manitoba neuroscience network

Neuregulin-1: a new emerging modulator and a therapeutic target for central nervous system injury and disease

SEMINAR & VISITING SPEAKER SERIES

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ZOOM LINK

MEETING ID PASSCODE

SPEAKER

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BIO

Soheila Karimi is a Professor and Neuroscientist with the Department of Physiology and Pathophysiology, in Rady Faculty of Health Sciences at the University of Manitoba, and a scientist with the Children's Hospital Research Institute of Manitoba. Soheila has had a long-term interest in neural regeneration and stem cell research. She received her PhD from the University of Saskatchewan in 2001, followed by a CIHR postdoctoral fellowship at the University of Toronto and Toronto Western Hospital Research Institute. Her postdoctoral work developed novel neural stem cell and pharmacological therapies for promoting spinal cord repair and regeneration, and was recognized by several fellowships and awards including a Synthes Award from the American Association of Neurological Surgeons (AANS) and two AOSpine New Investigator Awards in 2007 and 2008. In 2007, Soheila joined the University of Toronto as an adjunct Assistant Professor until 2010 when she established her laboratory at the University of Manitoba. Soheila's research program contributes to both basic and applied translational discoveries aiming at developing regenerative therapies for multiple sclerosis (MS) and spinal cord injury (SCI). Using preclinical models as well as transgenic and in vitro/ex vivo systems, Karimi's team has discovered novel disease mechanisms that play major roles in regulating immune response, cell replacement, neuroregeneration and myelin repair in MS and SCI. Her team has applied the gained knowledge towards development of new therapies for these conditions. Karimi's research has been supported continuously by concurrent Tri-council, national and international grants. Soheila is also involved in outreach, mentorship and leadership activities in Canada and internationally. She currently serves as the Secretary of the International Neurotrauma Society and sits in the Executive Committee of the International Women in Multiple Sclerosis, and the Scientific Program Committee of the Canadian Association for Neuroscience, among several other national and international peer-review and advisory committees in neuroscience. Soheila was named one of the Canada's Top 100 Most Powerful Women in 2020 by the Women Executive Network for her contributions to science and technology.

RESEARCH

The adult spinal cord has a limited capacity for self-repair following injuries and diseases that result in permanent neurological impairments. This limitation is largely attributed to a dysregulated microenvironment driven by activated glia and a complex neuroinflammatory response. Karimi's team has discovered that dysregulation of Neuregulin-1 (Nrg-1) pathway contributes to the imbalanced glial and immune responses in spinal cord injury (SCI) and multiple sclerosis (MS). Nrg-1 is a signaling protein with well-known roles in neuronal differentiation and maintenance, axon guidance, synaptogenesis and myelination in the developing CNS. Nrg-1 consists of multiple isoforms through alternative mRNA splicing. All Nrg-1 isoforms share an epidermal growth factor (EGF)-like domain that is the ligand site essential for binding and activation of tyrosine-protein kinase receptors, ErbB2, ErbB3, and ErbB4. Our parallel in vivo and in vitro studies have uncovered the functional impact of Nrg-1 dysregulation on endogenous cell responses in SCI and MS. In SCI, our in vitro and in vivo characterizations have identified significant neuroprotective and immunomodulatory roles for Nrg-1, which were previously unknown. We show restoring Nrg-1 levels in SCI by peptide therapy can improve the hostile milieu of acute SCI by immunomodulation, protecting neurons and oligodendrocytes from inflammation and oxidative damage, and enhancing remyelination that culminate in reduced tissue degeneration and improved functional recovery. In MS, using human samples and MS animal models, our work has associated dysregulation of Nrg-1 with MS pathogenesis and progression. In experimental autoimmune encephalomyelitis animal model of MS, Nrg-1 dysregulation precedes disease onset and progression, and its systemic restoration is sufficient to delay symptoms and alleviate disease burden. Taken together, our new findings propose an important role for Nrg-1 in immune homeostasis and repair process in SCI and MS suggesting its broader therapeutic potential in CNS injuries and disease. This talk will provide a timely overview of these findings.

OBJECTIVES

1. Provide an overview on the emerging role and mechanisms of Neuregulin-1 in regulating pathophysiology of SCI and MS.

2. Discuss how Neuregulin-1 dysregulation is a key modulator of glial and immune responses after SCI and MS.

3. Discuss the potential of Neuregulin-1 as an immune modulatory and neuro-regenertaive target for SCI and MS.

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