Oral Defense Announcement

University of Missouri – St. Louis Graduate School

An oral examination in defense of the dissertation for the degree
Doctor of Philosophy in Biology with an emphasis in Cell and Molecular Biology

Ariel Bulmash

B.S., Biology, Life University, 2016

Puf Protein-Mediated Regulation of mRNAs From Yeast to Humans, and Characterization of a Dopaminergic SH-SY5Y Cell Model

Date: August 30, 2024
Time: 10:30 a.m. to 11:30 a.m.
Place: 235 Benton Hall

Abstract

Modulation of gene expression is essential for adapting cellular processes in response to external and internal cues. The Puf family of RNA binding proteins are critical post-transcriptional regulators of mRNA stability in eukaryotes. In *Saccharomyces cerevisiae*, Puf3p is known to regulate nuclear-encoded mRNAs involved in mitochondrial biogenesis and function in a carbon condition-specific manner. The first project of this dissertation investigates the mechanism of this regulation, with the findings providing evidence for a model whereby Yak1p interaction with Puf3p is carbon condition-dependent, which modulates Yak1p's proximity to the Puf3p-bound mRNA and thus its ability to phosphorylate Pop2p in the vicinity. Consequently, phosphorylation of the decay factor Pop2p influences its ability to interact with Puf3p, resulting in altered Puf3p target stability in a carbon condition-dependent manner. Puf proteins are also known to regulate neuronal development and function. Recently, human Puf proteins PUM1/2 were confirmed as post-transcriptional regulators of two Parkinson's disease-implicated genes. Parkinson's disease is a neurodegenerative disease that targets dopaminergic neurons of the substantia nigra pars compacta. SH-SY5Y cells are a human neuronal-like cell line that is commonly used as an *in vitro* model for Parkinson's disease-related work. This cell line is primarily employed in its undifferentiated cell state, representative of immature neuronal-like cells. However, chemical agents can induce SH-SY5Y cell differentiation to a more mature cell state and influence the neuronal identity of the cells. The research presented in the second project of this dissertation expands understanding of the molecular phenotype of RA/TPA-differentiated SH-SY5Y cells and highlights transcriptomic changes that support the use of RA/TPA differentiation to generate a more mature dopaminergic-like SH-SY5Y model for Parkinson's disease-related research. Finally, to examine the complexity of PUM1/2 regulation in human neurons and across neuronal differentiation, the last project in this dissertation knocks down PUM1/2 to globally explore the cellular functions that are indirectly and directly regulated by PUM1/2 in undifferentiated and RA/TPA-differentiated SH-SY5Y5 cells. As the role of RNA binding proteins becomes a focal point in neurodegenerative disease research, this work contributes evidence to support a role for PUM1/2 regulation of multiple cellular processes and pathways implicated in Parkinson's disease.

Defense of Dissertation Committee

Wendy M. Olivas, PhD, Chairperson
Bethany K. Zolman, PhD
Lon M. Chubiz, PhD
Michael R. Nichols, PhD