# A Signal Through OX40 Prevents the Shut Down of CD4 T Cell IFN Production in a Model of Peripheral Tolerance.

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In our model of peripheral tolerance, naïve $CD4^+$ T cells from moth cytochrome c (MCC) peptide-specific TCR transgenic mice (AND) are injected into antigen-transgenic recipients expressing an MCC peptide covalently attached to the $I\text{-}E^k$ chain under the control of a class II promoter. The transferred T cells expand rapidly in the spleen within a few days, infiltrate the liver and lung, but then slowly disappear without causing any obvious autoimmunity in the host animal. Recovered donor AND T cells are unresponsive to antigen stimulation *in vitro* even upon addition of IL-2. Injection of the host animal with an agonist antibody for the TNFR family member OX40 upon transfer of the donor cells results in a greater accumulation of AND T cells, liver damage, and death of the host animal in 7 - 12 days. AND T cells recovered from OX40 treated mice, in comparison to those from mice treated with an isotype control antibody, are larger and more granular by flow cytometry, highly CD25 (IL-2R) positive, and secrete IFN independently of stimulation with peptide antigen *in vitro*. Recovered T cells from OX40-treated animals respond to *in vitro* stimulation with IL-12 and IL-18 by secretion of IFN, and proliferate in response to IL-2, while cells from animals treated with an isotype antibody remain unresponsive. Our results suggest that a signal through OX40 on $CD4^+$ T cells prevents shut down of effector cytokine secretion, blocking the induction of peripheral tolerance in this model.