**37th Annual**

**Frontiers in Physiology (FIP) Research Symposium**

DEPARTMENT OF PHYSIOLOGY

UNIVERSITY OF TORONTO

May 9th, 2017

**CALL FOR ABSTRACTS**

* **Eligibility:** All undergraduate project students and graduate students
* **Deadline for abstract submission**: Wednesday March 15th, 2017 11:59 PM

ABSTRACT APPLICATION FORM

Name:

Lab:

LEVEL OF TRAINEE

[ ] Undergraduate [ ] MSc student [ ] PhD student

**PREFERENCE FOR PRESENTATION**

Note: All submissions will be considered for a poster presentation. Please indicate

whether you would like to be considered for an oral presentation.

Oral : Yes / No

**PLATFORM (Please check ONE that is the most relevant to your study)**

[ ] Reproduction & Development [ ] Cardiovascular [ ] Endocrine & Diabetes

[ ] Brain Research & Integrated Neurophysiology

**ABSTRACT FORMAT**

* **All size 10 Cambria**
* **Title: BOLD, ALL CAPS**
* **Authors: Primary Author Bold (First Initial and Full Last Name) with affiliation number in superscript**
  + **Other authors:** Same format, but not bold
* **Affiliations:** italics, superscript before the department name; separate different institutions by semicolons. Please provide province/state and country.
* **Abstract Body:** no bold, regular text. No subheadings, all one paragraph.

The abstract should be no longer than **300 words** and should strictly follow the sample provided below. Please submit an electronically submit your abstracts in Microsoft Word format to [uoftfip@gmail.com](mailto:uoftfip@gmail.com)

**SAMPLE ABSTRACT**

## OAT BLOCKADE TO IMPROVE BETA CELL FUNCTION IN DIABETES

**1J.A. Eversley**, 1K.J. Prentice, 1Y. Liu, 1B. Batchuluun, 1E. Burdett, 1M.B. Wheeler

*1Department of Physiology, University of Toronto, ON, Canada*

The furan fatty acid metabolite 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) is elevated in humans with type 2 diabetes (T2D) and prediabetes, and rapid elevations in CMPF accelerate T2D progression. We previously showed CMPF enters the beta cell through Organic Anion Transporter 3 (OAT3), causing beta cunction. Here, we deliver intraperitoneal CMPF for 7 days—elevating plasma CMPF to T2D concentrations—prior to 6 weeks high fat diet (HFD)-feeding (CMPF-HFD vs. CON-HFD) to investigate long-term effects of CMPF on islet function. Remarkably, CMPF-HFD mice display persistent islet dysfunction with impaired glucose-stimulated insulin secretion (GSIS) and glucose tolerance up to 6 weeks following cessation of CMPF delivery.  Mechanisms behind this persistent CMPF action on the beta cell were uncovered using DNA from human islets treated with CMPF *in vitro* and the Illumina 450K Array which reveals whole-genome epigenetic alterations. To discover novel therapeutic targets to prevent these persistent effects of CMPF in prediabetes/T2D, we investigate whether OAT blockade *in vivo* inhibits CMPF action on the beta cell. To achieve this we block CMPF transport using (i) pharmacological OAT inhibition—by co-treatment with the competitive OAT inhibitor, probenecid—and (ii) genetic elimination of Oat3 (Oat3KO). As above, wildtype mice (co-treated with probenecid) or Oat3KO mice received CMPF prior to 6 weeks HFD-feeding. As anticipated, *in vivo* CMPF treatment alone decreased islet GSIS, increased islet reactive oxygen species, and impaired glucose tolerance. Importantly, Oat3KO mice or mice co-treated with probenecid were protected against CMPF islet phenotypes, rescuing glucose tolerance and islet function. These novel studies demonstrate a persistent effect of CMPF on islet function and a requirement of OAT transport to do so, highlighting the potential for OAT inhibition to prevent CMPF-induced diabetes: a metabolite highly elevated *prior* to diabetes onset which has a persistent effect on islet function, and accelerates disease progression.

**Abstract**