

Title: Tracing the Role of Nur77 in the Negative Selection of Autoreactive Thymocytes

Authors: Samuel G. Edmondson, Hyung J. Cho, Arden D. Miller, MacLean Sellars, Allison L. Tan, Shawn T. Alexander, Jennifer A. Punt

Abstract: Autoreactive thymocytes can be eliminated by clonal deletion during their development in the thymus. The precise developmental stage(s) at which clonal deletion occurs in a normal thymus has been difficult to assess, in large part because of the absence of a specific marker for TCR-mediated apoptosis. We reveal that Nur77 expression can be used as a specific marker of clonal deletion in an unmanipulated thymus and directly identify TCR^{int}CD4⁺CD8⁺ and semi-mature CD4⁺CD8⁻ thymocytes as the principal targets of deletion. These data indicate that clonal deletion normally occurs at a relatively late stage of development, as cells mature from CD4⁺CD8⁺ thymocytes to single positive T cells. We also reveal that immature thymocytes and mature lymphocytes exhibit differences in the regulation of Nur77.