IN BRIEF

NEUROIMMUNOLOGY

Neuronal GPCR controls innate immunity by regulating noncanonical unfolded protein response genes

Sun, J. *et al. Science* **332**, 729–732 (2011)

In this study, the model organism *Caenorhabditis elegans* was used to identify a novel link between the nervous and immune systems. The authors found that *C. elegans* lacking OCTR-1 — a G protein-coupled catecholamine receptor that is expressed by sensory neurons — showed increased survival following infection with the pathogenic bacterium *Pseudomonas aeruginosa*. Comparable bacterial loads were found in wild-type and OCTR-1-deficient *C. elegans*, suggesting that the increased survival in OCTR-1-deficient worms was due to enhanced resistance to *P. aeruginosa* infection. This greater resistance resulted from increased activity of an unfolded protein response (UPR) pathway regulated by cell death abnormality protein 1 (CED-1) and required for innate immunity in *C. elegans*. By rescuing OCTR-1 expression, the authors found that neurons involved in chemosensory behaviour negatively regulate this UPR pathway in *C. elegans* through OCTR-1. Importantly, the study shows that neurons in contact with the external environment have the potential to regulate an animal's immune status.

NKT CELLS

Innate and cytokine-driven signals, rather than microbial antigens, dominate in natural killer T cell activation during microbial infection

Brigl, M. *et al. J. Exp. Med.* 9 May 2011 (doi:10.1084/jem.20102555)

Invariant natural killer T (iNKT) cells recognize microbial and endogenous lipid antigens presented by CD1d molecules. In the case of self antigens, co-stimulation with interleukin-12 (IL-12) is required for iNKT cell activation. This study shows that innate cell-derived IL-12 is also essential for full iNKT cell activation by bacteria, irrespective of whether the bacteria express cognate lipid antigens. Defective Toll-like receptor signalling or IL-12 deficiency in dendritic cells resulted in low interferon-γ production by iNKT cells in response to bacterial infection. Moreover, iNKT cells were shown to constitutively express the IL-12 receptor, which may allow for their fast activation. Thus, iNKT cell activation depends primarily on innate immune signals.

VACCINES

Protective T cell immunity in mice following protein-TLR7/8 agonist-conjugate immunization requires aggregation, type I IFN, and multiple DC subsets

Kastenmüller, K. *et al. J. Clin. Invest.* **121**, 1782–1796 (2011)

A key goal of an effective vaccine is to induce protective multifunctional T cell immune responses. Here, Seder and colleagues generated a vaccine in which a protein antigen was conjugated to a TLR7 and TLR8 (TLR7/8) agonist to mimic more closely what dendritic cells (DCs) encounter during infections. Subcutaneous immunization of mice with this vaccine led to increased migration of DCs to the draining lymph node, increased antigen uptake by both resident and migratory DCs, and enhanced antigen-specific T helper 1 (T_H1) cell and $CD8^+$ T cell responses compared with immunization with non-conjugated antigen and TLR7/8 agonist. The effects of the conjugate vaccine were due to protein aggregation and TLR7/8-dependent type I interferon production. Finally, in addition to resident $CD8^+$ DCs, migratory langerin-negative dermal DCs activated $CD8^+$ T cell responses and primed T_H1 cells.