The Kidney Foundation of Canada Research Awards

2017 Awardees and Lay Summaries

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ALPORT SYNDROME FOUNDATION GRANT

Dr. Alessia Fornoni

University of Miami



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Alport Syndrome

Targeting podocyte lipotoxicity in Alport Syndrome.

Lay Summary:

Alport Syndrome (AS) is a hereditary disease of glomerular basement membranes (GBM) linked to mutations in genes coding for different chains of collagen type IV. Although the GBM is primarily composed of laminin and Collagen type IV, the de novo production of the α1 chain of collagen type I (Col I) has been observed in experimental models of AS.

Discoidin domain receptor 1 (DDR1) is a unique receptor tyrosine kinase that is activated by extracellular matrix but that can also be activated by collagen. DDR1 deletion in Col4a3 knockout (KO) mice, a mouse model for AS, improves survival and renal function. Podocytes and their proper interaction with the GBM are crucial to maintain the permeability of the glomerular filtration barrier. Our in vitro and in vivo preliminary data indicate that DDR1 can be activated by collagen I in human podocytes. Furthermore, we demonstrate that Col I-induced or genetic activation of DDR1 causes cellular lipotoxicity, a phenomenon that we recently demonstrated to be a key determinant of podocyte injury in other glomerular diseases. In particular, we show that the uptake of free fatty acids (FFAs) is increased in Col I treated podocytes and requires the activation of DDR1 which will ultimately lead to intracellular lipid accumulation due to increased fatty acid (FA) uptake. This phenomenon is also reflected in Col4a3 KO mice, where increased DDR1 activity in kidney cortexes correlates with blood urine nitrogen (BUN) and is associated with increased lipid deposition and increased expression of scavenger receptor B, cluster of differentiation 36 (CD36), a protein involved in FA uptake, cholesterol absorption and activation of inflammatory pathways. Studies by others have shown that CD36 activation can be blocked by the clinically available compound Ezetimibe. The goal of this proposal is to demonstrate a novel mechanism of podocyte lipotoxicity in AS that is amenable to therapeutic intervention through a repurposing strategy of Ezetimibe.

We will test the novel hypothesis that DDR1-induced podocyte injury in AS requires CD36 dependent fatty acid and cholesterol uptake and that inhibition of CD36-dependent lipotoxicity with Ezetimibe can prevent the progression of kidney disease in Alport Syndrome.

We will address this hypothesis using a combined in vitro and in vivo approach to investigate the role of DDR1 in lipid induced podocyte damage and to determine if CD36 inhibition can prevent intracellular lipid accumulation and podocyte injury in Col4a3 KO mice. If our hypothesis is confirmed, repurposing strategies for the use of Ezetimibe to treat patients with AS should be fast and safe, as Ezetimibe is an already FDA-approved drug currently labeled for the treatment of patients with hypercholesterolemia.

Biography:

Dr. Fornoni is tenured Professor of Medicine and Molecular and Cellular Pharmacology at the University of Miami Miller School of Medicine. She is the Chief of the Division of Nephrology and Hypertension and serves as Director and Chair of the Peggy and Harold Katz Drug Discovery Center. She is also the Associate Director of the MD PhD program. In 2013 Dr. Fornoni gained experience in drug development as Global Head of Discovery in Cardiovascular and Metabolism at Hoffman-La Roche in Basel. She is currently the Vice-President and Chief Scientific Officer of L&F Health LLC, a small start-up company focused on finding a cure for patients affected by chronic kidney diseases.

As a physician-scientist who has maintained a resolutely focused research program that has provided novel and seminal contributions to our understanding of the pathogenesis of kidney disease, her research has been supported by grants from National Institutes of Health, industry and private foundations. She has received prestigious awards, she is a member of ASCI, she serves on the editorial board of Diabetes and Kidney International, she was visiting professor at more than 50 academic institutions and international meetings worldwide. She serves as grant reviewer for NIH, DOD, ADA, AHA, UK-diabetes and the Italian Ministry of Health. Her contributions have been published in high impact journals: Journal of Clinical Investigation, NEJM, Nature Medicine, Science Translational Medicine, Journal of Biological Chemistry, Diabetes among others. She successfully trained several graduate students and post-doctoral fellows, further supporting her accomplishments, dedication and perseverance, and more importantly her unstinted commitment as a physician-scientist.

Moving forward, her vision is one that brings industry, investors and not for profit organizations around the table with the intent to match science with innovation and patients' motivation to find a cure for kidney diseases.

Dr. Constantinos Deltas

University of Cyprus



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Alport Syndrome

Repurposing of FDA approved chemical chaperones to the rescue of a mouse model of Alport Syndrome

Lay Abstract:

The mutations inherited by about 40-50% of patients with Alport syndrome lead to defective collagen IV genes and abnormal folding and breakdown of the protein before it gets to the basement membrane. The basement membranes are important structures of the kidney that serve a key role in blood filtration. Additionally, the misfolded collagen molecules also elicit an abnormal intracellular phenotype, triggering the hyper-activation of a related signalling cascade.

This research project aims to use small synthetic molecules, called PBA and TUDCA, as medicines to help improve the three-dimensional folding of the mutated collagen molecules and to promote its effective trafficking to the basement membrane outside the cells. These medicines will be used to treat a mouse model of Alport syndrome that the researchers prepared and are studying in Cyprus. The effective secretion of collagen IV molecules in the extracellular basement membrane, even if they have a missense mutation, is hypothesized to improve the three-dimensional network and the long-term outcome of kidney disease. Importantly, the medicines to administer to the mice have been approved by the FDA for use in other human conditions; thus, repurposing them may save time in proving their safe and efficacious application.

Biography:

Professor Deltas graduated in 1982 from the National and Kapodistrian University of Athens with a degree in Pharmaceutics. He then earned a PhD degree in Biochemistry, from Rutgers University, The State University of New Jersey, USA in January 1988. His PhD Mentor was Prof. Darwin J. Prockop, a well renowned scientist in connective tissue research. After a few more years in the USA, having worked at the Jefferson Institute of Molecular Medicine and at Duke University Medical Center, in 1991 he was offered a job at the newly established Cyprus Institute of Neurology and Genetics, in his home country, Cyprus. He was always fascinated by the DNA world and he was one of very few who first developed molecular medical diagnostics and genetics research in the Greek world, with emphasis on inherited kidney disorders. His work was instrumental in several

related fields. He was involved in the mapping and cloning of the PKD2 gene; his group mapped the first gene for medullar cystic kidney disease (MCKD1 or MUC1) and has had major contribution in promoting the concept that familial “benign” hematuria is not always benign, associating hereditary forms of focal and segmental glomerulosclerosis and hematurias, with collagen IV mutations. His group showed for the first time a putative role of the unfolded protein response signaling cascade in Alport Syndrome and developed the first knock-in mouse model for Alport Syndrome. They are going to use these mice for a pre-clinical study of FDA approved chaperones with funding by the Alport Syndrome Foundation (ASF, USA), The Kidney Foundation of Canada and the Pedersen family.

ALLIED HEALTH RESEARCH GRANTS

Dr. Dayna Lee-Baggley

Nova Scotia Health Authority



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Dialysis

Predicting and reducing non-adherence in kidney disease: validating a novel clinical tool

Lay Abstract:

Regularly attending prescribed dialysis is a key health behaviour that can improve the health of individuals living with kidney disease. Attending dialysis is both a lifesaving and a difficult health behaviour for individuals with kidney disease. The proposed study aims to improve the lives of people affected by kidney disease by studying an innovative clinical tool which may help improve attendance (i.e., reduce "no-shows") for dialysis treatment.

No-shows or non-adherence can be understood by assessing a patient's readiness to engage in the recommended health behaviour. However, current means of assessing readiness are cumbersome or too long to use in a clinical context. In the proposed study we present a novel means of assessing the likelihood of no-shows called the Traffic Light Assessment. The Traffic Light Assessment is a 4-question interview that allows a healthcare provider to capture whether a patient is ready (i.e., green light), on the fence (i.e., yellow light), or not ready (i.e., red light) to attend dialysis.

In order to test if the Traffic Light Assessment can predict whether a patient will attend dialysis, each participant will participate in a Traffic Light Assessment with a trained research assistant the day before their prescribed dialysis treatment for the upcoming week. Their attendance at dialysis will be tracked through their hospital charts. The research assistant will also contact the participant at the end of the week to learn more about anything that may have affected their attendance during the week and the impact of the Traffic Light Assessment on the participant's behaviour. To test the longer-term impact of the Traffic Light Assessment, we will examine attendance rates for the participant for 3 months prior to the Traffic Light Assessment and for 3

month and 6 months after the Traffic Light Assessment. These rates will be compared to rates for patients who have not yet received the Traffic Light Assessment.

Consistent with the mission of the Kidney Foundation of Canada to promote education and access to high quality healthcare, the results of this study will be shared with healthcare providers and will help to improve attendance for dialysis, thereby reducing wasted time due to no-shows or expensive emergency services and improving access for those who need dialysis. In testing an innovative clinical tool designed to predict and reduce no-shows for dialysis, this project has a high potential to directly impact the health and well-being of individuals living with kidney disease.

