FINAL DISSERTATION DEFENSE

Ana Dincas

Development of Tafazzin Enzyme Replacement Therapy in Mammalian Models of Barth Syndrome

Barth Syndrome (BTHS) is a devastating disorder caused by a single gene mutation in the mitochondrial transacylase, tafazzin (TAZ), which results in impaired lipid metabolism leading to dysfunction in highly energetic tissues, such as the heart and skeletal muscle. TAZ remodels, cardiolipin (CL), a multifaceted phospholipid with roles in mitochondrial bioenergetics, protein import and apoptosis. BTHS, the first known disorder of CL metabolism, manifests through a wide range of symptoms, from severe impairment in cardiac function to hypotonia and recurring infections. Current treatment strategies are merely ameliorative in nature and up to 30% of patients still succumb to the disease early in life. A curative treatment is still an unmet need. TAZ enzyme replacement therapy (ERT) could significantly benefit patients suffering from this disorder. The studies presented here focus on the design and development of a recombinant TAZ protein containing a cell penetrating peptide for the treatment of BTHS, along with characterization of TAZ deficient mammalian models critical for efficacy tests. To better understand the structure of TAZ, the mitochondrial localization signal of TAZ was determined. If successful, these studies could lead to significant improvements in quantity and quality of life for BTHS patients.

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2:00 PM
BROTMAN AUDITORIUM (UW SLU)

Program: MBD

Department: Pathology

Lab PI: Michael Chin

Email: ana.dinca@gmail.com

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