

## IPC AT THE 75TH SOCIETY FOR INVESTIGATIVE DERMATOLOGY ANNUAL MEETING

### IPC symposium focuses on research advances

By Megan Noe, MD, MPH



Megan Noe, MD, MPH, is a clinical instructor and post-doctoral research fellow in the University of Pennsylvania dermatology department. Dr. Noe graduated with research honors from Tufts University School of Medicine, earning both a medical degree and a master's degree in public health, and

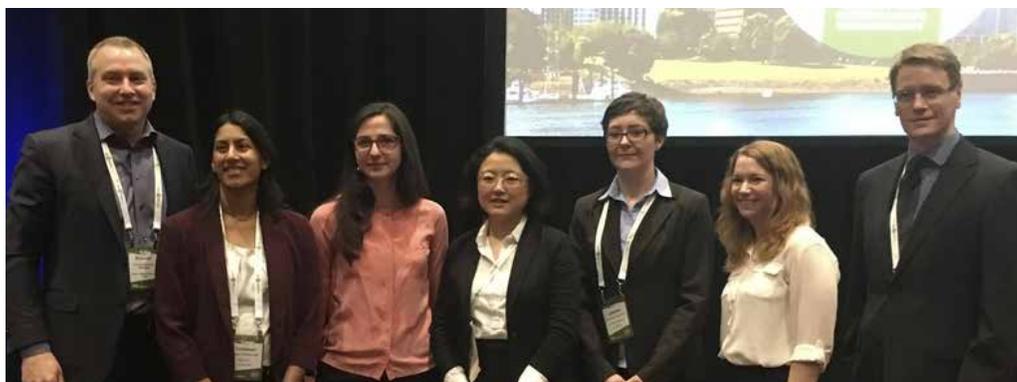
then completed her dermatology residency at the University of Iowa.

Research advances in the immunology and epidemiology of psoriasis were the focus of a symposium sponsored by IPC during the Society for Investigative Dermatology Annual Meeting held in Portland, Oregon, in April. The symposium was organized and chaired by IPC Councilors Dr. Johann Gudjonsson, University of Michigan, and Dr. Andrew Blauvelt, Oregon Medical Research Center, who helped bring together clinicians and researchers from around the country. Five investigators made presentations, which are summarized below.

- Interleukin (IL)-17 is an important cytokine that drives inflammatory signaling in psoriasis and is the target for several newer biologic agents. Beatrice Dyring-Andersen, MD, PhD, Brigham and Women's Hospital, presented her research investigating the relative contribution of neutrophils to total IL-17 production in the skin of psoriasis plaques. Using immunostaining of human psoriatic lesions and normal skin, she found that neutrophils may be an important source of IL-17A production in the skin. In a separate experiment, neutrophils cultured with keratinocytes show increased activation compared to neutrophils cultured alone, and production of IL-17A, IL-17F, and IL-22 was upregulated in those neutrophils cultured with keratinocytes. These results suggest that neutrophils may be an important source of inflammatory cytokines in psoriasis.

- Sylviane Lambert, PhD, University of Michigan, also focused her research on IL-17. Her work examined the role of an SNP (single nucleotide polymorphism) variant (D10N) in the TRAF3IP2 gene on IL-17 signaling. TRAF3IP2 has been previously identified as a genetic susceptibility locus that encodes for the protein Act1. Act1 binds to the IL-17 receptor and activates transcription factors through the MAPK and NFκB pathways, promoting a pro-inflammatory state. She isolated keratinocytes and fibroblasts from individuals carrying the wild type variant (protective) and those with the psoriasis-associated SNP variant D10N. They found that the D10N variant was associated with a significant increase in TRAF3IP2 expression in keratinocytes, but not in fibroblasts. The presence of the SNP variant, D10N, led to increased IL-17A production following polyclonal stimulation, consistent with the evidence that D10N is a genetic susceptibility locus associated with an increased risk for psoriasis.
- In addition to TRAF3IP2, genome-wide association studies (GWAS) have identified many genetic susceptibility loci for psoriasis. It is not well understood, however, how each locus contributes to the overall risk of psoriasis. Zhaolin Zhang, PhD, also from the University of Michigan, discussed her research identifying ways to study changes in the chromatin landscape and gene regulatory mechanisms related to psoriasis immune cells, specifically CD4 and CD8 skin homing T cells. This work may provide better understanding of how genetic variation affects the development of psoriasis. She isolated skin homing T cells from peripheral blood to assay the chromatin landscape around known psoriasis susceptibility loci using ATAC-seq (Assay for Transposase-Accessible Chromatin and Sequencing). This research confirms that ATAC-seq can be used to characterize the chromatin landscape of skin-homing T-cells, and future research will be focused on defining these changes in CD4 and CD8 T cells found in psoriasis lesions.
- Previously, epidemiology research has shown that individuals with psoriasis are at an increased risk for many medical comorbidities. Megan Noe, MD, MPH, at the University of Pennsylvania, examined the risk of

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Speakers at IPC's symposium at the Society for Investigative Dermatology Annual Meeting were, from left, IPC Councilor Dr. Andrew Blauvelt, Oregon Medical Research Center, program co-chair; Megha Tollefson, Mayo Clinic; Beatrice Dyring-Andersen, Brigham and Women's Hospital; Zhaolin Zhang and Sylviane Lambert, University of Michigan; Megan Noe, University of Pennsylvania; and IPC Councilor Johann Gudjonsson, University of Michigan, program co-chair.

mortality in psoriasis patients compared with population-based controls in a medical records database from the United Kingdom. Previous mortality research had used "treatments received" as a proxy for severity, which may not adequately capture the risk of mortality in all individuals. In this study, Dr. Noe used a prospective cohort of patients with a physician-confirmed diagnosis of psoriasis and physician-reported measures of psoriasis severity. Using this prospective, population-based cohort of patients with psoriasis and controls, she concluded that patients with >10% psoriasis BSA had an increased risk of death, compared to age and sex-matched controls. This increased risk was maintained even after controlling for baseline health status, suggesting underlying comorbidities are not completely responsible for the increased risk of death. These results suggest that preventive health efforts should be targeted toward patients with psoriasis whose BSA is >10%.

- An increased incidence in comorbidities was also seen in children with psoriasis. Megha Tollefson, MD, from the Mayo Clinic, presented her research examining the relationship between psoriasis, obesity, and

other comorbidities. Using medical claims data from the US, she found that children with psoriasis were more likely to develop hyperlipidemia, hypertension, metabolic syndrome, polycystic ovary disease, diabetes, non-alcoholic liver disease, and elevated liver enzymes than children without psoriasis. Importantly, children with psoriasis are at an increased risk of developing these comorbidities, regardless of their obesity status, so psoriasis is an independent risk factor for the development of co-morbidities. These results suggest that all children with psoriasis, regardless of their weight, should be monitored for the development of other medical conditions.

In conclusion, the IPC symposium at the Society for Investigative Dermatology meeting highlighted recent advances in psoriasis research from immunology to genetics to co-morbidities. Continued collaborative research will help researchers and clinicians better understand the complex pathophysiology of psoriasis, develop new treatments, and improve the overall care of patients with psoriasis. ■

Children with psoriasis are at an increased risk of developing comorbidities that include hyperlipidemia, hypertension and metabolic syndrome regardless of their obesity status.