Biography:

Dr. Dayna Lee-Baggley is a Registered Clinical Psychologist. She obtained her master's and Ph.D. in Clinical Psychology with an emphasis in health psychology from the University of British Columbia. She is a Clinical Health Psychologist at the Nova Scotia Health Authority (NSHA) for the Multi Organ Transplant Program, which provides liver, kidney, and pancreas transplants to Atlantic Canadians. She is also a Core Faculty of the Behaviour Change Institute (NSHA). She holds an Assistant Professor appointment in the Department of Family Medicine at Dalhousie University and an Adjunct Professor appointment in the Department of Industrial and Organizational Psychology at Saint Mary's University. She is the president of the Atlantic Chapter of the Association for Contextual Behavioral Science and the vice-chair of the Halifax Chapter of the Canadian Obesity Network. Her areas of expertise include self-management of chronic disease, facilitating health behavior change, managing and treating obesity, and professional resiliency for healthcare providers. She provides training to healthcare providers in behaviour change skills for chronic disease management. She has an active research program on behavior change, chronic disease self-management, obesity, and Acceptance and Commitment Therapy. In the last 5 years she has presented over 45 workshops and presentations to more than 2,500 healthcare providers, researchers, and members of the public. Dr. Lee-Baggley has been funded by local, provincial, and national research granting agencies. She has over 35 peer-reviewed publications and over 110 scholarly presentations.

Dr. Marisa Battistella

University Health Network

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$99,500	Dialysis; Quality of Life



Targeted deprescribing in patients on hemodialysis to reduce polypharmacy

Lay Abstract:

Polypharmacy has been associated with an increased risk of non-adherence to medication regimens, adverse drug events, falls, hospital admissions and mortality. Patients with end stage renal disease on hemodialysis (HD) are exposed to polypharmacy by taking on average 12 medications per day. Deprescribing tools have been developed to reduce polypharmacy and have been successful in the elderly population, but these tools have not been applied directly to the CKD population. Furthermore, many medications currently used in HD patients lack the high-quality evidence for efficacy and safety seen in the general population and the role of these medications in HD patients is often not known.

The aim of this initiative is to develop tools to guide the re-assessment and deprescribing of specific medications that lack evidence for efficacy and safety in HD patients and to determine the effectiveness of these tools in reducing polypharmacy. Through a review of the literature and discussion with stakeholders within the care team, medication classes fitting the criteria of poor evidence for efficacy and evidence of patient safety concerns in the HD population will be identified. Using the available evidence, medication specific algorithms will be developed and validated to guide re-assessment and potential deprescribing of these medications in HD patients. This initiative will be the development of national consensus driven medication deprescribing algorithms that will be implemented in clinical practice for hemodialysis units across Canada.

Biography:

Marisa graduated from the Faculty of Pharmacy at the University of Toronto in 1998 and completed her pharmacy residency at Sunnybrook and Women's Health Sciences Centre in 1999. She has worked at the University Health Network since 1999 in various positions, including cardiology and internal medicine. In 2002, Marisa completed her Pharm D thru Idaho State University. She has worked as a clinical pharmacist specialist in the hemodialysis unit at the University Health Network since 2002. Marisa has published several papers and given many presentations on drug therapy in the area of nephrology. Marisa also maintains an active teaching involvement, with the University of Toronto, Leslie Dan Faculty of Pharmacy.

As a Clinician Scientist in Pharmacy at the University Health Network and the Leslie Dan Faculty of, Marisa maintains an active teaching role and focuses much of her time on clinical research in the area of nephrology. Marisa was also the Chair and education coordinator to the Renal Pharmacists Network (RPN), a national organization for renal pharmacists and currently is the external liaison co-ordinator for the RPN.

BIOMEDICAL RESEARCH GRANTS

Dr. Andras Kapus

St. Michael's Hospital



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Kidney Biology

Mechanotransduction pathways and fibrogenic reprogramming

Lay Abstract:

Chronic kidney disease (CKD) is a major health problem, which is often called an "epidemic" as it affects 12% of the population. In Canada 2.6 million people suffer from or are at risk for CKD, which most often develops because of common conditions such as diabetes and hypertension. In children the leading cause of CKD is the obstruction of the free flow of the urine due to various developmental defects. Unfortunately, we have no cure for CKD, which usually progresses toward chronic kidney scarring (called fibrosis). This process destroys the kidney architecture and function, necessitating dialysis or transplantation as the only means to prolong life. These "solutions" are associated with profound human suffering, are extremely expensive (e.g. dialysis costs more than $80,000/patient/year and there are over 23,000 dialyzed patients in Canada) and require lifelong medication, putting a huge burden on the patients and society alike.

Therefore, there is a dire need to understand the cellular and molecular basis of kidney fibrosis, since without this knowledge we cannot hope to reverse the disease process and restore function. Previous research from our lab and others has uncovered that in addition to certain chemical mediators, mechanical stress (such as increased fluid pressure, stretch or tissue stiffness) are critical triggers of the development of fibrosis. Such stress leads to transport of certain proteins (so called transcription factors) into the nucleus of kidney epithelial cells and modifies the activity of genes. Ultimately this leads to the release of fibrosis-provoking compounds (cytokines), which induce scarring. Currently we do not understand how mechanical stress is sensed by kidney cells, and how this input leads to the reprogramming of genes. Here we propose to study the mechanisms that link the stress sensor molecules to the activation of mechanically regulated gene-modifying transcription factors in the nucleus. Specifically, we hypothesize that a certain ion channel, called TRPV4 regulates the activation of

mechanically sensitive, recently discovered transcription factors (MRTF, TAZ, YAP). To test this hypothesis, we will employ a variety of cell and molecular biology techniques and animal models.

Identification of this mechanism has huge clinical relevance because TRPV4 can be inhibited by specific drugs, and such compounds (currently tested in humans for other conditions) might be efficient means to lessen or halt kidney fibrosis.

Biography:

Dr. Kapus obtained his MD (1986) and PhD (1990) in cell physiology at the Semmelweis University, Budapest Hungary. He was postdoctoral fellow at the Division of Cell Biology in the Hospital for Sick Children (1992-1995) in Toronto and was then recruited as a basic scientist to the Toronto General Hospital Research Institute and Dept. Surgery in 1997. He was a Medical Research Council of Canada Scholar (1999-2004). Since 2005 he works at the St. Michael's Hospital/Keenan Research Centre (KRC) for Biomedical Research. He is a full professor (Dept. Surgery and Dept. Biochemistry) and the Associate Vice Chair of Research, Department of Surgery, at the University of Toronto, Head of Research Training Centre and Director of the Critical Care/Trauma/Inflammation Research Platform at KRC.

His research area is basic cell (patho)physiology and cell biology, specifically cellular stress signaling, volume and pH regulation, cytoskeleton remodeling and the role of the cytoskeleton in gene expression, epithelial-mesenchymal transition, and cell plasticity. He explores molecular mechanisms whereby the cytoskeleton regulates nuclear traffic of transcription factors and thereby cell fate and phenotype. This has strong relevance to his current major focus: the pathobiology organ (kidney) fibrosis.

He has published more than 145 peer-reviewed papers, (H-index: 54), and has been continuously supported by the Canadian Institutes of Health Research (CIHR), The Kidney Foundation of Canada and the National Sciences and Engineering Research Council of Canada (NSERC). He has been involved in the graduate training of >50 students. He was the recipient of the Elsie Winifred Crann Memorial Trust Award for Medical Research, of a Medical Research Council of Canada scholarship, and also received the Premier’s Research Excellence Award, the Mel Silverman Mentorship Award and the James Waddell Mentorship Award.

Dr. Andrew Advani

St. Michael's Hospital



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Kidney Biology

Epigenetics of focal segmental glomerulosclerosis

Lay Abstract:

Focal segmental glomerulosclerosis (FSGS) is a serious kidney disease. We urgently need new treatments. FSGS can have a number of different causes but, regardless of its causes, all forms of FSGS are associated with damage to particular cells in the kidney called podocytes. In our earlier work, we have discovered that the health of podocytes is maintained by a group of processes that go on in cells called "epigenetics". The term epigenetics refers to changes in the way genes carry the genetic code to make proteins that do not involve changes in the typical DNA code. For example, in order for each long DNA strand to be packed inside of a cell, it has to be tightly wrapped around spools of proteins called histones. If these spools are modified by chemical reactions this can affect how genes nearby make the proteins that they code for. We have discovered that taking away a particular chemical change from histone proteins (called demethylation) causes damage to podocytes and worsens FSGS.

In this proposal, we will look to see whether blocking the enzymes that take away this chemical reaction (called demethylases) can be used as a treatment for FSGS. The experiments will be performed by treating podocytes grown in Petri dishes and mice with FSGS with a new experimental medication (called an inhibitor) that stops the demethylases from working. The studies will shed new light on how FSGS occurs, potentially paving the way for the development of a new treatment for FSGS.

Biography:

Dr. Andrew Advani is an Associate Profession/Clinician Scientist and Staff Endocrinologist at St. Michael's Hospital and the University of Toronto. He completed his medical degree at Edinburgh University (UK) in 1996 and his PhD at Newcastle University (UK) in 2003 and he was appointed as a Principal Investigator at St. Michael's Hospital in 2008. His clinical interests are focused on the care of young people with Type 1 diabetes. Dr. Advani's research program is concentrated on understanding the causes of the long-term complications of diabetes, particularly diabetic kidney disease. Within this field, his lab studies the ways that epigenetic processes contribute towards or protect against the development of kidney disease. Supported by the Kidney Foundation of Canada, Dr. Advani's lab is working to see how these epigenetic processes may also affect the development of non-diabetic kidney diseases, in particular, focal segmental glomerulosclerosis. Dr. Advani has a keen interest

in the mentorship of postgraduate trainees who wish to develop research skills in diabetes and kidney disease. He has published over 60 peer-reviewed articles and he was the recipient of the 2015 Dr. Charles Hollenberg Young Investigator Award from the Canadian Society of Endocrinology and Metabolism.

Dr. Anne-Marie Côté

Université de Sherbrooke



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Hypertension

Detection of acute glomerular injury in the hypertensive disorders of pregnancy

Lay Abstract:

Preeclampsia is a very serious condition of pregnancy. It can be life threatening for both mother and baby. For the mother, one important sign includes high blood pressure, a condition called hypertension. Women who already have hypertension before pregnancy or during the first half of pregnancy are at even higher risk of preeclampsia.

