# DEPARTMENT OF Queense VIEW DEPARTMENT OF VIEW 2020

Queen's CardioPulmonary Unit (QCPU)



# CD68 (Myeloid Cells) CD20 (B Cells) CD3 (T Cells) Granzyme B α-actin DNA

#### **MESSAGE FROM OUR DIRECTOR**



Dr. Stephen Archer, MD. FRCP, FRSC, FAHA, FACC Scientific Director of QCPU

"The remarkable thing about QCPU in this very unusual pandemic year is its people. The team at QCPU has been at work, in person, throughout almost the entirety of the pandemic. Through challenges with lockdowns, stay home orders, vanishing childcare and more, we have been at work doing science. Draped in gowns and masked we have continued to advance science at Queen's, both in the COVID-19 domain and in the study of heart, lung blood and vascular diseases (and much more). This commitment reflects our shared belief that research is truly an essential service, the need for which is only highlighted by the pandemic. By sticking to our mission of advancing research for trainees and faculty alike we ensured that graduate education continued, grants were written, and faculty members research aspirations were advanced. Remarkably research at QCPU proceeded at a pace similar to that seen pre-pandemic. We even added a new scientist to our team and opened a state-of-the-art histology core.

I am proud of Team QCPU. Their dedication and skill and their willingness to work even more than usual to keep the scientific boat of Queen's researchers afloat and moving forward has made the pandemic tolerable.

> I am proud of Team QCPU. Their dedication and skill and their willingness to work even more than usual to keep the scientific boat of Queen's researchers afloat and moving forward has made the pandemic tolerable. We at QCPU see ourselves as worthy adversaries to COVID-19 and we are proud to take it on with creativity, flexibility and good humor. We will not be defeated, and we will ultimately emerge from this trial as an even stronger, more skilled and battle-tested research centre. QCPU's positive impact, both inside the FHS and beyond, is something that the entire research community at Queen's University can celebrate."

Dr. Stephen L Archer *MD. FRCP, FRSC, FAHA, FACC* Scientific Director of QCPU

Elizabeth Smith Distinguished University Professor C. Franklin and Helene K. Bracken Chair Head Department of Medicine, Queen's University Program Medical Director for Medicine at KHSC and Providence Care " In spite of the pandemic restrictions, I'm happy to say that I've managed to visit the QCPU, not once, but twice in my first few months as Dean of the Faculty of Health Sciences. It is an exceptional facility, beautifully designed from a scientific and an aesthetic perspective. But most importantly, I sensed the curiosity and drive of the research team. There was a palpable energy among the scientists, who have been recruited from across the globe, to join this translational medicine unit at Queen's. The discoveries that are enabled by the QCPU have already had a positive impact on human health and I have no doubt that the team will continue as a model of excellence, inspiring the future for health research at Queen's."

**DR. JANE PHILPOTT** (Dean of Health Sciences)



The Queen's CardioPulmonary Unit (QCPU) is an \$8 million dollar, 8000 square foot research facility that is focused on a Bench-to-Bedside philosophy with emphasis on heart, lung, blood and vascular diseases. QCPU was funded by a Canadian Foundation for Innovation (CFI) grant and opened in 2017 with Dr. Stephen Archer as the founding scientific director. QCPU is comprised of a state-of-the-art basic science research facility and also includes an on-site Kingston Health Sciences Center (KHSC) satellite echocardiography clinic. This clinical facility does over 1000 patient studies each year and offers an imaging resource in support of clinical trials research. Built on existing institutional investments by Queen's University, QCPU enhances existing links between clinical and basic investigators at Queen's and fosters new collaborations between researchers in other faculties and at other institutes. QCPU is funded by the Department of Medicine, the Faculty of Health Sciences (FHS) and through cost recovery for services provided. QCPU's mission includes growing the extramurally funded research enterprise at Queen's University.

Housed within the Bioscience Complex, located in the heart of Queen's campus, QCPU is within close proximity to the School of Medicine Building, KHSC and other key departments within FHS. QCPU embodies research excellence and will ensure that Queen's University is recognized internationally as a center for translational research.

Due to the global COVID-19 pandemic, QCPU has had to pivot in its focus and practices, like many other units on campus. We were proud to be one of the first labs at Queen's to return to in-person work, in April 2020. Our team of 5 scientists have been hard at work providing critical research services for the many labs that could not return to in-person research while also supporting many COVID-19 research projects.



#### **CLINICAL SATELLITE UNIT**



Number of echocardiograms (ECHO) per day QCPU opened its clinic doors in 2019 as an official KHSC Satellite and typically the clinic performs 8 echocardiograms (ECHO) per day. However, due to the pandemic the clinic was closed for a portion of the year due to public safety concerns and the cancellation of non-emergency procedures. While this cancellation was necessary until our understanding of COVID-19 improved, our clinic was able to safely return to operation in July 2020. The clinic is home to 1 full time receptionist and 3 sonographers. All clinical images are linked and stored on the Xclera server at KHSC. Since mid-summer of 2019, the QCPU clinic became the site for central booking for all local ECHOs. In 2020 we saw clinical services expand into using contrast agents for ECHO, which has had a positive impact on patient wait lists. Once the pandemic is over, we are looking forward to establishing several exciting research projects at our clinic. QCPU has a unique partnership with KHSC which allows 25% of the imaging capacity for use in clinical research studies. This partnership provides KHSC with a state-of-the-art imaging facility, and provides our researchers with access to the services of expert sonographers and ongoing maintenance of the equipment.

#### TRANSLATIONAL RESEARCH UNIT



This portion of QCPU is staffed by 5 scientists and is comprised of 5 different laboratories including:

- Physiology and experimental therapeutics
- · Molecular and cellular imaging
- · Cell culture and cytometry
- · Genomics, transcriptomics and molecular medicine
- · Mass cytometry, histology and proteomics

Number of scientists on staff at QCPU

05

Number of laboratories within QCPU

The centre offers faculty across the university access to state-of-the-art equipment, much of which exists only within QCPU. Notably, our model is innovative in that services are provided for faculty by QCPU's scientists on a cost-recovery basis. Examples of key equipment include:

- MILabs Tri-modality micro-CT/SPECT/PET nuclear imaging platform
- Illumina NextSeq550 Sequencing for next-generation sequencing services
- Sony SH800 flow cytometer and sorter
- · Leica SP8 confocal and super-resolution microscope upgraded with 2-photon laser
- MultiPep RSi peptide array technology
- Fluidigm Helios/Hyperion mass cytometer
- XCelligence cell culturing system
- \*NEW\* Histology services and electron microscopy

#### **BY THE NUMBERS**

QCPU was established as a cost-recovery funding model. We provide Queen's researchers with the **services of experienced scientists** and access to cut-ting-edge technology **so that they can elevate** their research to the next level.





