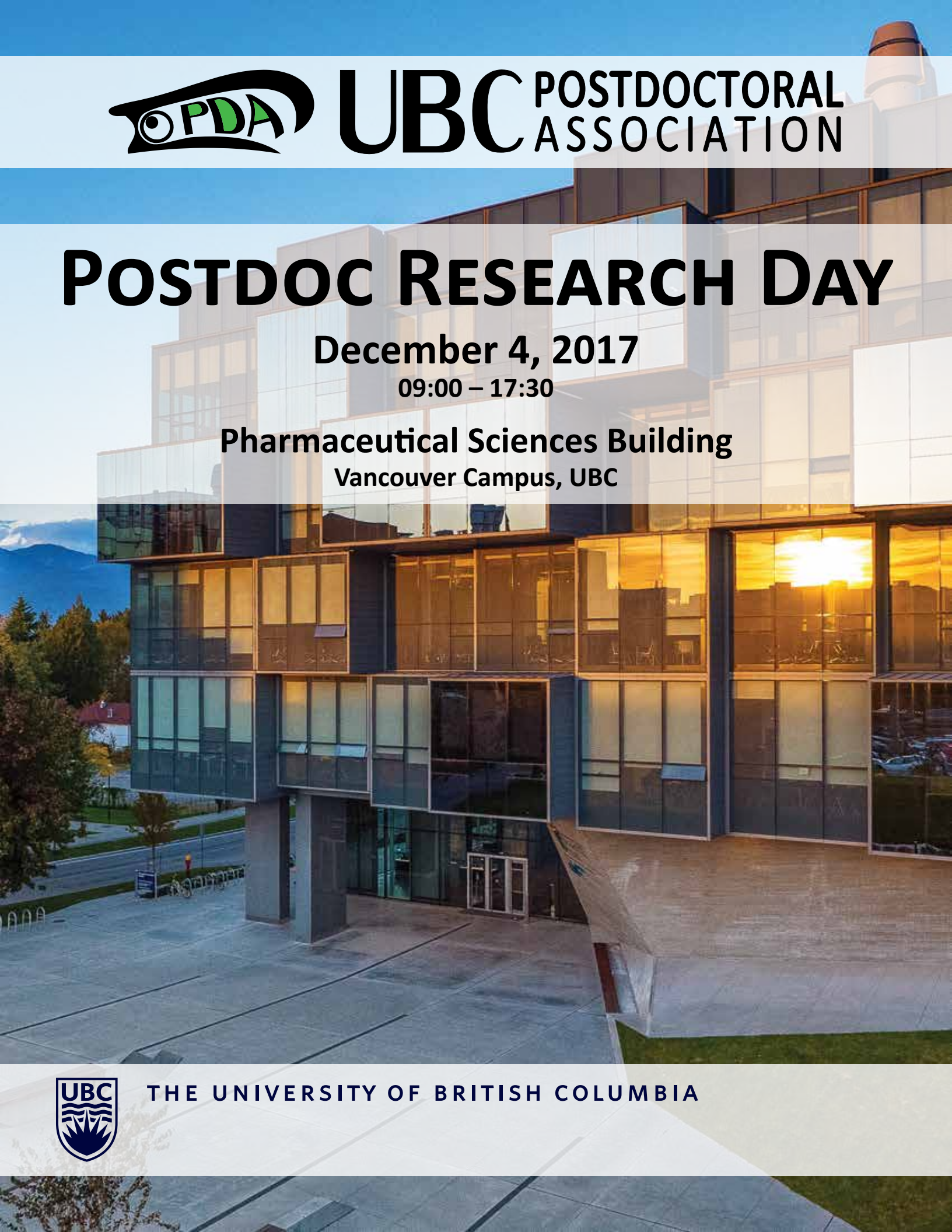

UBC POSTDOCTORAL ASSOCIATION

# POSTDOC RESEARCH DAY

## December 4, 2017

**09:00 – 17:30**

## Pharmaceutical Sciences Building

**Vancouver Campus, UBC**

THE UNIVERSITY OF BRITISH COLUMBIA

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# Thanks and Acknowledgements

