



uOttawa

University of Ottawa – Project UO6

Title: Plasminogen activator inhibitor-1, diabetes, and associated vascular disease

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Keywords: cardiovascular disease, biomarker, plasminogen activator inhibitor-1

Field: Translational research

Duration: 12 weeks

Project context:

We wish to establish that PAI-1 is a potential biomarker and mediator for major adverse cardiac events (MACE) (ie. death, stroke, and myocardial infarction) in patients with diabetes with established coronary artery disease at the University of Ottawa Heart Institute. Platelet and megakaryocyte precursors in diabetes have elevated PAI-1 expression potentially increasing platelet-mediated thrombogenicity and increased complications after intervention. We seek to better understand the regulatory mechanism behind this elevated PAI-1 expression. Ultimately, we wish to translate our understanding of the signaling mechanism and develop a novel therapy which can inhibit PAI-1 expression to improve clinical outcomes of diabetes in our patient population.

Currently, we have multiple equipment which examines agonist-induced platelet activation. However, we currently lack a model where we can examine shear-induced platelet activation. For this project, the student will have the opportunity to design an *ex vivo* thrombus formation model where we will examine thrombus formation in real-time after stent deployment takes place in the silicone tube. Once the method has been validated, we will employ different platelet and/or PAI-1 inhibitors and evaluate its effect in real time using clinical samples with the goal of designing a novel antiplatelet/PAI-1 regimen that we can translate from bench-to-bedside.

Methods and learning outcomes: As we are primarily a translational medicine lab, students will apply their molecular biology techniques to ultimately gain a greater appreciation and understanding of platelet hyper-reactivity resulting in heart attacks. In addition, the student will learn how to design their own experiments under the guidance of other clinician-scientists.

Stages d'été en recherche à l'international pour étudiants du premier cycle (SÉRI) Summer Undergraduate International Research Internships (SIRI)

By the end of this rotation, the student should: i) develop their molecular biology techniques (ie. flow cytometry); ii) exposed to clinical research; iii) learn critical thinking skills for translational sciences.

Time allocation: The student will spend their rotation developing a foundational knowledge and experimental techniques in cardiovascular research.

- **Week 1-4** – student will learn the basics of platelet biology using platelet-aggregation equipment
- **Weeks 5-12** – student will design an *ex vivo* thrombus formation model where we will be able to visualize thrombus formation in real time using clinical samples

The student will be supervised by Dr. Hibbert along with other clinician-scientists in training at the Hibbert Lab at the University of Ottawa Heart Institute.