SPP 1757

Functional heterogeneity and dynamic of astrocytes in the adult mouse hippocampus

Speaker:

Dr. Ruth Beckervordersandforth
Friedrich-Alexander-Universität Erlangen-Nürnberg
Emil-Fischer-Zentrum
Institut für Biochemie

Funding period:

since 2017

Project description:

The brain works as a functional co-operation unit between neurons and glial cells. This unit differs in its physiological properties in distinct brain regions and developmental stages. Neuronal diversity has been extensively investigated in the last decades. Recent works now suggests that also astrocytes are molecularly and functionally distinct, yet still very little is known about astrocyte heterogeneity. Most present studies focus on comparing astrocytes from different brain regions or developmental stages. However, if and to what extend astrocyte diversity within a specific region contributes to network function and plasticity has not been addressed yet. Using a genetic labeling strategy, I found that the adult hippocampal dentate gyrus is populated by morphologically distinct astrocytes that are localized to specific compartments. In sharp contrast to the prevailing assumption that astrocytes are postmitotic in the non-injured adult brain, preliminary experiments revealed proliferation of astrocytes in the adult dentate gyrus. Even more surprising was the finding that morphologically distinct astrocytes show a differential proliferation response in the context of specific stimuli (voluntary exercise and ageing). Here, I will pursue the novel hypothesis that the dentate gyrus is composed of molecularly and functionally distinct astrocytes whose dynamics are critical modulators for hippocampal adaption to changing conditions. What is the "connectome" of distinct astrocyte subtypes? Structural analysis by confocal and electron microscopy and assessment of the dynamics of astrocyte generation under distinct physiological conditions will reveal how astrocyte subtypes are embedded into the neurogenic niche and how cellular interactions and astrogenesis are modulated by physiological stimuli. What is the origin of adult generated astrocytes? In aim 2, I will investigate potential lineage relationships of astrocyte subtypes and radial glia-like neural stem cells. As structural heterogeneity of astrocytes may be a reflection of their functional properties, I aim to identify the molecular fingerprint of astrocyte subtypes by single-cell sequencing as aim 3. This data set will be used to analyse distinct molecular properties of astrocytes and to identify new markers for better targeting of astrocyte subgroups. Collectively, my studies will significantly promote our understanding of structural and molecular diversity and dynamic of astrocytes populating the same region. Furthermore, it will pave the way for selectively manipulating astrocyte subtypes in the future to address their specific functions.

Quelle:
https://gepris.dfg.de/gepris/projekt/387494543