**Anti-Nuclease Antibodies Contribute to Pathogenesis in Hidradenitis Suppurativa**

Autoimmune and inflammatory diseases can have impaired degradation of neutrophil extracellular traps (NETs), and NETs are abundant in skin lesions in patients with hidradenitis suppurativa (HS), a chronic skin disease characterized by painful lesions in the axillae, groin, and other intertriginous areas. Oliveira et al. reported that HS serum samples exhibit reduced NET degradation. Although the addition of exogenous DNase I and MNase could restore this degradative capacity, some patient samples did not exhibit this improved NET degradation. Further investigation revealed that decreased DNase I activity was present in these patient samples, concomitant with circulating and tissue anti-DNase antibodies. The presence of these antibodies correlated with the chronic stages of HS and impaired NET degradation. These findings shed new light on the immunological mechanisms underlying HS disease and offer DNase I and associated autoantibodies as potential biomarkers or therapeutic targets. See page 57.

**GWAS Reveals Autoimmune Overlap in Chronic Spontaneous Urticaria**

Although chronic spontaneous urticaria (CSU) was originally considered a severe allergic disease, more recent evidence has supported the notion that CSU is actually an autoimmune disease. To identify susceptibility SNPs associated with CSU, Zhang et al. performed a GWAS in 1,230 patients with CSU and 1,382 healthy controls in the Chinese Han population. Of the 5 genome-wide significant SNPs identified, 4 were in linkage disequilibrium with autoimmune-related diseases, and all 5 were enriched in immune processes. Together, these data support the genetic overlap between CSU and autoimmune diseases, and suggest that genetic factors that predispose individuals to CSU are associated with autoimmune traits. See page 67.

**Multipronged Comparison of Psoriasis Disease Variants**

To probe the similarities and differences in the inflammatory processes involved in psoriasis vulgaris, palmpoplantar pustular psoriasis (PPP), and nonpustular palmpoplantar psoriasis (NPPP), Wang et al. combined RNA sequencing, histologic assessment, focused proteomic analysis, and exome sequencing. Increased neutrophils were observed in PPPP lesional skin, whereas infiltration of CD8+ T cells characterized NPPP lesional skin. PPPP skin also exhibited activation of T helper (Th)17 pathway genes and keratinocyte response genes to IL-36, whereas NPPP skin exhibited activation of Th1/IFN-γ-associated genes. As both PPPP and nonpustular psoriasis disease variants showed IL-36 pathway expression, the underlying palmpoplantar psoriasis disease spectrum appears to be systemic and potentially mediated by the IL-36 pathway, supporting the exploration of targeting of IL-36 pathways for therapeutic benefit. See page 87.

_Clinical Snippets_

**Cytokine Profiles Distinguish Regular Bullous Pemphigoid and Dipeptidyl Peptidase 4 Inhibitor-Associated Bullous Pemphigoid**

Previous use of dipeptidyl peptidase 4 inhibitors (DPP4is) for treatment of type 2 diabetes is a strong risk factor for the development of medication-associated bullous pemphigoid (BP), a blistering skin disease characterized by a disruption of the dermal-epidermal junction by autoantibodies to BP180. Tuusa et al. showed that skin cytokine expression differed between patients with regular BP and DDP4i-BP. Specifically, cytokines mediating B-cell survival and targeting were more strongly expressed in lesional skin from patients with regular BP. Cytokines related to eosinophils were increased in samples from patients with DDP4i-BP, and these cytokine levels correlated with anti-BP180 autoantibody levels. These distinct profiles highlight differences in disease mechanisms between regular BP and DDP4i-BP. See page 78.

**Proliferative T Lymphocytes Predict Survival in Cutaneous B-Cell Lymphomas**

Tumor-infiltrating lymphocytes (TILs) are a vital component of the tumor microenvironment, and Menguy et al employed multiplex immunofluorescence to characterize the TILs in primary cutaneous B-cell lymphoma (PCBCL) subtypes. TILs from PCBCL-leg type samples were sparsely intermingled within the tumor infiltrate, comprised primarily CD8+ and CD4+ T cells, and contained abundant proliferative cells. Although the tumor microenvironment of all of the PCBCL subtypes was heterogeneous, the presence of proliferative T cells was associated with better survival, suggesting that therapeutic stimulation of the T-cell response may be worthwhile in patients with PCBCL. See page 124.