nerve activity are T cell dependent. It is known that choline acetyl transferase-expressing (ChAT⁺) T cells synthesize and release acetyl-choline 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 differentia-tion 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 irradi-ated 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 the splenic nerve is functionally connected to corticotropin-releasing hormone (CRH)-producing neurons originating in two particular fore-brain areas known to be involved in the body's responses to stress and threats — the central amygdala and the paraventricular nucleus of the hypothalamus. Genetic ablation or pharmacogenetic inhibition of these neurons impaired SPPC for-mation after immunization, whereas activation of the neurons boosted the number of SPPCs produced. Indeed, exposure of mice to mild stress activated these neurons and stimulated the production of SPPCs after immunization.

This study provides evidence for a direct pathway through which brain activity can tune immune system functioning, adding to our growing understanding of brain–body interconnectivity.

Katherine Whalley, Senior Editor,
Nature Reviews Neuroscience
This article is modified from the original in *Nat. Rev. Neurosci.* (https://doi.org/10.1038/s41583-020-0316-0)

ORIGINAL ARTICLE Zhang, X. et al. Brain control of humoral immune responses amenable to behavioural modulation. *Nature* **581**, 204–208 (2020)

Credit: Ievgen Chabanov/Alamy

with a T cell-specific *Tfam* deficiency (*Tfam^fl/fl Lck^Cre* mice) and these animals also showed premature age-associated multi-morbidity.

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^fl/fl Cd4^Cre* and *Tfam^fl/fl Lck^Cre* mice. Incubation of hepatocytes or pre-adipocytes with serum from *Tfam^fl/fl Cd4^Cre* mice or with TNF was sufficient to induce p21 expression, suggesting that the increased expres-sion 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^fl/fl Cd4^Cre* mice. Boosting levels of the metabolic cofactor NAD⁺ (which is known to decline during ageing) also had a protective effect in *Tfam^fl/fl Cd4^Cre* mice. The authors propose that these new mouse models could help to identify other beneficial therapeutics for patients with age-associated inflammatory diseases.

Yvonne Bordon

ORIGINAL ARTICLE Desdín-Micó, G. et al. T cells with dysfunctional mitochondria induce multimorbidity and premature senescence. *Science* https://doi.org/10.1126/science.aax0860 (2020)

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/10.1101/2020.05.03.20089300 (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 socio-economic status, being male, non-white ethnic back-ground 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 socio-economic 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/10.1101/2020.05.06.20092999 (2020)

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The authors declare no competing interests.