Greater coronary plaque prevalence in psoriasis patients

Psoriasis is associated with increased cardiovascular risk, likely stemming from chronic inflammation and the increased burden of subclinical coronary artery disease. In an effort to probe the underlying cardiovascular risk, Lerman and colleagues performed coronary computed tomography angiography on psoriasis patients, patients with hyperlipidemia and increased traditional cardiovascular risk who were 10 years older than the psoriasis patients, and healthy volunteers. Patients with psoriasis had an increased noncalcified coronary plaque burden compared with the older hyperlipidemia patients. Additionally, levels of high-risk coronary atherosclerotic plaques, which are associated with prospective cardiovascular events, were similar in the psoriasis and hyperlipidemia patient groups but were much greater than in healthy volunteers, suggesting that psoriasis patients and older patients with hyperlipidemia have similar coronary artery disease risk. The investigators followed 50 consecutive psoriasis patients for 1 year and found that reduction in psoriasis severity was associated with improvement in noncalcified coronary plaque burden. These studies support efforts to reduce systemic inflammation in psoriasis patients in order to minimize coronary artery disease. (Circulation 136:263-276, 2017) Selected by J. Celland

Personalized cancer immunotherapy advances

Anti-tumor immunity is driven by T cells directed against mutant neoantigens, which are HLA-presented peptides that arise from tumor-specific mutations. These neoantigens are highly immunogenic as they are not encoded in germline DNA and not expressed by healthy cells. Sahin and colleagues and Ott and colleagues investigated the use of vaccination with neoantigens to enhance tumor control in melanoma patients. Immunized melanoma patients exhibited T cell responses against multiple neoantigens, harbored T cells that discriminated between mutated and wild-type antigens, and experienced reduced disease recurrence. While these studies were independent, the overarching conclusions were similar: targeting of individual cancer mutations by RNA neo-epitope vaccines is clinically feasible and promotes strong T cell-mediated antitumor activity in melanoma patients, supporting further exploration of this personalized medicine strategy. (Nature 10.1038/nature23003; 10.1038/nature22991, 2017) Selected by I. Brownell

Hair follicle stem cell plasticity

Stem cells in the skin exhibit plasticity following injury or transplantation, yielding cell types normally derived from other stem cell compartments. Hoeck and colleagues investigated the role of leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5)þ hair follicle stem cells in stem cell plasticity. LGR5 is a stem cell marker and receptor involved in Wnt signaling. Ablation of Lgr5þ stem cells by diphtheria toxin (DT) administration in a mouse model activated adjacent CD34þ stem cells in concert with upregulation of Myc and NF-kB, transcription factors that function in inflammation and proliferation. Discontinuation of the DT treatment resulted in recovery of the Lgr5þ stem cell pool, restoration of anagen induction, and renewed hair growth. After DT treatment, CD34þ bulge stem cells were directly converted to Lgr5þ hair germ stem cells in a Wnt-dependent manner. Together, these results show that disruption of one stem cell compartment induces an inflammatory response concomitant with stem cell activation in additional stem cell types. (Nat Cell Biol 19:666-676, 2017) Selected by I. Brownell

Link between immune homeostasis and tumor programming

Homeostatic immune programming to prevent autoimmunity may impact tumor immunosurveillance. In the skin, a tissue that has rapid self-antigen turnover and the highest cancer prevalence rates, migrating dendritic cells direct self-tolerance and initiate immunity to foreign antigens when induced by danger signals. Nirschl and colleagues found that all tissue mononuclear phagocyte subsets share a conserved homeostatic differentiation program impacting 227 transcripts, despite ultimate functional specialization. Interferon (IFN)γ is required and plays an instructive role by inducing this program. Increased expression of the IFNγ-related inflammation and mononuclear phagocytic immune signatures are higher in primary melanoma than in healthy skin or nevi and is associated with improved clinical outcomes in metastatic melanoma. These programs were also found to be enriched across multiple human cancers, suggesting that IFNγ instructs anti-tumor immunity via induction of this differentiation program. These studies provide a link between immune homeostasis and anti-tumor immunity and escape and support the concept that the tumor microenvironment co-opts tissue-specific immune development to evade tumor surveillance. Specifically, suppressor-of-cytokine-2 (SOCS2) protein in mononuclear phagocytes is induced by IFNγ and limits adaptive anti-tumor responses, suggesting that this protein may be a new target for cancer therapy. (Cell 170:127-141, 2017) Selected by D. Kaplan

Small molecule modulation of pigmentation

Fair-skinned individuals are more likely to develop skin malignancies than darkly pigmented individuals. Thus, the ability to modulate pigmentation in the skin may have clinical benefits. Mujahid and colleagues demonstrated that the small molecule inhibitor of salt-inducible kinase (SIK) HG 9-91-01 induces expression of microphthalmia-associated transcription factor (MITF) that regulates expression of enzymes that promote biosynthesis of eumelanin. Furthermore, a new generation of SIK inhibitors was developed with optimized molecular size and lipophilicity to penetrate the skin. These topical skin inhibitors upregulated MITF expression and the synthesis of melanin and also induced melanosomal maturation, export, and localization. These studies describe a UV-independent, topical small molecule approach to rescue eumelanin synthesis in human skin with the potential to impact UV protection and mitigate skin cancer risk. (Cell Reports 19:2177-2184, 2017) Selected by C. Niessen