FOR 1336

Role of the Transcription Factor IRF-8 for Microglia Homeostasis and Function

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Project Description:

Only few factors are known so far that regulate microglia quiescence under non-diseased conditions. Interferon regulatory factor (IRF)-8 has a well-known role for the development, maturation and expansion of myeloid cells such as granulocytes, monocytes, plasmacytoid and CD8+ dendritic cells and bone marrow-derived macrophages but also B cells. Notably, IRF-8 mutations were also recently described in humans associated with severe defects in overall innate immune responses. However, very few is known about the function of IRF-8 in myeloid cells of the primitive haematopoiesis, especially microglia in the brain. We will therefore investigate in this project the precise role of IRF-8 for microglia function during health and disease. In preliminary experiments we found that IRF-8 deficiency profoundly changed cellular architecture and function of microglia in vivo. Thus, IRF-8 function will be examined during development and expansion of microglia after birth as well as during homeostasis in the adult brain. In detail, we intend to decipher the molecular pathways of IRF-8 function and the interaction partners involved. Next, the regulation of IRF-8 transcription will be investigated and finally, we will generate inducible microglia-specific IRF-8 mutants to delineate the function of IRF-8 for CNS diseases.

Reference: https://gepris.dfg.de/gepris/projekt/165233992