SPP 1757

Subproject
Heterogeneity of NG2-glia: its role and implication in the adult brain

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Project Description:

The adult central nervous system consists of neurons and glial cells. An important glial cell type resembles the oligodendrocytes, which are building the myelin, a structure that is responsible for the fast, saltatory nerve conduction. Myelination was thought to take place only during development and should be completed in young adolescence. Interestingly, the cell type that gives raise to mature oligodendrocytes during development was identified some years ago also in the adult brain and spinal cord. These oligodendrocyte progenitor cells (OPCs) that in the adult they are also named NG2-glia (as they express the proteoglycan NG2) are the only proliferating cells in the adult brain outside the neurogenic niches. However, despite their high number (around 5% of the neural cells), their role and potential in the adult brain is still unknown. Although further functions have been speculated, NG2-glia have been shown to differentiate into mature myelinating oligodendrocytes in a region dependent manner and with recent transplantation experiments, we could show that NG2-glia in distinct regions are intrinsically different, pointing to a heterogeneous population. In addition, we generated a novel BAC-transgenic mouse line, the GPR17-iCreERT2 line and could recently identify the GPR17+ cells as a subpopulation of NG2-glia in the adult brain that does not have the ability to differentiate, at least within 3 months after recombination.

The heterogeneity issue is of highly importance as myelin repair in disease or after injury is not sufficient in the adult brain although NG2-glia exist. Here we aim to understand and unravel the mechanisms dealing with the heterogeneity of adult NG2-glia at two levels: a/ the interregional heterogeneity: study the differences of NG2-glia in different regions of the brain b/ the intraregional heterogeneity: study the differences of GPR17+ and GPR17- NG2-glia in the cerebral cortex. We want to identify candidate genes and signal transduction pathways that lead to enhanced differentiation of NG2-glia as well as to gain insights of major biochemical and cell biological processes in the adult NG2-glia.

To achieve this aims we will address following questions: i/ What are the regional differences of adult brain NG2-glia and what is the implication on their differentiation behavior? ii/ What is the potential and role of GPR17+ cells amongst the total NG2-glia population?

By answering these questions we are very confident that we can identify key candidates playing a major role in the proliferation and differentiation properties of NG2-glia. These candidates could then be used to develop new therapeutic strategies to improve remyelination in demyelinating and neurodegenerative diseases.

Reference: https://gepris.dfg.de/gepris/projekt/255015192