COVID-19

Memory B cell induction

Sci. Immunol. https://doi.org/10.1126/sciimmunol.abi6950 (2021).

The induction of memory B cells by mRNA vaccines remains poorly understood. In *Science Immunology*, Wherry and colleagues assess circulating antibodies and antigen-specific memory B cells over the course of first and second immunizations in a cohort of 33 individuals who were SARS-CoV-2 naive and 11 individuals who had recovered from SARS-CoV-2 infection. In SARS-CoV-2-experienced individuals, the first dose induces a response similar to that induced by the boost dose in naive individuals by significantly increasing the amount of spike- and RBD-specific antibodies as compared to pre-existing or first-dose levels and by inducing a robust increase in neutralization. In naive individuals, the first dose induces and the second dose expands spike- and RBD-specific memory B cells, while in SARS-CoV-2-recovered individuals, the first dose robustly expands pre-existing memory B cells, with no additional boosting after the second dose. The baseline for antigen-specific memory B cells in recovered individuals correlates with the antibody response post-first dose, indicating that memory B cells are the major contributors to antibody recall responses post-vaccination. *IV*

https://doi.org/10.1038/s41590-021-00952-y

IMMUNOPATHOGENESIS

Cellular disturbances in COVID-19

Nat. Med. https://doi.org/10.1038/s41591-021-01329-2 (2021).
Nature https://doi.org/10.1038/s41586-021-03570-8 (2021).

Two recent studies utilizing multi-omics single-cell analyses provide new insights into potential immunopathogenesis associated with severe COVID-19. In *Nature Medicine*, Stephenson et al. performed gene expression analysis on peripheral blood mononuclear cells obtained from a cohort of patients with COVID-19 of varying severity. Notably, they identify a *C1Q*-expressing $CD16^+$ monocyte subset associated with more severe disease. $C1q^+CD16^+$ monocytes had increased interaction with platelets, a finding that is linked with increased platelet activation and increased frequencies of mobilized megakaryocyte precursors in patients' blood. In *Nature*, Delorey et al. present a single-cell and spatial cell atlas of gene expression in lung samples obtained at autopsy of patients with critical COVID-19. They show severe reductions in lung AT2 epithelial cells along with reduced surfactant production and perturbations in the regeneration of AT1 epithelial cells, which ultimately lead to compromised lung function. Both studies can serve as rich dataset resources for further hypothesis-driven investigations of COVID-19-associated immunopathology. *LAD*

https://doi.org/10.1038/s41590-021-00953-x

FUNGAL IMMUNITY

Macrophages do origami

Proc. Natl Acad. Sci. USA https://doi.org/10.1073/pnas.2020484118 (2021).

Macrophage-mediated phagocytosis is a major mechanism for controlling fungal infection; however, dimorphic fungi such as *Candida* are thought to counter this by assuming hyphal forms, which, by their sheer size, are challenging to engulf. In the *Proceedings of the National Academy of Sciences*, Brown and colleagues describe a mechanism by which macrophages can handle large hyphae. Using live cell imaging, the authors observe that macrophages are able to fold hyphae—often several cell diameters in length—into more manageable pieces that can be readily engulfed. Effective hyphal folding is dependent on macrophages exerting mechanical forces via their cytoskeleton and expressing both the fungal pattern-recognition receptor Dectin-1 and β2 integrin. This may be a generalized mechanism carried out by macrophages, since cells from a variety of sources are able to carry out this process and can do so to hyphae of distinct fungal species. Folding physically damages the hyphae and impairs their viability; therefore, mechanical damage can be added to the antimicrobial arsenal of macrophages. *ZF*

https://doi.org/10.1038/s41590-021-00955-9

NEUROIMMUNOLOGY

Illuminating the nervous system to treat colitis

Immunity https://doi.org/10.1016/j.immuni.2021.04.007 (2021).

The nervous system can exert control over the immune system via sympathetic innervation of immune organs, but tissue-specific functions are difficult to analyze. A study now published in *Immunity* by Schiller et al. utilizes optogenetic technology to overcome this limitation and shows that sympathetic signaling in the colon can limit dextran sulfate sodium–induced colitis in mice. The authors crossed channelrhodopsin-2 (Chr-2) mice with a tyrosine hydroxylase-Cre line to make mice that express Chr-2 in sympathetic neurons. Next they inserted a blue light–emitting probe intrarectally into the colon to photostimulate these cells, reducing local inflammation and increasing barrier function, an effect they attribute to sympathetic inhibition of the expression of MAdCAM-1, an endothelial adhesion protein that drives extravasation of immune cells. Although high MAdCAM-1 expression is already associated with intestinal inflammation in humans and is thereby already a potential therapeutic target, this paper elegantly demonstrates how sympathetic signals can control localized immune responses to affect health and disease. *NJB*

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