Signaling via the MyD88 Adaptor Protein in B Cells Suppresses Protective Immunity during Salmonella typhimurium Infection.

The myeloid differentiation primary response gene 88 (Myd88) is critical for protection against pathogens. However, we demonstrate here that MyD88 expression in B cells inhibits resistance of mice to Salmonella typhimurium infection. Selective deficiency of Myd88 in B cells improved control of bacterial replication and prolonged survival of the infected mice. The B cell-mediated suppressive pathway was even more striking after secondary challenge. Upon vaccination, mice lacking Myd88 in B cells became completely resistant against this otherwise lethal infection, whereas control mice were only partially protected. Analysis of immune defenses revealed that MyD88 signaling in B cells suppressed three crucial arms of protective immunity: neutrophils, natural killer cells, and inflammatory T cells. We further show that interleukin-10 is an essential mediator of these inhibitory functions of B cells. Collectively, our data identify a role for MyD88 and B cells in regulation of cellular mechanisms of protective immunity during infection.