## Panellists

**Leslie Grad** PhD
Manager, Research Programs (Design & Development),
*Michael Smith Foundation for Health Research*

**Chayne Piscitelli** PhD
Scientist, Protein Engineering,
*Zymeworks Inc.*

**Mark Romanish** PhD, JD
Senior Business Development Officer,
*STEMCELL Technologies*

**Nirupa Goel** PhD
Research and Project Manager,
*BC Centre for Substance Use*

**Elizabeth Rideout** PhD
Assistant Professor,
*Cellular and Physiological Sciences*

## Judges

### Oral Presentations

**Lori Brotto** PhD
Professor and Executive Director,
*Women's Health Research Institute*

**Ora Johannsson** PhD
Adjunct Professor,
*Zoology*

**Brian Wetton** PhD
Professor and Director,
*Institute of Applied Mathematics*

**Leslie Grad** PhD
Manager, Research Programs
(Design & Development),
*Michael Smith Foundation for Health Research*

**Susan Porter** PhD
Dean and Vice-Provost,
*Graduate & Postdoctoral Studies*

**Calvin Yip** PhD
Associate Professor,
*Biochemistry & Molecular Biology*

**Ryan Ziels** PhD
Assistant Professor,
*Civil Engineering*

### Poster Presentations

**Helen Burt** PhD
Professor and Associate Vice President,
*Research and Innovation*

**Kristina McBurney** PhD
Program Manager, Scientific
Communications and Marketing
*STEMCELL Technologies*

**Thomas Chang** PhD
Professor and Associate Dean,
Graduate and Postdoctoral Studies
*Pharmaceutical Sciences*

**Mark Romanish** PhD, JD
Senior Business Development Officer,
*STEMCELL Technologies*

**Thank you to all our presenters and attendees!**

# Schedule

| *Time* | *Session* | *Venue* |
|---|---|---|
| 08:45 – 09:00 | **Registration** | Atrium |
| 09:00 – 09:15 | **Welcome & Introduction**<br>Kieran Hudson, *President, UBC PDA* | London Drugs Lecture Theatre, room 1201 |
| 09:15 – 10:15 | **Research Session 1**<br>Jerome Robert, *Pathology & Laboratory Medicine*<br>Catherine Jutzeler, *Kinesiology*<br>Hyeju Jang, *Computer Science*<br>Jordan Burke, *Forestry* | London Drugs Lecture Theatre, room 1201 |
| 10:15 – 10:45 | ***SCWIST* Coffee Break** | Atrium |
| 10:45 – 11:45 | **Research Session 2**<br>Katharina Rothe, *Medical Genetics*<br>Stephanie Hobbis, *Anthropology*<br>Miling Li, *Earth, Ocean & Atmospheric Science*<br>Romain Tisserand, *Kinesiology* | London Drugs Lecture Theatre, room 1201 |
| 11:45 – 13:00 | **Lunch & Poster Session 1** | Atrium |
| 13:00 – 14:00 | **Keynote Lecture**<br>Lori Brotto, *Director, UBC Sexual Health Laboratory* | London Drugs Lecture Theatre, room 1201 |
| 14:00 – 15:00 | **Research Session 3**<br>Paul Pickell, *Forestry*<br>Eve Limbrick-Oldfield, *Psychology*<br>Murat Kilic, *Mechanical Engineering*<br>Sophie Stukas, *Pathology & Laboratory Medicine* | London Drugs Lecture Theatre, room 1201 |
| 15:00 – 16:00 | **Coffee Break & Poster Session 2** | Atrium |
| 16:00 – 17:15 | **Postdoc Careers Panel Discussion** | London Drugs Lecture Theatre, room 1201 |
| 17:15 – 17:30 | ***STEMCELL* Prizes & wrap-up**<br>Kieran Hudson, *President, UBC PDA* | London Drugs Lecture Theatre, room 1201 |
| 17:30 – 20:00 | ***Zymeworks* evening reception**<br>Drinks and a light supper | Atrium |

# Keynote Presentation 13:00 – 14:00

## **Lori Brotto** PhD

### From postdoc to promotion: Making a career out of sexual health

In contemporary times of stress and quick fixes and societal misconceptions about sex, it is perhaps no wonder that a third of individuals experience distressing sexual concerns. This talk will focus on how the practice of acceptance can lead to change with regards to sexual response. It will share the story of how a light-bulb moment during my Postdoctoral Fellowship paved the way for a productive program of research leading to promotion and a book and a number of stumbling blocks along the way.

### Biography

Dr. Lori Brotto is a Professor in the UBC Department of Obstetrics and Gynaecology, and a Registered Psychologist in Vancouver, Canada. She is the Executive Director of the Women's Health Research Institute of BC located at BC Women's Hospital. Dr. Brotto holds a Canada Research Chair in Women's Sexual Health. She is the director of the UBC Sexual Health Laboratory where research primarily focuses on developing and testing psychological and mindfulness-based interventions for women with sexual desire and arousal difficulties and women with chronic genital pain. Dr. Brotto is an Associate Editor for the Archives of Sexual Behavior, has 150 peer-reviewed publications, is the Sexual Health expert writer for the Globe and Mail, and is frequently featured in the media on topics related to sexuality. Her book, Better Sex Through Mindfulness: How Women Can Cultivate Desire is a trade book of her research demonstrating the benefits of mindfulness for women's sexual concerns, and is in press with Greystone Publishing and will be released in April 2018.

# Oral Presentations

## Research Session 1

| *Talk* | *Time* | *Details* |
|---|---|---|
| 1 | 09:15 – 09:30 | **Bioengineering blood vessels to study Alzheimer's disease**<br>– Jerome Robert, *Pathology & Laboratory Medicine* |
| 2 | 09:30 – 09:45 | **Teaching old drugs new tricks: Repurposing acute medications for enhanced recovery after spinal cord injury**<br>– Catherine Jutzeler, *Kinesiology* |
| 3 | 09:45 – 10:00 | **Finding structure in figurative language: Metaphor detection with topic-based frames**<br>– Hyeju Jang, *Computer Science* |
| 4 | 10:00 – 10:15 | **Population state-dependent invasion potential of the mountain pine beetle in Alberta**<br>– Jordan Burke, *Forestry* |

## Research Session 2

| | | |
|---|---|---|
| 5 | 10:45 – 11:00 | **Exploiting cellular recycling to kill cancer**<br>– Katharina Rothe, *Medical Genetics* |
| 6 | 11:00 – 11:15 | **Gendered violence 2.0? Women's empowerment and digital technologies in Melanesia**<br>– Stephanie Hobbis, *Anthropology* |
| 7 | 11:15 – 11:30 | **Insights from stable isotopes into life history of aquatic biota**<br>– Miling Li, *Earth, Ocean & Atmospheric Science* |
| 8 | 11:30 – 11:45 | **You must stop balancing before you can walk: vestibular control of balance during locomotor transitions**<br>– Romain Tisserand, *Kinesiology* |

## Research Session 3

| | | |
|---|---|---|
| 9 | 14:00 – 14:15 | **An early warning system for human-caused wildfires**<br>– Paul Pickell, *Forestry* |
| 10 | 14:15 – 14:30 | **The psychology of gambling**<br>– Eve Limbrick-Oldfield, *Psychology* |
| 11 | 14:30 – 14:45 | **Design and implementation of a tool condition monitoring system for the shop floor**<br>– Murat Kilic, *Mechanical Engineering* |
| 12 | 14:45 – 15:00 | **Generation of paediatric reference intervals for blood detection of the axonal proteins tau and neurofilament-light**<br>– Sophie Stukas, *Pathology & Laboratory Medicine* |

# Oral Presentation #1 09:15 – 09:30

## Bioengineering blood vessels to study Alzheimer's disease

**Jerome Robert** PhD
*Pathology & Laboratory Medicine*

Alzheimer's Disease (AD) is the leading cause of senile dementia with over 44 million affected persons and an economic burden of over $600 billion. Amyloid plaques, consisting of deposited beta-amyloid (Aβ), are a neuropathological hallmark of Alzheimer's Disease (AD). Cerebral vessels play a major role in AD, as Aβ is cleared from the brain by pathways involving the cerebrovasculature, most AD patients have cerebrovascular amyloid (cerebral amyloid angiopathy (CAA), and cardiovascular risk factors increase dementia risk. Here we present a notable advance in vascular tissue engineering by generating the first functional 3-dimensioinal model of CAA in bioengineered human vessels. We show that lipoproteins including brain (apoE) and circulating (high-density lipoprotein, the "good" cholesterol, HDL) synergize to facilitate Aβ transport across bioengineered human cerebral vessels. Taken together, our results establish the utility of human engineered cerebral vessels as highly innovative *in vitro* platform to study key mechanistic questions relevant to lipoprotein and AD.

