



ANNOUNCEMENT

Interested Members of the University community are invited to attend the Final Oral Examination for the degree of **Master of Science** of

Allyssa Hooper

of the Department of Biomedical Sciences (Ontario Veterinary College) on Tuesday, July 17th at 9:00am in Biomedical Sciences Room 1642 (Seminar); and OVC Main Building 3648 (Examination)

*MicroRNA Regulation of Ovarian Angiogenesis & Folliculogenesis
in Bovine Cystic Ovarian Disease*

Examination Committee

Dr. Jim Petrik, Advisor

Dr. Jonathan LaMarre, Committee Member

Dr. Eduardo Ribeiro, Graduate Faculty

Dr. Tarek Saleh, Exam Chair

Advisory Committee

Dr. Jim Petrik

Dr. W. Allan King

Dr. Jonathan LaMarre

ABSTRACT

Cystic ovarian disease (COD) is a major contributor to infertility in cattle, with 30% of cows developing ovarian cysts during a given lactation and becoming anovulatory. The cause of COD has remained elusive and is thought to be multifactorial, with angiogenic and genetic contributions proposed. There is an increasing body of work suggesting that microRNAs (miRNAs) may be involved in a number of ovarian-based reproductive disorders. Changes in miRNA expression can affect a multitude of genes and may be important regulators of the dynamic processes involved in each ovarian cycle. We hypothesize that miRNAs are integral to the regulation of critical ovarian processes such as angiogenesis and follicular development and that altered miRNA expression contributes to the onset and progression of ovarian dysfunction and reproductive disorders. Based on this hypothesis, we have identified eight miRNAs (miR-15a, -18a, -20a, -21, -29a, -126, -132, Let7a) that have been shown in the literature to target vascular endothelial growth factor (VEGF), a pro-angiogenic factor, or thrombospondin-1 (TSP-1), an anti-angiogenic factor, as well as play a role in both angiogenesis and folliculogenesis.

MiRNA expression was analyzed via qPCR in endothelial and granulosa cell lines following treatment with recombinant VEGF and 3TSR. A significant increase in miR-15a, -29a, -126, and -132 was observed in endothelial cells following recombinant protein treatment. In addition, miRNA, mRNA, and protein expression was analyzed in large and cystic bovine follicles using qPCR, western blot, and immunohistochemistry. miR-29a was found to be upregulated in cystic follicles, whereas miR-132 was downregulated. VEGF expression increased in cystic follicles at both the transcript and protein level, while no significant differences in TSP-1 expression was observed.

Our findings suggest that miR-15a, -29a, -126, and -132 may be playing an important role in maintaining the balance between VEGF and TSP-1 expression in the ovary, and if disrupted, could potentiate ovarian-based reproductive disorders.

PRESENTATIONS

Hooper A, Petrik J. *Upregulation of miRNA expression in bovine granulosa and endothelial cells due to recombinant VEGF and TSP-1 Treatment*. Poster presented at: 51st Annual Meeting of the Society for the Study of Reproduction, 2018 July 10-13; New Orleans, LA.

Hooper A, Del Castillo S, Petrik J. *Characterization of microRNA, mRNA, and protein expression in large and cystic bovine ovarian follicles*. Poster presented at: OVC Graduate Student Research Symposium, 2018 June 22; Guelph, ON.

Hooper A, Del Castillo S, Petrik J. *MicroRNA regulation of angiogenic factors in bovine cystic ovarian disease*. Oral presented at: 46th Annual Southern Ontario Reproductive Biology Conference, 2018 May 18; Guelph, ON.

Hooper A, Dynes J, Petrik J. *Identification of miRNAs that regulate VEGF and TSP-1 expression in the ovary*. Poster presented at: Oncology Research and Education Day, 2017 June 16; London, ON.

Hooper A, Dynes J, Petrik J. *Identification of miRNAs that regulate VEGF and TSP-1 expression in the ovary*. Poster presented at: 45th Annual Southern Ontario Reproductive Biology Conference, 2017 May 12; London, ON.

PUBLICATIONS

Lepage S, Robson N, Gilmore H, Davis O, **Hooper A**, St. John S, Kamesan V, Gelis P, Carvajal D, Hurtig M, Koch T. (2018). A look below cartilage: the role of the osteochondral unit in joint health and disease. *Tissue Engineering*, Submitted.

Dynes J, Osz K, **Hooper A**, Petrik J. (2017). Low Dose Metronomic Delivery of Cyclophosphamide is Less Detrimental to Granulosa Cell Viability and Ovarian Function Than Maximum Tolerated Dose Delivery in the Mouse. *Biology of Reproduction*, 97(3): 449-65.

BIOGRAPHICAL DATA

Allyssa graduated from McGill University in 2015 with a Bachelor of Science degree majoring in Physiology. Her interest in reproductive biology developed after working as a summer student and undergraduate research project student in the Department of Obstetrics and Gynecology at McGill, where she studied the role of TGF-beta signaling in embryo-uterine communication. Allyssa joined the laboratory of Dr. Jim Petrik in September 2016 as a Master of Biomedical Sciences student and then transferred to the Master of Science program in May 2017. Her research focuses on the role of miRNAs in regulating ovarian angiogenesis and folliculogenesis. Allyssa has been accepted into the Doctor of Medicine program at the University of British Columbia and is hoping to continue research in reproductive biology and pursue a career in Obstetrics and Gynecology.

AWARDS RECEIVED

Pari K. Basrur Travel Scholarship	2018
Barbara Kell Gonsalves Memorial Scholarship	2018
OVC Graduate Student Recognition Award – Biomedical Sciences	2018
Biomedical Sciences Teaching Assistant Excellence Award	2017
Dr. Casey Buizert Memorial Scholarship	2017
Ontario Veterinary College Masters Scholarship	2017 - 2018