Proceedings & Key Messages from the AHRS Scientific Session and Annual General Meeting

Webinar Program Ancillary Meeting of the 2021 SID Virtual Meeting

Webinar Program held on Friday/May 7, 2021





Victoria Ceh, MPA, Executive Director, American Hair Research Society

Background

The American Hair Research Society (AHRS) was pleased to present its annual scientific meeting as an ancillary meeting of the 2021 Society for Investigative Dermatology Virtual Meeting. Held as an interactive Zoom meeting on May 7, 2021, 150 persons were registered for the event with 66% coming from North America and 19% from South & Central America.



Welcome & Opening Remarks

Dr. Antonella Tosti, AHRS President, welcomed the audience and gratefully acknowledged the corporate sponsors—Concert Pharmaceuticals, Inc. and Pfizer. She referenced the exhibit showcase on the AHRS website with additional information and literature from the sponsors. She thanked the esteemed Annual Meeting Committee, headed by Dr. John Seykora, for organizing the program. Dr. Tosti relayed the Board of Directors' enthusiasm for the great turnout and invited nonmembers to consider joining the Society. She thanked the outgoing Board

members whose terms expired with this annual meeting, including Maria Fernanda R. Gavazzoni Dias, MD, PhD, Lynne Goldberg, MD, and John Seykora, MD, PhD. She congratulated and introduced the newly elected Board members including Isabella Doche, MD, PhD, Natasha Mesinkovska, MD, PhD, and Maryanne Makredes Senna, MD.

2021 David A. Whiting, MD Leadership & Research Award Presented to Hideo Uno, MD, PhD

Dr. Maria Hordinsky presented the 2021 Whiting Award to Dr. Hideo Uno noting his three major research areas: skin biology and disease in human and nonhuman primates, general pathology and aging in nonhuman primates, and nervous system and brain pathology in nonhuman primates. She went on to review his immense contribu-



tions to the field of hair research and touched on selected publications, several using the stumptailed macaque. Dr. Uno was unfortunately unable to attend, but he did prepare an acceptance speech that Dr. Hordinsky read. Notably, he mentioned, "The species of East Asian monkey, Stumptailed macaque, showed unique frontal alopecia resembling human androgenetic alopecia. Using this monkey model, we found that DHT triggered the dermal papilla cells to induce some factors diminishing the size of hair follicles in the frontal scalp. Furthermore, the inhibitor of DHT can block this phenomenon and clinically prevent the alopecia in both monkeys and human subjects. Now, it is widely known and using both minoxidil and finasteride for therapeutic use of androgenetic alopecia."

Progressive Dysfunction of Hair Follicle Dermal Stem/Progenitor Cells Contributes to Age-Related Hair Loss

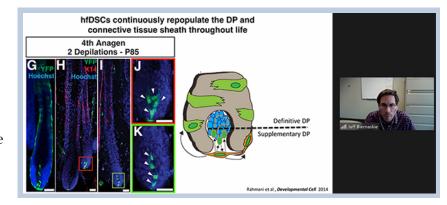
Keynote Speaker: Jeff Biernaskie, PhD

Professor, Stem Cell Biology and Regenerative Medicine, University of Calgary | Canada

Summarized by Jin Yong Kim, MD, PhD, Columbia University | New York, NY, USA

The scientific session launched with an informative Keynote Lecture. Take-home points included the following:

- Hair follicle dermal stem cells (hfD-SCs) function to populate the supplementary dermal papilla (DP), but can be co-opted to replenish the permanent DP in order to maintain inductive capacity.
- Aging prompts increased mobilization of hfDSCs into the permanent DP, likely to replace damaged cells.



- With advanced age, hfDSCs acquire senescence associated features and consequently exhibit diminished self-renewal and an inability to adopt appropriate DP fates, which may contribute to the diminished regenerative capacity of aged hair follicles.
- Effective treatment of hair loss may require targeted therapies to preserve or rejuvenate hfDSC health in order to maintain potency and proliferative capacity.