# Oral Presentation #2 09:30 – 09:45

## Teaching old drugs new tricks: Repurposing acute medications for enhanced recovery after spinal cord injury

**Catherine Jutzeler** PhD
*Kinesiology*

There are currently no medications that help people recover after a spinal cord injury (SCI). This means that lost sensation and muscle strength rarely fully return, and people with SCI are left with severe disabilities. While promising new treatments are being discovered, these are still in the early stages of development, and are likely years away from being tested in patients. Nearly every person sustaining a spinal cord injury (SCI) receives medications to manage pain in the acute stage of injury. But we have little information on how these medications affect their recovery. Some medications (e.g., opioids to treat pain) have been shown to limit the recovery of locomotor function. In contrast, anticonvulsants, a particular class of pain medication, have been examined as "neuroprotective" in preclinical animal models of CNS damage as they help to restore lost connections in the injured spinal cord. In line, we recently discovered that patients with SCI, who receive anticonvulsants, achieve greater returns of muscle strength compared to patients who receive other pain medications. Our work emerged with new meaning when experimental studies in rodents identified neural regeneration associated with the acute administration of a specific type of anticonvulsant (i.e., pregabalin) in an experimental model of SCI. In the interim of developing more effective interventions, evaluating current standards of acute care represents an intriguing alternative strategy to improve the lives of people with SCI by increasing the amount of muscle strength they recover.

# Oral Presentation #3 09:45 – 10:00

## Finding structure in figurative language: Metaphor detection with topic-based frames

**Hyeju Jang** PhD
*Computer Science*

Metaphor is a common linguistic tool in communication, in which two dissimilar concepts are compared. Accurate metaphor detection still remains an open challenge in natural language processing despite the importance of metaphor in human language. Previous approaches to automatically detecting metaphor have relied on the notion of violation of semantic or syntactic constraints at the sentence level. Although previous approaches were effective at capturing some expressions of metaphor, the space of ways of using contextual and situational information for more effective modeling of metaphor in interaction is still wide open. In this presentation, I will introduce my work towards a new type of clue for metaphor detection at the discourse level in an online medical support community.

# Oral Presentation #4 10:00 – 10:15

## Population state-dependent invasion potential of the mountain pine beetle in Alberta

**Jordan Burke** PhD
*Forestry*

The mountain pine beetle (*Dendroctonus ponderosae*, MPB) has caused hundreds of millions of dollars in damage to timber interests in Canada and the US in recent years, as a consequence of climate warming and past land use practices. The beetle has expanded in range well beyond historical limits, and are now found much farther north and east than in the past. Infestations are now occurring in the boreal forests of Alberta, as the beetle has invaded stands of the novel host, jack pine (*Pinus banksiana*). MPB is an eruptive species, where epidemic periods are regularly interspersed between long normative periods of low density. Prior research at UBC and the University of Alberta indicates that jack pines are likely more susceptible to infestations when the beetle population is large. However, progression of the infestation into boreal jack pine has slowed, and may be receding. Current research from the Forest Insect Disturbance Ecology Laboratory at UBC Forestry demonstrates that this may partially be due to low survival and persistence of populations during low-density phases, due to novel competitive interactions. This means the beetle's potential to invade the boreal forest is density-dependent, and the lack of coevolution with jack pine leads to beneficial effects for the beetle at high density, but detrimental effects at low density. We present a series of experiments in the field and laboratory on the effect of host migration on the competitive interactions between MPB and other insects, and between MPB external microbiome fungi and antagonistic saprotrophs.

# Oral Presentation #5 10:45 – 11:00

## Exploiting cellular recycling to kill cancer

**Katharina Rothe** PhD
*Medical Genetics*

Our body is composed of about 38 Trillion cells that form our extremities and our inner organs. Like we have a stomach, every single cell has organelles that have the ability to break down and digest material to obtain nutrients and to generate energy. This recycling process at the cellular level is called “autophagy” and is important for our body to keep us healthy 365 days a year. However, things can go wrong and this cellular recycling mechanism is abused by cancer cells to help them grow faster and to outcompete healthy cells. More specifically, our lab was the first group to show that one component of the recycling machinery, ATG4B, the catalyzer of the reactions, is deregulated in leukemias (blood cancers). ATG4B’s expression is not only increased in patient-derived leukemic cells, it also allows the autophagic process to occur much more efficiently in these cells to support their high energy demands. On the other hand, if we delete ATG4B from the cancerous cells they start to grow much slower and become sensitive again to standard chemotherapeutic drugs. These results have led to innovative collaborations between cell biologists, chemists and clinicians at UBC and SFU with the goal to develop and test novel ATG4B-specific drugs in different cancers and other autophagy-related diseases. In my talk, I will present how targeting of ATG4B is possible in leukemias and combined with standard chemotherapy may be the first therapy to fully eradicate a cancer.

# Oral Presentation #6 11:00 – 11:15

## Gendered violence 2.0? Women's empowerment and digital technologies in Melanesia

Stephanie Hobbis PhD
*Anthropology*

Papua New Guinea and Solomon Islands have some of the worldwide highest rates of gendered violence outside a conflict zone. Approximately two-thirds of women are raped or assaulted in their lifetime. In their efforts to address this violence and gendered inequalities more broadly, local, national, and international organizations increasingly turn towards digital technologies, in particular, mobile phones. Hotlines are launched. Social media such as Facebook or YouTube are used as platforms for awareness campaigns. Digital technologies are imbued with great promise. They allow for horizontal (rather than top-down) information dissemination, for private (confidential) communication, and for at least partially bridging the distance between urban service providers and a primarily rural population. However, digital technologies also bring great uncertainties. The proliferation of digital technologies in Melanesia, including an increasingly stable 3G and 4G mobile network in urban areas, has fueled gendered tensions. Some young men have justified raping of young women based on movies watched on their mobile phones. Mobile phones also make adultery easy, or at least easier; and they have been linked to an increase in domestic disputes. Thirteen months of field research in Solomon Islands and Papua New Guinea, an accompanying digital ethnography of relevant Facebook Groups, and an extensive survey of the literature suggest that digital technologies solidify gendered inequalities and contribute to violence against women in Melanesia. In particular, non-elite women are relegated further into the domestic (private) sphere and subordinated to men's increasing participation in digitizing public discourses.

