IN BRIEF

SIGNALLING

NF-κB signalosomes on the ER

This study shows that stimulation of a range of innate and adaptive immune receptors results in the accumulation of ubiquitylated components of the nuclear factor-κB (NF-κB) signalling cascade on the cytoplasmic leaflet of the endoplasmic reticulum (ER) membrane. ER membrane fractions from stimulated cells could activate inhibitor of NF-κB kinase (IKK) in a cell-free system, which indicates that the ER membrane anchors a signalosome that is sufficient to propagate NF-κB signalling. The ER-resident protein metadherin was shown to associate with ubiquitylated NF-κB signalling components, and knockdown of metadherin in both B and T cells inhibited the accumulation of ubiquitylated signalling components on the ER and selectively decreased NF-κB activation downstream of various immune receptors. The results support a role for the ER in outside-in signalling.

ORIGINAL RESEARCH PAPER Alexia, C. *et al.* The endoplasmic reticulum acts as a platform for ubiquitylated components of nuclear factor κB signaling. *Sci. Signal.* **291**, ra79 (2013)

REPRODUCTIVE IMMUNOLOGY

How NK cells affect pregnancy outcome

Interactions between killer cell immunoglobulin-like receptors (KIRs) expressed by maternal decidual natural killer (NK) cells and HLA-C molecules expressed by fetal trophoblast cells affect the extent of trophoblast invasion of the maternal blood supply by unknown mechanisms. This study reports that decidual NK cells expressing the activating receptor KIR2DS1 produce greater amounts of granulocyte–macrophage colony-stimulating factor (GM-CSF) in response to HLA-C2 than NK cells expressing the inhibitory receptor KIR2DL1 or those expressing both KIR2DS1 and KIR2DL1. Trophoblast cells were shown to express GM-CSF receptor-α, and stimulation with GM-CSF increased their migration through fibronectin-coated transwells. The authors suggest that women expressing KIR2DL1, with or without KIR2DS2, who carry a HLA-C2^{+} fetus will have decreased GM-CSF production in the decidua and hence decreased trophoblast invasion, which correlates with pregnancy disorders such as pre-eclampsia and fetal growth restriction.

ORIGINAL RESEARCH PAPER Xiong, S. *et al.* Maternal uterine NK cell-activating receptor KIR2DS1 enhances placentation. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI68991 (2013)

IMMUNE REGULATION

IL-27 induces immunosuppressive DCs

This study shows that, instead of directly affecting T cells as was previously thought, interleukin-27 (IL-27) modulates dendritic cells (DCs) to suppress T cells. Pretreatment of DCs with IL-27 decreased their ability to promote the differentiation of T helper 1 (T_H1) and T_H17 cells and increased their ability to generate regulatory T cells. Consistent with the increased induction of pathogenic T_H cell subsets, chimeric mice containing IL-27 receptor α-chain (IL-27RA)-deficient DCs developed faster onset and more severe experimental autoimmune encephalomyelitis (EAE) than control mice. Microarray analysis of IL-27-treated DCs showed upregulation of expression of CD39, which reduced extracellular concentrations of ATP and suppressed nucleotide-dependent activation of NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3). Finally, vaccination with IL-27-conditioned DCs suppressed EAE and reduced epitope spreading.

ORIGINAL RESEARCH PAPER Mascanfroni, I. D. *et al.* IL-27 acts on DCs to suppress the T cell response and autoimmunity by inducing expression of the immunoregulatory molecule CD39. *Nature Immunol.* http://dx.doi.org/10.1038/ni.2695 (2013)