IN BRIEF

HAEMATOPOIESIS

Regulation of lymphoid versus myeloid fate 'choice' by the transcription factor Mef2c

Stehling-Sun, S. *et al. Nature Immunol.* 25 Jan 2009 (doi:10.1038/ni.1694)

This study describes a new function for myocyte enhancer factor 2c (MEF2c) as a crucial component of the transcriptional network that regulates the fate of multipotent progenitor cells. MEF2c deficiency in haematopoietic stem cells and early progenitor cells led to defective generation of B cells, T cells, natural killer cells and common lymphoid progenitors owing to a block in development at the lymphoid-primed multipotent progenitor (LMPP) stage. By contrast, MEF2c deficiency led to increased myeloid-cell development, even in conditions that promote lymphoid-cell differentiation. Gene expression profiling revealed that MEF2c is required for the transcription of lymphoid-cell-associated factors, but it antagonizes the transcription of the myeloid-cell-associated factor CCAAT/enhancer-binding protein-α (C/EBPα). Further analysis indicated that MEF2c functions downstream of the transcription factor PU.1 to promote lymphoid-cell development.

T-CELL RESPONSES

Complete but curtailed T-cell response to very low-affinity antigen

Zehnm, D., Lee, S. Y. & Bevan, M. J. *Nature* 28 Jan 2009 (doi:10.1038/nature07657)

This study challenges the prevailing view that high-affinity T-cell receptor (TCR) ligation is required for T-cell activation. The authors looked at the responses of OT-I TCR-transgenic T cells transferred into mice that were then infected with *Listeria monocytogenes* engineered to express ovalbumin peptides that bind the OT-I TCR with varying affinities. They found that even very weak TCR–ligand interactions were sufficient to activate naive T cells, induce initial proliferation and generate effector and memory T cells. However, the weaker the ligand, the earlier the cells reached their proliferative limit and began to contract. Weakly stimulated T cells also exited the lymphoid organs sooner than those stimulated by high-affinity ligands. Together, the findings support the idea that the responding T-cell pool initially has a broad range of ligand affinities and changes over time to favour high-affinity T cells, which have a more prolonged expansion.

CELL MIGRATION

TLR2-induced calpain cleavage of epithelial junctional proteins faciliates leukocyte transmigration

Chun, J. & Prince, A. *Cell Host Microbe* **5**, 47–58 (2009)

To reach the alveolar airways and fight an infection in the lungs, neutrophils must first cross the vascular endothelium and then the epithelial barrier layer. We know a lot about transendothelial migration, but much less is known about the molecular mechanisms of transepithelial migration. This study shows that the calcium flux initiated by Toll-like receptor 2 (TLR2) signalling following exposure to heat-killed *Pseudomonas aeruginosa* or to a synthetic TLR2 ligand activated calpains. These cysteine proteases specifically degraded the junctional proteins occludin and E-cadherin, resulting in enhanced transepithelial migration of neutrophils. Importantly, the epithelial barrier to ion and solute flux remained intact. Therefore, TLR2 signalling not only induces chemokine expression to recruit neutrophils, but it also initiates signals for modulation of the epithelial barrier to facilitate transmigration.