5th Anniversary
CENTER FOR DERMAL RESEARCH

TRI Princeton
RESEARCH EDUCATION SERVICE

"RUTGERS' CENTER FOR DERMAL RESEARCH (CDR) SEMINAR SERIES
CO-HOSTED WITH TRI PRINCETON"

Guest speaker: **Angela Christiano**

Columbia University

Rutgers, The State University of New Jersey,
Life Sciences Auditorium **April 18, 2016**

Lecture begins at 6:30pm
Reception in LSB Lobby from 5:30-6:30pm
Light appetizers, wine/beer/soft drinks will be served

"Efficacy of JAK Inhibitors in the Treatment of Alopecia Areata"

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ABSTRACT:

Alopecia areata (AA) is a common autoimmune disease with a lifetime risk of 1.7%. Current treatments including corticosteroids and other immunomodulators are not FDA-approved and have demonstrated variable efficacy. In 2010, we published the first genome wide association study in AA, which revealed several susceptibility loci shared with other autoimmune diseases and in key pathways that regulate adaptive and innate immunity. This evidence, in conjunction with gene expression profiling, pointed to key members of the interferon-gamma (IFN γ) pathway, whose expression levels are markedly upregulated in AA. Since the IFNγ pathway is regulated in part by Janus kinases (JAKs), we recently conducted pre-clinical studies to ask whether immunosuppression with JAK inhibitors could induce hair regrowth in the C3H/HeJ graft mouse model of AA. We found that both systemic as well as topical treatment with ruxolitinib (JAK1/2 inhibitor) or tofacitinib (JAK3 inhibitor) reversed established disease, a response that persisted for up to 3 months in 100% of mice treated. We next initiated an open label, proof-of-concept clinical trial for the treatment of moderate to severe AA in humans, using oral ruxolitinib 20mg BID. Twelve patients presented with severe, stable AA (greater than 50% hair loss) and were enrolled for 3-6 months of treatment. Nine out of 12 (75%) of patients demonstrated a remarkable response to the treatment, with up to 50% hair regrowth compared to baseline. By three months of therapy, responding patients had substantial hair regrowth compared to baseline, together with molecular evidence for normalization of biomarker signatures in scalp skin interrogated by gene expression profiling. Similar clinical efficacy has also been observed in our ongoing open-label trial of tofacitinib in moderate to severe AA. Unexpectedly, recent work from our lab also found that JAK inhibition can also induce anagen hair growth in the mouse, and elongate the hair shaft in human organ culture assays, uncovering a new role for JAK inhibitors in modulating the normal hair cycle. Collectively, our results point to the potential benefit of JAK inhibitors in the treatment of alopecia areata, and potentially other forms of hair loss.

BIOGRAPHY:

Dr. Angela Christiano is the Richard and Mildred Rhodebeck Professor of Dermatology. She is also Director of the Basic Science Research Group of Dermatology at CUMC. Dr. Christiano's major focus of research is the study of inherited skin and hair disorders in humans, through a classical genetic approach including identification and phenotyping of disease families, genetic linkage, gene discovery and mutation analysis, and most recently, functional studies relating these findings to basic questions in epidermal biology. Molecular aspects of the cutaneous basement membrane zone, adhesion junctions including hemidesmosomes and desmosomes, and epidermal appendages such as hair and teeth are major basic science interests in her laboratory. A long-range goal of the research is to develop rationally designed genetic therapies for skin and hair diseases through understanding the underlying pathogenetic mechanisms. Dr. Christiano earned a Master of Science in Molecular Pathology in 1990, and a Doctor of Philosophy in Genetics in 1991, both at Rutgers University. From 1991-1992 she was a Post-Doctoral Fellow in the Department of Dermatology at Jefferson Medical College in Philadelphia, PA. Her research interests include inherited skin and hair disorders and stem cells.

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