# Oral Presentation #7 11:15 – 11:30

## Insights from stable isotopes into life history of aquatic biota

**Miling Li** PhD
*Earth, Ocean & Atmospheric Science*

Anthropogenic activities are having dramatic impacts on ocean chemistry and marine resources. Theoretical and modelling studies suggest that climate change could exert a large effect on food web structure and dynamics but at present, we lack the quantitative data to evaluate these models and determine how the life history of aquatic biota responds to environmental changes. This presentation will cover the application of stable isotopes in environmental and ecological studies, with an emphasis on recent advancements of using heavy stable isotopes (e.g., lead, mercury, strontium, cadmium) to understand migratory species' foraging ecology history, contamination profile, and changes in physical environment. Commercially important species like salmon and tuna as well as common prey fish such as herring and smelt have been studied. Our results show that these naturally occurring heavy stable isotopes can provide insights into environmental pollution sources, feeding habitats and species migration pattern. Heavy stable isotopes can be complementary tools to traditional stable isotopes (carbon, nitrogen) in studying life history of aquatic biota.

# Oral Presentation #8 11:30 – 11:45

## You must stop balancing before you can walk: vestibular control of balance during locomotor transitions

**Romain Tisserand** PhD
*Kinesiology*

To initiate a movement, a recent motor control theory (optimal feedback control) suggests that the central nervous system (CNS) needs to switch between motor control policies. Deficits in switching motor tasks is common in patients suffering from Parkinson's Disease (PD) and likely to disturb balance, increasing their risk of fall. By mapping the sensorimotor control of balance using vestibular stimulation, we investigated whether the CNS performs a discrete change between a postural control policy and a locomotor policy when humans transition between a quiet standing posture and locomotion. Healthy subjects initiated and terminated gait while receiving a continuous-changing-polarity electrical vestibular stimulation. Ground reactions forces where recorded for quiet standing periods and the three first/last steps. Time-frequency coherence between vestibular inputs and reaction forces was performed. A null coherence period preceding the onset of the first biomechanical action related to the locomotor transition was observed, both during initiation and termination. Moreover, coherence was significant during locomotion only when the vestibular error was distributed to the frontal plane. Thus, our results show that (1) a discrete change of motor control policy is performed by the CNS to transition between a quiet standing posture and locomotion, suggesting that humans must "stop balancing" when they stand before they can walk, and (2) human locomotion requires an active control of balance only in the mediolateral direction. Future work is considered with PD patients, to determine if freezing of gait episodes can origin from deficits in switching motor policies.

# Oral Presentation #9 14:00 – 14:15

## An early warning system for human-caused wildfires

**Paul Pickell** PhD
*Forestry*

The majority of wildfires in Alberta are caused by humans. Human-caused wildfires tend to pose greater danger than lightning-caused fires because of their proximity near homes, roads, and settlements. The majority of human-caused wildfires tend to occur during what is known as the spring burning window, a period of time in the growing season when snow cover has melted to expose vegetation that does not yet have leaves. The spring burning window is the most dangerous time of year for human-caused wildfires because fire can spread rapidly through the drier, leafless vegetation. We developed a system to predict the timing of leaf growth from satellite imagery that can be used to forecast the spring burning window. The early warning system was developed and tested over approximately 400,000 $km^2$ of forested land in Alberta. We simulated the real-world availability of satellite imagery from the years 2000 to 2014 to test the accuracy of each weekly forecast and further validated the forecasts using remote ground-based cameras that were installed in the forests to take photos of vegetation condition on a daily basis throughout the spring burning window. The system was able to predict the timing of onset leaf growth with 10-day accuracy for approximately 76% of fire-protected forests by the end of March, before the start of the official fire season in April. This early warning system could assist wildfire managers with more effective and strategic deployment of fire protection personnel and equipment over large areas.

# Oral Presentation #10 14:15 – 14:30

## The psychology of gambling

**Eve Limbrick-Oldfield** PhD
*Psychology*

Gambling is a popular leisure activity around the world. In British Columbia, tax revenue earned from gambling is greater than that earned from tobacco and alcohol combined. Whilst this revenue is, in part, returned to the community to fund community resources, a proportion of those who gamble develop gambling problems, with approximately 1% of the population meeting diagnostic criteria for Gambling Disorder. Research over the past few decades has led to a change in how we think about this disorder. It is now thought to be similar in many ways to substance use disorders. My work focuses on understanding why some people develop problematic gambling behaviour whilst others are able to gamble at a safe level, much like how only a small proportion of those who consume alcohol develop an addiction to alcohol. Here I report several functional MRI studies looking at markers of vulnerability for the disorder, and how brain activity is related to craving, a key construct in Gambling Disorder that can predict relapse. Finally, I will describe how these studies can inform our understanding of substance use disorders.

# Oral Presentation #11 14:30 – 14:45

## Design and implementation of a tool condition monitoring system for the shop floor

**Murat Kilic** PhD
*Mechanical Engineering*

In an airplane, the jet engine consists of the most critical components, which are exposed to high thermal and mechanical stress while rotating at high speeds. Due to very strict engineering design criteria, machining of such components are highly critical; an unexpected tool failure may scrap the workpiece and cost very high to the producer. Therefore, tool condition monitoring systems are popular due to their capacity to protect the production lines by automatically detecting tool failure. However, it is a challenging step to apply these systems at the shop floor since they are not possible to be adjusted to eliminate false alarms, and they require extensive operator training and integration periods which cause interruption to the production tasks. This paper presents a general purpose, open architecture tool condition monitoring software: It is (1) easy to adapt to any machine tool and operation, (2) intuitive with minimized user involvement, and (3) flexible to tune up current functions or to add new functions for the fast changing production requirements. Firstly, we present the modules, user interface and feature extraction capacity of the software. Then, preliminary tests are done using data from a milling operation at the shop floor. Using healthy process data, the dynamic threshold is modified in order to eliminate false warnings and alarms.

