

# 09



HEART &  
STROKE  
FOUNDATION  
OF BC & YUKON

*Finding answers. For life.*

## HIGH SCHOOL Summer Research Program

final  
presentations  
Thursday, July 23<sup>rd</sup>, 2009

# program

**9:00 am**

**FOUNDATION WELCOME**

Robert Hager, VP of Finance and Administration

**9:10 - 11:30 am**

**STUDENT PRESENTATIONS and  
INTRODUCTION TO POSTER SESSION**

Introduction by Jeff Sommers, Manager of Research and Science

**12:00 pm**

**LUNCH**

# students

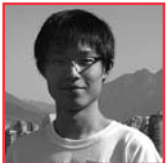
## 2009 High School Summer Research Program



**Ravina Binning**  
**Tamanawis Secondary, Surrey**

Ravina had the opportunity to work in Dr. Aly Karsan's lab at the BC Cancer Research Centre. Ravina's research focused on key cardiac development processes.

Congenital heart defects due to anomalies in heart development occur in 1% of newborns. Two key processes in the development of the heart are heart septation and valve formation. Both these processes require Notch signaling. Ravina's assignment was to evaluate a novel Notch target that participates in heart septation and valve formation. For this to take place, a subgroup of cells that line the inside of the heart called endocardial cells, transform into mesenchymal cells. This process is termed endothelial-to-mesenchymal transition (EMT). Ravina performed embryonic dissections to isolate the heart tissues for explantation and used chemical staining to measure amounts of EMT.



**Steven Cheng**  
**St. George's School, Vancouver**

Steven has been working at the Centre for Blood Research in UBC with Dr. Leslie Burtnick and his lab team. His topic of focus was the structure and functions of actin and actin-binding proteins. Actin is a protein that is found in all eukaryotic cells. Its importance is

evident in cell motility, apoptosis, cytokinesis, intracellular organelle movement, and the microfilament backbone. During apoptosis, the contents of the cell spill out into the blood, and actin polymerizes into long strands. This is of great interest to blood researchers because these long strands increase the viscosity of blood and the chances of a blockage in smaller blood vessels. To counter this, gelsolin severs the long strands of actin and caps them off so they do not repolymerize. Steven has learned to extract actin from the rabbit muscle tissue and to isolate G-actin by employing ultracentrifugation, gel filtration column, and dialysis to evaluate its purity by SDS-PAGE. The final goal was to solve the structures of the actin complexes with CapG, villin, and gelsolin by using x-ray crystallography.



**Lisa Choi**  
**Semiahmoo Secondary, Surrey**

Lisa has worked at the iCapture Centre under the supervision of Allen Xiao and Jerry Wong in Dr. Honglin Luo's lab. Lisa investigated the role of the Coxsackievirus B3 (CVB3) in heart failure. CVB3 is a small RNA virus and is one of the primary causes of viral

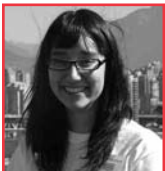
myocarditis, an inflammation of the myocardium. Lisa focused on the role of serum response factor (SRF) in CVB3 induced myocarditis. SRF is

a transcription factor that binds to the serum response element (SRE) in the promoter region of many cardiac specific genes that are important for the development and function of the heart. The overarching hypothesis of her project is that CVB3 infection leads to the cleavage of SRF. CVB3 infection not only decreases the amount of SRF but also produces a SRF fragment that blocks normal SRF function, which contribute to the down-regulation of cardiac function in infected hearts. Lisa explored several laboratory techniques, including transformation, DNA purification, transient transfection and Western Blotting in hopes of confirming the mechanism of SRF cleavage.



