CD8 T Cells With High Oxidative Phosphorylation Predict Immunotherapy Responses In Melanoma

For solid cancers, including melanoma, the advent of immune checkpoint inhibitor (ICI) therapies that target PD-1/PD-L1 has revolutionized treatment. However, responses are not universal, highlighting an unmet need for the development of tools for predicting ICI efficacy. Li et al. (2022) identified a subset of melanoma-infiltrating CD8 T cells that expressed high levels of cytotoxic and exhausted markers concomitantly with increased levels of oxidative phosphorylation and the ectonucleotidases, namely CD38 and CD39. These highly bioenergetic cells were increased in ICI-resistant patients, leading to the development of a blood-based gene expression profile that can predict responses to ICI in patients with melanoma. The discovery of this CD8 T-cell population also opens up possibilities for improved immunotherapies, with a focus on the manipulation of specific tumor-infiltrating CD8 T cells. (J Exp Med 219:e20202084, 2022; https://doi.org/10.1084/jem.20202084) Selected by T. Schwarz

Roadmap For Researchers In Reporting Human Microbiome Research

Reporting of results of human microbiome research has been challenged by a lack of reporting standards. A group of bio-informaticians, epidemiologists, biostatisticians, physicians—scientists, genomicists, and microbiologists convened to design a standardized reporting checklist to promote research consistency, harmonize publications, and encourage reproducibility. Using previously developed related guidelines from microbiome research and other fields as a jumping-off point, these collaborators developed the Strengthening The Organizing and Reporting of Microbiome Studies (STORMS) checklist to report the results of human microbiome studies. This checklist was designed to be easy to understand by researchers from different fields, to be organized in a manuscript format, and to represent a consensus across multiple disciplines involved in human microbiome research. The STORMS checkpoint, which will be evaluated and updated annually, can serve as a useful roadmap for authors in organizing their manuscripts and as a beneficial tool for reviewers and readers to guide their reviews of the studies. (Nat Med 27:1885–92, 2021; https://doi.org/10.1038/s41591-021-01552-x) Selected by I. Brownell

Immunity to Common Coronavirus Lends Protection To Severe Acute Respiratory Syndrome Coronavirus 2 Infection

The outcome of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains unpredictable, although age and comorbidities have been associated with more severe disease. Efficacious vaccines and mAb treatments have been introduced, but humoral antibody responses to acute disease, in correlation with outcomes, have yet to be precisely delineated. Kaplon et al. (2021) profiled humoral immune responses in early stages of infection with SARS-CoV-2 in patients and uncovered an association between FcR-binding S2-specific humoral immune responses and survival, with S2 class-switched IgG antibodies that could bind to multiple FcRs emerging rapidly after infection. Although these antibodies are not strongly neutralizing, their ability to induce innate effector responses may be critical. In addition, survival from severe and mild diseases correlated with the presence of OC43-specific antibodies early in infection, presumably from previous infections with this common seasonal coronavirus strain. This study offers insight not only into humoral immune responses to SARS-CoV-2 infection but also into the vaccine and boosting regimen development. (Sci Immunol 6:ebj2901, 2021; https://doi.org/10.1126/sciimmunol.abj2901) Selected by M. Udey

IL-23 Inhibition Not Beneficial In Severe Asthma

IL-23 has been implicated in asthma and is a therapeutic target for psoriasis and Crohn’s disease. The effects of inhibition of IL-23 on disease control and airway inflammation in asthma remain unknown. In a phase 2a, multicenter, randomized, double-blind, placebo-controlled, parallel-group trial, Brightling et al. (2021) examined the efficacy and safety of the anti–IL-23 p19 mAb risankizumab in 214 adult patients with severe asthma. The time to first asthma worsening, which was the primary endpoint of the study, was shorter in the risankizumab group than in the placebo group, whereas the annualized rate of asthma worsening was higher in the risankizumab group than in the placebo group. Analysis of sputum samples revealed similar cell counts between the groups and attenuated gene pathways associated with IL-23, cytotoxic T cells, and NK cells in the risankizumab group compared with that in the placebo group. Although there were no obvious safety concerns with risankizumab treatment in this study, targeting IL-23 with this mAb offered no benefit to patients with severe asthma, ultimately undermining the potential of targeting IL-23 and the T helper 17 axis for the treatment of asthma. (N Engl J Med 385:1669–79, 2021; https://doi.org/10.1056/NEJMoa2030880) Selected by J. Gelfand

Staphylococcus Aureus Inhibits Perforin-2 in Nonhealing Diabetic Foot Ulcers

Both recurrent Staphylococcus aureus infection and chronic unresolved inflammation are principal contributors to delayed wound healing in diabetic foot ulcers (DFUs). Pastar et al. (2021) showed that in DFU epidermis keratinocytes, S. aureus suppresses perforin-2, a protein associated with broad-spectrum bactericidal activity against intracellular bacteria and implicated in limiting the proliferation and dissemination of bacteria. S. aureus also induced activation of the AIM2 inflammasome and assembly of the pyroptosome, which facilitates a highly inflammatory form of cell death, and increased IL-1β levels in chronic diabetic ulcers even in the absence of notable clinical infection. In a longitudinal clinical study, although all DFUs accumulated S. aureus and induced pyroptosome assembly, tissue samples from healing DFUs exhibited decreased pyroptosome assembly and function and S. aureus accumulation compared with the samples from nonhealing DFUs. These findings suggest that suppression of perforin-2 in DFU tissue may identify patients at higher risk of further complications. (J Clin Invest 131:e133727, 2021; https://doi.org/10.1172/JCI133727) Selected by M. Udey