Due on or before October 21 2016. Forms received after this date will not be posted on the website.

**SUPERVISOR INFORMATION**

Supervisor Name: Professor Stephen G. Matthews

Mailing Address: Dept Physiology, 1 King’s College Circle, Toronto, Ontario, M5S 1A8

Telephone Number: 416-978-1974

Email Address: stephen.matthews@utoronto.ca

Degree (MD, PhD, MD/PhD): PhD

Academic Rank: Full Professor

Field of Research: Developmental Neurobiology

Graduate School Appointment (IMS, IHPME etc..): Physiology

*Please note that you must be appointed to the SGS in order to be a supervisor in the Scholar Program*

Research Institute Affiliation (if applicable): Associate Scientist LTRI

Allocation of student contact time (# of hours per week you are available to the student for any concerns or to review progress): Weekly lab meeting (Tuesdays 9-12), open-door policy at all other times
**PROJECT INFORMATION**

Project Title: **Epigenetic and Transcriptional Signatures of Early Experience**

Project Description (max 500 words):

Fetal adversity can result from maternal stress and anxiety as well as from pregnancy complications including pre-eclampsia and placental insufficiency. Such early adversity results in increased fetal glucocorticoid exposure and can place individuals on trajectories towards chronic disease and disability, including hypertension, obesity, diabetes, learning disabilities, disruptive behaviours and neurodegenerative disease. These conditions come at great personal, societal, and economic cost. **Indeed, it is predicted that by 2030, chronic diseases will account for 50% of global disease burden, costing the world economy $47 trillion.** Our research program integrates discovery and translational science together with human research. Our overall goals are to; 1) determine the mechanisms by which the fetal environment (particularly fetal glucocorticoid exposure) programs life-long susceptibility to neurologic deficits including learning difficulties and behavioral problems; 2) develop strategies to identify individuals at risk and; 3) create interventions that prevent or reverse the negative life-long consequences resulting from early adversity and increased glucocorticoid exposure. 'Programming' is defined as modified development resulting in long-term functional change.

Using an animal model (guinea pig) that closely mimics human neurodevelopment, we have shown that maternal stress or maternal synthetic glucocorticoid (sGC) treatment programs HPA function, behaviors and learning in first generation (F1) offspring. Mechanistically, we have shown antenatal sGC exposure to cause dramatic epigenetic and transcriptional changes in the prefrontal cortex, hippocampus and hypothalamic paraventricular nucleus (PVN); areas of the brain that regulate HPA function, behaviors and learning. This is highly clinically relevant as 10% of all pregnancies end in preterm birth and sGC are administered to women ‘at risk’, in order to mature the fetal lungs and improve respiratory function in the premature newborn.

The successful CREMS scholar will participate in a research program focused towards establishing epigenetic and transcriptional signatures (biomarkers) in blood or saliva leukocytes after prenatal sGC exposure, and determine if these translate to the human. In **Aim 1**: we will identify epigenetic and transcriptional biomarkers of prenatal sGC exposure in whole blood as well as blood and salivary leukocytes derived from juvenile guinea pigs, and determine how these epigenetic and transcriptional modifications map onto those in the PFC, hippocampus and PVN. In **Aim 2**, we will determine if the same biomarkers exist in human infants. Utilizing the Ontario Birth Study (OBS), we will compare DNA methylation and gene expression signatures in cord blood and salivary leukocytes of infants whose mothers were treated with sGC in late pregnancy.

This study will identify novel **biomarkers** of prenatal adversity / glucocorticoid exposure. In the longer term, new mechanistic knowledge may be **translated** to help create interventions that prevent the negative health consequences of a sub-optimal early environment and, in doing so, begin to decrease the burden of chronic disease.

If human subjects are involved, has Ethics been obtained?

☐ YES X ☐ NO ☐ Application Submitted ☐ N/A

*The OBS has full ethics approval, though additional supplemental approval will be required

Do you expect this work will be published within 20 months?
Student’s Roles / Responsibilities (Please be as specific as possible) Please indicate who will serve as the student’s direct report. (PI, PDF, PhD student, technician etc…):

The CREMS Scholar will work closely with a post-doctoral fellow and graduate students on the project, which will also be supported by laboratory technicians. The PDF will supervise day-to-day operations, but the CREMS Scholar will interact with the PI on a daily basis in the laboratory.