Universitätsmedizin Rostock

Centre for Transdisciplinary Neurosciences Rostock

"Hyperactivation of the Astrocytic Nrf2/ARE System promotes spinal cord injury recovery"

Freitag, 25. September 2020, 12.00 Uhr
Institut für Anatomie, großer Hörsaal
(um Voranmeldung unter markus.kipp@med.uni-rostock.de wird gebeten)

Speaker: Dr. Adib Zendedel, Institute of Neuroanatomy, RWTH Aachen

Host: Prof. Markus Kipp, Institute of Anatomy, Rostock University Medical Center

Abstract: After spinal cord injury (SCI), astrocytes play a crucial role in SCI pathology through a phenotypic change known as reactive astrogliosis. In this process, naive astrocytes sequentially exhibit opposite phenotypes, first as reactive astrocytes and then as scar-forming astrocytes (SAs). SAs are the main source of reactive oxygen species (ROS), and the deficiency of antioxidant function in these cells plays an essential role in the progress of SCI. Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) is the main transcriptional regulator against oxidative stress through the antioxidant response element (ARE)-directed induction of several antioxidant enzymes. Additionally, Nrf2 has been suggested to play an important role in modulating neuroinflammation. Using *GFAP-Cre::keap1*$^{flox/flox}$ KO mice, we investigated the effects of astrocyte-specific hyperactivation of Nrf2-signaling in a mouse model of spinal cord contusion injury. In a first step, we used transgenic ARE-Luc mice to investigate the quantitative pattern of Nrf2/ARE-activation after experimental SCI. Our results show a significant induction of luciferase-activity in the spinal cord and also brain after SCI. To confirm Nrf2-activity, RT-qPCR was performed for different Nrf2-target genes such as NQ1, Hmox1, GCLC and TxnRD1; gene expression of all genes was significantly induced in both CNS parts. Beyond, we observed that genetic hyperactivation of astrocytic Nrf2 inhibits axonal damage and astrogliosis post SCI. Furthermore, overexpression of Nrf2 improves motor function and protects the oligodendrocyte-myelin unit. Our results demonstrate that strengthening of the Nrf2 system in astrocytes is sufficient to prevent the gliosis, the development of demyelinating, neuroinflammation and axonal damage in SCI.

Most important recent papers:

1. *Hypoxia Induces Astrocyte-Derived Lipocalin-2 in Ischemic Stroke.*
   Fatemeh Ranjbar Taklimie, Natalie Gasterich, Miriam Scheld, Ralf Weiskirchen, Cordian Beyer, Tim Clarner, **Adib Zendedel**
   Int J Mol Sci. 2020: 13;20(6). pii: E1271. doi: 10.3390/ijms20061271.

2. *Estrogen Attenuates Local Inflammasome Expression and Activation after Spinal Cord Injury.*
   Adib Zendedel, Fabian Mönnink, Gholamreza Hassanzadeh, Arash Zaminy, Malek Masoud Ansar, Pardes Habib, Alexander Slowik, Markus Kipp, Cordian Beyer
   Molecular Neurobiology 2018; DOI:10.1007/s12035-017-0400-2.

3. *Post-Stroke Inflammasome Expression and Regulation in the Peri-Infarct Area by Gonadal Steroids after Transient Focal Ischemia in the Rat Brain.*
   Leoni Lammerding, Alexander Slowik, Sonja Johann, Cordian Beyer, **Adib Zendedel**
   Neuroendocrinology. 2016; 103(5)., DOI:10.1159/000439435

Everybody is very welcome!