nerve activity are T cell dependent. It is known that choline acetyltransferase-expressing (ChAT⁺) T cells synthesize and release acetylcholine in response to noradrenergic stimulation. Here, the authors show that NP-KLH immunization increases ChAT⁺ T cell numbers in the spleen, and ablation of these cells suppresses the generation of SPPCs.

This implies that the differentiation of SPPCs may be enhanced by acetylcholine and, indeed, the authors show that nicotinic acetylcholine receptor (nAChR) subunits are expressed by spleen B cells. Next, they transplanted bone marrow cells from animals in which the α9 nAChR subunit gene was deleted into irradiated mice. The capacity of these animals to produce SPPCs following NP-KLH immunization was impaired, indicating that splenic nerve activity enhances SPPC production through the activation of B cell nAChRs.

Many autonomic responses are subject to top-down modulation by the brain. Through viral-mediated retrograde tracing, optogenetic stimulation and electrophysiological recordings, the authors showed that with a T cell-specific Tfam deficiency (Tfam⁻/⁻ Lck⁻/⁻ mice) and these animals also showed premature age-associated multimorbidity.

Why then does loss of mitochondrial function in T cells have this effect? Transcriptomics showed upregulation of senescence-associated markers (including p21) in various tissues of Tfam⁻/⁻ Cd4⁺ and Tfam⁻/⁻ Lck⁻/⁻ mice. Incubation of hepatocytes or pre-adipocytes with serum from Tfam⁻/⁻ Cd4⁺ mice or with TNF was sufficient to induce p21 expression, suggesting that the increased expression of pro-inflammatory cytokines in T cells with defective mitochondria may drive senescence and morbidity.

In support of this idea, TNF blockade prevented systemic senescence and multi-morbidity in Tfam⁻/⁻ Cd4⁺ mice. Boosting levels of the metabolic cofactor NAD⁺ (which is known to decline during ageing) also had a protective effect in Tfam⁻/⁻ Cd4⁺ mice. The authors propose that these new mouse models could help to identify other beneficial immunotherapies for patients with age-associated inflammatory diseases.

Yvonne Borden

**ORIGINAL ARTICLE** Desdín-Micó, G. et al. T cells with dysfunctional mitochondria induce multimorbidity and premature senescence. Science 370, 860 (2020)

**COVID-19**

**ResearCh highlights**

**COVID-19**

**IN BRIEF**

**COVID-19**

**Innate T cells in COVID-19: friend or foe?**

Jouan et al. report reduced frequencies of mucosal-associated invariant T (MAIT) cells and invariant natural killer T (iNKT) cells in peripheral blood of critically ill patients with COVID-19-induced ARDS. By contrast, MAIT cells were increased in endotracheal aspirate (ETA) samples, suggesting enhanced recruitment to the airways. Moreover, ETA innate T cells were more activated in samples with higher pro-inflammatory cytokine levels, suggesting that innate T cells contribute to local inflammation. In early COVID-19, the level of MAIT and iNKT cell activation in peripheral blood correlated with preserved lung oxygenation, suggesting that activation status of innate T cells may be predictive of disease severity. Further studies are needed to dissect the potentially ambiguous role of innate T cells in COVID-19.

**ORIGINAL ARTICLE** Jouan, Y. et al. Functional alteration of innate T cells in critically ill Covid-19 patients. Preprint at medRxiv https://doi.org/10.1101/2020.05.01.20089394 (2020)

**COVID-19**

Kawasaki disease linked to COVID-19 in children

An unusually high incidence of Kawasaki disease in children was reported in a French centre for emerging infectious diseases: 17 cases in 11 days, in contrast to an average of 2 cases per month in 2018–2019. In 82% of the cases, IgG antibodies for SARS-CoV-2 were detected, suggesting an association between the virus and this syndrome in children. Although only six patients had recent history of an acute respiratory infection, all patients had gastrointestinal symptoms before the onset of Kawasaki disease symptoms. Remarkably, almost 60% of the patients originated from sub-Saharan Africa or Caribbean islands, and 12% from Asia, raising a possible genetic predisposition. Although Kawasaki disease-like syndromes have previously been linked to other viral infections, these patients showed higher levels of pro-inflammatory markers than other cohorts, which may reflect a particularly strong immunological reaction to SARS-CoV-2.

**ORIGINAL ARTICLE** Toubiana, J. et al. Outbreak of Kawasaki disease in children during COVID-19 pandemic: a prospective observational study in Paris, France. Preprint at medRxiv https://doi.org/10.1101/2020.05.10.20097394 (2020)

**COVID-19**

Risk factors for death from COVID-19

To identify risk factors for hospital deaths from COVID-19, the OpenSAFELY platform examined electronic health records from 17.4 million UK adults. The authors used multivariable Cox proportional hazards model to identify the association of risk of death with older age, lower socioeconomic status, being male, non-white ethnic background and certain clinical conditions (diabetes, obesity, cancer, respiratory diseases, heart, kidney, liver, neurological and autoimmune conditions). Notably, asthma was identified as a risk factor, despite prior suggestion of a potential protective role. Interestingly, higher risks due to ethnicity or lower socioeconomic status could not be completely attributed to pre-existing health conditions.

**ORIGINAL ARTICLE** The OpenSAFELY Collaborative et al. OpenSAFELY factors associated with COVID-19 related hospital death in the linked electronic health records of 17 million adult NHS patients. Preprint at medRxiv https://doi.org/10.1101/2020.05.06.20099299 (2020)

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