Sequestering the sequester

Pathogenic bacteria often enhance virulence through the expression of siderophores for capturing iron from their hosts. In *Nature*, Aderem and colleagues show that mice infected with *Escherichia coli* mount countermeasures. Signaling through Toll-like receptors induces expression of lipocalin 2, a protein that binds to the bacterial siderophores, abrogating their ability to acquire iron. Mice deficient in lipocalin 2 had increased bacteremia and increased lethality to bacterial challenge, despite having otherwise intact immune cell functions. Thus, lipocalin 2 is crucial in the innate immune response to bacterial infection. *LAD*

Nature **(7 November 2004) doi:10.1038/nature03104**

Chromatin switches

Repressed chromatin is associated with specific histone modifications and binds to corepressor complexes. Chromatin remodeling is required before specific loci become accessible to transcriptional transactivators. In *Molecular Cell*, Hoberg *et al.* report that the kinase IKKα can initiate such transitions for transcription factor NF-κB binding sites. IKKα phosphorylates a chromatin-bound corepressor called SMRT and causes its export from the nucleus. SMRT is responsible for the recruitment of histone deacetylase complexes that maintain chromatin repression. Cells overexpressing mutant SMRT that cannot be phosphorylated do not derepress pro-survival genes, which are targets for NF-κB activity, and show increased susceptibility to apoptosis. Thus, IKKα phosphorylation of SMRT is a requirement for the exposure of NF-κB-regulated genes for transcriptional activation. *LAD*

Mol. Cell **16**, 245–255 (2004)

Chronic exhaustion

Because the maintenance of memory T cells is mainly antigen independent, it is unclear why protective immunity against certain chronic infections requires antigen persistence. In the *Proceedings of the National Academy of Sciences USA*, Wherry *et al.* find that $CD8^+$ T cells generated during chronic infection are less 'fit'. In contrast to memory T cells generated after an acute infection, chronically stimulated T cells are inefficient in homeostatic proliferation, respond poorly to both interleukin-7 (IL-7) and IL-15, do not secrete IL-2 and do not express the lymph node homing receptors CD62L and CCR7. These findings present new challenges for the use of persistent vaccines and for the treatment of chronic infections and tumors. *PTL*

Proc. Natl. Acad. Sci. USA (25 October 2004)
doi:10.1073/pnas.0407192101

Acid gut

Dendritic cells (DCs) from Peyer's patches or mesenteric lymph nodes 'imprint' gut-homing specificity onto T cells. In *Immunity*, Song and colleagues show that retinoic acid is critical in this process. Retinoic acid produced by DCs from gut-associated lymphoid organs enhanced $\alpha_4\beta_7$ and CCR9 expression. This increased the chemotactic activity of T cells toward the CCR9 ligand TECK and resulted in preferential homing of T cells to gut-associated secondary lymphoid organs *in vivo*. Activated memory T cells ($\alpha_4\beta_7{}^+CCR7^+$) were absent from the intestinal lamina propria of vitamin A–deficient mice, which lack retinoic acid. Thus, retinoic acid 'imprints' gut-homing specificity on T cells. *JDKW*

Immunity **21**, 527–538 (2004)

Written by Laurie A. Dempsey, Peter T. Lee and Jamie D.K. Wilson.

The double life of nuclear receptors

The orphan nuclear receptors LXRα and LXRβ promote cholesterol efflux in macrophages. In *Cell*, Joseph *et al.* show that LXRα is also involved in the innate immune response. LXR-deficient mice were highly susceptible to *Listeria monocytogenes* infection. Normally, listeria induce LXRα mRNA through the NOD signaling pathway in macrophages. In the absence of LXRα, macrophages contained more viable intracellular bacteria, were more prone to apoptosis and had reduced basal and LXRα ligand–induced expression of the anti-apoptotic factor SPα compared with that of wild-type cells. Forced expression of LXRα or SPα in LXRα-deficient macrophages promoted antimicrobial activity and cell survival. Thus, LXRα is unexpectedly important in the innate immune response to intracellular bacteria. *JDKW*

Cell **119**, 299–309 (2004)

Terminating autoreactivity

Bone marrow–derived cells, but not medullary thymic epithelial cells (MTECs), are thought to delete autoreactive thymocytes. Thus, how T cells that recognize tissue-specific antigens expressed on MTECs are tolerized is unclear. In the *Journal of Experimental Medicine*, Gallegos and Bevan observe that MTECs can efficiently delete antigen-specific $CD8^+$ T cells. In addition, bone marrow–derived cells also induce the deletion of these T cells through cross-presentation of the MTEC-expressed antigen. Unexpectedly, bone marrow–derived cells exclusively mediate tolerance of an MHC class II–restricted antigen expressed on MTECs. Although the precise requirements of the tolerance process are unclear, it is likely to involve T cell receptor–peptide–MHC avidity. *PTL*

J. Exp. Med. **200**, 1039–1049 (2004)

Interaction without recognition

DCs and $V_\gamma1$ T cells quickly appear in the lungs after *Mycobacterium tuberculosis* infection. In the *European Journal of Immunology*, Dieli *et al.* show that infected DCs induce $V_\gamma1$ T cells to secrete interferon-γ (IFN-γ) and to acquire cytotoxic activity in a T cell receptor–independent but IL-12-dependent way. $V_\gamma1$ T cells, in turn, enhance the secretion of IL-12 by DCs through IFN-γ. The 'conditioned' DCs are more effective in activating $CD8^+$ than $CD4^+$ T cells. Thus, mycobacteria induce two-way interactions between DCs and $V_\gamma1$ T cells that do not need cognate recognition. *PTL*

Eur. J. Immunol. **34**, 3227–3235 (2004)