27

We serve 27 research groups across 16 departments, and 3 faculties.

blocks of 208 (SuperUser A plan) or 104 (SuperUser B plan) hours/year or winners of a Translational Institute of Medicine (TIME) incubator grant competition.

defined as users who purchase service in

In 2020 QCPU boasts 13 SuperUsers,

73

11

QCPU scientists have assisted or mentored over 73 trainees, including research staff, medical students, post-doctoral fellows, graduate students and undergrads. QCPU has contributed to 11 publications in the past year.

#### **QCPU PROFILES**



#### **Dr. Stephen Archer**

Head, Department of Medicine, Scientific Director, QCPU stephen.archer@queensu.ca @DrStephenArcher

Dr. Stephen Archer is physician scientist and graduate of Queen's University (Meds '81). He is a practicing cardiologist who specializes in the care of patients with various forms of pulmonary hypertension. His other interests include strategies for improving cardiovascular care and training the next generation of physicianscientists. In his spare time, he enjoys spending time with family and is an avid hockey player, guitarist and coffee drinker.

Dr. Archer directs a CIHR-funded research lab, where he and his associates study basic mechanisms of oxygen sensing in the vasculature. He investigates the role of mitochondria, both as oxygen sensors and regulators of cell proliferation and apoptosis. His research focuses on exploring cellular and molecular mechanisms of oxygen sensing and mitochondrial metabolism and dynamics. He also develops experimental therapeutics for pulmonary hypertension and cancer.

After training at the Royal Columbian Hospital in BC and the Minneapolis Veteran Affairs Medical Center he joined the faculty at the University of Minnesota in 1988. He spent a decade on faculty and attained the rank of Professor under the guidance of his mentor and friend, Dr. E.K. Weir. He then served as Chief of Cardiology at the University of Alberta (1998-2007). Subsequently he served as Chair of Cardiology and Harold Hines Jr Professor at the University of Chicago (2007-12). In late 2012 Dr. Archer returned to Queen's University as the Head of Medicine and Program Medical Director for Kingston Health Sciences Center (KHSC; includes Hotel Dieu Hospital, Kingston General Hospital, and Providence Care). Dr Archer is the founder and Scientific Director of the Queen's CardioPulmonary Unit (QCPU) a \$8 million dollar, 8000 squarefoot research facility, with a Bench-to-Bedside philosophy. QCPU is designed to support faculty and trainees who perform heart, lung, blood and vascular research. QCPU is comprised of a state-oftheart basic science research facility that is complemented by an onsite KHSC satellite clinic with clinical trials research capacity. He has over 300 publications and his H-index is 99, with over 41,000 citations. He has mentored over 60 trainees, many of whom are leaders in science and medicine. His translational cardiovascular research has been recognized with numerous awards, including being elected as a Fellow of the Royal Society of Canada and being awarded Distinguished Scientist Awards from the American Heart Association and American College of Cardiology. He received the AFMC President's Award for Exemplary National Leadership in Academic Medicine in 2019 and was named the Chicago American Heart Association Coeur d'Or recipient in 2013. In 2020 he was appointed the School of Medicine's C. Franklin and Helene K. Bracken Chair.

#### **Brooke Ring-Snetsinger**

Manager, Facilities & Operations QCPU, Research Scientist at QCPU ringb@queensu.ca @Brooke\_Ring

Brooke has 10 years of research experience specializing in molecular biology, cytometry, microscopy and laboratory management. She graduated



with a BSc. Hons in Biochemistry and Molecular Medicine and MSc. in Life Sciences from Trent University. She managed a virology laboratory at Trent University and taught Virology and Infectious Diseases before coming to Queen's University in 2012.

She worked as the research assistant for clinician-scientist, Dr. Michael Rauh in Pathology and Molecular Medicine. Prior to joining QCPU she provided lab management for multiple research labs in the Pathology department, including the Queen's Laboratory for Molecular Pathology (QLMP). She has expertise running confocal microscopy, flow cytometry, NanoString Technology and Next-Generation Sequencers.

In 2019, she became the Manager of Operations and Facilities at Queen's CardioPulmonary Unit (QCPU). Brooke oversees operation of both the KHSC satellite clinic's daily operations, as well as, the state-of-the-art research centre. She not only lends her strong background in lab management research centre. She not only lends her strong background in lab management to QCPU, but her significant bench experience as a Research Scientist, aiding in the Genomics, Molecular Imaging and Cytometry labs. Throughout 2020 Brooke has engaged with numerous researchers helping them to adapt to research in the COVID-19 era. She created content to showcase QCPU's work as highlighted in CFI's #GoResearch campaign, and Queen's Review.



## CLINICAL SATELLITE TEAM

#### Dr. Amer Johri

Associate Professor, Onsite physician, QCPU, Director of the CINQ lab cinq.research@gmail.com @amerjohri

Dr. Johri joined the Echocardiography group at Queen's University in 2010 after completing an Advanced Fellowship in Echocardiography (Level III) and

Multi-modality Imaging at Harvard University Medical School, Boston MA. He is the Founder/Director of the Cardiovascular Imaging Network at Queen's (CINQ) and has the distinction of Fellow of the American Society of Echocardiography (ASE) in recognition of his various contributions to the advancement of the field of ultrasound.

His particular interest is in 3D echocardiography, quality control in the echo lab, interventional echocardiography, and Handheld Cardiac Ultrasound. He also has extensive experience in echo-guided CRT optimization and TEE guided percutaneous aortic valve replacement (TAVI). Dr. Johri's current research interests include the investigation of carotid intimal medial thickening, and 3D strain and 3D stress testing. He serves as an executive member of the ASE Standards and Guidelines Committee is actively participating in the development and review this society's position statement on Hand-Held Cardiac Ultrasound. His laboratory is supported by the Canada Foundation for Innovation and the SEAMO Clinical Scientist Development Program.



