NCGG SEMINAR

"ROLE OF NAMPT AND NAD+ IN HIPPOCAMPAL-DEPENDENT COGNITIVE PHENOTYPES OF AGED MICE"

Mr. Sean E. Johnson

Molecular Cell Biology Program student,
Departments of Developmental Biology,
Washington University School of Medicine,
St. Louis, MO, USA

November 22, 2017 (Wed), 4-5pm

The 2nd floor Conference Hall Small
in the 1st Research building, NCGG

Nicotinamide adenine dinucleotide (NAD) is a vital cofactor for many biological processes including redox reactions, cellular signaling, and inter-tissue communication. During the course of aging, NAD^+ levels decline in a variety of tissues, including the hippocampus. This NAD^+ decline reduces the functionality of NAD^+ dependent enzymes and may cause declines in tissue functionality. We found aged B6 mice showed a strong phenotype in their response to contextual fear conditioning. Our previous work has shown the importance of nicotinamide phosphoribosyltransferse (NAMPT) in the functions of hippocampal and cortical excitatory neurons and neural stem cells. To further assess the role of NAMPT-mediated NAD^+ biosynthesis in the hippocampus, we created CA1 specific NAMPT knockdown mice. Behavioral analysis of these mice showed striking changes in contextual fear conditioning, mimicking the results observed in aged mice. Furthermore, nicotinamide mononucleotide (NMN), a key NAD^+ precursor produced by NAMPT, was able to ameliorate the age-associated decline in hippocampal dependent cognitive functions. We have identified CASK (calcium/calmodulin serine kinase) as a potential downstream effector of this pathway. We hypothesize the NAD^+ pool in hippocampal cells is diminished with age, leading to a cascade of gene expression changes and a decline in hippocampal cognitive functions. We are investigating the mechanism by which this occurs and the therapeutic treatment of NMN to restore the NAD^+ pool of aged mice and restore learning and memory deficits due to aging.

Contact: Akiko Satoh, SARR (TEL: 0562-44-5651 ext.7855)