Abstract Book
St. Boniface BGU Find a Partner Event

List of St. Boniface PIs who are interested in working with BGU in a collaborative project. Their research programs are described in the following pages:

Neurodegenerative Disorders Research
Dr Paul Fernyhough
Dr Ben Albensi
Dr. Toby Martin

Cardiovascular Research
Dr Larry Hryshko
Dr Amir Ravandi
Dr Rakesh Arora
Dr Michael Czubryt
Dr Elissavet Kardami
Dr Sanjiv Dhingra
Dr Todd Duhamel
Dr Jeff Wigle
Dr Lorrie Kirshenbaum
Dr Pawan Singal
Dr Davinder Jassal
Dr Ross Feldman
Dr. Ian Dixon

Nutraceutical and Functional Food Research
Dr Michel Aliani
Dr Harold Aukema
Dr Thomas Netticadan and Dr Shelley Zieroth
Dr Peter Zahradka and Dr Carla Taylor
Dr Hope Anderson
Dr Heather Blewett
Dr Karmin O

Neurodegenerative Disorders Research

Dr. Paul Fernyhough - Neurodegenerative Disease Laboratory

1. What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc): I study neurodegenerative diseases, CNS and PNS, with a focus on mechanisms of mitochondrial dysfunction

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc): Main focus is disease of the PNS such as found in diabetes but also in cancer and HIV. I also have some interest in co-morbidity between diabetes and cognitive dysfunction.

3. What type of research does your lab carry out? (basic science or clinical trials or both): We are primarily basic research, however, I am in the midst of commercializing our discoveries and phase 1/phase 2 trials are ongoing.

4. What projects are currently underway in your lab (250 word max)?

   Selective or specific muscarinic acetylcholine type 1 receptor (M_1R) antagonists induce elevated neurite outgrowth in adult sensory neurons. We overexpressed M_1R in sensory neurons and discovered depletion of functional mitochondria at the growth cone and a subsequent decrease in neurite outgrowth. The mitochondrial deficit in axons was associated with discontinuity in the □-tubulin cytoskeletal structure that, in turn, suppressed mitochondrial trafficking. This structural defect was corrected by treatment with muscarinic antagonists pirenzepine (PZ) and muscarinic toxin 7 (MT7). Recruitment of G-proteins and increased Ca^{2+} signaling in the neurites mediated this protective drug effect. In vivo studies with rodent models of type 1 and 2 diabetes reveal that systemic or topical PZ or MT7 can prevent and reverse structural and functional abnormalities in peripheral nerve (and other neuropathic diseases). A novel mechanism is being studied in which modulation of M_1R influences mitochondrial distribution in nerve terminals and controls axonal outgrowth and regeneration. This work has recently been accepted for publication in *Journal of Clinical Investigation*.

Dr. Ben Albensi – CNS Disorders Laboratory

1. What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc):
   Our main focus is on CNS disorders/disease.

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc):
   Memory impairments associated with dementia (includes both Alzheimer's disease (AD) dementia and vascular dementia); acquired epilepsy associated with brain injury/dementia; TBI/head trauma leading to CNS disorders (eg, Alzheimer's).

3. What type of research does your lab carry out? (basic science or clinical trials or both):
   We are involved in basic science (eg, *in vitro,* LTP, molecular/cell biology, *in vivo* memory testing), translational research (eg MRI/PET), and collecting critical preclinical data for establishing a rationale to test nutritional products in clinical trials (eg, creatine).

4. What projects are currently underway in your lab (250 word max)?
   Currently, we are using several experimental modalities to conduct the research described above, including MRI/PET, electrophysiology (e.g., LTP), cell/molecular biology, behavioral tests of memory, and computational modeling. Some of our projects characterize biological processes of memory and mechanisms of memory impairments. In addition, we are actively investigating inflammatory responses in CNS disease/disorders, such as those mediated by NF-kB signaling and activated microglia. In addition, we are investigating changes in energy metabolism in AD and have focused on the role of mitochondrial dysfunction. We use several transgenic strains of mice (TgCRND8, 3xTg, NF-kB KO) in addition to using human tissue samples. We also have tested or will be testing several nutritional products including creatine, flax, and choline (papers in preparation or submitted). One hypothesis under investigation is if mitochondrial function is affected differently in males vs. females. To date, we have collected statistically significant data showing mitochondrial function becomes impaired in our AD mice at 2 mos of age in females (but not males). Furthermore, we have multiple collaborations in Canada and the USA that add additional strength to our research experimental capability and scope. These projects are led by 3 postdoctoral fellows and assisted by 2 laboratory technicians. Other trainees also regularly rotate through our lab.

5. Is there anything else important that we should know (in one sentence) about your research? We have discussed collaborations with Dr. Alon Friedman at BGU on projects of mutual interest as described here.

Dr. Toby Martin, Applied Behaviour Analysis

1. *What disease/condition is the focus of your lab?*

Autism spectrum disorders (ASD), developmental disabilities, intellectual disabilities.

2. *Upon what subset of this disease/condition do you focus?* In terms of population, much of my work is either with children with ASD, or adults with severe or profound ID.
3. *What type of research does your lab carry out? (basic science or clinical trials or both):* Primarily applied, or translational.
4. *What projects are currently underway in your lab (250 word max)?*

We have several ongoing projects to evaluate variants of Early Intensive Behavioural Intervention (EIBI) for children with ASD. We're investigating: long-term (e.g. > 5 y) post-program outcomes (i.e. in cognitive, adaptive, social etc. domains), the effects on outcomes of varying service setting, program model, and service intensity, and the outcomes and social validity of short-term pre-Kindergarten intervention for children at risk of aging-out of service.

We are evaluating the use of an eHealth case management and data collection program by front-line staff to promote specific service quality measures in an EIBI program from children with ASD. Measures include data collection accuracy for discrete trials teaching and challenging behaviour intervention, as well as time intervals within the clinical decision cycle.

Innovative methods for staff and parent training to support children with ASD are another research focus, driven by service funding challenges. This work can be characterized as "knowledge translation science," per the Canadian Institutes of Health Research. The knowledge translated includes behavioural procedures to identify reinforcers, determine causes of challenging behaviour, and deliver discrete trials teaching.

Another objective regarding staff training is to experimentally evaluate the benefits of promoting mindfulness among caregivers. Evidence suggests that mindful staff experience lower stress and increased engagement, and their clients may display fewer challenging behaviours and increased quality of life. We have several projects aimed at elucidating the mechanisms by which these benefits occur.

