Increased Risk of Liver Disease in Psoriasis Patients

In a population-based study of patients with the inflammatory disorders psoriasis and psoriatic arthritis, Ogdie and colleagues uncovered an elevated risk for new liver disease diagnosis (both non-alcoholic fatty liver disease and cirrhosis) even after adjustment for gender, body mass index, alcohol intake, and smoking. Patients with psoriasis who were treated with systemic therapy had greater risk of liver disease. Patients with psoriasis and psoriatic arthritis also had higher risk of liver disease than patients with rheumatoid arthritis, another inflammatory disease, independent of systemic therapy. These findings may inform systemic medication treatment for inflammatory diseases and encourage healthcare providers to counsel psoriasis and psoriatic arthritis patients on the increased risk of liver disease. See page 760.

Therapeutic Potential of Gentamicin for NPPK

The autosomal recessive disease Nagashima-type palmoplantar keratosis (NPPK) results from loss-of-function nonsense mutations in the SERPINB7 gene, which is highly expressed in the stratum granulosum. These mutations create a premature termination codon, which typically targets mRNAs for nonsense-mediated decay to prevent production of deleterious proteins. Natural suppression of the premature termination codon and subsequent readthrough can restore expression of full-length protein. Ohguchi and colleagues reported that gentimicin, a recently identified readthrough-enhancing drug, enhanced readthrough of the common c.796C>T mutation in the last exon of SERPINB7 in vitro and promoted full-length SERPINB7 protein expression in NPPK cells. These results are consistent with their observations that topical gentamicin treatment ameliorated hyperkeratosis in several patients with NPPK. These studies highlight possible treatment strategies for NPKK. See page 836.

Targeting Kinases to Treat Psoriasis

Pro-inflammatory cytokines and T lymphocytes that contribute to psoriasis pathogenesis have become targets for therapeutic development. Using the Rac1V12 and imiquimod-induced psoriasis mouse models, Fuhriman and colleagues investigated the effects of the PRN684 small molecule inhibitor of the ITK and RLK kinases that function downstream of T cell lymphocyte activation and are upregulated in psoriatic skin on disease. This inhibitor attenuated psoriasis severity, and also reduced tumor necrosis factor-alpha production and CD3+ and γδ T cell infiltration. Epidermal proliferation and thickness were also reduced in PRN684 treated animals. Collectively, these findings support further exploration of inhibitors of these kinases for treating psoriasis. See page 864.

Success of Second-line Biologics for Psoriasis

Biologic therapies are efficacious for moderate-to-severe psoriasis, but 11-35% of patients fail their first biologic therapy during the first year of treatment due to ineffectiveness or adverse events. In a large prospective study, Iskandar and colleagues found that the majority of patients who experienced failure of a first-line treatment continued a second biologic treatment (adalimumab, etanercept, or ustekinumab) for at least a year, especially if initial discontinuation occurred because of ineffectiveness. Patients who experienced an adverse event with the first biologic were more likely to experience one with the second biologic. The outcome of initial treatment with a biologic therapy may be predictive of subsequent experiences with biologics. See page 775.

IL-1 Neutralization Improves Hidradenitis Suppurativa

Kanni and colleagues examined the effects of treatment of hidradenitis suppurativa (HS) patients with the human monoclonal antibody MABp1 that targets and neutralizes interleukin-1α (IL-1α), which is known to participate in the inflammatory process underlying HS. Clinical responses were observed in 60% of patients and they persisted after treatment cessation, perhaps as a result of inhibition of neovascularization or modulation of IL-8 and human β-defensin-2 production. This antibody may be useful for HS in patients who are not candidates for treatment with the tumor necrosis factor inhibitor adalimumab due to either refractoriness or contraindications. See page 795.