KRESCENT

# KRESCENT Award Recipients:

## 2015-2019

kidney FOUNDATION

FONDATION DU rein

Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

CIHR IRSC
Institute of Nutrition, Metabolism and Diabetes
Institut de la nutrition, du métabolisme et du diabète

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# 2015 KRESCENT Award Recipients

## Dr. Sri Nagarjun Batchu, PhD

### Keenan Family Foundation - KRESCENT Joint Fellowship



**Supervisors**: Dr. Andrew Advani and Dr. Kim Connelly
**Institution**: Keenan Research Centre for Biomedical Science, Li Ka Shing Knowledge Institute - St. Michael Hospital
**Year**: 2015-2018

Dr. Sri Nagarjun Batchu will complete his post-doctoral fellowship under the supervision of Dr. Andrew Advani and Dr. Kim A. Connelly at the Keenan Research Centre for Biomedical Science and Li Ka Shing Knowledge Institute of St. Michael's Hospital in Toronto. Dr. Batchu's project is focused on identifying and developing new treatments for cardiorenal disease.

Kidney disease is a major cause of illness and death amongst Canadians. When kidney disease reaches the stage where the kidneys stop working people need treatment with dialysis or with a kidney transplant. However, many people with kidney disease will never reach this stage but will instead die of cardiovascular diseases such as heart attack or heart failure. The term "cardiorenal disease" refers to the situation where heart disease and kidney disease affect the same person and where the presence of one of the conditions affects the development of the other. Dr. Batchu's project is focused on understanding the role that a particular protein called HDAC6 plays in the development of kidney disease and heart disease. HDAC6 is an enzyme that is present in all our cells and changes the chemical structure of certain other proteins by a process that is called "deacetylation". Dr. Batchu hopes that his work will pave the way to the development of inhibitors (or blockers) of HDAC6 as a new treatment that can slow the progression of kidney failure and heart failure in the millions of people at risk.

## Carole Campion, PhD

### KRESCENT Fellowship



**Supervisors**: Dr. Johanne Tremblay
**Institution**: Centre de Recherche du CHUM
**Year**: 2015-2018

Dr. Carole G. Campion will pursue her post-doctoral fellowship under the supervision of Dr. Johanne Tremblay at the CRCHUM-Research Center, Centre hospitalier de l'Université de Montréal. Dr. Campion wishes to identify new therapeutic strategies for improving tissue repair after renal injury.

The pathophysiology of kidney damage is complex and is further complicated by the fact that renal aggravation often exists in the context of multiple organ failure. Due to a lack of understanding of signaling culprits involved in the pathogenesis of

nephropathy, no promising therapies are currently available for the management of patients' treatment. Dr. Campion's research focuses on a new candidate therapeutic protein, HCaRG/COMMD5 (Hypertension-related, Calcium-Regulated Gene). This protein has the potential to accelerate the recovery of renal tissue integrity and corresponding physiological functions, characterized by a reduction in the expression of pro-inflammatory genes after renal insult. Dr. Campion will try to identify potential partners of HCaRG at the molecular level as crucial mediators of kidney repair after injury. A better understanding of these signaling pathways is essential for developing new therapeutic strategies to prevent, repair or delay kidney disease.

## Maryam Demian

PhD Candidate



### KRESCENT Allied Health Doctoral Scholarship

**Supervisors**: Dr. Wendy Loken-Thornton and Dr. Jean Shapiro
**Institution**: Simon Fraser University
**Year**: 2015-2018

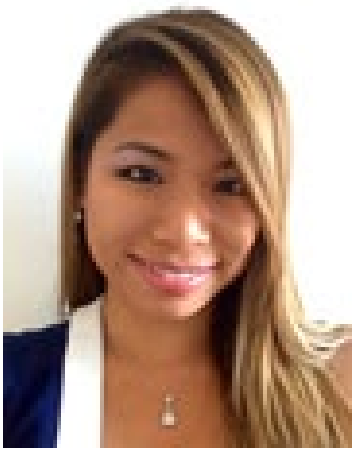
Ms. Maryam Demian will complete her fellowship under the supervision of Dr. Wendy Loken-Thornton and Dr. Jean Shapiro at Simon Fraser University, where she obtained a master's in clinical psychology and is currently pursuing a Ph.D. in clinical psychology (neuropsychology stream).

Kidney transplant recipients must follow a complex immunosuppressant regimen to prevent complications related to non-adherence (e.g., decreased organ function and graft rejection). Unfortunately, the rates of non-adherence in the kidney transplant population are high. There are many reasons for low levels of adherence. This research project focuses primarily on health literacy as an under-appreciated factor in determining non-adherence to prescribed medication regimens. In various other medical populations health literacy has been extensively studied, and many studies have demonstrated that poor health literacy is linked to worse disease outcomes. The objective of the current project is to build on this research by developing and testing a health literacy educational program, with the goal of supporting and improving immunosuppressant adherence in people who have received kidney transplants.

This project will help determine whether this novel approach of targeting medication adherence through improving health literacy may be effective in this population. Supporting medication adherence in this way can then be more uniformly integrated with healthcare professionals' current care practices, with the ultimate goal of enhancing the management of treatment and organ function in kidney transplant recipients.

# Dr. Ngan Lam

## KRESCENT New Investigator Award



**Institution**: McGill University
**Year**: 2015-2018
**KRESCENT Infrastructure Support**: 2015-2016

Dr. Ngan Lam is a new investigator and transplant nephrologist (Assistant Professor, Division of Nephrology) at the University of Alberta. She completed her fellowships in Nephrology and Clinical Kidney Transplantation at Western University. Dr. Lam also completed her Master of Science in Clinical Epidemiology and Biostatistics at Western University and is a graduate of the KRESCENT Post-Doctoral Fellowship (2012-2015) under the mentorship of Dr. Amit Garg.

Dr. Lam's research focuses on the long-term outcomes of kidney transplant recipients, particularly understanding and reducing cardiovascular disease. Cardiovascular events are a major cause of morbidity and mortality in kidney transplant recipients accounting for 30% of deaths with a functioning graft and remains the number one cause of death in recipients. Her research will utilize healthcare administrative databases to develop her research theme in pharmaco-epidemiology and drug safety in the prevention of cardiovascular disease in Canadian kidney transplant recipients.

# Dr. Fabrice Mac-Way

## Fonds de Recherche du Quebec Santé (FRQS) - KRESCENT Joint New Investigator Award



**Institution**: CHU de Québec Research Center, Hôtel-Dieu de Québec Hospital
**Year**: 2015-2018
**KRESCENT Infrastructure Support**: 2015-2016

Dr. Fabrice Mac-Way is a nephrologist and clinician scientist at Centre de Recherche du CHU de Québec. He is also an Assistant Professor in Laval University's Division of Nephrology. Dr. Mac-Way completed his post-doctoral training in bone biology at Université de Lyon, St-Etienne, where he developed an expertise in the assessment of bone microarchitecture, mineralisation and remodelling (bone histomorphometry analysis) in the context of Chronic Kidney Disease (CKD).

Bone and mineral disorders affect every patient with CKD and are characterized by anomalies of bone morphology and vessel structure. These anomalies then lead to increased morbidity and mortality through bone fractures and enhanced vascular pathology. Recent studies suggest that anomalies in osteocytes (the most abundant bone cells) may contribute to the development of bone remodelling and vascular defects through sclerostin secretion in CKD populations. The objective of Dr. Mac-Way's research is to determine how osteocyte dysfunction leads to bone disorders in CKD through translational research from animal models to humans. Understanding this pathway could lead to new therapies to prevent the development of bone and vessels anomalies in the chronic kidney disease population.

## Dr. Ruth Sapir-Pichhadze, PhD

### KRESCENT New Investigator Award



**Institution**: McGill University
**Year**: 2015-2018
**KRESCENT Infrastructure Support**: 2015-2016

Dr. Sapir-Pichhadze is a new investigator at the McGill University Health Centre and an Assistant Professor, Division of Nephrology and Multi-Organ Transplant Program, at McGill University. She completed subspecialty training in nephrology and kidney transplantation at the University of Toronto, and also completed the Eliot Phillipson Clinician Scientist Program and the Royal College of Physicians and Surgeons of Canada Clinician Investigator Program, where she undertook a Ph.D. in clinical epidemiology and health care research. Her doctoral studies focused on the pathogenesis, diagnosis, and prognosis of antibody-mediated injury secondary to the production of anti-human leukocyte antigen antibodies in kidney transplant recipients and candidates.

