Inheritance Spectrum

Examination of a two-year-old patient diagnosed with the rare condition epidermolytic ichthyosis (EI) revealed a mutation with predicted deleterious functional effects in the previously implicated keratin 1 gene (KRT1). Nousbeck and colleagues also identified this mutation in a heterozygous state in the seemingly unaffected parents of the proband. Although the father reported no skin manifestations, histopathology revealed calluses over the palms and thickening of the plantar surfaces along with less extensive epidermolytic changes. This report—the first to identify semidominant inheritance in EI—suggests that mild mutations in KRT1 may be a rare cause of simple and common callosities. See page 2626

Sequencing Power

Using the power of whole-exome sequencing, Cui and colleagues recently unearthed six mutations in the α- and γ-adaptin–binding protein p34 gene (AAGAB) in Chinese patients with punctate palmoplantar keratoderma type 1 (PPKP1). A total of 14 mutations have now been identified in AAGAB in PPKP1 patients with Scottish, Irish, Japanese, Tunisian, Croatian, German, and Chinese ancestries. Although these identified mutations account for only a fraction of cases, the success of this technique suggests that other genes carrying mutations can be identified in the unresolved patients. See page 2631

Ceramides in Psoriasis

Because reduced expression of an important ceramide synthesis enzyme, serine palmitoyltransferase (SPT), has been noted in psoriatic lesions, deficiency of ceramides, which function in barrier homeostasis, and the resultant barrier disruption may be important for development of psoriasis. Nakajima and colleagues generated keratinocyte-specific SPT conditional knockout mice and demonstrated that a lack of this enzyme results in barrier dysfunction, immunological alterations, and the psoriasis phenotype. The failure of repeated barrier insults to induce this phenotype in wild-type mice indicates that ceramide deficiency, as opposed to barrier abnormality per se, contributes to the development of psoriasis in these animals. These mice will be used to further our understanding of the relationship between epidermal dysfunction and immunological abnormalities in psoriasis. See page 2555

Making a Map

To explore the process of keratinocyte differentiation from the basal layer to spinous, granular, and cornified cells, Gulati and colleagues combined laser-capture microdissection to isolate reticular dermis, basal epidermis, and suprabasal epidermis with gene expression profiling. The transcriptional profiles of these three regions were distinctly separated by principal components analysis. Elucidation of 286 upregulated genes and 310 downregulated genes in the basal versus suprabasal epidermis facilitated the creation of a differentiation-specific human epidermis genomic map, which can serve as a basis for comparison with specific cell types from various disease states. See page 2640

Reaction Prediction

Life-threatening dapsone-induced hypersensitivity reactions (DIHR) occur in approximately 2% of leprosy patients treated with dapsone. Wang and colleagues found that the HLA-B*1301 haplotype is strongly associated with DIHR development in the Chinese population, indicating that this antigen can serve as a useful biomarker for predicting DIHR prior to dapsone administration in leprosy patients in this population. Interestingly, the mechanism of DIHR in these patients appears to be related to HLA immunologically but not to dapsone metabolism, shedding light on our murky understanding of this dangerous reaction. See page 2642