and other possible target fungi.
EFFECT ON INFLAMMATORY CYTOKINE LEVELS IN PATIENTS WITH SEBORRHEIC DERMATITIS USING NEW-FORMULA SHAMPOO

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Introduction
Scalp seborrheic dermatitis (SD) is a chronic inflammatory disease associated with sebum secretion and proliferation of Malassezia species. Previous studies reported that the Malassezia yeast has a causative role in SD and can induce the production of interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)- in vitro. Topical corticosteroids and antifungal agents are still the mainstream of treatment for SD. However, long-term use of topical corticosteroids may bring inevitable complications such as skin atrophy and antifungal agents are not always effective for treatment of SD.

Objective
This study aimed to evaluate the effect on inflammatory cytokines of a new-formula shampoo containing rose extracts, epigallocatechin gallate (EGCG), zinc pyrithione, and climbazole for patients with SD.

Materials & Methods
Twenty five patients with SD were enrolled. All patients were instructed to massage their scalps for at least 5 minutes with the new-formula shampoo and then rinse with water three times a week for 4 weeks. We examined the level of inflammatory cytokines (IL-1, IL-6, IL-8, IL-10, and TNF-) before and after 4 weeks of treatment.

Results
We found that IL-1 and IL-8 were significantly decreased after 4 weeks of new-formula shampoo treatment (median of percent change form baseline = -63.1 and -83.1, p < 0.01 and < 0.01, respectively). In contrast, IL-10 was significantly increased after 4 weeks of new-formula shampoo treatment (median of percent change form baseline = 77.8, p < 0.01).

Comment
We observed that the new-formula shampoo decreased pro-inflammatory cytokines and could induce expression of the anti-inflammatory cytokine IL-10. These findings suggest that the new-formula shampoo containing rose extracts, EGCG, zinc pyrithione and climbazole is a useful option for the treatment of scalp SD.
Introduction

Olfactory receptors (OR) are part of an evolutionarily ancient chemosensory signaling system, which regulates many cell functions beyond olfaction. We have recently shown that human hair follicle (HF) epithelium engages in OR-dependent chemosensation via the OR2AT4 receptor and that continuous signaling through this receptor is required for anagen maintenance ex vivo. OR2AT4 is expressed mainly in the suprabulbar outer root sheath (ORS) and selectively targeted by the synthetic sandalwood odorant (Sandalore®).

Intriguingly, microarray analysis revealed that Sandalore® strongly up-regulates dermcidin (DCD) transcription in microdissected HFs ex vivo. DCD is an antimicrobial peptide with broad antimicrobial activity against pathogenic microorganisms Staphylococcus aureus, Staphylococcus epidermidis, and many gram-negative bacteria like Pseudomonas aeruginosa and Escherichia coli by interacting with bacterial membrane phospholipids and forming pores in the cell membrane.

Previously, DCD was thought to be produced only by sweat gland epithelium, which is absent in amputated microdissected HF ex vivo. Therefore, we asked whether Sandalore® I) actually up-regulates intrafollicular DCD peptide production, and II) renders organ-cultured human HFs less susceptible to bacterial contamination/infection.

Methods

By in situ hybridization and immunofluorescence microscopy epithelium of freshly embedded human scalp skin samples from three healthy donors, we show that, in vivo, DCD shows almost negligible mRNA and peptide expression in the HF epithelium and is mainly restricted to eccrine glands. However, DCD mRNA (qRT-PCR) and protein expression (immunofluorescence) is slightly increased in microdissected anagen HFs, but is transcribed in both anagen and catagen HFs (5 donors, qRT-PCR).

Results

Importantly, after 6 days of HF stimulation with Sandalore® (500 M) ex vivo, the intrafollicular production of DCD peptide in ORS keratinocytes was significantly increased, and (less pronouncedly) also after topical Sandalore® administration to organ-cultured human scalp skin. Most importantly, Sandalore® significantly reduced microbial contamination of human scalp HFs organ-cultured in the absence of antibiotics.

Conclusion

These data show that stimulation of OR2AT4 by Sandalore® increases the antimicrobial activity of human HFs by stimulating DCD production. Thus, our data suggest that “olfactotherapy” of hair follicle diseases characterized by major dysbiosis such as acne vulgaris or bacterial folliculitis, with selected odorants is a realistic possibility.
Background
Hypertrichosis describes the growth of an excessive amount of hair on any area of the body. Though hypertrichosis is not an uncommon condition, the dermatologists can have some difficulty for its exact diagnosis or management. On the contrary to hirsutism, hypertrichosis can occur in male and involve any nonvolar areas.
It can be classified based on its distribution (generalized versus localized) and the age of onset (congenital versus acquired). Many cases of localized hypertrichosis have been reported, but clinical research focused on clinical features in accordance with causes of localized hypertrichosis is rarely reported.

Objectives
The purpose of this study was to investigate the clinical features of localized hypertrichosis.

Methods
We performed a retrospective review of medical chart during a period of 12 years (2007-2018). Congenital and acquired localized hypertrichosis with various causes were included, but hypertrichosis accompanied with congenital melanocytic nevus and Becker’s nevus were excluded in this study.

Results
We included 48 patients with localized hypertrichosis. The ratio of male to female patients was 1:2.4. The ratio of congenital to acquired hypertrichosis was 1:2.2. The most common suspected cause of congenital and acquired hypertrichosis was congenital smooth muscle hamartoma (46.7%), and topical minoxidil (27.2%), respectively. The most common site of involvement was lower extremities (32.7%), followed by face (25.6%), and trunk (14.5%). Coexistent hyperpigmentation was also observed in 16 cases (33.3%), especially highly in patients with history of previous trauma (87.5%).

Conclusion
Clinical features in accordance with various causes of localized hypertrichosis in this study could be helpful for dermatologists managing hypertrichosis.
Introduction

Alopecia is a common condition with a high burden of disease, perhaps amplified in ethnic populations. Currently, dermatologists do not utilize an objective measure for hair texture, yet hair texture reflects hair shaft shape, fragility and may intimate unique styling practices. This lack of objectivity lowers dermatologists’ ability to confidently address hair disorders in these patients.

The lay public has developed, adopted and now widely uses objective classification schemes for hair texture, or curl pattern, that allow for communication amongst the curly-haired community regarding optimal hair products and styling. Classification schemes depict curl pattern with visual charts of photographs and/or illustrations of hair from straight to coiled, allowing individuals to self-classify.