Higher amounts of protein are also found in the urine of women with preeclampsia. This is known as proteinuria. Preeclampsia can damage the mother's kidneys making them leak more protein than usual into her urine. It can also lead to other organ damage in the mother. Complications for babies can also be severe, including preterm birth and very low birthweight. The accurate measurement of proteinuria is therefore crucial to the care of hypertensive women evaluated for preeclampsia. Important decisions such as hospitalization, drug prescription, and time of delivery all take into consideration proteinuria laboratory results amongst other signs and symptoms.

It is known that methods that are currently used to detect kidney damage during pregnancy need to be improved. One method is to measure albumin, one of the many proteins contained in urine. This is called albuminuria. Albuminuria has been shown to be better than proteinuria in persons with kidney disease or at risk outside of pregnancy (for example, when searching for kidney damage in diabetic patients). We think that albuminuria is also better for pregnant women.

Because special kidney cells called podocytes were recently found in the urine of women with preeclampsia, we will also assess if measuring specific podocyte proteins will help to further detect kidney

damage in addition to albuminuria. We will also measure proteins in the blood that are linked to small vessel damage in women with preeclampsia.

Our goal is very straightforward: to improve the detection of kidney damage in women with high blood pressure during pregnancy by providing simple and accurate laboratory methods. This is crucial to the timely detection of preeclampsia and will help prevent its complications for mothers and their babies. Our project will also ensure Canadian leadership in this field.

Biography:

Dr. Anne-Marie Côté, MD, MHSc, FRCPC, is a nephrologist and obstetrics consultant at the CIUSSS of the Estrie-CHUS and an associate professor in the Faculty of Medicine and Health Sciences at the Université de Sherbrooke. A member of the Centre de recherche du CHUS as a clinician scientist and the recipient of a FRQS-SQHA Jacques-de-Champlain Award, her research interests focus on renal impairment and the diagnosis of hypertensive disorders during pregnancy. Her research program is supported by, among others, the CIHR and The Kidney Foundation of Canada. She collaborated on updating the SOGC's 2008 and 2014 clinical practice guidelines for hypertensive disorders of pregnancy, has been a member of the hypertension and pregnancy committee of Hypertension Canada since 2016, and sits on the boards of the Société Québécois d'Hypertension Artérielle, the North American Society for the Study of Hypertension in Pregnancy, and the Groupe d'Étude en Médecine Obstétricale du Québec.

Dr. An-Wen Chan

Women's College Hospital

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$99,958	Transplantation



Nicotinamide chemoprevention for keratinocyte carcinoma in kidney transplant recipients: a pilot, randomized, placebo-controlled, internal pilot trial

Lay Abstract:

As patients live longer after receiving organ transplants, there is a need to better prevent the long-term effects of anti-rejection drugs, which are used to prevent organ rejection. In particular, long-term use of these drugs increases the risk of skin cancer. Skin cancer is now a leading cause of illness and disfigurement after kidney transplantation. Given the increased risk and burden of skin cancer in transplant recipients, prevention is critical.

Nicotinamide is a form of vitamin B3 that has been shown to protect against skin cancer in the general population. However, it is unclear whether nicotinamide is safe and effective among immune-suppressed transplant recipients.

Methods: We will conduct a preliminary study to evaluate the use of oral nicotinamide (500 mg twice daily) to prevent skin cancer in 120 high-risk adult kidney transplant patients who have previously had at least one skin cancer. Patients will receive nicotinamide or sham tablets for 12-16 months. Our main objective is to determine the feasibility of conducting a larger, definitive trial that will involve more patients and longer follow-up. We will recruit patients from the University Health Network's Multi-Organ Transplant program and St Michael's Hospital kidney transplant program, which are two of the largest transplant centres in Canada.

Relevance: Kidney transplants are a life-altering treatment for people with severe kidney disease. Given the scarcity of kidney donors and the risks involved with transplantation, it is important that everything possible is done to maintain long-term health and quality of life for these patients. This study will provide useful information about the safety and effectiveness of nicotinamide to prevent skin cancer in kidney transplant patients in Canada. Nicotinamide is readily available and evidence of its safety and effectiveness could be immediately translated into clinical practice. Prevention could help to avoid premature death and suffering from aggressive skin cancer, ultimately improving the lives of kidney transplant patients.

Biography:

Dr. Chan is a clinical epidemiologist and Mohs skin cancer surgeon at Women's College Hospital in Toronto, Canada. He is the Phelan Scientist at Women's College Research Institute, Associate Professor of Medicine at University of Toronto, and Director of Transplant Dermatology at University Health Network. After obtaining his doctorate as a Rhodes Scholar at University of Oxford, Dr. Chan served as Special Advisor to the Canadian Institutes of Health Research and helped coordinate the World Health Organization's International Clinical Trials Registry Platform. His research interests include the epidemiology and management of high-risk skin cancer in solid organ transplant recipients, as well as addressing issues of transparency and biases in clinical trials. He currently chairs the international SPIRIT initiative to improve the quality of clinical trial protocols.

Dr. Christopher McIntyre

Lawson Health Research Institute



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Dialysis

Understanding the pathophysiology of uremic symptoms: a pilot mechanistic study of dialysate cooling to protect against hemodialysis induced liver and gut dysfunction

Lay Abstract:

An alarming 24,000 Canadians (and over two million people worldwide) suffer from serious kidney failure and rely on a dialysis machine to clean their blood. Dialysis poses significant challenges; one in three patients die within a year of starting dialysis and those who undergo long-term dialysis treatment experience an array of adverse symptoms. For example: toxins, which would have normally been removed by the kidneys, can cause itch and other unpleasant effects. Some of these toxins come from the gut and should normally be partially processed by the liver before they even get to the rest of the body. However, if the liver does not work properly, the patient's blood can be flooded with more toxins than dialysis can eliminate.

Dialysis has been shown to cause damage to different organs (such as the heart, brain, intestine and kidney). We propose that dialysis also leads to liver damage, starving it of blood to the point where it cannot manage the breakdown of these toxins coming from the gut, and resulting in a buildup of toxins in the blood. To investigate this, we will examine the function and blood supply of the liver using a special form of CT scanner and compare the condition of the liver to the symptoms experienced by dialysis patients. We will then examine whether changes in the dialysis treatment can help improve liver function by maintaining sufficient blood supply. We have previously shown that the safe and simple measure of cooling the dialysis fluid is effective at protecting other organs from damage, such as the heart and brain.

This study will be the first to examine the role of the liver in dialysis. It will provide entirely new insights into the reasons why dialysis patients experience undesirable symptoms and allow us to uncover new ways to improve these symptoms by focusing on modifying dialysis treatment.

Biography:

Dr. McIntyre is Professor of Medicine, Professor of Medical Biophysics, Professor of Paediatrics and Robert Lindsay Chair of Dialysis Research and Innovation at Western. He also serves as Director of the Lilibeth

Caberto Kidney Clinical Research Unit at London Health Sciences Centre, where he is also a practicing Clinical Nephrologist. He leads a team of multidisciplinary researchers focused largely on the pathophysiology of the effecting cardiovascular, brain, liver and gastro-intestinal structure and function in patients with chronic kidney disease. These studies include basic clinical science, natural history studies and the development and application of novel therapeutic strategies into large scale randomized controlled trials. These studies have increasingly focused on the adverse consequences resulting from dialysis therapy itself and the improvement in outcomes by the reduction of preventable harm. Multimodal imaging plays an important role in these studies including ultrasound, CT, PET and MRI.

Research Areas: Hemodialysis, Applied Imaging (CT, MRI, PET, Imaging), Chronic Kidney Disease, Peritoneal Dialysis, Cardio Renal Medicine

Dr. Elena Torban

McGill University Health Centre Research Institute



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Kidney Development

PCP effector Fuzzy in renal development and pathogenesis of CAKUT

Lay Abstract:

In the Western world, between 2-6 out of every 1000 newborns are born with small kidneys and/or defects of the lower urinary tract– the compilation of diseases known as Congenital Anomalies of Kidney and Urinary Tract (CAKUT). In the most severe cases, kidneys are not formed at all; this condition is not viable. Even the milder congenital (developmental) defects are associated with progressive loss of kidney function, necessitating renal transplantations or urological surgeries. In Canada, the serious consequences of renal birth defects have doubled over the last 10 years. In order to understand the basis for these defects, it is important to decipher the molecular programs which regulate development of the kidneys and lower urinary tract.

In our laboratory, we recently discovered that a novel gene, Fuzzy, is crucial for normal renal development. When we generated transgenic mice lacking Fuzzy, we found that embryos had very small kidneys and ~ 15% of mutant embryos did not form kidneys at all. These data, for the first time, revealed that Fuzzy is a critical regulator of kidney formation. In this project, we propose to investigate how Fuzzy contributes to kidney development and how Fuzzy disruption leads to this severe kidney phenotype. We propose to combine the

analysis of our mutant mice with studies of cultured cells derived from their tissues by immunofluorescence and other advanced methods. Based on preliminary data, we believe our studies will implicate Fuzzy into pathogeneses of CAKUT.

Biography:

Dr. Elena Torban is an associate professor at McGill University and a basic scientist in the Division of Nephrology, McGill University Health Center. She received her PhD in kidney development at McGill and her post-doctoral training at the Montreal Neurological Institute and at McGill, where she studied the novel Planar Cell Polarity pathway in development. Dr. Torban's current research focuses on the molecular and cellular mechanisms of congenital and acquired kidney disease. Congenital anomalies of the kidney and urinary tract (CAKUT) arise in 1 in 500 births and account for considerable morbidity in the pediatric population. Increasingly, CAKUT cases have been attributed to mutant genes, including those that encode proteins of primary cilia. In contrast, many diseases of the renal filtration apparatus reflect pathologies acquired throughout life. The overall objective of Dr. Torban's research program is to identify and understand the pathomechanisms that underlie rare human kidney diseases, in order to develop new personalized therapies. Her lab is currently supported by the Kidney Foundation of Canada to study the role of Planar Cell Polarity genes in kidney development and renal cystic disease.

Dr. Emmanuelle Cordat

University of Alberta



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Water, salt, and calcium handling by the kidney

Deciphering mechanisms of acid-base balance in collecting duct intercalating cells

Lay Abstract:

Distal renal tubular acidosis (dRTA) is a kidney disease that causes metabolic acidosis, difficulties to thrive in children, recurrent kidney stones and can ultimately lead to renal failure. dRTA is due to a malfunction of intercalated cells (ICCs) in the collecting duct, a specialized cell type that excretes the excess of protons we produce to the urine while reabsorbing the physiological buffer bicarbonate into the blood. dRTA can be caused by hereditary mutations in the gene encoding the bicarbonate transporter called Anion Exchanger 1 (kAE1). However, within the same cells, another bicarbonate transporter, SLC26A7, is present but it is unclear why this protein cannot compensate the lack of function of kAE1 in dRTA.

Our previous results showed that in dRTA conditions, SLC26A7 is downregulated by an unknown mechanism. In this project, we will dissect the mechanisms that down-regulate the SLC26A7 transporter, with the aim of identifying pharmacological ways to manipulate its function to restore bicarbonate reabsorption in dRTA patients with a mutated anion exchanger 1. Understanding these mechanisms is not only relevant to dRTA patients but also to the growing cohort of Canadian patients with chronic kidney disease who have symptoms similar to those of dRTA patients.

Biography:

Dr. Emmanuelle Cordat is an Associate Professor in the Department of Physiology at the University of Alberta, Edmonton. She joined the University as an Assistant Professor in 2007 after completing a six year-postdoctoral training at the University of Toronto under the supervision of Dr. Reinhart Reithmeier. Her undergraduate training was completed at the University of Nice/Sophia-Antipolis (France), where she also obtained her Ph.D. in Cellular and Molecular Pharmacology. Her research focuses on the physiology and pathophysiology of the collecting duct and more specifically how cells in this nephron segment regulate pH and electrolyte homeostasis. Abnormal pH homeostasis is a hallmark of chronic kidney disease, which affects millions of Canadians every year. Our laboratory is working towards a better understanding of the role of this nephron segment in maintaining a normal plasma pH and electrolyte composition.

Dr. Heather Reich

University Health Network

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Glomerulo-nephritis



Non-invasive markers of outcome and treatment response in the MENTOR study

Lay Abstract:

Membranous glomerulonephritis (MN) is one of the most common causes of glomerulonephritis, which are a group of diseases affecting the filters of the kidney. Patients with MN are at high risk of life-threatening complications including blood clots, infections, and heart attack and stroke.

The outcome of patients with MN is variable: up to 40% of patients with MN will develop kidney failure, half of the remaining patients will have chronic kidney disease, and the remainder may have spontaneous remission. The varying outcome of patients with MN and potential toxic side effects of treatment make the utility

of predicting patient response to treatment of clear benefit. Clinical markers available to doctors (creatinine, urine protein) lack sensitivity and often do not reflect the severity of progressive kidney injury. Furthermore, long-term treatment of MN with agents such as cyclosporine carries a risk of treatment-related kidney toxicity. Urinary biomarkers (measurement of specific proteins) can provide a window into the molecular processes within the kidney. We propose to evaluate the relationship between a panel of urinary biomarkers and treatment-specific response a in patients with MN enrolled in the MENTOR study.

This is the largest study ever performed in patients with MN and is a multicentre randomized controlled trial of cyclosporine versus rituximab. The identification of urinary biomarkers that are associated with disease and treatment response will allow personalized tailoring of treatment to minimize drug toxicity and optimize outcomes of patients with progressive kidney disease.

Biography:

Dr. Reich is a graduate of McGill University Faculty of Medicine. She completed her post-graduate clinical training and PhD at the University of Toronto where she is an Associate Professor and holds the Gabor Zellerman Chair in Nephrology Research. She works as a nephrologist-scientist at the University Health Network and is passionate about improving the clinical care and outcomes of patients with glomerulonephritis.

Dr. Reich's research objective is to identify clinical and molecular markers of progressive glomerular diseases, and she is scientific director of the Toronto GN Registry. Her translational research program focuses on the study of human biologic samples to elucidate the mechanisms responsible for progression of kidney disease towards kidney failure. This molecular work is complemented by studies to identify clinical risk factors for disease progression in glomerulonephritis. She enjoys teaching and is the co-director of the annual educational pre-course in glomerulonephritis for the American Society of Nephrology.

Dr. John S. D. Chan

Centre de recherche du CHUM

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Diabetes



Oxidative stress and molecular regulation of renal angiotensin-converting enzyme-2 (Ace-2) and angiotensin 1-7 receptor (MasR) expression in diabetic nephropathy

Lay Abstract:

Diabetes and hypertension are major risk factors for the development of kidney failure in diabetes. Clinical and animal experimental studies demonstrate that chronic treatment with blockers of a hormonal system called the "renin-angiotensin system (RAS)" is effective in lowering blood pressure and in delaying the progression of kidney failure but not the cure. These findings establish that RAS activation is a major risk factor in the development of hypertension and kidney failure in diabetes.

Angiotensin-converting enzyme-2 (Ace2) is the key enzyme (or protein) in the RAS that converts angiotensin-II (Ang II) to angiotensin 1-7 (Ang 1-7). Ang 1-7 interacts with its own receptor called MasR that is downregulated in diabetic kidneys. The regulation of renal Ace2 and MasR expression, however, is not well understood. In this proposal, Dr. John Chan is examining a protein, called nuclear factor erythroid 2-related factor 2 (Nrf2) and how this protein is involved to down-regulate the expression of renal Ace2 and MasR in aggravating kidney damage in diabetes. Dr. Chan's studies will identify whether Nrf2 could be a therapeutic target in preventing nephropathy progression in diabetes.

Biography:

Dr. Chan is currently a Professor of Medicine at the Université de Montréal and the Chief of the Laboratory of Molecular Nephrology and Endocrinology at the Research Centre of Centre hospitalier de l'Université de Montréal (CRCHUM). Dr. Chan's research program seeks to understand the role(s) of intrarenal renin angiotensin system (RAS) and oxidative stress in the pathogenesis of diabetic nephropathy, with special emphasis on renal angiotensinogen gene expression and reactive oxygen species (ROS) generation on tubular apoptosis in diabetes. Dr. Chan has published over 100 papers in scientific journals and presented more than

250 abstracts in various scientific societies. Dr. Chan's research program is supported by several peer-reviewed granting agencies including the Canadian Institutes of Health Research, The Kidney Foundation of Canada, Canadian Diabetes Associate and Canadian Foundation of Innovation.

Dr. Karthik Tennankore

Nova Scotia Health Authority



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Transplantation

Frailty and the kidney transplant wait list

Lay Abstract:

Every year, a growing number of Canadians are waiting for a kidney transplant who will not receive one because of the short supply of available kidneys. It is important to ensure that individuals who are on the kidney transplant waiting list are able to benefit from a transplant and that the process of deciding who is eligible is fair and objective.

Many people with advanced kidney disease will benefit from a kidney transplant. However, some people are not eligible because they have health conditions that would make the transplant surgery too risky or would put them at a high risk of poor health after transplant. Deciding who is able to receive a transplant involves a detailed evaluation of a person's health and a review by kidney transplant specialists who are knowledgeable about the risks.

Some people with kidney disease who are being considered for a kidney transplant have difficulties in many areas of their health that put them at a risk for a shortened lifespan. This is often referred to as frailty. Being "frail" may affect how people walk, (for example, using walking aids or supports), their level of function, (for example, trouble with daily activities like dressing or bathing), their fitness, and their activity. We know that being frail may lead to negative health consequences after receiving a kidney transplant. However, we do not know how being frail might affect people who are waiting for a kidney transplant, because assessing their function, fitness, and activity is not a standard part of the evaluation. Knowing this information could be helpful for individuals and kidney transplant specialists in several ways. If individuals who are frail are at a much higher risk of death, being removed from the waitlist or dying soon after transplant, it may become a new tool that transplant specialists use to determine eligibility for the list. This tool would then allow transplant specialists to make objective decisions about eligibility, and not rely only on their clinical impression. It may help the kidney

transplant team to identify individuals that have been accepted to the kidney transplant wait list that might need closer monitoring. Finally, it might provide a more complete picture of a person's overall health that complements the tests that are currently used, and this information could be used to better inform patients who are inquiring about being put on the kidney transplant waitlist.

In this study, we aim to examine what happens to people who are frail and being waitlisted for a kidney transplant. This study will include individuals with kidney disease from several centers across Canada in the provinces of Nova Scotia, New Brunswick, Newfoundland, and Ontario. We will use three different tools to assess frailty. We will then follow individuals closely to see if they experience a decline in health and are removed from the waitlist or die before they can receive a transplant. We will also follow those individuals who are eventually transplanted to see if they die or lose function of their transplanted kidney in a short time.

Finally, we will also see how frailty status changes for those who are waiting for a transplant. We hope that the findings will contribute to the practice of transplantation across Canada and perhaps worldwide. In the future, we hope that this study will be the first step to a national, standardized evaluation of a patient's function, fitness, and activity when being considered for a kidney transplant. The Kidney Foundation strives to better support people affected by kidney disease, and a key element of this is timely access to kidney transplantation and care for patients who are waiting for a transplant. Knowing how frailty impacts someone's health may lead to better allocation of this important, limited resource.

Biography:

Dr. Karthik Tennankore received his MD at the University of Western Ontario and completed Internal Medicine and Nephrology at Dalhousie University. He went on to complete a two-year clinical fellowship in home dialysis at the Toronto General Hospital (University of Toronto) and concurrently obtained a master's degree in clinical Epidemiology through Harvard University.

He joined the Dalhousie Division of Nephrology in 2013. His clinical expertise includes in-center and home dialysis. From a research perspective, he is interested in studying and improving outcomes of patients after initiation of dialysis and transplantation, and in studying the effect of frailty on dialysis and transplant patient outcomes. He is involved in clinical trials and conducts several prospective cohort studies in nephrology.

Co-applicants: Ian Alwayn; Marc Dorval; Nessa Gogan; Tammy Keough-Ryan; Bryce Kiberd; Sean Martin; Amanda Miller; Kenneth Rockwood; Laura Sills; Kenneth West; Seychelle Yohanna

Dr. Katalin Szaszi

St. Michael's Hospital



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Kidney Biology; Renal Failure

Claudin-2 as a regulator of RhoA and epithelial phenotype in tubular cells

Lay Abstract:

Chronic kidney disease is a significant problem that poses a large burden on individuals and society. We currently do not have a treatment and therefore we need more research to understand how the disease develops and to design new therapies. This project is aimed to provide fundamental new knowledge about the molecular events that cause chronic kidney disease. The kidney tubules are made of specialized cells called epithelial cells, which create and maintain a barrier and allow only highly regulated exchange of materials through the layer.

These cells are vital for kidney function. In recent years it also became clear that the injury of these cells leads to pathological changes that contribute to chronic kidney disease. Specifically, injury induces the production of mediators in these cells, and these mediators augment scar formation in the tissue. Scar formation, a disease called fibrosis, is the outcome of chronic kidney disease, and it is incurable and cannot be halted. It destroys normal kidney tissue and causes the kidneys to fail. The details of how this happens, however, are not clear. The tubular cells are connected to each other through a protein complex that creates a specialized transport pathway between the cells. This complex is called the tight junction. We found that one of the proteins residing in the tight junctions, claudin-2, is lost in a chronic kidney disease mouse model. Further, when we mimicked experimentally this loss, we found that tubular cells had augmented production of fibrosis-generating mediators, suggesting that claudin-2 is a regulator of this important process.

Therefore, in this project, we have three main objectives. First, using cultured tubular cells, we wish to define the cellular and molecular pathways through which claudin-2 controls epithelial activity and production of harmful mediators. Second, we wish to demonstrate in animal models that claudin-2 indeed has the ability to control the generation of fibrosis. Third, we have designed interventions that can interfere with the loss of claudin-2 and will test whether these can improve the generation of fibrosis.

Our studies will uncover new mechanisms underlying molecular events during kidney disease and will start assessing approaches that could benefit by slowing the disease process.

Biography:

Katalin Szaszi MD, PhD is a scientist at the Keenan Research Center (KRC) for Biomedical Science of the St Michael's Hospital and an associate professor at the University of Toronto (Dept Surgery). She obtained MD and PhD degrees at the Semmelweis University in Budapest, Hungary and completed post-doctoral trainings at the Hospital for Sick Children and Toronto General Hospitals in Toronto. She was appointed as a scientist at the KRC in 2005.

Dr. Szaszi is a cell biologist studying tubular epithelial biology and pathophysiology in inflammation and fibrosis in the context of kidney disease. Their work is funded by CIHR, NSERC and The Kidney Foundation of Canada. She was a recipient of a KRESCENT New Investigator award from The Kidney Foundation and CIHR (2007-2010) and an Early Research Award from the Ontario Ministry of Innovation. She has more than 60 peer-reviewed well cited publications.

Dr. Keir Joe Menzies

University of Ottawa



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$99,990	Renal Failure

Removal of mitochondrial health to improve the outcome of acute kidney injury

Lay Abstract:

Acute kidney injury is the most common renal disease with no effective treatment. Acute kidney injury affects 3-7% of hospitalized patients with a patient mortality rate that exceeds that of breast and prostate cancers, heart failure and diabetes combined. After adverse kidney events or toxic cancer treatments in humans, there is a pronounced loss and dysfunction of various cells within the kidney that results in the evolution of acute kidney injury.

Importantly, certain kidney cells are extremely rich in mitochondria, the organelle of a cell that provides energy, and are therefore sensitive to the decline in mitochondrial health that occurs during acute kidney injury. Mitochondrial health relies greatly on a family of proteins named sirtuins, which may therefore be an ideal target for treating injured kidney cells. Interestingly, the activity of sirtuins relies on a cellularly-limited metabolite called NAD+, thus we hypothesize that treatments that boost NAD+ levels will possess clinical potential in acute

kidney injury. These NAD+ treatments can include diet supplements of nicotinamide riboside (NR), which is a known component of certain foods such as milk and is a precursor for NAD+ production. NR has proven to be a very effective at raising NAD+ levels and sirtuin activity in cells to enhance metabolism. In fact, over the last year our research alone has shown that NAD+ boosters can treat metabolic diseases, improve stem cell health during aging and even extend the lifespan of mice. Beyond NR there are other NAD+ boosters that include inhibitors for a family of proteins called PARPs, which consume NAD+, and a novel inhibitor for an enzyme that diverts precursors away from NAD+ production, called ACMSD.

Thus, we propose to explore and compare the ability of these NAD+ boosters to improve mitochondrial health in two mouse models of kidney injury. We plan to treat rodents with NAD+ boosters following kidney injury in a therapeutic approach, mimicking a real-life treatment for a sudden acute kidney injury event. We expect that NAD+ boosters will help recover mitochondrial health in kidneys and improve the outcome of this type of injury. We will examine the signaling events that occur with this treatment strategy using a primary cell culture model of kidney cell injury. As each of the NAD+ boosters we propose to use can be administered in food, this approach could have immediate translational potential to the clinic. In addition, NR is already sold as a food supplement and PARP inhibitors, such as Olaparib (used in this study), are currently being used in combinatorial cancer therapies.

Biography:

Keir Menzies is an assistant professor at the Interdisciplinary School of Health Sciences, Faculty of Health Sciences, and is cross-appointed to the department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa. His research examines metabolism in various organs with a special interest in energy-signalling pathways that support kidney function and health. By understanding these signalling pathways, he hopes to create new treatment options for metabolic dysfunction in kidneys during disease or injury. Previously, he has helped define various metabolic pathways that are controlled by the energy-sensing group of NAD+-dependent enzymes named sirtuins. Using nutraceutical or pharmaceutical strategies that boost tissue NAD+ levels, followed by the activation sirtuin enzymatic activity, his research has led to new treatments for metabolic dysfunction in muscular dystrophy, non-alcoholic fatty liver disease and stem cells during aging in mice. Optimization of these treatment strategies will eventually include mapping whole body NAD+ homeostasis as a predictive biomarker of metabolic dysfunction during injury, disease and aging.

Dr. Kevin Burns

Ottawa Hospital Research Institute



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Renal Failure

Exosomal transfer of MicroRNA-486-5p in acute kidney injury repair

Lay Abstract:

Acute kidney injury (AKI) is a serious condition in which kidney function declines rapidly, often over minutes to hours. Therapy often involves use of dialysis, with the hope that the kidneys will eventually recover their function, although this occurs in only about one half of patients. Unfortunately, there are no treatments to accelerate the repair of injured kidneys after AKI.

Use of stem cells has been proposed to help injured kidneys recover their function. Recently, we isolated different "progenitor" cells from human umbilical cord blood and infused them into mice with AKI, induced by temporary blockage of blood supply to the kidneys. We found that one population of cells protected the mice from kidney injury. Furthermore, the cells themselves did not incorporate into the injured kidneys, but rather released factors that appeared to stimulate healing. In this regard, the cells shed tiny membrane particles ("exosomes") that are enriched in a substance called "miR-486-5p". Injection of mice with the exosomes strongly protects them from kidney injury, and the benefits appear to be at least partly due to transfer of miR-486-5p to the kidney.

Using exosomes to treat humans with AKI represents an exciting long-term research goal. Indeed, exosomes may offer distinct advantages over cell treatments, including a low risk of immune "rejection", reduced chance of abnormal cell growth, and less potential to cause blockage of blood vessels due to their small size. However, a number of questions remain to be answered before studies can be conducted in humans. How can we optimize the delivery of exosomes to the kidneys after AKI, and do infused exosomes target specific kidney cells to promote repair? What is the effect of transfer of miR-486-5p in the protective response associated with exosome use after kidney injury, and what role does prevention of cell death play? What other molecular pathways in the kidney are affected by exosomes and miR-486-5p? In this grant, we will conduct animal studies to address each of these key questions. Our proposal represents the critical next step in developing new treatments for humans with AKI.

Biography:

Kevin D. Burns, MD, FRCP(C) is Professor of Medicine in the Division of Nephrology and Vice-Chair for Research in the Dept. of Medicine at the Ottawa Hospital and the University of Ottawa. He is Senior Scientist and Director of the Kidney Research Centre of the Ottawa Health Research Institute, University of Ottawa, and is cross-appointed to the Department of Cellular and Molecular Medicine. Dr. Burns received his B.Sc. and M.D., C.M. from McGill University, and completed Internal Medicine Residency at the University of Ottawa. Following a clinical fellowship year in Nephrology in Ottawa, he undertook basic science research training at Vanderbilt University Medical Center. In 1992, he was awarded a 5-year Scholarship from the Medical Research Council of Canada, and he returned to Ottawa as a clinician-scientist. His research program has been supported by funds from the Canadian Institutes of Health Research (CIHR), the Kidney Foundation of Canada (KFOC), and the Canada Foundation for Innovation/Ontario Innovation Trust.

