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

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B.S. in Biology, December, 2005, University of Missouri-St. Louis

Puf Proteins: Regulation of Condition-Specific mRNA Decay
and Contributions to Ribosome Biogenesis in Yeast

Date: November 15th, 2018
Time: 11:15 a.m. to 12:15 p.m.
Place: 428 Benton Hall

Abstract
Regulation of protein expression is critical to organism survival. Multiple disease states arise from aberrant accumulation/aggregation of proteins or reduced production of key enzymes. Cells have many ways to manipulate protein levels, including transcription factors, chromatin modification, modification of messenger RNA (mRNA), and manipulation of proteolytic protein decay. Cells can indirectly control protein volume by controlling mRNA lifespan, which is directly correlated with protein output. Often, sequence-specific elements in mRNA contribute to this lifespan. The Puf family of RNA-binding proteins is ubiquitous throughout eukarya, and plays important cellular and developmental roles through mRNA lifespan regulation. Puf proteins contain a C-terminal conserved domain primarily responsible for binding target mRNA (via conserved sequences in the mRNA’s 3’ untranslated region) and protein cofactors including mRNA decay machinery. Mechanisms regulating Puf protein stimulation of mRNA decay, especially signal transduction pathways from environmental stimuli, are poorly understood. Here, I demonstrate how Puf3p activity in the yeast Saccharomyces cerevisiae is regulated through alteration of Pop2p binding and activity, which is influenced by the protein kinase Yak1p. Pop2p is a scaffolding protein allowing decay factors to bind Puf3p and degrade target mRNA. In carbon sources that inhibit Puf3-mediated decay stimulation, Puf3p binds Yak1p, which phosphorylates Pop2p in the vicinity of the bound mRNA. Phosphorylation of Pop2p is detrimental to decay stimulation by Pop2p, not only for Puf3p targets but also non-targets, indicating a general cellular mechanism for modulating Pop2p activity. Separately, I show that both combinatorial and opposing regulation of mRNA targets encoding ribosome biogenesis factors by Puf proteins 1-5 of S. cerevisiae is critical for proper ribosome biogenesis and trafficking. Specifically, while Puf proteins 2, 4 and 5 stimulate decay of the target mRNAs, 1 and 3 stabilize mRNAs. Puf protein levels are critical for ribosome biogenesis, as overexpression of Puf4p leads to aberrant ribosome biogenesis and trafficking. Together, these two bodies of work expand our knowledge of the plasticity with which Puf proteins regulate their mRNA targets, reveal new roles for Puf proteins in mRNA stability and ribosome biogenesis, and reveal a mechanism by which Puf protein activity can be modulated by environmental conditions.

Defense of Dissertation Committee
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