IN BRIEF

T CELLS

Memory CD4 T cells emerge from effector T-cell progenitors.

Harrington, L. E. *et al. Nature* 5 March 2008 (doi:10.1038/nature06672)

CD8$^+$ T cells undergo a large clonal expansion in response to some infections, so it has been reasonably easy to show that long-lived memory CD8$^+$ T cells arise from effector T cells. By contrast, fewer CD4$^+$ T cells are generated during infection and it has therefore proved more challenging to determine the origin of memory CD4$^+$ T cells. Harrington and colleagues have developed two new cytokine reporter mouse models in which effector T cells producing interferon-γ after infection with lymphocytic choriomeningitis virus were stably marked and in which they could track the development of memory T cells from both CD4$^+$ and CD8$^+$ T-cell effectors. Their results show that, in responding to the same pathogen, a similar relationship exists between effector and memory CD4$^+$ T cells as has previously been shown for CD8$^+$ T cells.

INNATE IMMUNITY

UNC93B1 delivers nucleotide-sensing toll-like receptors to endolysosomes.

Kim, Y.-M. *et al. Nature* **452**, 234–238 (2008)

The membrane protein UNC93B1 is known to physically interact with the nucleotide-sensing Toll-like receptors (TLRs; TLR3, TLR7 and TLR9) that are located in endosomes, and is crucial for signalling through these receptors. It is now shown that UNC93B1 delivers these TLRs from the endoplasmic reticulum (ER) to the endosomes. Accordingly, stimulation of wild-type bone-marrow dendritic cells (BMDCs) with nucleic-acid ligands led to the re-localization of TLR7 and TLR9 from the ER to the endosomes. By contrast, in BMDCs expressing a mutant form of UNC93B1 that abrogates the interaction with these receptors, TLR7 and TLR9 remained in the ER. TLR9 also failed to translocate to phagosomes in UNC93B1-mutant cells incubated with polystyrene beads; this might explain the defect in cross-presentation observed in these cells. The trafficking of mutant UNC93B1 itself was also defective, and it is thought that this could be due to disruption of interactions with another as-yet-unidentified protein.

HIV

Transcription factor FOXO3a controls the persistence of memory CD4$^+$ T cells during HIV infection.

van Grevenynghe, J. *et al. Nature Med.* **3**, 266–274 (2008)

If we could understand how HIV infection is naturally controlled in some infected individuals (referred to as elite controllers), we may stand a better chance of fighting the disease in other patients. Here, the authors provide a mechanism to explain how memory CD4$^+$ T-cell responses are maintained in elite controllers. Memory CD4$^+$ T cells from elite controllers were shown to be less susceptible to FAS-mediated apoptosis and persisted longer after stimulation *in vitro* compared with cells from aviremic successfully treated subjects or HIV-negative controls. This increased T-cell survival correlated with increased phosphorylation of the transcription factor FOXO3A, which led to inhibition of anti-apoptotic gene transcription. Accordingly, knockdown of FOXO3A expression extended the survival of cells from treated aviremic subjects to a level equal to that of elite controllers, suggesting that interference of the FOXO3A pathway could be a therapeutic strategy against HIV.