“Developing extracellular anti-amyloids in Drosophila”

Summary of research interests: Dr. Pedro Fernandez-Funez has used Drosophila melanogaster as a model to study protein misfolding and neurodegenerative diseases. Using a Drosophila model created in his laboratory, Dr. Fernandez-Funez has focused his research on understanding how the amyloid-β (Aβ42) peptide induces neurotoxicity. Alzheimer’s disease (AD) is the most common neurodegenerative disorder and is characterized by progressive cognitive deterioration. AD is triggered by the overproduction of Aβ42, which rapidly misfolds and accumulates in toxic aggregates. Despite the identification of the molecular trigger leading to neuronal loss and dementia, no disease-modifying therapies exist currently to treat this devastating disease. Dr. Fernandez-Funez’s lab has recently pursued a strategy to generate Aβ42-binding agents that block Aβ42 neurotoxicity. One approach consists in engineered antibodies that can be expressed from a single cDNA – single chain variable fragment (scFv) antibodies. Two scFvs targeting the N- and C-terminus of Aβ42 showed protective activity in transgenic flies expressing Aβ42. A different strategy consists in engineered molecular chaperones that are secreted to the extracellular space, where they can interact with Aβ42. Secretion of Hsp70 resulted in dramatic reduction of Aβ42 neurotoxicity, confirming the protective activity of Hsp70 in the absence of co-chaperones. Overall, these novel approaches illustrate the advantages of using Drosophila as a platform to identify novel anti-Aβ42 agents.

Recent publications:

Dr. Pedro Fernández-Fúnez
Department of Neurology and Center for Translational Research on Neurodegenerative Diseases, University of Florida, Gainesville, Florida. USA
pedro.fernandez@neurology.ufl.edu