Casey Salata ECHO lab sonographer



Siew-Li Leaman ECHO lab sonographer



Peter Leaman ECHO lab sonographer



Liz Bullet QCPU Clinic Administrator

#### **QCPU PROFILES**

### TRANSLATIONAL RESEARCH UNIT TEAM

#### **Dr. Charlie Hindmarch**

Assistant Professor (Adjunct), Genomics, Transcriptomics and Molecular Medicine Specialist, Scientific Operations Director, Translational Institute of Medicine (TIME) <u>c.hindmarch@queensu.ca</u> @DrHindmarch

Dr. Charlie Hindmarch is Associate Professor (Adjunct) of

Medicine and Director of the Genomics, Transcriptomics, and Molecular Medicine laboratory within Queen's CardioPulmonary Unit (QCPU). Dr Hindmarch is also Scientific Operations Director for the new Translational Institute of Medicine (TIME).

Dr. Hindmarch graduated in 2001 with a BSc in Marine Biology in 2002 (University of Plymouth), in 2003 with an MSc in Biochemical Pharmacology (University of Soton) and in 2009 with a PhD in

Neuroscience and Endocrinology (University of Bristol). Following his PhD, Hindmarch held two consecutive Postdoctoral Fellowships in University of Bristol, and the role of Senior Research Associate. Dr Hindmarch has previously held visiting Professorships at the University of Malaya (Malaysia) and at the Federal Rural University of Rio de Janeiro (Brazil). Dr Hindmarch has been at Queen's University since early 2016 and currently has 45 published papers with an h-index of 18.

Dr Hindmarch is Director of the Genomics, Transcriptomics and Molecular Medicine laboratory at QCPU where he is responsible for Next Generation Sequencing and bioinformatics. Dr Hindmarch also runs the mass cytometer (Cytometric Time of Flight; CYTOF) which is a high throughput proteomic tool that can resolve up to 50 antibodies in both cell suspension and in tissue (using laser ablation). This year he received a National Scientist Award from the Canadian Network of Scientific platforms.



#### **Dr. Elahe Alizadeh**

Assistant Professor (Adjunct), Imaging & Radiation Physics Specialist elahe.alizadeh@queensu.ca @ElizaAlizadeh\_

Elahe Alizadeh graduated with a BSc. in Applied Physics and an MSc. in Medical-Radiation Physics Program, both from AmirKabir University of Technology (Tehran Polytech-



nic) in Tehran, Iran. She then obtained her PhD in Nano-Bio-Physics from the University of Innsbruck, Austria. In 2010, she joined Prof. Sanche's lab at the Department of Radiobiology (at Université de Sherbrooke, QC, Canada) as a postdoctoral research fellow; where she designed and constructed a new X-ray apparatus to investigate the radiation damage on DNA complexed with radiosensitizing chemo-therapeutic agents for chemoradiation therapy. Her achievement was recognized with the Radiation Research Society Jack Fowler Award in 2013 as an outstanding research in medical physics / radiobiology.

In January 2016 she joined the Department of Medical Imaging (University of Saskatchewan) to establish a pre-clinical research program for developing novel radiopharmaceuticals combining both therapeutic and diagnostic capabilities. She was managing the imaging facility with a  $\mu$ PET/SPECT/CT scanner and a radio-chemistry lab. She was also a member of the Occupational Health Committee at the Saskatchewan Cyclotron Centre (Sylvia Fedoruk Canadian Centre for Nuclear Innovation) and obtained the Radiation Safety Officer (RSO-1) certificate from the Radiation Safety Institute of Canada in May 2018.

Since July 2018, Elahe directs the nuclear imaging facility located at QCPU. She is responsible for the coordination and performance of pre-clinical imaging projects using tri-modality µPET/SPECT/CT scanner (VECTor4CT from MILabs; Utrecht, Netherlands). So far, she has developed many innovative approaches for ex vivo and non-invasive in vivo imaging in animal models for cancer, cardiac and pulmonary hypertension studies including: cardiac- and respiratory-gated techniques to capture and visualize 3D / 4D images, as well as enhancedcontrast CT. She is also a member of the Canadian Radiation Protection Association (CRPA) and serves as a member of the Queen's Radiation Safety Committee in the Department of Environmental Health and Safety.



#### **Dr. Patricia Lima**

Assistant Professor (Adjunct), Molecular Imaging & Cytometry Specialist pdal@queensu.ca @Limapda

Dr. Lima is a scientist and an Assistant Professor (Adjunct) at the QCPU. She is QCPU's Molecular Imaging and Cytometry Specialist and provides scientific assistance for over 30 ongoing

research projects. Driven by the philosophy of "Let's get this done and get it right", Dr Lima is well known by her competence, organization skills and scientific knowledge. She co-supervises graduate students focusing on the development of their scientific skills and critical thinking. At QCPU, Dr. Lima directs the Imaging Lab (housing the super-resolution SP8 Leica MP and confocal microscope) and the Culture and Cytometry Lab (a fully equipped risk level 2+ facility with a cell sorter and an enclosed culture system).

Dr. Lima graduated with a degree in Biological Sciences and obtained her Ph.D. in one of the top Universities in Brazil - UNI-CAMP in collaboration with Queen's University. She has focused her graduate studies in Reproductive Immunology, specifically looking into the regulatory mechanisms of Natural Killer cells (NK) during pregnancy and the role of these cells in complications such as miscarriages and preeclampsia. During her postdoctoral training (Queen's University and Ottawa Hospital Research Institute), Dr. Lima narrowed her research interest to study the immunological and metabolic aspects of women's health particularly focusing on diabetes during pregnancy and infertility-driven by endocrine and metabolic disorders such as Polycystic Ovarian Syndrome. Over the years, Dr. Lima has accumulated relevant publications and several awards recognizing the excellence of her research. Currently, she has four major research interests: 1) macrophage polarization and metabolism in pulmonary hypertension (PH), 2) NLRP3 inflammasome activation in PH, 3) the phenotyping of neutrophils in risk stratification and prognostics of sepsis, and 4) complement activation in membranous nephropathy.

