resulted in an increased production of $CD4^+$ T cells, in contrast to the transplantation of *Cd83*$^{-/-}$ epithelial cells.

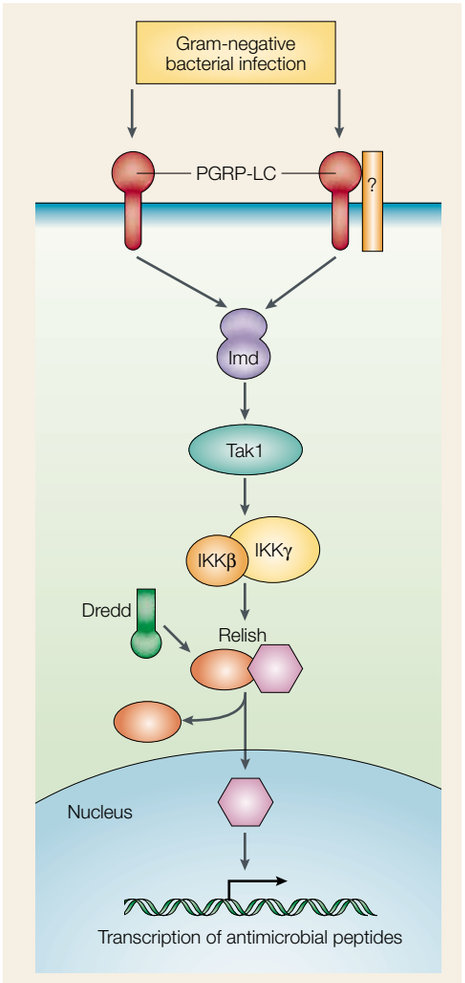
These results imply that the developmental defect that is seen in *Cd83*$^{-/-}$ mice is due to an impaired thymic microenvironment in these mice and that the expression of CD83 by non-lymphoid cells within the thymus is required for $CD4^+$ T-cell development. This work is the first to show the importance of CD83 engagement for the regulation of $CD4^+$ T-cell differentiation in the thymus.

Jenny Buckland

References and links

ORIGINAL RESEARCH PAPER Fujimoto, Y. *et al*. CD83 expression influences $CD4^+$ T-cell development in the thymus. *Cell* **108**, 755–767 (2002)

FURTHER READING Anderson, G. & Jenkinson, E. J. Lymphostromal interactions in thymic development and function. *Nature Rev. Immunol*. **1**, 31–40 (2001)



AUTOIMMUNITY

Different cuts

Local variations in proteasome composition might regulate organ-specific autoimmunity, according to a recent report in *The Journal of Experimental Medicine*.

Ulrike Kuckelkorn and colleagues set out to investigate why self-antigens that are expressed ubiquitously can drive organ-specific autoimmune responses. They used a mouse model in which T-cell-receptor-transgenic $CD8^+$ T cells that cross-react with the ubiquitous self-antigen heat-shock protein 60 (Hsp60) are transferred into T-cell-deficient mice. The resulting autoimmune response is restricted to the small intestine, despite similar migration of transgenic T cells to the colon. The authors wondered if tissue-specific differences in the proteolytic processing of Hsp60 epitopes might account for this.

A key player in the generation of peptide epitopes that are recognized by $CD8^+$ T cells is the proteasome, which consists of a cylindrical active core with a regulatory complex at each end. The core — which is known as the 20S proteasome — consists of two α-rings and two β-rings, each of which is formed by seven subunits. The basic 20S proteasome is expressed constitutively. However, interferon-γ induces the expression of components that replace the constitutive β-subunits; this forms the 'immunoproteasome', which has altered activities.

The authors examined the composition of 20S proteasomes from various tissues by two-dimensional gel electrophoresis. Comparing the small intestine with the colon, they found organ-specific expression patterns of the inducible β-subunits. Differentially expressed variants of α4 and α6 subunits (which interact with the regulatory complexes) were identified also.

Proteasomes from different organs were shown to have distinct cleavage-site preferences for the processing of Hsp60 *in vitro*. Notably, the Hsp60-derived peptide that is recognized by the pathogenic T cells was produced most efficiently by the proteasomes of the small intestine.

But, are the quantitative and qualitative differences in peptide production relevant to $CD8^+$ T-cell recognition? This was tested in a chromium-release assay, in which target cells were pulsed with peptide products that had been generated *in vitro* by proteasomes isolated from various tissues. Only target cells that had been pulsed with peptides processed by small-intestine-derived proteasomes were lysed by the transgenic T cells.

The authors propose that this organ-specific generation of epitopes, "represents an important mechanism to control the reactivity of autoreactive $CD8^+$ T cells that escape thymic deletion".

Jennifer Bell

References and links

ORIGINAL RESEARCH PAPER Kuckelkorn, U. *et al.* Link between organ-specific antigen processing by 20S proteasomes and $CD8^+$ T-cell-mediated autoimmunity. *J. Exp. Med.* **195**, 983–990 (2002)

FURTHER READING Kloetzel, M. P. Antigen processing by the proteasome. *Nature Rev. Mol. Cell Biol*. **2**, 179–188 (2001) | Steinhoff, U. *et al.* Autoimmune intestinal pathology induced by hsp60-specific CD8 T cells. *Immunity* **11**, 349–358 (1999)