Rejection is the leading cause of kidney transplant loss. Antibody-mediated rejection occurs when kidney transplant recipients develop antibodies towards the donor tissue. Donor-specific antibodies emerge as a consequence of structural incompatibility between donor-recipient Human Leukocyte Antigens (HLAs). The objective of Dr. Sapir-Pichhadze's research is to identify strategies that minimize mismatches between donors and recipients and thereby diminish the risk of rejection and kidney transplant loss.

## Oraly Sanchez-Ferras, PhD

### KRESCENT Fellowship



**Supervisors**: Dr. Maxime Bouchard
**Institution**: Goodman Cancer Research Center - McGill University
**Year**: 2015-2018

Dr. Oraly Sanchez-Ferras will pursue her post-doctoral fellowship under the supervision of Dr. Maxime Bouchard at the Goodman Cancer Research Center of McGill University in Montreal. Dr. Sanchez-Ferras seeks to better understand the genetics of CAKUT by studying the molecular pathways and forces that control morphogenesis of the nephric duct during embryonic development.

Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) are amongst the most common congenital diseases and a leading cause of end-stage kidney disease in children. In spite of this clinical relevance there is still a poor understanding of the genes and molecular mechanisms involved in CAKUT. The Nephric Duct (ND) or Wolffian duct is a central component of the urogenital system. A failure of – or inappropriate timing in – ND formation, migration, guidance or insertion into the cloaca is a well-known cause of CAKUT. Dr. Sanchez-Ferras's research will focus on studying the molecular and cellular mechanisms that control morphogenesis of the nephric duct and identify critical regulators of ND collective cell migration downstream of the transcription factor Gata3. Dr. Sanchez-Ferras uses a combination of murine genetics (particularly the CRISPR/Cas9 genome editing technology) as well as time lapse live imaging. With this strategy she expects to find potential therapeutic targets for CAKUT and better understand the genetic networks implicated in renal diseases.

# 2016 KRESCENT Award Recipients

## Dr. Moumita Barua



### KRESCENT New Investigator Award

**Institution**: University Health Network, University of Toronto
**Year**: 2016-2019
**KRESCENT Infrastructure Support**: 2016-2017

Dr. Moumita Barua is a Clinician Scientist and Assistant Professor in the Division of Nephrology at University Health Network and the Department of Medicine at the University of Toronto. She is Associate Director of the Hereditary Kidney Disease Clinic, where individuals with genetic conditions affecting the kidney are seen. She is a Scientist within the Advanced Diagnostics Division at the Toronto General Hospital Research Institute. Dr. Barua completed a KRESCENT postdoctoral research fellowship in one of the leading laboratories in genetic kidney disease at Brigham & Women's Hospital & Beth Israel Deaconess Medical Center.

Dr. Barua's primary research focus is focal and segmental glomerulosclerosis (FSGS), a disorder characterized by abnormalities of the kidney filter. Affected individuals manifest with abnormal protein loss in their urine, leading to a constellation of symptoms collectively called nephrotic syndrome comprising edema, vulnerability to infection and hypercoagulability. More than 50% of patients with FSGS will not respond to standard immunosuppressive treatment, progressing to kidney failure necessitating dialysis or transplantation.

Mutations in more than 40 genes have been found in FSGS and the list continues to grow. Despite advances in the understanding of the genetic causes of disease, there remain significant gaps in knowledge, which limits diagnostic and treatment capability. Past low throughput screens consisting of only a few genes due to constraints of sequencing technology and the rareness of each genetic cause have been a limiting factor in advancing the field and generating knowledge to inform clinical practice.

Dr. Barua's laboratory focuses on developing next-generation sequencing based testing as a diagnostic clinical tool while leveraging it to discover new FSGS genes. Ultimately, her laboratory aims to translate research findings to help guide interpretation of genetic testing in the clinical setting to personalize the care of patients with FSGS in reaching diagnoses, selecting suitable at-risk kidney donors and tailoring treatment options. The laboratory also uses clinically relevant genetic models for mechanistic based studies with the eventual goal of developing targeted therapies to halt or delay disease progression.

## Dr. Justin Chun, PhD

### KRESCENT Post-Doctoral Fellowship



**Supervisors**: Dr. Martin Pollak
**Institution**: Beth Israel Deaconess Medical Center/Harvard Medical School
**Year**: 2016-2019

Dr. Justin Chun will pursue his post-doctoral fellowship under the supervision of Dr. Martin Pollak at the Beth Israel Deaconess Medical Center/Harvard Medical School in Boston, Massachusetts. Dr. Chun will use novel imaging techniques such as super-resolution microscopy to characterize the podocyte slit diaphragm and mutations that cause Focal Segmental GlomeruloSclerosis (FSGS).

Mutations or injury to specialized kidney cells called podocytes can lead to disruption of the kidney's filtration barrier and diseases such as FSGS. Identifying the causes of – and developing treatments for – FSGS has been difficult, due in part to the limitations of experimental methods and models used to study the kidney. Our goal is to combine innovative, state-of-the-art imaging techniques with improved experimental models of the kidney to characterize the podocyte's ultrastructure and how genetic mutations and injury lead to FSGS. We plan to use super-resolution microscopy, an imaging technique awarded the Nobel Prize in chemistry in 2014, to study molecules regulating nano-scale renal architecture. In addition, we will use kidney organoids grown from human stem cells combined with gene editing to study the podocyte slit diaphragm. An improved understanding of the molecular machinery regulating the podocyte slit diaphragm will help identify therapeutic targets to treat FSGS.

## Dr. Ana Konvalinka, PhD

### KRESCENT New Investigator Award



**Institution**: University Health Network, University of Toronto
**Year**: 2016-2019
**KRESCENT Infrastructure Support**: 2016-2017

Dr. Ana Konvalinka is a nephrologist and clinician scientist at the University Health Network, and Assistant Professor at the University of Toronto. She completed training in nephrology and clinical transplantation in Toronto, as well as a Ph.D. in basic science, the Clinician Scientist Training Program, and the Clinician Investigator Program at the University of Toronto. The focus of her doctoral studies is the effect of angiotensin II on the proteome of primary human proximal tubular cells and the relevance of this effect in vivo. During her doctoral research she developed expertise in inflammatory and fibrotic mechanisms of kidney disease progression, as well as approaches based in proteomics and systems biology. Dr. Konvalinka currently leads the Multi-Organ Transplant biobank, which encompasses renal, pancreatic and hepatic programs.

Dr. Konvalinka's main clinical and research interests are in antibody-mediated rejection, which is the leading cause of premature kidney allograft loss. The pathophysiology of antibody-mediated rejection is not completely understood, and therapeutic options are limited. This type of rejection is linked to antibodies directed against the donor allograft; however, not all antibodies lead to allograft injury. Dr. Konvalinka will utilize systems biology and proteomic approaches to identify

antibodies that cause graft injury by studying human tissues and cells, developing improved tests for monitoring such antibody-mediated graft injury as well as identifying potential new treatments for antibody-mediated rejection.

## Yulu Cherry Liu, PhD

### KRESCENT Post-Doctoral Fellowship

**Supervisors**: Dr. Adrian Salic
**Institution**: Harvard Medical School
**Year**: 2016-2019
**Study Title**: Understanding chronic kidney diseases caused by defective retrograde trafficking in the primary cilia, and devising strategies to correct it

#### LAY SUMMARY

In the human body, the main function of cilia is to serve as “cellular antennas”, for detecting and interpreting various environmental signals. Cilia are vital for proper development and function of multiple organs and tissues. Cilia defects lead to human diseases collectively termed ciliopathies, which encompass a wide spectrum of symptoms, including retinal degeneration, polycystic kidney, and skeletal abnormalities. In spite of their critical importance, how cilia defects cause disease remains poorly understood. The main goal of the present proposal is to decipher the molecular link between cilia and disease. Specifically, I aim to elucidate how mutations that affect a critical ciliary process called retrograde trafficking, impair the Hedgehog cell-cell signalling pathway, which plays fundamental roles in embryonic kidney development. To achieve my aim, I propose taking a multidisciplinary approach, combining state-of-the-art biochemistry, proteomics, and chemical biology. First, I will employ complementary strategies to define the molecular organization and protein-protein interactions of the Hedgehog pathway in primary cilia, and to uncover Hedgehog regulation by retrograde trafficking. Next, I will determine precisely how impaired retrograde trafficking, as it occurs in chronic kidney disorders, leads to defective Hedgehog signalling. Finally, through screening and chemical biology, I will discover and characterize small molecules capable of “rescuing” Hedgehog signalling compromised by defective retrograde trafficking. Together, my findings will make important strides toward understanding how ciliopathies develop, and towards novel strategies for treating these devastating human conditions.