These classification schemes have gained significant publicity with features in lifestyle and beauty magazines, including Glamour and Allure. Dermatologists under-utilize these classification schemes, however, adoption in clinical practice has the potential to guide assessment and treatment recommendations. In this cross-sectional survey study we demonstrate that curl pattern classification, in addition to race, has additional utility as a risk-stratification tool in alopecia.

Methods

This was an IRB-approved, case-control study of women with a clinical and/or histopathologic diagnosis of androgenetic alopecia (AGA), traction alopecia (TA), frontal fibrosing alopecia (FFA), central centrifugal cicatricial alopecia (CCCA), alopecia areata (AA) or telogen effluvium (TE). During a clinical encounter, the provider assigned a curl pattern score: pattern 1 (straight), pattern 2 (wavy), pattern 3 (curly) and pattern 4 (coiled). Curl pattern score and the patient’s form of alopecia were recorded. Statistical analyses were performed with Fisher’s exact tests.

Results

A total of 74 patients were enrolled. Regarding forms of alopecia of the patients (N=74), 30 patients had FFA, 25 had AGA, 7 had CCCA, 6 had TE, 5 had AA, and 1 had TA. Overall, the forms of alopecia are stratified between the 4 curl patterns with significance (p=0.011), primarily between patterns 1 (straight) and 4 (coiled) (p=0.0009).

Although AGA occurs with similar frequency across the 4 curl patterns, CCCA, occurs more frequently in curlier hair: pattern 1 (straight)=0/7, pattern 2 (wavy)=2/7, pattern 3 (curly)=1/7, pattern 4 (coiled)=4/7.

Conclusion

Dermatologists lack an objective measure of curl pattern, yet the lay public widely utilizes classification schemes on curl pattern to communicate hair care practices.

We show that curl pattern is associated with some forms of alopecia and dermatologists can use curl pattern classification to risk stratify for forms of alopecia, including CCCA. Additionally, we aim to introduce this under-utilized, visual tool to dermatologists as it will guide assessment and patient-centered communication in clinical practice.
Introduction

Over the past years concomitant involvement of the genitalia and the scalp in females with lichen planus (LP) has been extensively studied (A. Chew, et al., 2014; M. Olszewska, et al., 2016). However, only limited and conflicting data are available on the frequency of the involvement of the scalp in patients with vulvar erosive LP.

The goal of our study was to evaluate the frequency and peculiarities of clinical manifestations of the scalp involvement in females with erosive vulvar LP.

Material & Methods

We observed 14 patients with erosive vulvar LP including three patients with the vulvo-vaginal-gingival syndrome. The diagnosis was confirmed by histological examination in all cases. The patients were 28 to 75 years old (51.1 ± 15.1 years). Lichen planus of the scalp was diagnosed in 4 (28.5%) patients, who composed the main group. 10 patients with erosive vulvar LP without involvement of the scalp were included in the comparison group.

The age of patients in the main group and in the comparison group was 59.2 ± 12.4 and 47.1 ± 14.76 years, respectively.

Results

In all patients of the main group and three patients of the comparison group, the involvement of the vulva was represented with erosions of the vestibulum, adhesions between the clitoris and the clitoral hood, synechiae and resorption of the labia minora. The rest of the patients of the comparison group demonstrated demarcated vulvar erosions without any pronounced alterations of vulva architecture. Three patients in the main group and four patients in the comparison group demonstrated involvement of the oral mucosa. Skin lesions were observed in one patient in the main group and 3 patients in the comparison group.

The involvement of the scalp in 3 patients of the main group was represented by a classical type of LPP. Three patients had large areas of scarring alopecia with follicular papules along the periphery of the lesions. LPP was accompanied by the involvement of the glabrous skin and non-scarring alopecia of the axillary regions in one patient (Graham-Little-Piccardi-Lassueur syndrome), as well as frontal fibrosing alopecia. The lesions on the scalp in two patients of the main group developed before the vulvar disease.

Comment

Thus, the scalp involvement is observed in 28% patients with erosive vulvar LP. The involvement of the genitalia in patients with a combined disorder is more severe and is very likely to be associated with structural changes in the vulva. Quite often, it is also accompanied by oral mucosa lesions. The most common type of the disease of the scalp is classical LPP with the development of multiple/large foci of scarring alopecia. The Results of our study confirm the need for further studies of clinical manifestations of LPP in patients with the vulvar disorder. More patients should be enrolled, and the diagnostic and prognostic criteria for the combined disease should be developed.
Introduction
Naltrexone is a competitive antagonist of µ, κ and γ opioid receptors, synthesized in 1963 and approved by the FDA in 1984 for treatment of alcoholism and opioid addiction. It is a fat-soluble substance absorbed from the gastrointestinal tract and biotransformed in the liver into 6-betanaltrexol, its active metabolite, which crosses the blood-brain barrier, promoting attenuation or complete and reversible blockade of the opioid effects. It is routinely available in 50 mg tablets and also it can be administered by subcutaneous, intravenous or intramuscular injections.

Low-dose naltrexone (LDN) has been used off-label in several diseases. The use of naltrexone at doses lower than 5 mg daily has a paradoxical effect, leading to an increase in endogenous opioids, including beta-endorphins, which have anti-inflammatory properties. LDN also plays a role in modulating the neuroimmune axis. These mechanisms may also justify their possible role in the treatment of inflammatory conditions. Therefore, it became a potential adjuvant therapy in many inflammatory conditions. We aim to discuss the use of LDN as an adjuvant therapeutic option in symptomatic alopecias.

Comment
Trichodynia is defined as scalp discomfort of variable intensity. It seems to be related to release of substance P and it is suggested that perifollicular inflammation may be a causative agent. It has been previously associated with alopecia areata (AA), telogen effluvium, lichen planus pilaris (LPP) and its variants. Trichodynia is a common and undervalued symptom in patients with hair loss that negatively impacts quality of life. It may be refractory to conventional therapies and does not yet have a specific therapeutic guideline. For these cases, LDN would be a possible alternative adjuvant therapy.

In alopecias, the use of LDN has already been reported in LPP and AA. In clinical practice, although without consensus, the suggested dose ranges from 1 to 5 mg / day, usually starting at 3 mg and increasing gradually to 5 mg / day.

