Is expressing type I IFN good or bad?

Type I interferons (IFNs) elicit potent innate antiviral activities and also stimulate the generation of adaptive immune responses. So expression of the type I IFNs, IFN-α and the various IFN-βs should be good if you are infected by microbes. However, in the *Journal of Experimental Medicine*, O'Connell *et al.* show that mice deficient in type I IFN receptors (*Ifnar1*$^{-/-}$) or IFN regulatory factor 3 (*Irf3*$^{-/-}$), a transcription factor activated by signaling from the receptor, have a survival advantage over their wild-type kin when infected by the intracellular bacterial pathogen *Listeria monocytogenes*. Boosting expression of type I IFNs in wild-type mice also lessened their survival after challenge with an otherwise sublethal dose of bacteria. Wild-type mice had severe liver and spleen pathologies after *L. monocytogenes* infection that were exacerbated when type I IFN production was increased. In contrast, both *Irf3*$^{-/-}$ and *Ifnar1*$^{-/-}$ mice could clear their bacterial infection without producing ancillary liver damage. *L. monocytogenes* induced expression of IFN-γ, interleukin 6 (IL-6) and IL-1β to a similar extent in wild-type and mutant mice, but only wild-type mice had increased expression of proapoptotic molecules such as TRAIL. Thus, *L. monocytogenes* takes advantage of the overzealous induction of apoptosis induced by type I IFNs. *LAD*
J. Exp. Med. **200**, 437–445 (2004)

Complementing virus immunity

The complement component C3 has been linked to the generation of antiviral CD8 T cell immunity. However, mice doubly deficient in receptors for fragments of C3, CR1 and CR2, have normal antiviral CD8 T cell responses, which suggests that other complement receptors may be involved. In the *Journal of Immunology*, Kim *et al.* examine whether the receptor for the complement fragment C5a (C5aR) is critical for mounting antiviral CD8 T cell responses. Treatment of influenza type A–infected mice with a C5aR peptide antagonist reduced the frequency and absolute number of CD8 T cells specific for influenza. Consistent with this, CD8 T cells from the lungs of treated mice were defective in IFN-γ production and cytotoxic activity in response to influenza. These data suggest that C5a is essential for the optimal generation of antiviral CD8 T cell responses, but how C5a mediates this effect is yet to be determined. *JDKW*
J. Immunol. **173**, 2524–2529 (2004)

Whooping up immunity

Protection against *Bordetella pertussis*, the causative agent of the infection known as whooping cough, requires a T helper type 1 (T_H1) response. However, because T cell responses are suppressed during the acute infection phase and T cells do not seem to be important in confining *B. pertussis* in the lungs, the source of the cytokine IFN-γ that would promote a T_H1-type response is unclear. In the *European Journal of Immunology*, Bryne *et al.* show that natural killer (NK) cells are the primary source of IFN- γ after infection. In the absence of NK cells, mice have increased bacteria counts and die within 3 weeks of challenge. NK cell depletion results in enhanced production of T_H2 cytokines and associated immunoglobulin G1 antibody. Thus, in addition to providing an early innate response, NK cells seem to be essential in shaping protective adaptive immunity to *B. pertussis* infection. *PTL*
Eur. J. Immunol. **34**, 2579–2588 (2004)

Communicating with skin

IL-22 is a member of the IL-10 cytokine family that is secreted mainly by activated T_H1 cells. In *Immunity*, Wolk *et al.* investigate the targets and physiological function of this cytokine. T cells, B cells, NK cells, monocytes, macrophages and dendritic cells (DCs) neither expressed the IL-22 receptor nor responded to IL-22 in functional assays. Instead, IL-22 receptor expression was restricted to nonimmune tissues of the skin, gut and respiratory systems. Receptor expression was particularly high in keratinocytes, which upregulated β-defensin 2 (hBD2) and β-hBD3 mRNA in response to IL-22 treatment. High IL-22 expression in the skin of patients with inflammatory skin disease also correlated with β-HD mRNA expression. Thus, IL-22 serves as a link between the adaptive immune system, via activated T cells, to the innate immune response of tissues. *JDKW*
Immunity **21**, 241–254 (2004)

Neutrophils direct traffic

Migration of antigen-primed $CD8^+$ T cells into the skin is important for allergic contact hypersensitivity responses. Although the chemokine CXCL1, produced in the local milieu, is known to be important in this process, it is not a chemoattractant for T cells. In the *Journal of Leukocyte Biology*, Engeman *et al.* show that CXCL1 acts via neutrophils to recruit the $CD8^+$ T cells. Depletion of neutrophils in sensitized mice prevents the migration of antigen-specific $CD8^+$ T cells into the skin. This movement is dependent on inflammatory signals from the neutrophil rather than antigen-specific cues. Thus, unrelated antigens that induce neutrophil infiltration in primed mice could enhance the migration of $CD8^+$ T cells into the challenged site, albeit without causing a hypersensitivity response. In addition, injection of neutrophils with a suboptimal dose of antigen is sufficient to recruit the $CD8^+$ T cells and induce contact hypersensitivity. Thus, an early neutrophil response directs the trafficking of antigen-specific T cells. *PTL*
J. Leukocyte. Biol. (Aug 2004) doi:10.1189/jlb.0304193

DCs ruffled by TLRs

Toll-like receptor (TLR) signals are known to stimulate DC maturation. This maturation leads to the increased antigen presentation and costimulatory molecule expression necessary for effective priming of naive T cells. However, the endocytic activity of mature DCs is thought to be much less than that for immature DCs. In *Science*, Watts and colleagues show that TLR ligands induce transient changes in rearrangements of actin cytoskeleton in DCs within an hour of receptor engagement. Multiple TLRs stimulated membrane ruffling and endocytic activity. Conversely, in the same time frame TLR signaling decreased the number of podosomes, F-actin clusters thought to be involved in cell migration. New protein synthesis was not required for these responses, but both ERK and p38 MAP kinases contributed to the observed effects. Hence, after microbial challenge, DCs rapidly alter their cytoskeletal assemblies to allow for increased antigen uptake and then shut down these same activities to 'fix' antigen presentation. *LAD*
***Science* 305, 1153–1157 (2004)**

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