## Dr Amber Molnar



### Geoffrey Posen Memorial KRESCENT New Investigator Award

**Institution**: University of Alberta
**Year**: 2016-2019
**KRESCENT Infrastructure Support**: 2016-2017

Dr. Amber Molnar is a new investigator and nephrologist (Assistant Professor, Division of Nephrology) at McMaster University/St Joseph’s Healthcare Hamilton. She completed her fellowship in Nephrology and Master of Science in Epidemiology at the University of Ottawa. Dr. Molnar is a graduate of the KRESCENT Post-Doctoral Fellowship (2013-2015) under the mentorship of Drs. Greg Knoll and Carl van Walraven.

Dr. Molnar's research focuses on improving the care of patients with chronic kidney disease, with a particular focus on cardiovascular complications and improving pre-dialysis care. Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular disease and congestive heart failure. Despite this well known increased risk, patients with CKD are commonly excluded from cardiovascular therapeutic trials. Dr. Molnar will utilize healthcare administrative databases in the province of Ontario to study the effectiveness and safety of commonly prescribed cardiovascular medications in the CKD population. Her research findings will ultimately help guide the design of cardiovascular therapeutic trials in patients with CKD.

## Kara Schick-Makaroff, PhD

### Can-SOLVE CKD - KRESCENT New Investigator Award



**Institution**: University of Alberta
**Year**: 2016-2019
**KRESCENT Infrastructure Support**: 2016-2017

Dr. Kara Schick-Makaroff is a New Investigator at the University of Alberta. She obtained her PhD in Nursing from the University of Victoria. She completed her Post Doctoral Fellowship, funded by the KRESCENT program, with Dr. Anita Molzahn at the University of Alberta.

Building on her Post Doctoral research, Dr. Schick-Makaroff's program of research broadly focuses on enhancing quality of life, enriching person-centred care, and improving services for people affected by chronic kidney disease. This illness significantly impacts peoples' views of their health, emotions, work, and relationships. Clinicians need patients' views about how chronic kidney disease impacts their overall life so that they can respond to any concerns. One way to do this is to use patient-reported outcomes that ask people to share the impact of an illness on their life. Examples of patient-reported outcomes include surveys asking about quality of life or symptoms. Patient-reported outcomes provide vital and often missing information to the healthcare team. The purpose of Dr. Schick-Makaroff's research is to study the impact of routine use of electronically provided patient-reported outcomes data in kidney care settings and to influence positive change in health services. Findings of this research may ultimately improve the quality of health services for Canadians living with chronic kidney disease.

# 2017 KRESCENT Award Recipients

## Dr. Ioan-Andrei Iliuta



### Otsuka Pharmaceuticals Canada - PKD Foundation of Canada - KRESCENT Joint Fellowship

**Supervisors**: Dr. York Pei and Dr. James W. Scholey
**Institution**: University Health Network
**Year**: 2017-2020

After receiving his medical degree at Laval University in 2010, Dr. Iliuta completed residency training in internal medicine (2010-2013) and nephrology (2013-2015) in Quebec City. He then pursued a fellowship in hereditary kidney disease under the supervision of Dr. York Pei at Toronto General Hospital, University Health Network, while undergoing graduate training in the Translational Research Program at the Institute of Medical Science, University of Toronto. His clinical interests range from autosomal dominant polycystic kidney disease to tuberous sclerosis complex and inherited tubulopathies. His current research focuses on investigating novel disease-modifying therapies for the treatment of polycystic kidney disease. In the fall, he will be starting a Ph.D. in biomedical science at the University of Toronto, with a focus on the therapeutics of AMP kinase in polycystic kidney disease.

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is an inherited form of kidney disease that manifests in adults in which numerous cysts enlarge progressively until they cause severe kidney failure requiring dialysis or a transplant. Although ADPKD is a major cause of kidney failure in North America, effective treatments to slow disease progression are lacking. By acting on specific pathways involved in the metabolism of cyst cells (specifically, energy sensing and production) in APDKD either through drug combinations or dietary changes, we hope to attenuate the severity of renal disease: this would result in smaller kidneys, better quality of life, and a longer interval to kidney failure.

## Vinusha Kalatharan



PhD Candidate

### KRESCENT Allied Health Doctoral Scholarship

**Supervisors**: Dr. Amit Garg and Dr. York Pei
**Institution**: University of Western Ontario
**Year**: 2017-2018

Ms. Vinusha Kalatharan will complete her fellowship under the supervision of Dr. Amit Garg and Dr. York Pei at The University of Western Ontario, where she is currently pursuing her Ph.D. in epidemiology and biostatistics.

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a genetic disorder with no cure. Urinary tract stones are five to ten times more common in patients with ADPKD compared to the general population and increase morbidity by causing pain and accelerating disease progression. For these reasons, stones require effective management in patients with ADPKD. Recurrent pain, blood in urine, urinary tract obstruction, or infection caused by stones may demand an urgent intervention to remove the stone. However, reduced kidney function and distorted kidney anatomy in this population may make performing these interventions more challenging than the general population. Strong evidence on the safety and efficacy of urological interventions as well as the associated operative and post-operative healthcare costs for urinary tract stone removal in patients with ADPDK is lacking.

Ms. Kalatharan aims to:

1) Describe and compare the incidence of urological interventions for urinary tract stone removal in patients with ADPKD to non-ADPKD counterparts;
2) Describe and compare the 30-day incidence of complications following a urological intervention for stone removal in patients with ADPKD to non-ADPKD counterparts; and
3) Describe and compare the operative and perioperative healthcare costs of urological intervention for stone removal in patients with ADPKD to their non-ADPKD counterparts.

She will conduct several population-based studies using Ontario's healthcare administrative databases held at the Institute for Clinical Evaluative Sciences, applying statistical and health economics analyses to address these objectives. Research findings from these studies may help modify and inform future clinical practice guidelines on the management of urinary tract stones in ADPKD.

## Dr. Thomas Kitzler

### KRESCENT Fellowship



**Supervisors**: Dr. Friedhelm Hildebrandt
**Institution**: Boston Children's Hospital – Harvard Medical School
**Year**: 2017-2020

Dr. Thomas Kitzler will complete his research fellowship under the supervision of Dr. Friedhelm Hildebrandt at Boston Children's Hospital – Harvard Medical School. His project focuses on the discovery and characterization of novel kidney disease genes by means of whole-exome sequencing and zebrafish animal models. These models will then be used to screen for novel targeted therapies. Dr. Kitzler completed his medical residency at the Department of Medical Genetics at McGill University, where he was also involved in basic research in the field of nephrology. Dr. Kitzler obtained his degree at the Medical University of Graz, Austria.

Nephronophthisis (NPHP) is an autosomal-recessive cystic kidney disease and is the most frequent genetic cause of Chronic Kidney Disease (CKD) in the first three decades of life. It has been demonstrated in recent years that NPHP shows a high degree of genetic heterogeneity. Elucidating the underlying genetic and molecular pathomechanisms of hereditary kidney disease is paramount for identifying at-risk individuals and the development of novel targeted therapies to alter or hopefully even reverse disease progression.

Dr. Kitzler will characterize novel NPHP candidate genes. He will then use zebrafish models to screen for novel targeted therapies for genetic causes of kidney disease for which no treatment currently exists.

Dr. Friedhelm Hildebrandt at the Boston Children's Hospital is a world leader at identifying new genes which, when altered, cause kidney disease. The goal of Dr. Kitzler's project is to better understand the role of a recently identified kidney disease gene discovered in a family from Montreal. He will use Dr. Hildebrandt's database of more than 1,500 families with unsolved cases of kidney disease to screen for other families with changes in this gene. To do this, he will use state-of-the-art technology such as whole-exome capture and next-generation sequencing. These methods allow us to look at a vast number of genes in an efficient manner. He will then use well-known animal models of nephronophthisis, such as zebrafish, to further detail how this gene causes kidney disease and screen for new therapies, hopefully leading to the development of new treatment options for genetic forms of kidney disease.