Because many opioid receptors are located in the same nuclei that are active in sleep regulation, nocturnal use is recommended. LDN has no drug interactions described with the drugs commonly used for the treatment of alopecias presenting trichodynia. However, it is important to note that LDN can hypersensitize patients to exogenous opioids. Thus, physicians should be aware to drug interactions in patients taking opioid analgesics.

Due to its anti-inflammatory properties, analgesic potential, low cost and few adverse effects described, LDN seems to be a complementary option in the therapeutic arsenal in alopecias presenting trichodynia. Although patients report improvement of symptoms, it is not known how much the anti-inflammatory action would aid in the course of the underlying disease. Further studies are needed to standardize posology, to better understand its mechanism of action and to evaluate its potential therapeutic indications.
Background
Tinea capitis, a dermatophyte infection involving scalp hair, occurs primarily in prepubertal children. The information of this disease entity in adults is very scarce.

Objectives
Tinea capitis, a dermatophyte infection involving scalp hair, occurs primarily in prepubertal children. The information of this disease entity in adults is very scarce.
We aimed to study the epidemiological, clinical and mycological characteristics of tinea capitis of adult population in Korea.

Methods
We retrospectively evaluated 82 adults (44.3%) among the 185 patients with tinea capitis who visited our hospital between June 2000 and June 2017.

Results
Mean age of patients was 66.9 ± 15.8 years (20 - 90 years) with female predominance (male: female = 1:3.1). Mean duration of disease onset until the mycological diagnosis was 22.5 weeks (1 - 144 weeks) and the misdiagnosed rate through only clinical examination was 65.9%.
Concomitant underlying chronic systemic illness were found in 61 patients (74.4%). On clinical features, most common subtype was diffuse pustular (26.8%), followed by seborrheic dermatitis-like scaling (25.6%), gray patch (23.2%), kerion celsi (22.0%), and black dot (2.4%) type. Accompanying localized or diffuse alopecia was shown in 46 patients (56.1%). Forty-eight patients (58.5%) also had the tinea infection at other skin area. Among 23 culture-positive patients, Microsporum canis (n=13, 56.5%) was the most common causative organism, followed by Trichophyton rubrum (n=5, 21.7%), Trichophyton mentagrophytes (n=4, 17.4%), and Trichophyton verrucosum (n=1, 4.4%).

Most patients (93.9%) showed complete resolution with systemic anti-fungal agents and/or topical antifungal agents, oral corticosteroid and antifungal shampoo. Seven patients (9.1%) demonstrated recurrence.

Conclusion
To the best of our knowledge, this is the largest case series of tinea capitis in adult to date. Our study shows distinctive epidemiological, clinical, and mycological features comparing with those of prepubertal children. Atypical clinical presentation of tinea capitis in adults may lead to wrong or delay in diagnosis. Therefore, high index of suspicion and mycological examination is always warranted in inflammatory scalp condition in adults.
MACROFIBRILS, THE MAIN BUILDING BLOCK OF HAIR, ARE LEFT HANDED.

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Introduction

The main structural component of hair shafts is the cortex. Like all components of hair, the cortex is composed of sacrificed cell remnants filled with cornified keratin. In cortical cells, the main keratin building block is the macrofibril. These are long bundles of keratin intermediate filaments (KIFs) embedded in a matrix of keratin-associated proteins and are about 500 nm in diameter and of uncertain length. The KIFs can be helically arranged around the macrofibril axis, with KIF helical pitch increasing linearly from macrofibril core to edge. Macrofibril formation within follicles appears to be largely a mesophase-based self-assembly process in which the precursors of macrofibrils first appear as liquid-crystal tactoids, and this is driven initially by interactions between pre-keratinized KIFs. Differences in the nature of these KIF-KIF interactions during self-assembly can result in different proportions of macrofibrils with different twist handedness.

Objective

Our objective was to establish if macrofibrils are all a single handedness or if they form 50:50 mixtures of handedness within each cortical cell. Earlier work from our laboratory, in which we modelled macrofibril structure from electron tomography data suggested that both left and right-handed forms exist.

Methods

We data-mined 41 electron tomograms containing three-dimensional macrofibril data from previously published studies of Japanese and Caucasian scalp hair, and also different types of wool.

Results

In all we examined 644 macrofibrils and found that within each tomogram all macrofibrils have the same handedness.

Discussion

Due to the pattern of results we concluded that earlier reports of left and right handed macrofibrils were due to artefacts of imaging or data processing. To validate our initial conclusion, we used a handedness marker and re-imaged some of the original sections from earlier studies to establish that in all cases all macrofibrils are left-handed around the macrofibril axis. With agreement within human samples and sheep, we provisionally conclude that this state is universal within mammalian hair.

Conclusion. This also supports the conclusion that the origin of macrofibril twist is the expression of chiral twisting forces between adjacent KIFs, rather than mesophase splay and bending forces relaxing to twisting forces acting within a confined space (such as a cortex cell).
Introduction
Pityriasis amiantacea (PA) has been reported as a reaction pattern of various inflammatory diseases of the scalp. However, the data on PA are scarce in the literature. We studied to know the epidemiologic and clinical characteristics of PA.

Methods
We retrospectively analyzed a series of 44 PA patients in a single tertiary hospital from March 2008 to May 2017.

Results
The mean age of the patients was 42.4 ± 23.4 years with a female predominance (M:F=1:1.6). PA was localized in 21 patients (47.7%), widespread in 16 patients (36.4%), and involved the whole scalp in 7 patients (16.0%). Alopecia was also present on the scalp in 21 patients (48.5%). The underlying skin diseases were eczema (38.6%), followed by primary cicatricial alopecia (25%), psoriasis (11.4%), pemphigus (11.4%), tinea capitis (4.5%), and drug-related skin reaction (2.3%). Three patients (6.8%) were not associated with other skin diseases. Bacteria were isolated in 16 of the 22 cases (72.7%), the majority of which was Staphylococcus aureus. The majority of patients were adequately treated with topical agents in combination with variable systemic agents targeting underlying conditions. In recalcitrant cases, physical removal achieved a satisfactory clinical outcome.

Conclusion
PA appears to be a distinct clinical manifestation secondary to a wide spectrum of scalp dermatitis or medication in susceptible individuals. Individualized treatment depending on the underlying conditions is necessary.
ORWIN’S THRESHOLD IS A KEY POINT IN THE ANAGEN FOLLICLE; WHAT IS IT, WHERE IS IT, AND WHY?

