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Molecular heterogeneity of oligodendrocytes: novel role and regional relevance of a chemokine-like signaling protein in brain function

Speaker:

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Project description:

CNS myelin is provided by mature oligodendrocytes, which display regional heterogeneity with respect to morphology and electrophysiological properties. However, underlying molecular-genetic diversity has not been reported. We hypothesized that regional oligodendrocytic heterogeneity is reflected at the molecular level in the protein composition of myelin. In pilot experiments, we have used quantitative mass spectrometry to determine the proteome of myelin purified from various regions of healthy mouse brains. While the abundance of major structural myelin proteins, such as PLP or MOG, is largely similar across the analyzed brain regions, several non-structural proteins display considerable heterogeneity of abundance, e.g. in myelin from the cortical gray matter compared to the subcortical white matter. To select proteins for more detailed analysis, we have evaluated our datasets for heterogeneously abundant myelin proteins with a probable function in cellular metabolism or intercellular signaling. In a pilot experiment, we identified CMTM5 (chemokine-like factor MARVEL transmembrane-domain containing protein 5) and genetically deleted its expression specifically in oligodendrocytes. Based on our unpublished observations we will test the hypothesis that CMTM5 is not involved in the biogenesis of myelin per se but in oligodendrocytic signaling to myelinated axons. This project will involve biochemistry/proteomics, mouse genetics, electron microscopy and assessment of mouse behaviour. We anticipate that signaling proteins such as CMTM5 contribute to establishing regionally distinct functions of oligodendrocytes; this novel concept will be tested in vivo.

Quelle:
https://gepris.dfg.de/gepris/projekt/387227149?language=en