IN BRIEF

T-CELL DEVELOPMENT

Tox: an HMG box protein implicated in the regulation of thymocyte selection.

Wilkinson, B. *et al. Nature Immunol.* **3**, 272–280 (2002)

T-cell receptor (TCR) signalling is vital for the positive selection of mature T cells. How these signals are translated into changes in gene expression that are required for T-cell maturation and lineage commitment is unknown. This study describes the identification of *Tox*, which encodes an High Mobility Group (HMG) box family DNA-binding protein. Tox mRNA and protein are upregulated in T cells undergoing positive selection, and *Tox* transgenic mice have increased $CD8^+$ and reduced $CD4^+$ thymocytes. This perturbed lineage commitment might result from Tox-mediated changes in gene expression.

SOMATIC HYPERMUTATION

Activation-induced cytidine deaminase turns on somatic hypermutation in hybridomas.

Martin, A. *et al. Nature* **415**, 802–806 (2002)

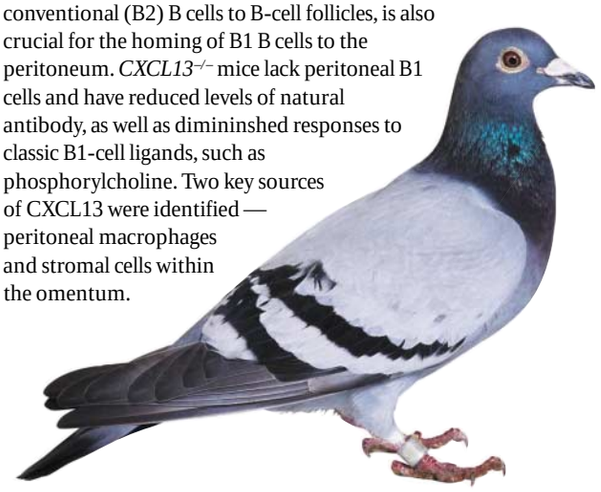
Activation-induced cytidine deaminase (AID) is essential for somatic hypermutation, although its actual role is not understood. Here, hybridomas, which represent an antibody-secreting B-cell stage that does not normally undergo hypermutation, were transfected with *AID*. Surprisingly, this was sufficient to induce hypermutation of *V* genes, indicating that other factors expressed by germinal centre-stage B cells are not essential for the induction of hypermutation. This discovery opens up the possibility of recapitulating affinity maturation *in vitro* to improve the binding of monoclonal antibodies.

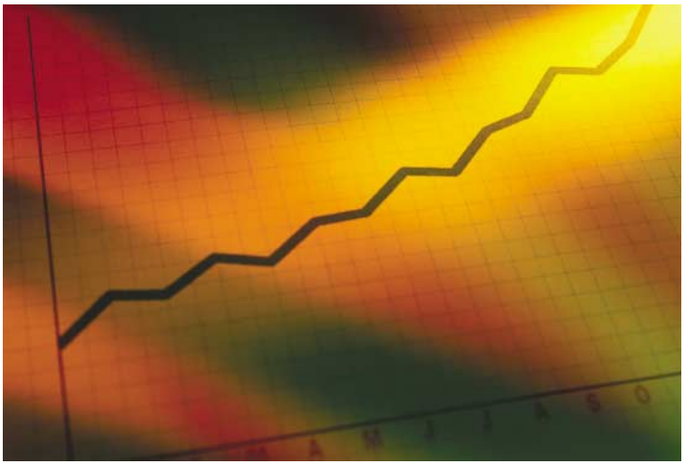
LYMPHOCYTE MIGRATION

CXCL13 is required for B1-cell homing, natural antibody production and body cavity immunity.

Ansel, K. M., Harris, R. B. & Cyster, J. G. *Immunity* **16**, 67–76 (2002)

B1 cells predominate in the body cavities and participate in innate defence by producing natural antibody. Here the authors show that the chemokine CXCL13, which is essential for the homing of conventional (B2) B cells to B-cell follicles, is also crucial for the homing of B1 B cells to the peritoneum. *CXCL13*$^{-/-}$ mice lack peritoneal B1 cells and have reduced levels of natural antibody, as well as dimininshed responses to classic B1-cell ligands, such as phosphorylcholine. Two key sources of CXCL13 were identified — peritoneal macrophages and stromal cells within the omentum.





VIRAL IMMUNITY

Positive prospects

The CC chemokine receptor CCR5 is an important co-receptor for HIV, and patients who lack this receptor have a reduced susceptibility to infection. Anti-CCR5-based therapies for HIV are being developed, but the role of CCR5 in normal antiviral responses has not been directly investigated. Nansen and colleagues now report in *Blood* that CCR5 is not crucial for T-cell-mediated antiviral immunity, validating the use of CCR5 as a target for HIV therapies.

The authors used the murine lymphocytic choriomeningitis virus (LCMV) model to compare the antiviral responses of *CCR5*$^{-/-}$ and wild-type mice. Infection with LCMV normally induces the generation of activated $CD4^+$ and $CD8^+$ T cells, which are important for clearing the viral infection and which cause inflammation of infected organs. Intracerebral infection leads to fatal T-cell-mediated meningitis. To investigate the importance of CCR5 expression for the generation of LCMV-specific T cells, the frequency of virus-specific $CD4^+$ and $CD8^+$ T cells in the spleens of *CCR5*$^{-/-}$ and wild-type mice were compared. Virus-induced clonal expansion of antigen-specific T cells, particularly $CD4^+$ cells, was actually enhanced in the *CCR5*$^{-/-}$ mice.

Do these *CCR5*$^{-/-}$ LCMV-specific T cells clear the virus effectively? The kinetics of viral clearance in the spleen, liver and lungs was similar in the *CCR5*$^{-/-}$ and wild-type mice, showing that cytolytic T-cell function in, and homing to, infected organs is not affected in the absence of CCR5. Despite lacking expression of CCR5, the knockouts succumb to lethal T-cell-mediated meningitis following intracerebral infection. In addition, the authors found no significant differences between the knockout and wild-type mice in the recruitment of monocytes/macrophages to the inflamed meninges or in the cerebral chemokine and CCR gene expression. Analysis of the long-term $CD8^+$ T-cell-mediated response to LCMV also showed a redundant role for CCR5 in the memory phase of LCMV infection.

The authors conclude that CCR5 expression is not crucial for T-cell-mediated antiviral immunity and that there are positive prospects for anti-CCR5 HIV therapies.

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References and links

ORIGINAL RESEARCH PAPER Nansen, A. *et al.* The role of CC chemokine receptor 5 in antiviral immunity. *Blood* **99**, 1237–1245 (2002).

FURTHER READING Sallusto, F. *et al.* The role of chemokine receptors in primary, effector, and memory immune responses. *Annu. Rev. Immunol.* **18**, 593–620 (2000).

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Chemokines