Jianrong Li, J Neurol Disord 2016, 4:9(Suppl)
http://dx.doi.org/10.4172/2329-6895.C1.014

Galectin-9 modulates inflammatory demyelination and myelin repair

Jianrong Li
Texas A&M University, USA

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS). Local inflammatory reactions induced by infiltrating leukocytes and activated glia are believed to be the main culprit for myelin destruction and axonal damage. Recent studies suggest that galectins, the β-galactoside-binding lectins, can modulate immune tolerance and inflammatory responses. Galectin-9 is significantly elevated in MS lesions, however, its function in CNS immune responses and demyelination remains largely unexplored. We found that galectin-9 was markedly induced in microglia and reactive astrocytes during experimental autoimmune encephalomyelitis (EAE), an animal model of MS, as well as in reactive astrocytes and microglia/macrophages surrounding active MS lesions. Pro-inflammatory cytokines such as TNF and IL-1β triggered galectin-9 production from astrocytes, which in turn acted in a feed-forward fashion to further enhance microglial TNF production. TNF-stimulated Lgals9$^{+/+}$ astrocytes induced greater extent of encephalitogenic T-cell apoptosis and proliferation arrest than that of Lgals9$^{-/-}$ astrocytes, indicating that galectin-9 negatively regulates encephalitogenic T cells. During MOG_{35-55}-induced EAE, Lgals9$^{-/-}$ mice exhibited worse clinical symptoms, which were associated with heightened Th17 responses in the CNS and demyelination when compared with littermate Lgals9$^{+/+}$ controls. In autoimmunity-independent toxin models of CNS demyelination, spontaneous remyelination was delayed in Lgals9$^{-/-}$ mice. Immunohistochemistry analyses revealed that although Lgals9$^{-/-}$ mice had similar number of oligodendrocyte precursor cells in the lesions as control mice, the number of mature oligodendrocytes was significantly reduced. Consistently, recombinant galectin-9 promoted oligodendrocyte maturation in mixed glial cultures. Collectively, our data suggest a role for galectin-9 in suppressing T lymphocytes in the CNS and facilitating oligodendrocyte maturation and myelin repair.

Recent Publications

1. Steelman A R, Zhou Y, Koito H, Kim S J, Payne H R, Lu Q R and Li J (2016) Activation of oligodendroglial Stat3 is required for efficient remyelination. Neurobiology of Disease 91:336-346.
2. Steelman A R and J Li (2014) Astrocyte galectin-9 potentiates microglial TNF secretion. J Neuroinflammation 11:144.
3. Steelman A J, Smith R, Welsh C J and Li J (2013) Galectin-9 is up-regulated in astrocytes by TNF and promotes encephalitogenic T-cell apoptosis. J Biol Chem 288:23776-23787.
4. Kim S and Li J (2013) Caspase blockade induces RIP3-mediated programmed necrosis in Toll-like receptor activated microglia. Cell Death & Disease 4(7):716-725.
5. Kim S, Steelman A J, Zhang Y, Kinney H C and Li J (2012) Aberrant upregulation of astroglial ceramide potentiates oligodendrocyte injury. Brain Pathology 22: 41-57.

Biography

Jianrong Li is an Associate Professor in Neuroscience at Texas A&M University. She has received her PhD in Biochemistry from University of Hawaii and Post-doctoral training from University of Pittsburgh and Children's Hospital Boston, Harvard Medical School. Her research interests include elucidating the molecular basis of oligodendroglial cell injury in developmental and demyelinating diseases and uncovering key pathways for myelin repair. She has been awarded multiple research grants from the National Multiple Sclerosis Society and National Institutes of Health and has authored over 40 peer-reviewed research articles.

jrli@cvm.tamu.edu

Notes: