FOR 1336

Role and Function of Microglia Cells in Autoimmune CNS Inflammation

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Project Description:

Unlike other glia cells, microglia originate from the myeloid cell lineage and therefore often are considered resident brain macrophages. They act in the first response to direct injury or peripheral insults. However, the exact role microglia play during the process of autoimmune disease in the CNS is not yet clear. In this proposal we suggest the utilization of currently available mouse lines and their combination with newly developed strains to further determine the role of microglia in a mouse model of multiple sclerosis. Focusing on the activation of microglia we will first make use of mouse lines that allow for the conditional deletion of two deubuiquitinating (DUB) enzymes, CYLD and A20, in microglia. As these DUB enzymes normally suppress inflammatory mediators such as the NFκB pathway, their deletion should lead to hyper-activation of microglia. Furthermore we will analyze the role of ionotropic glutamate receptors in microglia activation as rising evidence propose their contribution in the pathogenesis of neuroinflammation and moreover their relevance in microglia activation. In a more generalized approach we will deplete microglia during CNS inflammation and progression and analyze the altered disease outcome.

Reference: https://gepris.dfg.de/gepris/projekt/165235933