Montagna Symposium 2009: Genetic–Epigenetic Basis of Skin Diseases

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The 2009 Montagna Symposium, Genetic–Epigenetic Basis of Skin Diseases,* was attended by approximately 100 scientists, clinicians, residents, students, industrial representatives, and representatives from the National Institutes of Health. The program was held over three days and included five sessions: (i) "Genetic Control of Skin Morphogenesis," (ii) "Epigenetics, Skin Development, and Diseases," (iii) "Developmental Genetics and Epigenetics," (iv) "Genetic Basis of Disease and Genomic Approaches," and (v) "Novel Opportunities for Therapies for Genetic Diseases."

An important theme was compartments of the skin, both epidermis and dermis, and how regulation of gene expression is achieved by both genetic and epigenetic mechanisms. The sessions were ordered to reflect increasing complexity, beginning with the molecular controls of gene regulation, working through the cellular consequences of genetic changes (i.e., what happens when these processes are disturbed in different diseases), and finally addressing how our knowledge of the genetic basis of disease can be used to generate novel therapeutic strategies.

In addition to talks by invited speakers, several short talks were selected from abstracts. Ample discussion time was included after each talk, and on the last day the attendees broke into small groups to discuss specific research questions and future research priorities. The relatively small size of the meeting facilitated interaction among attendees.

The meeting opened with a keynote address by Howard Chang (Stanford University), who gave an overview of noncoding RNAs and epigenetics. Dr. Chang explained that while both genetic and epigenetic changes in DNA are heritable, epigenetic changes are distinct in that they are reversible and do not involve sequence changes in the DNA itself. Using the hox locus as an example, he described how long noncoding RNAs are an ancient, conserved mechanism of DNA regulation involved in positional identity of the dermis during skin morphogenesis, with a potentially broader role in disease.

The first full day of the meeting began with the session entitled "Genetic Control of Skin Morphogenesis." The goal of this session was to explore the role of developmental signaling pathways and their downstream effectors (transcription factors) in normal and abnormal skin growth. Sarah Millar (University of Pennsylvania) and Andrezj Dlugosz (University of Michigan) presented results of a study in which the genetic control of hair follicle formation was disrupted. They revealed that if wnt or shh signaling is perturbed, both the numbers and the morphogenesis of hair follicles and other skin appendages, such as teeth, are perturbed and can be directed toward tumor formation. This was followed by three talks discussing the roles of various transcription factors in skin and hair development. Carol Trempus (National Institute of Environmental Health Sciences, North Carolina) reported that if the T-box transcription factor Tbx1 is increased, tumor formation is inhibited. Arup Indra (Oregon State University) discussed the necessity of balance of the chicken ovalbumin upstream promoter (COUP) transcription factor CTIP-2 during development, showing that misexpression results in barrier function defects. Maranke Koster (University of Colorado, Denver) demonstrated that an imbalance of the p63 isoforms during development results in ectodermal dysplasia. Later, Benjamin Yu (University of California, San Diego) and Laura Hansen (Creighton University) discussed the regulation of skin phenotypes by varying the levels of receptors and/or ligands for the receptors, with an emphasis on fibroblast growth factor– and epidermal growth factor–dependent signaling.

In the second scientific session, "Epigenetics, Skin Development, and Diseases," Rui Yi (University of Colorado) and Robert Lavker (Northwestern University) showed how varying levels of microRNAs can regulate gene expression in the developing epidermis. Radhika Atit (Case Western Reserve University) then showed that wnt signaling can affect the developmental programs of the skin in different body sites. Mangalam Subramanian (Texas Women's University) discussed histone acetylation and deacetylation in the regulation of global DNA repair. Finally, Colin Jamora (University of California, San Diego) described how perturbation of Snail-mediated

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cross-talk between epithelial cells and leukocytes can lead to skin carcinoma.