# Oral Presentation #12 14:45 – 15:00

## Generation of paediatric reference intervals for blood detection of the axonal proteins tau and neurofilament-light

**Sophie Stukas** PhD
*Pathology & Laboratory Medicine*

Traumatic brain injury (TBI) is one of the most difficult brain disorders to study as it can happen to anyone at any time, with injuries ranging from concussion to life threatening. Diagnostic and prognostic markers are needed to help establish the correct diagnosis, direct appropriate care, risk stratify for intervention trials, and prognosticate long-term outcome. This is especially true for paediatric cases due to barriers in communication, potential for abuse, risks associated with neuroimaging and radiation exposure, and the rapid brain growth and development that takes place during these years. Due to technological advances, we can now detect biomarkers of brain injury and recovery within blood samples. A critical first step in blood biomarker development is the establishment of a normative baseline by generating reference intervals (RI) – partitions that give upper and lower limits of biomarker concentration based on age and sex groupings. Using ultrasensitive robotic technology, we have measured two axonal proteins, called tau and neurofilament-light (NF-L), in serum samples taken from over 300 healthy community dwelling children age 1-18. While there was no correlation with sex, there was a significant negative correlation between age and both tau and NF-L levels, with the highest and most variable levels of tau being observed in children under 4. Four age partitions were generated for tau: age 1-<4, 4-<9, 9-<15, and 15-<19y, while only two age partitions were required for NF-L: age 1-<10, and 10-<19y. Generation of this normative database will allow for future comparison of tau or NF-L measured following TBI.

# Poster Presentations

| Poster | Presenting Author |
|---|---|
| 1 | **Estimating worker exposure to silica using offline analysis and real-time proxy measurements**<br>– **Alberto Baldelli** PhD, *Mechanical Engineering* |
| 2 | **The Meaningful Patient Engagement in Research (PEIR) Framework – an empirically based conceptual framework**<br>– **Clayon Hamilton** PhD, *Physical Therapy* |
| 3 | **Matrix stability of circulating blood-based biomarkers of brain injury: pre-analytical methodological considerations**<br>– **Colin Wallace** PhD, *Pathology & Laboratory Medicine* |
| 4 | **Multiple jobholders are less likely to return to work than single jobholders**<br>– **Esther Maas** PhD, *School of Population and Public Health* |
| 5 | **Natural bacterium-mediated repression of virulence factor production by human fungal pathogens**<br>– **François Mayer** PhD, *Michael Smith Laboratories* |
| 6 | **Lipid nanoparticles co-loaded with siRNA and taxane prodrugs for combination treatment of prostate cancer**<br>– **Roy van der Meel** PhD, *Biochemistry and Molecular Biology* |
| 7 | **Human islets exhibit heterogeneity in macronutrient-stimulated insulin release that cannot be explained by gross donor characteristics**<br>– **Jelena Kolic** PhD, *Cellular & Physiological Sciences* |
| 8 | **Development of highly efficient Hydrogen Evolution Reaction (HER) catalysts for PEM water electrolysis**<br>– **Liu Gaoyang** PhD, *Chemical & Biological engineering* |
| 9 | **Depupylase Dop requires inorganic phosphate in the active site for catalysis**<br>– **Marcel Bolten** PhD, *Michael Smith Laboratories* |
| 10 | **Treatment of type III endoleak in aneurysm using a novel stent design**<br>– **Mohammad Fazel Bakhsheshi** PhD, *Mechanical Engineering* |
| 11 | **Exploring the evolutionary continuum from commensalism to pathogenesis in rhizosphere-dwelling Pseudomonas**<br>– **Ryan Melnyk** PhD, *Microbiology and Immunology* |
| 12 | **A triple combination approach involving nerve transplantation, glial scar digestion and passive exercise promotes cardiovascular recovery after spinal cord injury**<br>– **Rahul Sachdeva** PhD, *International Collaboration On Repair Discoveries (ICORD)* |
| 13 | **Salmonella mediated alteration of host DNA methylation patterns during infection**<br>– **Jennifer L Rowland** PhD, *Michael Smith Laboratories* |
| 14 | **Differential functional connectivity of the subgenual and rostral anterior cingulate cortex predict treatment outcome with repetitive transcranial magnetic stimulation for treatment-resistant depression**<br>– **Ruiyang Ge** PhD, *Psychiatry* |

# Poster 1

## Estimating worker exposure to silica using offline analysis and real-time proxy measurements

**Alberto Baldelli** PhD
*Mechanical Engineering*

Mining dusts, especially inhalable silica, can be a health hazard. Regulations on this matter concern particles in the range of 0.3 to 10 µm for an exposure of 8 to 10 hours and PM 4. Nanozen Dustcount 8899 is a well calibrated wearable tool that records in real-time respirable particles smaller than 4 µm. Real-time data collection combined with portability allows this aerosol monitor to have a much greater capacity for measuring exposure to aerosols. Off-line measurements, such as X-ray diffraction or mass spectroscopy, have been used extensively for silica detection in aerosol. Off-line analysis of collected samples can be laborious (often involving ashing of filters) and usually requires more than a milligram of material – which can be difficult to collect in practice. There are few reported attempts to determine the mass of crystalline silica in aerosols collected on filters and using real-time measurements. Challenges encountered in measuring silica in aerosol dusts collected on PVC filters are commonly related to the lower amount of aerosol required by a characterization device, the fragility of PVC filters, the differentiation of different silicates present in the aerosol dust, and the interference of the PVC to the silica signal in few characterization devices.

# Poster 2

## The Meaningful Patient Engagement in Research (PEIR) Framework – an empirically based conceptual framework

**Clayon Hamilton** PhD
*Physical Therapy*

BACKGROUND:
Engaging patients as partners on research teams is promoted to improve the quality of health research. However, there is little empirically based conceptualization of what makes patient engagement in research *meaningful* to the patient partners. We aimed to develop a conceptual framework for meaningful patient engagement in research from a patient perspective, that would useful to guide the planning, implementing, and evaluating of patient engagement in research.

METHODS:
We conducted a qualitative secondary analysis of in-depth interviews with 18 patient partners from a research centre–affiliated patient advisory board. Data analysis involved three phases: identifying the themes, developing a framework, and confirming the framework. Thematic analysis was conducted to identify and explore the emergent themes. Directed content analysis was conducted to derive concepts from 18 publications related to patient engagement in research to supplement, confirm or refute, and extend the emergent conceptual framework. The framework was reviewed by the four patient partners on our research team.

FINDINGS:
Participants' experiences of working with researchers were generally positive. Eight themes emerged: *Procedural Requirements, Convenience, Contributions, Support, Team Interactions, Research Environment, Feel Valued*, and *Benefits*. These themes were interconnected and formed the Patient Engagement in Research (PEIR) Framework to explain the phenomenon of meaningful patient engagement in research from a patient perspective.