**Shelly Chopra**  
**Sir Winston Churchill, Vancouver**

Shelly had the privilege of working in Dr. David Granville's lab at iCapture at St. Paul's Hospital. Her work was focused on atherosclerosis and the role of Granzyme B—a protein involved in apoptosis—on plaque stability within the arteries. As the disease progresses, immune cells infiltrate the plaque and contribute to plaque destabilization through the induction of SMC and macrophage apoptosis and by the release of matrix-degrading enzymes. Granzyme B has been hypothesized to not only induce SMC death but degrade the extracellular matrix that provides structural support to these specialized cells. Shelly has been involved in testing the effect of varying levels of PI-9—an inhibitor of Granzyme B produced by smooth muscle cells—and its role in promoting plaque stability. With Alon Hendel and Alison Müller, Shelly was able to not only learn about the role of Granzyme B on atherosclerosis but also how to perform histological staining and immunohistochemistry techniques on mice and human arterial tissues as well as perform Western Blotting.



**Lauren Cuthbertson**  
**York House School, Vancouver**

Lauren was very excited to work at UBC's Brain Research Centre in Dr. Yu Tian Wang's Laboratory. Over the past three weeks she has worked on a project with researcher Ted Lai to discover a method for rapid, efficient, and selective degradation of specific proteins. Current techniques to study protein function, such as DNA knockout and mRNA knockdown, have many limitations, therefore selective degradation would add great value to research. The first target protein Lauren studied was Homer1b, which may be an important protein that mediates ischemia-induced cell death in the brain of stroke patients. Lauren has learned how to clone and genetically alter DNA as well as transform her genetically engineered DNA into bacterial cells, and then extract it from the host bacteria after repeated amplification (bacterial/DNA growth). She has also learned how to transfect her purified DNA from bacteria into mammalian cell cultures, and to study them under a fluorescent microscope.



**Andrew Guy**  
**Lambriek Park, Victoria**

Andrew has had the privilege of working with Dr. Ed Pryzdial and his Canadian Blood Services team (especially Scott Meixner) at the UBC Centre for Blood Research. The Pryzdial lab investigates the biochemistry of blood protein function and the involvement in vascular diseases, such as thrombosis. Hemostasis, or the normal control of bleeding, requires a strict balance between blood coagulation (clot generation), anticoagulation (prevention of unneeded clot formation) and fibrinolysis (clot busting). When imbalances occur, clots may form when they should not, causing thrombosis. Using classical biochemical techniques such as gel electrophoresis, the Western Blot, and protein imaging, Andrew has been investigating a specific blood protein known as factor Xa, which is essential for life. The Pryzdial laboratory has found that factor Xa can function to enhance clot busting. The discovery of this novel link between coagulation and fibrinolysis is of significant importance because new targets for improved clot busting medicines and diagnostic tests are suggested.



**Shoshanna Kervin**  
**Port Hardy Secondary, Port Hardy**

Shoshanna is investigating the expression of Matrix metalloproteinase -12 (MMP-12) - as a potential diagnostic tool for detection of viral myocarditis. MMP-12 is an enzyme that digests the extracellular matrix (ECM) during viral infection. Dr. McManus' laboratory is investigating better ways for the clinician to diagnose virus induced myocarditis, or inflammation of the heart. This disease has numerous causes and can be mistaken for a heart attack in patients admitted to emergency with chest pain. Currently there is no single standardised marker for virus infection of the heart. Shoshanna is detecting MMP-12 in virus infected biopsied tissue samples from patients with myocarditis, as well as patients with myocarditis that is not viral. She is using immunohistochemistry which specifically stains the MMP-12 produced by virus infected cells. The research has started to show that MMP-12 is a robust biomarker of viral myocarditis and is absent in non-viral myocarditis samples.



**Marie Low**  
**Hatzic Secondary, Mission**

Marie was given the opportunity to work at the iCapture Centre at St. Paul's Hospital in Dr. Decheng Yang's lab with Dr. Mary Zhang. Marie has been studying the molecular pathogenesis of Coxsackievirus B3 (CVB3) infection, specifically the role of p58IPK in CVB3-infected cells. p58IPK is a protein that inhibits protein kinase R (PKR) and PKR-like ER protein kinase (PERK), which target the eukaryotic translation initiation factor eIF2- $\alpha$  and regulate protein translation. This protein is one of the many proteins that are involved during endoplasmic reticulum (ER) stress, which can occur in response to viral infections. To study how p58IPK affects the CVB3 replication and the fate of CVB3-infected cells, p58IPK over-expressed cells and

p58IPK knocked-down cells were infected by CVB3. The infections supernatants and the cell lysates were used for experimental analysis of p58IPK function. Expression levels of ER stress proteins, apoptotic proteins and viral proteins in these cells were analyzed using Western Blots, MTS assays, and plaque assays.