## Dr. Caroline Lamarche

### KRESCENT Fellowship



**Supervisors**: Dr. Megan Levings
**Institution**: BC Children's Hospital/University of British Columbia
**Year**: 2017-2020

Dr. Lamarche will complete her post-doctoral fellowship under the supervision of Dr. Megan Levings at BC Children's Hospital/University of British Columbia, where she will work on methods to tailor antigen-specific regulatory T cells for their use in transplantation.

Transplantation is the best and sometimes only treatment for end-stage organ failure. In the last ten years the lives of more than 20,000 Canadians have been improved, extended, or saved by donated organs. Immunosuppressive drugs make transplantation possible, but since these drugs suppress the entire immune system and not just the cells reactive to the transplanted organ they come at the price of an increase in infection and cancer risk. The drugs are also not perfect; many organs are still lost to rejection.

Our goal is to improve transplantation success by finding ways to re-educate the recipient's immune system to tolerate the transplanted organ. Our strategy is to harness the natural immunosuppressive properties of a type of white blood cell called T regulatory cells (Tregs). Tregs naturally regulate immune responses by ensuring the immune system attacks infectious or harmful substances without over-reacting to self or non-harmful foreign proteins. In the last 10 years research has shown that Tregs could be used as a cell-based therapy to induce immune tolerance and prevent organ rejection. The efficacy of Treg cell therapies can be significantly enhanced if the cellular product is enriched for Tregs that recognize a target specific to the transplanted organ. Dr. Levings's lab developed a method to improve the potency of Tregs by engineering them to express an activator protein when they are in the presence of a transplant. Dr. Lamarche's goal is to study the potential of those engineered Tregs to control allograft rejection and lower the chances that transplant recipients will reject the donor organ.

# Dr. Matthew Lanktree, PhD

## KRESCENT Fellowship



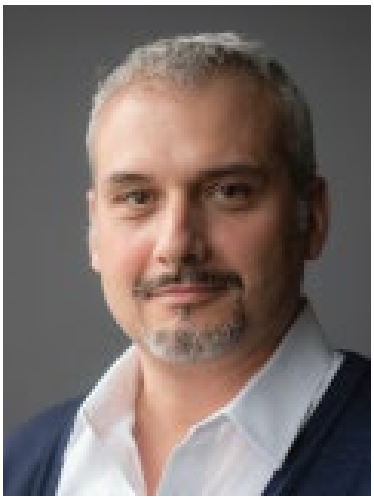
**Supervisors**: Dr. Andrew D. Paterson and Dr. York Pei
**Institution**: University Health Network
**Year**: 2017-2019

Dr. Matthew Lanktree began research training during an undergraduate degree in bioinformatics at the University of Waterloo, followed by a combined M.D./Ph.D. at the University of Western Ontario studying complex disease genetics. He then completed a residency in internal medicine and a clinical fellowship in nephrology at McMaster University before moving to the University of Toronto to pursue a post-doctoral research fellowship in heritable kidney diseases that include polycystic kidney disease. Dr. Lanktree has received funding from the Canadian Institutes of Health Research and the American Society of Nephrology, and is a member of the Kidney Foundation's KRESCENT program. Over the last 15 years Dr. Lanktree has published over 50 articles in high impact journals in genetics and medicine and has set a goal of improving outcomes for patients with polycystic kidney disease.

Therapies for polycystic kidney disease attempt to maintain kidney function and slow progression towards kidney failure, which eventually results in dialysis or kidney transplantation. Patients at the highest risk of disease progression have the most to benefit from early initiation of aggressive therapy. Large kidney size can help identify patients at high risk of progression, as can identification of the associated genetic mutation. We seek to incorporate these data sources, imaging and genetics, and clinical risk factors to improve our ability to identify patients at highest risk of kidney failure. Additionally, we will further stratify patients and attempt to identify new treatments and possibly a cure for polycystic kidney disease through the analysis of genetic and molecular tests of blood, urine and kidney cyst fluid combined with "big data" from international collaborations.

# Dr. Mathieu Lemaire, PhD

## KRESCENT New Investigator Award



**Institution**: University Health Network, University of Toronto
**Year**: 2017-2020
**KRESCENT Infrastructure Support**: 2017-2018

### 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. Then, he went to Yale University (New Haven, CT) to pursue a PhD in Investigative Medicine under the supervision of Dr Richard P. Lift on 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

## LAY SUMMARY:

Blood vessels are like roads that can reach any cell of our body. We call the cells that line blood vessels "endothelial cells". Blood flows fast in normal blood vessels, but it is slow when there is damage. It forms a blood clot. This is similar to a “good traffic jam”: it helps repair injured blood vessels. The body must control the machines that help with repair to avoid “bad traffic jams”. Healthy blood vessels don't need blood clots. In the lab, we study the function of endothelial cells in the kidneys. We work on a disease called "atypical hemolytic-uremic syndrome". For simplicity, we call it "aHUS". Patients with aHUS get kidney failure. Why? Blood clots form in the blood vessels of the kidneys. These clots prevent normal blood flow in kidneys. Blood flow is important to deliver food and oxygen to the kidneys.

We found that mutations in the gene DGKE can cause aHUS. Each cell in the body contains DNA, a code made of genes. Genes make proteins—the building blocks of cells. Mutations are changes in the DNA that cause abnormal function of a protein. For our patients, the mutations prevent DGKE from working well. DGKE is an enzyme that work on fats. DGKE stands for "diacylglycerol kinase epsilon". Diacylglycerol is also called DAG. Enzymes are like machines that do specific tasks in cells. For example, a kinase adds a phosphorus group to its target. DGKE is a kinase that targets one type of fat named DAG. Cells use DAG as a signal to turn on specific functions. It is like a light switch. When DGKE modifies DAG, it turns off the signal in the cell. When DGKE can't work, it is as if the light switch is left on too long. When that happens, patients cannot prevent blood clotting in their kidneys. These patients develop kidney failure, and we have no treatment to offer.

We study endothelial cells that have no DGKE at all. We have found three clues that help guide this project. First, we found that when DGKE does not work, it affects the function of AKT, another protein that is like a light switch. In particular, AKT turns on another protein called eNOS. Second, we also found that the function of eNOS is abnormal in cells that have no DGKE. AKT and eNOS play a major role in making sure that blood vessels stay open and are not too sticky. We don't know how DGKE deficiency causes problems with AKT and eNOS, or how this affects blood vessels. Third, we also noticed that endothelial cells that have no DGKE protein have difficulties to function normally when exposed to blood flow. The endothelial cells are like flags that are not well attached to their pole when there is high wind: they fly away leaving blood vessels without a lining.

This project will tackle four different tasks to help us understand better DGKE function in endothelial cells:

1) Figure out how a deficiency in DGKE leads to abnormal AKT function in endothelial cells
2) Find out how abnormal eNOS function affects the function of blood vessels that have no DGKE protein
3) Determine how DGKE deficiency prevents endothelial cell to withstand normal blood flow
4) Study how DGKE mutations found in patients with aHUS affect the function and structure of DGKE enzymes

This research is important so we can start thinking about new treatment for this disease. Studies on the function and structure of DGKE could be helpful to diagnose patients with new mutations. It will also teach us a lot about how normal blood vessels prevent blood clot formation.

# 2018 KRESCENT Award Recipients

## Dr. David Collister, PhD

### KRESCENT Fellowship



**Institution**: McMaster University
**Year**: 2018-2020
**Study title**: Dialysis Symptom Control-Restless Legs Syndrome (DISCO-RLS) trial

### LAY SUMMARY

Patients with kidney disease are often excluded from research studies examining new drugs and technologies because of their renal dysfunction. This puts kidney disease patients at a disadvantage, as they are often afflicted with other illnesses independent of their kidney disease. The Kidney Foundation has previously prioritized the investigation of knowledge gaps in the treatment of patients with kidney disease by increasing the number of research studies focused on key questions related to patients, their caregivers and their doctors, and acknowledges the need for high quality studies and the creation of networks to investigate relevant questions through randomized clinical trials. These types of studies are Dr. Collister's area of focus and constitute some of the most reliable evidence to guide clinical decision-making.

Restless Legs Syndrome (RLS) is a disorder of the nervous system that causes an uncontrollable urge to move your legs or other body parts. RLS affects 30% of dialysis patients and is bothersome, disrupts sleep and decreases quality of life. Symptoms are common in dialysis patients but are not optimally managed despite being a patient, caregiver and physician research priority. In patients without kidney disease there is a significant amount of research dedicated to treating this condition, but in individuals with kidney disease – in which the disorder is thought to be possibly different in its origins – only a handful of clinical trials have been performed and each is associated with specific limitations.

