SPP 1757

Nature and functionality of adult neural stem cell derived oligodendroglial cells.

Speaker:

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Funding period:

from 2014 to 2019

Project description:

Within the adult mammalian central nervous system a certain degree of cell replacement can be observed. This is mainly based on two resident cell populations within the adult brain and spinal cord. The first population is represented by oligodendroglial precursor cells while the second population consists of neural stem cells. Whereas oligodendroglial precursor cells represent a widespread and equally distributed cell type which upon activation can generate myelinating oligodendrocytes, adult neural stem cells are located in at least two discrete niches and possess a multipotent character. Our research focuses on glial cell differentiation mechanisms and regulatory aspects of myelination. In this context, we have identified a potent intrinsic regulator, encoded by the p57kip2 gene. We found that the p57kip2 protein efficiently blocks both peripheral Schwann cell maturation as well as oligodendroglial differentiation. Upon long-term suppression a number of differentiation associated processes such as cell-cycle exit, morphological maturation, gene expression and myelin production were affected and maturation was clearly promoted. In addition, we recently identified p57kip2 as a glial fate decision regulator of adult neural stem cells. Suppression of p57kip was found to neutralize bone morphogenetic protein signalling and to promote oligodendroglial precursor cell generation at the expense of astrocytic differentiation in vitro as well as in vivo. This raises the question, if generated oligodendroglial cells from p57kip2-suppressed adult neural stem cells can give rise to mature oligodendrocytes or to oligodendroglial-like cells, only, and to what degree these stem cells can therefore contribute to glial heterogeneity of the adult brain. Moreover, fate determination events must clearly be separated from processes involved in (accelerated) cellular differentiation within a given lineage. In the here propose study we will investigate whether these stem cell descendants can equally mature in white- and grey matter structures and whether they behave similar to grey matter derived- or to white matter derived resident oligodendroglial precursor cells. To this end we will investigate the fate determination process that is initiated by means of a forced p57kip2 downregulation using gene expression profiling. Resulting patterns will be compared to oligodendroglial gene expression patterns corresponding to either white or grey matter oligodendroglial precursor cells and to patterns of either neonatal or adult origin. In order to study these cells functionally, we will transplant control stem cells as well as p57kip2 suppressed stem cells into white and grey matter structures of the adult brain and investigate site-specific differentiation, tissue integration, neurophysiological properties as well myelin sheath generation capacities.

Quelle:
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