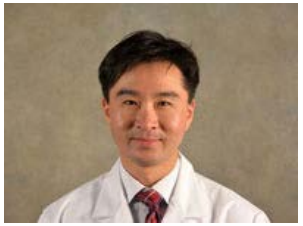
INTERDISCIPLINARY GRADUATE PROGRAM IN

MOLECULAR AND CELLULAR BIOLOGY

DISSERTATION SEMINAR



"Tau associates with protein tyrosine phosphatase SHP2"

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PhD Candidate

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2117 Medical Education Research Facility (MERF)

"Tau associates with protein tyrosine phosphatase SHP2"

The microtubule-associated protein tau normally functions to bind to and stabilize microtubules. However, evidence now indicates that tau may also play a critical role in signaling pathways linked to neuronal development and neurodegeneration. The tau association with numerous signaling proteins such as tyrosine kinases, adaptor proteins, and scaffold proteins support this hypothesis. Phospho-Y18 tau was previously found in Alzheimer's disease (AD) brain. Interestingly, this phosphorylation appeared to be regulated during neurodegeneration possibly by a tyrosine phosphatase(s). Identifying a candidate phosphatase, our lab found the association between tau and SHP2 in a neuronal cell line and dephosphorylation of phospho-Y18 by protein tyrosine phosphatase SHP2 *in vitro*. Since both tau and SHP2 play a critical role in NGF-induced signaling pathway, these findings raised the possibility that the tau-SHP2 association has a role in NGF signaling.

The aim of this dissertation research is to characterize the tau-SHP2 association and its role in neuronal signaling. Here, we provide evidence that tau phosphorylation is not required for SHP2 association but significantly enhances the interaction. The SHP2 binding region of tau napped to residues 256-273, which contain the microtubule binding repeat 1 of tau. Using *in situ* proximity ligation assay (PLA), we also showed the presence of endogenous tau-SHP2 and tau-activated SHP2 complexes in neuronal cells. The number of complexes was increased in the cells in response to NGF. Our PLA data also showed the localization of these complexes to actin ruffles. In NGF signaling, we showed that phosphorylation at T231 of tau was necessary for the increase in tau-SHP2 association. Lastly, we provide evidence that tau-SHP2 complexes are present in mouse primary neuronal cultures and mouse brain sections. Together, these findings show a role for tau phosphorylation in SHP2 binding and a potential role for tau-SHP2 interaction in neuronal signal transduction. Based on our findings, we speculate that there is a role for tau-SHP2 association during early brain development and in neurodegenerative disease.

Future studies will aim to further understand a role for tau-SHP2 association in physiological and pathological conditions. We will attempt to find a SHP2 association-defective tau mutant which would be a useful tool to investigate the role for tau-SHP2 association in MAPK signaling. We will also investigate tau as a substrate for SHP2 in cells. The membrane localization of tau-SHP2 complexes during MAPK signaling would be investigated. Lastly, we will determine the tau-SHP2 complexes in AD brain and AD-cell culture models.

Yohan Kim
Biographical Sketch

Yohan Kim was born in Suwon, South Korea. In his college years, he had studied Veterinary Medicine in Jeju National University, Jeju, South Korea. Since Yohan was not interested being a veterinarian, after graduation in 2006, he was looking for chances to study areas related to human diseases. Because Yohan wanted to study abroad, he came to the US for the first time that year to study English in Eastern Washington University, WA. In 2008, he entered the master program in Biology at the same school and joined Dr. Charles Herr's lab to study ovarian cellular dynamics. In 2011, he graduated and earned a master of science in biology at EWU, WA. Realizing that research fulfilled his thirst for discovery and understanding of how things work at a molecular level, Yohan decided to pursue his PhD. In 2011, he entered the Molecular and Cellular Biology PhD program at University of Iowa. After his rotations, Yohan joined Dr. Gloria Lee's lab to study a role for abnormally phosphorylated tau protein in Alzheimer's disease. Since Lee's lab had found an association between tau and protein tyrosine phosphatase SHP2, Yohan investigated the mechanism for this association and its role in MAPK signaling which is involved in both developing and degenerating neurons. Yohan will continue his work on tau and SHP2 in AD brain sections with Dr. Lee to further investigate this association and its role in disease pathogenesis.

When not at the lab, Yohan enjoys spending time with his family (two little princesses and his wife). He also enjoys watching movies, listening to music, and playing various sports.

Yohan would like to thank the people he has met during his time at the University of Iowa, in particular Dr. Gloria Lee and the members of the Lee lab, and MCB. He is honored to have worked alongside these individuals and very grateful for the opportunities they have brought into his life.

DISSERTATION COMMITTEE

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