**RESEARCH HIGHLIGHTS**

**IN BRIEF**

**COVID-19**

Cross-reactive memory T cells abort SARS-CoV-2 infection

A study in health-care workers showed that some people, despite likely exposure to SARS-CoV-2, never develop PCR or antibody positivity. Swadling et al. hypothesized that pre-existing cross-reactive memory T cells, as described in pre-pandemic samples, may lead to abortive seronegative infections in these individuals. Indeed, they found T cell and innate transcript evidence for abortive infections. They also showed that these individuals frequently had memory T cells directed at the early transcribed replication transcription complex, which has high sequence conservation between human seasonal coronaviruses and SARS-CoV-2. Boosting such T cells with vaccines may allow for pan-reactivity against endemic and emerging coronaviruses.

**ORIGINAL ARTICLE** Swadling, L. et al. Pre-existing polymerase-specific T cells expand in abortive seronegative SARS-CoV-2. Nature https://doi.org/10.1038/s41586-021-04186-8 (2021)

**COVID-19**

Defective viral genomes can protect against SARS-CoV-2 variants and other respiratory viruses

Based on the unexpected observation that the Sabin Poliovirus vaccine not only protects against polio but also against other viruses, Andino and colleagues explored whether virus-like entities can be used as broad-spectrum antivirals to stimulate innate immune defences. They generated a liposome-encapsulated poliovirus-derived defective viral genome (eTIP1) that was administered intranasally to mice infected with different respiratory viruses, including influenza, SARS-CoV-2 and its Alpha, Delta and Epsilon variants. eTIP1 reduced viral loads, facilitated adaptive immune responses and prevented lethal infections when given up to 48 hours before to 24 hours after viral exposure. Protection was dependent on eTIP1 being replication competent. The authors hypothesize that, by mimicking natural infection, eTIP1 recruits different arms of immunity, providing a potentially powerful broad-spectrum prophylactic and therapeutic weapon.

**ORIGINAL ARTICLE** Xiao, Y. et al. A defective viral genome strategy elicits broad protective immunity against respiratory viruses. Cell https://doi.org/10.1016/j.cell.2021.11.023 (2021)

**COVID-19**

Dexamethasone restrains neutrophils in severe COVID-19

Dexamethasone reduces mortality in patients with severe COVID-19, but the mechanism has been elusive. Using single-cell RNA sequencing and plasma proteomics, Rosin, Yipp, Biernaskie and colleagues investigated immune cell dynamics in patients with severe COVID-19 and acute respiratory distress syndrome (ARDS) who either did or did not receive dexamethasone, and compared these to patients with bacterial ARDS and healthy volunteers. COVID-19 seemed to promote the enrichment of specific neutrophil states characterized by increased type I interferon (IFN) activation (IFNactive) or by prostaglandin signaling. Dexamethasone treatment was associated with global alterations in neutrophil sub-states, a suppression of IFN networks, a depletion of IFNactive neutrophils and an expansion of immature and immunosuppressive neutrophils, indicating that dexamethasone limits neutrophil pathogenicity.

**ORIGINAL ARTICLE** Sinha, S. et al. Dexamethasone modulates immature neutrophils and interferon programming in severe COVID-19. Nat. Med. https://doi.org/10.1038/s41591-021-01576-z (2021)