Quality Control Measures for RCM Imaging

Reflectance confocal microscopy (RCM) used in concert with dermoscopy provides a noninvasive option for dermatology diagnostics with good specificity and sensitivity. However, quality assurance during image acquisition is critical. Kose et al. applied machine-learning techniques to objectively and accurately (82% sensitivity and 93% specificity) identify and quantify areas that were uninformative within a dataset of 117 RCM mosaics. As the location of the uninformative areas is important for diagnosis, a combination of the visual overlay of the diagnostically uninformative areas with the percentage of such areas within the lesion across the mosaic may indicate image quality at the time of image acquisition in the clinic, precluding patient call-backs for reimaging. See page 1214.

Itch Mediator Dispensable for Inflammation in AD

Although itch is the most debilitating symptom of the chronic inflammatory skin disorder atopic dermatitis (AD), the molecular mechanisms underlying this symptom remain unclear. Guo et al. revealed that kallikrein 7 (KLK7) is upregulated in the epidermis of lesional skin in mice and humans with AD. Kallikreins are serine proteases that previously have been implicated in AD pathology. In these studies, KLK7 was found to be dispensable for the development of AD-associated inflammation in mice but to be required for AD-associated itch, as mice deficient in this factor exhibited significantly reduced scratching behavior. Together, these findings may direct development of potential therapies that target kallikreins to mediate itch in AD. See page 1244.

Methylation Modification Related to Stem Cell Dysregulation in Psoriasis

Loss of the hydroxymethylation mark 5-hydroxymethylcytosine (5-hmC) induces alterations in skin stem cell regulation. Li et al. found that 5-hmC is lost in keratinocyte stem cells and transit-amplifying cells in human psoriasis and an imiquimod-induced mouse psoriasis model. Loss of 5-hmC was associated with decreased demethylation enzyme (TET) expression and decreased expression of genes involved in stem cell maintenance and Wnt/β-catenin signaling. Derivatives of ascorbic acid have been found to increase 5-hmC. In this study, treatment of keratinocyte stem cells with ascorbic acid resulted in restored TET function, increased 5-hmC, corrected downstream gene expression, and improved squamoid differentiation, suggesting that such restoration of stem cell dynamics may provide therapeutic efficacy for psoriasis. See pages 1127 and 1266.

Platelet-Lymphocyte Complexes Predict Response to Anti-TNF Therapy in Psoriasis

Sanz-Martinez et al. demonstrated increased platelet-lymphocyte complexes (PLYCs) in patients with psoriasis. Platelet activation, which results in PLYC formation, is correlated with psoriasis disease severity and vascular disease occurrence and is reduced by TNF-α therapy. Patients with psoriasis treated with anti-TNF-α therapy exhibited normalized numbers of PLYCs, and the basal level of PLYCs including T helper cells was higher in the TNF-α therapy responders. These studies indicate that chronic inflammatory responses and activation of platelets induce PLYCs, which may modulate the immune response in psoriasis, and that these complexes may serve as a predictor for response to TNF-α therapy in patients with psoriasis. See page 1176.

T-Cell Clonality May Distinguish Graft-versus-Host Disease

Cutaneous manifestations of graft-versus-host disease (GVHD) and drug hypersensitivity reactions (DHRs) have overlapping clinical and histological features, creating a diagnostic challenge. As GVHD is mediated by clonal expansions of a limited repertoire of T cells, Chang et al. explored the utility of T-cell clonality in differential diagnosis. Sequencing of the T-cell receptor β chain from 17 patients with either GVHD or DHR revealed significantly higher clonality in patients with GVHD. As use of clonality assessment information yielded a sensitivity of 60% and specificity of 71% for GVHD diagnosis, the potential for incorporation of clonality assessments with clinical features such as facial or palm/sole involvement may offer a more robust diagnostic tool to differentiate GVHD and DHR. See page 1282.