Jared Sterneckert Group

Project: Characterize the role of ribonucleoprotein (RNP) granules in the pathogenesis of amyotrophic lateral sclerosis (ALS)

Motor neurons (MNs) have very long axons that require local translation of mRNAs transported from the soma via RNP granules. RNP granules are condensates that protect mRNA from degradation in a translationally arrested state. There are many different types of RNP granules found in MN axons, and MNs are able to disassemble individual granules at specific times and locations in order to support specialized functions such as metabolism or injury repair. However, mutations in RNA-binding proteins such as FUS, which are components of axonal RNP granules, cause axonal degeneration, leading to ALS. Thus, a better understanding of RNP granules could lead to novel therapeutics to protect MN axons against degeneration in ALS. To achieve this objective, our team seeks to build a single molecule model of axonal RNP granule dynamics in human induced pluripotent stem cell (iPSC)-derived MNs. We will use synthetic mRNA reporters to assess mRNA transport and translation of individual mRNAs in living axons to identify disease-associated changes to RNP granule assembly, transport, and translation in different compartments of MNs, including soma and axons. Using dCas13d-mediated proximity labeling, we will analyze disease-associated alterations in the proteins localized to RNP granules. Finally, together with other team members, we will explore if specific oligonucleotides could offer an effective strategy for reversing disease-associated alterations in RNP granules, thereby protecting against ALS pathogenesis.

Preferred Course of Study/Expertise of Candidate: Mammalian cell culture, immunofluorescence