Nonreceptor-Mediated Effects of High-Dose IgG Treatment in Inflammatory Diseases

Intravenous IgG treatment is associated with clinical remission in patients with the autoimmune skin disease epidermolysis bullosa acquisita (EBA); however, the mechanism underlying this efficacy remains unknown. Pipi et al. examined the effects of intraperitoneal high-dose IgG treatment in experimental murine EBA models. High-dose IgG reduced the levels of antibodies against type VII collagen, which causes the clinical disease manifestations of EBA, likely through an FcRn-dependent mechanism. Complement, proteases, and ROS are known drivers of skin inflammation in EBA, and in the animal models, high-dose IgG functioned by reducing complement deposition at the dermal–epidermal junction, acting as a scavenger for ROS, and serving as a competitive substrate for proteases. This study highlights the multiple modes of action of high-dose IgG in the treatment of immune complex–induced, neutrophil–dependent autoimmune diseases such as EBA. See page 1552.

Tape Stripping Offers Noninvasive Sampling for High-Resolution Molecular Analysis of Psoriasis

Understanding the transcriptomic changes underlying inflammatory skin diseases is critical for the development of novel therapies; however, invasive biopsies are typically utilized to gain samples for RNA sequencing. Tsoi et al. compared high-resolution RNA sequencing on samples obtained by tape stripping with that on biopsy from lesional and nonlesional skin from patients with psoriasis. Tape stripping captured transcriptomic changes in the differentiated keratinocyte layers, such as the inflammatory response, the regulation of genes implicated in antigen processing and presentation, and feed-forward immune response amplification in psoriatic skin. In addition, a subclinical low-grade inflammatory state was identified in samples obtained by tape stripping from nonlesional skin. Tape stripping offers an alternative minimally invasive means to obtain cells for analysis from the skin of patients with psoriasis and may be a useful method to identify biomarkers or track treatment response. See page 1587.

Nuclei-Specific Changes Predict BRAF Mutation in Melanoma

BRAF mutations are common in melanoma and are detected through biopsy-acquired tissue samples. In an effort to explore the utilization of image-based analysis as a method for mutation detection, Kim et al. utilized a deep convolutional neural network approach and a pathomics pipeline to analyze nuclear differences for digitized whole-slide images. The convolutional neural network model accurately differentiated melanomas from benign tissue, and pathomics found that BRAF-mutated nuclei were larger and rounder than those with wild-type BRAF. Furthermore, predictive performance of the model was improved dramatically on a combination of input from pathomics, deep learning, and clinical features, supporting future integration of this automated approach for predicting treatment response or survival in patients with melanoma. See page 1650.

HLA-C*06:02 Defines Psoriasis Clinical Endotypes

Previous studies have suggested that patients who carry the HLA-C*06:02 allele exhibit a distinct psoriasis clinical phenotype. Using two large cross-sectional datasets comprising >9,000 individuals from the United Kingdom, Douroudis et al. confirmed that the presence of this allele is associated with positive family history, early age of onset, guttate psoriasis, and reduced nail involvement. These studies further identified an HLA-C*06:02–negative association with later age of onset, large plaque disease, palm/sole involvement, obesity, and other cardiometabolic comorbidities. The stratified subgroups delineated by this primary genetic susceptibility allele in psoriasis may be useful for targeted management approaches, screening, and early intervention. See page 1617.

Statins Reduce Vascular Endothelial Inflammation in Psoriasis

Patients with psoriasis have frequent dyslipidemia and an increased risk of cardiovascular disease. On the basis of reports of successful reduction in cholesterol and cardiovascular risk in general populations after treatment with statins, Garshick et al. conducted a randomized open-label controlled trial to examine the effects of high-intensity atorvastatin treatment on vascular endothelial inflammation in patients with moderate psoriasis severity and low cardiovascular risk. Atorvastatin decreased vascular endothelial proinflammatory transcript expression, which is a surrogate marker of cardiovascular risk. This improvement was correlated with low-density lipoprotein cholesterol reduction but not with high-sensitivity C-reactive protein. These findings underline the need for larger studies to conclusively determine whether long-term statin use may decrease cardiovascular risk in patients with psoriasis. See page 1749.