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IN BRIEF

REPRODUCTIVE IMMUNOLOGY

Constraints in antigen presentation severely restrict T cell recognition of the allogeneic fetus.

Erlebacher, A. *et al. J. Clin. Invest.* **117**, 1399–1411 (2007)

Why does the maternal immune system not recognize the fetus as foreign? Determining how fetal antigens are presented to maternal T cells might hold the answer. In this paper, the authors developed a system to visualize T-cell responses to the fetus, and found that fetal antigens are presented to both maternal $CD4^+$ and $CD8^+$ T cells exclusively through indirect antigen presentation. This pathway of presentation ensures that the large population of T cells that are activated by direct presentation and that typically drive acute transplantation rejection are unaware of the fetal allograft. In addition, defective priming and clonal deletion of $CD8^+$ T cells was observed following exposure to fetal antigens, and antigen presentation commenced only at mid-gestation. So, by limiting how maternal T cells recognize fetal antigens, the fetus can escape rejection by the maternal immune system.

EVOLUTION

Evolution and diversification of lamprey antigen receptors: evidence for involvement of an AID-APOBEC family cytosine deaminase.

Rogozin, I. B. *et al. Nature Immunol.* 29 April 2007 (doi:10.1038/ni1463)

Jawless vertebrates, including lampreys and hagfish, do not have immunoglobulins but instead have variable lymphocyte receptors (VLRs). VLRs are somatically rearranged receptors composed of diverse leucine-rich repeats but the mechanism of their assembly is not known. Here, Rogozin and colleagues assembled a draft of the sea lamprey genome. Comparison of genomic sequences with mature VLR sequences revealed that mature VLRs are assembled from multiple genomic cassettes in a gene-conversion-like process. The authors also identified genes encoding two members of the AID-APOBEC cytosine deaminase family and found that these putative deaminases might be involved in VLR diversification and could therefore represent a primordial mechanism of the AID-induced DNA strand breaks that are required for immunoglobulin gene conversion.

T-CELL DEVELOPMENT

RANK signals from $CD4^+3^-$ inducer cells regulate development of Aire-expressing epithelial cells in the thymic medulla.

Rossi, S. W. *et al. J. Exp. Med.* 14 May 2007 (doi:10.1084/jem.20062497)

Central tolerance occurs in the thymus when developing thymocytes interact with specialized medullary thymic epithelial cells (mTECs) which express autoimmune regulator (AIRE), a transcription factor that controls the expression of tissue-restricted antigens by mTECs. To date, the molecular mechanisms controlling mTEC development have been undefined. Now, Rossi and colleagues show that $CD4^+CD3^-$ lymphoid-tissue inducer cells — which have previously been associated with the development and function of secondary lymphoid tissue — are present in the thymus and express the RANK (receptor activator of nuclear factor-κB) ligand. These cells control the development of mature $AIRE^+$ mTECs from $RANK^+AIRE^-$ mTEC progenitor cells. When $RANK^-$ thymic stromal cells were transplanted into immunodeficient hosts, this resulted in autoimmunity similar to the disease that occurs when AIRE is defective, confirming a key role for RANK as a regulator of central tolerance.