IN BRIEF

IMMUNE RESPONSES

Eosinophil granules function extracellularly as receptor-mediated secretory organelles

Neves, J. S. *et al. Proc. Natl Acad. Sci. USA* **105**, 18478–18483 (2008)

Eosinophils are characterized by cytoplasmic granules that release their contents when activated by stimuli such as interferon-γ (IFNγ) and eotaxin. This study shows that free eosinophil granules, which are commonly seen in tissues in which a T-helper-2-type response is occurring, can function as extracellular secretory organelles. Following their isolation by density centrifugation, the authors showed that free eosinophil granules released cationic proteins and cytokines in a dose-dependent manner when they were exposed to IFNγ. Furthermore, this secretion was found to be triggered by receptor activation and controlled by intragranular signalling pathways and membranotubular networks. This work suggests that free eosinophil granules can influence immune responses and that other immune-cell types might also produce such secretion-competent granules.

THYMOCYTE DEVELOPMENT

Cutting Edge: Thymic crosstalk regulates Delta-like 4 expression on cortical epithelial cells

Fiorini, E. *et al. J. Immunol.* **181**, 8199–8203 (2008)

Bidirectional crosstalk between developing thymocytes and thymic epithelial cells (TECs) is crucial to establish the appropriate environment for T-cell development. A key example of this crosstalk is the necessary interaction between Notch1 on the lymphoid progenitors and Delta-like ligand 4 (DLL4) on cortical TECs (cTECs). By generating a new monoclonal antibody to closely monitor DLL4 expression in the thymus, this study shows that thymic crosstalk influences the amount of DLL4 that is available to support T-cell development. DLL4 expression by cTECs was high in fetal and neonatal mice (when thymopoiesis is most productive) but low in adult mice. Analysis of mutant mice in which thymocyte development is blocked at different developmental stages revealed that the downregulation of DLL4 in adult mice required progression beyond the double-negative 3 stage of thymocyte development. Thymocyte reconstitution experiments confirmed that thymic crosstalk regulates thymopoiesis by controlling DLL4 expression levels in cTECs.

INNATE IMMUNITY

Autophagosome-independent essential function for the autophagy protein Atg5 in cellular immunity to intracellular pathogens

Zhao, Z. *et al. Cell Host Microbe* **4**, 458–469 (2008)

Autophagy proteins have recently been implicated in the control of infection by intracellular pathogens, but until now their importance during infection *in vivo* was unknown. Here the authors show that mice that specifically lack expression of the autophagy protein ATG5 in macrophages and granulocytes are more susceptible to infection with intracellular pathogens, such as *Toxoplasma gondii* and *Listeria monocytogenes*. ATG5-deficient macrophages failed to clear *T. gondii* from parasitophorous vacuoles following stimulation with lipopolysaccharide (LPS) and interferon-γ (IFNγ). This failure to cause LPS- and IFNγ-induced damage to parasitophorous vacuoles was associated with the impaired recruitment of an IFNγ-inducible GTPase to the vacuole membrane. Given that the authors did not find evidence of autophagosomes enveloping *T. gondii*, they suggest that ATG5 can function in autophagy-independent processes, such as GTPase trafficking during immunity to intracellular pathogens.