IN BRIEF

AUTOIMMUNITY

Chromogranin A is an autoantigen in type 1 diabetes

Stadinksi, B. D. *et al. Nature Immunol.* 7 Feb 2010 (doi:10.1038/ni.1844)

Several diabetogenic $CD4^+$ T cell clones have been isolated from non-obese diabetic (NOD) mice; some of these clones are specific for insulin peptides, but the other antigenic targets have remained unknown. This study shows that the target antigen of certain BDC T cell clones, which are known to react to pancreatic islets in an insulin-independent manner, is a peptide (WE14) from the neuroendocrine secretory protein chromogranin A. WE14 was shown to bind I–A^{g7} MHC class II molecules in an atypical manner, occupying the carboxy-terminal half of the MHC peptide-binding groove. ***In vitro***, BDC T cells produced interferon-γ in response to wild-type pancreatic β-cells, but did not respond to chromogranin A-deficient β-cells. As chromogranin A is widely expressed outside the pancreas, the authors suggest that pancreas-specific post-translational modification of chromogranin A-derived peptides could explain why NOD mice do not develop autoimmune responses against other tissues.

IMMUNE TOLERANCE

Mechanism of T cell tolerance induced by myeloid-derived suppressor cells

Nagaraj, S. *et al. J. Immunol.* 8 Feb 2010 (doi:10.4049/jimmunol.0902661)

This study explains how T cell tolerance to tumours can be antigen specific. Nagaraj ***et al.*** show that when antigen-specific $CD8^+$ T cells were exposed to myeloid-derived suppressor cells (MDSCs) presenting their cognate antigen, T cell receptor (TCR) signalling was not induced. The presence of MDSCs also inhibited T cell stimulation by dendritic cells (DCs) presenting the same peptide. Using a T cell line expressing two different TCRs, MDSC-mediated suppression was shown to affect only the TCR response to the peptide presented by the MDSCs; signalling by the other TCR was not affected. ***In vivo*** assays using tumour-bearing mice confirmed that T cell suppression was specific for the antigen expressed by the tumour cells. Imaging studies revealed that the mechanism involved dissociation of the TCR complex caused by nitrosylation of molecules at the point of contact between MDSCs and T cells.

DENDRITIC CELLS

Mature dendritic cells use endocytic receptors to capture and present antigens

Platt, C. D. *et al. Proc. Natl Acad. Sci. USA* 8 Feb 2010 (doi:10.1073/pnas.0910609107)

Immature dendritic cells (DCs) use various mechanisms for antigen uptake, but activation of DCs leads to decreased endocytosis and the loss of MHC class II molecules from late endocytic compartments. Therefore the current dogma has been that fully mature DCs no longer acquire antigen. This view has been challenged by Platt ***et al.*** who show that fully mature DCs can still accumulate antigen from their surroundings. Bone marrow-derived DCs ceased to show macropinocytosis following activation with lipopolysaccharide, but these cells continued to acquire antigen by receptor-mediated endocytosis or phagocytosis. Mature DCs could efficiently present newly acquired antigens to T cells. The authors suggest that previous uptake studies (where immature or mature DCs have been exposed to large doses of antigen ***in vitro***) have chiefly measured macropinocytosis; consequently, we may have underestimated the ability of activated DCs to continue to take up new antigens.