Quantity and Quality of T-Cell Infiltrate Impact Prognosis in Merkel Cell Carcinoma

T cells play roles in regulating the growth of tumors, including Merkel cell carcinoma (MCC), and controlling progression. Farah et al. found that primary MCC with higher Simpson’s Dominance indices (SDom), which represent the relative abundance of independent T-cell clones and reflect antigen-driven T-cell expansion, yielded fewer metastases and had lower disease stages at presentation. MCCs with high densities of CD3+ or CD8+ T cells as well as high SDom associated with longer disease-specific survival, suggesting that the use of these objective prognostic markers may help identify patients with MCC who require more aggressive therapies and those who may benefit from observation and less toxic therapy. See page 2146.

Serpin Mutation Underlies Some Cases of Palmoplantar Keratoderma

To date, more than 20 different genes have been implicated in the pathogenesis of palmoplantar keratodermas (PPKs), which comprise a heterogeneous group of hereditary disorders characterized by abnormal epidermal differentiation. However, a considerable number of inherited cases lack known genetic mutations. Mohamad et al. identified nonsense variants in SERPINA12, which encodes the serine protease vaspin, in two unrelated cases of recessive diffuse PPK. Functional studies revealed that these variants result in the loss of vaspin inhibitory activity, leading to increased downstream kallikrein (KLK) activity. Because overexpression of KLK7 causes increased epidermal thickness and hyperkeratosis in mouse models, these findings provide evidence for a role of epidermal protease networks in skin dermatoses and indicate that alteration in SERPINA12 underlies some cases of PPK. See pages 2111 and 2178.

BCL2 Inhibition Quells Steroid-Refractory Graft Versus Host Disease

Nearly one third of patients with graft versus host disease (GVHD), a condition that commonly occurs after allogeneic hematopoietic stem-cell transplantation for hematological malignancies, are refractory to initial steroid treatment. Strobl et al. reported that the anti-apoptotic regulator BCL2 was upregulated before the onset of GVHD symptoms, and that the higher expression of BCL2 at GVHD onset correlated with mortality and steroid-refractory disease. In mixed leukocyte reactions, small molecule BCL2 inhibitor reduced cytotoxic effector cells through the induction of apoptosis in cells expressing high BCL2 levels. In vitro BCL2 inhibition induced apoptosis in CD4+ and CD8+ T cells from patients with steroid-refractory GVHD, supporting additional investigations into the use of BCL2 inhibition for the treatment of steroid-refractory GVHD. See page 2188.

Antidrug Antibodies Impair Clinical Responses to Ustekinumab

Only about half of patients with psoriasis experience good clinical responses with the biologic ustekinumab, which targets the p40 subunit of IL-12 and IL-23. Differences in drug levels between responders and nonresponders suggest that antidrug antibodies (ADAs) block drug–antigen interactions and prevent drug effectiveness. Loeff et al. demonstrated that ADAs that were detected in patients with psoriasis treated with ustekinumab were primarily neutralizing and that ADA positivity in these patients was associated with lower drug levels and poor clinical responses. Determination of drug and ADA levels in ustekinumab-treated patients may guide clinical decisions, including dose modification or change in biologics. See page 2129.

Psychometrics of Itch-Related Scales

Many patients with atopic dermatitis (AD) and psoriasis report severe chronic pruritus that impacts their QOL, sleep habits, and health. To gather psychometric data on self-reported pruritus scales, Heckman et al. evaluated the results of the Scratch Intensity and Impact Scale and the Sleep-Related Itch and Scratch Scale in a cohort of 137 patients with psoriasis or AD. These two itch-related measures exhibited a significant correlation with each other and with other itch-related measures. These results highlight the possible utility of these scales to provide a better understanding of scratching and sleep problems of patients and to inform treatment strategies that address these issues. See page 2138.