**RESEARCH HIGHLIGHTS**

**IN BRIEF**

**Covid-19**

**SARS-CoV-2 has a sweet tooth**

To help understand why uncontrolled diabetes is a risk factor for severe COVID-19, Campos Codo et al. looked at the relationship between glycolysis and SARS-CoV-2 replication in monocytes. Glucose enhanced SARS-CoV-2 viral load and mRNA expression of pro-inflammatory cytokines and type I/III interferons in these cells in a dose-dependent manner. Pretreating human peripheral blood monocytes with metabolic inhibitors showed that these effects of glucose depend on mitochondrial reactive oxygen species (mtROS) and HIF1α. The transition to aerobic glycolysis in SARS-CoV-2-infected monocytes facilitated viral replication and the production of soluble mediators that may contribute to lung damage. Additional studies are needed to investigate the potential for therapeutic targeting of mtROS, HIF1α and glycolysis signalling while maintaining antiviral type I/III interferons.

**ORIGINAL ARTICLE** Campos Codo, A. et al. Elevated glucose levels favor Sars-Cov-2 infection and monocyte response through a HIF-1α/glycolysis dependent axis. Preprint at bioRxiv https://doi.org/10.1101/2020.05.27.118870 (2020)

**Covid-19**

**A versatile mouse model of COVID-19**

Israelow et al. report a novel mouse model of COVID-19 using adeno-associated virus (AAV)-mediated expression of human ACE2 (hACE2) in the respiratory tract, which supports productive SARS-CoV-2 infection. Infected mice had acute infiltration of innate and adaptive immune cells to the lungs and developed specific neutralizing antibodies. Transcriptomic analysis showed robust upregulation of cytokines and of interferon-stimulated genes (ISGs), largely overlapping with the signature seen in patient lungs. A key advantage of this model is its application to mice of different genetic backgrounds and age. Infection of AAV-hACE2 mice lacking IFNAR1 or IRF3 and IRF7 showed that type I interferon signalling is required for ISG expression and the recruitment of pro-inflammatory cells to the lungs during infection. Potential future applications of this model include testing therapeutics and vaccines for COVID-19.

**ORIGINAL ARTICLE** Israelow, B. et al. Mouse model of SARS-CoV-2 reveals inflammatory role of type I interferon signalling. Preprint at bioRxiv https://doi.org/10.1101/2020.05.27.118871 (2020)

**Covid-19**

**Neutralizing antibodies in convalescent patients**

In a cohort of 149 convalescent patients with variable COVID-19 severity, Robbiani et al. report an overall low neutralizing capacity of plasma serum for SARS-CoV-2. Repertoire analysis of six representative convalescent patients revealed the presence of recurrent and clonally expanded IgG+ B cells, with specific IGHV and IGKV gene combinations being shared between different individuals. Potent neutralizing antibodies were found in individuals independently of their overall serum neutralizing capacity. Furthermore, the antibodies targeted distinct neutralizing epitopes on the SARS-CoV-2 glycoprotein spike. These findings indicate that despite low plasma neutralizing capacity, most individuals can generate potent IgG neutralizing antibodies independently of the severity of their symptoms, which has important implications for the design of an effective vaccine.

**ORIGINAL ARTICLE** Robbiani, D. F. et al. Convergent antibody responses to SARS-CoV-2 infection in convalescent individuals. Preprint at bioRxiv https://doi.org/10.1101/2020.05.27.118019 (2020)

**MACROPHAGES**

**Peritoneal sex differences**

Body cavity macrophages have crucial roles in immune surveillance. Of these, peritoneal macrophages have been best studied, with previous results describing differences between the sexes in terms of in vitro function. Bain et al. now show that the sexual dimorphism of peritoneal macrophages is determined by differences in both their rate of turnover and environmental signals.

The major peritoneal macrophage population consists of long-lived F4/80+CD102+ cells that derive from embryonic progenitors but are later replaced by bone marrow-derived cells. Previous studies have shown that their rate of turnover is higher in male mice than in female mice. Using sex-matched or sex-mismatched, tissue-protected bone marrow chimeric mice, Bain et al. show that this dimorphism is driven by the peritoneal environment rather than cell-intrinsic differences. Furthermore, using a genetic fate-mapping approach, they show that in prepubescent mice the frequency of newly differentiated F4/80+CD102+ macrophages is the same in male and female mice, whereas by sexual maturity male mice have more newly differentiated macrophages. Bilateral ovariectomy increased the rate of macrophage turnover in female mice, which was not reversed by exogenous oestriol. Thus, the female reproductive system decreases the turnover of peritoneal F4/80+CD102+ macrophages in an oestriol-independent manner.