

SOCS1 Regulates TCR-Mediated Signaling

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Suppressor of Cytokine Signaling 1(SOCS1) is a cytokine inducible inhibitor of Janus kinases. SOCS1^{-/-} mice die between days 10 and 20 following birth, however, OTI transgenesis rescues this defect prolonging life. Study of SOCS1^{-/-} T cells has been hampered by their spontaneous activation. OTI SOCS1^{-/-} peripheral T cells have a central memory phenotype: CD25^{neg}, CD69^{neg}, CD44^{hi}, CD62L^{hi} and Ly6C^{hi}. IL-2 receptor b-chain is elevated in these cells. OTI SOCS1^{-/-} thymi have increased percentage of CD8 single positive cells and corresponding reduction in the double positive (CD4+ CD8+) population. The CD8 single positive cells have a naïve phenotype: CD44^{lo} CD69^{neg}, CD25^{neg}. OTI SOCS1^{-/-} thymic single positive and peripheral T cells respond better than wild type to stimulation with antigen. SOCS1^{-/-} T cells upregulate CD25 and CD69 faster. They also secrete more IL-2 and IFN γ . These cells are hyperproliferative to IL-2 and IL-15 alone as well as TCR stimulation by antigen or anti-CD3. SOCS1^{-/-} T cells exhibit lower TCR expression levels at all stages of development. Calcium flux is equivalent to lower in SOCS1^{-/-} T cells following TCR-ligation. SOCS1 clearly plays a role in the regulation of T cell responsiveness to antigen and appears to directly regulate TCR-mediated signaling.