IN BRIEF

DENDRITIC CELLS

Defective antiviral functions in neonatal DCs

Ruckwardt *et al.* have compared how adult and neonatal dendritic cells (DCs) respond to respiratory syncytial virus (RSV) infection in mice. They focused on tissue-resident $CD103^+$ and $CD11b^+$ DCs, which capture antigen in the lungs and migrate to the mediastinal lymph nodes (MLNs). The authors found that both DC subsets can be directly infected by RSV and can induce $CD8^+$ T cell activation. However, the antiviral DC response is markedly affected by age. Following RSV infection, neonates had tenfold fewer $CD11b^+$ DCs in the MLNs compared with adult mice. Neonatal DCs also showed defects in antigen uptake and processing, and expressed lower levels of co-stimulatory molecules. Finally, adult and neonatal DCs preferentially expanded distinct populations of RSV-specific $CD8^+$ T cells. These differences in DC function could explain why neonates are so vulnerable to RSV infection.

ORIGINAL RESEARCH PAPER Ruckwardt, T. J. *et al.* Quantitative and qualitative deficits in neonatal lung-migratory dendritic cells impact the generation of the $CD8^+$ T cell response. *PLoS Pathog.* http://dx.doi.org/10.1371/journal.ppat.1003934 (2014)

T CELLS

Memory cells need more (not less) antigen

Current dogma implies that the ability of memory T cells to respond rapidly to repeat encounters with antigen is due to a minimal requirement for co-stimulation and antigen. However, a new study suggests that naive $CD8^+$ T cells, but not central memory $CD8^+$ T cells, proliferate in response to low levels of antigen. This study shows that although both naive and memory T cells are stimulated by low antigen doses *in vivo*, only naive T cells enter the cell cycle. This effect is intrinsic to naive T cells owing to the degradation of the cyclin-dependent kinase inhibitor p27 and the activation of cell cycle effectors in response to low antigen levels. Compared with naive T cells, central memory T cells less efficiently activate the T cell receptor (TCR) signalling component ZAP70, have lower levels of surface TCR and have higher levels of protein tyrosine phosphatases that inhibit TCR signalling. Together, this suggests that memory $CD8^+$ T cells require stronger TCR stimulation than naive $CD8^+$ T cells to enter the cell cycle, which may safeguard against harmful reactions to self antigen.

ORIGINAL RESEARCH PAPER Mehlhop-Williams, E. R. & Bevan, M. J. Memory $CD8^+$ T cells exhibit increased antigen threshold requirements for recall proliferation. *J. Exp. Med.* http://dx.doi.org/10.1084/jem.20131271 (2014)

INFLAMMATION

To sleep, perchance to DREAM

DRE-antagonist modulator (DREAM) is a transcriptional repressor that binds to downstream regulatory elements (DREs) in its target genes. This study shows that DREAM binds to the gene encoding the deubiquitinase A20, repressing its transcription and promoting inflammation. *Dream*$^{-/-}$ mice survived severe lipopolysaccharide (LPS)-induced lung injury better than wild-type mice, showing reduced neutrophil influx and pro-inflammatory cytokine production. Knockdown of A20 expression in *Dream*$^{-/-}$ mice confirmed that upregulated A20 was responsible for limiting inflammation in these mice. DNA-binding analysis revealed that, in the presence of LPS, DREAM binding to the promoter of the gene encoding A20 is replaced by the transcription factor upstream stimulatory factor 1 (USF1), which suggests a coordinated regulation of A20 transcription by DREAM and USF1. DREAM-mediated suppression of A20 expression enabled the activation of nuclear factor-κB signalling and the downstream target genes responsible for inflammation.

ORIGINAL RESEARCH PAPER Tiruppathi, C. *et al.* The transcription factor DREAM represses the deubiquitinase A20 and mediates inflammation. *Nature Immunol.* http://dx.doi.org/10.1038/ni.2823 (2014)