Specific help for T_{RM} cells

CD4+ T cells are important for the formation of memory CD8+ T cell responses through the licensing of dendritic cells and the generation of chemokine gradients in the draining lymph nodes. In *Immunity*, Kaech and colleagues show that CD4+ T cells also promote the formation of CD8+ tissue-resident T cells (T_{RM} cells) during infection of mice with influenza virus by promoting expression of the integrin CD103 on virus-specific CD8+ T_{RM} cells and, thus, their localization in the lung airway. In the absence of CD4+ T cell help to CD8+ T_{RM} cells, there is less recruitment of virus-specific CD8+ T cells and less protection during secondary infection. CD4+ T cell help is required during the first week of infection and is dependent on the production of interferon-γ by CD4+ T cells. CD8+ T_{RM} cells that did not receive help have higher expression of T-bet than their counterparts that did receive help, and high expression of this transcription factor represses the TGF-β-mediated induction of CD103 in virus-specific CD8+ T cells, which provides a potential mechanism for these observations. ***IV***

***Immunity* 41, 633–645 (2014)**

Dampening T_H1 cells by *Mycobacteria*

Over millennia of infecting humans, *Mycobacterium tuberculosis* has evolved numerous ways to manipulate host immune responses. In *Mucosal Immunology*, Xing and colleagues identify a mechanism through which *M. tuberculosis* dampens the induction of T_H1 cells, a response critical for controlling infection by this bacterium. Mouse hosts deficient in the adaptor DAP12 have more robust T_H1 responses and a lower bacterial burden in both the spleen and lungs following infection with *M. tuberculosis*. Mechanistically, DAP12 is required for induction of the negative regulatory kinase IRAK-M following the infection of antigen-presenting cells (APCs) with *M. tuberculosis*. Activated IRAK-M triggers production of the immunosuppressive cytokine IL-10, and such APCs are ineffective at priming T_H1 responses in lung-draining lymph nodes. By upregulating IRAK-M via DAP12 in host APCs, *M. tuberculosis* has yet another means by which it can thwart effective immune responses. *ZF*

Mucosal Immunol. 7, 670–683 (2014)

Alveolar macrophages in asthma

Alveolar macrophages (AMs) make up the vast majority of leukocytes in the lower respiratory tract under steady-state conditions; however, their role in asthma has been relatively poorly characterized. In the *Journal of Immunology* Peters-Golden and colleagues use clodronate liposomes administered either intratracheally or intravenously to achieve selective depletion of either AMs or peripheral monocytes, respectively, to determine the contribution of each population to experimental asthma. In the absence of AMs, typical allergic asthma-associated cytokines such as IL-4, IL-5 and IL-13 are increased and inflammatory parameters are worsened. In contrast, the loss of peripheral monocytes ameliorates the asthma phenotype. Together these results suggest that AMs have a restraining role in asthma, whereas inflammatory monocytes recruited to the lungs are involved in driving the disease. ***ZF***

***J. Immunol.* 193, 4245–4253 (2014)**

Written by Laurie A. Dempsey, Zoltan Fehervari & Ioana Visan

From lung to gut

Respiratory infection with influenza virus induces gastroenteritis-like symptoms, such as nausea, vomiting and diarrhea, especially in young children. In *The Journal of Experimental Medicine*, Wang *et al.* show that during infection of mice with influenza virus, $CCR9^+CD4^+$ T cells from the respiratory mucosa migrate to the intestinal mucosa, where they cause changes in the intestinal microbiota and induce immunological injury. Influenza virus is not detected in the small intestine during intranasal infection, but lung-derived interferon-γ-producing $CD4^+$ cells are recruited to the intestine in a manner dependent on the chemokine CCL25 and its receptor CCR9; there, they induce changes in the composition of intestinal microbiota. In turn, the imbalance of the microbiota causes intestinal injury through a process dependent on polarization to the T_H17 subset of helper T cells and production of interleukin 17A (IL-17A). Intragastric infection with influenza virus does not cause intestinal injury, which demonstrates that these effects are truly secondary to the lung pathology. *IV*

J. Exp. Med. **211**, 2397–2410 (2014)

Rhinoviruses induce IL-25

Respiratory viruses such as rhinoviruses can exacerbate allergen-driven asthma. In *Science Translational Medicine*, Beale *et al.* report that patients with atopic asthma produce more IL-25 in response to infection with rhinovirus than do healthy people, which contributes to the severity of allergic inflammation and airway hyper-reactivity. Infection with rhinovirus also enhances the production of IL-25 by bronchial epithelial cells in mouse allergy models. This response correlates with greater production of type 2 cytokines, enhanced recruitment of leukocytes and accumulation of cells expressing IL-17RB (the IL-25 receptor) in the infected lungs. However, such allergen-sensitized mice have higher viral loads in their airway tissues, which suggests that this response interferes with antiviral immunity. Blocking IL-17RB in the mouse lungs relieves the exacerbation of asthma and diminishes the viral load. Thus, targeting IL-25 signaling pathways may have therapeutic effects that lessen the disease severity and morbidity associated with viral exacerbation of asthma. ***LAD***

***Sci. Transl. Med.* 6 (1 October 2014) doi:10.1126/scitranslmed.3009124**

Scavenger receptor B1 in lung immunity

The scavenger receptor B1, known for its regulation of high-density lipoprotein complexes in plasma and uptake of vitamin E, is expressed in AMs and epithelial cells, but its role in lung immune responses has not been explored. In *Mucosal Immunology*, Gowdy *et al.* show that SR-B1 is required for host survival in settings of bacterial pneumonia. SR-B1-deficient mice fail to control infection with *Klebsiella pneumoniae* despite developing neutrophilia and expressing more TNF and CXCL5 in their infected lung tissues than do similarly infected wild-type mice. Their bacterial counts are systemically higher, which indicates that loss of local control contributes to dissemination of the pathogen and sepsis. SR-B1-deficient neutrophils show defects in the clearance of lipopolysaccharide, bacterial phagocytosis and killing. The last defect is associated with deficient generation of reactive oxygen species by the intracellular NADPH oxidase complex. These findings should spur further research into how scavenger receptors influence immunity. *LAD*

Mucosal Immunol. (22 October 2014) doi:10.1038/mi.2014.88

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