



## ANNOUNCEMENT

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

*Priya Mistry*

of the Department of Biomedical Sciences (Ontario Veterinary College) on Friday, December 7<sup>th</sup> at 1:00pm in the Pathobiology Building, Room 1812 (Seminar); and Room 3826 (Examination)

### *The Role of the Circadian Microbiome in Healing Post-Myocardial Infarction*

#### Examination Committee

Dr. Tami Martino, Advisor

Dr. Emma Allen-Vercoe, Committee Member

Dr. John Dawson, Graduate Faculty

Dr. Matthew Vickaryous, Exam Chair

#### Advisory Committee

Dr. Tami Martino

Dr. Emma Allen-Vercoe

Dr. Roger Moorehead

## ABSTRACT

The circadian clock is critical for cardiovascular physiology and plays a role in the pathophysiology of cardiovascular disease. The gut microbiome is involved in many diseases and has been linked to cardiovascular disease, however the role of the circadian microbiome in benefiting outcome post-myocardial infarction (MI) is unknown. This thesis investigates the contributions of the circadian microbiome to healing processes post-MI. Here, we demonstrate that disrupting the gut microbiome with antibiotics leads to worsened cardiac outcomes post-MI. Mechanistically, this is attributed with reduced functional metabolites of the microbiome and correlates with altered immune responses required for infarct healing post-MI. Re-establishing a healthy microbiome can rescue cardiac outcomes post-MI, despite microbiome disruption. Importantly, the circadian clock coordinates microbiome responses post-MI, as *Clock*<sup>Δ19/Δ19</sup> mice with gut dysbiosis have preserved cardiac structure

and function. Collectively, these are the first studies to demonstrate the pivotal role of the circadian microbiome in post-MI outcome.

## **ABSTRACTS/PRESENTATIONS**

**Mistry P**, Reitz CJ, Khatua TN, Oliphant K, Al-Abdul-Wahid MS, Allen-Vercoe E, and Martino TA. Circadian Microbiome Benefits Outcome Post-Myocardial Infarction. Centre for Cardiovascular Investigations (CCVI)/Southern Ontario Cardiovascular Research Association (SOCRA) Cardiovascular Research Day, University of Guelph, October 11, 2018.

**Mistry P**, Reitz CJ, Khatua TN, Oliphant K, Al-Abdul-Wahid MS, Allen-Vercoe E, and Martino TA. Circadian Microbiome Benefits Healing Post-Myocardial Infarction (Heart Attack). Graduate Student Research Symposium, University of Guelph, June 22, 2018.

Joshua J, **Mistry P**, Niel L, and Martino TA. Building a Better ICU: Monitoring Veterinary Care Settings to Benefit Animal Health and Welfare. Graduate Student Research Symposium, University of Guelph, June 22, 2018.

**Mistry P**, Reitz CJ, Oliphant K, Allen-Vercoe E, and Martino TA. Circadian Microbiome Benefits Outcome Post-Myocardial Infarction (Heart Attack). Third Conference of the Canadian Society for Chronobiology, York University, May 19-21, 2017.

**Mistry P**, O'Sullivan ML, Reitz CJ, Alibhai FJ, Daw A, Barry J, Wright GA, Ghugre NR, and Martino TA. Pre-clinical Translation of ACE Inhibitor Chronotherapy for Treatment of Myocardial Infarction Using the Porcine Ischemia/Reperfusion Model. Centre for Cardiovascular Investigations (CCVI) Cardiovascular Research Day, University of Guelph, September 29, 2016.

## **PUBLICATIONS**

**Mistry P**, Reitz CJ, Khatua TN, Oliphant K, Al-Abdul-Wahid MS, Allen-Vercoe E, Martino TA. Circadian CLOCK Regulates Microbiome and Benefits Outcome Post-Myocardial Infarction in Mice. *Circ Res*. In preparation.

**Mistry P**, Duong A, Kirshenbaum L, Martino TA. (2017) Cardiac Clocks and Preclinical Translation. *Heart Fail Clin*. 13 (4):657-672. PMID: 28865775

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O'Sullivan ML, Reitz CJ, Alibhai FJ, Tsimakouridze EV, **Mistry P**, Daw A, Barry J, Wright GA, Ghugre NR, Martino TA. Beneficial effects of chronotherapy on remodeling after myocardial infarction. *Sci Transl Med*. In preparation.

## **BIOGRAPHICAL DATA**

Priya Mistry graduated from the University of Guelph in 2016 with a Bachelor of Science Honours degree in Bio-Medical Sciences. Priya's interest for cardiovascular research began when she was a research assistant at the Hamilton General Hospital in the cardiac surgery department. Interested in the translation of research to clinical practice, she joined Dr. Tami Martino's lab as a 4<sup>th</sup> Year Research Project student investigating the benefits of chronotherapy for treating heart disease in a pre-clinical porcine model. Priya further pursued her research interests in the circadian system and cardiovascular health and enrolled in the Master of Science program in Biomedical Sciences with Dr. Tami Martino in the fall of 2016. Supported by CIHR and OVC funding, Priya's research focuses on the role of the circadian gut microbiome in healing post-myocardial infarction (heart attack) and how to therapeutically target this system to improve outcomes. Throughout her Master's, Priya has also been Co-Chair of the Student Executive Council for the Centre for Cardiovascular Investigations (CCVI) to promote the outstanding cardiovascular research at the University of Guelph and provide networking opportunities for students.

## **AWARDS RECEIVED**

CIHR Canada Graduate Scholarship – Masters (2017-2018)

OVC Incentive Stipend Fund, University of Guelph (2018)

Ontario Graduate Scholarship (MSc), University of Guelph (2017-2018)

OVC MSc Scholarship, University of Guelph (2016-2018)

Gary Partlow Prize for Leadership and Academic Performance, University of Guelph (2016)

Biomedical Science Research Award of Merit, University of Guelph (2016)

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