The third scientific session, "Developmental Genetics and Epigenetics," began with a general overview of the genetic basis for pigmentary skin diseases by Vincent Hearing (National Cancer Institute), who showed that many of the genes controlling melanogenesis in skin development result in pigmentary disease when mutated. Michael Marks (University of Pennsylvania) discussed the regulation of melanosome biogenesis and how disruption of trafficking results in Hemansky–Pudlak syndrome. Maite Huarte (Harvard Medical School) identified a relationship between large intergenic noncoding RNAs and p21 misregulation in cancer. Next, Elena Ezhkova (Rockefeller University) and Richard Eckert (University of Maryland) discussed epigenetic regulation of skin stem cells and keratinocyte survival, with a particular emphasis on the role of the polycomb family of proteins. Maria Morasso (National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)) discussed the role of DLX3 in the morphogenesis of hair follicles and other epidermal appendages and the role of DLX3 in different ectodermal dysplasia phenotypes. Stephanie Shirley (University of Texas, MD Anderson) reported that UV light increased Snail family members, resulting in melanoma. Finally, Michael Fessing (University of Bradford, UK) presented emerging work on the three-dimensional architecture of DNA into "chromosome territories" and discussed how this higher-order organization can add an additional level of control to gene expression.

In the session entitled "Genetic Basis of Disease and Genomic Approaches," Irwin McLean (University of Dundee) described the genetic basis of atopic dermatitis and the role of filaggrin mutations in this common disease. He then presented new findings illustrating common genetic associations between eczema and asthma. Anne Bowcock (Washington University, St Louis) followed, discussing the complex genetic basis of psoriasis and outlining several innovative systems biology approaches for integrating gene expression data on copy number variants with the analysis candidate loci that arise from genome-wide association studies. Chrisophe Cataisson (National Cancer Institute) discussed the genetic regulation of tumor formation. Christina de Guzman Strong (National Human Genome Research Institute (NHGRI)) described a comparative genetic approach to disease gene discovery by studying conserved elements across species, with an emphasis on the epidermal differentiation complex genes. Later, Allan Balmain (University of California, San Francisco) reported on several mouse models of skin cancer and how the power of mouse genetics could be used to discover genetic susceptibility. Rebecca Morris (Hormel Institute, Minnesota) reported that *BMP5*, a candidate stem cell regulatory gene that she identified from a screen for quantitative trait loci, affects tumor susceptibility. Shirley Russell (Vanderbilt University) then discussed keloids as a model of epigenetically altered wound healing. Carl Baker (NIAMS) ended the session with information about NIAMS funding for genetic and epigenetic research.

In the final session, on translational research—"Novel Opportunities for Therapies for Genetic Diseases"—Ervin Epstein (Children's Hospital Research Institute, Oakland, CA) outlined the potential for novel therapies in the shh pathway for basal cell carcinoma (BCC), including mouse models of the disease and what these have taught us about treating patients with BCC. Julie Segre (NHGRI) discussed her new studies determining the diversity of the skin microbiome on various body sites using global genomic approaches. Two industrial scientists working on skin-related diseases spoke next. Patrick Iversen (AVI Biopharma) discussed antisense-based therapies for both genetic and acquired inflammatory diseases, and Roger Kaspar (TransDerm) discussed the development of small interfering RNA skin therapeutics for targeting dominant mutations in an allele-specific manner using topical delivery. Al Klingelhutz (University of Iowa) ended the session with a description of a human model for studying telomere shortening in aging skin and a model for dyskeratosis congenita.

2009 SID Eugene M. Farber Travel Awards for Young Investigators

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

Caitlin Cloud
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Elena Ezhkova, PhD
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Géraldine Guasch, PhD
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Stephanie Harkey Shirley, PhD
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Department of Pathology, The Ohio State University, Columbus, OH

Valerie Verstraeten, MD
Department of Medicine, Brigham and Women's Hospital, Harvard University, Boston, MA and Department of Dermatology, University of Maastricht, The Netherlands

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*The 2009 Montagna Symposium, "Genetic–Epigenetic Basis of Skin Diseases," was held at the Salishan Resort, Gleneden Beach, Oregon, USA, 8–12 October 2009. 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 2010
"Small Molecules: Skin as the First Line of Defense"
7–11 October 2010, Salishan Resort, Gleneden Beach, Oregon

Program Chair: Richard Gallo, MD, PhD
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