Decoding the Molecular Anatomy of Skin

Keynote Speaker: Maria Kaspar, PhD

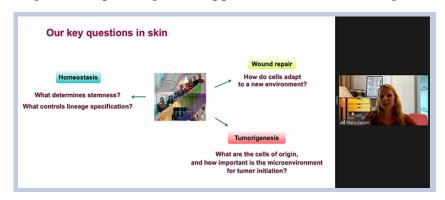
Researcher, Skin and Stem Cell Biology, Karolinska Institute | Sweden

Summarized by Eunice Lee, MPhil, Columbia University | New York, NY, USA

Dr. Maria Kasper from Sweden's Karolinska Institute gave the second Keynote. She provided an extensive and informative overview of her laboratory's single-cell sequencing-based approaches to understanding

the cellular heterogeneity contributing to various skin- and hair-related biological phenomena. Take-home points included the following:

Single-cell RNA sequencing (scRNA-seq) and RNA FISH provided an atlas
of full-thickness mouse skin and
identified 56 cell types that define the
telogen and anagen phases of the hair
cycle.



- Downstream analyses such as trajectory inference and receptor-ligand analyses mapped the differentiation of anagen hair follicle cells and defined distinct subpopulations of the outer root sheath, as well as their interactions with the surrounding stroma.
- A collaboration with Dr. Valentina Greco's laboratory defined the trajectory of epidermal stem cell differentiation that was characterized by gradual transcriptional changes as opposed to discrete cellular states.
- scRNAseq-based approaches are currently being used to decode the molecular design of early skin development.
- Science is advanced through collaboration and the sharing of data. See <u>kasperlab.org/tools</u> to explore Dr. Kasper's and her laboratory's data online.

AHRS Annual General Meeting

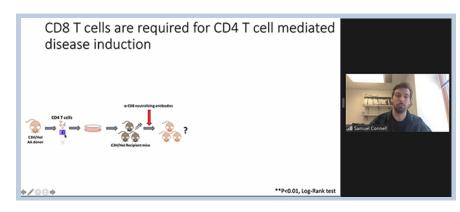
Dr. Maria Hordinsky, Immediate Past President, conducted the annual general business meeting. She reviewed membership numbers noting there are 297 total members, with the regional breakdown as follows: 63% North American, 21% South American, 4% Central American, and the remainder from Europe, Asia, the Middle East, and Australasia. She noted a renewal rate of 87% who paid their 2021 dues. She explained about the 2021 Virtual Mentorships and stated the 2022 Mentorships Program is planned to open in July 2021 for applications with a deadline of Nov. 30, 2021. Dr. Hordinsky thanked the donors of the AHRS Grant Fund. She announced the AAD Hair Loss and Alopecia Initiative in Research (HAIR) Grant Program. She encouraged the membership to save the date and submit abstracts for the 2022 World Congress for Hair Research, scheduled for April 22-25, 2022, in Melbourne, Australia.

Abstract Talks

Five abstracts were selected for oral presentations, all of which provided excellent and informative information. Key take-home points are noted as provided by the presenters.

Induction of Hair Loss by Expanded CD4 T Cells from Previously Affected AA Mice Samuel J. Connell, BA, The University of Iowa Graduate College | Iowa City, IA, USA

- There is an increased presence of interferon gamma producing CD4+ T cells in the skin-draining lymph nodes (SDLNs) of alopecia areata (AA)-affected C3H/HeJ mice.
- Isolated CD4+ T cells from the SDLNs of AA mice that underwent in vitro activation and expansion are able to induce disease in recipient mice as compared to CD4+ T cells from unaffected (control)



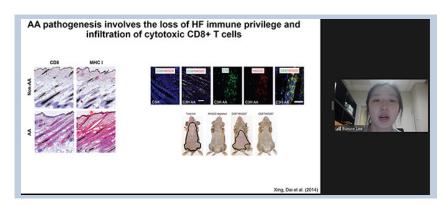
donor mice, and this disease induction occurs in a dose-dependent manner.

 The endogenous CD8+ T cell population is needed in mice in order for disease to develop when induced by CD4+ T cells; however, the endogenous CD4+ T cell population is not required when disease is induced by CD8+ T cells.