Dr. Collister's research focuses on treating symptoms in dialysis patients so they feel better and have a better quality of life. He will be performing a pilot clinical trial of two different types of medication – individually and in combination – compared with placebo(s), (pills that look, smell, taste and feel the same as real drugs but do not contain any medication), for RLS in dialysis patients to determine the feasibility of a larger study. The larger study will include multiple sites across Canada with the goal of identifying the best way to control symptoms associated with this challenging condition in the context of the cluster of symptoms that are common in dialysis patients, including depression, anxiety, fatigue, itchiness and pain. Dr. Collister also hopes to study these latter symptoms in future clinical trials of drugs and other interventions that will eventually help kidney disease patients and their families.

# Dr. Casimiro Gerarduzzi, PhD

## KRESCENT New Investigator Award



**Institution**: Hôpital Maisonneuve-Rosemont
**Year**: 2018-2021
**Study title**: The role of matricellular proteins in kidney repair and development

### LAY SUMMARY

The proper functioning and survival of cells require an accommodating environment, similar to a seed surrounded by fertile soil. This soil, which we call the ExtraCellular Matrix (ECM), surrounds cells (seeds) with the optimal conditions required for cells to thrive and function correctly.

Diabetic patients develop significant damage to the kidney's ECM structure (composition and texture), which then requires continuous repair using new ECM materials. ECM repair can remain continuously activated in patients with diabetic kidney disease, and although it seems counterintuitive this "turned on" repair is harmful to cells due to a continuous buildup in new ECM material that eventually replaces the cells needed for proper kidney function. By attempting to return a chronically injured kidney back to health this process actually leads to serious and life-threatening complications and eventually death.

The ECM is also very important in kidney cancer. ECM "soil" is markedly different between normal cells and cancerous cells, and researchers have recently discovered that the structure of cancerous ECM (bad soil) evolves to be different from that of a normal kidney (good soil), thereby developing into an optimal environment for the continued growth of cancer cells (bad seeds). Cancerous ECM evolves even further in a way that supports cancer metastasis, allowing cancer cells to spread to other parts of the body. In this context, identifying and inhibiting factors that regulate ECM expression and processing represent an attractive therapeutic avenue to inhibit the growth and metastasis of cancer cells in Renal Cell Carcinoma patients (RCC).

Learning more about the ECM is an exciting opportunity to correct its regulation during excessive and uncontrolled ECM remodeling in life-threatening conditions such as diabetic kidney disease and RCC. Our laboratory has taken the approach of screening large amounts of genes and proteins in RCC and diabetic kidney disease to identify those involved in ECM regulation. We have an excellent team of nephrologists and renal biomedical researchers working together to validate our identified genes/proteins in diabetic kidney disease and RCC patients, and we will then be able to better understand their relevance to diabetic kidney disease and RCC in well-established animal models. Finally, we will use our animal models to test for new therapeutic options that will improve the quality of life of patients with kidney disease.

# Dr. Paraish Misra, PhD

## KRESCENT Fellowship



**Supervisor**: Dr. Maria Cristina Nostro and Dr. Darren Yuen
**Institution**: University of Toronto
**Year**: 2018-2021
**Study title**: Characterizing the potential of stem cell-derived insulin-producing cells as a treatment for diabetic nephropathy

### LAY SUMMARY

Diabetes is the most common cause of kidney failure in Canada and the United States. Diabetic kidney disease is usually the result of the inadequate control of blood sugar, which is common among patients treated with standard insulin therapy. It has been demonstrated that pancreatic transplantation can normalize blood sugar levels and reverse diabetic kidney disease, but this therapy is limited by a scarcity of organs for transplantation.

Insulin-producing cells can now be generated in vitro from human stem cells, and these so-called “beta-like cells” are currently being tested in clinical trials for the treatment of diabetes. Similar to pancreatic transplantation, beta-like cells normalize blood sugar levels in diabetic animals and may thus be effective for the treatment of diabetic kidney disease.

The aim of this project is to determine whether transplantation with human beta-like cells can be used to treat diabetic kidney disease. As one of the first ever studies of its kind, these cells will be tested in an animal model of diabetes. After studying the natural course of diabetic kidney disease in this model, untreated and transplanted diabetic animals will be followed for the development of changes in kidney structure and function. In this way the effect of beta-like cells on diabetic kidney disease will be determined.

This project has the potential to identify a novel therapy for diabetic kidney disease for which few treatments are currently available. By determining the potential benefits of beta-like cell therapy, this work will hopefully contribute to their application in clinical practice and improve the quality of life of diabetic patients.

# Dr. Samuel Silver

## KRESCENT New Investigator Award



**Institution**: Queen's University
**Year**: 2018-2021
**Study title**: Primary care physician involvement and quality of care for patients on dialysis

### BIOGRAPHY

Samuel Silver is an Assistant Professor in the Division of Nephrology at Queen’s University in Kingston, Ontario, Canada. He completed his clinical training in internal medicine and nephrology at the University of Toronto. He holds a Master of Science in quality improvement and patient safety and completed the Veteran Affairs Quality Scholars program at the University of California-San Francisco. Samuel then trained as a research fellow at Stanford University, with a focus on health services research. The objective of his research program is to use administrative data and systematic reviews to inform the design of quality improvement interventions that may improve patient outcomes. Samuel’s research interests

focus on the delivery of care for patients with acute kidney injury, both during the inpatient and outpatient setting. He is also starting to expand his work to patients on in-center hemodialysis. Samuel currently lives in Kingston, Ontario, with his wife and three young children.

## LAY SUMMARY

**Background**: Patients on dialysis have high healthcare needs that go beyond their regular dialysis treatments. Therefore, their care also includes preventative health, symptom management, mental health, and acute illness. Given patients' frequent presence in the dialysis unit, they may lose contact with their family doctor. The nephrologist is often asked to fill this gap and provide primary care despite little training dealing with issues that are more commonly handled by family doctors. This situation may lead to poor quality care. In other illnesses like diabetes and heart disease, patients who see their family doctors more often have better outcomes. No study has looked at whether the same applies to patients on dialysis, which could help change care for patients that respects patient time, healthcare provider expertise, and healthcare system costs.

**Research Plan**: The study aims are to describe the current role family doctors play for patients on dialysis, identify barriers to family doctor visits, and determine which processes and outcomes are improved by more frequent visits to a family doctor. To reach these goals, we will complete several studies using routinely collected patient and healthcare system information from 2003 to 2012 that is stored at the Institute for Clinical Evaluative Sciences (ICES) in Ontario, Canada. This data will allow us to compare patients with more family doctor visits to patients with fewer family doctor visits. We will look for an effect on care processes, (flu vaccination, cancer screening tests, and rehabilitation after a stroke or heart attack), selection of home dialysis, admission to hospital, and death.

**Impact**: My research program involves a stepwise approach to identify problems in healthcare that can then be targets for improvement:

1. Identify problems with routinely collected health information
2. Meet with patients and healthcare provides to develop solutions
3. Test different solutions on a small-scale in real clinical practice
4. Evaluate solutions on a larger scale, with a focus on studies that can be evaluated with routinely collected health information at ICES

This work will clarify the role that family doctors currently play for patients on dialysis and determine whether more contact with a family doctor improves patient outcomes. Once these studies are complete, future work will involve meeting with patients, family doctors, and nephrologists to discuss the results and develop strategies for better integration of the care provided to patients in dialysis programs and primary care settings.

# Vanessa Silva e Silva

PhD Candidate



## KRESCENT Allied Health Doctoral Scholarship

**Supervisor**: Dr. Joan Tanmer
**Institution**: Queen's University
**Year**: 2018-2020
**Study title**: Determining the influence of processes, structure and inter-professional relational networks within organ donation programs in Ontario

### LAY SUMMARY

**Background**: To optimize the impact of organ donation and transplantation the nature and impact of complex organizational characteristics, such as inter-professional roles and relationships and the hospital organization's structure and processes, need to be understood. We know that performance indicators vary among hospitals in the same province, even in the presence of common program structures and support. Therefore, the overall aim of this research is to understand and measure the nature and impact of relationships within the organizational context of organ donation programs in Ontario.

