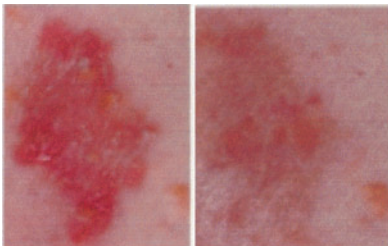


Fine-Tuning Immune Linkage to AA



Susceptibility to alopecia areata (AA) and other autoimmune diseases is associated with human leukocyte antigens (HLA), encoded by the major histocompatibility complex on chromosome 6; non-HLA molecules, including the major histocompatibility complex class I chain-related gene A (*MICA*), are also associated with autoimmune diseases. To investigate associations between AA and the HLA loci, Barahmani and coworkers genotyped two genes and eight microsatellite markers spanning this region in a two-phase study involving a total of 94 multiplex families. They found *MICA**6 to be significantly associated with all forms of AA, and *MICA**5.1 to be significantly associated with patchy AA. The results suggest that *MICA* is both a candidate gene and part of an extended HLA haplotype that may contribute to susceptibility to AA. *See page 74*

Fool the Mutant Gene



Recent studies have shown the potential of aminoglycoside antibiotics to induce readthrough of nonsense mutations in human cells; although this group of antibiotics has been used experimentally to reverse the effects of pathogenic nonsense mutations in various genetic disorders, this effect had not been demonstrated for any of the human genodermatoses. Kellermayer and colleagues used a yeast model to test at the molecular level whether topical aminoglycosides may be beneficial for the treatment of Hailey-Hailey disease (HHD) patients carrying nonsense mutations. HHD is linked to mutations in the *ATP2C1* gene encoding the human secretory pathway $\text{Ca}^{2+}/\text{Mn}^{2+}$ ATPase (hSPCA1). The researchers found that paromomycin — an aminoglycoside capable of inducing efficient readthrough in yeast — stimulated growth of the yeast strain expressing hSPCA1-R468X as compared with the same yeast strain expressing hSPCA1 with a pathogenic missense mutation. This suggests a rationale for clinical studies of topical aminoglycosides as therapeutic agents for patients harboring *ATP2C1* premature stop mutations. *See page 229*

Salivary Antigen Is the Culprit



Although bites from the common bedbug (*Cimex lectularius*) are now rather uncommon, they have been noted recently in immigrants, international travelers, and inhabitants of old frame houses. Leverkus and colleagues, characterizing the host immune response and potential protein antigens present in the saliva of *C. lectularius*, describe a patient with bullous bite reactions after sequential contact with these bugs' bites over 1 year's time. The authors demonstrate that bullous cimicosis may be the late-phase response of an allergic IgE-mediated hypersensitivity to *C. lectularius* nitrophorin. *See page 91*

Journal of Investigative Dermatology (2006) **126**, 2. doi:10.1038/sj.jid.5700079

MC1R Dimers and Skin Phototype

The melanocortin 1 receptor (MC1R) is a key regulator of mammalian pigmentation and a determinant of human skin phototype and cancer risk. Sánchez-Laorden *et al.* showed that MC1R forms dimers with a wide range of functional consequences. The MC1R–melanocortin system is unexpectedly complex, paralleling the diversity of hair color, skin phototypes, and sun sensitivities. Subtle changes of functional properties may be associated with different MC1R haplotypes and contribute to skin phenotype. *See page 172*

Tail Wagging the Head

Ichthyosis hystrix Curth-Macklin (IHCM) is characterized by severe fissuring, mutilating palmoplantar keratoderma, and dark hyperkeratotic plaques over joints. Richardson and coworkers report a keratin 1 (KRT1) gene mutation that completely alters the K1 tail domain in a patient with clinical features of IHCM. In addition, these researchers characterize a new size polymorphism of KRT1, which is especially prevalent among African Americans. These observations illustrate the puzzling phenotypic heterogeneity among K1 disorders and suggest the existence of distinct pathogenetic pathways. *See page 79*