Project 9: TLR-induced natural immunity and defense against infection in Arylhydrocarbon-Receptor-Repressor (AhRR)-deficient mice

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Summary:
The Arylhydrocarbon Receptor (AhR) is a ligand-activated transcription factor, which is activated by polycyclic aromatic compounds (also called xenobiotics), which may enter our body as environmental pollutants, food constituents or cosmetics. Upon ligand binding the AhR activates the transcription of xenobiotic-metabolizing enzymes and has a strong impact on the regulation of immune responses. The activity of the AhR is apparently controlled by the AhR-Repressor (AhRR) through negative feedback inhibition. Using a gene targeting approach, in which the AhRR is replaced by a green fluorescent protein (GFP), we could recently show that besides a proportion of keratinocytes and fibroblasts of the skin, the AhRR is mainly expressed by a subset of CCL17+ dendritic cells present in the gut- and skin-associated lymphoid tissue, as well as T cells of the gut mucosa. Induction of AhRR expression in dendritic cells mainly occurs through stimulation with microbial pathogens, i.e. toll-like receptor (TLR) ligands, like lipopolysaccharide. Thus, the AhR-AhRR system is linked to natural immunity and infection. In this project, we want to investigate whether the AhRR influences the course of microbial infection via the skin or intestinal mucosa. For this purpose, we will analyze the ability of AhRR-deficient mice to react against cutaneous infections with *Staphylococcus aureus* and to respond to house dust mite antigens, which also represent TLR ligands and are major inducers of allergic responses. In addition, oral infection with *Listeria monocytogenes* will be analyzed. Our goal is to further explore the impact of the AhR/AhRR system as a sensor of environmental stimuli on the immune defense against infection.