Conserved PRRs

In mammalian systems, macrophages can directly recognize microorganisms *via* pattern recognition receptors (PRRs) such as the mannose receptor and the scavenger receptors (SRs). In contrast, no transmembrane macrophage PRR for bacteria has been definitively characterized in insects. In *Immunity*, Ezekowitz and colleagues showed that the *Drosophila* scavenger receptor dSR-Cl is a PRR capable of recognizing Gram-negative and Gram-positive bacteria but not yeast. The dSR-Cl accounted for 20–30% of the total bacterial binding activity in S2 cells, suggesting that insects have additional, but as yet undefined, PRRs. These results suggest that scavenger receptor bacterial recognition is conserved between insects and mammals and could represent one of the most primitive forms of bacterial recognition.

Immunity **15**, 1027–1038 (2001)

Bet on T_H1

T-bet is expressed by NK cells, $CD4^+$ and $CD8^+$ T cells and appears to regulate lineage commitment in $CD4^+$ and $CD8^+$ T lymphocytes, in part by activating IFN-γ. In *Science*, Szabo *et al.* firmly establish, using T-bet–deficient mice, that T-bet is required for controlling IFN-γ production in $CD4^+$ T cells and NK cells, but not in $CD8^+$ T cells. The role of T-bet in T_H1 lineage commitment is further supported by another report in *Science*, by Finotto *et al.* They showed T-$bet^{-/-}$ mice and SCID mice receiving T-$bet^{-/-}$ $CD4^+$ T cells spontaneously develop an asthmatic phenotype, a condition associated with airway infiltration by T_H2 cells. These results suggest that, as a regulator of T_H1 lineage commitment, T-bet could be a target for the development of anti-asthmatic drugs.

Science **295**, 336–338 & 338–342 (2002)

Selective intestinal epithelium

One of the main routes to infection by HIV-1 is the mucosal surface. HIV-1 isolated from acutely infected individuals is predominantly R5 (CCR5-tropic), yet both R5 and X4 (CXCR4-tropic) viruses are typically inoculated into the mucosa. In *Nature Medicine*, Meng *et al.* showed that primary intestinal epithelial cells (IECs) express galactosylceramide, an alternative primary receptor for HIV-1, and CCR5, the coreceptor for R5 viruses. IECs, however, do not express CXCR4 or CD4. Consistent with their phenotype, IECs could transfer R5, but not X4, viruses to $CCR5^+$ indicator cells, which efficiently replicated virus. Transcytosis of HIV-1 was microtubule-dependent. Thus, $CCR5^+$ IECs account for the preferential transmission of R5 HIV-1 in primary infection acquired across the mucosal surface.

Nature Med. **8**, 148–154 (2002)

BAFF in Sjögren's syndrome

Sjögren's syndrome is an autoimmune disease associated with salivary and lacrimal gland pathologies, which lead to deficient secretion of saliva and tears. In the *Journal of Clinical Investigation*, Groom *et al.* describe a Sjögren's-like disorder that develops in aged BAFF (BLyS)-transgenic mice. These mice had enlarged and inflamed submaxillary glands, reduced saliva flow and increased incidence of submaxillary tumors. Large numbers of marginal zone–like B cells were present in the infiltrates. Humans diagnosed with Sjögren's syndrome also displayed elevated serum BAFF concentrations and increased numbers of BAFF-expressing cells in diseased labial glands. Thus, development of Sjögren's syndrome appears to be linked to dysregulation of B cell homeostasis at the immature transitional stage where BAFF signals contribute to B cell survival.

J. Clin. Invest. **109**, 59–68 (2002)

HCV inhibits NK cells

How does hepatitis C virus (HCV) evade the immune system, despite the patient's ability to mount both cellular and humoral responses? Two reports in the *Journal of Experimental Medicine*, by Crotta *et al.* and Tseng and Klimpel, show that HCV inhibits NK cells by engaging CD81 through its E2 envelope protein. Unlike ligation of CD81 in T cells, cross-linking of CD81 on NK cells with immobilized E2 or with anti-CD81 blocks their cytolytic activity and IFN-γ production, even after stimulation with IL-12 or IL-15. CD81 engagement blocked signals emanating from ligation of CD16, thus CD81 participates in a negative signaling pathway in NK cells. These studies also establish a major role for NK cells in controlling HCV infection.

J. Exp. Med. **195**, 35–41 & 43–49 (2002)

Targeting nonsense mRNA

During lymphoid development, V(D)J recombination often generates nonfunctional receptor transcripts due to nonsense codon usage. How lymphocytes ignore these aberrant transcripts to focus on functional receptor mRNAs remained puzzling. In the *EMBO Journal*, Gudikote and Wilkinson identify a *cis* element in the V(D)J exon and flanking intron sequences that targets TCR mRNAs containing premature termination codons for decay. This element targeted heterologous nonsense mRNAs for decay but functional cognate transcripts, lacking nonsense codons, over 30-fold more stable. Nonsense codons had to be within or downstream of this negative signal to target mRNA instability. Several TCR V_β gene families include such negative *cis* elements in their transcripts, suggesting its conserved function. Thus, V(D)J genes also encode signals to clean up any mistakes that they may leave behind.

EMBO J. **21**, 125–134 (2002)

Increasing HSC frequency

How are hematopoietic stem cell numbers regulated in the bone marrow? In the *Journal of Immunology*, Clarke and colleagues identify a region of mouse chromosome 17 that confers increased HSC frequencies. Bone marrow cells from AKR/J mice consistently yield higher success in long-term self-renewing HSC engraftment into irradiated recipient mice than those of C57BL/6 mice. This trait was confined to increased HSC numbers, but not for differences in restricted progenitors, and was recessive in F_1 progeny. Genetic mapping narrowed the region to a 20-cM interval encompassing the H-2 locus. This region is rich in genes encoding factors that regulate immune responses and cell cycle control. Sorting out which factors influence HSC frequency and turnover will shed light on HSC biology and has potential clinical value.

J. Immunol. **168**, 635–642 (2002)