Credit: lorenzo rossi/Alamy

lungs of basophil-depleted mice on day 7 after infection showed lower levels of neuromedin B receptor (NMBR) expression than ILC2s from control animals, suggesting that basophils regulate ILC2 responses by altering their ability to respond to neuromedin B (NMB).

Consistent with an inhibitory role for NMB, wild-type mice treated with recombinant NMB 7 days after infection showed reduced ILC2 responses and eosinophilia in the lungs. Deletion of NMBR expression by haematopoietic cells mimicked the effects of basophil depletion on *N. brasiliensis* infection. Finally, in vitro studies confirmed a direct effect of NMB on ILC2s. Culturing in the presence of recombinant NMB led to reduced production of IL-5 and IL-13 by lung ILC2s from infected control mice but not from infected basophil-depleted mice, and co-culturing ILC2s with activated basophils resulted in elevated surface expression of NMBR, together indicating that basophils prime ILC2s for NMB-mediated inhibition. This 'priming' was shown to involve expression of prostaglandin E_2 by basophils, which increased NMBR expression and decreased proliferation by ILC2s.

So, basophil-derived prostaglandin E_2 and neuron-derived NMB cooperate to temper ILC2 cytokine production and proliferation, keeping helminth-induced tissue pathology at bay.

Lucy Bird

ORIGINAL ARTICLE Inclan-Rico, J. M. et al. Basophils prime group 2 innate lymphoid cells for neuropeptide-mediated inhibition. *Nat. Immunol.* https://doi.org/10.1038/s41590-020-0753-y (2020)

extravillous trophoblasts, 3D placental villous explants as well as decidual macrophages and dendritic cells, in which decidual NK cells reduced bacterial loads while sparing the infected cells.

To investigate the cell contact dependency of the bacterial killing, the authors tracked cytotoxic mediators in co-culture assays. Granulysin, but not granzyme B, was transferred to infected and non-infected trophoblasts after 3 hours of co-culture with decidual NK cells or activated peripheral NK cells, which have upregulated granulysin expression. By also labelling for actin and lymphocyte function-associated antigen 1 (LFA1), which is expressed by NK cells not trophoblasts, confocal microscopy revealed that NK cells did not form classical immune synapses with JEG-3 cells and instead cytoplasmic extensions resembling nanotubes connected the cells, occurring more frequently from decidual NK cells than from peripheral NK cells. Moreover, granulysin was observed within the nanotubes connecting decidual NK cells and trophoblast cells. Granulysin transfer and bacterial killing was reduced by inhibition of actin polymerization but not by inhibition of endocytosis or microtubule formation, confirming the role for nanotubes.

Lastly, the in vivo relevance was evaluated using mice expressing human granulysin. Uterine NK cells from these mice selectively reduced intracellular bacteria while sparing the infected trophoblasts in vitro, in a granulysin-dependent, perforin-independent manner. Compared with wild-type mice, pregnant granulysin-transgenic mice had much lower bacterial loads in the placenta and fetus and no evidence of systematic spread following infection with *L. monocytogenes*. Most importantly, granulysin-transgenic mice were protected from infection-induced pregnancy loss.

So, delivering cytotoxic molecules via nanotubes ensures that decidual NK cells protect against infection and preserve maternal–fetal tolerance.

Lucy Bird

ORIGINAL ARTICLE Crespo, Â. C. et al. Decidual NK cells transfer granulysin to selectively kill bacteria in trophoblasts. *Cell* https://doi.org/10.1016/j.cell.2020.07.019 (2020)

IN BRIEF

COVID-19

Long-lasting SARS-CoV-2-specific T cell memories

Memory T cells may provide long-term protection against SARS-CoV-2 even if antibodies wane. Screening 26 convalescent patients and 25 healthy donors, the authors of this preprint identified immunodominant SARS-CoV-2 epitopes that elicit pre-existing and newly induced $CD8^+$ T cell responses and measured the frequency, immunophenotype and function of these T cells. Notably, SARS-CoV-2-specific T cells were present even in seronegative convalescent patients. Longitudinal analyses in one patient showed in vivo priming and rapid expansion of SARS-CoV-2-specific $CD8^+$ T cells, followed by a long contraction phase, with T cells but not antibodies still detectable 109 days post infection. Therefore, T cells might help to control SARS-CoV-2 infection and serve as correlates of protective immunity. Further studies are needed to evaluate T cell-mediated protection from reinfection.

ORIGINAL ARTICLE Schulien, I. et al. Ex vivo detection of SARS-CoV-2-specific $CD8^+$ T cells: rapid induction, prolonged contraction, and formation of functional memory. Preprint at *bioRxiv* https://doi.org/10.1101/2020.08.13.249433 (2020)

COVID-19

Immune correlates of SARS-CoV-2 protection

The protective potential of SARS-CoV-2 neutralizing antibodies (nAbs) has not been validated in humans. This preprint study analysed an outbreak on a fishing vessel ($n = 122$) with an infection rate of 85%. Before departure, all individuals with available data ($n = 120$) were negative for SARS-CoV-2 infection by RT-PCR but 6 were positive for IgG against viral nucleoprotein. Of the 6 seropositive individuals, 3 had antibodies to SARS-CoV-2 spike protein and its receptor-binding domain (RBD) that could both neutralize pseudotyped lentiviruses and block the interaction between the RBD and the virus entry receptor ACE2. These 3 individuals did not get infected, unlike the 103 individuals who lacked pre-existing nAbs, suggesting that nAb titres are a correlate of viral immunity and, potentially, vaccine efficacy.

ORIGINAL ARTICLE Addetia, A. et al. Neutralizing antibodies correlate with protection from SARS-CoV-2 in humans during a fishery vessel outbreak with high attack rate. Preprint at *medRxiv* https://doi.org/10.1101/2020.08.13.20173161 (2020)

COVID-19

Inhaled nanobodies against COVID-19

Nanobodies (Nbs) are naturally occurring single-domain antibody fragments from camelid heavy-chain antibodies. They have unique biophysical properties, including small size and thermostability, that allow aerosolized administration. In this preprint, Gai et al. describe Nb phage display libraries from camels immunized with the SARS-CoV-2 spike receptor-binding domain (RBD). Out of 381 Nbs identified, 7 blocked the interaction between the virus entry receptor ACE2 and 8 RBD variants. Nb11-59, a candidate with the highest neutralizing activity, was further selected to validate its interaction with the RBD by structure prediction analysis. Production of Nb11-59 in a yeast expression system followed by its nebulization showed potential for rapid and high-quality manufacturing.

ORIGINAL ARTICLE Gai, J. et al. A potent neutralizing nanobody against SARS-CoV-2 with inhaled delivery potential. Preprint at *bioRxiv* https://doi.org/10.1101/2020.08.09.242867 (2020)

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The authors declare no competing interests.