Dr. Burns was University and Hospital Division Head of Nephrology from 1997-2005. He is Past President of the Canadian Society of Nephrology (CSN) (2004-2006) and is Chair of the Steering Committee for the KRESCENT Program. Dr. Burns' research is focused on the function and regulation of the intrarenal renin-angiotensin system, as this system pertains to the pathogenesis of kidney diseases, including diabetic nephropathy and hypertension. His laboratory uses a variety of methods in cell and molecular biology, as well as animal models of kidney disease. Dr. Burns is also involved in clinical research studies that aim to transfer knowledge from the laboratory bench to the patient's bedside.

Dr. Mathieu Lemaire

The Hospital for Sick Children (SickKids)

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$99,000	Kidney Biology



Glomerular sialic acid deficiency as a novel cause of hemolytic-uremic syndrome

Lay Abstract:

Kidneys play a very important role in your body. Among other functions, they help filter wastes created by the body daily. To do that, enormous amounts of blood need to be brought to the kidneys every hour. The filter is called the glomerulus: it acts like a sieve in that it keeps all of the big molecules and cells in the blood (like noodles) and filters out all of the small molecules and water in the urine. Because of that, it is very important to keep the blood flowing smoothly to the kidneys. How the kidney blood vessels can do this remains a fascinating puzzle.

There are diseases in which the main problem is that blood flow in the kidney is abnormal or stops altogether because of blood clots. This may cause a lot of problems for the patient because the kidney is then unable to filter out the body wastes properly. Patients with severe infections caused by a bacterium called pneumococcus can develop blood clots in their kidneys. Most of these patients are children that will need dialysis while they are sick because their kidneys are not working at all. Many will also have kidney problems even after the infection is over. We do not know why blood clots are forming in their kidneys. We also do not know how to treat it: right now, all we can offer to patients is a “tincture of time” (we hope that the kidneys can repair themselves over time).

One hint that we have relates to an enzyme called sialidase that the bacteria release in the blood of patients. An enzyme is like a little engine that can do one thing very, very well. Sialidases have only one goal: to seek and remove a specific sugar, called sialic acid, found on proteins on the outside surface of cells. Proteins with sialic acids normally play important roles on cells: they can be used as a docking station by some blood cells whereas they may repel others. All patients who develop kidney disease during pneumococcus infection have a lot of sialidases in their blood (sialidases are never found in the blood of healthy people). The big problem: we do not know why having sialidase in the blood causes problems in the kidneys.

We recently discovered a new genetic disease where patients also develop blood clots in their kidneys. The interesting part of this story is that these patients have mutations in a gene called ST3GAL1 that also works

with sialic acid in cells. In fact, its function is the exact opposite of sialidases: it is an enzyme that adds the very sialic acid to proteins that the sialidase likes to remove! Experiments done in our lab show that these mutations prevent this enzyme from working normally. The bacterial and genetic diseases may thus be mirror images of each other.

We propose to study the two diseases at the same time to try to figure out what may be the common thread between them. Indeed, this may help us understand why abnormal sialic acid biology causes so many problems for patients. We think there must be specific proteins with sialic acid normally on them that play an important role to prevent the formation of clots in the kidney blood vessels. A better understanding of these diseases is required if we want to develop specific treatments for these patients.

Biography:

Dr. Mathieu Lemaire finished his medical training at McGill University in 2004 and then moved to Toronto to learn Paediatrics and Nephrology at The Hospital for Sick Children. He then went to Yale University (New Haven, CT) to pursue a PhD in Investigative Medicine under the supervision of Dr. Richard P. Lifton as a KRESCENT post-doctoral fellow. The focus of his project was on the genetics of rare paediatric kidney diseases, with a particular focus on atypical hemolytic-uremic syndrome (aHUS). Dr. Lemaire returned to the University of Toronto in mid-2014 as Assistant Professor of Paediatrics: he joined the Division of Nephrology at The Hospital for Sick Children as Assistant Professor of Paediatrics, and the Cell Biology Program of the SickKids Research Institute as Scientist-Track Investigator. He is cross appointed at the University of Toronto with the Institute of Medical Sciences and in the Biochemistry Department. His main research interest is to do translational research that pertains to rare paediatric kidney diseases using genomic tools for gene discovery followed by careful functional dissection of candidate genes using cutting-edge microscopic, cell biology and biochemical methods. The goal is to not only contribute to a better understanding of disease pathophysiology but also aim to translate these findings into tangible changes in clinical care. He played a central role in the identification of the first non-complement gene that causes a recessive form of aHUS, diacylglycerol kinase epsilon. His laboratory continues to work on teasing out the mechanisms by which DGKE deficiency causes thrombosis restricted to small blood vessels of the kidneys. His team continues to do gene discovery on a variety of rare paediatric kidney diseases using whole-exome sequencing: functional work is on the way for yet another novel gene that causes complement-independent aHUS.

Dr. Michael Zappitelli

McGill University Health Centre Research Institute



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Screening & Prevention

11-year renal outcomes after pediatric intensive care unit admission: acute kidney injury and disease progression

Lay Abstract:

Many critically ill children admitted to the intensive care unit (ICU) experience injury to their kidneys, or what is referred to as acute kidney injury (AKI). AKI usually happens because of the disease which brought children to the ICU (e.g., severe infection, cardiac surgery) or the treatments they need to receive (e.g., medication toxic to kidneys). AKI can cause many problems, like fluid retention with heart failure, hormone problems, difficulty feeding and sometimes AKI requires treatment with dialysis. In children, we know that AKI in ICU children is associated with death in the ICU and longer hospital stay.

In adults, it is known that kidney tissue damage occurring with AKI can lead to chronic (long-term, ongoing) kidney damage. This long-term damage can lead to chronic kidney disease or high blood pressure (hypertension) and even increase risk for long-term death in adults. However, little is known about how AKI which occurs in hospitalized children, affects long term child kidney health. Chronic kidney disease and hypertension are a significant burden to populations and are very important risk factors for heart disease. Early life events like AKI may be an important risk factor for chronic kidney disease and hypertension in children. Importantly, early treatment and prevention of chronic kidney disease and hypertension in children could lead to significant improvements in kidney and heart health and decrease health system burden.

To begin clarifying if AKI in children admitted to the ICU leads to chronic kidney disease or hypertension, we previously studied a group of children, 6 years after they were in the ICU. Chronic kidney disease and hypertension were remarkably common. Yet, we know that most children who are admitted to the ICU are not followed up for kidney function or blood pressure problems after discharge from hospital. Therefore, chronic kidney disease and hypertension in our group of children would have otherwise gone undetected. There is a need to change how ICU children are followed-up after discharge, to detect, prevent and treat chronic kidney disease and hypertension. We will follow-up our large group of children previously admitted to the ICU (whom we followed already at 6 years after ICU admission), at 11 years after ICU admission. We will do this to understand if and by how much kidney function, kidney damage or blood pressure worsen over time, from 6 to

11 years after ICU admission. We will also study whether new urine tests of kidney damage measured in children at 6 years after ICU admission can help us predict what children will have worsening, or improving, kidney function and blood pressure at 11 years follow-up.

This study will be unique in the world and will give us the information we need to start changing how children are followed up and treated by their doctors and tell us what children need to be followed closely to prevent long-term kidney damage and promote long-term kidney health, after an illness causing AKI. We will be able to do this work, because we are a group of kidney, ICU, cardiology and general pediatric doctors who have worked together for many years to understand the negative effects of AKI on child health. We will also work together with family representatives and health care administrators to make sure that the guidelines on kidney follow-up that we recommend at the end of our study, are based on outcomes important to families and patients and are feasible within our current health care system.

Biography:

Dr. Michael Zappitelli is a pediatric nephrology fellow who obtained his MD at McGill University in Montreal and completed a post-doctoral fellowship with Dr. Stuart Goldstein at Baylor College of Medicine and Texas Children's Hospital in Houston, one of the largest pediatric centres in North America.

His research is on acute kidney injury (AKI) in children. AKI mostly occurs in hospitalized patients and must be better understood in order to detect the disease earlier, lessen the most serious risks and improve patients' long-term health. His clinical research laboratory is characterizing this disease by evaluating definitions and performing studies to assess the effect of AKI on various outcomes in several diagnostic populations. Included are patients on nephrotoxic medications, patients undergoing cardiac surgery and critically ill patients. His latest studies examine the long-term outcomes of AKI in cardiac and non-cardiac critically ill patients and in children treated for cancer with cisplatin. He aims to evaluate whether AKI is a risk factor for chronic kidney disease (CKD) and whether new AKI biomarkers of renal tubular damage can be used to better diagnose patients at risk of CKD. Other projects focus on discovering and characterizing novel AKI urine protein biomarkers for AKI diagnosis.

Dr. Nina Jones

University of Guelph



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Kidney Biology

Role of Nck adaptor proteins in kidney podocyte morphology

Lay Abstract:

Chronic kidney disease (CKD) is a major public health issue that continues to rise coincident with the diabetes epidemic, and ~15% of Canada's population is already living with this devastating illness. Very few treatments are available for advanced kidney disease, and these approaches are associated with considerable morbidity, mortality and health care costs, prompting a demand for new and more effective treatment strategies.

Fundamental discoveries over the past decade have highlighted the key role of the podocyte in the pathogenesis and progression of CKD. The ability of podocytes to remain anchored to the basement membrane and maintain filtration despite fluctuating hemodynamic forces is closely tied to their unique morphology. Podocytes extend a series of interdigitating actin-rich foot processes that respond to their environment and alter their shape via a specialized cell junction known as the slit diaphragm. One of the earliest features of kidney disease is remodeling of podocyte foot processes and collapse of the actin cytoskeleton, resulting in slit diaphragm loss and proteinuria.

