GEORGE MASON UNIVERSITY
COLLEGE OF SCIENCE
BIOLOGY DEPARTMENT SEMINAR
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"Is tau the how behind Alzheimer's?"

Tau is an axonal protein that binds to and regulates microtubule function. Hyper-phosphorylation of Tau reduces its binding to microtubules and it is associated with β-amyloid deposition in Alzheimer's disease. Paradoxically, Tau reduction may prevent β-amyloid pathology, raising the possibility that Tau mediates intracellular Aβ clearance. The current studies investigated the role of Tau in autophagic and proteasomal intracellular Aβ1-42 clearance and the subsequent effect on plaque deposition.

Tau deletion impaired Aβ clearance via autophagy, but not the proteasome, while introduction of wild type human Tau into $Tau^{-/-}$ mice partially restored autophagic clearance of Aβ1-42, suggesting that exogenous Tau expression can support autophagic Aβ1-42 clearance. Tau deletion impaired autophagic flux and resulted in Aβ1-42 accumulation in pre-lysosomal autophagic vacuoles, affecting Aβ1-42 deposition into the lysosome. This autophagic defect was associated with decreased intracellular Aβ1-42 and increased plaque load in $Tau^{-/-}$ mice, which displayed less cell death. Nilotinib, an Abl tyrosine kinase inhibitor that promotes autophagic clearance mechanisms, reduced Aβ1-42 only when exogenous human Tau was expressed in $Tau^{-/-}$ mice. These studies demonstrate that Tau deletion affects intracellular Aβ1-42 clearance, leading to extracellular plaque.

TUESDAY September 15, 2015

3:00-4:15 PM

JC Meeting Room F