Credit: RUNSTUDIO/Getty

sialylated ligands but not those masked by 9-O-acetylation, so the authors investigated whether pregnancy-induced deacetylation of IgG stimulates CD22-dependent inhibition of B cells. CD22 was shown to be essential for the protective efficacy of pIgG in neonatal mice, but vIgG efficiently protected B cell-deficient neonates from *Lm* infection. Together, the results suggest that a subset of neonatal B cells suppresses IgG-mediated protection against *Lm* but that pregnancy-induced modification of *Lm*-specific antibodies enables CD22 binding and inhibition of the suppressive B cell subset.

B cells producing the immunosuppressive cytokine IL-10 have been previously shown to promote *Lm* susceptibility, and in this study, pIgG but not vIgG was shown to inhibit IL-10 production by these cells in a CD22-dependent manner. As pIgG selectively inhibited *Lm*-activated B cells, the authors propose that IgG may bridge activating and inhibitory receptors on B cells by simultaneously binding *Lm* and CD22.

In summary, SIAE-mediated deacetylation of antibodies during pregnancy allows for maternally transferred IgG to inhibit a regulatory B cell population in neonates, which in turn presumably prevents the IL-10-mediated suppression of innate immune responses to *Lm*.

Kirsty Minton

ORIGINAL ARTICLE Erickson, J. J. et al. Pregnancy enables antibody protection against intracellular infection. *Nature* https://doi.org/10.1038/s41586-022-04816-9 (2022)

that these are not only upregulated in germinal centre B cells, where the RNA exosome is known to be involved in class switch recombination and somatic hypermutation, but also during B cell development in the bone marrow and fetal liver.

As observed with *Skiv2l*, conditional deletion of *Exosc10*, *Dis3* or *Exosc3* in early mouse B cells also led to a developmental block at the pro/pre-B cell stage and to defective V(D)J rearrangement. A knock-in of *VDJ* genes at the IgH locus partly rescued the pre-B cell population in *Dis3*-deficient mice, but these cells then showed defective V-J recombination at the κ light chain locus (the λ light chain locus was less affected). Transcriptomic analysis revealed an accumulation of noncoding RNAs (ncRNAs) in the absence of *Dis3*, including a marked increase in antisense germline transcription that overlapped the J_H and *D* genes, and an accumulation of ncRNAs on V_H genes and recombination signal sequences. Moreover, gene-set enrichment analysis showed increased expression of p53 pathway-associated genes in *Dis3*-deficient pro-B cells.

The authors hypothesize that germline transcription at the V(D) locus is a consequence of accessible chromatin, and that the resulting ncRNAs are normally resolved by the RNA exosome. If the RNA exosome is defective, the accumulation of chromatin-associated ncRNA or RNA:DNA hybrid-associated non-B DNA structures may interfere with loop extrusion kinetics during V(D)J recombination and DNA binding of the RAG recombinases. This obstructs the first step of D to J_H recombination and leads to p53-mediated apoptosis of pro-B cells.

Together, these studies demonstrate that the RNA exosome is an essential component in the process of V(D)J recombination.

Alexandra Flemming

ORIGINAL ARTICLE Yang, K. et al. The mammalian SKIV2L RNA exosome is essential for early B cell development. *Sci. Immunol.* https://www.science.org/doi/10.1126/sciimmunol.abn2888 (2022) | Laffleur, B. et al. RNA exosome drives early B cell development via noncoding RNA processing mechanisms. *Sci. Immunol.* https://www.science.org/doi/10.1126/sciimmunol.abn2738 (2022)

IN BRIEF

COVID-19

When 'mild' COVID-19 is not so mild

Neurological symptoms are common even after 'mild' COVID-19. Using a mouse model of SARS-CoV-2 infection limited to the respiratory tract, this study shows that even after viral clearance, there is prolonged microglial reactivity in subcortical and hippocampal white matter and increased levels of CCL11 in the cerebrospinal fluid. Loss of myelin-forming oligodendrocytes and reduced hippocampal neurogenesis were also observed. CCL11 administration in mice causes hippocampal microglial reactivity and impaired hippocampal neurogenesis. Increased plasma levels of CCL11 were also observed in patients with Long COVID with cognitive symptoms, and white matter microglial reactivity was observed in patients who died while infected with SARS-CoV-2 without severe COVID-19. Influenza A virus infection also resulted in neuroinflammation but without the prolonged effects on subcortical white matter.

ORIGINAL ARTICLE Fernández-Castañeda, A. et al. Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation. *Cell* https://doi.org/10.1016/j.cell.2022.06.008 (2022)

COVID-19

Neutralization susceptibility of Omicron lineages

Two studies in *Nature* and *Cell* look at the ability of vaccine-induced and infection-induced sera to neutralize the newer BA.2.12.1, BA.4 and BA.5 sublineages of SARS-CoV-2 Omicron compared with BA.1 and BA.2. Tuekprakhon et al. and Cao et al. show that serum from triple-vaccinated individuals (Pfizer, AstraZeneca or CoronaVac), and from vaccinated individuals who experienced a breakthrough infection with BA.1, has reduced ability to neutralize BA.4/5 and BA.2.12.1 compared with BA.1/2 as a result of L452R and F486V (BA.4/5) and L452Q (BA.2.12.1) mutations in the receptor binding domain (RBD). Similar results were reported for most commercially available monoclonal antibodies in terms of further reduced neutralization activity against the newer Omicron sublineages. Tuekprakhon et al. also report that the RBD of BA.4/5 has higher affinity for the host receptor ACE2 than BA.1/2, whereas Cao et al. find that the ACE2-binding affinities are similar.

ORIGINAL ARTICLE Cao, Y. et al. BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection. *Nature* https://doi.org/10.1038/s41586-022-04980-y (2022) | Tuekprakhon, A. et al. Antibody escape of SARS-CoV-2 Omicron BA.4 and BA.5 from vaccine and BA.1 serum. *Cell* https://doi.org/10.1016/j.cell.2022.06.005 (2022)

COVID-19

Mechanistic insights into Long COVID in hamsters

Using a golden hamster model, Frere et al. compared the short- and long-term responses to SARS-CoV-2 and influenza A virus (IAV) infection to better understand the mechanisms that account for persistent COVID-19 symptoms. At 3 days post infection (3dpi), both viruses induced a robust type I interferon response that cleared acute infection from the respiratory tract. Both viruses also induced an acute inflammatory response in peripheral tissues such as heart, kidney and lung, but by 31dpi (which would be defined as Long COVID in humans), SARS-CoV-2-infected hamsters had greater evidence of peripheral organ damage than IAV-infected hamsters. Furthermore, SARS-CoV-2-infected hamsters uniquely had prolonged inflammation in the olfaction system and various brain regions including striatum and cerebellum. This inflammation was evident in the absence of infectious virus and was associated with behavioural changes.

ORIGINAL ARTICLE Frere, J. J. et al. SARS-CoV-2 infection in hamsters and humans results in lasting and unique systemic perturbations post recovery. *Sci. Transl. Med.* https://doi.org/10.1126/scitranslmed.abq3059 (2022)