Aside from science, Dr. Lima dedicates her time giving back to the community. She is also a volunteer firefighter at Athens Fire Department where she is a member of the executive and training team. She also leads yearly the Muscular Dystrophy Canada fundraising for research ("The Boot Drive"). At Queen's, Dr. Lima is the founder of the Women in Science at Queen's (WiSQ), which is popular amongst scientists of diverse fields, genders and professional levels. The group was funded by Queen's Inclusive Community Funding and has the support of several departments at Queen's.



#### **Oliver Jones**

#### Histologist and Electron Microscopist oj3@queensu.ca @OliverJ45751384

Oliver Jones is a histologist working for Queen's University, Ontario, Canada. Following his graduation in 2005 with a degree in Biochemistry with Biomedi-

cine at Lancaster University (United Kingdom), he was employed as a trainee in histopathology at Manchester Royal Infirmary, a large teaching hospital serving a city with a population of ~3 million people. During this training, Jones completed a Post Graduate Certificate (PGC) in Biomedical sciences, which allowed for his formal registration with the Institute of Biomedical Scientists in the UK. While in this position, Jones was trained to operate the on-site Transmission Electron Microscope and was in a position to receive samples, process them for imaging and generate the electron micrographs for pathologist review; his training here was conducted by clinical scientists working with the UK Health Protection Agency. In 2010, he was offered a position with a successful research group at Queen's University (Petrof Laboratory), where he adopted an instrumental role as the lab's histologist, performing image analysis on murine tissue (mainly colonic). This role allowed Jones to complement his clinical research background with experience in a non-clinical, laboratory research environment. His unique work experience combined with his growing reputation within Queen's University allowed him to secure a position within the Queen's Laboratory for Molecular

Pathology (QLMP) within the Pathology and Molecular Medicine department. Between 2013 and 2019, Jones performed a range of histological and microscopy services to the Queen's research community within the scope of a cost recovery model. In addition to the histology services that he provided, Jones built on his previous experience with electron microscopy providing services for researchers at Queen's University, Kingston Health Science Centre (KHSC), Canadian Cancer Trials Groups (CCTG). In this time, Jones also engaged in continuing professional development; training at Sick Kids Hospital in Toronto to prepare and analyze blood samples for dense granule testing on the electron microscope, and training at Queen's to use an updated electron microscope in the Radioactive Materials Testing Laboratory; Jones is now one of only a few authorized operators.

In 2018, Jones' considerable experience was recognized by St. Lawrence College where he teaches histopathology to students undertaking the Medical Laboratory Assistant (MLA) course. The successful MLA students may then register to work in clinical support laboratories in the hospital environment. The course was a combination of lecture-based theory and laboratory based hands-on techniques.

Most recently, Jones has been engaged in active research with Dr. Stephen Archer at Queen's University where he has been facilitating research by using electron microscopy to acquire images of mitochondria exposed to S. aureus from healthy volunteers. He officially joined the Queen's CardioPulmonary Unit (QCPU) in the summer of 2020 as the Histology and Transmission Electron Microscope specialist and provides his experience, knowledge and skills as a service to the Queen's research community.



" In the Adams-Holden research group, we have been working closely with Dr. Elahe Alizadeh to optimize the use of the Vector4CT to visualize, characterize and quantify the maladaptive changes in fine bone microarchitecture in rat tibias and as well as the associated calcification of blood vessels in chronic kidney disease. The results have been superb as Dr Alizadeh has been a committed and talented collaborator. This equipment has been key to advancing the research in our lab and the results will be central to several up-coming publications."

DR. MICHAEL ADAMS (Professor and Researcher DBMS Director of the Bachelor of Health Sciences Program) DR. MANDY TURNER Graduate (DBMS) DR. RACHEL HOLDEN (Professor and Clinician Researcher (DOM))

#### USER LISTS (PI, DEPARTMENT)

USER TYPE	PRINCIPAL INVESTIGATOR	DEPARTMENTW
SuperUser	Stephen Archer	Medicine
SuperUser	David Lillicrap	Pathology & Molecular Medicine
SuperUser	Mark Ormiston	Biomedical and Molecular Sciences / Surgery
SuperUser	Don Maurice	Biomedical and Molecular Sciences
SuperUser — TIME	Paula James	Medicine / Pathology & Molecular Medicine
SuperUser — GIDRU	Stephen Vanner	Medicine / Gastroenterology
SuperUser — GIDRU	Alan Lomax	Medicine / Gastroenterology
SuperUser — TIME/GIDRU	David Reed	Medicine / Gastroenterology
SuperUser	James Rutka	Surgery / University of Toronto
SuperUser	Robert Siemens	Urology
SuperUser —TIME	Amer Johri	Medicine
SuperUser —TIME	David Maslove	Medicine / Critical Care
SuperUser —TIME	Rachel Holden	Medicine / Biomedical and Molecular Sciences
User	Michael Rauh	Pathology & Molecular Medicine
User	Peter Davies	Biology / Biomedical and Molecular Sciences
User	Charles Graham	Biomedical and Molecular Sciences
User	Martin Petkovich	Biomedical and Molecular Sciences
User	Michael Adams	Biomedical and Molecular Sciences
User	Fredrick Kan	Biomedical and Molecular Sciences
User	Jagdeep Walia	Pediatrics / Biomedical and Molecular Sciences
User	Myron Szewczuk	Biomedical and Molecular Sciences
User	Simon Hesp	Chemistry
User	Richard Oko	Biomedical and Molecular Sciences
User	Chandra Tayade	Biomedical and Molecular Sciences
User	Andrew Winterborn	Animal Care Services
User	Kurt Prins	University of Minneapolis
User	Christopher Spencer	Geology
User	Jacob Rullo	Optometry & Opthomology / Biomedical and Molecular Sciences

#### SUPERUSER PROFILES



#### **Dr. Stephen Archer**

Dr. Archer is a CIHR and CRC Tier 1 funded cardiologist and physician scientist. Dr. Archer is the scientific director of QCPU, his research focus is on defining molecular mechanisms of oxygen sensing, defining mechanisms of disordered mitochondrial metabolism and dynamics and development of mitochondrial metabolic therapies for pulmonary hypertension (PH) and cancer.