5. *Is there anything else important that we should know (in one sentence) about your research?*

My research occurs in the context of an interdisciplinary research centre (colleagues who are expert in nursing, community health) and a large publicly-funded community service agency.

Cardiovascular Research

Dr Larry Hryshko – Ion Transport and Heart Transplant Laboratory

1. Our laboratory focuses on cardiovascular disease.

2. The specific cardiovascular diseases/conditions under investigation include ischemia-reperfusion injury, arrhythmias and heart failure.

3. We are a basic science laboratory with a strong interest in translational research.

4. Our laboratory has a long standing interest in evaluating the role of sodium-calcium exchange in various cardiac pathologies, such as ischemia-reperfusion injury, arrhythmias and heart failure. We have been investigating this family of proteins using electrophysiological, biophysical and molecular biological techniques. Our research focuses on elucidating the mechanism of action of several novel sodium-calcium exchange inhibitors, including SEA0400, KB-R7943 and SN-6 as well as the mitochondrial NCX inhibitor CGP 37157. We continue to investigate the therapeutic potential of these compounds in clinically relevant models of cardiac injury with an emphasis on understanding the benefits and limitations of currently available agents. The pharmacological manipulation of sodium-calcium exchange represents a promising therapeutic target, despite the limitations in our understanding of the inhibitory mechanisms of action for these agents. We also continue to investigate the unique characteristics of different members of the sodium-calcium exchange family from a functional/regulatory perspective as well as by studying their different pharmacological sensitivities to available inhibitors. Understanding this differential sensitivity is critically important for understanding therapeutic possibilities and limitations of sodium-calcium exchange inhibitors in vivo. Finally, we are utilizing our knowledge of sodium-calcium exchange inhibitors and excitation-contraction coupling to devise novel strategies that can be directly applied to human heart transplantation.

5. Our interests in the role of sodium-calcium exchange in various cardiovascular ailments are shared by several Investigators at Ben-Gurion University of the Negev as well as other Investigators in Israel.

Dr. Amir Ravandi - Cardiovascular Lipidomics Laboratory

The general focus of Dr. Ravandi's laboratory is to study lipid oxidation products and their contribution to cardiovascular pathology. The laboratory uses LC/MS/MS Lipidomic platform for quantitation and identification of lipid oxidation products in both animal models and clinical conditions to determine the involvement of oxidized lipids in both cardiac and vascular lesions. The ultimate goal is to not only identify the contribution of bioactive lipids to cardiac muscle injury but also to determine new therapeutic approaches to prevent the pathological effects of oxidized lipids.

2. Upon what subset of this disease/condition do you focus? Myocardial Ischemia and reperfusion; Lung Inflammation; Renal Reperfusion injury

3. What type of research does your lab carry out? (basic science or clinical trials or both): We carry out both clinical studies and basic sciences.

4. What projects are currently underway in your lab (250 word max)?

Lipidomic analysis of plasma in patients presenting with STEMI; Cell death in cardiomyocytes mediated by fragmented OxPC molecules; Role of Fragmented Oxidized phospholipid in asthma, COPD and reactive airway disease.

For many years lipids were considered to be only cellular building blocks with very little biological activity. Due to their susceptibility to oxidation they are modified in the presence of reactive oxygen species. Apart from impairment of their structural function, oxidation makes oxidized phospholipids (OxPL) acquire novel biological activities not characteristic of their unoxidized precursors. The effects of OxPLs described in vitro and in vivo suggest their potential relevance in different pathologies, including atherosclerosis, acute inflammation, lung injury, and many other conditions. The actions of OxPL can vary depending upon the specific species of phospholipid being oxidized. Recently, oxidized phosphatidylcholines (OxPC) have been recognized as not only products of oxidative damage but also mediators of its progression. Recent advancements in softer methods of ionization, such as electrospray mass spectrometry, has allowed us to identify and quantitate OxPL's in biological tissues. Our group has over the past decade developed mass spectrometric techniques that can identify and quantitate oxidized lipids within atherosclerotic plaques, oxidized Low Density Lipoprotein (OxLDL), and other biological tissues. As we move forward in trying to better understand the role of OxPL in cardiovascular pathology, it necessitates a detailed understanding of the oxidized lipidome within cardiac tissue such as ischemic myocardium or in plasma from patients with acute coronary syndromes. Using this knowledge as a platform, we are investigating the role of OxPL in cardiovascular pathology and will be able to tailor therapies to prevent OxPL induced injury.

5. Is there anything else important that we should know (in one sentence) about your research? We are truly a translational lab that tries to answer pertinent clinical questions through basic science techniques.

Dr. Rakesh Arora – Delerium Post Surgery Laboratory

1. What is the disease/focus of your lab? We interested in the perooperative outcomes in the older adult with cardiovascular disease.

2. What subset of this disease? We study frailty (including cognition), delirium and mental health in the older adult with cardiovascular disease, primarily following cardiac surgery.

3. What type of research? Database outcomes, prospective cohort and clinical trials.

4. What projects:

Validating the 4AT screening tool for detection of delirium in post-cardiac surgery patients: At least 1 in 5 patients experience delirium following cardiac surgery in Manitoba, with 20-30% of incident delirium occurring for the first time on the postoperative ward. However, when patients were interviewed in a 1-year follow-up clinic, approximately 25% of patients categorized "non-delirious" by the Confusion Assessment Method (CAM) reported having symptoms consistent with delirium following their operation . This suggests that delirium was under-detected with our current screening method and that more sensitive methods are needed. Delirium is associated with increased mortality, long-term morbidity, and cognitive decline, therefore improved detection is crucial in the vulnerable cardiac patient. We are conducting a single centre prospective observational study using the 4 A's Test (4AT; see www.the4AT.com) as a screening tool for delirium on the postoperative ward (Cardiac Surgery Inpatient Unit). The 4AT is simple to administer, brief (<2 min), and requires no special training. We anticipate patient enrollment of up to ~250 over a 4-month period. Enrolled patients will undergo daily assessments using 4AT by a reference rater (BSc. Student), regular nurse CAM assessments, and a neuropsychiatic examination as a reference standard with the diagnosis of delirium made using DSM-5 criteria. Confidence intervals for sensitivity, specificity, positive predictive value, and negative predictive value will be calculated using a Clopper-Pearson methodology. We expect it to yield results of high sensitivity and specificity, with improved detection of delirium in the postoperative ward.

