The strong MINT

Notch signaling promotes marginal-zone (MZ) B cell differentiation but suppresses follicular (Fo) B cell generation in the spleen. The DNA binding protein RBP-J, a *Drosophila* homolog of Suppressor of Hairless (Su(H)), mediates notch signaling. Su(H) is negatively regulated by Hairless in flies, but no vertebrate homolog of this protein is known. In *Immunity,* Honjo and colleagues identify an RBP-J–interacting protein called MINT (Msx2-interacting nuclear target protein) that competitively repressed notch-RBP–mediated transcription. MINT was expressed strongly in Fo B cells but weakly in MZ B cells. MINT-deficient B cells preferentially differentiated into MZ B cells. These data suggest that MINT negatively regulates MZ B cell development by suppressing notch-RBP-J signaling and that MINT could be the homolog of fly Hairless.

Immunity **18**, 301–312 (2003)

Conjugating IFN-α/β signals

Type I interferons, produced in response to viruses, poly(I-C) and some bacteria, induce reversible modification of intracellular proteins by a ubiquitin-like molecule called ISG15. In *Genes & Development*, Zhang and colleagues show that ISG15 conjugation regulates signaling *via* the JAK-STAT1 pathway. Cells that lack the protease UBP43, which specifically removes ISG15 from modified proteins, show heightened and prolonged responses to IFN-α or IFN-β and are more sensitive to apoptosis. UBP43-deficient mice die soon after poly(I•C) treatment. In the *Journal of Biological Chemistry*, the same group identify JAK1, STAT1, ERK1 and PLCγ1 as targets of ISG15 modification. How ISG15 modification enhances the signaling properties of these molecules is not known. Yet it is clear the ISG15-UBP43 axis regulates responses to type I interferons.

Genes Dev. **17**, 455–460 & *J. Biol. Chem.* Feb. 11, 2003 (M208435200)

Virological synapses

Because lymphocytes naturally infected with human T cell lymphotropic virus type 1 (HTLV-I) produce very few cell-free virions, contact between cells is thought to mediate virus transmission. In *Science*, Bangham and colleagues analyzed the mechanism of HTLV-I cell-to-cell spread by confocal microscopy. Both HTLV-I Gag protein and the virus genome polarized to the cell-cell junction and were transferred to the uninfected cell. Polarization of virus protein and nucleic acid was associated with reorientation of the microtubule organizing center (MTOC) towards the area of cell-cell contact. Yet cytoskeletal polarization was not triggered by TCR-mediated recognition of HTLV-I antigens presented by neighboring T cells. Thus, this structure should be considered more a virological than an immunological synapse, enabling HTLV-1 to mediate infection between cells.

Science Feb. 13, 2003 (doi:10.1126/science.1080115)

MAIT of the gut

A conserved subset of αβ T cells bearing the canonical V_α7.2-J_α33 in humans and V_α19-J_α33 TCRα chain in mice, paired with an oligoclonal repertoire of $TCRV_\beta$ chain, was identified previously. However, their selection and tissue distribution were unknown. In *Nature*, Treiner *et al*. show that these cells are preferentially found in the gut lamina propria and thus represent mucosal-associated invariant T (MAIT) cells. The selection and/or expansion of MAIT cells require B cells that express the β_2-microglobulin–dependent MHC class Ib molecule MR1. The number of MAIT cells is reduced in germ-free mice, suggesting that their homeostasis is dependent on microbial stimulation. Thus, MAIT cells may emerge as a population of invariant T cells that regulates immune responses at mucosal surfaces.

Nature March 13, 2003 (doi:10.1038/nature01433)

Attenuating adhesion

Lymphocyte adhesion to endothelial cells or to components of the extracellular matrix requires β_2 integrin activation. However, these interactions need to be transient to allow cells to migrate through tissues. In the *EMBO Journal*, Boehm *et al*. identify an adaptor, CYTIP, that binds to the guanine exchange factor cytohesin-1 and regulates its ability to transmit integrin signals. Both CYTIP and cytohesin-1 are recruited to the cell membrane upon integrin activation; however, this localization does not require a physical interaction between CYTIP and cytohesin-1. Rather, CYTIP associates with cytohesin-1 at the membrane and triggers its detachment and relocalization to the cytosol, attenuating the signaling complex initiated by integrin adhesion. Thus, CYTIP can control the duration of β_2 integrin signaling.

EMBO J. **22**, 1014–1024 (2003)

Energy control in combat

Granulocytes and macrophages are adapted to function at sites of inflammation where oxygen and glucose concentrations are low. Although operating under these extreme conditions is likely to involve the hypoxia-inducible transcription factor-1 (HIF-1), its role in inflammation is unclear. In *Cell*, Cramer *et al*. show that conditional deletion of HIF-1 in macrophages reduced glycolysis-dependent generation of ATP, resulting in diminished killing of intracellular bacteria. The disruption of ATP generation also reduced cell movement through artificial extracellular matrix, reduced cellular aggregation that promotes their tissue recruitment and decreased macrophage motility. Thus, HIF-1 directly regulates the cascade of events that allows efficient macrophage and granulocyte response to inflammation.

Cell **112**, 534–657 (2003)

Accessibility & allelic exclusion

Successful rearrangement of antigen-receptor genes can preclude further recombination by a feedback process known as allelic exclusion. In *Immunity*, Chowdhury and Sen showed that allelic exclusion of immunoglobulin heavy-chain rearrangement involves regulation of *Igh* chromatin accessibility. Signals mediated by the cytokine IL-7 induce histone acetylation of the 5′ V_H locus, which is correlated with accessibility to the V(D)J recombination machinery. Loss of IL-7R signaling, as occurs in developing B cells that have successfully rearranged one *Igh* allele and expressed protein, leads to histone deacetylation within the V_H region and cessation of further recombination at the *Igh* locus. These results were further confirmed using Abelson virus–transformed B cell lines, which mimic IL-7 signals. Thus, IL-7 signals control *Igh* chromatin accessibility. What remains unclear is how triggers the loss of IL-7 signals.

Immunity **18**, 229–241 (2003)