Lack of host gut microbiota alters immune responses and intestinal granuloma formation during schistosomiasis.

Fatalities from schistosome infections arise due to granulomatous, immune-mediated responses to eggs that become trapped in host tissues. Schistosome-specific immune responses are characterized by initial T helper type 1 (Th1) responses and our previous studies demonstrated that myeloid differentiation primary response gene 88 (Myd88)-deficient mice failed to initiate such responses in vivo. Paradoxically, schistosomal antigens fail to stimulate innate cells to release proinflammatory cytokines in vitro. Since Schistosoma mansoni infection is an intestinal disease, we hypothesized that commensal bacteria could act as bystander activators of the intestinal innate immune system to instigate Th1 responses. Using a broad spectrum of orally administered antibiotics and anti-mycotics we analysed schistosome-infected mice that were simultaneously depleted of gut bacteria. After depletion there was significantly less inflammation in the intestine, which was accompanied by decreased intestinal granuloma development. In contrast, liver pathology remained unaltered. In addition, schistosome-specific immune responses were skewed and faecal egg excretion was diminished. This study demonstrates that host microbiota can act as a third partner in instigating helminth-specific immune responses.