Impact of physical activity on depression after cardiac surgery (IPAD-CS): We have previously performed a prospective observational cohort analysis in 431 patients undergoing elective cardiac surgery (see. The Canadian Journal of Cardiology, 29(12), 1649–56; The Journal of Thoracic and Cardiovascular Surgery, 145(5), 1400–6). In these studies it was found that one-third of cardiac surgery patients have symptoms consistent with depression at time of hospital discharge. The IPAD-CS is

one of the largest clinical study of its kind and has been a highly accessed article at the Canadian Journal of Cardiology as well as been reference in the media and internet news blogs (i.e. the Huffington Post). We are currently examining the long-term impact of depression through data linkages with the Manitoba Centre of Health Policy. Importantly, the study that was originally attached with this project has return to complete a PhD on the PREHAB study.

The PREHAB study: In Canada, when a patient requires heart surgery, they are placed on a "waiting list" for as long as 2-4 months. Many patients on the waiting list experience feelings of powerlessness and are fearful of "making things worse", which cause them to stop being active. This is problematic for the already deconditioned frail, older adult patient. At present, there is no formal process for engaging frail older adult patients during this wait period. This wait period, therefore, presents a significant opportunity to optimize preoperative risk factors in these vulnerable patients. We have recently received funding from CIHR (budget: $620,000) for a study seeking to address this issue entitled: the PREHAB (Pre-operative REhabilitation for reduction of Hospitalization After coronary Bypass and valvular surgery) study (NCT02219815). I have the honour of acting as the Principal Applicant for this interdisciplinary model of care that seeks to maximize the physical, nutrition, psychological reserve and cardiac risk profile of "frail" older adult patients undergoing cardiac surgery (see: BMJ Open, 5(3), e007250–e007250). This trial is currently underway and is supporting both a MSc and PhD student at the University of Manitoba.

5. Anything else

The PI is a Co-Founder and President of the CANadian CARdiovascular critical carE (CANCARE) Society (see: www.cancaresociety.com) and the Past-President of the American Delirium Society (see: www.americandeliriumsociety.org)

Dr. Michael Czubryt, Molecular Pathophysiology Lab

1. What disease/condition is the focus of your lab? Cardiovascular disease.

2. Subset? Our primary focus is cardiac fibrosis, but we are interested in any fibrotic diseases, including perivascular and lung fibrosis.

3. What type of research does your lab carry out? We are a basic science laboratory, but maintain a focus on knowledge translation; as a result, we have been issued one patent on our work, with another about to issue and a third in process. We have also just started a collaboration with a clinical colleague (Dr. Jassal) to perform a non-invasive human study.

4. What projects are currently underway in your lab? We study a transcription factor called scleraxis, which we have shown is a key regulator of cardiac fibroblast phenotype and function. Our published data in isolated primary cells and in mice has shown that scleraxis induces fibroblast to myofibroblast conversion via direct transcriptional regulation of various key genes including fibrillary collagen type I, fibronectin, and a-smooth muscle actin. Conversely, loss of scleraxis expression or activity attenuates this conversion and blocks extracellular matrix synthesis. Scleraxis is over-expressed in the collagen-rich cardiac infarct scar, and in response to pressure overload. We demonstrated that common pro-fibrotic signaling pathways induce scleraxis expression, and performed the first analysis of scleraxis post-translational modifications. Our preliminary data has shown that scleraxis gene deletion attenuates pressure overload-induced cardiac fibrosis. This is important, since cardiac fibrosis is an independent and powerful risk factor for heart failure and arrhythmias in human patients, yet there are no medications currently approved for cardiac fibrosis. We are currently working with a European group to identify small molecule inhibitors of scleraxis which we hope to exploit as a first-in-man therapy.

   We are completing a related study showing a similar requirement for scleraxis in lung fibrosis, and will soon be investigating systemic sclerosis. We hypothesize that scleraxis is a key driver of fibrosis not only in the heart, but in multiple tissues throughout the body. Attenuation of scleraxis function may thus provide an avenue for treatment of multiple fibrotic diseases. <u>We will collaborate on fibrotic diseases in any tissue.</u>

5. Additional information: Our laboratory is proficient in molecular biology methods, including DNA/RNA/protein manipulation and mutagenesis, primary cell culture (cardiomyocytes, cardiac fibroblasts, vascular smooth muscle), luciferase reporter assay, electrophoretic mobility shift assay, chromatin immunoprecipitation assay (and re-ChIP), adenoviral gene delivery, and transgenic animal creation (including DOX-ON/OFF

and Cre/Lox systems). Key pieces of equipment in our lab include a Zeiss epifluorescence microscope with 3D deconvolution software, and an Affymetrix microarray system.

Dr. E. Kardami

1. LAB FOCUS: CARDIOVASCULAR DISEASE
2. DISEASE SUBSET: CARDIAC HYPERTROPHY, HEART FAILURE
3. TYPE OF RESEARCH: BASIC SCIENCE
4. CURRENT PROJECTS:
(a). Endogenous factors (FGF-2) affecting cardiac remodeling from hemodynamic or chemotherapy-drug-induced stress.
Cardiac tissue contains growth factors exported from cells (mainly fibroblasts) and acting locally on all cells within the heart. Amongst these, fibroblast growth factor-2 (FGF2), produced as high and low molecular weight isoforms (hmw, lmwFGF2), has both benign (cardioprotection, repair) and deleterious (hypertrophy, fibrosis) roles, as our lab has shown in *in vitro* studies. We are now using mouse models, engineered to express only hmwFGF2 or only lmwFGF2, to test the hypothesis that lmwFGF is primarily protective while hmw is, in the long term, deleterious. Our models are subjected to surgically induced hemodynamic stress producing hypertrophy and loss of function, assessed by echocardiography. In a parallel project, mice are exposed to doxorubicin (chemotherapy drug), which eventually causes heart failure. Cell culture models are used in parallel, to examine mechanisms activated by hmwFGF versus lmwFGF, to find new targets to prevent maladaptive heart remodeling.

(b). Studying the role of different cardiac mitochondrial populations in cardioprotection and protein quality control. Mitochondrial well-being is fundamental for the proper functioning of cardiomyocytes. There is currently strong interest in mechanisms maintaining mitochondrial health during stress, including mitophagy. We are investigating how different cardiac mitochondrial populations (subsarcolemmal-SSM) versus inter fibrillar (IFM) may be targeted by mitophagy. We are also examining the direct effect of cytoplasmic growth factors on cardiac mitochondrial ability to become protected from calcium overload and oxidative stress.

