HSV-8p in both strains — should have a similar relative effect in each strain. But, if breadth of the repertoire is important, depletion of V β 8⁺ T cells would affect the outcome differentially. When V β 8⁺ T cells were depleted, B6 mice showed enhanced mortality, whereas bm8 mice showed no difference in mortality compared with non-depleted mice. This provides evidence that CTL repertoire diversity can influence resistance to infection. In addition, CTLs from bm8 mice had higher avidity for antigen and were better able to kill target cells in a CTL assay.

The authors suggest that MHC-polymorphism-driven diversification of the TCR repertoire in bm8 mice allows high-avidity CTLs to be generated more readily, and that this might be the link between MHC polymorphism and resistance to infection.

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References and links

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IMMUNOLOGICAL MEMORY

SAPping B-cell memory

Mutations of SAP (SH2 domain protein 1A) are responsible for X-linked lymphoproliferative disease, a syndrome that is characterized by three main phenotypes — fulminant infectious mononucleosis, B-cell lymphomas and dysgammaglobulinaemia. But, the precise role of SAP in controlling immune responses remains unclear. A new study, reported in *Nature*, shows that the expression of SAP by CD4⁺ T cells is important for controlling the development of long-term humoral immunity.

B-cell responses were investigated in SAP-deficient mice after infection with lymphocytic choriomeningitis virus (LCMV). Wild-type mice generate strong primary responses, clear an infection with LCMV quickly and develop long-term specific B- and T-cell responses. SAP-deficient mice also make good primary responses, and they develop a similar number of virus-specific antibody-secreting cells (ASCs). When virus was cleared in the wild-type mice, the number of LCMV-specific ASCs decreased and then stabilized at about 10% of peak levels. But in SAP-deficient mice, ASCs were barely detectable by day 15. The number of long-lived plasma cells in the bone marrow was also much lower in SAP-deficient mice than in wild-type mice.

Next, the authors looked at the kinetics of the immunoglobulin-G response in the serum of SAP-deficient mice, and these were found to be comparable

to the kinetics of ASCs. No significant differences in isotype switching were detected between wild-type and SAP-deficient mice. However, germinal centres were significantly reduced in both size and number in SAP-deficient mice, which indicates that germinal centres are necessary for the development of long-lived plasma cells.

So, which cell type is responsible for the defective development of long-lived plasma cells and of B-cell memory in SAP-deficient mice? To determine this, adoptive-transfer experiments were carried out. Mice that received SAP-deficient T cells and wild-type B cells followed by infection with LCMV had defective development of long-term humoral immunity. Further experiments showed that SAP must be expressed by CD4⁺ T cells to enable long-term humoral immunity to develop.

This study has uncovered an unusual effect of a genetic defect, in which normal numbers of antigen-specific CD4⁺ T cells are generated and early B-cell help occurs, but in which SAP deficiency is not permissive for the B-cell help that is necessary for the development of long-term humoral immunity.

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References and links

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