IN BRIEF

EVOLUTION

Female sticklebacks count alleles in a strategy of sexual selection explaining MHC polymorphism.

Reusch, T. B. H., Häberli, M. A., Aeschlimann, P. B. & Milinski, M. *Nature* **414**, 300–302 (2001)

Several mechanisms have been suggested by which allelic diversity at the major histocompatibility complex (MHC) is maintained. Reusch and co-workers now describe a newly discovered mechanism — rather than selecting a mate with a dissimilar MHC genotype, female sticklebacks 'count' the number of MHC alleles and prefer males with greater allelic diversity as opposed to males with fewer alleles.

TOLERANCE

Corticotropin-releasing hormone promotes blastocyst implantation and early maternal tolerance.

Makrigiannakis, A. *et al. Nature Immunol.* **2**, 1018–1023 (2001)

This paper describes a new mechanism of maternal tolerance. Corticotropin-releasing hormone (CRH) is released after embryo implantation and was shown to induce Fas ligand expression by trophoblast cells, leading to apoptosis of activated T cells that express the death receptor Fas. CRH inhibition was shown to reduce successful embryo implantation in rats. These results indicate that CRH-induced expression of Fas ligand leads to the killing of activated T cells that would otherwise harm the embryo during implantation.

ALLERGY

Hyper immunoglobulin E response in mice with monoclonal populations of B and T lymphocytes.

de Lafaille, M. A. *et al. J. Exp. Med.* **194**, 1349–1360 (2001)

IgE production driven by T_H2 cells is a central pathogenic mechanism in allergy. When mice with monoclonal populations of ovalbumin (OVA)-specific B cells and haemagglutinin (HA)-specific $CD4^+$ T cells were immunized with OVA–HA, unusually high levels of IgE were produced. But this hyper IgE response was prevented by transferring normal, polyclonal $CD4^+/\alpha\beta^+$ T cells. Both $CD25^+$ and $CD25^-$ regulatory T-cell subsets can mediate this effect, which involves inhibition of T_H2 development.

NATURAL KILLER-CELL ACTIVATION

Activation of NK cell-mediated cytotoxicity by a SAP-independent receptor of the CD2 family.

Bouchon, A., Cella, M., Grierson, H. L., Cohen, J. L. & Colonna, M. *J. Immunol.* **167**, 5517–5521 (2001)

Marco Colonna's group has identified a new member of the CD2 family called CD2-like receptor activating cytotoxic cells or CRACC. Although CRACC has cytoplasmic motifs similar to those that recruit SAP (SLAM-associated protein) to other CD2 molecules, CRACC can activate natural killer cell-mediated cytotoxicity in the absence of SAP via an extracellular signal-regulated kinase-dependent signalling pathway.

IMMUNE TOLERANCE

Random reflections

T cells are able to recognize foreign antigens and contribute to disease protection, and yet they are tolerant to the myriad of self-antigens they are exposed to. Tolerance to self-antigens is developed in two ways — central tolerance to ubiquitously expressed proteins and blood-borne self-antigens occurs in the thymus, and peripheral mechanisms are required for the development of tolerance to self-antigens that are expressed in specific tissues. However, tissue-specific antigens have been detected within the thymus. The cells responsible for this 'promiscuous' gene expression have, until now, been undefined. Reporting in *Nature Immunology*, Derbinski and colleagues now show that medullary thymic epithelial cells (mTECs) express a range of tissue-specific antigens in the thymus.

To investigate gene expression within the thymus the authors purified cortical and medullary TECs, macrophages and dendritic cells and analysed their gene expression profiles by reverse-transcription polymerase chain reaction (RT-PCR). The expression of a range of genes (including enzymes, structural proteins and genes of restricted tissue distribution) was studied. mTECs consistently expressed a wide range of tissue-specific self-antigens.

Further experiments showed that the scope and level of promiscuous gene expression by mTECs was maintained throughout the period of thymic T-cell output and did not decline with age. This is important, for if the expression of tissue-specific genes in the thymus is to shape the T-cell repertoire it needs to be maintained as long as T cells are being produced.

The authors also showed that the ability of mTECs to express self-antigens is not dependent on intact T-cell development and is a cell-autonomous property of mTECs.

But is this promiscuous gene expression important in the generation of tolerant T cells? To address this question, Derbinksi and colleagues generated chimeric mice for serum amyloid P component (Sap), the main acute-phase protein in mice. Mice either expressed Sap within mTECs exclusively ($Sap^{+/+}$ thymus transplanted into thymectomized $Sap^{-/-}$ recipients) or Sap expression by mTECs was excluded ($Sap^{-/-}$ thymus transplanted into thymectomized $Sap^{+/+}$ recipient). The results showed that for Sap, promiscuous expression in mTECs was sufficient, but not necessary, to induce $CD4^+$ T-cell tolerance.

In conclusion, the authors describe the thymus as an immunological homunculus, in that it expresses a range of randomly selected self-antigens that mirror and anticipate the peripheral self.

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References and links

ORIGINAL RESEARCH PAPER Derbinski, J., Schulte, A, Kyewski, B. & Klein, L. Promiscuous gene expression in medullary thymic epithelial cells mirrors the peripheral self. *Nature Immunol.* **2**, 1032–1039 (2001)

FURTHER READING Klein, L & Kyewski, B. "Promiscuous" expression of tissue antigens in the thymus: a key to T-cell tolerance and autoimmunity? *J. Mol. Med.* **78**, 483–494 (2000)