5. OTHER: our studies (project b) are applicable to brain degenerative diseases relating to mitochondrial damage.

Dr. Sanjiv Dhingra – Cardiac Regeneration and Tissue Engineering Lab

1. What disease/condition is the focus of your lab? Cardiovascular disease.

2. Upon what subset of this disease/condition do you focus? Cardiac stem cell therapy and tissue engineering.

3. What type of research does your lab carry out? Basic translational.

4. What projects are currently underway in your lab (250 word max)?
   My research program is directed toward following three themes:
   (1) Allogeneic stem cell therapy for cardiac regeneration: Allogeneic (un-related donor) mesenchymal stem cells from young and healthy donors have demonstrated potential to restore heart function following a cardiac injury. However, data from initial clinical trials indicate that transplanted cells provoke host immune response and are rejected in the heart. Therefore, current projects in my lab in this area are focused to study immunogenicity of allogeneic stem cells. We use pre-clinical rodent models to study mechanisms of transplanted stem cell rejection in the heart. Our long term goal is to develop clinically relevant strategies to prevent the rejection and enhance benefits of transplanted stem cells in the heart.
   (2) Synthesis and application of biomaterials for cardiac tissue engineering: My research program under this theme consists of several different projects focusing on synthesis and application of novel biomaterials for cardiac tissue engineering. Our key projects in this area are focused on 1.) Designing immunomodulatory hydrogels and scaffolds for stem cell delivery. 2.) Developing conductive polymers for cardiac tissue engineering.
   (3) To establish induced pluripotent stem cells (iPSC) based *in vitro* cardiac models: Our current projects in this area are focusing on the generation of *in vitro* cardiac tissue models for hereditary mitochondrial disorders involving cardiomyopathies. We collect blood from patients with rare mitochondrial diseases, reprogram blood cells to iPSC and differentiate iPSC to cardiomyocytes. Established in vitro models are being used to study disease mechanisms and perform drug screening studies.
5. Is there anything else important that we should know (in one sentence) about your research? I have had initial discussions with Dr. Rivka Ofir from Ben-Gurion University to start a collaborative study on iPSC based disease modeling and establish a Canada-Israel bio-bank to store iPS cells. Through this we want to reprogram and archive multiple iPSC lines to represent the genetic diversity and have comprehensively HLA-matched cells for cell therapy and novel drug testing.

Dr. Todd Duhamel – Physical Activity Lab

1. What disease/condition is the focus of your lab? Cardiovascular disease

2. Upon what subset of this disease/condition do you focus? Primary and secondary prevention of adverse cardiovascular events

3. What type of research does your lab carry out? (basic science or clinical trials or both): My research examines the role of physical activity for modifying cardiovascular disease processes. I am an exercise physiologist and have experience working with human participants as well as model systems (rodents and cells). My basic research examines the basic science of how exercise influences metabolic signaling and calcium transport in models of disease. My clinical research examines how physical fitness and frailty influence the development of cardiovascular diseases.

4. What projects are currently underway in your lab (250 word max)?
   - My team is leading the multi-site PREHAB randomized controlled trial (ClinicalTrials.gov Identifier: NCT02219815). This trial will determine if exercise "prehabilitation" prior to cardiac elective surgery will reduce post-operative hospital length of stay and post-surgical outcomes in older, frail adults.
   - My basic science lab utilizes exercise interventions to identify signaling pathways that protect the regulation of calcium-transport proteins in the diseased hearts of rodents and humans. We work with isolated cell models, rodents and human heart tissue removed and discarded as a normal part of surgery.
   - Our group is conducting the HAPPY Hearts study to screen for cardiovascular disease risk in a cohort of 1000 women. Projects have grown out of this work to examine: (1) health psychology; and, (2) health promotion interventions.
   - We recently developed a health promotion app to support people to reduce their sedentary behaviour and to increase physical activity levels. The next phase of this work will test the efficacy of the tool in populations with elevated cardiovascular disease risk.

5. Is there anything else important that we should know (in one sentence) about your research?
   - I enjoy collaborating with Clinician (e.g. cardiac surgeons, cardiologists, nurses, nephrologists and psychiatrists) and PhD (Physiologists, biochemists, health psychology) researchers. My research program also engages community partners to facilitate integrated knowledge translation.

Dr. Jeffrey Wigle – Molecular Cardiovascular Pathology Lab

1. What disease/condition is the focus of your lab?
   Cardiovascular disease

2. Upon what subset of this disease/condition do you focus?
   Cardiac fibrosis post- myocardial infarction
   Vascular and lymphatic function

3. What type of research does your lab carry out? (basic science or clinical trials or both)
   Basic Science

4. What projects are currently underway in your lab (250 word max)?
   A) We are investigating the potential of natural products such as resveratrol and cyandin-3-glucoside to preserve cardiac function and blunt cardiac fibrosis following a myocardial infarction. In this project, we are determining whether these polyphenolic compounds are capable of preserving heart function in a rat model of myocardial infarction (left anterior descending artery (LAD) ligation) as determined by echocardiography. We are analyzing the ventricles for alterations in reactive oxygen species, TGFβ signaling, collagen deposition and expression of myofibroblast markers.
   B) Following a myocardial infarction, resident fibroblasts in the heart become activated and convert into myofibroblasts, which actively deposit extracellular components particularly collagens. We are studying the transcriptional mechanisms that control this switch between a cardiac fibroblast and myofibroblast. We are looking at the role of two transcription factors- Meox2 and Zeb2. By understanding how this important checkpoint is controlled, we will be better able to block its activation and those reduce fibrosis in the areas of the heart that were not infarcted and thus preserve cardiac function.
   C) Adipocytes secrete hormones (adipokines) that regulate the function of the cardiovascular system. In contrast to many adipokines, Adiponectin secretion is decreased as adipocytes enlarge during obesity and adiponectin has beneficial cardiometabolic effects. We are studying how adiponectin is processed in the body and the mechanisms that underly the sex-dependent nature of its actions.

5. Is there anything else important that we should know (in one sentence) about your research?
   We have a longstanding interest in how transcription factors control the acquisition of cellular phenotypes.

Dr. Lorrie Kirshenbaum – Molecular Cardiology Lab

1. **What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc):** Cardiovascular disease

2. **Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc):** Ischemia/hypoxia-reoxygenation injury of myocardial infarction and heart failure. We also have studies directed toward understanding cell proliferation, regeneration and cancer metabolism.

