

Tracking down the thymocyte precursors of agonist-selected T cells.

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In the gut epithelium resides an abundant population of TCR $\alpha\beta$ ⁺ intraepithelial lymphocytes (IEL) that express the CD8 $\alpha\alpha$ molecule. Recently, it has been shown that these T cells are selected within the thymus in the presence of agonist self-peptides that cause negative selection of conventional T cells. These opposing outcomes may reflect the utilization of different cellular signaling pathways. Up until now the expression of CD8 $\alpha\alpha$ has been restricted to cells within the gut, however we have discovered that a subpopulation of double positive (DP) thymocytes expresses CD8 $\alpha\alpha$. To understand the development of agonist selected T cells, we took advantage of evidence from IL-15/IL-15R α deficient animals that suggest IL-15 plays a role in the development, expansion and/or survival of the CD8 $\alpha\alpha$ expressing cells. Ex vivo culturing of CD4-CD8 α -double negative (DN) thymocytes in the presence of IL-15 lead to the expansion of a CD8 $\alpha\alpha$ expressing TCR $\alpha\beta$ ⁺ population. These cells also showed pronounced expression of the IL-15 receptor together with enhanced levels of the anti-apoptotic factors Bcl-2 and Bcl-x_L. We therefore hypothesize that the SP CD8 $\alpha\alpha$ expressing thymocytes represent precursors of the agonist selected T cells that develop in the thymus, possibly through a triple positive stage and undergo agonist selection in an IL-15 dependent way.