Abundant allergen

Exposure to allergens results in the recruitment of cells producing T helper type 2 cytokines and alternative activation of tissue-resident macrophages. In *Nature*, Locksley and colleagues show that chitin, a prevalent natural biopolymer, is required for the initiation of allergic responses to the parasite *Nippostrongylus brasiliensis*. Parasite injection results in the expression of chitinases, whose enzymatic activity suppresses parasite-induced allergic responses. Purified chitin elicits the recruitment of interleukin 4–producing eosinophils and basophils and triggers alternative activation of tissue-resident macrophages. Chitin-induced recruitment of eosinophils and basophils occurs independently of TLR4 and transcription factor STAT6 but depends on macrophage production of the chemoattractant leukotriene B4. These data emphasize that mammalian chitinases are crucial in limiting allergic responses to a commonly encountered allergen. ***CB***

***Nature* (22 April 2007) doi:10.1038/nature05746**

Omenn's syndrome

Patients with Omenn's syndrome suffer autoimmunity, immunodeficiency and atopy. In the *Journal of Clinical Investigation* Marrella *et al.* and Khiong *et al.* describe mouse models that closely reproduce the human disease. Mice with hypomorphic mutations in the recombination-activating genes *Rag1* or *Rag2* produce oligoclonal populations of B and T lymphocytes, including fewer functional T_{reg} cells. These mice also show altered negative selection resulting from severely disrupted thymic architecture, as well as lower *Aire* expression. In the periphery, memory-like T cells predominate, probably because of homeostasis-driven proliferation, and the $CD4^+$ T cell population is skewed toward T helper type 2 polarization. The last findings help to explain the hyper–immunoglobulin E production and atophy of the clinical disease. Thus, altering the efficiency of variable-diversity-joining recombination alone leads to the profound defects in lymphocyte repertoires and immune regulation of Omenn's syndrome. *LAD*

J. Clin. Invest. **117**, 1260–1269 & 1270–1281 (2007)

DC-SIGNing TLRs

Binding of the mycobacterial cell wall component ManLAM to the C-type lectin receptor DC-SIGN suppresses TLR-dependent lipopolysaccharide (LPS)-induced maturation of DCs and increases production of interleukin 10 (IL-10). In *Immunity*, Geijtenbeek and colleagues investigate how ManLAM mediates these effects. Activation of Raf-1 kinase by Ras GTPase occurs after stimulation of DC-SIGN with ManLAM and LPS. Activated Raf-1 mediates phosphorylation of serine 276 of the transcription factor NF-κB p65 subunit, an event which then induces acetylation of several lysines within p65 by the histone acetyltransferases CBP and p300. Acetylated NF-κB has prolonged and increased transcriptional activity at promoters such as for *Il10*, a classic anti-inflammatory cytokine. Candida, mycobacteria, HIV and measles virus all bind DC-SIGN and induce acetylation of p65. Thus, signaling induced by several pathogens modulates TLR signaling and inflammation conditions. ***DCB***

***Immunity* 26, 1–12 (2007)**

Research notes written by Christine Borowski, Douglas C. Braaten and Laurie A. Dempsey

MicroMatters

The functions of microRNA (miRNA) in the immune system remain mostly unknown. Three new reports, one in the *Proceedings of the National Academy of Sciences* and two in *Science,* indicate key regulatory functions for *miRNA-150* and *miRNA-155* in lymphocytes. Zhou *et al.* find that overexpression of *miR-150* in hematopoietic cells results in profoundly altered B cell development. The Rajewsky and Turner groups separately developed mutant mice with *miR-155* gain or loss of function. Several hematopoietic lineages express *miR-155*. Few germinal center B cells develop in mice lacking *miR-155*, leading to lower immunoglobulin production. T cell function is also affected by deficiency in *miR-155*, as cytokine production is altered. Turner and colleagues show that vaccinated *miR-155*-deficient mice succumb to lethal challenge by salmonella. These findings begin to identify the functions of miRNA in immune function. *LAD*

Proc. Natl. Acad. Sci. USA **104**, 7080–7085; *Science* **316**, 604–608 & 608–611 (2007)

Suppression strategy

Extracellular ATP promotes inflammation, whereas extracellular adenosine suppresses it. In *Blood*, Falk and coworkers show that regulatory T (T_{reg}) cells are equipped with 'machinery' capable of converting ATP into adenosine. Most mouse $CD4^+CD25^+Foxp3^+$ T_{reg} cells express the CD39 ectonucleoside triphosphate diphosphohydrolase, which converts ATP to AMP. CD39 is also expressed on a subset of human T_{reg} cells with potent immunosuppressive properties that contain large amounts of the transcription factor Foxp3. The ATPase activity of CD39 increases with activation of mouse T_{reg} cells and is required for the survival and proliferation of mouse T_{reg} cells in the presence of abundant extracellular ATP. The proportion of $CD39^+$ T_{reg} cells, but not of total T_{reg} cells, is higher in healthy humans than in patients with multiple sclerosis. Along with published data showing that T_{reg} cells express the ectonucleosidase CD73, which converts AMP into adenosine, these findings indicate that T_{reg} cell–mediated 'squelching' of extracellular ATP might contribute to T_{reg} cell–mediated immunosuppression. ***CB***

***Blood* (20 April 2007) doi:10.1182/blood-2006-12-064527**

Regulating RIG-I

The helicase RIG-I is a cytosolic RNA sensor that is activated by single-stranded RNA bearing 5′ phosphates. In the *Proceedings of the National Academy of Sciences*, Shimotohno and colleagues find that expression of the ubiquitin E3 ligase RNF125 is induced by treatment of cells with interferon or poly(I:C) double-stranded RNA; RNF125 then binds to RIG-I and reduces its expression through ubiquitination of RIG-I. Overexpression of RNF125 in mouse primary embryonic fibroblasts decreases RIG-I and leads to reduced 'downstream' signaling after Sendai virus infection, whereas 'knockdown' of RNF125 via small interfering RNA increases signaling. RNF125 also interacts with the other known cytosolic helicase RNA sensor, Mda5, and the 'downstream' adaptor IPS-1, also used by RIG-I. Ubiquitination of Mda5 and IPS-1 by RNF125 reduces their expression. These findings provide insight into how these key innate immune signaling molecules are regulated after cells encounter RNA-bearing pathogens. *DCB*

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