Functional Interrogation of Immune Cell Types Identified by Single-Cell RNA **Sequencing in Alopecia Areata**

Eunice Lee, BA, Columbia University | New York, NY, USA

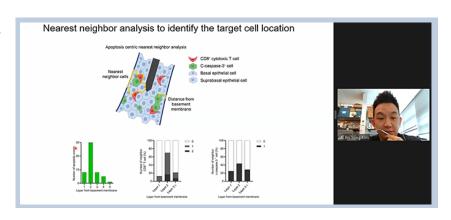
- Single-cell RNA sequencing of skin immune cells in C3H/HeJ mice with long-standing AA and age/sexmatched controls showed significant changes in the distribution of immune cell types across disease condition.
- The major cell types represented in our single-cell study of AA skin using antibody-mediated depletion were functionally interrogated.
- Consistent with the significant expansion of CD8+ T cells in AA skin, only anti-CD8 depletion completely prevented AA onset. Anti-CD4 and anti-CD25 delayed but did not prevent AA. Depletion of gd T cells and NK cells had no effect on AA onset.



Asynchronous and Perturbed Catagen Regression in C3H/HeJ Mice Precedes the **Onset of Alopecia Areata**

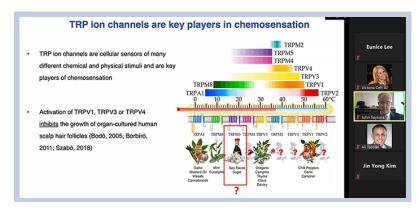
Jin Yong Kim, MD, PhD, Columbia University | New York, NY, USA

- Both extrinsic and intrinsic apoptotic pathways drive premature hair follicle regression in alopecia areata (AA).
- Henle's layer (K71+ inner root sheath) selectively targeted by cytotoxic CD8+ T cells in AA-affected C3H/HeJ mice.
- Asynchronous regression and delayed epithelial apoptosis were observed in catagen of C3H/HeJ mice.
- In catagen of C3H/HeJ mice, epithelial debris is cleared by activated immune phagocytes.



Hair Follicle Chemosensation: TRPM5 Signaling Is Required for Anagen Maintenance Andrei Mardaryev, MD, PhD, Monasterium Laboratory | Münster, Germany

- TRPM5 is a non-selective cation channel that is activated by a rapid and transient increase in intracellu-
- lar Ca2+ in response to G-protein coupled membrane receptor activation. However, its role in human hair follicle (HF) biology remains unclear.
- First, we showed TRPM5 prominent expression in the epithelial HF compartments, such as the outer root sheath (ORS) and hair matrix.
- In human HF organ culture, siRNA-mediated TRPM5 knockdown induced catagen transition associated with apoptosis and

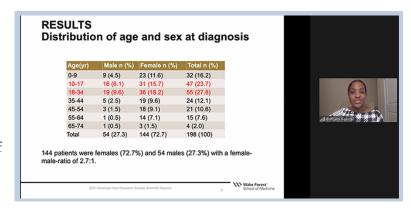


- reduction in cell proliferation in the hair matrix and proximal bulb ORS. A similar effect was observed in HF treated with a selective inhibitor triphenylphosphine oxide.
- Pharmacological TRPM5 activation with putative pheromones 2-heptanone and 2,5-dimethylpyrazine
 maintained HFs in the anagen stage at levels similar to or even greater than vehicle controls. Finally,
 we identified that TRPM5 controls the expression of well-known hair growth regulators, such as IGF1,
 TGFB1/2 and SFRP1. These data suggest that TRPM5 is a novel modulator of human hair growth, and
 specific TRPM5 activators or inhibitors maybe used to promote hair growth or inhibit unwanted hair
 growth, respectively.

Epidemiology of Alopecia Areata in Black Patients

Brittany Feaster, MHS, Wake Forest University School of Medicine | Winston-Salem, NC, USA

- Results of our study demonstrated a female predominance and increased prevalence of alopecia areata in younger patients. At the time of diagnosis, most patients were within the 18-34 year age group followed secondarily by the 10-17 year age group.
- Of our study population, there was increased prevalence of the comorbidities of diabetes mellitus, thyroid disease, obesity, hypertension, and depression. The highest prevalence of all the comorbidities evaluated was in atopic conditions.



Closing Remarks

After a wonderful session, Dr. Seykora opened the floor to final questions and comments. He concluded by thanking the presenters and audience.