EASTERN MICHIGAN UNIVERSITY

Chemistry Department

M. S. Thesis Seminar

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Monday, April 28th 4:00 pm

Science Complex Room 156

Deciphering the Mechanism by which Humanin Binding to IGFBP3 Inhibits Neuronal Cell Death in Alzheimer's Disease

Nuclear translocation of IGFBP3 by importin β1 is a prerequisite for apoptosis induced by IGFBP3 in Alzheimer's disease (AD). The neuroprotective peptide humanin (HN) counteracts this IGFBP3-induced cell death. Unfortunately, the natural synthesis of this peptide decreases with age coincident with the time that people are likely to develop AD. In addition, the precise mechanism of action of HN is currently unknown. We have synthesized residues 3 to 19 of HN known to be sufficient for its neuroprotective function by solid phase peptide synthesis. Using competitive ligand dot blotting and co-immunoprecipitation, we show here that this 17 amino acid peptide interferes with importin β1 binding to IGFBP3 *in vitro*, suggesting a possible mechanism of action as an inhibitor of IGFBP3 nuclear translocation, blocking apoptosis. Future work will examine whether the decline in cell death due to HN is accompanied by a corresponding decrease of the nuclear accumulation of IGFBP3 *in vivo*.