ANNOUNCEMENT

Interested Members of the University community are invited to attend the Final Oral Examination for the degree of Doctor of Philosophy of

Allison Tscherner

of the Department of Biomedical Sciences (Ontario Veterinary College) on Friday, December 8\textsuperscript{th} at 9:00am in the Lifetime Learning Centre Room 1715 (Seminar); and OVC Room 3648 (Examination)

MicroRNA expression is regulated by complex mechanisms in the cumulus-oocyte complex and preimplantation embryo and may reflect developmental potential

Examination Committee

Dr. Jonathan LaMarre, Advisor
Dr. John Vessey, Committee Member
Dr. Barbara Vanderhyden, External Examiner
Dr. Jim Petrik, Graduate Faculty
Dr. Matthew Vickaryous, Exam Chair

Advisory Committee

Dr. Jonathan LaMarre
Dr. John Vessey
Dr. W. Allan King
Dr. Alicia Viloria-Petit
ABSTRACT

This thesis is an investigation of the regulatory mechanisms that control microRNA (miRNA) abundance in the mammalian oocyte and preimplantation embryo. MiRNAs are highly conserved, short non-coding RNAs that act as potent effectors of post-transcriptional gene regulation. They are abundantly expressed in the mammalian oocyte and early embryo during critical developmental periods when transcription is very low or absent and post-transcriptional mechanisms for the regulation of gene expression predominate. Based on these characteristics miRNAs have emerged as strong candidate regulators of RNA stability during oocyte maturation and during the transition from maternal to zygotic control of the genome. The hypothesis addressed by the studies described here is that specific miRNAs represent key regulators of oocyte maturation and subsequent early developmental events, are transcribed and processed in cumulus-oocyte complexes, and have the potential to reflect gamete and embryo health. To begin to test this hypothesis, precursor and mature forms of miR-21 and miR-34 miRNAs were examined in an in vitro model of bovine oocyte maturation and preimplantation embryo development. The dynamics of these two important miRNA families were used to evaluate the following potential mechanisms of miRNA regulation: 1) transcriptional control in the oocyte and surrounding cumulus oophorus cells, 2) post-transcriptional regulation by rate-limiting availability of the miRNA-processing enzyme Drosha, 3) delivery of sperm-borne miRNA to the zygote upon fertilization. Evidence supported roles for transcriptional and post-transcriptional regulation of miRNA abundance in the cumulus and oocyte compartments of the cumulus-oocyte complex, however the miRNAs analysed in this thesis did not appear subject to regulation from the paternal gamete. Importantly, the transcriptional regulation of miR-21 in the somatic/cumulus cell compartment of the cumulus-oocyte complex during in vitro maturation was sensitive to an inhibitor of the transcription factor STAT3. Ligands that act predominantly through the JAK/STAT pathway play well-established roles in the ovary and have been found to improve oocyte cytoplasmic maturation and competency in vitro, which suggests that miR-21 has the potential to be used as an informative marker of cumulus-oocyte complex quality and oocyte competency. The studies presented here have explored several distinct aspects of miRNA biology in the oocyte and strongly support the overall importance of miRNA biology in bovine gamete and embryo biology, as well as their potential utility in fertility assessment.
PUBLICATIONS


SELECTED PRESENTATIONS


Tscherner A, Gilchrist G and LaMarre J. Regulatory mechanisms controlling miRNA abundance in the oocyte: miR-21 expression throughout bovine in vitro oocyte maturation. Short talk presented at: 44th Annual Southern Ontario Reproductive Biology Meeting, 2016 May 13; Kingston ON


Tscherner A, Smith N, and LaMarre J. Variation in miR-34 family expression in bovine gametes and early embryos. Poster presented at: Keystone Symposium on RNA Silencing, 2014 January 31-February 5; Seattle WA

BIOGRAPHICAL DATA

Allison earned a B.Sc. in Anatomy and Cell Biology from McGill University in 2011. As an undergraduate student she developed a strong interest in molecular biology and became involved in research projects ranging from the maintenance of cell polarity in the mammary epithelium, to the tethering of particle transport vesicles in yeast. In 2012 she joined the laboratory of Dr. Jon LaMarre at the University of Guelph as a M.Sc. student, where she focused her interest on the unique RNA biology of the mammalian oocyte and early embryo. She transferred to a PhD program shortly thereafter. Allison is a trainee member of the Society for the Study of Reproduction.

AWARDS RECEIVED

USDA-NIFA-AFRI Merit Fellow 2015 & 2017
Dr. Pari K. Basrur Travel Scholarship 2017
Ontario Graduate Scholarship 2015 - 2016
Betty Goldhart Scholarship 2016
Dobbin Scholar, Ireland Canada University Foundation 2015
OVC Doctoral Fellowship, Ontario Veterinary College 2013 - 2016
Queen Elizabeth II Graduate Scholarship in Science and Technology 2013
OVC Master's Fellowship, Ontario Veterinary College 2012 - 2013