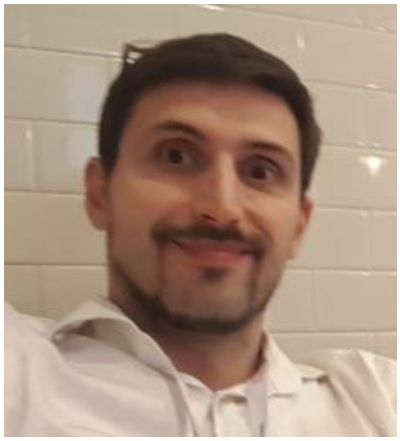
**Methods**: We will systematically investigate the interactions of the health professional network in the context of the organ donation process, and the influence of these interactions on the outcomes of Ontario organ donation programs by applying a social network analysis approach. We will also explore the influence of organizational attributes, processes of organ donation programs, and individual collaboration on organ donation performance amongst Ontario hospitals using a multiple case-study approach. Finally, we will compare similarities and differences of the influence of social networks and organizational attributes on the performance of organ donation programs amongst Ontario hospitals. Our study will include at least five trauma centre hospital partners of Ontario's Organ Procurement Organization.

**Expected outcomes**: Our research will result in novel findings regarding the enablement of organizational attributes and processes relevant to organ donation programs. We will also determine the utility of applying detailed organizational evaluations to this complex process. Aligned with the Kidney Foundation's mission, our findings will guide the development of organizational interventions designed to optimize the organ donation process and corresponding outcomes. These interventions should, in turn, enhance the availability of organs for transplant and improve the overall organ donation process. The end result should be shorter organ transplant waiting lists, to the benefit of at-risk individuals affected by kidney disease or any other chronic conditions that lead to organ failure.

# 2019 KRESCENT Award Recipients

## Sergi Clotet-Freixas, PhD

### KRESCENT Post-Doctoral Fellowship



**Supervisor**: Dr. Ana Konvalinka
**Institution**: University Health Network
**Year**: 2019-2022
**Study title**: Sex and Human Kidney Metabolism: New Insights into Diabetic Kidney Disease

### BIOGRAPHY

Dr. Sergi Clotet-Freixas completed his Bachelor of Biotechnology at the Universitat Autònoma of Barcelona (2010), and a Master's degree in Biomedical Research at the University of Barcelona (2011). In 2012, he embarked on a PhD in basic science at the Hospital del Mar in Barcelona. The aim of his PhD was to explore the effect of sex on experimental diabetic kidney disease (DKD) and the renin-angiotensin system. Dr. Clotet-Freixas uncovered a critical role of androgens and a sex-specific role of angiotensin-converting enzyme 2 in DKD progression. These observations are relevant from a clinical perspective, as they may shed new light on sex-specific approaches to the treatment of DKD. As a PhD student, Dr. Clotet-Freixas also discovered a novel link between male sex hormones and impaired energy metabolism in the diabetic kidney, which may help to understand the more rapid kidney disease progression associated with male sex. Since completion of his PhD, he has been working as a post-doctoral fellow in the lab of Dr. Ana Konvalinka at the University Health Network in Toronto. Dr. Clotet-Freixas is continuing to study the role of cell sex and sex hormones on the metabolic function of renal tubular cells, and these studies have received funding support from CIHR Catalyst Grant. Dr. Clotet-Freixas is also expanding his expertise in other kidney-related disease settings by studying the mechanisms involved in antibody-mediated rejection, acute cellular rejection and acute tubular necrosis after kidney transplantation.

### LAY SUMMARY

Being a man is harder for the kidney than being a woman. Male sex predisposes to the development of several diseases affecting the kidney, known as chronic kidney disease (CKD). People with diabetes are at high risk of CKD as their kidneys are injured by high levels of glucose. These patients may develop diabetic kidney disease (DKD), the most predominant type of CKD. The harmful effect of male sex in DKD and CKD may be due to actions that the male sex hormones (known as androgens) exert on the kidney cells. However, researchers are still trying to discover what happens in kidney cells when they are in contact with androgens. Understanding how androgens are able to damage kidneys will allow the clinicians to apply more personalized treatments of kidney disease, depending on the patient's sex.

Dr. Clotet-Freixas discovered that androgens affected the metabolism of kidney cells. Kidney cells with impaired metabolism may not be able to take up nutrients from their environment and use them to generate energy and work properly. Altered metabolism could be the reason why androgens are bad for the kidney. Metabolism is a very complex process based on the actions of many proteins that transform the nutrients to metabolites, used to make energy and build cellular machinery. He will study which of these proteins and the molecules that transport these proteins into the kidney

cells are more implicated in the bad effects of androgens in the kidney. He will also study how estrogens (the female sex hormones) alter these processes in a different way, and may also predispose diabetic women to develop kidney diseases, but at a later moment and in a different fashion than men. In this project, he will discover proteins and processes through which androgens damage the kidneys faster and to a greater extent than estrogens, and propose how this can be stop, thus preventing CKD and DKD. The proposed research may lead to sex-specific therapies for kidney diseases.

# Dr. Meghan J. Elliott

## KRESCENT New investigator award



**Institution**: University of Calgary
**Year**: 2019-2022
**Study title**: Supporting Engagement in Chronic Kidney Disease Care and Research

### BIOGRAPHY

Dr. Meghan Elliott is a nephrologist and Clinical Assistant Professor at the University of Calgary. She completed her clinical nephrology training at the University of Calgary and earned a Master of Science degree in Clinical Epidemiology at the University of Toronto in 2018. Her graduate work focused on patient and stakeholder engagement in chronic kidney disease research. Her research program aims to support patient, family and provider engagement in person-centered kidney care and research. Using qualitative and mixed methods research approaches, she is exploring patient and provider care experiences, strategies to implement best evidence, and approaches to meaningfully partner with patients in research. She is involved in supporting knowledge translation and patient engagement within the national, patient-oriented kidney research network, Can-SOLVE CKD.

### LAY SUMMARY

Chronic kidney disease, commonly referred to as CKD, affects 1 in 10 adults in Canada. People living with CKD can experience many symptoms (such as fatigue and nausea) and may develop kidney failure that requires dialysis or kidney transplantation. By taking an active role in their own kidney health, persons living with CKD can gain knowledge, skills, and confidence about their condition and ensure they receive the care that is best for them. The same is true about patient involvement in kidney health research. It has become increasingly common for research teams to involve patients as partners in their projects; that is, doing research “with” patients rather than doing research “on” or “about” them. Involving patients as partners in kidney research can help them gain knowledge, skills, and a shared sense of community, as well as ensure the research is more relevant and impactful. The purpose of Dr. Elliott research is to better understand the needs and experiences of people living with CKD so that they can meaningfully participate in their care and in kidney health research.

Her research plan will include 4 projects: (1) Understanding the roles of patient partners within the patient-oriented kidney research network, Can-SOLVE CKD; (2) Understanding how symptoms are reported and addressed in hemodialysis units; (3) Exploring the support needs for patients with early stages of CKD, including the role of peer support; (4) Exploring the experiences of hospitalized CKD patients and developing a strategy to treat CKD complications outside of the hospital setting. The topics addressed by the proposed research, particularly those related to symptoms and CKD supports, have been identified as research priorities for persons living with CKD. All projects have a patient focus, meaning they aim to understand patient needs and experiences so that CKD care can be provided for the person as a whole -- physically, emotionally, mentally, and socially. She will be engaging with patient partners in different ways and in many aspects of this research, including conducting qualitative interviews and analysis, and observing symptom reporting in dialysis units.

Findings will help us better understand CKD patients' experiences and needs related to their kidney health and their involvement in research. This will directly impact how care for persons with CKD is provided (for example, how symptoms are managed on dialysis, or how peer support needs are addressed) and will also identify strategies to enhance research partnerships with patients.

## Janine Farragher, PhD

### KRESCENT Post-Doctoral Fellowship



**Supervisor**: Dr. Brenda Hemmelgarn
**Institution**: University of Calgary
**Year**: 2019-2022
**Study title**: A Pilot randomized control trial of the PEP Program for Adults on Chronic Dialysis with Fatigue

### BIOGRAPHY

Dr. Janine Farragher is an occupational therapist and a postdoctoral research fellow at the University of Calgary, where she is supervised by Dr. Brenda Hemmelgarn. Dr. Farragher completed her PhD in Rehabilitation Sciences Institute at the University of Toronto, where her dissertation focused on fatigue in people with kidney disease who undergo dialysis. Fatigue is a very common symptom of kidney disease, which can interfere with people's ability to live their lives to the fullest.

