Conditional knockout of CXCR5 on CD11c+ cells prevents protective Th2 response following T. muris infection

Introduction

The expression of the chemokine receptor CXCR5 by dendritic cells and their homing to B-cell follicles are suggested requirements for the generation of T-helper type 2 (Th2) cells in response to infection. Previous studies revealed that bone marrow chimeric mice deficient in CXCR5 in dendritic cells or CD4+ T-cells impaired the development of both T-follicular helper (Thf2) or Th2 cells after infection1. Trichuris muris (T. muris) is a gastrointestinal parasite capable of naturally infecting mice, and is used as a model for the human parasite Trichuris trichuria which affects over 1 billion people in predominantly developing countries. Infection with Trichuris spp. elicits a spectral immune response. A strong Th2 response results in immunity and expulsion of the parasites, whereas a Th1-biased response results in susceptibility and persistent infection. High dose infection with T. muris stimulates a Th2-dominated response in resistant mouse strains such as C57Bl/6 with worm clearance within 21 days. We therefore infected CD11cCre:CXCR5fl and CXCR5fl (control) transgenic mice with T. muris and monitored their response to infection.

Methods

LoxP sites were gene-targeted flanking the open reading frame (ORF) of the CXCR5 gene in C57Bl/6 mice. CXCR5fl mice were bred to homozygosity with or without CD11cCre2. Mice were gavaged with ~250 embryonated T. muris eggs and sacrificed 30 days post infection.

Results

CD11cCre:CXCR5fl transgenic mice are persistently infected with T. muris 30 days post infection (d.p.i.) unlike CXCR5fl (control) mice.

Conclusions

The expression of the chemokine receptor CXCR5 by dendritic cells and their homing to B-cell follicles are suggested requirements for the generation of T-helper type 2 (Th2) cells in response to infection. Conditional knockout of the chemokine receptor CXCR5 in CD11c+ cells renders C57Bl/6 mice susceptible to high dose T. muris infection. Cytokine profiling from mesenteric lymph nodes revealed an increase in CD11c+ cells in the absence of increased CXCR5 expression and altered cytokine profile with reduced IL4 and increased IL13, IL6 and IFNG. Persistently infected CD11cCre:CXCR5fl mice reveal inflammatory changes within the colon with recruitment of CD11b+ cells to specific areas.

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