#### **Dr. David Lillicrap**

Dr. Lillicrap is a CIHR and CRC Tier 1 funded researcher. His research explores the molecular aspects of blood coagulation to improve the diagnosis and treatment of patients with bleeding disorders. His research team use a combination of molecular technologies to improve the understanding of common inherited bleeding disorders, such as hemophilia and von Willebrand disease to identify cures.



#### **Dr. Mark Ormiston**

Dr. Ormiston is an investigator who is funded by CIHR and a Tier 2 CRC. Dr. Ormiston serves on the management board of QCPU. He studies how impairment of a specific immune cell 'Natural Killer (NK) cells' may be critical to development of pulmonary hypertension and how targeting these cells may offer a new avenue for treatment. His team also works on techniques to isolate and genetically modify patient-derived stem cells, with the ultimate goal of creating tailored immune cell therapies that can reverse the vascular changes that affects the lungs of patients with pulmonary arterial hypertension (PAH).

#### **Dr. Don Maurice**

Dr. Maurice is a CIHR funded researcher and serves on the management board of QCPU. The Maurice Lab studies the role of cyclic nucleotide (cAMP and cGMP) compartmentalization and cyclic nucleotide signaling in human arterial endothelial cells and arterial smooth muscle cells. Since virtually all cells are either directly or indirectly influenced by cAMP and or cGMP, this pathway represents a potential therapeutic target in multiple cardiovascular diseases, such as atherosclerosis and restenosis, and is also important for angiogenesis.



#### **Dr. Paula James**

Dr. James is the director of our TMED graduate program. Her primary research interest is focused on investigating the genotype/phenotype interactions in patients with von Willebrand disease and Hemophilia. She studies the molecular genetic basis of these inherited bleeding disorders and is also heavily involved in clinical investigation of patients with these diseases. The James lab has a focus on the quantitation of bleeding symptoms in women with von Willebrand disease and on understanding the relationship between bleeding scores and the molecular basis of disease.

#### **Dr. David Reed**

Dr. Reed is a young investigator. His clinical interest is in gastrointestinal motility disorders. His research interest is how the interaction of luminal factors (e.g. dietary components) with stress or the microbiota modulates pain signaling and motility in disorders such as irritable bowel syndrome. " Dr. Johri and the Cardiovascular Imaging Network at Queen's was awarded a TIME project grant entitled "Virtual Histology and Molecular Environment of Atherosclerotic Plague by a Novel 3D-Guided Ultrasound Tool for Atherosclerosis Risk Detection - VANGUARD" in the inauguration year of the program. In collaboration with QCPU's scientists, Dr. Charles Hindmarch and Oliver Jones, CINQ has been investigating the use of 3D ultrasound to detect high risk atherosclerotic plaques that can cause strokes or heart attacks. In this study, patients undergoing endarterectomy surgery receive a carotid ultrasound and the removed plaque is then collected for histological analysis. The histological specimens are correlated back to the ultrasound images to identify key features associated with rupture prone plaques. Oliver has provided us with exquisite images that are currently being analyzed for cell identification. Dr. Marie-France Hétu (CINQ) has been leading the 3D ultrasound image analysis for the project. Dr. Hindmarch is further helping elucidate the presence of inflammatory biomarkers, present in the histological samples, through Hyperion imaging. The VANGUARD Study uses ultrasound because it is an inexpensive, radiation-free, non-invasive, portable method that is ideal for imaging blood vessels, detecting the presence of plague, and may help risk stratify patients at risk of cardiovascular events. We would like to thank Oliver and Charlie for all their hard work so far on this project.

DR. AMER JOHRI (Associate Professor and Researcher in Medicine Director of the CINQ lab)

#### SUPERUSER PROFILES



#### **Dr. Rachel Holden**

Dr. Rachel M. Holden is a nephrologist and an Associate Professor in the Department of Medicine with a cross-appointment to the Department of Biomedical and Molecular Sciences at Queen's University. Dr. Holden and her associates study basic mechanisms of vascular calcification in chronic kidney disease. A focus of her research program is clinical, basic and translational aspects of vitamin K metabolism and specifically the role of vitamin K in the inhibition of vascular calcification. Her clinical interests include mineral bone disorders in chronic kidney diease and hemodialysis patients.

#### **Dr. Stephen Vanner**

Dr. Vanner is a CIHR funded researcher and is the scientific director of the Gastrointestinal Diseases Research Unit (GIDRU) and the Translational Institute of Medicine (TIME). Dr. Vanner has expertise in gastrointestinal motility disorders. He has an established translational research program that examines mechanisms underlying pain signaling and motility in the gastrointestinal tract, relevant to irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

#### **Dr. James Rutka**

Dr. Rutka is a CIHR and CRC funded researcher and is Chair of the Department of Surgery at the University of Toronto. His laboratory has focused on two areas of related research regarding astrocytomas (malignant brain tumors: 1) Cytoskeletal:matrix interactions, and 2) Cell cycle control mechanisms.

#### **Dr. Robert Siemens**

Dr. Siemens is the head of the Department of Urology at Queen's University. His research focus is on urological oncology. His research endeavors have led to novel observations of the role of the tumour microenvironment and its interactions with the oncogenic drivers of malignant progression, with a specific interest in translating these findings to clinically effective cancer immunotherapy approaches.



#### Dr. Amer Johri

Dr. Johri is a mid-career researcher funded by the Heart and Stroke Foundation. He serves on the management board of QCPU. He is also founder and director of the Cardiovascular Imaging Network at Queen's (CINQ). His research interests include 3D echocardiography, quality control in the echo lab, interventional echocardiography, and Hand-Held Cardiac Ultrasound. Dr. Johri's current research interests include the investigation of carotid intimal medial thickening as a surrogate to diagnose vulnerable coronary artery atherosclerotic plaques.