### LAY SUMMARY

People who have kidney failure (ESRD) often feel unusually tired, which interferes with their ability to live life normally. During her doctoral degree, Dr. Farragher has created a program (The PEP Program) that teaches people with ESRD how they can manage their energy during their everyday life, using strategies like prioritizing, organizing home and workspaces, and using good body postures. These techniques have been found to help people who have fatigue because of other illnesses (eg. multiple sclerosis) but haven't been tested for people with ESRD. A large study is needed to see whether the PEP program is helpful for people with ESRD, but first, Dr. Farragher will need to do a smaller-scale practice (or pilot) study to help plan this large study.

The purpose of this practice study is to see whether people with ESRD are able to do the PEP program, to see what they think of the program, and to see how many people need to be included in the large study. She plans to invite 40 people with ESRD from dialysis units across Calgary, Alberta to participate. People with ESRD who report feeling unusually tired a lot of the time (based on a symptom assessment tool completed every 2 months) will be asked to take part in the study. People who agree will either do the PEP program, or another program that gives them general information about kidney disease. She will measure whether the PEP program helps people feel less tired, by asking them to complete questionnaires before and after the study. She will also interview people after they participate in the study, to learn what they think. This practice study will help plan next steps for the PEP program, with an aim to improve the lives of people with kidney failure.

# Dr. Tyrone Harrison

## KRESCENT Post-Doctoral Fellowship



**Supervisor**: Dr. Brenda Hemmelgarn
**Institution**: University of Calgary
**Year**: 2019-2022
**Study title**: Improving the perioperative care of patients with end-stage renal disease

### BIOGRAPHY

Dr. Harrison received his medical degree from the University of Calgary in 2013, which was followed by residency training in Internal Medicine and Nephrology (completed in 2018). Dr. Harrison has now begun his doctoral studies at the University of Calgary by pursuing a PhD in Health Services Research, as part of the Clinician Investigator Program. He is completing this training with supervisor and clinician-scientist Dr. Brenda Hemmelgarn. His research, while a KRESCENT post-doctoral fellow, is focused on understanding and improving the perioperative management of patients with end-stage kidney disease.

### LAY SUMMARY

In Canada, approximately one in nine adults have a surgical procedure each year, and of those, one in twenty have a major cardiovascular event (heart attack, heart failure, stroke etc.) around the time of surgery. These cardiovascular events around the time of surgery have significant implications with one third of cases resulting in death, in addition to prolonged hospitalization, and increased health care costs. End-stage renal disease (ESRD), or kidney failure, requires either kidney transplantation or dialysis initiation as life sustaining therapy. Patients with ESRD have an overall risk of cardiovascular death 10-20 times that of the general population. Despite this high risk, little is known about the risk faced by ESRD patients around the time of surgery, and how best to detect individuals at highest risk. Recommendations from current Canadian guidelines include risk scores and blood tests to be drawn prior to surgery, but these tools are not well-understood in patients with ESRD.

Research is needed to provide care for ESRD patients that is specifically designed for use in this important patient population. With this KRESCENT supported research, Dr. Harrison will first characterize predictors of post-operative cardiovascular events and death in ESRD patients in a population-based cohort of patients, which will lead to development of an ESRD-specific risk prediction model for use in the perioperative period. Finally, patients and perioperative experts will be consulted to identify consensus-based best-practices to be incorporated into perioperative pathways for the care of ESRD patients. Ultimately, if researchers are able to understand and predict the risk of ESRD patients around the time of surgery, the developed ESRD care pathway will reduce and prevent unnecessary and potentially life-threatening cardiovascular events for patients.

# Dr. Gregory Hundemer

## KRESCENT New Investigator Award



**Institution**: Ottawa Hospital Research Institute, University of Ottawa
**Year**: 2019-2022
**Study title**: Characterizing Renal Outcomes in Overt and Subclinical Aldosterone Excess

### BIOGRAPHY

Dr. Greg Hundemer is a nephrologist and clinician-scientist at The Ottawa Hospital/University of Ottawa. He completed his nephrology training at the Brigham and Women's Hospital/Massachusetts General Hospital Joint Fellowship Program in Boston, Massachusetts. During his fellowship, Dr. Hundemer was awarded the 2017 Young Investigator Award by the International Aldosterone Society, the F32 National Research Service Award and the K23 Research Career Development Award from the National Institutes of Health in support of his research under the mentorship of Dr. Gary Curhan and Dr. Anand Vaidya.

Dr. Hundemer's research focuses on the effects of overt and subclinical forms of aldosterone (a hormone which stimulates absorption of sodium by the kidneys and so regulates water and salt balance) excess on renal and cardiovascular outcomes. Primary aldosteronism, a form of secondary hypertension defined by autonomous aldosterone secretion from the adrenal glands, is increasingly recognized as a common, yet vastly under-diagnosed, form of hypertension. Primary aldosteronism results in disproportionately higher rates of renal and cardiovascular disease compared with other forms of hypertension. The goals of Dr. Hundemer's research are: 1) to identify treatment strategies to improve health outcomes in patients with primary aldosteronism; and 2) to study the long-term consequences of subclinical forms of primary aldosteronism on renal and cardiovascular health.

### LAY SUMMARY

Dr. Hundemer is a Clinician-Investigator in the Division of Nephrology at the Ottawa Hospital, an Assistant Professor at the University of Ottawa, and an Associate Scientist at the Ottawa Hospital Research Institute. His research focuses on hormonal causes of renal and vascular disease, in particular overt and subclinical forms of aldosterone excess. His non-traditional background has been instrumental in preparing for a career in clinical research. Following medical school, while serving multiple combat deployments as a United States Air Force flight surgeon for the U-2 high altitude spy plane, he helped manage an outbreak of decompression sickness among the pilots through clinical investigation. The findings resulted in a government expenditure of $8.7 million in 2013 to increase the U-2 cockpit pressurization; no further episodes of decompression sickness have occurred since.

This unique experience sparked a passion for clinical research, resulting in obtaining a Master of Public Health degree from Johns Hopkins University concurrent with his military service. Following his service, he returned to medicine completing his internship and residency in internal medicine at Massachusetts General Hospital (2012-15) and his fellowship in nephrology at the joint Massachusetts General Hospital/Brigham and Women's Hospital training program (2015-18). During his fellowship, he developed a keen interest in the renal and cardiovascular effects of aldosterone excess.

Under the mentorship of Dr. Gary Curhan, he was the lead investigator for multiple high-impact studies demonstrating that the current guideline-recommended treatment approaches to primary aldosteronism are inadequate at mitigating adverse renal and cardiovascular outcomes. However, utilizing renin as a biomarker to guide therapy could dramatically improve

outcomes in the future. The degree of renin suppression serves as a biomarker for subclinical primary aldosteronism, a condition affecting a large, but currently unrecognized, population.

# Dr. Matthew Lanktree, PhD

## KRESCENT New investigator award



**Institution**: McMaster University
**Year**: 2019-2022
**Study title**: Assessing the Omnigenic Contribution to Chronic Kidney Disease

### BIOGRAPHY

Dr. Matthew Lanktree is a clinician scientist in nephrology genetics at McMaster University. Dr. Lanktree obtained an undergraduate degree in bioinformatics at University of Waterloo, followed by a combined MD/PhD at Western University with special training in human genetics. Moving to McMaster, he completed clinical training in internal medicine and nephrology, before moving to University of Toronto for a post-doctoral research fellowship in heritable kidney disease under Drs. York Pei and Andrew Paterson. Dr. Lanktree has received funding from the Canadian Institutes of Health Research, is the recipient of the Jared G. Grantham Fellowship of the American Society of Nephrology, and a post-doctoral fellowship followed by a new investigator award from the Canadian Kidney Research Scientist Core Education National Training (KRESCENT) program. Over the last 15 years, Dr. Lanktree has published over 60 articles in high impact journals in genetics and medicine, including recent articles in Journal of the American Society of Nephrology, and Nature Reviews Nephrology. Dr. Lanktree has set his goal to translate genetic studies into improved care of patients with kidney disease. The genetics field has been quick to recognize the importance of large collaborations to generate samples sizes required to confidently identify genetic variants with small but important effects. He has been fortunate to lead and participate in such collaborations and want to work to include more multi-disciplinary professionals, as well as patient partners, into his research program in his new position as a clinician scientist at McMaster University.

