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HDAC7 regulates apoptosis in developing thymocytes

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Abstract

Central immune tolerance is established in the thymus for T cells via a complex selection process that involves interactions between CD4+CD8+ double-positive thymocytes and antigen-presenting cells. Cells that express antigen receptors interacting strongly with self peptide MHC complexes are deleted from the repertoire via activation-induced apoptosis, a process termed negative selection. Cells that express an appropriate signal are positively selected and mature into single positive naïve T cells, either CD4 or CD8 positive. The balance between positive and negative selection is thought to play a critical role in the elimination of self-reactive clones and in the establishment of central immune tolerance. We have recently reported that HDAC7, a class II histone deacetylase, is highly expressed in CD4+CD8+ double positive thymocytes. HDAC7 inhibits Nur77 expression, an orphan receptor involved in antigen-induced cell death and in negative selection. The inhibitory effect of HDAC7 on the Nur77 promoter is mediated via the transcription factor MEF2D. During T cell receptor activation, HDAC7 is exported from the nucleus leading to the derepression of Nur77 expression and the induction of apoptosis. These observations define HDAC7 as a regulator of Nur77 and apoptosis in developing thymocytes and indicate that HDAC7 is likely to play an important role in the control of central immune tolerance.

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