#### **Dr. David Maslove**

Dr. Maslove is an NSERC-funded young investigator and Clinician Scientist with the Department of Medicine and Critical Care Department. His research focuses on informatics, genomics, and the use of biomedical Big Data to address current challenges in Critical Care Medicine. The Maslove's lab leverages the power of randomization in a clinical trial of vitamin C in sepsis in order to ask: Are there molecular subtypes of wsepsis that portend a positive response to treatment, and why do certain subtypes respond to vitamin C better than others?.

#### **Dr. Alan Lomax**

Dr. Lomax is a CIHR funded researcher. His lab investigates how interactions between the microbiota, nervous system and the immune system can contribute to symptom generation in inflammatory bowel disease. His lab also investigates the regulation of neurogenesis in the enteric nervous system.

#### SUPERUSER PROFILES



(Above: Dr. Hindmarch)

#### **COURSES AND EVENTS**



#### **COURSES AND EVENTS AT QCPU**

While we normally host many groups and events at QCPU, due to the COVID-19 pandemic we have moved to an online format and were still about to run the following events:

- TMED811 Next-Generation Sequencing: (Dr. Charlie Hindmarch) – Winter 2019. This course teaches students the theoretical and practical basis of high-throughput genomics and transcriptomics.
- Joint Vascular Biology Research Day between the Ottawa Hospital Research Institute (OHRI) and QCPU – Organized by Dr. Ormiston. This is an annual event that showcases each center's current research and achievements. The event took place on September 10th and was attended by approximately 60 people
- Queen's for Teens (partnered with WiSQ and the Kingston Public Library)

" I first began interacting with the QCPU as an undergraduate summer research student and was impressed at how committed their scientists were in facilitating our labs' research. Beyond providing access to state-of-the-art scientific equipment such as the VECTor4CT micro-CT machine, Dr. Elahe Alizadeh was thoroughly engaged in our project and actively assisted with troubleshooting, workflow design, and educating me about the QCPU equipment concerning our labs' project. The QCPU's promotion of a learning environment and willingness to collaborate was a great asset to the success of my project."

#### SONO KHAN

(4th year undergraduate in the Biochemistry program MSc Candidate)

#### NOTABLES

#### **HIGHLIGHTS**

#### Histology Core and New Infrastructure:

The summer of 2020 saw the completion of QCPU's final laboratory, the Histology Core. Equipped with standard histology equipment (processor, embedder, cryostat and microtome) our experienced technologist Oliver Jones, can move fresh and frozen tissue to application ready slides. Oliver is the newest member of our team, and can advise researchers on advanced histology techniques, recommend special stains and generally consult on how they can get the most out of their precious tissue. As an instructor for the MLA course at St. Lawrence college, he is eager to educate researchers and students in histology practices to foster the learning environment that QCPU prides itself on. In addition to standard histology, Oliver is also a skilled TEM electron microscopist with special training and access to the Reactor Material Testing Laboratory (RMTL) for imaging on their state-of-the-art digital TEM. Since introducing this new service halfway through the year, it has become one of our most popular offerings - both because of its affordability and quality.

At the beginning 2020, QCPU secured a MultiPep 2 and slide spotting robot. The combination of the two units provides our users with access to a best-in-class peptide synthesizer. This automated synthesizer has unmatched flexibility for screening hundreds of peptides in parallel.

Another new piece of equipment acquired at QCPU is the xCELLigence system housed within our cell culturing suite. This instrument can perform real-time cell invasion and migration assays while obtaining detailed data time points, using special plates and an electronically integrated Boyden chamber.

#### **Research despite COVID-19:**

The global COVID-19 pandemic underlined the important role QCPU plays in helping researchers tackle the pandemic. In March of 2020, when Queen's campus went into lockdown, QCPU is proud to have secured early approval to return to the bench. This saw us back to work by end of April, after a very short hiatus. We



were pivotal in continuing research for faculty members across the Faculty of Health Sciences. We ensured that research which could not be halted was continued and thus served as a bridge for numerous researchers, sustaining them until their research group had approval to return to work. By the end of summer 2020, QCPU was actively contributing to the preliminary planning and experiments for several COVID-19 related projects.

We promoted our belief that scientists are essential workers by accepting an opportunity to promote research and development to the public in CFI's #GOResearch campaign. Our video, 'Part of the Cure' helped to spotlight our own unique COVID-19 research and contributed to the campaign's goals of emphasizing the fact that Canadian researchers are ready to perform science under the most urgent circumstances. Creating state-of-the-art centers like QCPU allows Canadian scientists to perform essential research that benefits the country and the world.

Locally, Drs. Lima, Alizadeh and Johri were featured in the Queen's Alumni Review Magazine photo assay and a complimentary Queen's Gazette article 'The New Normal'. With a distribution of 125,000 readers, these articles explored how the landscape of research and education changed at Queen's University over the past year. Dr. Lima and Alizadeh were also featured in their role as QCPU researchers for studies they are performing with the Archer lab on developing small molecule therapeutics that block SARSCoV-2 mediated mitochondrial damage in lung cells. These small molecules may have therapeutic potential for patients with COVID-19 pneumonia. Dr. Johri's laboratory was highlighted for their inspiring adaption to the pandemic by shifting to develop on-line educational materials related to point of care ultrasound (POCUS) for medical students and staff. His ARTICA project, (Accelerated Remote Tele-POCUS in Cardiopulmonary Assessment) received national recognition by the Canadian Cardiovascular Society. ARTICA will meet the pandemic challenge using novel technological innovation - the use of live-streaming of imaging by an expert to support learners and provide a Virtual Learning Lab.

#### **QCPU joins Navigator:**

Navigator is an on-line national directory of research facilities that are open to collaboration between industry, academia and government. Launched by CFI, Navigator helps people locate and connect with 750 facilities with research expertise and stateof-theart equipment in labs located across Canada's universities, colleges, and hospitals. On QCPU's Navigator profile you can find a list of our research services, infrastructure and areas of expertise.

#### Women in Science at Queen's University (WiSQ)

Women in Science Queen's (WiSQ) is Queen's University's second Employee Resource Group funded by the Inclusive Community Fund (ICF) provided by the Human Rights and Equity Office.