Our laboratory provided some of the first evidence that signaling from the slit diaphragm directly regulates actin dynamics and foot process morphology, and we have since validated the importance of such signaling in podocyte injury and repair. Our studies are now revealing that significant crosstalk exists between the slit diaphragm and focal adhesions, which attach the podocyte to the basement membrane. We have identified the adaptor protein Nck as a molecular hub linking these signaling centres, and the studies proposed here will use mutant mouse models and complementary cell lines to explore the role of Nck in focal adhesion remodeling. Emerging studies are highlighting the molecular heterogeneity of glomerular diseases; thus, our long-term objective is to translate this knowledge into rational design of more targeted therapies for the podocyte.

Biography:

Dr. Nina Jones is an Associate Professor and Canada Research Chair in Eukaryotic Cellular Signalling at the University of Guelph, Ontario. She completed Ph.D. studies at the University of Toronto and obtained

postdoctoral training at the Lunenfeld Tanenbaum Research Institute with the late Dr. Tony Pawson before her recruitment to Guelph in 2006. Her research investigates fundamental mechanisms of cell communication, and she has made significant contributions in understanding how such signalling pathways become deregulated in prevalent human pathologies such as kidney disease, cardiovascular disease and cancer. Dr. Jones has received numerous awards throughout her career, including a KRESCENT New Investigator Award, an Ontario Early Researcher Award, an NSERC-University Faculty Award, and a KFOC Merit Award for Outstanding Community Partner, and she is a member of the Royal Society of Canada College of New Scholars, Artists and Scientists. Research in Dr. Jones's lab is presently supported by KFOC, CIHR and NSERC.

Dr. Sacha de Serres

Université Laval



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Transplantation

The role of dendritic cells and follicular helper T-cells in antibody-mediated rejection of the kidney graft

Lay Abstract:

In the last twenty years, considerable progress has been achieved in kidney transplantation. However, the life expectancy of transplanted kidneys has not increased as much as expected. In Canada, the percentage of kidneys from deceased donors that are still functional 5 years after transplant is only slightly above 80%. In other words, young patients transplanted today may need 2, 3 or even more grafts during their lifetime. Adequate graft survival would be that once a patient receives a kidney, he or she will die with this graft functioning. Given that each year in dialysis costs over $50,000 dollars more than a year with a functioning transplant, there is a clear economic incentive to improve graft survival.

Premature graft loss is most often due to late rejection, which is caused by anti-HLA antibodies. Although many agents have been tested to treat antibody-mediated rejection, so far none of them has been very successful. Once the patient develops these antibodies, he or she is somewhat 'vaccinated' against the graft. To improve outcomes, we need to block the immune system at a checkpoint before antibody generation.

The purpose of the proposed research is to better understand how innate immune cells called dendritic cells can instruct specialized T cells called follicular helper cells to interact with B cells that produce anti-HLA

antibodies. We previously described that, dendritic cells can invade the graft slowly in patients following transplantation, and that they are in close contact with activated T cells. More recently, we confirmed that patients with class II anti-HLA antibodies have a predominance of follicular T cells in their blood and in their kidney biopsy, that was not observed with class I anti-HLAs. We now want to better characterize this dendritic cell – T cell interaction in humans in vitro and in vivo. We want to determine whether specific inhibition of cytokines involved in the dendritic cells – follicular T cells crosstalk can prevent donor-specific antibody formation by human B cells. The hope is to find an immunological target(s) (single or in combination) that will block the pathway to antibody formation before the process reaches the B cells checkpoint. Some cytokine candidates, such as anti-IL21, are already in development for other diseases. Moreover, this work will clarify whether inhibition of follicular helper cell generation seems an interesting target for class II anti-HLA only, or also for class I anti-HLAs.

Biography:

Dr. Sacha De Serres is a new investigator at Laval University. He obtained his M.D. at Université de Montréal and trained in Internal Medicine and Nephrology at Laval University. He then completed a KRESCENT Post-Doctoral Fellowship in Transplantation Immunology at the Brigham and Women's Hospital at Harvard University in Boston. Dr. De Serres' research focuses on the innate immunity in transplantation.

The aim of his project is to study the interaction between two specific types of cells, the dendritic cells and the follicular helper T cells, during kidney rejection. More precisely, Dr. De Serres' aim is to decipher how these cells instruct the B cells to produce antibodies against the graft. Dr. De Serres' hope is that this knowledge will help to individualize immunosuppressive therapy and thus reduce the side effects of the anti-rejection drugs. It should also help to develop better treatments for chronic rejection, which will ultimately increase the life expectancy of the transplanted kidneys. These tools might prove beneficial not only to kidney transplant recipients, but eventually to the recipients of other organs.

Dr. Soham Rej

Lady Davis Institute for Medical Research



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$96,664	Water, salt, and calcium handling by the kidney

Statins in the treatment of lithium-induced nephrogenic diabetes insipidus: a pilot randomized controlled trial

Lay Abstract:

Lithium is a commonly used treatment in several medical conditions, including bipolar disorder and major depressive disorder. It is also being studied in dementia, stroke, and even cancer. Currently, lithium is used by approximately 350,000 Canadians and more patients could potentially benefit from using it. However, doctors are avoiding lithium because of chronic kidney disease, which is often irreversible. Lithium exposure can increase the risk of chronic kidney disease by 3 times through Nephrogenic Diabetes Insipidus (NDI), a condition characterized by excessive urination and thirst. A recent preliminary study found that statins, commonly used cardiovascular medications, are associated with a lower risk of NDI in lithium users, but a randomized clinical trial is needed.

In this first clinical trial, Dr. Soham Rej will test a statin called atorvastatin (Lipitor) in treating NDI in people using lithium. The trial will recruit 60 lithium users, randomly selected to receive either atorvastatin (20mg/day) or placebo for 12 weeks, to observe whether statins can improve NDI. If successful, this pilot study will generate the information needed to plan future large clinical trials that can confirm whether statins can treat NDI and potentially prevent chronic kidney disease in lithium users. This could improve people's health and prevent the use of costly health services for kidney disease and other medical problems. This study supports the mission of the Kidney Foundation of Canada by helping reduce the burden of kidney disease through innovation.

Biography:

Dr. Soham Rej is a Geriatric Psychiatrist and an Assistant Professor at the Department of Psychiatry, Jewish General Hospital, Lady Davis Institute, McGill University, Montreal, Canada. His primary research interest has been to understand renal side-effects related to the use of psychotropic medication in older adults. In particular, using pharmacoepidemiology and clinical trial approaches, he has been investigating the risk of nephrogenic diabetes insipidus and chronic kidney disease related to lithium, and approaches to minimizing this risk.

Dr. Soham Rej is also interested in the psychosocial health of patients with chronic kidney disease, including a recently completed randomized controlled trial examining meditation in the treatment of depression and anxiety in hemodialysis patients. Dr. Rej is very thankful to the Kidney Foundation of Canada for supporting his research and hopes that his work can improve the lives of Canadians currently dealing with or at future risk for kidney disease.

Dr. Todd R. Alexander

University of Alberta

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Renal Failure



Molecular mechanisms mediating paracellular intestinal Pi absorption and the development of CVD

Lay Abstract:

The most common cause of death in persons with kidney failure is cardiovascular disease. In persons with chronic kidney disease and end-stage renal disease, blood phosphate levels directly correlate with cardiovascular diseases including heart attack and stroke. This is because phosphate can bind calcium in the blood-forming calcifications in blood vessels and the subsequent sequalae, heart attack and stroke. Unfortunately, we do not completely understand, at a molecular level, how phosphate (a common food preservative) is absorbed into the blood. We aim to decipher this, so that we can block intestinal phosphate absorption thereby preventing cardiovascular diseases in persons with kidney disease. What is known is that most of the ingested phosphate is absorbed between intestinal cells.

The Alexander laboratory has significant experience understanding the movement of substances between cells. We have observed that preventing the movement of sodium through intestinal and kidney cells prevents the movement of ions and small molecules between cells. This is because blocking sodium movement somehow makes the connection between cells tighter. In this proposal, we seek to understand how this occurs and tease out the signaling molecules mediating this, such that they can be manipulated to prevent phosphate absorption and cardiovascular disease in persons with kidney disease. This proposal also seeks to identify the proteins in the connection between intestinal cells that permits or prevents the movement of phosphate between them. The Alexander laboratory has generated mice genetically engineered to lack one such protein,

called claudin-12. Preliminary data infers that claudin-12 forms a phosphate barrier between epithelial cells. This project will clearly define the role of this protein in intestinal phosphate absorption.

Further, given the proposed effect of claudin-12 on intestinal phosphate flux, i.e., it prevents it, this model will be used to examine the effect of increased intestinal phosphate absorption on the tendency to develop cardiovascular disease. Ultimately these studies will provide new therapeutic targets for the treatment of cardiovascular disease in persons with kidney disease.

Biography:

Dr. Alexander is a Pediatric Nephrologist at the Stollery Children's Hospital and Associate Professor in the Department of Pediatrics with an adjunct appointment to Physiology at the University of Alberta. Dr. Alexander completed his MD at the University of Western Ontario. Training in Pediatrics was performed at Memorial University in Newfoundland and Pediatric Nephrology at the Hospital for Sick Children. After this, he received a Ph.D. in Cell Biology from the University of Toronto. He then completed a post-doctoral fellowship in renal tubular physiology at St Radboud University in the Netherlands. The focus of Dr. Alexander's research is primary transport mechanisms by which the renal tubule regulates the body's electrolyte, acid/base and calcium balance. In particular he seeks to understand the molecular mechanisms responsible for altered tubular salt absorption leading to the development of hypertension and the related process of how perturbations in tubular calcium transport induce kidney stone formation. His work is supported by the Canadian Institute of Health Research, the Natural Sciences and Engineering Research Council, the Kidney Foundation of Canada and the Women and Children's Health Research Institute. Dr. Alexander is the Canada Research Chair (tier 2) in Renal Epithelial Transport Physiology.

