T-CELL DEVELOPMENT

Thymocyte-selected CD4$^+$ T cells

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Two papers published in 2005 showed that, in addition to positive selection of thymocytes on MHC-class-II-positive thymic epithelial cells (TECs), human thymocytes themselves express MHC class II molecules and can mediate positive selection of other thymocytes. Mouse thymocytes do not express MHC class II, so Li and colleagues generated mice with MHC-class-II-positive thymocytes by expressing the MHC class II transactivator — a transcription factor that is required for the expression of several molecules involved in MHC class II antigen presentation — as a transgene under the control of the *Cd4* promoter (termed CIITA^{Tg} mice). The current study shows that by comparison to TEC-selected CD4$^+$ T cells, thymocyte-selected CD4$^+$ T cells retain characteristics of both T helper 1 (T_H1) and T_H2 cells.

The authors first compared cytokine production from T cells isolated from wild-type mice (which only have TEC-selected CD4$^+$ T cells) and from CIITA^{Tg} mice (which have a mixed population of CD4$^+$ T cells selected on both TECs and thymocytes). T cells from CIITA^{Tg} mice produced both interleukin-4 (IL-4) and interferon-γ (IFNγ) and at higher levels compared with T cells from wild-type mice, showing that T cells from CIITA^{Tg} mice have hallmarks of both T_H1 and T_H2 cells.

To look at cytokine production from thymocyte-selected cells only, the authors isolated T cells from CIITA^{Tg} mice on a CIITA-deficient background. Even under T_H1-polarizing conditions, thymocyte-selected CD4$^+$ T cells expressed both IL-4 and IFNγ. Bone-marrow chimaera experiments further substantiated these results. Strikingly, even though the signal transducer and activator of transcription 6 (STAT6) signalling pathway is crucial in T_H2-cell differentiation, thymocyte-selected CD4$^+$ T cells from *Stat6*-knockout mice were able to produce IL-4.

The authors next looked at the role of thymocyte-selected CD4$^+$ T cells in an antigen-induced airway inflammation model using a T_H2-cell-inducing allergen. Although thymocyte-selected CD4$^+$ T cells can produce T_H2-type cytokines, CIITA^{Tg} mice were less susceptible to airway inflammation, as shown by reduced numbers of eosinophils and neutrophils in lung tissue and a reduction in IgE levels compared with wild-type mice. The explanation for this phenomenon is not yet clear.

This study shows that the thymic selection pathway influences the effector function of CD4$^+$ T cells and suggests that further studies might be warranted to address the role of thymocyte-selected CD4$^+$ T cells in immune responses in humans.

Elaine Bell

ORIGINAL RESEARCH PAPER Li, W. *et al.* Thymic selection pathway regulates the effector function of CD4 T cells. *J. Exp. Med.* **204**, 2145–2157 (2007)