Shaping responses

Candida albicans can switch between yeast and filamentous morphologies. In the *EMBO Journal*, Underhill and colleagues investigate whether the morphological differences between these two forms affect innate immune cell recognition. Dectin-1, a receptor for the fungal cell wall component β-glucan, recognizes yeast but not filamentous forms of *C. albicans*. Most yeast β-glucan is shielded from dectin-1 recognition except for β-glucan exposed at scar sites formed during the budding process. *C. albicans* yeast, unlike filaments, can induce dectin-1-mediated macrophage phagocytosis and trigger reactive oxygen production. During filamentous growth, scar sites are not formed, making β-glucan inaccessible to dectin-1 recognition and unable to induce dectin-1-mediated innate immune responses. Thus, the shape of *C. albicans* affects how phagocytes recognize this fungus. *JDKW*

EMBO J. (24 February 2005) doi:10.1038/sj.emboj.7600594

Allergic oil

Pollen grains are carriers of proteinaceous allergens. However, it is unknown whether lipids such as phytoprostanes, which are chief components of pollen grains, can also mediate an immune response. In the *Journal of Experimental Medicine*, Traidl-Hoffmann *et al.* find that lipids from birch pollen promote partial maturation of dendritic cells (DCs), resulting in their enhanced capacity to stimulate allogeneic T cells. However, the lipid-containing pollen extracts selectively inhibit lipopolysaccharide- or CD40 ligand–induced interleukin 2 (IL-12) secretion by DCs and consequently skew $CD4^+$ T cells to a T helper 2 (T_H2) type response. The PPE_1 class of phytoprostanes mediates this modulation of IL-12. Thus, lipids from pollens can condition DCs to trigger an allergic-promoting T_H2 response. *PTL*

J. Exp. Med. **201**, 627–635 (2005)

Food for thought

Prions, the causal infectious agent of spongiform encephalitis, can destroy tissues of the central nervous system. Prion replication occurs in follicular DCs in lymphoid tissues before any evidence of disease is apparent. In *Science*, Aguzzi and colleagues show that chronic inflammation, which correlates with neogenesis of aberrant lymphoid tissues that contain follicular DCs, increases the organ distribution of prions. Increased prion infectivity is noted in several models of pancreatitis, hepatitis and nephritis, whereas no infectivity is associated in the same organs from wild-type animals in the absence of ongoing inflammatory disease. Thus, animals without neurologic disease symptoms may still pose risks of prion transmission. *LAD*

Science **307**, 1107–1110 (2005)

Kick-starting c-Maf

IL-6 promotes the polarization of $CD4^+$ T cells toward a T_H2 phenotype. In the *Journal of Immunology*, Yang *et al.* examine the molecular mechanism of IL-6-induced differentiation of T cells and report that it directly triggers the transcription factor c-Maf, which is essential for IL-4 secretion *in vivo*. Activation of c-Maf is mediated by the STAT3 signaling molecule 'downstream' of IL-6 receptor. DC-derived IL-6 elicits c-Maf expression within hours of stimulation. The activation of c-Maf is independent of IL-4 and the IL-4 transcription factor STAT6. However, c-Maf expression requires additional calcium-mediated signaling through the T cell receptor (TCR). Thus, IL-6 and TCR engagement seem to be important triggers of the early events of IL-4 production. *PTL*

J. Immunol. **174**, 2720–2729 (2005)

Illuminating NF-κB activation

Caspase-8 is an integral component of the death receptor pathway. Paradoxically, caspase-8-deficient patients demonstrate immunodeficiency due to impaired activation of T, B and natural killer cells. In *Science*, Hu *et al.* show that caspase-8 deficiency prevents activation of the transcription factor NF-κB. This defect affects T, B and natural killer cells through specific antigen receptors including T and B cell receptors, Toll-like receptor 4 and the Fc receptor. Caspase-8 acts by recruiting the enzyme complex IKK to the adaptor complex Bcl10-MALT1 associated with the TCR. Subsequent phosphorylation of IKK complex leads to translocation of NF-κB into the nucleus. The enzymatic activity of caspase-8 is important for this process. Thus, caspase-8 provides the critical link between Bcl10-MALT1 and IKK that results in lymphocyte activation. *PTL*

Science **307**, 1465–1468 (2005)

A toll for cross-presentation

Antigen cross-presentation is crucial for the development of cytolytic T lymphocyte responses to viruses that do not infect DCs. In *Nature*, Schulz *et al.* show that $CD8\alpha^+$ DCs cross-prime cytolytic T lymphocytes after phagocytosis of virally infected cells. Viral antigen presentation is dependent on DC expression of Toll-like receptor 3 (TLR3), which recognizes internalized duplex RNA (dsRNA). TLR7, MyD88 and PKR, a kinase activated by cytosolic dsRNA, are not required for $CD8\alpha^+$ DC cross-presentation. Inhibition of phagosome internalization or acidification blocks viral antigen presentation. Thus, signals originating in the endosome recognized by TLR3 are key to this cross-priming pathway. This work suggests incorporation of dsRNA as vaccine adjuvants may increase the efficacy of antiviral or antitumor vaccines. *LAD*

Nature **433**, 887–892 (2005)

Making a negative of a positive

Src family kinases such as Hck and Fgr are thought to positively regulate G protein–coupled receptor signaling. In *Immunity*, Zhang *et al.* make the unexpected observation that several chemokines can augment Erk activation, actin polymerization and chemotactic responses in $Hck^{-/-}Fgr^{-/-}$ neutrophils and $Fgr^{-/-}$ DCs. The mechanism for Src-mediated inhibition of chemokine signaling is associated with the inhibitory receptor PIR-B, as PIR-B-deficient neutrophils and DCs are also hyperresponsive to chemokine signaling. Furthermore, Hck and Fgr deficiency reduces PIR-B phosphorylation and its association with the tyrosine phosphatases SHP-1 and SHP-2. Neutrophils and DCs from SHP-1 mutant mice also show enhance signaling responses to chemokines. These data suggest Src kinases can function as negative regulators by regulating PIR-B phosphorylation. *JDKW*

Immunity **22**, 235–246 (2005)

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