### LAY SUMMARY

Kidney disease affects 1 in 10 Canadians. 35,000 Canadians currently have kidney failure needing dialysis or a kidney transplant. A cause for the kidney failure is not found in 35% of patients. Diet and the environment can contribute to kidney disease but our genes also play an important role. Each person has 30,000 genes and breaking even one can cause a kidney disease. A "broken" gene results from a genetic change that makes the gene unable to make a working protein. Mutations are just bad luck and inherited from your parents. Mutations that result from exposure to a toxin can cause cancer but haven't been linked to kidney disease so far. Genetic studies have thus far focused on families with many relatives affected by kidney disease and discovered over 200 single gene kidney diseases where one gene is broken. However, all of these 200 kidney diseases are uncommon and they together explain a small percentage of patients. Instead of looking for one broken gene, Dr. Lanktree will look for many poorly working genes leading to kidney disease. He will collect blood and urine from 1000 patients with kidney disease and use cutting edge genetic and computer technology. He will compare test results from kidney disease patients with 500,000 people from the general public and focus on patients who remain without a diagnosis to look for new types of kidney disease.

Kidney disease has no symptoms until it has advanced. This creates a big window to treat and slow the disease before it causes problems. However, treating a disease the patient does not know they have is difficult. Especially when it causes no symptoms. As well, most available treatments to slow kidney disease remain fairly ineffective. This is why we need research. Dr. Lanktree would like to be able to tell patients what is causing their kidney disease and to predict who is going

to get worse, even in early stages of kidney disease. Treatment can be targeted to those who need it most. This research could prevent kidney disease from getting worse at an earlier stage and could help to reassure people unlikely to progress to kidney failure. It could also lead to new ways to treat the specific kidney disease of each patient.

## Dr. Mathieu Lemaire, PhD



### KRESCENT Program Partnership with CIHR IHDCYH

**Institution**: The Hospital for Sick Children
**Year**: 2019-2022
**Study title**: Studying why abnormal fats in blood vessel leads to blood clots in the kidneys of children with a rare genetic disease (DGKE deficiency)

### LAY SUMMARY

Blood vessels are like roads used to deliver food and oxygen to our body. A thin carpet of cells called endothelium lines the blood vessels. One of their important functions is to help make sure that blood flow is smooth. When a blood vessel is injured, blood flow slows down so a repair can happen. If this is a “good" traffic jam, it is critical to avoid "bad" ones, that is clotting in healthy blood vessels. Dr. Lemaire studies two diseases that lead to blood clots in the kidneys, causing kidney failure. He will study them together because what is found for one disease can help understand the other.

The first disease is called HELLP syndrome. It affects about 1% of all pregnant women. It is a terrible disease because sometimes the mother or the fetus dies. An injury to the placenta causes the clotting problem for the mother. The placenta sends special proteins in the blood of the mother that trigger clotting in the kidney. The only things doctors can do to help is using a machine to clean the mother's blood or deliver the baby. Dr. Lemaire is trying to understand how this protein from the placenta causes these troubles.

The second disease is caused by DNA changes (mutations) in a gene called DGKE. Affected children have kidney blood clots after most infections up until age 5. Because of the repeated kidney injuries, the kids develop chronic kidney failure over the next 10 years. Infections can cause the release of the same special proteins made by the placenta in the blood of patients. Researchers try to understand why their blood vessels are “stickier” after an infection to find a way to prevent it. Could we make them feel better by using the same machine used to clean the blood of mothers? A better understanding of how and why these two diseases occur is essential to develop new treatments.

# Claire Martin, PhD

## KRESCENT Post-Doctoral Fellowship



**Supervisor**: Dr. Anne-Claude Gingras
**Institution**: Mount Sinai Hospital, University of Toronto
**Year**: 2019-2022
**Study title**: Proteomic mapping of the kidney's blood filtration barrier.

### BIOGRAPHY

Claire Martin will be completing her post-doctoral fellowship in the lab of Dr. Anne-Claude Gingras at the Lunenfeld-Tanenbaum Research Institute at Mount Sinai Hospital/University of Toronto. She will work to establish a proteomics pipeline tailored to studying the kidney, with the goal of identifying roles for previously unknown molecules in renal disease.

The kidney's principal utility is to filter the blood, a critical task carried out by specialized cells called "podocytes". Disruption of these cells is commonly observed in the various forms of kidney disease; however, the mechanics that lead to podocyte disorder remain poorly understood. As a doctoral student in the lab of Dr. Nina Jones at the University of Guelph, she has worked to understand the molecular basis of podocyte dysfunction by studying several key proteins required for podocyte stability. She now seeks to advance this knowledge as a postdoctoral fellow by leveraging rapidly advancing technologies within the proteomics field.

### LAY SUMMARY

Chronic kidney disease constitutes a major health issue in Canada and worldwide. Nearly 3 million Canadians are living with this disease and its incidence is predicted to continue to rise coincident with rates of obesity, diabetes and hypertension, all which greatly increase the likelihood of disease. Currently, there is no cure for kidney disease and treatments focus instead on limiting its progression. However, the early stages of disease are often asymptomatic and nearly 3/10 newly diagnosed individuals in Canada each year are already in renal failure. Dialysis and transplantation remain the only forms of treatment for advanced kidney disease, approaches that are associated with considerable morbidity, mortality and healthcare costs. Understanding the changes that contribute to disease in the kidney is imperative to our ability to diagnose it at early stages and to develop new therapies. However, the molecular and cellular basis of kidney disease remains poorly understood.

The kidney's principal function is to filter the blood. The kidney's sorting mechanism is carried out by specialized cells called "podocytes". These cells associate with one another to form a sieve-like structure that is capable of distinguishing between essential blood components that the body must retain from wastes, which are eliminated as urine. During disease, the organization of podocyte filters becomes disrupted, which results in the loss of blood proteins into the urine, the clinical hallmark of chronic kidney disease. Grasping a firm understanding of mechanism by which these podocyte sieves become dysfunctional provides an avenue for us to better understand the development and progression of kidney disease.

Proteins represent the building blocks of all cellular functions. They act as structural elements, molecular machines, sensors and transporters. They rely on interactions with each other to perform their functions. Therefore, in order to understand the mechanisms by which the kidney's blood filter functions, we must understand how the proteins communicate with each other. Leveraging a cutting-edge molecular technique called proteomics, Dr. Martin will first

generate a molecular ‘map’ of protein-protein interactions within the kidney’s filtration sieve. These investigations are poised to reveal the involvement of previously undetectable molecules in podocyte function and how these proteins coordinate to facilitate blood filtration. Ultimately, these findings will move us closer towards grasping the molecular basis of kidney function and dysfunction, representing a new frontier towards the treatment of kidney disease.

# Dr. Marko Skrtic, PhD

## KRESCENT Post-Doctoral Fellowship



**Supervisor**: Dr. Lisa Robinson
**Institution**: Hospital for Sick Children
**Year**: 2019-2022
**Study title**: Pro-resolving mediators and Slit2-Robo pathway in acute kidney injury

### BIOGRAPHY

Dr. Skrtic grew up in the industrial city of Hamilton. After undergraduate studies in Biology at McMaster University, he pursued the MD PhD program at the University of Toronto where he completed his PhD under the supervision of Dr. Aaron Schimmer studying mitochondrial biology in acute myeloid leukaemia. Afterwards, he completed internal medicine training at the University of Toronto, now followed by Nephrology fellowship at McMaster University. His research post-doctoral studies will be with Dr. Lisa Robinson at the Hospital for Sick Children studying inflammation in acute kidney injury.

### LAY SUMMARY

Acute kidney injury occurs in 4-10% of adults during hospital admission. Although scientific research over the past fifty years has learned more about the biology of this condition, a proven treatment is yet to be determined. The inflammatory response in the body is part of the immune system machinery in response to injury. Dr. Skrtic previously demonstrated that the Slit family of protein machinery is important in the immune system response to repair kidneys after injury. More recently, omega-3 derived fats in the body have been implicated in the inflammatory response. He proposes to further understand the impact of the Slit proteins in the body on omega-3 derived fats during the kidney injury response.

He will carry out experiments in different cells of the immune system and in mice models of kidney scarring to better understand the interaction of Slit proteins and omega-3 derived fats. The second goal is to test the use of Slit protein and omega-3 derived fat therapy for prevention of kidney injury. He will also use mouse models of kidney injury to study the combination of these two possible therapies. When the immune system is hyperactive during an injury response in the body, long-term scarring may occur. The resulting information will enable the planning of new early clinical studies in human patients with kidney injury.

The long-term goal of this research is to improve the outcomes of patients with kidney injury. The body’s fat compounds have recently been recognized to be important parts of the immune system. This research may also potentially provide future insight into new therapies of acute kidney injury that are targeting the regulation of the body’s immune system.