

IN BRIEF

IMMUNE TOLERANCE

Regulatory T cells require constant reassurance

Regulatory T (T_{Reg}) cells require T cell receptor (TCR) signalling for their development, but it has been unclear how TCR signals contribute to their functions in the periphery. Vahl *et al.* used an inducible deletion system to specifically ablate TCR expression on mature peripheral T_{Reg} cells in mice. They found that TCR ablation did not affect T_{Reg} cell expression of forkhead box P3 (FOXP3) or epigenetic remodelling at key T_{Reg} cell-associated gene loci. TCR ablation also did not affect T_{Reg} cell expression of molecules that are required for lymph node homing. However, T_{Reg} cells lacking TCRs did not undergo homeostatic proliferation and were progressively lost from the periphery. Furthermore, TCR-deficient T_{Reg} cells lost their expression of key anti-inflammatory mediators, including interleukin-10. Finally, ablation of TCR expression on T_{Reg} cells led to the spontaneous development of colitis and splenomegaly in mice. Therefore, continuous restimulation through the TCR seems to be essential for the suppressive functions of T_{Reg} cells.

ORIGINAL RESEARCH PAPER Vahl, J. C. *et al.* Continuous T cell receptor signals maintain a functional regulatory T cell pool. *Immunity* <http://dx.doi.org/10.1016/j.immuni.2014.10.012> (2014)

REPRODUCTIVE IMMUNOLOGY

Hyaluronan protects the cervix from infection

During the later stages of pregnancy there is increased synthesis of cervical hyaluronan and it has been assumed that this is important for remodelling of the cervix to facilitate birth. Surprisingly, when Akgul *et al.* conditionally depleted hyaluronan from the female reproductive tract in mice, they found that this did not affect tissue compliance and matrix remodelling in the cervix during pregnancy and parturition. Instead, hyaluronan depletion compromised cervical epithelial cell differentiation and led to disruption of epithelial barrier function. This increased the susceptibility of mice to vaginal bacterial infections, with hyaluronan-depleted mice showing increased rates of preterm birth in response to vaginal inoculation with *Escherichia coli*. These findings may aid in the development of new therapies for preterm birth, which is responsible for 3.3 million perinatal deaths globally each year.

ORIGINAL RESEARCH PAPER Akgul, Y. *et al.* Hyaluronan in cervical epithelia protects against infection-mediated preterm birth. *J. Clin. Invest.* <http://dx.doi.org/10.1172/JCI78765> (2014)

ANTIVIRAL IMMUNITY

Whipping up a remedy for rotavirus infection

Rotavirus infection is a major cause of gastroenteritis and 600,000 infants die from this infection each year. This study shows that treatment with bacterial flagellin can protect mice against subsequent infection with rotavirus and promote the clearance of this virus from chronically infected mice. Flagellin induced protective immunity by activating both Toll-like receptor 5 (TLR5) and NOD-, LRR- and CARD-containing 4 (NLRC4), leading to the production of interleukin-22 (IL-22) and IL-18, respectively. These cytokines seemed to operate via distinct antiviral mechanisms; IL-22 induced protective gene expression in intestinal epithelial cells, whereas IL-18 upregulated a pro-apoptotic pathway. Co-treatment with IL-18 and IL-22 recapitulated the protective effects of flagellin, suggesting that these cytokines could have antiviral applications in the clinic.

ORIGINAL RESEARCH PAPER Zhang B. *et al.* Prevention and cure of rotavirus infection via TLR5/NLRC4-mediated production of IL-22 and IL-18. *Science* <http://dx.doi.org/10.1126/science.1256999> (2014)