Egalitarian OcaB

OcaB (also called Bob-1 and OBF-1) interacts with Oct proteins to allow B cell–specific transcription of Ig light chain genes and V(D)J recombination. In *Cell*, Casellas *et al.* provide an explanation for the puzzling observation that OcaB-deficient mice have near-normal numbers of mature B cells. OcaB differentially regulates germline expression in V_κ genes; recombination of $V_\kappa 4$ or $V_\kappa 3$ was absolutely dependent on OcaB, whereas $V_\kappa 8$ was not; thus, $OcaB^{-/-}$ mice have skewed Ig repertoires. Surprisingly, OcaB is not required for gene accessibility to basal transcription components. OcaB confers transcriptional and recombinational competence to V_κ genes that lack an 18-bp element found near the ATG start site in expressed V_κ genes. Thus, OcaB enables greater V_κ gene heterogeneity, which promotes greater Ig diversity.

Cell **110**, 575–585 (2002)

Presenting myeloids

Unlike myeloid $CD8^-$ DCs, only lymphoid $CD8^+$ DCs can cross-present cell-associated antigen to $CD8^+$ T cells *in vivo*. In the *Journal of Experimental Medicine*, den Haan and Bevan now show that both $CD8^+$ and $CD8^-$ DC subsets derived from mice treated with OVA–anti-OVA immune complexes can cross-present OVA in the context of MHC class I. In contrast, $CD8^-$ DCs, but not $CD8^+$ DCs, lose the ability to cross-present immune complexes to $CD8^+$ T cells if the activating receptors FcγRI and FcγRIII are not present. However, the decreased ability of FcγR-deficient $CD8^-$ DCs to cross-present MHC class I was not due to a decrease in uptake of antigen complexes. Collectively, these data suggest $CD8^+$ DCs can cross-present exogenous antigens constitutively, whereas $CD8^-$ DCs require activation *via* FcγR ligation.

J. Exp. Med. 9 September 2002 (doi:10.1084/jem.20020295)

Gut signaling

The IL-6 cytokine family helps maintain the normal functioning of the gastrointestinal mucosa by regulating epithelial cell homeostasis. Cytokine family members can trigger a STAT1 and STAT3 (STAT1/3) or an SHP2-Ras-Erk signaling pathway *via* gp130. In *Nature Medicine*, Tebbutt *et al.* investigated the role played by each pathway in the gastrointestinal tract. Mice with defective SHP2-Ras-Erk signaling develop gastric adenomas similar to trefoil factor 1 (TFF1)–deficient mice. However, mice with ablated STAT1/3 signaling or with defective IL-6–mediated gp130 signaling exhibit impaired colonic mucosal wound healing, a phenotype exhibited by TFF3-deficient mice. The SHP-Ras-Erk pathway induced TFF1 transcription and the STAT1/3 pathway stimulated intestinal TFF3 transcription. Thus, mucosal wound healing is STAT1/3-dependent, whereas gastric hyperplasia results from disrupting both STAT1/3 and SHP2-Ras-Erk pathways.

Nature Med. **8**, 1089–1097 (2002)

Triggering arthritis

The pathogenesis of erosive arthritis in K/BxN mice is mediated by autoantibodies, complement components, Fc receptors and cytokines. However, the cellular link between the soluble factors and inflammatory arthritis is not known. In *Science*, Lee and colleagues found that mast cell–deficient mice (W/W^v and Sl/Sl^d), unlike wild-type controls, had little clinical joint inflammation or histopathologic abnormalities after transfer of K/BxN serum. Mast cell engraftment restored the susceptibility of W/W^v mice to K/BxN serum–induced arthritis. Furthermore, one hour after K/BxN serum transfer, only synovial mast cells had striking degranulation. These data suggest mast cells are the cellular targets of autoantibodies, complement components and Fc receptors in the development of inflammatory arthritis.

Science **297**, 1689–1692 (2002)

E-xtend life

Vitamin E supplementation increases total lymphocyte counts and immunodeficient HIV-infected patients have decreased concentrations of serum vitamin E. In the *Journal of Clinical Investigation*, Li-Weber *et al.* report a possible molecular mechanism behind these related observations: vitamin E can inhibit CD95L expression on T cells and thus can prevent activation-induced cell death. Vitamin E inhibits the expression of CD95L by blocking the binding of the transcription factors NF-κB and AP-1 to the promoter region of the gene for CD95L. *In vitro* culture of vitamin E with cells from HIV-positive patients decreases expression of CD95L and inhibits apoptosis, which suggests a potential therapeutic application for AIDS. These data also shed light on mechanisms by which vitamins with antioxidant properties may enhance the immune system.

J. Clin. Invest. **110**, 681–690 (2002)

Introducing inflammasome

IL-1β is an inflammatory cytokine that requires processing from its inactive cytoplasmic form by caspase-1. However, the process that generates active caspase-1 is unknown. In *Molecular Cell*, Martinon *et al.* show that similar to the "apoptosome" observed in apoptotic cells, the formation of a complex of proteins is required to process IL-1β. The term "inflammasome" was coined for this complex and comprises a member of the nucleotide binding-site family (NALP1), an adaptor protein (Pycard), caspase-1 and caspase-5. The inflammasome is important in facilitating the cleaving of both caspase-1 and caspase-5 to their active forms. Depletion of Pycard by antibodies in cell lysates and by a dominant negative construct in whole cells shows that Pycard is an essential component of the inflammasome for generating active IL-1β.

Mol. Cell **10**, 417–426 (2002)

Integrin activation

How intracellular signals trigger integrin activation to unmask high-affinity ligand binding sites has remained a mystery. Two reports in *Cell* describe how disrupting cytoplasmic interactions between membrane-proximal domains of integrin α and β subunits induce major structural changes in their extracellular domains. Vinogradova *et al.* show that, in the inactive state, the cytoplasmic tails of the two chains interact. Disrupting this αβ association with integrin activators such as talin—which competes for the β chain molecular interface—induces a shift in the register between the two chains. Takagi *et al.* show that this "pull" allows the inactive integrin to extend its ectodomains, which were previously folded back onto itself, and thus expose the high-affinity ligand-binding site.

Cell **110**, 587–597 & 599–611 (2002)