Project 16: Comparative analysis of immunmodulating functions of type I interferon-producing cells during Cytomegalovirus versus Listeria monocytogenes Infections

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Project summary

Due to the high structural and pathophysiological similarity of the human cytomegalovirus (HCMV) and its murine counterpart MCMV and because the latter is a natural mouse pathogen the MCMV infection model provides the unique opportunity to examine a medical relevant virus in vivo during the course of infection in its natural host. Type I interferons, which comprise IFNβ and the different subtypes of IFNα, are of great importance for the immune defense against MCMV. However, while type I interferons are in general essential for an optimal antiviral immune response it has been shown recently that this cytokine family can mediate adverse effects in anti-infectious immune responses: Type I interferons were defined as detrimental for the host during the systemic Infection with intracellular bacteria such as Listeria monocytogenes.

Utilizing a fluorescence-based IFNβ-reporter mouse model our lab demonstrated for the first time directly ex vivo that in viral and bacterial infections, respectively, distinct and highly specialized cell types were responsible for the production of IFNβ. The mechanism of these specific host-pathogen interactions that lead to the induction of this cell type specific type I IFN response are still ill defined.

This project centers on comparative analyses of the IFNβ-producing cell populations in the course of the infection with MCMV vs. Listeria in dependence of the route of infection. Using modern visualization techniques the spatio-temporal modes of in vivo interaction of these cells with the respective pathogen will be defined. A special focus lies on the functional role of these IFNβ-producers in the generation of a protective versus detrimental immune response, that will be defined in molecular and cell biological assays in vitro and in vivo.