Founded by Dr. Patricia Lima, who was looking to help other women as they explore and build upon their careers at Queen's while at the same time helping foster equity within science. WiSQ goals include promoting discussions about gender bias in science; incentivizing the active participation and leadership of women; and establishing a visible,

![](_page_20_Picture_3.jpeg)

equitable, diverse and inclusive community promoting the development and retention of women across all scientific disciplines.

WiSQ became official in 2019, its monthly seminars and workshops are attended by 30+ people per session. In 2020, WiSQ had gone virtual, hosting 10 seminars of guest lectures, including a variety of topics to discuss issues of equity, career development, retention in STEM and work-life balance. As part of their plan to start more community outreach WiSQ held a joint lunch with the Queen's Women's Network for International Women's Day on March 6th, 2020 which was attended by almost 100 attendees. In addition, WiSQ partnered with QCPU to hold a joint event 'Queen's for Teens' with the Kingston Public library where scientists discussed their personal scientific journies and engaged with teenagers in the Kingston area about science at Queen's University. Once the pandemic ends WiSQ is excited to return to inperson seminars and workshops, and plan to hold more external events.

Please follow us on Twitter (@womeninscience6) to find out about our events or add our group (Women in Science at Queen's – WiSQ) to Queen's outlook calendar.

#### **VISITORS AT QCPU IN THE PAST YEAR**

**Patrick Deane** (Principal of Queen's University)

**Dr. Jane Philpott** (Dean of Faculty of Health Sciences)

#### Jim Balsillie and Neve Peric

(Founder of Research in Motions, Communications specialist for the The Centre for International Governance Innovation)

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#### FUNDING AND PUBLICATIONS

![](_page_21_Picture_1.jpeg)

(left) CT image of lung vasculature after barium perfusion via left ventricle in a mouse (right) CT scan of cardiovasculature under hypoxia by perfusion of Omnipaque contrast agent via rabbit's pups' left ventricle

#### **EXTERNAL GRANTS** (submitted)

#### **Ontario COVID-19 Rapid Research**

Synthesis and preclinical testing of novel small molecule therapies for COVID-19

#### CIHR - 2020 Rapid Research Funding Opportunity

SARS-CoV-2-mitochondriopathy impairs oxygen-sensing and causes lung injury: discovery and pre-clincial evaluation of new therapies to treat happy hypoxemia and COVID-19 pneumonia

#### **Heart and Stroke**

The Sex Paradox: The Role of Sex Hormones in Right Ventricular Failure in Pulmonary Arterial Hypertension

#### **NSERC - Alliance Grant**

Synthesis and preclinical testing of novel small molecule therapies for COVID-19

#### CFI –

#### **Exceptional Opportunities Fund**

*MICROSCOPE*: Molecular Imaging of Coronavirus SARS-CoV-2 for Pharmacologic Exploration.

#### New Frontiers in Research Fund - Transformation

Engineering Human Models of Human Disease Using iPSC Derived Lung and Vascular Cells: A Personalized Medicine Approach to Identify Novel Mitochondrial Treatments for COVID-19 and Pulmonary Hypertension

#### CIHR – Project Grant Spring/Fall 2020

Dysregulation of TET2 and DNMT3A promotes pulmonary arterial hypertension (PAH) through inflammation: A new mechanism of PAH. Rauh / Archer - FUNDED

#### CIHR – Project Grant Spring/Fall 2020

Role of trained immunity in the response to BCG immunotherapy of bladder cancer. Graham / Seimens /Berman / Cotechini / Hindmarch / Jackson / Koti / Pare - FUNDED

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(left) Dr.'s Lima and Alizadeh

#### **INTERNAL GRANTS** (submitted)

# RAPID RESPONSE QUEEN'S SARS COV-2

Synthesis and preclinical testing of novel small molecule therapies for COVID-19 (*Archer, Hindmarch, Lima, Alizadeh*) - *FUNDED* 

#### SEAMO-COVID-19 Innovation Fund

Synthesis and preclinical testing of novel small molecule therapies for COVID-19 (Archer, Hindmarch, Lima, Alizadeh) – FUNDED

#### Faculty of Health Science SPEAR Grant

Validating multimodality microCT/PET/ SPECT for Assessment of Right Ventricular Function and Metabolism in Experimental Pulmonary Hypertension. (**Archer** and **Alizadeh**) - *FUNDED* 

#### DOM Research Award – CIHR Pillars:

The role of complement in membranous nephropathy. (**Moran and Lima**) *- FUNDED* 

#### **TIME Incubator Grant**

TIMEKeeper: A Comprehensive Cardiovascular Biobank Linked to Clinical and Outcomes Data to Support Implementation of Personalized Medicine through Translation Research. (**Archer**, Vanner, **Hindmarch**, Johri) - *FUNDED* 

#### **PUBLICATIONS SUPPORTED BY QCPU**

Bentley R, **Hindmarch C**, Dunham-Snary K, Read A, Mewburn J, **Lima P**, **Archer SL**. Examining Oxygen-Induced Changes in Gene Expression of Human Ductus Arteriosus Smooth Muscle Cells Using Transcriptomics. Free Radical Biology and Medicine. 2020 Nov 1;159:S86.

Potus F, Martin AY, **Snetsinger B, Archer SL**. Biventricular Assessment of Cardiac Function and Pressure-Volume Loops by Closed-Chest Catheterization in Mice. J Vis Exp. 2020 Jun 15;(160). doi: 10.3791/61088. PMID: 32597858.

Tian L, Xiong PY, **Alizadeh E, Lima PDA**, Potus F, Mewburn J, Martin A, Chen KH, **Archer SL**. Supra-coronary aortic banding improves right ventricular function in experimental pulmonary arterial hypertension in rats by increasing systolic right coronary artery perfusion. Acta Physiol (Oxf). 2020 Aug;229(4):e13483. doi: 10.1111/ apha.13483. Epub 2020 May 17. PMID: 32339403; PMCID: PMC7363583.

Tian L, Wu D, Dasgupta A, Chen KH, Mewburn J, Potus F, **Lima PDA**, Hong Z, Zhao YY, **Hindmarch CCT**, Kutty S, Provencher S, Bonnet S, Sutendra G, **Archer SL**. Epigenetic Metabolic.