3. **What type of research does your lab carry out? (basic science or clinical trials or both):** Basic research with a strong translational component through collaborations with clinicians within and outside our institution.

4. **What projects are currently underway in your lab (250 word max)?**
   We have several interrelated research projects in our laboratory that include:
   1) Understanding the cellular and molecular mechanisms underlying cell death in the heart and cancer. We study how the inducible death gene Bnip3 which is cloned by my laboratory, mediates mitochondrial injury, cell death and heart failure following myocardial infarction.
   2) We have ongoing studies that examine the role of mitochondrial dynamism and metabolism on mitophagy autophagy in cancer and cardiac cells.
   3) We have ongoing investigations to understand how the chemotherapeutic drug doxorubicin mediates cardiac dysfunction and heart failure.
   4) We have ongoing studies to examine the regulation of apoptosis, necrosis and autophagy in the pathogenesis of cancer.
   5) We have ongoing studies that address cardiac cell regeneration and cell cycle control and inflammatory processes after myocardial infarction and in response to cytokines.
   6) We have ongoing studies that examine how polyphenolic compounds modulate cell metabolism mitochondrial function and cell death during hypoxia and ischemic injury.

5. **Anything else?**
   The work carried out in my laboratory is internationally recognized and published in the highest quality of top ranked scientific journals. We have been pioneers and have contributed in a major and significant way toward understanding the role of cell death in heart disease and cancer. We look forward to expanding our research program through new collaborations with research investigators at BGH.

Dr. Pawan Singal – Oxidative Stress Laboratory

1. *What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc)?* Pathogenesis of Cardiovascular disease to understand heart failure for its prevention as well as better management.

2. *Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc)?* The role of the "vicious cycle of oxidative stress and inflammation" in the ischemic heart disease and heart failure.

3. *What type of research does your lab carry out? (basic science or clinical trials or both)?* Principally, we have a basic science approach but also have interest in patient studies which are carried out in collaboration with Dr. Davinder Jassal (Chief of Cardiology), where we examine the cardiotoxic effects of anti-cancer drugs both at the bench as well as in the clinics.

4. *What projects are currently underway in your lab (250 word max)?*
   We have two main projects on the go at this time: Role of cytokines in the activation of innate signaling to promote or to prevent apoptosis in cardiac dysfunction. In particular we examine the regulation of Toll-like receptors 2 and 4 in response to Interleukin-10 (IL-10), and tumor necrosis factor alpha (TNF-α) in global ischemia/reperfusion in isolated hears as well as cardiomyocytes; and we also study the cardiotoxic side effects of anticancer drugs (Doxorubicin, Trastuzumab, Sunitinib). For more information, please consult our review paper (Khaper, et. al.; Anti. Redox Signal. 13: 1033-1049, 2010) and couple of research papers (Ludke, et. al.; Am. J. Physiology. 303:645-653, 2012; Bagchi, et.al.; Cytokine 61: 304-314, 2013;

5. *Is there anything else important that we should know (in one sentence) about your research?*
   We have experience in international collaborations where we have had joint projects with the scientists in Mayo Clinic (USA), Heart Institute, Bratislava (Slovak Republic), Post–Graduate Institute, Chandigarh (India) and Physiology, Porto Alegre (Brazil). In any joint proposal with BGU, our hope would be to have at least one clinical laboratory with us from ICS and one or two laboratories from BGU participating in the proposed joint research.

Dr. Davinder Jassal – Cardiac Performance Lab

1. What disease/condition is the focus of your lab? Cardio-Oncology

2. Subset of this disease? Prevalence, early detection, and prevention of cardiotoxicity due to common anti-cancer drugs including Doxorubicin, Trastuzumab, Bevacizumab, and Sunitnib.

3. What type of research does your lab carry out? Translational research extending from the basic science to the clinical arena.

4. What projects are currently underway in your lab?

1. Cardio-Oncology: Breast Cancer and Heart failure

Breast cancer and cardiovascular disease are major public health concerns in Canada. The two diseases are intricately involved as treatment of one disease may lead to detrimental effects in the other. Although the current combination of surgical resection, radiotherapy, and chemotherapy may lead to remission in breast cancer patients, the administration of chemotherapeutic based agents, in particular Doxorubicin, are associated with an increased risk of cardiotoxicity. The introduction of novel monoclonal antibodies in breast cancer therapy which target growth factor receptors further compounds this issue of drug induced cardiac dysfunction. Trastuzumab (Herceptin), a humanized monoclonal antibody against the extracellular domain of the HER-2 protein, is used in both the adjuvant and metastatic settings of breast cancer. Despite its clear therapeutic benefits, cardiotoxicity is a major concern, especially when Trastuzumab is used in combination with anthracyclines. Although clinical trials have demonstrated that the risk of developing LV systolic dysfunction after receiving Trastuzumab is up to 10%, recent studies have shown an even higher risk of nearly 1 in 4 women developing this drug induced cardiomyopathy. An understanding of the potential mechanisms for the deleterious cardiac effects of HER-2 blockade may be beneficial in improving breast cancer therapy. Our current focus is to evaluate the cardioprotective effect of flaxseed against the drug-induced cardiotoxicity caused by Doxorubicin and Traztuzumab. The anticipated goal of our Cardio-Oncology research program is to improve overall morbidity and mortality in cancer patients treated with chemotherapy, while at the same time, preventing any detrimental side effects of these drugs on cardiac health.

2. ASICS (Avastin and Sutent Induced Cardiotoxicity Study)

Colorectal and kidney cancer are major public health concerns in North America, affecting both men and women equally. Although the current combination of surgery, radiation, and chemotherapy may lead to remission in this cancer population, the administration of chemotherapeutic drugs is associated with an increased risk of developing heart failure. While the recent addition of Bevacizumab (BVZ) and Sunitinib (SNT) may improve the long-term outcomes in individuals with colorectal and kidney cancers, these two drugs may also increase the risk of developing heart failure. We are currently

evaluating the use of RAS inhibitors (Aliskiren, Perindopril, or Valsartan) as prophylactic agents in the prevention of BVZ and SNT mediated cardiotoxicity.

5. Anything else? Our research program is multidisciplinary involving Basic Scientists, Clinicians in Cardiology and Oncology.

