RESEARCH SCHOLAR PROGRAM 2017
SUPERVISOR/PROJECT INFORMATION FORM

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

SUPERVISOR INFORMATION

Supervisor Name: Eyal Grunebaum

Mailing Address: Dr. Eyal Grunebaum, Head, Division of Immunology and Allergy, Hospital for Sick Children, 555 University Avenue, Toronto , Ontario M5g 1X8

Telephone Number: 4168138625

Email Address: eyal.grunebaum@sickkids.ca

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

Academic Rank: Associate professor

Field of Research: Immunology and Allergy

Graduate School Appointment (IMS, IHPME etc..): IMS, Immunology
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): Sickkids Research Institute, Developmental and Stem Cell Biology Program

Allocation of student contact time (# of hours per week you are available to the student for any concerns or to review progress): As a clinician scientist, I have 70% protected time for research, I will be available for contact with the student 2-3 times per week, for 1-2 hours on each of these days.

Do you have a student that you have already agreed to work with? No
Please note, you may go ahead with a self-initiated project with a student of your choosing. If you choose this option, your project will not be posted online, meaning it will not be open to student applicants.

PROJECT INFORMATION

Project Title: The effect of platelet activating factor on vascular cells- a potential explanation for anaphylaxis severity.

Project Description (max 500 words):

Background: Anaphylaxis following exposure to food, venom, medications or other allergens is a rapidly growing health concern in Canada, particularly now when food allergies affect >5% of Canadian children. Anaphylaxis is associated with skin flushing and urticaria, tongue swelling, vomiting and diarrhea as well as constriction of the airways. In addition, one of the most life threatening complications of anaphylaxis is hypotension, attributed to vascular dilatation and increased permeability of vascular endothelial cells (EC). Also, adults experiencing anaphylaxis often suffer from coronary vasoconstriction, suggesting different effects of anaphylaxis on different blood vessels.

Histamine, leukotrienes, prostaglandins and platelet-activating factor (PAF) have been shown to mediate anaphylaxis. Indeed, in a recent landmark paper, serum PAF levels were significantly higher in patients with anaphylaxis and correlated with the severity of anaphylaxis. Animal studies further supported PAF ability to induce anaphylaxis, suggesting that antagonizing PAF activity might ameliorate anaphylaxis.

Hypothesis: We hypothesize that PAF may have different effects on different blood vessels, and that blocking PAF activation in vascular EC may stop the anaphylactic cascade.

Research plan: We will use cells representing blood vessels of different calibers, location and function (available from ATCC). These cells include primary and immortalized human umbilical vein EC (HUVEC), immortalized human microvascular EC (HMEC1 foreskin derived), primary dermal microvascular EC from, primary pulmonary artery EC, primary coronary artery EC, etc. The EC will be stimulated by PAF, epinephrine, Vascular Endothelial Growth Factor (VEGF) and basal Fibroblast Growth Factor (b-FGF). Phosphorylation of the transcription factor STAT3, as well as MAPK/ERK, implemented in intracellular signaling of PAF and epinephrine will be determined by phosphor-flow cytometry and/or Western blotting. Calcium influx and cAMP concentrations will also be determined, as they were shown to be affected by PAF in muscle cells. The ability of the Rupatadine (a commercially available PAF receptor antagonists) as well as calcium depletion and nifedipine on EC responses will be measured.

Significance: Importantly, understanding the effects of PAF on EC, including intracellular pathways responses will provide novel targets for pharmacological intervention as well as better management of food allergies and anaphylaxis.

If human subjects are involved, has Ethics been obtained?

☐YES ☐NO ☐Application Submitted ☒N/A

Do you expect this work will be published within 20 months?

☒YES ☐NO ☐Uncertain

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 student's roles and responsibilities will include selecting, maintaining and growing the various EC as well as stimulating/blocking the EC. The student will also be responsible for analyzing EC responses by flow cytometry and/or Western blotting.
The student will report daily and directly to Dr. Matilde Leon-Ponte, an experienced post-doctoral project manager in the research lab. Additionally, the student will report 2-3 times/week to Dr. Eyal Grunebaum.
The student will also be involved in writing the manuscript summarizing the results of this study.