IMPLICATIONS:
The PEIR Framework provides guidance on aspects of patient engagement in research to operationalize for engagement to be meaningful. It could be particularly useful when patient-researcher partnerships are led by researchers with little experience of engaging patients in research.

# Poster 3

## Matrix stability of circulating blood-based biomarkers of brain injury: pre-analytical methodological considerations

**Colin Wallace** PhD
*Pathology & Laboratory Medicine*

BACKGROUND AND AIM:
A broad panel of potential blood-based biomarkers has been identified for traumatic brain injury (TBI); however, appropriate pre-analytical considerations have yet to be examined. Human plasma and serum are the common matrices for clinical studies of TBI, yet no study has described the methodology of sample collection. The aim of this study is to investigate the stability of blood-based biomarkers across 3 distinct matrices.

METHODS
Blood samples were collected from 10 healthy donors into 3 different blood collection tubes: K3EDTA-lined tubes yielded plasma; lithium heparin-lined tubes yielded plasma; and serum separator tubes (SST)-yielded serum. Biomarkers included tau, neurofilament light (NF-L), glial fibrillary acidic protein (GFAP) and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1). Analysis was performed on the Simoa HD-1, a digital analyzer 1000x more sensitive than conventional immunoassays.

RESULTS:
All data are presented as (mean ± standard deviation). A matrix effect was seen for NF-L
($p < 0.05$). GFAP concentration was greater in lithium heparin tubes (88.6 ± 40.6 pg/mL) compared to serum separator tubes (80.1 ± 35.0 pg/mL) ($p < 0.05$). Tau concentration was higher in lithium heparin tubes (2.02 ± 0.79 pg/mL) compared to both EDTA (0.55 ± 0.38 pg/mL) ($p < 0.05$) and SST (0.17 ± 0.10 pg/mL) ($p < 0.01$). No matrix effect was demonstrated for UCH-L1.

CONCLUSIONS:
This study highlights the importance of proper blood sample collection when quantifying blood-based TBI biomarkers; demonstrated matrix effects were seen for GFAP, NF-L, and tau. These findings have the potential to influence future TBI biomarker research.

# Poster 4

## Multiple jobholders are less likely to return to work than single jobholders

**Esther Maas** PhD
*School of Population and Public Health*

The objective of this study was to examine the association between multiple jobholding and return-to-work (RTW) for workers with a work-related musculoskeletal disorder (MSD).

We used administrative workers' compensation data to identify injured workers with accepted MSD lost-time claims and an injury date between 2010-2014 in British Columbia, Canada (N=125,639 SJHs and 9,029 MJHs). The outcome was time until RTW within one year following the first time-loss day. The MJH and SJH cohorts were balanced using coarsened exact matching, which yielded a matched cohort of 8,922 MJHs and 8,992 SJHs. The outcome was estimated with Cox regression, using piecewise models.

MJHs were less likely to RTW compared to SJHs within the first six months after the first time-loss day. This applied to men and women, and workers with any type of MSD except dislocations. No difference between MJHs and SJHs was found for workers who had a six- or seven-day work week preceding MSD, workers with an annual income <$20 000, and for workers who were still off work after six months.

Overall, MJHs with a workweek of maximum five days per week and those earning more than minimum are disadvantaged compared to SJHs in terms of RTW following a work-related MSD within the first six months after the first time-loss day. This difference might be caused by more precarious job contracts for MJHs that challenges RTW in terms of support (e.g. by modified work offerings), a higher workload, and their reduced likelihood to file a workers' compensation claim.

# Poster 5

## Natural bacterium-mediated repression of virulence factor production by human fungal pathogens

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Inter-species and inter-kingdom microbial interactions are ubiquitous in nature. As a consequence of competition for space and food, a considerable proportion of these interactions are antagonistic. The meningitis-causing human fungal pathogen *Cryptococcus neoformans* is acquired from the environment by inhalation of spores and/or desiccated yeast cells. In immunocompromised individuals these fungal cells are able to infect lung tissue and, eventually, to further disseminate to and infect the brain. Here, we hypothesized that *C. neoformans* is likely exposed to other microbes in nature that may possess anticryptococcal properties. We have identified the soil bacterium *Bacillus safensis* as a potent inhibitor of *C. neoformans* melanization, capsule formation, urease secretion, and biofilm formation, all of which are key cryptococcal virulence factors. Interestingly, *B. safensis* was also found to inhibit the yeast-to-hyphal transition in *Candida albicans*, another major human fungal pathogen that, in contrast to *C. neoformans*, is obligately associated with warm-blooded animals. In *C. neoformans*, the antifungal activity of *B. safensis* appeared to be mediated by direct contact and live bacteria were required. We show that at least part of the antifungal activity appears to be the result of a targeted influence on the fungal cell wall via bacterial chitinase activity. These results may help in the identification of new antibiotic drug targets, as well as in the discovery of novel antifungal mechanisms.

# Poster 6

## Lipid nanoparticles co-loaded with siRNA and taxane prodrugs for combination treatment of prostate cancer

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Treatments that prolong the survival of patients with advanced prostate cancer include inhibition of its fundamental driver, the androgen receptor (AR), and taxane-based chemotherapy. Nevertheless, expression of constitutively active AR splice variants (AR-Vs) which lack the ligand binding domain often occurs, rendering current AR inhibitors ineffective. At the same time, taxane chemotherapy is hampered by dose-limiting adverse effects. To address this, lipid nanoparticles (LNPs) co-loaded with taxane prodrugs and siRNA for knockdown of AR and AR-Vs were developed to induce enhanced therapeutic effects, lower taxane-mediated adverse effects and overcome resistance to AR inhibition.

LNPs containing the ionizable cationic lipid DLin-MC3-DMA for efficient encapsulation of siRNA against AR N-terminal domain (ARNTD) and lipophilic prodrugs of docetaxel/cabazitaxel were formulated by a rapid mixing method using a T-junction mixer. Physicochemical analysis indicated mean LNP size of 50 nm and >90% siRNA and taxane prodrug encapsulation efficiency. LNPs containing ARNTD siRNA with and without taxane prodrugs induced >80% knockdown of AR-V7 in 22Rv1 cells as determined by qPCR. MTS assays demonstrated that LNPs containing both siRNA and taxane prodrugs induced significantly greater inhibition of 22Rv1 cell viability when compared to control formulations while no difference was observed in AR-negative PC3 cells. Incorporation of taxane prodrugs did not affect LNP circulation time in mice after i.v. administration.

