Driving Dermal Inflammation

The pathogenesis of systemic sclerosis (SSc) involves both immune activation and fibrosis. These factors in combination with increased Toll-like receptor (TLR) activity in SSc sera led Farina and colleagues to examine the function of TLR ligands, which commonly mediate innate immune activation, in a murine model. The TLR3 agonist polyinosinic/polyrictidyl acid upregulated IFN-γ and transforming growth factor-β-responsive genes in dermal fibroblasts. Furthermore, chronic stimulation with this ligand in mice resulted in the development of dermal inflammation and skin remodeling that resembled SSc skin, providing a mechanistic link between inflammation and matrix remodeling. See page 2583

At the Frontline of Innate Immunity

The pattern recognition receptors (PRRs), which include Toll-like receptors (TLRs) and C-type lectin receptors, serve as the frontline defense of innate immune surveillance to sense a wide variety of pathogen ligands. The chronic inflammatory disease atopic dermatitis is characterized by increased skin infection, whereas psoriasis is characterized by increased expression of antimicrobial peptides. In a comprehensive analysis of PRRs in normal and inflamed human epidermis, de Koning and colleagues found that many PRRs are expressed in normal epidermis. Dectin-1 was remarkably upregulated in psoriatic lesions. In-depth investigations into the function of this C-type lectin in psoriasis will offer insight into the biology of skin inflammation. See page 2611

Proallergy Action

IgE is a key type I allergy component. Because the T helper type 17 (Th17) cytokine IL-17A promotes B-cell activity, Milovanovic and colleagues investigated the role of IL-17A in IgE production by B cells. Indeed, IL-17A was found to exert a proallergenic action on B cells by triggering the production of IgE. Th17 cells were increased in allergic subjects and were involved in IgE production. These results uncover a molecular link between the enhanced IL-17A activity and increased IgE levels found in allergic subjects and highlight IL-17A as a potential therapeutic target for intervention for allergies. See page 2621

Impaired Tolerance for Light

Polymorphic light eruption (PLE), which is induced via exposure to UVR, is a common skin disorder that resembles a contact allergy reaction to an as yet undiscovered antigen. Koulu and colleagues employed a fixed irradiation dose that suppressed contact allergy induction in 50% of control patients. In addition to the short-term immunosuppression following exposure, this dose resulted in compromised induction of immunotolerance in PLE subjects following subsequent resensitization compared with healthy volunteers. The investigators concluded that a diminished ability to become tolerized to UVR is a critical immune deviation in PLE patients. See page 2578

Polymorphic CAT

Oxidative stress may be important in melanocyte degeneration in vitiligo. The activity of catalase, an enzyme that protects cells from oxidative stress, is often low in vitiliginous melanocytes. Liu and colleagues found that at least one catalase (CAT) polymorphism (−89A>T), as well as genotypes with more than one variant allele, was associated with an increased risk of vitiligo in a case-controlled study of the Chinese population. Thus, polymorphisms in the CAT promoter may decrease CAT activity and contribute to vitiligo pathogenesis in the Chinese population. See page 2647