GEORGE MASON UNIVERSITY
COLLEGE OF SCIENCE
DEPARTMENT OF BIOLOGY SEMINAR

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National Institutes of Health

"Role of DNA Damage and Repair in Neurodegeneration"

Alzheimer's disease (AD) represents a major medical challenge for modern society. While insights into AD have emerged, real mechanistic understanding of the disease remains enigmatic, thus complicating the discovery of therapeutics to treat this terrible disease. Brains from AD patients and mice contain more DNA damage than controls and human postmortem AD brains show reduced base excision DNA repair activity. Thus, it was our hypothesis that proficient DNA repair contributes to neuronal health and viability. To investigate the importance of DNA repair in AD, we crossed DNA polymerase β heterozygous mice (Polβ $^{+/-}$) into the 3xTg AD mouse model to create a DNA repair-deficient AD mouse (3xTgAD/Polβ$^{+/-}$). Polβ is active in the base excision DNA repair pathway which is responsible for the repair of oxidative DNA damage. Significantly, after a reduction of Polβ, AD pathologies were aggravated including Aβ and pTau pathologies, synaptic dysfunction, neuronal death and cognitive impairment. To further investigate the mechanism of how DNA damage contributes to neurodegeneration, we proposed persistent DNA damage caused activation of polyADP ribose (PARP). PARPs catabolize nicotinamide adenine dinucleotide (NAD+) and cause loss of cellular NAD^+. The implications of NAD^+ loss and supplementation in our AD mouse model will be discussed. Our results underscore the importance of DNA repair in neurodegeneration.

TUESDAY November 28, 2017
3:00-4:15 PM
Innovation Hall Room 207