Co-loading LNPs with ARNTD siRNA and lipophilic taxane prodrugs is an attractive strategy to develop effective combination treatments for advanced prostate cancer.

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# Poster 7

## Human islets exhibit heterogeneity in macronutrient-stimulated insulin release that cannot be explained by gross donor characteristics

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Type 2 diabetes (T2D) impacts more than 3 million Canadians, and obesity, which increases the risk of T2D, has reached epidemic proportions. Despite numerous treatment options, many obese and/or T2D patients suffer from decreased quality of life. However, obesity and its complications can be prevented in mice genetically-protected from diet-induced hyperinsulinemia. While this has not been shown in humans, long-term insulin treatments induce weight gain. Taken together, these data suggest that a reduction in insulin levels is beneficial to the metabolic health of an individual with hyperinsulinemia.

While glucose is the main driver of insulin secretion, other macronutrients can potentiate insulin release. We measured insulin secretion in response to glucose, leucine, or oleate/palmitate from 20 non-diabetic human islet donors. We find that insulin release in response to these macronutrients is highly variable. Glucose (15 mmol/L) stimulated insulin release by 2 to 24-fold. Leucine (5 mmol/L) induced insulin release by 2 to 21-fold, and oleate/palmitate (1.5 mmol/L; 1:1 mix) stimulated insulin release by 4 to 16-fold. We find that these donor-donor variations in insulin secretion are poorly correlated to islet isolation parameters, or gross donor characteristics (age, BMI, HbA1c).

This heterogeneity could explain how macronutrient intake can have distinct effects on weight loss and diabetes risk in individuals, and shed light on why ‘low-carb’ diets that aim to keep insulin levels low are only effective in some individuals. Ongoing studies correlating insulin responses to genomic factors aim to elucidate the mechanistic underpinnings of this heterogeneity.

# Poster 8

## Development of highly efficient Hydrogen Evolution Reaction (HER) catalysts for PEM water electrolysis

**Liu Gaoyang** PhD
*Chemical & Biological engineering*

To date, Pt-based catalysts can catalyze the HER effectively and are widely used, but the high cost largely prevents their practical application. Non-Pt catalysts, especially for molybdenum disulfide (MoS2), has been extensively studied as the catalysts for the HER because of its comparable activity to Pt-based catalysts. Recent studies have shown that the HER activity of MoS2 is highly dependent on the exposed edges, and most of the present works are focusing on getting more active exposed edges of the MoS2 catalyst by chemical peeling, porous morphology, lattice distortion, crystal structure defects, physical grinding and sonication methods. It should be noted that lots of the in-plane domains of the MoS2 catalyst are useless.

In this research, novel MoS2 based non-Pt catalyst towards HER will be developed. Unlike the stratified structure of MoS2, the hexagonal Ni2P usually maintains particle structures. Thus, highly dispersed Ni2P tiny particles both in amorphous state and the multi-phase crystalline state will be supported on the in-plane domains of MoS2 (Ni2P/MoS2). The active areas in the composite catalyst will be greatly improved due to the synergistic effect of both the Ni2P tiny particles and the exposure edges. Then, novel electronic and protonic conductive carbon papers will be prepared to support the active phase. The highly mixed protonic and electronic conductive support with intimate interconnection between nanosized MoS2 or Ni2P/MoS2 will be expected to offer excellent charge transfer behavior and increase the electrochemical performance of MoS2 or Ni2P/MoS2.

# Poster 9

## Depupylase Dop requires inorganic phosphate in the active site for catalysis

**Marcel Bolten** PhD
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Analogous to eukaryotic ubiquitination, proteins in actinobacteria can be post-translationally modified in a process referred to as pupylation, the covalent attachment of prokaryotic ubiquitin-like protein Pup to lysine side chains of the target protein via an isopeptide bond. Like in eukaryotes, an opposing activity counteracts the modification by specific cleavage of the isopeptide bond formed with Pup. However, the enzymes involved in pupylation and depupylation have evolved independently of ubiquitination and are related to the family of ATP-binding and hydrolyzing carboxylate-amine ligases of the glutamine synthetase type. Furthermore, the Pup ligase PafA and the depupylase Dop share close structural and sequence homology and have a common evolutionary history despite catalyzing opposing reactions. Here, we investigate the role played by the nucleotide in the active site of the depupylase Dop using a combination of biochemical experiments and X-ray crystallographic studies. We show that, although Dop does not turn over ATP stoichiometrically, the active site nucleotide species in Dop is ADP and inorganic phosphate rather than ATP, and that non-hydrolyzable analogs of ATP cannot support the enzymatic reaction. This finding suggests that the catalytic mechanism is more similar to the mechanism of the ligase PafA than previously thought and likely involves the transient formation of a phosphorylated Pup-intermediate. Evidence is presented for a mechanism where the inorganic phosphate acts as the nucleophilic species in amide bond cleavage and implications for Dop function are discussed.

# Poster 10

## Treatment of type III endoleak in aneurysm using a novel stent design

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*Mechanical Engineering*

Aortic aneurysms are common disorder as progressive dilation due to weakening of the aortic wall with high risk for death caused by rupture. Endoleak is defined as the persistent of blood flow into and within the aneurysmal sac after endovascular repair. Endoleaks are seen in up to 30-40% of the cases with endovascular aneurysm repair and have been pointed out as adverse events, which can cause migration of the stent-graft and rupture of the aneurysm. About 46% of endoleaks required additional treatment. Despite advances in the treatment of cardiac arrest, we believe that there is still a great need for technology that improves patient outcomes. In the present study, we investigated a Venturi tube stent in the treatment of aortic aneurysms, and its effect on aneurysm and aortic wall stress. Specifically, we analyzed the ability of the Venturi stent to reduce pressure in sac area and absorb the stresses in the aneurysm wall in the phenomena of endoleaks, i.e., an expanding sac with elevated sac pressure due to mechanical failure of endovascular stent. Computational fluid dynamic techniques are applied to model the blood flow by numerically solving the three-dimensional continuity equation and the time-dependent Navier–Stokes equations for an incompressible fluid. Our numerical results showed that a stent with Venturi structure was able to significantly reduce the wall shear stress and average pressure at the artery's wall in the event of endoleak type III.

