Sand Fly Contributes to Induction of Fogo Selvagem

Brazilian investigators have hypothesized that hematophagous insects play a role in the pathogenesis of fogo selvagem (FS), a blistering disease that is endemic to Brazil and characterized by autoantibodies to the keratinocyte adhesion protein desmoglein 1 (DSG1). Diaz et al. reported that patients with FS had greater concentrations of IgG4 antibodies against the Lutzomyia longipalpis sand fly salivary proteins than non-endemic controls. These antibodies were crossreactive with recombinant DSG1 but did not bind human or mouse epidermis. Identification of surface-exposed homologous residues with the human DSG1 ectodomain and the LJM17 salivary antigen from L. longipalpis offers a potential site for crossreactivity. These results suggest that introduction of L. longipalpis salivary proteins may result in DSG1-crossreactive antibodies and FS in genetically predisposed individuals. See page 2332.

Proinflammatory Lipid Mediator in Hidradenitis Suppurativa

Hidradenitis suppurativa (HS) is an inflammatory disease involving hair follicles, although the immunopathogenic events leading to this disease remain to be elucidated. Because the skin is a site of active lipid metabolism and fatty acids are integral to skin integrity, Penno et al. assessed lipid metabolic pathway mediators using targeted liquid chromatography-mass spectrometry and transcriptomics in patients with HS. These studies uncovered dysregulation of the 5-lipoxygenase (LO) and 15-LO pathways in lesional skin of patients with HS, with overexpression and activation of the 5-LO pathway that is responsible for proinflammatory lipid biosynthesis and downregulation of the 15-LO pathway that is involved in anti-inflammatory prohomeostatic lipid biosynthesis. Hyperactivation of 5-LO in lesional macrophages resulted in leukotriene B4 production, which induced neutrophil influx and activation, suggesting that this pathway may contribute to HS pathogenesis. See page 2421.

Intracutaneous Delivery of Adenovirus Vaccine Enhances Cytotoxic Response

In efforts to enhance efficacy of genetic immunizations based on recombinant DNA technology, Erdos et al. demonstrated that microneedle array delivery of the toll-like receptor 3 agonist polynosinic:polycytidylic acid along with an adenoviral vector encoding the model antigen ovalbumin induced proinflammatory changes in the skin. This immunization was characterized by a significantly improved antigen-specific cellular response and equivalent antibody response compared with immunization with the adenoviral vector encoding ovalbumin alone. These observations support further development of adjuvanted adenovirus vaccines for microneedle array delivery because of the ease of production, application, and storage combined with improved immunogenicity. See page 2528.

Dual TYK2/Jak1 Inhibitor as a Psoriasis Therapy

Jak and TYK2 inhibitors have been efficacious for treatment of patients with plaque psoriasis. Forman et al. reported that, over the course of a 4-week induction period and an 8-week maintenance period, the dual TYK2/Jak1 inhibitor PF-06700841 yielded a significantly greater improvement in disease severity from baseline than placebo in a phase IIa, randomized, placebo-controlled multicenter trial in patients with moderate-to-severe plaque psoriasis. Greater proportions of treated patients achieved a 75% or 90% reduction in severity from baseline than those who received placebo, and the inhibitor was well tolerated at all tested doses and strategies with a favorable safety profile. See page 2359.

Propranolol Offers Possible Treatment for Neutrophil-Mediated Disease

Development of safe and effective treatments for autoimmune blistering diseases, including the pemphigoid-like disease epidermolysis bullosa aquisita, is warranted because of the side effects of the mainstay treatment of long-term corticosteroids. Stüssel et al. showed that in a mouse model of neutrophil-dependent epidermolysis bullosa aquisita, propranolol, an adrenergic beta blocker, enhanced neutrophil chemotaxis and reduced immune complex–induced neutrophil ROS release, which is an important pathogenic event in pemphigoid-like diseases. Propranolol was not toxic to human neutrophils, and it is unlikely to induce adverse events similar to corticosteroids, as this drug does not affect other immune cell types, supporting further investigations of this drug for use in dermatological autoimmune diseases. See pages 2326 and 2408.