FOR 1336

The Role of PU.1 in Homeostasis and Function of Brain Macrophages

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Project Description:

The PU.1 transcription factor is essential for the differentiation of hematopoietic stem cells into early myeloid progenitors, but its role in mature myeloid cells is poorly understood. To elucidate whether PU.1 is required for macrophage homeostasis in the brain, we have generated a mouse model in which the PU.1 gene can be inductively deleted in macrophages using the myeloid-specific CX3CR1GFP-ERT-Cre allele. Unexpectedly, our preliminary data suggest that PU.1 ablation leads to an expanded rather than reduced brain macrophage compartment, and skews peripheral blood myeloid cells towards inflammatory monocytes. In the upcoming funding period, we aim on extending our investigation of the functional role of PU.1 in adult macrophage homeostasis, with a particular focus on macrophages of the brain. Moreover, we will explore whether PU.1 controls macrophage function during a pathological scenario within the central nervous system. Finally, we will use genome-wide technologies to identify PU.1 target genes and PU.1-occupied chromatin sites in brain macrophages, and will compare these data with those of macrophages from another tissue. Taken together, these experiments will provide important novel insight into the mechanistic regulation of brain macrophage homeostasis and function.

Reference: https://gepris.dfg.de/gepris/projekt/165157194