Montagna Symposium 2008: The Biologic Basis of Psoriasis

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More than 100 physicians, scientists, residents, students, and pharmaceutical company representatives attended the 2008 Montagna Symposium, The Biologic Basis of Psoriasis,* including most of the world's leading research experts working on psoriasis. The program was divided into four major sections: (i) the genetics of psoriasis, (ii) mouse models of psoriasis, (iii) T cell and keratinocyte biology, and (iv) translational/human studies. In addition to major talks by invited speakers, the meeting included short talks selected from meritorious abstracts, ample discussion time after each talk, and interactive breakout sessions with small groups that focused on specific research questions and future research priorities. Because of the intimate lodge setting and the relatively small size of the meeting, attendees had numerous opportunities to interact during the scientific sessions as well as during both planned and unplanned social events.

The meeting began with a keynote address by Rene de Waal Malefyt, who has been an integral member of a research team that performed pioneering studies on the IL-23/T helper (Th)17 inflammatory pathway. Dr. de Waal Malefyt described the rationale behind the science that led to the discovery of IL-23, delineated the differentiation pathways for both human and murine Th17 cells, explored the role of IL-23–driven Th17 responses versus IL-12–driven Th1 responses in well-defined mouse models of autoimmunity, and summarized the data implicating IL-23 and Th17 cells as major players in psoriasis pathogenesis. This talk provided the perfect backdrop for the meeting, because many talks in subsequent sessions required a basic understanding of the fundamental discoveries with regard to the IL-23/Th17 inflammatory pathway.

During the first full day of the meeting, geneticists from around the world took center stage. J.T. Elder and Anne Bowcock presented soon-to-be-published results from a genome-wide association study of psoriasis supported by the Genetic Association Information Network. This revealed strong support for the association of at least seven genetic loci with psoriasis, including *HLA-C*, IL-12/23p40, IL-23p19, IL-23R, IL-4/13, TNFAIP1, and TNFAIP3. Eniko Sonkoly then described altered expression of microRNAs in psoriasis. MicroRNAs are small molecules (approximately 20 bases) that play an important role in translational regulation. Recent evidence from Dr. Sonkoly and her group, as well as Cailin Joyce in Anne Bowcock's group, indicates that the expression of several microRNAs is altered in psoriasis, including miR-31, miR-21, miR-133a/b, and miR-203. Joost Schalkwijk described copy-number alterations in psoriasis, including those within the β-defensin cluster of genes, and the late cornified envelope cluster of genes within the epidermal differentiation complex. Christina de Guzman Strong described genomic analyses for identifying genetic regions important for normal skin barrier function. Frank Nestle outlined a gene-to-clinic example that involved IL-23 and included studies on polymorphisms encoding for IL-12/23p40, blocking this protein in a xenograft model of psoriasis and summarizing clinical data in patients treated with ustekinumab, a monoclonal antibody directed against IL-12/23p40. Last, Julie Segre presented ongoing groundbreaking work exploring the genetics of microbial flora present within normal skin, commonly referred to as the skin microbiome. Hundreds of bacterial species are present within normal skin, far more than can be simply cultured, and species appear to vary widely in different body parts and when sampled in different ways, such as by swabbing or biopsying skin.

The second scientific session centered on mouse models of psoriasis. John DiGiovanni and Shigetoshi Sano described transgenic mice that overexpressed *Stat3* within basal keratinocytes. These mice display many histologic and immunologic features of psoriasis, including the development of psoriasis-like lesions at sites of trauma. Xiao-Jing Wang summarized ongoing work using transgenic mice that overexpress *TGF-β1* within basal keratinocytes. Deleting T cells in these mice leads to a delay in, but not complete protection from, developing skin disease. The final portion of this session, introduced by Brian Nickoloff, included small but spirited group discussions on the relative merits and drawbacks of the many mouse models of psoriasis, as well as a discussion on the ways in which these models could be evaluated and scored in a standardized manner.

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The third scientific session began with talks focused on T cell biology. Rachael Clark discussed the phenotype and cytokine expression profile of populations of cutaneous T cells. Subsequent talks by Kevin Cooper and Hideaki Sugiyama centered on the role of regulatory T cells in the pathogenesis of psoriasis, including a delineation of how IL-6 contributes to dysfunction of these cells within psoriatic tissue. Andrew Blauvelt presented unpublished data showing high numbers of $CCR6^+$ Th17 cells in the blood of psoriatics (compared with that of healthy individuals), with decreased numbers of the cells following infliximab therapy. Allen Bruce presented interesting data on how cytokines derived from both Th1 and Th17 cells acted in synergistic ways to promote inflammation in psoriasis, in contrast to recent papers suggesting that Th1 responses downregulated Th17 responses and vice versa.

The second half of the third scientific session centered on keratinocyte biology. It began with Wenjun Ouyang describing how IL-22 and other IL-20 cytokine family members stimulate proliferation and production of antimicrobial peptides by keratinocytes. This theme was continued with a presentation by Andrew Johnston, who showed that EGFR signaling and IL-1 also contributed significantly to antimicrobial defenses in keratinocytes. Yuangang Liu showed how the chemokine CCL20 differentially regulated the expression of Trim32 and Piasy, two molecules involved in keratinocyte growth signaling pathways. Last, Ewout Baerveldt reported on how neuropeptides affect keratinocyte biology.

The translational/human studies session began with James Krueger describing numerous published and unpublished studies on cytokine mRNA and protein expression in skin samples obtained from individuals with psoriasis, atopic dermatitis, and healthy skin. Importantly, Dr. Krueger's work has been critical in the understanding of both Th17 and Th1 inflammatory networks in psoriasis and has resulted in the ability to develop and test comprehensive global hypotheses on the cellular immunology of psoriasis. Kristina Callis Duffin, who works with the Utah Psoriasis Initiative, described genotype–phenotype studies with an emphasis on particular genetic changes that correlated with how psoriasis was affected by pregnancy and smoking. The formal meeting ended with a presentation by Joel Gelfand, who reported on data linking moderate to severe psoriasis with increased risk of myocardial infarction, stroke, and mortality.

2008 SID Eugene M. Farber Travel Awards for Young Investigators

As in the past, nine young investigators were able to attend the Montagna Symposium thanks to a generous donation from the Eugene M. Farber family through the Society for Investigative Dermatology:

Ewout Baerveldt, MD
Departments of Dermatology and Immunology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Anne-Marie Broome, PhD, MBA
Departments of Biomedical Engineering and Radiology, Case Western Reserve University, Cleveland, OH

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Epithelial Biology Section/Genetics and Molecular Biology Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD

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Emma Guttman, MD, PhD
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Reto Huggenberger, MSC
Department of Pharmaceutical Sciences, Swiss Federal Institute of Technology, Zurich, Switzerland

Andrew Johnston, PhD
Department of Dermatology, University of Michigan, Ann Arbor, MI

Cailin Joyce, BS
Department of Genetics, Washington University in St. Louis, St. Louis, MO

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**The 2008 Montagna Symposium, "The Biologic Basis of Psoriasis," was held at the Salishan Resort, Gleneden Beach, Oregon, USA, 2–6 October 2008.*
Information about content and support of past Symposia and the next Montagna Symposium on the Biology of Skin can be found at http://www.montagnasymposium.org.

Montagna 2009

"Genetic–Epigenetic Basis of Skin Diseases"
October 8–12, 2009, Salishan Resort, Gleneden Beach, Oregon

Program Chair: Angela Christiano, PhD
Associate Professor, Departments of Dermatology and Genetics & Development
Columbia University Medical Center