Lack of antigen-specific Th1 response alters granuloma formation and composition in Schistosoma mansoni-infected MyD88-/- mice.

Abstract:

To evaluate the role of the innate immune system during schistosomiasis in vivo, we infected myeloid differentiation factor 88 (MyD88)-deficient mice with Schistosoma mansoni and analyzed their pathognomonic formation of hepatic granulomas and T cell responses. Even though the differences between knockout and wild-type mice in terms of mortality, liver damage, serum IgE and parasite burden were insignificant, the liver granulomas in the MyD88-deficient mice were significantly smaller, less cellular and contained a reduced percentage of eosinophils. Histologically, these granulomas revealed stronger fibrosis, confirmed also by increased levels of soluble collagen and IL-13, implying a Th2 bias. Spleen cells from infected MyD88-deficient mice also produced significantly less IFN-gamma than their wild-type controls upon restimulation with Schistosoma-egg-antigen (SEA). Furthermore, SEA-loaded APC from naive wild-type or MyD88-deficient mice induced equal amounts of proliferation and cytokine secretion by T cells from wild-type infected mice. In contrast, Ag-specific T cells from infected MyD88-deficient mice produced hardly any IFN-gamma but considerably more IL-10, again regardless of the APC type. These findings indicate that the loss of IFN-gamma production is not due to impaired antigen presentation but may
perhaps is due to suppression by IL-10-producing T cells. Thus, MyD88 plays an important role in cellular infiltration, granuloma composition and T cell responses during schistosomiasis.