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Introduction
The process of growing a hair is biologically, chemically and physically complex. If we are to fully understand how variation at the signalling, metabolic and genomic levels translate into functional differences in hair, we need to clearly understand how intervention at different points in the process will affect fibre construction. New tools and discoveries (e.g., microRNAs, live-follicle imaging) introduce opportunities to build the groundwork needed to develop new approaches that directly intervene in follicle activity to treat disorders, or enhance hair health (with implications also in the fields of agriculture and bio-based materials)

This will require a multi-disciplinary approach, and, in turn, will benefit from a common nomenclature for follicle features of morphological, chemical, biological and physical significance for hair shaft development and maturation.

Comment
While formal, technique specific, and ad-hoc systems exist for naming anagen follicle features, we recognise the power that a name gives to a cell type, structure or developmental threshold. A pertinent example is the Critical Level, defined by Aubert’s study of wool follicles to indicate the transition that distally migrating cells in the follicle bulb make from actively dividing and non-keratinous, to non-dividing and differentiating. Many just refer to this threshold as the Line of Aubert. Here we highlight another important developmental threshold, and landmark within the follicle, which replaces imprecise terms such as “top of the bulb”, or “end of the hair matrix.” “Orwin’s Threshold” is defined by a plane transecting the anagen follicle in line with the base of the most proximal point at which Henle’s layer of the Inner Root Sheath cornifies. This cornification event occurs very rapidly, within a single cell length, and therefore forms a clear anatomical landmark which is visible with both light and electron imaging under a wide range of conditions. It is also the point after which the remaining Inner Root Sheath and Hair Shaft cell lines are enclosed within a cornified tube.

Conclusion
Orwin’s Threshold, is named to acknowledge the scientific contribution of Dr. Donald Orwin to hair and follicle biology, and the location is relevant to multiple developmentally important events. These include the end of cortical cell reshaping and inter-cellular shuffling (elongation zone) and the end of nuclear function. It also marks the beginning of the post-transcriptional expression of numerous keratin associated proteins, major keratin accumulation (beginning of the keratogenous zone), changes in cytosolic chemistry from a reducing to an oxidising environment, the first signs of keratinization (keratin filament internal rearrangement and disulfide formation) and the first signs of an increase in cortical stiffness. This threshold corresponds to the transition from Zone B to Zone C in the ultrastructure-based fibre development scheme of Donald Orwin.
Introduction & Objective
The role of allergic contact dermatitis in patients with alopecia has not been well established. Allergic contact dermatitis of the scalp may potentially lead to further inflammation and irritation and exacerbate the alopecia. This case series aims to raise awareness of scalp allergic contact dermatitis with nickel and polyurethane-containing products and subsequent alopecia exacerbation.

Materials & Methods
Six patients (ages 3-65 years old) were identified as having allergic contact dermatitis coinciding with increased hair loss. Diagnosis of alopecia areata (n=3), alopecia areata and telogen effluvium (n=1), frontal fibrosing alopecia (n=1), and frontal fibrosing alopecia and androgenetic alopecia (n=1) were confirmed.
Five had reported use of nickel-containing hair accessories, and the sixth had polyurethane-containing hair extensions at hair loss sites.

Results
Patients were treated with high-potency topical corticosteroid and all patients discontinued use of allergen or employed protective barriers against offending agents such as the application of clear nail varnish on the accessories. All patients experienced improvement of scalp allergic contact dermatitis over the course of days to four weeks with these measures. They all declined patch testing due to fear of exacerbation of hair loss.

Conclusion
Patients with alopecia often use hair extensions or pieces to cover areas of hair loss. Many of these products are held in place using metal clips, glues or tapes, all which may contain potential allergens. The allergens may induce scalp allergic contact dermatitis, increase inflammation and cause further hair loss, contributing to patient morbidity. Early clinical recognition of scalp allergic contact dermatitis is important to prevent scalp irritation and further hair loss in patients diagnosed with alopecia.
Introduction
Hair disorders have a significant impact on patients’ lives. It is imperative, more often than not, to initiate treatment as early as possible, be it cicatricial or non-scarring alopecia.
For this purpose, it is important for dermatologists to know the awareness amongst the general population regarding prevalent hair care practices, whom to consult, options available, realistic expectations and so on. This helps in gauging the end-user’s knowledge and recognition of these parameters, which was the aim of this study.

Methodology
We used a self-administered online questionnaire, across adult male and female subjects. A total of 1184 individuals attempted the survey, out of which 1160 completed it.

Results
Out of a total of 1160 responses, 76% were in the age group of 20-40 years; 77% respondents were female; 51% of the individuals said that they were more likely to try home-remedies for hair problems versus only 24% that would consult a dermatologist; 44.8% individuals were unaware that they should consult a dermatologist for their hair problems.
A staggering 57.39% of individuals believed that oiling of hair cures a multitude of hair issues such as dandruff, hairloss and improves hair growth; 76% people spend an average of 500-1000 Rs on over-the-counter hair care products and hair grooming procedures monthly; 57% were unaware that medications and treatment options such as PRP, meso-

Discussion
Hair, in health and disease, has a significant psychosocial impact on society. It has proven, in due course of time, that is more than just a tactile organ, or one, limited purely to aesthetic function. This study has shown that people are unaware of the available treatment options and are often at loss regarding the right person to go to for a consultation. In a country like India, where quackery is quite prevalent, the common public is often misled, the media propaganda regarding OTC preparations often dictate their choice of treatment, so does the age-old tradition of using oil as the ultimate treatment option.

Conclusion
This survey helps us gauge the ignorance of the general population regarding hair care. Despite massive propaganda on alopecia and hair, a major chunk of the general population is still unaware about dermatologists as the primary care physicians for hair disorders.
It is imperative to bust certain myths and educate the masses through seminars, print and community awareness programs to sensitise them towards correct treatment options.
Introduction
Alopecia is an unusual manifestation in patients with mycosis fungoides (MF). In a retrospective study of 1150 patients with MF, just 2.5% presented alopecia. Among these patients, 66% presented alopecia associated with lesions of MF with clear epidermal changes such as patch, plaque and erythroderma. Thirty-four percent presented hair loss in an areata-like pattern. Epidermal changes, when present in these areas of baldness, were limited to mild erythema or scaling. The dermoscopy of MF areata-like can present perifollicular scaling, broken and short hairs.

