

TITLE:

Discovery of genes that mediate Alzheimer's disease pathogenesis in "humanized flies"

FACULTY MENTOR NAME, EMAIL PHONE NUMBER

Diego E. Rincon-Limas, PhD
Assistant Professor
Email diego.rincon@neurology.ufl.edu
Phone 273-9689

FACULTY MENTOR DEPARTMENT

Neurology

RESEARCH PROJECT DESCRIPTION (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications -- SHOULD NOT EXCEED ~ 250 WORDS)

Alzheimer's disease (AD) is an incurable neurological condition and the most prevalent form of dementia among the elderly. The two landmark lesions in the AD brain are extracellular amyloid plaques mainly formed by the amyloid beta-42 (Abeta42) peptide and intracellular neurofibrillary tangles containing aggregates of abnormal tau protein. Unfortunately, very little is known about how Abeta and tau trigger AD pathogenesis. To address this, we have created a new fruit fly model of AD that genetically produces both human Abeta42 and tau. These "humanized" flies display extracellular deposition of Abeta42, intracellular aggregation of pathological tau, and robust neurodegeneration, which provides a new platform to discover genes that can suppress disease pathogenesis. Therefore, we will cross these Alzheimer flies with thousands of strains engineered to specifically knockdown individual fly genes. We will first perform a primary screen in the fly eye, which provides a fast visual result of the effect of silencing every gene. Then, we will validate the identified suppressors for preservation of brain neurons and development of pathological markers. This effort will not only provide information about disease mechanisms, but also identify relevant therapeutic targets to approach this overwhelming disorder. The student will participate actively in the screen and will be exposed to a variety of molecular, histological and bioinformatic approaches.

Relevant papers in last 3 years were published in high-quality journals including PNAS, J Proteomics, Neurobiol Dis, Sci Rep, Exp Neurol, HMG, and J Exp Med to name a few. Funding is provided by Florida Department of Health.