Convalescent plasma harbors cross-neutralizing antibodies against SARS-CoV-2

Variants of severe acute respiratory syndrome coronavirus (SARS-CoV2) that have higher transmission or resistance to therapeutics have raised concern. Wang et al. (2021) examined blood from 22 convalescent patients who had recovered from infection with SARS-CoV-2 Washington-1 strain to investigate neutralizing antibody responses to these variants of interest. Highly potent neutralizing antibodies were identified in the blood of four convalescent patients, and the increased potency and breadth of such neutralizing antibodies were dependent on their binding to the receptor-binding domain but in regions outside of mutational hotspots that are major contributors to resistance in the variants. Studies of antibody selection pressure to mimic generation of virus strains with spike protein mutations that conferred antibody resistance in vitro revealed that antibody combinations with complementary recognition of the receptor-binding domain decreased the chances of emerging resistance. These studies support use of therapeutic combinations of antibodies to mitigate resistance development in SARS-CoV-2 variants. (*Science* 373:eabh1766, 2021; https://doi.org/10.1126/science.abh1766) *Selected by M. C. Udey*

Nucleotide transhydrogenase modulates melanosome maturation and pigmentation

The redox-regulating enzyme nicotinamide nucleotide transhydrogenase (NNT) is localized in the inner mitochondrial membrane of human melanocytes, fibroblasts, and keratinocytes (KCs). However, the role of NNT in skin pigmentation has not been described. Allouche et al. (2021) showed that NNT acts as a modulator of melanosome maturation and pigmentation. In human melanoma cell lines, NNT regulated pigmentation via a mechanism that is dependent on intracellular redox levels but independent of the classic cAMP–MITF pigmentation pathway. More specifically, NNT promoted ubiquitin–proteasome–dependent degradation of tyrosinase. Bioinformatics analyses revealed that some intronic SNPs in the *NNT* locus were associated with skin pigmentation, tanning, and sun protection use and that individuals with post-inflammatory hyperpigmentation or lentigines exhibited reduced NNT levels in the skin. Topical NNT inhibitors (N,N′-dicyclohexylcarbodimide and 2,3-butanedione) increased pigmentation and further protected skin from UVB-induced damage, suggesting use of such reagents in medical and cosmetic pigmentation therapies. (*Cell* 184:4268–83.e20, 2021; https://doi.org/10.1016/j.cell.2021.06.22) *Selected by C. Niessen*

Evaluation of overinterpretation of results in systematic reviews

Identification and evaluation of spin, a term that describes reporting results in a manner that leads readers to be more optimistic about the investigational intervention, are important to minimize misapplication of diagnostic results by clinicians and patients. McGrath et al. (2021) evaluated 137 systematic reviews of diagnostic accuracy studies published in journals with higher impact factors from January 2010 to January 2019. These higher impact journals have historically been associated with higher quality research, suggesting that overinterpretation in the publication may be more likely to be overlooked by clinicians. In these reviews, actual overinterpretation was present in 46% of abstracts and 38% of full-text reports, whereas potential overinterpretation was present in 79% of the reviews. These analyses revealed that compared with journals with all impact factors, high-impact journals are less likely to contain overinterpretation or spin in reviews of diagnostic accuracy. However, this conclusion did not remain significant after exclusion of the 80 reviews that were published in the Cochrane Database of Systematic Reviews, which is less likely to contain overinterpretation practices due in part to publication and review processes inherent in the database. Thus, caution in assuming that high-impact factor journals are less likely to contain spin is warranted. (*Clin Chem* 66:915–24, 2021; https://doi.org/10.1093/clinchem/hvaa093) *Selected by P. Spuls*

Obesity-induced metabolic stress accelerates hair loss

Obesity predisposes individuals to age-associated diseases, but the specific cell populations that are involved remain unclear. Morinaga et al. (2021) showed that cyclic hair regeneration is targeted by high-fat diet–induced stress, resulting in acceleration of hair thinning via depletion of hair follicle stem cells (HFSCs) in the bulge. These changes in HFSC fate were specifically induced at anagen on HFSC activation. Decreased expression of Shh was observed in anagen HFSCs from mice that were fed a high-fat diet. High-fat diet–induced stress led to activation of IL-1R signaling–induced inhibition of Shh signaling and subsequent progressive hair follicle miniaturization and hair loss. Obesity may therefore interact with repetitive hair-cycle– or aging-induced changes to decrease HFSC self-renewal, leading to hair thinning. These findings support the stem cell–centric theory of organ aging and suggest that lifestyle management may be an important mechanism to prevent somatic stem cell decline and organ dysfunction. (*Nature* 595:266–71, 2021; https://doi.org/10.1038/s41586-021-03624-x) *Selected by I. Brownell*

Relationship between microbiota and the immune system is controlled by endogenous retroviruses

Colonization of the skin by commensal microbes promotes accumulation of T cells in the absence of inflammatory responses. To understand the processes that underlie the initiation and regulation of this homeostatic immunity, Lima-Junior et al. (2021) investigated the role of endogenous retroviruses (ERVs). Colonization by *Staphylococcus epidermidis* in mice triggered an antiviral program in KCs and evoked IFN-1 to promote a T-cell response to this commensal microbe. Furthermore, *S. epidermidis* teichoic acid and lipoproteins induced the expression of endogenous retroelements in the skin in a reverse transcriptase–dependent manner. Treatment with antivirals not only interrupted *S. epidermidis* effects on induction of the gene expression program but also affected antimicrobial defense and tissue repair. In contrast, enhanced expression of ERVs promoted microbiota-induced inflammation. These findings support the concept that host endogenous virome influences the relationship between the microbiota and the immune system and highlight the importance of ERV responses to the microbiota in our understanding of inflammation and homeostatic immunity. (*Cell* 184:3794–811, 2021. https://doi.org/10.1016/j.cell.2021.05.020) *Selected by I. Brownell*

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