Case report
A 56-year-old woman presented with a one-year history of hair loss on the anterior hairline and eyebrows. She had a previous appointment with a dermatologist and was submitted to a skin biopsy with the diagnosis of Alopecia Areata. She was using topical tacrolimus 0.1% and had received intralesional injections of corticosteroids but without benefit. She also complained of generalized itching, but with no skin lesions. On clinical exam, she presented alopecia in all the anterior hairline (frontal and temporal) and loss of eyebrows (more intense on the right side) (Figure 1). Dry dermoscopy showed low hair density with a mild perifollicular scaling (Figure 2A).

On immersion dermoscopy of adjacent area, yellow dots, vellus and circle regrowing hairs were evident (Figure 2B). A punch biopsy was performed and the histologic evaluation showed mononuclear infiltrate damaging hair follicles and sweat glands, mucin deposition and folliculotropism with the presence of Pautrier’s abscess (Figure 3), confirming the diagnosis of folliculotropic microsys fungoides.

Conclusion
For a post-menopausal woman presenting hair loss on the anterior hairline and eyebrows with follicular scaling the most straightforward diagnosis would be frontal fibrosing alopecia, however the presence of vellus hairs and yellow dots on dermoscopy do not support this hypothesis. On the horizontal section of skin biopsy, MF areata-like can present peribulbar lymphocytic infiltrate, mimicking alopecia areata. Probably the initial misdiagnosis of alopecia areata in this case happened because of that. Multiple horizontal sections from bulb to the infundibulum could help to avoid this diagnostic error. As far as we know, this is the first description of MF areata-like in an ophiasis pattern.
Introduction

Alopecia is a very common condition observed in clinical practice. The common causes of alopecia are nutritional deficiencies, physical agents, medical disorders and drugs. Among drugs, anti-mitotic drugs induce alopecia with frequency and other uncommon drugs include anti-tuberculosis drugs. Adverse reactions to anti-tuberculosis drugs affect about 10% of patients.[1]

Hepatitis, polyneuropathy, and psychosis are relatively common adverse reactions. However, alopecia due to anti-tuberculosis drugs has rarely been reported in the literature. It is very uncommon and has been reported with only isoniazid, thiacetazone and ethionamide.

Case Report

A 64-year-old woman presented with erythematous patches with induration on her right lower leg for a duration of 2 weeks. The lesions were suspected as a cutaneous tuberculosis infection after skin biopsy and laboratory work-up. She was started on anti-tuberculosis chemotherapy initially containing isoniazid, ethambutol, rifampicin, pyrazinamide, and vitamin B6.

After 1 month of medication, the cutaneous lesion was gradually improved clinically. However, she complained of alopecia after 3 months of medication that became worsening over 2 months after that. The alopecia affected the frontal and both temporal area of the scalp.

On physical examination, there was no sign of inflammation or infection on the affected scalp and no sign of nutritional deficiencies, skin diseases. On the other hand, there were some findings suspected as other adverse reactions including oral ulcer and small lichenoid eruptions that started simultaneously with alopecia.

Because of these findings, we assessed the patient as drug-induced alopecia or drug-induced systemic lupus erythematosus. The further investigations were conducted, including blood tests for complete blood cell count, human immunodeficiency virus, anti-nuclear antibody and rheumatoid factor. With the exception of positivity for anti-nuclear antibody, all these investigations were unremarkable. Skin biopsy was also conducted on bladed scalp, and it revealed mononuclear cell infiltration on periappendageal areas consisted of eosinophils.

Therefore drug-induced alopecia was considered. Because the anti-tuberculosis regimen of the patient didn’t include thioacetazone or ethionamide, the causative agent of drug-induced alopecia was considered as isoniazid. Since then, isoniazid was stopped, and other drugs were continued. The hair regrowth was observed after 4 weeks with complete recovery after 8 weeks. The mechanism is not clearly understood.

Conclusion

However, physicians should be aware of this possible side effect.
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POSTERS

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ASSESSMENT OF THE “SKINSCREEN” SOCIAL MEDIA VIDEO LIBRARY TO AUGMENT PHYSICIAN-PATIENT EDUCATION

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Introduction
Most dermatologist-provided patient education relies on verbal communication to convey complex instruction. This overestimates patients’ appropriate use of medications, which may ultimately lead to unsatisfactory results and noncompliance.

Nearly 80% of Americans use the internet to obtain health information, although little oversight exists to monitor the quality of data presented. Additionally, many resources provide information that is either oversimplified or too complex for the general public. Social media is a leading source of health education for younger demographics, with 18 to 24 year olds being twice as likely to utilize such outlets compared to patients 45 to 54 years old. Of dermatology-related posts on Instagram, only 5% are written by a board-certified dermatologist, supporting the idea that dermatologists are slow to adopt effective technologies for health outreach. As dermatologists, we have the unique opportunity to shift the paradigm of patient education using social media with the implementation of high-quality and easy-to-use learning tools.

Methods
We hypothesized that specialized dermatologic social media-based instructional videos can enhance physician counseling, patient comprehension, user satisfaction, and medication compliance. We created and investigated a newly-created video library entitled “SkinScreen.” These short, stylized, patient-centric films address 30 commonly recommended skin and hair counseling topics. Examples of topics include biopsy wound care, application of emollients, minoxidil, topical retinoids, and pediatric bleach bathing techniques.

Results
Our study addresses dermatologist utilization of social media for patient education and public engagement with the SkinScreen library. As a control, dermatologists completed a questionnaire on the use of social media for patient education in their current practice. We implemented the SkinScreen video library in participating practices and studied metrics including current social media usage for patient education, satisfaction with available social media teaching resources, and amount of online engagement with patients. We found that the SkinScreen library significantly increased familiarity, satisfaction and utilization amongst dermatologists with social media tools for patient education.

We also assess the public’s engagement with SkinScreen on social media, with videos posted free of charge on Instagram and YouTube under the dedicated SkinScreen account. After each video, viewers provide an anonymous response on the value and usefulness of the educational content.

Conclusions
Our data collection includes video utilization rate, engagement, and user demographics. We summarize the responses from users to inform dermatologists on the enhancement, development, and targeting of social media content for patients. Moreover, these patient-tailored videos can be accessed rapidly in-office during patient counseling and can be easily distributed for public use.
Single hair properties, which can include diameter, curvature, bending stiffness, lustre and along-fibre changes, are important for defining human hair appearance. Hair properties are determined by combined morphological and compositional aspects of single fibres that are synthesized during the anagen phase of the follicle.

Understanding the structure-protein-properties relationships and their synthesis in the follicle is important for supporting future research that could influence hair appearance by controlling the shaft formation.