Dr. Tom D. Blydt-Hansen

University of British Columbia



FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$100,000	Transplantation

Pharmacometabolomics in pediatric transplant recipients and relationship to mycophenolate mofetil pharmacokinetics and pharmacogenomics

Lay Abstract:

Children with end-stage kidney failure benefit greatly from kidney transplantation to return them to more normal living. To prevent rejection, children must continue to take medications that suppress the immune system

for the rest of their lives. Because these medications can have side effects, the challenge is to give enough medication to prevent rejection but not so much that they have serious side effects.

Mycophenolate mofetil (MMF) is a medication that is difficult to use. It works very well to prevent rejection but also can cause blood and gastrointestinal toxicity (e.g., diarrhea). These side effects impact quality of life and can result in dose reductions. Unfortunately, these dose reductions also can increase the risk of rejection.

Unlike some other medications, there are no easy tests to monitor the level of MMF in the blood, making it difficult to adjust. There are also a lot of differences in people's metabolism, and MMF down more slowly in some people and too quickly in others. These differences are partly determined by our genes and so we are all unique in this way. But it means that it can be very hard to know the right dose for transplant recipients to keep their kidney safe and them feeling well.

Right now, there are two studies already taking place for children with kidney transplants, one in Canada and another in Mexico. We will work with these studies to develop a better monitoring test for MMF. Our research group will use comprehensive drug level testing (called pharmacokinetics) and urine testing for small molecules (called metabolites) to learn how to predict the right MMF dose for children. Some of these differences are genetics, so we will include genetic information about kidney transplant recipients to develop the test. This test can be done in the future on urine samples from clinic to screen for either risk of toxicity or low MMF drug levels that can cause rejection. There will be 80-100 children studied in Mexico, who will have pharmacokinetic testing done to see how much MMF is getting into their body on their regular dose of medication. We will first look for pattern of metabolites in urine, to see which ones are related to high or low levels of MMF. We fill find other metabolites by looking for patterns related to genes that affect MMF metabolism. This will give us the best combination of metabolite markers to develop a urine test. We will use this test to find how well this testing predicts side effects and kidney transplant failure.

More accurate testing and monitoring will permit kidney transplant doctors to adjust the dose of MMF so that children will have the benefit of blocking rejection and avoid some of the MMF side effects. Better adjustment of MMF will improve the quality of life of children after transplant and may extend their kidney transplant function by reducing the risk of rejection.

Biography:

Dr. Tom Blydt-Hansen received his MD, CM from McGill University in 1992. He trained in Pediatrics and Nephrology at the Montreal Children's Hospital and went on to receive further training in transplantation and research at the University of California, Los Angeles. He started his Nephrology career at the University of Manitoba in 2001 and went on to become Division Head of Nephrology from 2005-2014. Since 2014, he is Director of the Multi-Organ Transplant Program at BC Children's Hospital and a Senior Scientist at the BC Children's Hospital Research Institute.

His clinical and translational research program is focused on characterizing kidney allograft injury using urine metabolite profiling and other biomarkers. He is lead investigator in the PROBE study, a CIHR funded multi-center cohort study to identify non-invasive urine biomarkers of allograft rejection in pediatric kidney transplant recipients. Most recently, he received funding from Kidney Foundation of Canada to develop a test for mycophenolate treatment monitoring. He is also engaged in collaborations to identify urinary biomarkers (metabolomics) associated with chronic kidney disease, acute kidney injury, type 2 diabetes and cisplatin nephrotoxicity. He is co-investigator on several nationally funded transplant research studies including CKiD, iCARE, CAN-RESTORE and CNTRP.

ALLIED HEALTH DOCTORAL FELLOWSHIPS

Brennen Dobberthien

University of Alberta

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$58,000	Cancer



Assessing kidneys non-invasively with MRS: a potential tool for early detection of kidney cancer

Lay Abstract:

Kidney cancer kills thousands of Canadians a year, with incidence increasing every year. However, this cancer usually remains undetected in the earlier stages, with many cases being diagnosed at an advanced stage.

New strategies for early detection are needed. One potentially useful method is Magnetic Resonance Spectroscopy (MRS), which can detect chemicals that may have relevance to kidney cancer. Each chemical has a unique signal, which allows us to measure their individual levels with MRS. Typically, studies have been limited to MRS on kidney tissue samples. However, new MRS techniques offer an opportunity to measure these chemicals directly in kidney non-invasively. The number of such studies has been limited due to low sensitivity, breathing motion, and contamination from overlapping signals. This makes it difficult to detect a number of relevant chemicals such as glycine (Gly), glutamate (Glu), glutamine (Gln), gamma-aminobutyric acid (GABA), scyllo-inositol (Scyllo), and betaine (Bet). The levels of all of these chemicals have been shown to be altered in cancerous kidney tissue compared to normal tissue, and they may be valuable for early diagnosis.

In order to overcome the challenges associated with the use of MRS directly in kidney, we will look at optimizing techniques to improve measurements while mitigating the problems caused by low sensitivity, breathing motion, and signal contamination. We previously optimized a detection sequence for the improved measurement of Gly, Glu, and Gln in rat brain. Our goals include addressing the challenges of breathing motion, investigating the feasibility of measuring Glu, Gln, and GABA simultaneously, and exploring the measurement of Scyllo and Bet directly in rat kidney. This work will enable the assessment of kidney chemicals non-invasively and

can be applied to study kidney cancer in humans. The information gained from these studies may enable methods of early detection and diagnosis of kidney cancer.

Biography:

Mr. Brennen Dobberthien is a PhD candidate in Oncology – Medical Physics at the University of Alberta. His educational background includes a Bachelor of Science in Engineering Physics with Nanoengineering Option from the University of Alberta, awarded in 2012. He was admitted to a Master of Science program in Oncology – Medical Physics at the University of Alberta in the same year. In 2015, he transferred to a Doctor of Philosophy program in Oncology – Medical Physics and completed his Doctoral Candidacy Examination in 2016.

His area of study within Medical Physics is in-vivo nuclear Magnetic Resonance Spectroscopy (MRS), specifically spectral editing for single voxel MRS at 9.4 T, under the supervision of Dr. Atiyah Yahya. Brennen is passionate about in-vivo MRS because of its potential health care applications, specifically for cancer research and diagnosis. He will continue to pursue clinical medical physics as a career path because he is interested in the application of physics to medicine in an effort to improve the lives of cancer patients, including those with kidney cancers such as renal cell carcinoma.

Supervisor: Dr. Atiyah Yahya

Marie Leblond

Université de Montréal

FUNDING PERIOD	FUNDING AMOUNT	CATEGORY
2017-2019	$58,000	Transplantation



Identify among transplant recipient teens and parental roles in the context of living donation from a parent

Lay Abstract:

Adolescence is a period of development that is characterized by rapid growth and change. It is during this period that new issues surface, including identity development, considered as the leading issue of adolescence. Literature suggests that the question of identity development is intensified for teens living with a chronic disease since they must adapt not only to the challenges of normative development (i.e., of identity) but also to issues related to chronic illness and its associated treatments. In addition to forging their identities, teen

organ transplant recipients face other issues, including parental overprotection, social adaptation challenges, the attitude towards the organ donor, the quest for autonomy, and identification with their peers. These issues influence the development of identity and self-acceptance in adolescence. Teen transplant recipients cite the definition of identity among the greatest challenges associated with their health condition. Parents play an active and participatory role in the development of their teen's identity. In addition to assuming normal parenting roles, parents of children with a chronic illness must also take on the role of "caregiver". Family dynamics change in instances where a parent is an organ donor for his or her child. When the time comes to volunteer to act as a donor, some parents state that they don't feel they have a choice and that they sometimes feel alone in their decision-making process.

Given that the disease and its associated treatments make it difficult for these teens to develop their identities, particularly in terms of their body image, autonomy and independence, and given that parents tend to be over-protective of their children and play a dual role as parents and donors, this thesis aims to describe and understand the development of identity among young people who have received a kidney transplant from a parent, and the role of the parent in the child's identity development.

Biography:

Marie Leblond has been a PhD candidate at the Université de Montréal (research and treatment in clinical psychology) since 2014. Ms. Leblond completed her bachelor's at the Université du Québec à Trois-Rivières and the Institut René Descartes (Paris V), where she developed research projects on the physical and psychological health of French teens. Under the supervision of Dr. Marie Achille, Ms. Leblond has been drafting her doctoral thesis on identity development among teens who receive a kidney transplant and on parenting practices in situations where the parent is a living donor. She works in collaboration with Montreal's Hôpital Sainte-Justine and principal investigator, Dr. Marie-José Clermont, as well as Vancouver's BC Children's Hospital, under the supervision of Dr. Tom Blydt-Hansen. The research project's preliminary findings have been presented at scientific conferences held by the Canadian Society of Transplantation (2015/2016/2017) and the International Pediatric Transplant Association (2017). Ms. Leblond won the award for the subject that sparked the greatest interest among professionals working with transplant recipient children and teens.

Thanks to funding from The Kidney Foundation of Canada through its Allied Health Doctoral Fellowship, Ms. Leblond is able collect the data required for her thesis. She is conducting interviews with young patients and their parents in Montreal and Vancouver with the goal of describing and better understanding their experience in relation to living donation from a parent. The project's final results will be presented to the teams involved in 2018-2019 and may lead to the adaptation of current practices and a better understanding of parent-donor and teen-recipient dyads.