manitoba neuroscience network

Epigentic Regulation of Microglial Innate Immune Memory in the Brain

SEMINAR & VISITING SPEAKER SERIES

DATE
Monday, March 20th, 2023

11:00 AM

LOCATION
Apotex Centre 050

SPEAKER

Annie Vogel Ciernia, PhD
Assistant Professor, University of British Columbia,
Department of Biochemistry and Molecular Biology,
Djavad Mowafaghian Centre for Brain Health

BIO

Dr. Ciernia has a multi-disciplinary background in neurobiology and behavioral neuroscience as well as epigenetics, molecular biology and bioinformatics. She completed her PhD work in Dr. Marcelo Wood's laboratory at UC Irvine with a focus on examining the role of a neuron-specific nucleosome remodeling in regulating transcription and long-term memory. Her postdoctoral work with Dr. Janine LaSalle at UC Davis focused on understanding how DNA methylation and chromatin accessibility impact RNA expression in Rett syndrome and other mouse models of Autism Spectrum Disorders. Dr. Ciernia's current research combines experimental and computational approaches to understand how neuro-immune interactions are impacted by genetic and environmental risk factors for neurodevelopmental disorders. Her lab's goal is to discover how altered patterns of gene expression, epigenomic regulatory pathways and cellular functions in microglia and neurons drive brain and behaviour impairments in models of disease. Findings from her research will increase our understanding of the basic mechanisms regulating gene expression in the brain and form the basis for future development of novel therapeutics for neurodevelopmental disorders.

ABSTRACT

Microglia, the innate immune cells of the brain, protect the brain against invading pathogens and injury by rapidly increasing pro-inflammatory gene expression to promote immune system mobilization. However, in the context of neuropsychiatric and neurodegenerative disorders, microglia become chronically "stuck" in this pro-inflammatory state, causing long-term tissue damage that contributes to brain dysfunction. Little is known about the molecular reprogramming of microglia that drives this state change in disease. However, early life infections or brain injuries increases the risk of later life brain disorders, potentially through reprogramed microglial driven inflammation. After resolution of an infection or injury, microglia can retain an immune memory of the event, allowing for modulation of cellular immune responses to a subsequent immune activation event. Depending on type, strength and duration of the initial stimulation, the secondary response can either be enhanced (primed) or suppressed (tolerance). By mimicking infection with injections of lipopolysaccharide (LPS) that produce brain inflammation, my lab has recently developed a paradigm of microglia memory that can be manipulated to produce either microglia hyper-activation\(priming) or hypo-activation (tolerance) for weeks or months. We have identified novel epigenetic regulatory mechanisms governing the formation of training and tolerance in microglia. These epigenetic changes are long lasting and impact microglial gene expression and microglial interactions with neurons in the brain. Findings from this work can be applied to identify new therapeutic targets to "erase" microglial memories that lead to increased disease risk.

OBJECTIVES

1. Identify the role of epigenetic regulation in disease.
2. Explore how microglial regulation is altered in disease through the formation of immune memories.
3. Identify the epigenetic and transcriptional mechanisms controlling microglial immune memory.

For more information:

T: 204-235-3939
E: info@manitobaneuroscience.ca

@AvogelCiernia
https://ciernialab.med.ubc.ca/

Health Sciences Centre Winnipeg
Hôpital St-Boniface Hospital RECHERCHE • RESEARCH
University of Manitoba