Hair formation is a multi-scale and multi-variable process. Controlled study of specific aspects of hair growth in an experimental context is challenging using human subjects, and for this, model systems are valuable. For example, mice have been an important experimental tool for understanding the follicle cycle. Here we introduce an animal model selected for research on hair shaft development and maturation (anagen). Our model uses wool and follicles from natural sheep mutants (felting lustre mutants and English Leicester breed) with wool fibres that are variously straight and lustrous, and their wild-type relatives. To assess the value of the sheep as a model we investigated the emergent properties of the wool using proteomics, electron microscopy techniques and physical-chemical approaches.

Structural results showed that, while curved wild-type fibres had bilaterally arranged orthocortex and paracortex, and English Leicester fibres had a scatter of paracortex on a background of orthocortex, lustre mutant fibres typically had a complete or partial ring of orthocortex surrounding a paracortex core, and sometimes a central orthocortex (similar to straight human hair). Mutant fibres also had a reduced abundance of some high glycine-tyrosine proteins, normally associated with the orthocortex, with a possible relationship between the protein expression of the KAP8 and KAP16 protein families and fibre felting properties.

We conclude that through control of the internal fibre patterning, multiple-solutions to hair curvature are possible, but this variation may result in different mechanical phenotypes, with implications for how hair behaves on the head. Felting lustre mutant sheep will be a useful tool for discriminating cause and effect from non-causative correlation in a systems-biology approach to hair growth and assembly.
Lipids and lipid metabolism are critical elements in hair follicle (HF) biology and cholesterol has long been suspected to influence hair growth. The routes for cholesterol transport and compartmentalisation in the HF are yet to be defined, yet mutations in the putative cholesterol transporter, ABCA5, are known to cause an autosomal recessive congenital hypertrichosis. This study aims to determine the impact of ABCA5 activity on HF keratinocyte behaviour.

Materials & Methods
Primary keratinocytes isolated from the outer root sheath (ORSK) of plucked human HF are utilised as a model cell system for the siRNA-mediated knock down of ABCA5. mRNA and protein levels were detected by qPCR and western blotting, respectively. Differences in labelled cholesterol efflux to ApoA1 and HDL acceptors was determined. ORSK proliferation was measured by EdU incorporation. Immunofluorescent staining utilised antibodies against ABCA5, Lamp-1 and PDI.

Results
ABCA5 is expressed throughout the HF, with a strong immunofluorescent signal detected within the matrix keratinocytes and inner root sheath. ABCA5 is localisation to lysosomes and endoplasmic reticulum in ORSK. Knock down of ABCA5 reduced total and lysosomal cholesterol accumulation. ABCA1-mediated cholesterol efflux to ApoA1 was also reduced following ABCA5 knockdown.

No significant changes in ORSK proliferation were detected following knockdown of ABCA5. Loading of ORSK with free cholesterol resulted in the expected transcriptional changes associated with excess cholesterol, including up-regulation of cholesterol efflux genes (ABCA1, ABCG1) and down-regulation of de-novo cholesterol synthesis (HMGCR). Knockdown of ABCA5 prevented this transcriptional response to free cholesterol loading.

Conclusions
The maintenance of cholesterol homeostasis is vital for normal cellular function. As a pre-cursor for steroid hormone synthesis and regulator of signalling pathways associated with HF growth and cycling (i.e. Wnt/beta-catenin, Shh), changes in cellular cholesterol could have wide-ranging implications for skin and hair biology.

Data shown here demonstrate a role for ABCA5 in the intracellular compartmentalisation of free cholesterol in primary HF keratinocytes. Reduced movement of cholesterol to ApoA1 could indicate an indirect role for ABCA5 in the delivery of free cholesterol for ABCA1-mediated efflux. Crucially, the loss of normal homeostatic response to excess cholesterol delivery, following ABCA5 knockdown, suggests an impact on LXR-mediated transcriptional activity. We therefore speculate that the loss of ABCA5 could lead to impaired intracellular cholesterol transport and thus a reduction in oxysterol production and LXR activation.
Case Report
A 25-year-old Japanese women visited our department for evaluation of hair loss. She had been treated for depression and eating disorders, and she was receiving adalimumab and colchicine for two years for Behcet’s disease. She also had suffered from alopecia areata 1 year before. Her alopecia areata had completely subsided with 500mg methyl prednisolone pulse therapy and SADBE treatment. 3 months after complete remission of alopecia areata, she had attempted to commit suicide by taking 45mg of colchicine (90 tablets). 3 weeks after attempted suicide, she developed hair loss.

On clinical examining, she had diffuse non-scarring alopecia extending from the frontal area to vertex. There were no inflammatory signs such as erythema or crusts. Other body hairs were intact. Trichoscopy revealed yellow dots, broken hairs, exclamation mark hairs, and flame hairs. On performing a microscopic examination of the dislodged hairs, telogen roots characterized by the presence of a keratinous envelope were shown.

In her hematological and biochemical investigations, her hemogram, thyroid function, serum zinc level, and prolactin level were normal. We also performed 4mm punch biopsy on her scalp.

We devided a specimen by the Tyler technique. The sagittal section showed telogen follicles with an scant inflammatory in filtrates. The coronal section contained 13 follicles and 12 of them was in a stage of telogen. We diagnosed her with colchicine induced telogen effluvium. Her hairs regrew completely within 3 months without any treatment.

Comment
Colchicine inhibits microtubule polymerization by binding to tubulin and inhibits mitosis.

There are few reports in the literature describing colchicine induced hair loss, and 1 of them is agen effluvium caused by suicide attempt with colchicine (Combalia et al. 2016). Excessive colchicine can cause severe side effect and colchicine should be carefully prescribed for patients who may intend to commit a suicide.
Introduction
The trace elements such as copper are mainly required for enzyme function in carbonic anhydrase, superoxide dismutase, polymerase, and collagenase, as well as cell division, nucleic acid metabolism and coenzyme, hence they are required for approximately 300 enzyme functions. Copper deficiency is known to be responsible for the etiology of hair loss, however there has not been enough study supporting this finding so far.

Zinc is a component of zinc finger motifs for many transcription factors, which regulate hair growth through hedgehog signaling and is a catagen inhibitor via its inhibitory action on apoptosis-related endonucleases. In our previous study, we reported that hair loss patients showed lower serum zinc levels than health control, especially alopecia areata and telogen effluvium.

