Integrated Biomedical Science Graduate Program
1190 Graves Hall
333 W. 10th Avenue
Columbus, Ohio 43210
www.ibgp.org

Edward Chang
PhD Candidate

“Role of Tau Protein in Neurodegenerative Disorders”

May 21st, 2009
159 DHLRI
2:00 PM
VITA

Jan. 10, 1982 .......................... Born – Manhattan, KS

2000-2004 .......................... B.S. Microbiology
Ohio State University
Columbus, OH

2004-Present  ....................... Graduate Research Associate
Integrated Biomedical Science Graduate Program
Integrated Medical Scientists Program
Ohio State University

COMMITTEE MEMBERS

Jeff Kuret, PhD, Advisor
C. Glenn Lin, PhD
Chris Phiel, PhD
Michael Racke, MD

AWARDS AND HONORS

Susan Huntington Dean’s Distinguished University Fellowship (2006-2009)

FUTURE PLANS

As part of the Integrated Medical Scientists Program, Edward will enter Med 3 at the Ohio State University College of Medicine. He is particularly interested in the management of neurodegenerative disorders.
ABSTRACT

Aggregates of the microtubule-associated protein tau characterize several neurodegenerative disorders, including Alzheimer’s disease and the frontotemporal lobar degenerations. Because the temporal and spatial progression of tau lesions correlates with the clinical progression of symptoms, an understanding of factors that contribute to tau aggregation is of utmost importance. Furthermore, identifying small molecules that can interfere with the aggregation of tau may pave the way for development of therapeutics for these neurodegenerative diseases.

Mutations in the coding sequence for tau protein are associated with hereditary familial tauopathies. Some of these mutations were known to have effects on cellular regulation of tau, but whether these mutations directly affect the ability of tau to aggregate was unknown. The data showed that most mutations were able to increase tau’s intrinsic propensity to aggregate. Furthermore, different mutations acted at different steps in the aggregation process, providing a possible mechanism for the clinical heterogeneity of these mutations.

Tau protein is often found hyperphosphorylated in disease-associated aggregates. The use of a pseudophosphorylation mutant allows for analysis of the contribution of a specific phosphorylation site to aggregation propensity. Data showed that pseudophosphorylation of tau at site T212 increased tau...
aggregation propensity at multiple steps, similar to the effect of coding sequence mutations.

Pseudophosphorylation and exonic mutations, both disease-causing agents, show a common ability to promote tau aggregation. This suggests that interventions that can interfere with tau aggregation may be useful as therapeutic agents that can slow or halt the advance of neurodegeneration. We extended our lab’s previous work on a small molecule inhibitor of tau aggregation, N744, to determine a structure-activity relationship in inhibition of tau aggregation. Out of the panel of related cyanine dyes tested, one compound had inhibitory potency similar to that of N744 while showing improved predicted pharmacokinetic properties. These data show that it is possible to maintain tau inhibitory activity while developing more druglike molecules for potential future use.

**RECENT ABSTRACTS AND PRESENTATION**

**Chang, E.,** Congdon, E.E., Honson, N.S., Duff, K.E., and Kuret, J. Structure-activity relationship of cyanine dye tau aggregation inhibitors. The Ohio State University Medical Center Research Day, Columbus, OH. (2009)


**Chang, E.,** Honson, N.S., Johnson, R., Inglese, J. Austin, C., and Kuret, J. Pharmacological modulation of tau fibrillization in Alzheimer’s Disease. The Ohio State University Medical Center Research Day, Columbus, OH (2007)