SPP 1757

Impact and regional aspects of glia to neuron exosome transfer in the CNS

Speaker:

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Project description:

Oligodendrocytes myelinate axons and in addition maintain axonal integrity by providing support to neurons. We have shown that oligodendrocytes secrete nano-sized vesicles termed exosomes, which mediate bidirectional neuron-glia communication. However, their impact on brain physiology is largely unresolved. Exosomes are released by oligodendrocytes upon neurotransmitter signalling and internalized by neurons via endocytosis delivering a variety of biomolecules, including RNA, from oligodendrocytes to neurons. Cultured neurons that have received exosomes are more resilient to stress suggesting that oligodendroglial exosomes mediate neuroprotection. Modification of exosomes to carry reporter enzymes such as Cre recombinase is utilized to illustrate transfer of exosomes and their cargo to target neurons allowing the identification of target neurons in the brain. In this project, we aim to determine the brain regions, where exosome transfer from oligodendrocytes to neurons is prevalent, and the specific neuronal subpopulations targeted by exosomes. Our strategy utilizes tamoxifen-inducible CreERT2-mediated recombination of target cells to trace exosome transfer in the brain of reporter mice. In addition, the coupling of exosome transfer to neural electrical activity will be assessed. Exosome transfer from NG2-cells to neurons and mature oligodendrocytes to neurons will be compared regarding their targeting characteristics revealing potentially distinct functional implications. Furthermore, we will determine the influence of glial exosomes on the transcriptomic profile of target neurons. The project will reveal deeper insight into the prevalence of exosome-dependent neuron-glia communication in distinct brain regions and its functional relevance for neural performance and neural plasticity. This is particularly relevant for myelin diseases, where axons degenerate as a result of lacking oligodendrocyte-neuron communication. Establishing a spatio-temporal map of glial exosome transfer in the brain complies with the goals of the Priority Program aiming to resolve local determinants of brain activity and furthermore integrates an innovative concept of cell communication into the glia research network.

Quelle:
https://gepris.dfg.de/gepris/projekt/254941261?language=en