**Fraser Parlane**

**Kelowna Christian School, Kelowna**

Over the past month, Fraser studied Coxsackievirus B3 (CVB3) infection in Dr. Honglin Luo's laboratory, side-by-side with Allen Xiao and Jerry Wong at the iCapture Centre, St. Paul's Hospital. CVB3 is the leading cause of viral myocarditis (inflammation of the heart) and has a single-stranded RNA genome. AUF1 is a host protein that binds to the A+U-rich elements (ARE) of mRNA and marks it for degradation. The lab found that the CVB3 genome also contains ARE, and therefore could theoretically be bound and degraded by AUF1 mechanism. Degradation of CVB3 genome leads to the shutdown of RNA replication and viral protein synthesis. To ensure efficient viral replication, CVB3 infection leads to the cleavage of AUF1. Fraser explored how: (1) CVB3 cleaves AUF1 and (2) AUF1 affects CVB3 infectivity. Understanding of the role of AUF1 in CVB3 infection may lead to the development of new therapeutics for viral myocarditis.



**Bryson Siemens**

**DP Todd Secondary, Prince George**

For the past few weeks, Bryson has been working at the iCapture centre under the supervision of Jon Carthy. The lab is involved in determining the effects of the protein versican on atherosclerosis. Atherosclerosis is the build up of LDL-saturated macrophages called foam cells inside the artery. The build up of these foam cells cause a blockage to form in the artery, constricting blood-flow. If this pocket of foam cells ruptures, a blood clot could form and clog the entire artery. Large amounts of versican have been found in areas with a blockage, and it is believed that the protein plays a role in the disease. It is thought that the negatively charged carbohydrate chains on versican cause additional debris to stick to the side of the artery, increasing the speed of the build up of these blockages. Bryson has been performing immunohistochemistry to stain tissue samples and locate the presence of versican in arterial blockages.

# researchers

We wish to acknowledge and thank the following researchers and their lab personnel who have volunteered their time and expertise to the students.



**Dr. Leslie Burtnick**

Centre for Blood Research, UBC



**Dr. David Granville**

iCapture Centre, St. Paul's Hospital



**Dr. Aly Karsan**

BC Cancer Research Centre



**Dr. Honglin Luo**

iCapture Centre, St. Paul's Hospital



**Dr. Bruce McManus**

iCapture Centre, St. Paul's Hospital



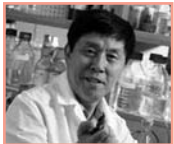
**Dr. Edward Pryzdial**

Centre for Blood Research, UBC



**Dr. Yu Tian Wang**

Brain Research Centre, UBC



**Dr. Decheng Yang**

iCapture Centre, St. Paul's Hospital

We would also like to express our sincerest gratitude to the following people who contributed their time, expertise, and enthusiasm:

Brenda Pasichnyk and James Chang, Chaperones

Dr. Jacques LeBlanc, BC Children's Hospital

Melissa Ashman, Brain Research Centre

Sandy Barabe, CPR Consultant

Katherine Wright, GF Strong Rehabilitation Centre

Dr. Michael Allard, iCapture Centre

Jacqui Brinkman, iCapture Centre

Hayley Spencer and Saranee Fernando, iCapture Lab Safety

Elizabeth Walker and Dr. Brian Rodrigues, Reviewers

Jim Milne, Telus

Dr. Nadia Khan, UBC

Elise Frketich, UBC Accommodations

Lynn Macdonald, UBC Committee on Animal Care

Philip Varghese, UBC Student Recruitment

Darlene Tanaka, Vancouver Community Kitchen

Staff, Heart and Stroke Foundation of BC & Yukon



The Heart and Stroke Foundation of BC & Yukon and the students of the 2009 High School Summer Research Program would like to thank...

**Mr. Daljit S. and Mrs. Pritam K. Dhillon  
and Family**

for their generous support of this program.