This time, we try to measure the hair copper and zinc levels and look into the correlation between hair copper, zinc level and hair loss.

Objectives
The purpose of this study is to evaluate the relationship between patient’s hair zinc and copper levels and several types of hair losses.

Methods
Serum zinc and copper levels were evaluated in 24 hair loss patients (5 alopecia areata, 8 telogen effluvium, and 11 pattern hair loss) and 32 health controls. And hair zinc and copper level analyses were performed in the 24 hair loss patients.

Results
The mean serum zinc level of hair loss patients was 80.63 14.95 g/dl, significantly lower than the control group (97.94 21.05 g/dl).

Whereas the patient’s mean level of hair zinc was 17.83 7.72 mg/dl. Furthermore, there was no patient who showed lower hair zinc level than normal reference ranges.

Comment
Meanwhile in all of the hair loss patients, the mean serum copper level was 96.96 18.65 g/dl. It was no different from the control group (96.29 28.84 g/dl). In addition, the patient’s mean level of hair copper was 2.2 2.19ppm. The highest hair copper level was 10.9ppm and the lowest level was 0.6ppm. All hair loss patients except four patients showed hair copper levels within normal range (0.9-39ppm).

Conclusions
In our previous study, we reported that hair loss patients showed lower serum zinc levels than health control. In this study all hair loss patients showed normal hair zinc level and it showed that the zinc level between serum and hair had little correlation. When it comes to copper, 20 out of 24 hair loss patients showed normal hair copper level. Besides, two patients showed higher hair copper level beyond the normal range. Therefore, hair copper level is not correlated with hair losses. It demonstrated that the copper level between serum and hair had no correlation.

Several studies on the relationship between serum and hair copper levels and hair loss are still controversial. Although the correlation as not significant in this study, additional studies are needed to improve the number of hair loss patients and control group.
NUCLEAR EXPRESSION OF HIF1A, ARNT AND NOTCH2 IN HUMAN HAIR FOLLICLES VS EPIDERMIS DEFINE THE ASSOCIATION OF HIF1 WITH DISTINCT PHYSIOLOGICAL PHENOMENA

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Introduction
HIF1α and HIF1β/ARNT proteins dimerize to form HIF1 transcription factor which drives general adaptive response to cellular/tissue stress and hypoxia. In keratinocytes in culture, HIF1 activity is linked to both, proliferation and cell cycle arrest. In the interfollicular epidermis (IFE) in vivo, HIF1α and ARNT enhance differentiation and barrier function by augmenting filaggrin expression. Also, elevated HIF1 activity is a feature of hyper-proliferative skin conditions. The divers outcomes of HIF1 activation in keratinocytes are likely to be controlled by other major signaling pathways. Mapping the expression of HIF1α/ARNT and referencing it to Notch status of the cell in hair follicle (HF) and IFE compartments would help to unravel multifaceted roles of HIF1.

Methods
Assessment of the distribution of HIF1α-, ARNT- and Notch2-nuclear positive cells in skin epithelia by immunofluorescence has revealed that in IFE, HIF1α and ARNT are co-expressed solely in a subset of granular layer cells, suggesting HIF1 association with late differentiation events. Nuclear Notch2 is evident in the stratum spinosum cells, i.e. “before HIF1”. Unlike the IFE, in full anagen HFs, nuclear accumulation of HIF1α and ARNT is present in ORS, while Notch2 is cytoplasmic, suggesting HIF1 activity “in the absence” of active Notch. In the hair matrix, strong nuclear signal is found for all three markers. Catagen is characterized by the loss of nuclear Notch2 and HIF1α in lower bulb cells. In telogen HFs, nuclear HIF1α and Notch2 signals are absent, while nuclear ARNT is expressed in a subset of the outer bulge cells.

Discussion
We propose a model for context-dependent physiological roles of HIF1 in skin epithelia. In essence, the outcome of HIF1 activation depends on the Notch-related history of the cell. In the IFE, “late” HIF1α/ARNT coupling in the granular layer cells “that have seen Notch before”, is implicated in late differentiation events. In the ORS, HIF1 activity in the absence of Notch is linked to cell cycle control w/o differentiation.

HIF1 activity is likely to be implicated in the fulfillment of increased metabolic demands, associated with the isometric growth and maintenance of ORS structure. Conjoint action of both Notch and HIF1 in the hair matrix is associated with acquisition of specific cell fates required for the formation of ascending HF layers and hair shaft production. HIF1α and ARNT uncoupling, along with the decrease of Notch activity, is associated with the entry of HF into regression and dormancy phases.
Introduction & Objectives
Tinea capitis is an infection caused by species of dermatophyte fungi, of the genera Trichophyton and Microsporum. The prevalence of each of these genera varies according to the geographical region. Despite principally affecting children from 3 to 7 years old, previous studies have shown that it is not infrequent in adults, especially in those immunosuppressed and in post-menopausal women. The objective of this study was to determine the incidence of tinea capitis in adults, the causal species and the predisposing factors.

Materials & Methods
A retrospective study was conducted over a period of 5 years, from July 2013 to October 2018, of cases of tinea capitis diagnosed in the Department of Dermatology of a reference center (Instituto de Dermatologia Professor Rubem David Azulay) in Rio de Janeiro, Brazil. The information collected included age, gender, medical history of immunosuppression and the results of direct examination and culture.

Results
In a total of 262 patients with a clinical hypothesis of tinea capitis, 68 cases obtained a positive culture for fungi. In this group, 39 (57.3%) and 29 (42.6%) were female and male, respectively. The age distribution was from 1 to 83 years; 51 (75%) of this patients were children under 10 years old with a mean age of 5.45 years, 12 (17.6%) were adolescents between 10 and 19 years old and 5 (7.3%) were adults older than 19. In the adult group, the mean age was 49.8 years, 4 (80%) were women and 2 (40%) of them were post-menopausal.

Comment
The prevalent genus was Trichophyton spp., which was isolated in 60 patients (88%) and Microsporum spp. in 8 patients (12%). More specifically, in the adult group 5 (7.35 %); Microsporum canis was isolated in 1 patient and Trichophyton spp. in 4 patients (T. rubrum and T. tonsurans). T. rubrum was the dermatophyte isolated in two elderly women over 60 years of age (40%). In addition, 2 patients (40%) had concomitant lesions in other regions of the body, with a positive culture for the same specie responsible for the tinea capitis.

