Luring DCs to the gut lumen

Continual sampling of the gut lumen alerts the immune system to the presence of potential pathogens and allows tolerance induction to commensal organisms. In *Science*, Niess *et al.* describe how myeloid dendritic cells (DCs) achieve this during salmonella infection. Intestinal epithelial cells, especially those of the ileum, express the transmembrane chemokine CX_3CL1 (also called fractalkine), which recruits circulating CX_3CR1-expressing DCs to the mucosal lamina propria. These cells are capable of extending dendrites through the epithelial border and have direct interaction with the intestinal contents. Mice lacking CX_3CR1 fail to broach this border and are more susceptible to intestinal pathogens. Thus, this pathway provides another means to 'interrogate' gut contents and might function in protecting against infection. *LAD*

Science **307**, 254–258 (2005)

Portal to T cells

T cells in the lymph nodes (LNs) access soluble antigens delivered from the periphery by two routes: antigens are transported by migrating DCs or they traffic to the LNs in a cell-independent way. In *Immunity*, Sixt *et al.* examine the cell-free movement of antigens and find that they drain from the afferent lymphatic vessels through a network of channels into the high endothelial venules. The network is ensheathed by reticular fibroblastic cells and resident DCs, which are able to take up and process traversing antigens. In contrast, DCs that have migrated from the periphery are not associated with the reticular network. Thus, soluble antigens are captured by specific DCs through the reticular network for probable presentation to LN T cells. *PTL*

Immunity **22**, 19–29 (2005)

Flexible migration

DCs from gut-associated lymphoid tissues 'imprint' gut-homing properties on $CD8^+$ T cells. In the *Journal of Experimental Medicine*, von Andrian and colleagues investigate T cell migration to the skin. DCs derived from skin-draining lymph nodes (PLN-DCs) increase $CD8^+$ T cell expression of the skin-homing P- and E-selectin ligands and enhance migration of the cells to inflamed skin. The ability of PLN-DCs to imprint a skin-homing phenotype is suppressed by the presence of intestinal DCs, while the homing properties of memory $CD8^+$ T cells can change depending on the tissue origin of the DCs used for reactivation. These data suggest that $CD8^+$ T cells will acquire skin-homing properties unless exposed to intestinal DCs but that the migratory phenotype is not fixed. *JDKW*

J. Exp. Med. **201**, 303–316 (2005)

Oblivious to Tolls

Ethylnitrosourea is a powerful mutagen used by Beutler and colleagues to generate a library of mutant mice. In *Nature*, Hoebe *et al.* describe one ethylnitrosourea-induced mutant mouse strain, oblivious, which has a selective defect in the recognition of some but not all Toll-like receptor 2 (TLR2) ligands. Macrophages from oblivious mice produce less tumor necrosis factor in response to lipoteichoic acid and the diacylated lipopeptide MALP-2. These mice develop spontaneous bacterial eye infections and have substantially reduced immunity to staphylococcal infection, although the defect is not as severe as that in *Tlr2*$^{-/-}$ mice. The oblivious mutation maps to *Cd36*, encoding the CD36 scavenger receptor. Thus, CD36 is involved in innate immunity by facilitating ligand recognition by TLR2. *LAD*

Nature **433**, 523–527 (2005)

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

The double life of IgA

Although serum immunoglobulin A (IgA) can bind FcαRI in the absence of antigen-induced aggregation, it is thought to have no biological effects. In *Immunity*, Pasquier *et al.* show that in the absence of sustained aggregation, ligand binding to FcαRI, in association with ITAM-bearing FcγR, inhibits IgE-dependent mast cell activation mediated by FcεRI. Ligand binding to FcαRI induces recruitment of the inhibitory phosphatase SHP-1 and prevents FcεRI-induced phosphorylation of Syk, LAT and Erk, which is required for IgE-mediated mast cell activation. *In vivo*, FcαRI targeting using anti-FcαRI Fab treatment prevents IgE-mediated asthma. Thus, FcαRI can function as both an activatory and an inhibitory receptor depending on whether IgA is aggregated by antigen. *JDKW*

Immunity **22**, 31–42 (2005)

SAPping NKT cells

SAP, an adaptor molecule, is critical for T and natural killer (NK) cell cytotoxicity and cytokine production. In *Nature Medicine*, Stein and colleagues analyze whether NKT cells also require SAP. NKT cell–enriched splenocyte samples from SAP-deficient mice show defects in cytokine production and an inability to activate other lymphoid lineages. Unlike the development of T and NK cells, NKT cell development is perturbed in SAP-deficient mice, as demonstrated by a notable reduction in peripheral NKT cell numbers. Mixed bone marrow chimera experiments show that the defects in NKT cell ontogeny are cell autonomous. Humans with X-linked lymphoproliferative disease (XLP), which is caused by mutations in the SAP gene, also have reduced NKT cell numbers. Thus, SAP is likely to contribute to XLP pathogenesis by affecting NKT cell development. *JDKW*

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High growth address

After an infection, the population of antigen-specific $CD8^+$ T cells contracts and persists as memory cells in both lymphoid and nonlymphoid tissues. In the *Journal of Immunology*, Becker *et al.* investigate the preferential site for homeostatic proliferation of these memory T cells. Bone marrow and the spleen contain the largest population of antigen-specific memory $CD8^+$ T cells after virus infection. However, memory cells in the bone marrow consistently show the greatest proliferation activity of all tissues examined. Labeling experiments suggest that the proliferated cells subsequently migrate out of the bone marrow. In agreement with previous studies, interleukin 15 is an important cytokine for the homeostatic proliferation. It is now necessary to understand the precise characteristic of the bone marrow milieu that supports the reservoir of memory T cells. *PTL*

J. Immunol. **174**, 1269–1273 (2005)