IN BRIEF

NEUROIMMUNOLOGY

Blocking TGF-β–Smad2/3 innate immune signaling mitigates Alzheimer-like pathology.

Town, T. *et al. Nature Med.* **14**, 681–687 (2008)

Despite chronic activation of innate immune cells in the brains of subjects with Alzheimer's disease, microglial cells ultimately fail to clear the build up of amyloid-β peptide that causes brain damage. Here, the authors show that blockade of signalling by transforming growth factor-β receptor type II (TGFβRII) through the expression of a dominant-negative form of the receptor in $CD11c^+$ macrophages attenuates disease in a mouse model of Alzheimer's disease. Specifically, disease-associated behavioural features, such as hyperreactivity, and pathological features, such as β-amyloid deposits, were markedly reduced by TGFβRII signalling blockade. Disease inhibition was associated with increased infiltration of amyloid-β-containing macrophages around cerebral vessels and β-amyloid plaques. However, although SMAD2 and SMAD3 activation downstream of TGFβRII was blocked in these cells, activation of alternative SMAD proteins was increased, and this might be responsible for increasing the phagocytic activity of the infiltrating macrophages.

IMMUNE REGULATION

A crucial role for HVEM and BTLA in preventing intestinal inflammation.

Steinberg, M. W. *et al. J. Exp. Med.* **205**, 1463–1476 (2008)

The tumour-necrosis factor receptor superfamily member HVEM (herpesvirus entry mediator) can mediate either pro- or anti-inflammatory effects, owing to its capacity to interact with both activating and inhibitory receptors. A recent study now shows that the interaction between HVEM and its inhibitory receptor BTLA (B- and T-lymphocyte attenuator) is important for limiting intestinal inflammation in a T-cell transfer model of colitis. Although the roles of HVEM and its receptors have been best characterized in T cells and antigen-presenting cells, the authors found that the lack of HVEM expression by a radiation-resistant non-lymphoid cell population in immunodeficient recipient mice, but not by the transferred T-cell population, led to rapidly lethal intestinal inflammation. So, the balance between activating and inhibitory effects of HVEM might be cell specific, and HVEM expression by non-lymphoid cells can modulate T-cell-mediated inflammation in the intestine.

T-CELL MEMORY

Cutting Edge: chromatin remodeling as a molecular basis for the enhanced functionality of memory CD8 T cells.

Northrop, J. K., Wells, A. D. & Shen, H. *J. Immunol.* **181**, 865–868 (2008)

Memory $CD8^+$ T cells are characterized by their rapid responsiveness to secondary stimulation. However, such a responsive state is not reached if the T cells are activated in the absence of adequate $CD4^+$ T-cell help. Here, the authors show that the defective phenotype of 'unhelped' memory T cells correlates with impaired histone modification. Memory $CD8^+$ T cells that were stimulated *in vitro* in the absence of $CD4^+$ T cells did not have increased levels of histone H3 acetylation (AcH3) at the interferon-γ (*Ifng*) promoter that were observed in 'helped' memory T cells. Moreover, unhelped T cells survived poorly following transfer into wild-type mice and produced less IFNγ following restimulation *in vitro*. Importantly, treatment with a chemical inhibitor of histone deacetylases restored AcH3 and full functional capabilities of unhelped memory T cells, including their ability to provide protective immunity, which supports a role for AcH3 in maintaining memory characteristics.