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# Innate Activation of IFN-γ-iNOS Axis During Infection With *Salmonella* Represses the Ability of T Cells to Produce IL-2

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## Abstract

Pathogenic *Salmonella* serovars are a major cause of enteric illness in humans and animals, and produce clinical manifestations ranging from localized gastroenteritis to systemic disease. T cells are a critical component of immunity against this intracellular pathogen. The mechanisms by which *Salmonella* modulates T-cell-mediated immune responses in order to establish systemic infection are not completely understood. We show that infection of mice with *Salmonella enterica* serovar Typhimurium (*S*. Typhimurium) suppresses IL-2 and increases IFN-γ and IL-17 production from T cells activated *in vivo* or *ex vivo* through the T cell receptor. Infection with *S*. Typhimurium brings about recruitment of $CD11b^{+}Gr1^{+}$ suppressor cells to the spleen. *Ex vivo* depletion of these cells restores the ability of activated T cells to produce IL-2 and brings secretion of IFN-γ and IL-17 from these cells back to basal levels. The reduction in IL-2 secretion is not seen in $IFN\text{-}\gamma^{-/-}$ and $iNOS^{-/-}$ mice infected with *Salmonella*. Our findings demonstrate that sustained innate activated IFN-γ production during progression of infection

with *Salmonella* reduces IL-2-secreting capability of T cells through an iNOS-mediated signaling pathway that can adversely affect long term immunity against this pathogen.