Dr Ross Feldman- Vascular Disease Laboratory

I. Disease: Vascular disease in women remains underappreciated, underdiagnosed and undertreated. The biological basis for the increased rate of rise in atherosclerosis risk and the increased rate of complications after revascularization in women after menopause remains very poorly understood.

II. Focus: Based on our recent studies examining the importance of the G protein linked estrogen receptor (GPER) as a regulator of i) blood pressure, ii) LDL cholesterol and iii) the response to vascular injury and our identification of a common GPER genetic variant that is hypofunctional we will now examine:
1. the importance of GPER in vascular smooth muscle phenotype switching between contractile and synthetic phenotypes and
2. the impact of carrying the hypofunctional GPER genetic variant in women as a predictor of the risk of complications following revascularization procedures.

III. Platforms: basic science and population research

IV. Current Research Programs:

1. Identification of novel GPER ligands. Following from our initial report in 2011, there have now multiple reports establishing the GPER-dependent effects of aldosterone in a range of cardiovascular models. However, related to the challenges inherent in performing radioligand binding using lipophilic ligands and the low cellular content of GPER in mammalian cells the biophysical characterization of GPER ligand interactions has lagged behind our understanding of the receptor's actions at a functional level. Based on our extensive background in radioligand binding techniques we are developing an SF9/baculovirus model of GPER expression with which to examine ligand-GPER-G protein interactions for aldosterone and a range of novel ligands suggested to interact with GPER.

2. Mechanisms of GPER regulation of LDL metabolism. Based on our recent report of the effects of GPER to regulate LDL receptor expression via regulation of PCSK9 expression, we are determining the receptor specificity (ER vs. GPER) of estrogen's effects on LDL receptor metabolism in HepG2 cells and human hepatocytes. Studies to date have uncovered novel mechanisms of effect of GPER activation on LDL receptor, PCSK9 as well as SREBP1 and SREBP2 expression.

3. Role of aldosterone in regulation of growth and spread of ovarian and prostate cancer. Based on our recent demonstration of the *in vitro* and *in vivo* effects of aldosterone in regulation of renal cell cancer metastases we are now examining those effects in ovarian and prostate cancer. *In vitro* we will assess indices of invasiveness, proliferation and apoptosis. *In vivo* we will examine aldosterone-mediated regulation of metastatic spread using implantation models in mice.

Ian Dixon – Molecular Cardiology Lab (ICS)

1.What disease/condition is the focus of your lab?:Cardiac fibrosis and heart failure after heart attack.

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc):
We are interested in cardiac fibrosis that occurs after heart attack or myocardial infarction (MI).

3. What type of research does your lab carry out? Basic science

4.What projects are currently underway in your lab (250 word max)?

The work carried out by the members of the lab addresses the signaling pathways responsible for cardiac fibrosis. Cardiac fibrosis is a primary contributor to heart failure. In many types of heart disease, cardiac fibrosis "sneaks up" on the myocardium and stiffens the heart so that relaxation becomes flawed, leading to problems in heart ventricle filling following contraction. Reduced filling equates to heart failure with preserved ejection fraction (HFpEF) in fibrosed hearts, and may slip through normal methods of detection (M-mode echocardiography). **In this context, we study the cell biology of cardiac myofibroblasts.** Myofibroblasts are activated fibroblasts, and play a large role in contributing to cardiac fibrosis. Myofibroblasts are not normally found in healthy heart muscle, but are very common in diseased and failing hearts of various etiologies.
To summarize, we investigate cellular control of myofibroblast phenotype and function (migration, activation, contraction) as these functions all contribute to wound healing and remodeling of extracellular matrix in diseased hearts.
Our group is interested in determining why natural inhibitors of wound healing undergo drastically reduced expression in injured or failing hearts. Our laboratory is known for its work on two such proteins, Smad7 and Ski. The expression of these naturally occurring fibrosis-inhibiting proteins are tightly regulated in cardiac wound healing, especially after myocardial infarction. Adapting their function with development of a new drug and applying it to failing hearts may allow us to alter the course of the progression of heart disease. Other than Smads and Smad repressors such as Ski and Sno, pathways of interest to us include the Hippo pathway effectors such as YAP1 and WWTR1 (eg, TAZ).
As cardiac myofibroblasts numbers are elevated in heart disease, we want to determine cellular control points for fibroblast cell death and viability. In this context, we are investigating mechanisms that trigger autophagy and apoptosis in these cells, which ultimately may control their numbers in the myocardium, and possibly regulate the rate of cardiac fibrosis. We have published that autophagy may be involved in non-apoptotic roles in these cells, including activation of myofibroblasts.

5.Is there anything else important that we should know (in one sentence) about your research?

Cardiac matrix is complex. Thus we are interested not only in fibrillar collagen isoform expression, but also on the regulatory points for collagen synthesis, as well as other key matrix proteins such as fibronectin and proteoglycans. We also have expertise in MMP function in failing hearts. Second, we are willing to expand our experimental models to hypertension or diabetes. Finally, we are interested in developing 3D culture methods of fibroblasts and myocytes eg, Biowire or microfluidics to more closely model fibrosis in vitro.

Nutraceutical and Functional Food Research

Dr. Michel Aliani –Metabolomics Lab

1. What disease/condition is the focus of your lab? My focus is to develop foods that can be designed for populations with pre-diabetics and diabetics. I also examine cardiovascular disease samples.

2. Upon what subset of this disease/condition do you focus? We create low glycemic index foods using dairy products as vehicles fortified with berry powders designed for pre-diabetics. We also examine tissue samples for cancer and cardiovascular disease.

3. What type of research does your lab carry out? (basic science or clinical trials or both): Both basic science and clinical trials. Creation of functional foods, sensory studies of the final foods destined to clinical trials, full characterization of food samples and metabolomics studies of biological fluids and tissues in post-prandial and/or clinical studies. Mass-spectrometry and NMR-based Metabolomics is the focus of my research activities. The application of metabolomics to foods and biological fluids collected from animal and human studies will provide valuable information to understand the effect of diet and nutrients on metabolism. As such, our Agri-Health metabolomics laboratory is currently collaborating with several research teams within Canadian and American universities. We also have extensive collaboration with food industries with international reputation (eg. Maple Leaf; Warburton's).

