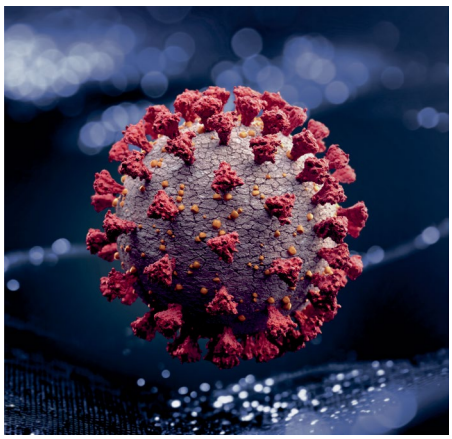
COVID-19

Changing the baseline



Whether and how baseline immune states may be altered by viral infections remains unclear. In *Nature*, Tsang and colleagues evaluated the immune responses to vaccination against influenza in healthy people who had not been vaccinated against COVID-19 and had recovered from non-severe COVID-19 (COVR; $n = 33$) versus those of age- and sex-matched control participants who had never had COVID-19 (HC; $n = 44$). Up to 150 days after COVID-19, monocyte frequencies were higher in male COVR participants than in female COVR or male HC participants, whereas male and female COVR participants had higher transcriptional signatures of T cell activation and lower expression of innate immune receptors in monocytes than those of HC participants. After vaccination against influenza, male COVR participants had stronger inflammatory responses, in particular interferon-γ-related transcriptional responses, and stronger influenza-specific antibody responses than those of male HC or female COVR participants, which correlated with enrichment for effector memory $GPR56^{+}CD8^{+}$ T cells that make interferon-γ in response to the cytokines IL-15, IL-12 and IL-18 (possibly in an antigen-independent manner) in male COVR participants before vaccination. Vaccination against influenza normalized the innate immune receptor transcriptional signature in monocytes, especially in female COVR participants, although the functional relevance of this change remains to be determined.

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Original reference: *Nature* https://doi.org/10.1038/s41586-022-05670-5 (2023)

Neuroimmunology

Aging in the CSF

Cerebrospinal fluid (CSF) contains populations of immune cells that are changed during Alzheimer's disease and dementia. In *Cell*, Piehl et al. provide in-depth profiling of the CSF from cognitively normal participants during aging and compared this with that of individuals with cognitive impairment (CI). T cells and non-classical monocytes were the most changed with age. Within the monocyte population, the expression of genes associated with lipid transport was increased with age but was decreased in individuals with CI. Non-classical monocytes were predicted to interact with $CD8^{+}$ T cells in all individuals, but communication between these populations via CXCL16 and CXCR6 was unique to individuals with CI. Transcriptionally, T cells from individuals with CI were more similar to those from older individuals than to those from younger individuals, and T cell clonal expansion was suggested as a driver of transcriptional dysregulation. Taken together, these data show that there are substantial changes to immune cell populations in the CSF during aging and CI.

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