Safety of Zinc Oxide Nanoparticle Sunscreens

Regular use of efficient sunscreens has been recommended to minimize the risks of skin aging and cancer caused by long-term exposure to UVR. Studies in cultured cells have shown that agglomerated zinc oxide nanoparticles (ZnO-NP) induce cytotoxicity, prompting some groups to question the safety of nanoparticulate-based sunscreens. Mohammed and colleagues addressed this concern using multiphoton tomography paired with fluorescence lifetime imaging microscopy. Following repeated hourly and daily application of topical ZnO-NP to the skin of human volunteers, these investigators reported minimal NP penetration through the stratum corneum and no detectable morphological or redox changes indicative of cellular toxicity, supporting the safety of repeated use of ZnO-NP-formulated sunscreens. See page 308.

Targeting PAR2 with A Pepducin in Atopic Dermatitis

PAR2 overactivation has been implicated in itch and inflammation in atopic dermatitis (AD). It is quite challenging to target this receptor in animals, in part due to involvement of multiple potential activating proteases, despite an urgent need for non-steroidal therapeutics for AD. Barr and colleagues reported that a cell-penetrating PAR2-targeting pepducin, PZ-225, attenuated skin thickening, inflammation, skin lesion severity, and itch in multiple chronic and acute mouse models of AD induced by chemicals, allergens, and genetic engineering. Furthermore, PZ-225 potently inhibited release of proinflammatory mediators by keratinocytes and mast cells. These experiments also demonstrated that PZ-225 was effective after antigen stimulation in mice, offering promise for the development of therapeutic PAR2-targeting pepducins to mitigate AD symptoms in patients. See pages 282 and 412.

Myeloid-Derived Suppressor Cells Are Expanded in Cutaneous Lupus

Cutaneous lupus erythematosus (CLE) occurs in 70-80% of patients with systemic lupus erythematosus. Mechanisms that counter regulate the hyperactivated immune response in CLE patients are incompletely characterized. Florez-Pollack and colleagues found that myeloid-derived suppressor cells (MDSCs), which suppress T-cell activity in cancer, infection, and autoimmunity, were increased in blood and skin samples from 20 CLE patients compared to healthy controls. These MDSCs, which inactivate T cells via ligation of co-receptors such as DC-HIL, were found to be juxtaposed to T cells in CLE specimens and were highly suppressive of T effector cells in a concentration-dependent manner in vitro, although the MDSCs were a minor population in clinical samples. Therapies that expanded this cellular subset might result in suppression of T cells and counteract immune dysfunction in CLE. See page 478.

Probing Autoantibody Targets in BP and Neurodegenerative Diseases

Patients with neurological diseases have an increased risk of bullous pemphigoid (BP), which is caused by autoantibodies to BP180, and these antibodies have also been detected in patients with neurological diseases. Tuusa and colleagues reported that patients with multiple sclerosis (MS) have BP180 antibodies that do not bind the cutaneous basement membrane like anti-BP180 antibodies in BP patients. Critical for future studies, autoantibodies in MS and Alzheimer’s disease patients target epitopes that differ from those in BP patients, suggesting that neurodegeneration could herald epitope spreading in some patients and result in development of BP. See page 293.

Prediction of the Response to Antimalarials in CLE

Oral antimalarials, such as hydroxychloroquine (HCQ), are first-line therapies for CLE. However, HCQ is only effective in 50% of patients, and the remaining non-responsive patients may benefit from the addition of quinacrine (QC). Zeidi and colleagues identified upregulated tumor necrosis factor-α gene expression and increased myeloid dendritic cells, which are known to play a role in CLE pathogenesis, in lesional skin of patients who were refractory to HCQ and required the addition of QC. Furthermore, HCQ and QC exhibited differential suppression of inflammatory cytokines. These inflammatory players may be useful as biomarkers for responsiveness to improve personalized therapy for CLE. See page 324.