4. What projects are currently underway in your lab (250 word max)? Many projects are currently underway including:

1) Application of metabolomics as an effective tool to investigate the health benefits of pulses (lentils, beans, peas), flaxseed and dairy products fortified with berry powders in animal models and/or population with PAD, hypertension, obesity and diabetes.
2) Metabolomics studies of biological samples (Plasma, sputum and exhaled condensate breath) from lung cancer patients
3) Metabolomics studies of asthma using rat models
4) A recent collaboration with the biggest bread company in UK (Warburton's) to develop healthy breads with selected pulses and to create the most comprehensive database related to pulses using our metabolomics platform
5) Collaboration with industry to improve meat flavor in meat products.

Dr. Harold Aukema - Oxylipin Laboratory

1. What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc): Our work on bioactive lipids has mostly been applied to kidney health and disease, but bioactive lipids are relevant to all diseases/conditions (e.g. our work on inflammation in obesity).

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc): The renal disease that we focus on most is the cystic kidney diseases such as polycystic kidney disease (PKD) and nephronophthesis (NPHP).

3. What type of research does your lab carry out? (basic science or clinical trials or both): Basic science and clinical trials

4. What projects are currently underway in your lab (250 word max)?
   Our lab is interested in nutritional and disease effects on bioactive lipids. In particular our focus is on oxylipins, which are oxygenated fatty acid metabolites such as prostaglandins, leukotrienes, protectins, resolvins and many more. These bioactive lipids are involved in the regulation of inflammation, blood flow, proliferation, reproduction, blood clotting, sleep, reproduction and many more physiological processes. See our recent invited review for more information: Gabbs et al, Adv Nutr 6:513-540, 2015; doi:10.3945/an.114.007732.
   Using a targetted lipidomics approach we are currently examining the effects of dietary fatty acids on oxylipin s in rat and mouse tissues. This work is relevant to recommendations for dietary fatty acids. We are also examining the role of oxylipins in inflammation in obesity in human trials, as well as using adipocyte, monocyte and endothelial cell culture to examine the mechanisms and associated signaling pathways involved. We are also undertaking studies on the role of oxylipins in the effects of dietary protein level and source in normal and diseased kidneys. The studies in normal kidneys are relevant to recommendations for dietary protein. Our work in diseased kidneys has shown that oxylipin alterations are present in cystic kidney diseases and that diet and drug approaches to treat these alterations are effective in slowing disease progression. Our work on this is continuing, as we examine other diet and drug approaches and their mechanisms of action. We also are involved in collaborations on the roles of oxylipins in fatty liver disease and in polycystic liver disease.

5. Is there anything else important that we should know (in one sentence) about your research? Our targetted lipidomics approach utilizing LC/MS/MS enables us to simultaneously quantify over 150 oxylipins.

Dr. Thomas Netticadan; Dr. Shelley Zieroth - Heart Failure Research Lab

OVERALL OBJECTIVE: To examine the cardioprotective effects of food-derived bioactive compounds.

BASIC RESEARCH

Project 1: Studying the standalone and combinatorial effects of a grape/berry polyphenol, resveratrol, and an ACE inhibitor, perindopril, on heart structure and function in an experimental model of myocardial infarction – the coronary artery ligated rat.

Project 2: Examining the effects of a berry polyphenol cyanidin glucoside on heart structure and function in the coronary artery ligated rat.

Project 3: Studying the effects of an oat polyphenol avenanthramide on heart structure and function in an animal model of hypertension – the spontaneously hypertensive rat.

Echocardiographic examinations are performed. The signalling pathways and target molecules underlying cardiac abnormalities in the infarcted/hypertensive heart, and the impact of test interventions, are being examined by biochemical analysis. Adult rat cardiomyocytes exposed to norepinephrine are used as an *in vitro* cell culture model of heart disease to further understand the mechanisms underlying effects of the test interventions.

REPRESENTATIVE PUBLICATIONS

a) Raj P et al. Resveratrol is equipotent to perindopril in attenuating post-infarct cardiac remodeling and contractile dysfunction in rats. *J Nutr Biochem*. 2016;28:155-63.

b) Louis XL, et al. Treatment with low-dose resveratrol reverses cardiac impairment in obese prone but not in obese resistant rats. *J Nutr Biochem*. 2012;23(9):1163-9.

CLINICAL RESEARCH

Project 1: We are examining the effects of resveratrol on heart function in patients with symptomatic heart failure in a randomized double blinded placebo controlled human clinical trial. Echocardiography and biochemical analysis are being performed. Dr. Amrit Malik is a co-investigator.

ClinicalTrials.gov Identifier: NCT01914081

5. Is there anything else important that we should know (in one sentence) about your research?

Our goal is to translate research findings on food-derived bioactive compounds from the bench to the bedside.

Dr. Carla Taylor & Dr. Peter Zahradka –Nutritional Research

1. Disease/condition: Obesity, cardiovascular disease, diabetes

2. Subsets of the disease/condition: Obesity, metabolic syndrome, pre-symptomatic atherosclerotic disease, type 2 diabetes

3. Type of research: Clinical trials (including nutritional interventions) and basic science research

4. Projects currently underway: The overall goal of our group is to identify nutritional interventions and dietary components capable of mitigating the adverse effects of metabolic and vascular dysfunction in the context of obesity, cardiovascular disease and diabetes.
   Clinical research studies focus on the following:
   i) Diet interventions with pulses (beans, peas, lentils, chickpeas): We have shown that consumption of ½ cup mixed pulses for 8 weeks improved the blood flow to the legs in individuals with peripheral artery disease. Ongoing studies are delineating the effects of the different pulse types on blood pressure, arterial stiffness, lipidemia, glycemic control, etc. in the disease conditions indicated above (#2). We have a suite of instruments for non-invasively assessing vascular health (arterial stiffness, endothelial dysfunction) and have a DEXA for determining body composition.
   ii) Effects of type of fat (eg omega-3) on inflammation and immune function: These studies are determining sex differences and effect of obesity-mediated inflammation.
   iii) Defining relationships between arterial stiffness and traditional risk factors for cardiovascular disease
   Basic sciences (each of these complements clinical research except item iv):
   i) Reversal of arterial remodeling by pulses (lentils, beans) in an animal model of hypertension and arterial stiffness
   ii) Modulation of adipocyte dysfunction, inflammation, and macrophage polarization by dietary factors
   iii) Mechanisms by which omega-3 fatty acids modulate endothelial function
   iv) Role of adiponectin in relation to metabolic disease; effects of adiponectin on vascular health

5. We are a multi-disciplinary team capable of translating the findings from cell culture and animal models to clinical studies.

