IN BRIEF

MAST CELLS

Mast cells can enhance resistance to snake and honeybee venoms.

Metz, M. *et al. Science* **313**, 526–530 (2006)

Snake and bee venoms activate mast cells, inducing degranulation and release of biologically active mediators. The idea that such mediators contribute to the tissue injury associated with a bite or sting has been overturned by a new study that shows, instead, that mast-cell activation ameliorates the pathogenic effects of venom. Mice lacking mast cells were tenfold more sensitive than wild-type mice when injected with venom or purified venom toxin. The transfer of mast cells from wild-type mice to the deficient mice restored resistance. Protection was mediated, in part, by proteases capable of digesting venom components. Because mast cells contain cytoplasmic granules that are rich in proteases, they could be active against toxins of diverse origin. So, in contrast to their widely known pathogenic role in allergic disorders, mast cells seem to have a beneficial role in host defence against animal venoms.

IMMUNOTHERAPY

Inhibition of T cell activation and autoimmune diabetes using a B cell surface-linked CTLA-4 agonist.

Fife, B. T. *et al. J. Clin. Invest.* **116**, 2252–2261 (2006)

Cytotoxic T-lymphocyte antigen 4 (CTLA4) has a crucial role in the regulation of T cells and immune tolerance. However, attempts to target CTLA4 directly as a means of suppressing T-cell-mediated autoimmune disorders, such as diabetes, have proved unsuccessful. Agonists of CTLA4 crossreact with other receptors, and CTLA4-specific antibodies administered alone do not stimulate the appropriate signals. In a new approach, the authors developed transgenic mice that have a single-chain, membrane-bound CTLA4-specific antibody expressed by antigen-presenting B cells, which have a crucial role in the non-obese diabetic (NOD) mouse model of diabetes. The presence of these B cells in NOD mice inhibited the spontaneous development of autoimmune diabetes, even in the absence of regulatory T cells. This model system shows that T-cell engagement of a CTLA4 agonist on B cells can block *in vivo* T-cell responses to antigens presented by these B cells, and it opens up a new avenue for immunotherapy.

HIV

Structural basis for targeting HIV-1 Gag proteins to the plasma membrane for virus assembly.

Saad, J. S. *et al. Proc. Natl Acad. Sci. USA* **103**, 11364–11369 (2006)

Targeting of the retroviral protein Gag (group-specific antigen) to the plasma membrane is essential for the assembly of immature HIV virions and for their budding and release from infected cells. Nuclear-magnetic-resonance studies have now shown that plasma-membrane targeting of Gag is achieved by binding of the matrix (MA) domain of Gag to the membrane lipid phosphatidylinositol-4,5-bisphosphate (PtdIns(4,5)P_2). Binding of the MA domain to PtdIns(4,5)P_2 leads to a conformational change that exposes a myristyl group in the MA domain, which can then attach to the plasma membrane and stabilize Gag binding. The authors suggest that blocking the MA–PtdIns(4,5)P_2 interaction could be a new therapeutic strategy, particularly because the relevant region of the MA domain does not seem to mutate much in HIV-1.