Project 12:

Analysis of the function of lymphotoxin β Receptor-dependent effector mechanisms in the immune response against intracellular pathogens

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Background:

The immunological functions of cytokine receptors of innate immunity and of interferon-γ induced murine 65kDa guanylate binding proteins (mGBPs) in intracellular pathogens are the central research topics of our projects.

The LTβR is a prototypical member of the TNF / TNFR superfamily, a group of approximately 50 receptors and their ligands that mediate a variety of functions in the regulation of inflammatory reactions, immune defense against infection, organogenesis of secondary lymphoid organs and maintenance of structural integrity of lymphoid organs. The role of the cytokine receptor LTβR in *T. gondii* infection has been insufficiently investigated so far, although numerous immunological studies with different pathogens have already been performed for LTβR$^{-/-}$.

Own previous work:

We have shown in previous work that mice deficient in the lymphotoxin β receptor (LTβR) exhibit increased susceptibility to *T. gondii* infection, which is particularly manifested during the chronic phase of infection. These mice show altered expression of mGBPs, which are essential for the survival of *T. gondii* infection. In this infection model, LTβR$^{-/-}$ mice were shown to have reduced frequencies of cytotoxic CD8+ T-cells compared to wild-type mice and to show defects in IgM and especially IgG production.

Aim of the project:

This project aims to characterize these findings in more detail and identify the molecular and cellular factors regulated by LTβR in *T. gondii* infection.

Work program:

We will identify the ligands of LTβR and the cell populations responsible for the described phenotype in *T. gondii* infection.

Tissue specific ablation of the LTβR will reveal the role of myeloid cells in the LTβR dependent immune response to *T. gondii*

Whole transcriptome studies will identify targets regulated by LTβR that will be analyzed in the context of infection.

The cellular distribution of *T. gondii* parasites during infection in WT and LTβR$^{-/-}$ mice will be analyzed with fluorescent parasites using FACS and microscopy.