Conclusions
The incidence of tinea capitis in adults was not high compared with similar studies in other geographical areas, including those carried out for shorter time periods. In this age group, we have not yet identified immunosuppression and women were the most affected, similarly to that reported in previous studies. In contrast with the literature published to date that indicated Microsporum canis as the prevailing agent of tinea capitis in Rio de Janeiro, most of the cases observed in our study, both in children and adults, were caused by infection with the anthropophilic dermatophyte Trichophyton tonsurans. This difference might be explained by the migratory movements to urban areas in recent years. It is worth highlighting the importance of this observation, as it has implications for preventive and therapeutic measures.
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TOWARDS DEVELOPMENT OF A COMPLETELY HUMAN MODEL SYSTEM FOR THE RE-INNERRVATION OF SCALP SKIN AND HAIR FOLLICLES EX VIVO

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Introduction

Human scalp hair follicles are densely innervated by sensory peripheral nerve fibers (NF), most prominently at the level of the bulge. Several studies have shown that neuromediators released by cutaneous nerve fibers highly impact on human HF activities, including hair growth, pigmentation, and stem cells activities. Vice versa, HF keratinocytes regulate cutaneous sensory nerve fiber remodelling by the release of neurotrophins. Imbalance of this complex bi-directional communication may contribute to the development of hair loss disorders, yet has been exceptionally difficult to dissect at the preclinical level in human skin. Building upon previous rat dorsal root ganglion reinnervation methodology of organ-cultured human skin by neurons, we report here the first fully human re-innervated long-term scalp skin ex vivo model.

Methods

For this purpose, we have placed full-thickness human scalp skin punches directly onto a layer of human iPSC derived neural stem cells (nSCs), or human iPSC-derived sensory neuron progenitors (snPs) and cultured them ex vivo at the air-liquid interface for 10, 12, and 15 days. The serum-free culture medium was either supplemented with only nerve growth factor (NGF) for nSCs, or NGF in combination with glial derived neurotrophic factor (GDNF), brain-derived neurotrophic factor (BDNF), and Neurotrophin-3 (NT-3) for snPs.

Results & Discussion

While no remaining nerve fibers were detected in human skin after 10 days of organ culture without supporting neuronal progenitors, PGP9.5+ nerve fibers around terminal HFs could be observed at day 10, 12, and 15 in scalp skin cultures with nSCs or snPs. Interestingly, some of these were positive also for NF200, a class of intermediate filaments present in myelinated fibers. While skin re-innervation did not induce major changes in overall HF morphology, the presence of neurons differentially regulated the proliferation or apoptosis of hair matrix and bulge keratinocytes. We are currently characterizing the phenotype of the neuronal progenitors and the axons generated by them, the neuromediators released by the newly generated nerve fibers; we are also characterizing the effect of reinnervation on HF keratinocyte functions ex vivo/in situ.

Conclusions

Once fully established, this novel assay can be utilized for dissecting and manipulating the bi-directional communication between defined HF cell populations and (sensory) human nerve fibers under stringently controlled ex vivo conditions. This represents a unique opportunity for industry to engage in the the animal-free testing of both cosmeceuticals and pharmaceuticals that target the cross-talk between human scalp HFs and cutaneous nerve fibers.
Background
Trichotillomania is an impulse control disorder characterized by unintentional but conscious pulling out of one’s own hair on any part of the body. It is common in children and young adolescents. The scalp is the most frequently involved site, followed by the eyebrows, pubic, and other body hairs. When involving scalp, it shows an artefactually patterned, either ill-defined or sharply demarcated area of alopecia. Unusual presentation of trichotillomania may pose difficulty in the diagnosis of patchy hair loss. Here we present a case of trichotillomania in patterned distribution.

Case Report
A 25yr old married woman presented to our outpatient department with widening of central partition since 1 year. Patient had been suffering from multiple vague symptoms like headache, chest pain, breathlessness. She also had multiple visits to different doctors during last one year. Patient denied history of pulling her hair. No significant history of any other illness was present.

On Cutaneous examination, a alopecic patch was present on midscalp simulating Christmas tree pattern of Female pattern hair loss. Hair pull test was positive. On further examination, patchy hair loss was seen on eyebrows. Trichoscopy examination was done which showed uneven broken off hair with few twisted hairs. Differential diagnosis of alopecia areata, trichotillomania and Christmas tree pattern of FPHL were kept. Scalp biopsy revealed distorted hair canal with pigment casts clinching the diagnosis of trichotillomania. Patient was started on N- Acetyl Cysteine 600mg BD and topical minoxidil 5% OD.

Conclusion
Trichotillomania can present in unusual patterns making diagnosis a difficult task. Trichoscopy and scalp biopsy helps to differentiate it from other hair disorders.
A CASE OF Tinea Capitis by Microsporum ferrugineum Treated Successfully with Terbinafine.

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Introduction
In Spain the dermatophytes most isolated in tinea capitis are: Microsporum canis, T. Mentagrophytes, T tonsurans and T violaceum. Ongoing changes are evident in the greater diversity of pathogenic species identified and a marked increase in anthropophilic dermatophytes, especially associated with immigration. Microsporum ferrugineum is most common in the far East, Northern China, Corea, Japan, the Middle East and Nigeria.
We report here the first case of M ferrugineum isolated from a patient of tinea capitis in Spain treated successfully with terbinafine.

Case Report
A 10-year-old girl was admitted for alopecia patches with diffuse scaling associated with annular desquamative lesions on the neck. The trichoscopy findings was diffuse scaling, zigzag hair, perifollicular scaling and pustules. Cultures of lesions yielded M ferrugineum after 4 weeks. Isolate was identified based on colony morphology on Sabouraud’s dextrose agar medium, microscopic morphology of slide culture, and biochemical reactions. The patient was treated successfully, both clinically and mycologically, with oral terbinafine administered for 10 weeks and daily washing with Ketoconazol shampoo.

Comment
M. ferrugineum is an anthropophylic dermatophyte causing tinea in humans. The clinical features of the disease caused by M. ferrugineum are similar to those of infections caused by other dermatophytes, Tinea corporis being the most common presentation. The most recommended treatment in previous publications is itraconazole, as it is a microsporum genre. In this patient, however, the treatment with terbinafine resulted in a cure in 10 weeks.

The increase of migratory movements has produced an epidemiological change of Tinea Capitis in our country. We must insist on correct diagnosis, treatment and prevention among contacts in order to avoid a rise in the prevalence of this disease.