Dr. Hope Anderson - **Vascular Pathophysiology Lab**

What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc.) Cardiovascular disease

1. *Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc.)* Hypertension; Cardiac hypertrophy; Microvascular disease

2. *What type of research does your lab carry out? (basic science or clinical trials or both) B*asic science

3. *What projects are currently underway in your lab (250 word max)?*
   - A significant interest of the lab is *novel signaling mechanisms that underlie cardiac hypertrophy*. One example is our focus on the endocannabinoid system. Having discovered that activated cannabinoid receptors stimulate anti-hypertrophic signaling and protect cardiomyocyte mitochondria, we are pursuing strategies (i.e. drug development) to manipulate the endocannabinoid system in a therapeutically-viable manner.
   - We are interested in the *role of resistance arteries in hypertension*. Blood pressure is influenced by peripheral resistance to blood flow, and resistance increases as the arterial lumen diameter narrows (whether by structural, functional, and/or mechanical mechanisms). An important therapeutic aim, for which we are testing *nutritional interventions*, is to prevent this narrowing. We reported the microvascular (and cardiac) effects of resveratrol, a stilbenoid polyphenol, but resveratrol exhibits low oral bioavailability and a short half-life. Thus, we are investigating stilbenoid compounds with improved bioavailability (i.e. pterostilbene, a dimethylated analog of resveratrol) or a history of medicinal use (i.e. gnetol). We assessed their cardiovascular effects in the spontaneously hypertensive heart failure rat and are now interrogating the signaling mediators involved.
   - Our newest project is predicated on our *hypothesis* that *aberrations of brain-penetrating arterioles contribute to cerebral vascular insufficiency in the context of cardiovascular disease, and that this potentiates the risk of cognitive decline and dementia during heart failure*. We are characterizing these aberrations using a combination of pressure myography and multi-photon laser scanning microscopy in isolated arteries and brain slices. We are also exposing co-cultured cerebral and vascular cells to mechanical strain and assessing signaling effectors by biochemical assays.

4. *Is there anything else important that we should know (in one sentence) about your research?*

- To achieve our research objectives, our laboratory uses – (i), models of escalating complexity ranging from cultured heart muscle and vascular cells, to isolated hearts and arteries, to hearts and arteries in vivo; (ii), a repertoire of experimental approaches such as pressure myography, echocardiography, multi-photon laser scanning microscopy, cytomechanics, bioenergetic analyses, metabolomics, and so on; and (iii), the expertise of valuable collaborators world-wide to implement these methodologies and research endeavors.

Dr. Heather Blewett – Human Nutrition and Immunology lab

1. What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc):
My lab has projects focused on immune function, diabetes, obesity and cardiovascular disease.

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease, etc):
My focus is on T-cell activation, reduction in postprandial glucose response, increased satiety and LDL cholesterol lowering.

3. What type of research does your lab carry out? (basic science or clinical trials or both):
My lab has research projects in both the basic science area and clinical trials.

4. What projects are currently underway in your lab (250 word max)?

I have several projects currently underway aimed at filling the gaps in the scientific literature that are necessary to substantiate the following food health claims for the following crops:

- Postprandial glucose reduction: peas, barley, Saskatoon berry
- Satiety: peas, barley, buckwheat, pinto beans
- LDL cholesterol lowering: flax

I am a team member of the Manitoba Personalized Lifestyle Research (TMPLR) project, whose overall objective is to bring together an interdisciplinary team to implement a cross-sectional study to identify the complex interactions that exist between lifestyle, genetics, and gut microbiota and explore how these relate to risk factors for chronic conditions in Manitoba. My focus is on immune function and how its dysregulation is related to lifestyle factors, genetics and gut microbiota. Please visit www.tmplr.ca for more information.

I also have projects that are investigating the effect of polyphenols extracted from berries on T-cell activation in animal models of hypertension and myocardial infarction.

5. Is there anything else important that we should know (in one sentence) about your research?
My lab has been collaborating extensively and successfully with Dr. Michel Aliani to also include metabolomics in all clinical trials we have been working on (Saskatoon berry, peas and flax) and Dr. Thomas Netticadan for his expertise in animal models of cardiovascular disease.

Dr. Karmin O - Renal Physiology Lab

1. What disease/condition is the focus of your lab? (i.e. cardiovascular disease, etc): Nutritional interventions and cardiovascular disease

2. Upon what subset of this disease/condition do you focus? (i.e. ischemic heart disease)

(1) Non-alcoholic fatty liver disease (NAFLD)
(2) Hyperhomocysteinemia
(3) Kidney ischemia-reperfusion (IR) injury and distant organ dysfunction

3. What type of research does your lab carry out? (basic science or clinical trials or both): Basic science (clinical trials in collaboration with others)

4. What projects are currently underway in your lab (250 word max)?

Project 1 High energy diet-induced non-alcoholic fatty liver disease (NAFLD associated with obesity and diabetes) in the C57/6J mouse model. The incidence of NAFLD and obesity has grown dramatically worldwide. In Western society, about 30% of the adult population exhibits NAFLD with the incidence increasing to 70-90% in obese and type 2 diabetes patients. If untreated, NAFLD may further progress to cirrhosis, liver failure and cancer. NAFLD patients often died of cardiovascular incidence. We are conducting mechanistic studies into (1) regulation of AMPK signaling pathway, hepatic lipid metabolism, oxidative stress (homocysteine - hydrogen sulfide – glutathione) and inflammatory response; (2) use of agricultural products (i.e. folate, tyrosol, berberine, berries, phenolic compounds) to improve hepatic metabolism and gut health, and to mitigate NAFLD associated abnormalities in the cardiovascular system.

Project 2 Ischemia-reperfusion induced renal and distant organ injury in the SD rat model. Our research is focused on identifying (1) the mechanisms underlying renal and distant organ injury (liver, heart, endothelia function) upon kidney ischemia-reperfusion injury; (2) the beneficial effects of nutraceuticals and herbal medicine; (3) clinical implication of homocysteine-hydrogen sulfide-glutathione imbalance in patients with renal disease. Feasibility: Animal models, cell culture (hepatocyte, macrophage, vascular endothelial cell and smooth muscle cell, cardiomyocyte, kidney tubular cell, gut epithelial cell) and techniques (biochemical and histological analysis, cell and molecular biology) are established in my lab.

5. Is there anything else important that we should know about your research?

We are also actively conducting research on oxidative stress, inflammation and gut health in livestock and poultry.