University of Victoria | Graduate Studies

Notice of the Final Oral Examination for the Degree of Master of Science

of

JENNIFER CHRISTIE

BSc (University of Victoria, 2009)

"Characterizing ARS2 Localization and Function in Differentiating Myoblasts"

Department of Biochemistry and Microbiology

Friday April 24, 2015
2:00 P.M.
Engineering and Computer Science Building
Room 130

Supervisory Committee:
Dr. Perry Howard, Department of Biochemistry and Microbiology, University of Victoria (Supervisor)
Dr. Robert Burke, Department of Biochemistry and Microbiology, UVic (Member)
Dr. Leigh Anne Swayne, Department of Biology, UVic (Outside Member)

External Examiner:
Dr. Juergen Ehlting, Department of Biology, UVic

Chair of Oral Examination:
Dr. Joan Wharf-Higgins, School of Exercise, Science, Physical Health and Education, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies

Abstract

ARS2 is a highly conserved protein that is essential for early mammalian development as evidenced by the embryonic lethality of *Ars2*-null embryos shortly after implantation. It has recently been established that ARS2 is a component of the nuclear cap-binding complex (CBC) and is critical for a number of RNA processing pathways including miRNA biogenesis and replication-dependent histone (RDH) pre-mRNA cleavage. In miRNA biogenesis, ARS2 interacts directly with the RNase III-type enzyme DROSHA of the Microprocessor and promotes pri-miRNA processing. The contribution of ARS2 to RDH pre-mRNA processing is less clear. ARS2 interacts with S-phase nuclear protein FLASH and in the absence of this interaction there is a reduction in total RDH mRNA and deficient S phase progression. The emerging model is that ARS2 acts as a master regulator of RNAPII transcript maturation by bringing capped RNA substrates together with the appropriate processing machinery. It remains unclear precisely how ARS2 functions in the context of stem and progenitor cell maintenance and differentiation. Here, I found that ARS2 is localized to the nucleus and the cytoplasm of proliferating myoblasts and post-mitotic, differentiating myotubes. Both ARS2-depletion and overexpression in myoblasts cause a block in myogenic differentiation. I also identify a new isoform of ARS2 that is localized to the cytoplasm and provide preliminary evidence that ARS2 is required for nonsense-mediated decay (NMD).