![](_page_23_Picture_5.jpeg)

(left) Histologist Oliver Jones

Reprogramming of Right Ventricular Fibroblasts in Pulmonary Arterial Hypertension: A Pyruvate Dehydrogenase Kinase-Dependent Shift in Mitochondrial Metabolism Promotes Right Ventricular Fibrosis. Circ Res. 2020 Jun 5;126(12):1723-1745. doi: 10.1161/ CIRCRESAHA.120.316443. Epub 2020 Mar 27. PMID: 32216531; PMCID: PMC7274861.

Potus F, Pauciulo MW, Cook EK, Zhu N, Hsieh A, Welch CL, Shen Y, Tian L, **Lima P**, Mewburn J, D'Arsigny CL, Lutz KA, Coleman AW, Damico R, **Snetsinger B**, Martin AY, Hassoun PM, Nichols WC, Chung WK, Rauh MJ, **Archer SL**. Novel Mutations and Decreased Expression of the Epigenetic Regulator TET2 in Pulmonary Arterial Hypertension. Circulation. 2020 Jun 16;141(24):1986-2000. doi: 10.1161/CIRCULATIONAHA. 119.044320. Epub 2020 Mar 20. PMID: 32192357; PMCID: PMC7299806.

Dasgupta A, Wu D, Tian L, Xiong PY, Dunham-Snary KJ, Chen KH, **Alizadeh E**, Motamed M, Potus F, **Hindmarch CCT**, **Archer SL**. Mitochondria in the Pulmonary Vasculature in Health and Disease: Oxygen-Sensing, Metabolism, and Dynamics. Compr Physiol. 2020 Mar 12;10(2):713-765. doi: 10.1002/cphy. c190027. PMID: 32163206.

Dasgupta A, Chen KH, Wu D, Hoskin V, Mewburn J, **Lima PDA**, Parlow LRG, **Hindmarch CCT**, Martin A, Sykes EA, Tayade C, Lightbody ED, Madarnas Y, SenGupta SK, Elliott BE, Nicol CJB, **Archer SL**. An epigenetic increase in mitochondrial fission by MiD49 and MiD51 regulates the cell cycle in cancer: Diagnostic and therapeutic implications. FASEB J. 2020 Apr;34(4):5106-5127. doi: 10.1096/fj.201903117R. Epub 2020 Feb 18. PMID: 32068312. Wu D, Dasgupta A, Chen KH, Neuber-Hess M, Patel J, Hurst TE, Mewburn JD, Lima PDA, Alizadeh E, Martin A, Wells M, Snieckus V, Archer SL. Identification of novel dynamin-related protein 1 (Drp1) GTPase inhibitors: Therapeutic potential of Drpitor1 and Drpitor1a in cancer and cardiac ischemia-reperfusion injury. FASEB J. 2020 Jan;34(1):1447-1464. doi: 10.1096/fj.201901467R. Epub 2019 Dec 2. PMID: 31914641.

Bonnet S, Boucherat O, Paulin R, Wu D, Hindmarch CCT, Archer SL, Song R, Moore JB 4th, Provencher S, Zhang L, Uchida S. Clinical value of non-coding RNAs in cardiovascular, pulmonary, and muscle diseases. Am J Physiol Cell Physiol. 2020 Jan 1;318(1):C1-C28. doi: 10.1152/ajpcell.00078.2019. Epub 2019 Sep 4. PMID: 31483703; PMCID: PMC6985837.

McNeill MC, Wray J, Sala-Newby GB, **Hindmarch CCT**, Smith SA, Ebrahimighaei R, Newby AC, Bond M. Nuclear actin regulates cell proliferation and migration via inhibition of SRF and TEAD. Biochim Biophys Acta Mol Cell Res. 2020 Jul;1867(7):118691. doi: 10.1016/j. bbamcr.2020.118691. Epub 2020 Feb 28. PMID: 32119877; PMCID: PMC7262588.

Dutra SGV, Paterson A, Monteiro LRN, Greenwood MP, Greenwood MP, Amaral LS, Melo MR, Colombari DSA, Colombari E, Reis LC, **Hindmarch CCT**, Elias LLK, Antunes-Rodrigues J, Murphy D, Mecawi AS. Physiological and Transcriptomic Changes in the Hypothalamic-Neurohypophysial System after 24 h of Furosemide-Induced Sodium Depletion. Neuroendocrinology. 2021;111(1-2):70-86. doi: 10.1159/000505997. Epub 2020 Jan 20. PMID: 31955161. "The facilities, personnel and expertise at the Queen's Cardio-Pulmonary Unit (QCPU) have been essential to advance our understanding of the cellular and health impacts of age-related clonal hematopoiesis (CH). Access to Molecular and Cellular Imaging, Physiology and Experimental Therapeutics, and Transcriptomics and Molecular Medicine facilities were instrumental in our recently successful CIHR project grant, studying the intersection of CH and pulmonary arterial hypertension. Working the Transcriptomics core, led by Dr. Charlie Hindmarch, and imaging specialist, Dr. Patricia Lima, we are also advancing an exciting project looking at the impact of CH mutations on neutrophil gene expression and function. As at least 10 to 15% of older adults have CH, it is essential we understand the impact of these mutations on neutrophils and their ability to manage infections and inflammation. Working closely with QCPU is enabling us to unlock these secrets and to consider personalized and preventive approaches to healthy aging."

DR. MICHAEL RAUH (Associate Professor and Researcher in Pathology & Molecular Medicine)

#### What is on the horizon for QCPU?

Our main goal is to establish ourselves as the Tier 1 medical research facility at Queen's University. In 2020, we hope to become recognized as an official institute, with the objectives of establishing research excellence by continuing to conduct leading edge research that captures both national and international recognition, creating significant impact. In the year ahead, we also plan on creating more opportunities for public outreach and engaging educational program by taking advantage of the ability to host online tours and lectures. QCPU is dedicated to the enhancement of local, national and international collaboration, and we hope to see an expanse of our metrics of success including increasing our publications, funding and research partnerships, and expanding our interdisciplinary and multi-faculty research while engaging in more community outreach and knowledge translation.

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To learn more about our research and service, please visit our website: <u>depmed.queensu.ca/research/teams/qcpu</u> or follow us on Twitter (@QueensuCPU).

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