# Poster 11

## Exploring the evolutionary continuum from commensalism to pathogenesis in rhizosphere-dwelling *Pseudomonas*

**Ryan Melnyk** PhD
*Microbiology and Immunology*

Small genetic changes can result in dramatically different bacterial lifestyles including the switch from commensal to pathogen. Unlike close relatives that promote plant growth and lateral root formation, *Pseudomonas* sp. FW300-N2C3 (N2C3) strongly inhibits *Arabidopsis thaliana* seedling development, ultimately resulting in plant death. Because closely-related strains within this genus can have such dramatically different effects on plant health, Pseudomonas is an ideal model to study the genetic basis and evolution of bacterial lifestyle transitions. We developed a novel computational pipeline for identifying orthologs in thousands of bacterial genomes and used this tool to identify a genomic island in N2C3 that is absent in related beneficial *Pseudomonas* strain. This island contains genes for non-ribosomal peptide synthases and an acyl homoserine lactone (AHL) quorum-sensing system, which are frequently found in known *Pseudomonas* plant pathogens. Deleting the AHL synthase within the island in N2C3 restored healthy seedling development, showing that N2C3-mediated plant death is quorum-dependent and that the island is associated with pathogenicity of N2C3. Further comparative genomics identified the island in other *Pseudomonas* strains. One of these strains is not pathogenic when applied to *Arabidopsis* seedlings, but it restores the pathogenicity of the AHL synthase mutant, suggesting a role for interspecies quorum-sensing systems in the rhizosphere. Use of well-studied and genetically tractable commensal microbes in the genus *Pseudomonas* coupled with high-throughput comparative genomics has allowed us to gain insights into the evolutionary history of the commensal-pathogen continuum.

# Poster 12

## A triple combination approach involving nerve transplantation, glial scar digestion and passive exercise promotes cardiovascular recovery after spinal cord injury

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*International Collaboration On Repair Discoveries (ICORD)*

INTRODUCTION:
A common impression of having spinal cord injury (SCI) is the inability to walk. But most people are unaware of its life-threatening consequences such as disrupted cardiovascular control. This is because the spinal pathways controlling heart and blood vessels get severely damaged by SCI and the individuals suffer from a condition called Autonomic Dysreflexia, where routine stimuli e.g. full bladder or bowel routine trigger life-threatening spikes in blood pressure (BP; up to 300mmHg). Although a single episode can be potentially fatal, these occur several times a day, putting the individual at serious health risk.

RATIONALE:
Restoration of cardiovascular control by spinal regeneration combined with reduction in the injury-associated sprouting of sensory pain fibers will reduce the severity of Dysreflexia.

METHODS:
The rats received a complete T3 SCI. In treatment group, the lesion was bridged using Tibial nerves isolated from donor rats. An enzymatic treatment was continuously delivered to the injury site to prevent scar formation. The rats also performed daily cycling exercise. Eight weeks later, functional regeneration was confirmed by measuring flow of electric current across the nerve bridge in anesthetized rats. Dysreflexia severity was tested by inflating a balloon in the animals' rectums.

RESULTS/CONCLUSION:
The combined regenerative and rehabilitative approach led to over 50% reduction in the Dysreflexia severity compared to untreated groups. The mechanism underlying recovery such as specific sources and targets of re-growing connections are also being evaluated. With possibility of clinical translation, this approach could improve autonomic function and the quality of life after SCI.

# Poster 13

## *Salmonella* mediated alteration of host DNA methylation patterns during infection

**Jennifer L Rowland** PhD
*Michael Smith Laboratories*

*Salmonella enterica* serovar Typhimurium (*S*. Typhimurium) is responsible for millions of gastrointestinal illnesses globally each year. As an intracellular pathogen, *S*. Typhimurium is adept at controlling host cells and creating a favorable environment for replication. Upon entry into a human host, *Salmonella* survive and replicate inside a variety of host cell types including intestinal epithelial cells and macrophages. To create a favorable replication environment, *Salmonella* disrupts the normal endocytic pathway of host cells, resulting in a vacuole containing the replicating *Salmonella*, using a variety of effector proteins.

Pathogens induce changes in host cell gene regulation at the chromatin level. These regulatory alterations are evidenced by changes in the host cell methylation pattern on DNA and by changes in the modifications of histone tails. Some of these epigenetic changes are the result of the host acting upon itself in response to infection, while others are the direct result of pathogen proteins that act both inside and outside the host nucleus. To determine whether and how *Salmonella* infection alters host DNA methylation, we infected the human macrophage-like cell line, THP-1, with both live and killed *S*. Typhimurium, as well as a strain lacking some effector secretion. Host DNA methylation was interrogated by bisulfite conversion followed by analysis on Illumina MethylationEPIC bead chip. At 24 hours post infection, all infections showed significant changes in DNA methylation compared to uninfected cells, suggesting that the altered methylation pattern is a host-driven response.

# Poster 14

## Differential functional connectivity of the subgenual and rostral anterior cingulate cortex predict treatment outcome with repetitive transcranial magnetic stimulation for treatment-resistant depression

**Ruiyang Ge** PhD
*Psychiatry*

Neuroimaging studies of patients with major depressive disorder have revealed predictive value of activity patterns in subgenual anterior cingulate cortex (sgACC) and rostral anterior cingulate cortex (rACC), and most of these studies suggest an opposite activity pattern of these two regions between patients who respond adequately and who respond inadequately to the treatment. However, studies investigating and comparing the predictive capability of the two regions at a system-level are missing. We hypothesized that the predictive capacity of those two regions is mediated via different functional networks. Pre-treatment resting-state functional MRI was measured in fifty patients with treatment-resistant depression to predict subsequent response to repetitive transcranial magnetic stimulation (rTMS). We used a priori seed-driven functional connectivity analysis to discover connectivity pairs that serve as candidate predictive biomarkers. The functional connectivity of the following regions with sgACC and rACC was associated with treatment improvement: left dorsolateral prefrontal cortex within the affective network and right lateral parietal cortex within the default mode network. Using sgACC and rACC connectivity pair as a feature, classification accuracy rate of 84% and 76% was demonstrated respectively. SgACC-related connectivity was significantly higher in non-responders than responders and negatively correlated with symptom improvement, whereas rACC-related connectivity showed the opposite pattern. Moreover, the connectivity pairs of sgACC and rACC were negatively correlated, and correlated with overlapped and specific depression symptoms. In summary, this is the first study to demonstrate that functional connectivity patterns of agACC and rACC provide predictive biomarkers of treatment response to rTMS, and they act as biomarkers through participating in different functional networks.