UCA1 Plays Negative Feedback Role in Melanogenesis

The long noncoding RNA UCA1 has been implicated in various cellular processes, including development of bladder cancer, breast cancer, and melanoma. As UCA1 is involved in melanoma, Pei et al. investigated the role of this molecule in melanogenesis. Expression of UCA1 was low in melanocytes and inversely correlated with melanin content. UCA1 inhibited melanogenesis by negatively regulating expression of melanogenesis-related genes, including the microphthalmia-associated transcription factor, via effects on cAMP or protein kinase A, extracellular signal–regulated kinase, and c-Jun N-terminal kinase signaling. Following UVB irradiation, UCA1 expression increased with concomitant downregulation of melanogenesis, highlighting a negative feedback role for UCA1 in UVB-induced melanogenesis. These studies suggest that manipulation of UCA1 in skin provides a potential treatment strategy for hyper- and hypopigmentation skin disorders. See page 152.

MicroRNA Ratios as Melanoma Biomarkers

Diagnosis of cutaneous melanoma by histopathology can be challenging, indicating the need for quantitative molecular diagnostic methods. More than 500 microRNAs (miRNAs), which have been touted as useful biomarkers for disease diagnosis, were found to be enriched in nevi or melanomas. Torres et al. utilized a machine-learning approach to probe miRNA data sets combined with genetic and clinical characteristics to identify miRNAs useful for melanoma diagnosis. These studies revealed that tumor cellularity and patient age are confounders that influence miRNA detection in biopsy samples. In addition, the investigators determined that use of expression ratios, as opposed to total levels, of six miRNAs reproducibly delineates melanocytic nevi from malignant melanoma, potentially leading to improved diagnosis, earlier treatment, and better patient outcomes. See pages 18 and 164.

Inhibition of Type 2 Inflammation Increases Microbial Diversity in AD

Previous clinical trials reported that dupilumab targeting of the IL-4 and -13 receptor subunit IL-4Rα improved the signs and symptoms of atopic dermatitis (AD) as well as skin barrier function. Callewaert et al. described additional skin microbiome alterations following dupilumab treatment. Before treatment, the skin microbiome in patients with AD exhibited low microbial diversity and increased presence of Staphylococcus aureus, which is known to be associated with exacerbated disease. After 16 weeks of dupilumab treatment, microbial diversity was increased and S. aureus abundance was decreased in lesional and nonlesional skin. This normalized microbial signature was also associated with reductions in serum biomarkers and improved clinical AD symptoms. See pages 15 and 191.

Immune Dysfunction Contributes to Second Primary Cancers

Invasive and in situ skin cancers occur more frequently in immunosuppressed individuals, and second primary cancers (SPCs) are significantly increased in these patients. Chattopadhyay et al. examined data from the nationwide Swedish Cancer Registry, which includes information from 1958 to 2015, to determine risks of SPCs in invasive and in situ skin cancers and of these skin cancers as SPCs. High bidirectional risks between immune-responsive skin cancers and most other cancers indicated that inherent or treatment-induced immune system dysfunction is a shared mechanism for SPC and suggested that immunotherapy may be efficacious for skin cancers as well as for SPCs in skin cancer patients. See page 48.

IL-12/IL-23 Blockade Improves Psoriasis and Reduces Vascular Inflammation

Psoriasis is associated with an increased risk of cardiovascular disease that is independent of traditional risk factors. In a randomized, double-blind, placebo-controlled trial including 43 patients with psoriasis, Gelfand et al. demonstrated that treatment with ustekinumab, an antibody that blocks disease-driving IL-12 and IL-23 cytokines and improves psoriasis, significantly decreased aortic vascular inflammation, which serves as a useful marker for future cardiovascular events. Although the change in aortic vascular inflammation was transient and coincident with therapy, a more durable reduction in serum inflammatory and lipid and glucose metabolism markers was observed, supporting additional efforts to determine the clinical benefits of this psoriasis treatment on development of cardiovascular disease. See page 85.