Natural killer memory

Traditionally, natural killer (NK) cells are classified in the innate immune system. However, in *Nature*, Lanier and colleagues report that NK cells, like T cells, undergo all four phases—population expansion, contraction, maintenance and recall—of an adaptive immune response to infection. In an adoptive-transfer model, Ly49H$^+$ NK cells are shown to proliferate 100-fold in the spleen and 1,000-fold in the liver after infection with murine cytomegalovirus (MCMV). After the contraction phase, memory-like NK cells with maturation markers and enhanced effector cytokine responses are detected for several months. These cells expand their populations after adoptive transfer into secondary mice challenged with MCMV and provide much better protection than do naive NK cells when transferred into newborn mice infected with MCMV. These data are beginning to challenge the classification of NK cells as purely cells of the innate immune system and will have implications for vaccination strategies. ***JDKW***

***Nature* (11 January 2009) doi:10.1038/nature07665**

Thymic fountain of youth

The cytokine IL-7 is essential for thymopoiesis. In the *Proceedings of the National Academy of Science*, Alves *et al.* identify two populations of thymic epithelial cells that produce abundant IL-7. These cells also express the chemokines CCL19, CCL25 and CXCL12 and Notch ligands Dll4 and Jag4. In adults, these cells are found in cortical-medullary junction regions and arise early in embryonic development around day 13.5 of gestation. However, IL-7^{hi} cell numbers decrease with age, beginning as early as 5 weeks of age. Their anatomical location as well as the correlation of their abundance with temporal thymocyte production suggest that they might control thymic output. Elucidation of the mechanisms regulating these cells should lend important insight into thymic function and potential therapeutic aims of thymic reconstitution. *LAD*

Proc. Natl. Acad. Sci. USA **106**, 1512–1517 (2009)

Clearing the path of PMNs

Bacterial engagement of Toll-like receptor 2 (TLR2) molecules lining the apical surface of airway epithelial cells results in release of chemokines and cytokines that recruit and activate polymorphonuclear leukocytes (PMNs). In *Cell Host & Microbe*, Chun and Prince explain how these activated PMNs traverse epithelial barrier tight junctions to enter the airway lumen and eliminate invading microbes. In a way dependent on TLR2 expression and calcium flux, exposure to heat-killed *Pseudomonas aeruginosa* induces calpain-mediated cleavage of the junctional complex components occludin and E-cadherin in airway epithelial cells. Calpain activity is essential for *P. aeruginosa*–mediated transmigration of PMNs across airway epithelial cell monolayers *in vitro* and into the lung lumen *in vivo*. As TLR2 signaling does not alter the permeability of airway epithelial cells to dextran or *P. aeruginosa*, further work is needed to understand precisely how TLR2-induced calpain activity facilitates permeability to PMNs. ***CB***

***Cell Host & Microbe* 5, 47–58 (2009)**

Written by Christine Borowski, Laurie A. Dempsey & Jamie D.K. Wilson

Using eosinophils

Although eosinophilia is known to be associated with helminth infection, the function of eosinophils in host defense against such parasites remains controversial. In the *Journal of Immunology*, Febre *et al.* analyze the effect of eosinophil deficiency on *Trichinella spiralis* infection. Although eosinophil ablation has no discernable effect on the intestinal phase of *T. spiralis*, it does compromise parasite survival in skeletal muscle compared with that of eosinophil-sufficient mice. Parasite killing is mediated by greater production of interferon-γ and nitric oxide. Consistent with that, inhibition of inducible nitric oxide synthase improves larval survival, whereas eosinophil-deficient mice that also lack interleukin 10 (IL-10), a cytokine known to downregulate interferon-γ and inducible nitric oxide synthase, show an enhanced ability to clear muscle larvae. These data suggest that the parasite requires eosinophils for survival. It remains unclear if other parasitic worms also use eosinophils to sustain chronic infection. *JDKW*

J. Immunol. **182**, 1577–1583 (2009)

cAMP: timing is everything

The adhesion of T cells to antigen-presenting cells increases the sensitivity of T cell antigen receptor (TCR) signaling. In *Immunity*, Randriamampita and colleagues show that cyclic AMP (cAMP), a molecule long thought to suppress T cell activation, facilitates adhesion-induced enhancements in TCR sensitivity. T cells that adhere to fibronectin have more phosphorylation of the kinase Erk and a spike in cAMP production. Adhesion promotes Erk phosphorylation by suppressing Erk phosphatases, including HePTP, a phosphatase known to be inhibited by the cAMP effector protein kinase A. Inhibition of adenyl cyclase or protein kinase A prevents adhesion-mediated augmentation of TCR-induced calcium flux. Transient but not sustained mobilization of cAMP in suspended T cells mimics the effect of adhesion on TCR signaling sensitivity. Antigen-independent contacts with dendritic cells are sufficient to elicit transient cAMP spikes. Further work is needed to determine if cAMP targets other than protein kinase A contribute to adhesion-induced increases in TCR sensitivity. ***CB***

***Immunity* 30, 33–43 (2009)**

ARNT-CD30 regulates NF-κB

CD30 is a member of the tumor necrosis factor receptor 'superfamily' and has commonly been associated with various hematopoietic malignancies. In *Science*, Wright and Duckett show that CD30 binds the aryl hydrocarbon receptor nuclear translocator (ARNT; also called hypoxia-inducible factor 1β). Ligation of CD30 induces a shift that promotes cytoplasmic retention of the otherwise nuclear ARNT. Nuclear ARNT specifically associates with the RelB subunit of the transcription factor NF-κB. Cells lacking ARNT have enhanced activation of genes regulated by NF-κB as a result of more recruitment of the NF-κB subunit RelA to target promoters and less binding of RelB-HDAC1 to chromatin. ARNT is hypothesized to be involved in maintaining the suppression of or contributing to the negative feedback of canonical NF-κB activity. The details of how CD30 regulates ARNT, and thereby NF-κB, remain to be elucidated. *LAD*

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