TED ROGERS CENTRE
FOR HEART RESEARCH



Donor Stewardship Report

APRIL 2022 – MARCH 2023

Presented March 2024

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Presidents' Message



Dr. Ronald Cohn



Dr. Kevin Smith



Professor Meric Gertler

On behalf of the Hospital for Sick Children, University Health Network, and the University of Toronto, we are pleased to provide you with the 2022/23 impact report for the Ted Rogers Centre for Heart Research.

Fueled by your family's visionary support and leadership, our three institutions are transforming the future of heart failure care and bringing the promise of a healthy heart to children and adults across Canada and beyond. Now a year into "Rogers 2.0", we would like to highlight the tremendous impact of your 2021 gift. Your ongoing support is critical to sustaining the work of the Ted Rogers Centre for Heart Research in perpetuity and to expanding its impact in a new era of precision health. Thank you for your unwavering commitment to this vital area of health research. Our respective institutions and researchers are united in a singular vision to make this the world's premiere centre for heart health research.

In its eighth year, the Ted Rogers Centre for Heart Research continued to advance health research and care, not least by developing an AI-based model for pediatric diastolic heart failure. In addition, the Centre researchers are utilizing the latest precision-medicine models to improve outcomes for heart failure patients—and have reduced hospitalizations by 50 per cent. Thanks to your renewed commitment, the Centre is bringing to life the promise of precision health, where patients are treated according to their unique genetic, structural, and environmental profiles.

This is no small feat.

Heart failure is among the world's deadliest conditions, one with many complex and overlapping causes that strike both old and young. There are no shortcuts in treatment and prevention—it takes nothing less than bringing together our most extraordinary medical talents across many fields, from engineering to cardiology, genomics, public health, and more.

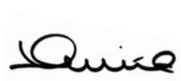
Since its creation, the Ted Rogers Centre for Heart Research has reduced hospitalizations while developing predictive, preventative, and personalized tools and treatments to slow and stop heart failure's fatal progression.

Your leadership and vision have made all of this possible.

In short, your family is directly helping people to live longer and more vital lives. We are tremendously grateful for your continued support of this critical priority in our healthcare system.



Dr. Ronald Cohn
President and CEO,
The Hospital for Sick Children



Dr. Kevin Smith
President and CEO,
University Health Network



Professor Meric Gertler
President,
University of Toronto



2022/23 at the Ted Rogers Centre

from Executive Director Dr. Mansoor Husain

In reflecting on our eighth year at the Ted Rogers Centre for Heart Research (TRCHR), it's inspiring to see the many advancements we have made through collaborations between the University of Toronto, University Health Network, and SickKids. Year 2022/23 brought back in-person showcase events where we celebrated the growth and success achieved by the TRCHR community. We hosted our first in-person Trainee Day for students and postgraduates which included almost 100 trainees from all three partners and 35 poster presentations. It's always wonderful to see the work our trainees are doing alongside the faculty and staff here at TRCHR.

Additionally, 2022 was our first hybrid Heart Failure Symposium since the COVID-19 pandemic, with an excellent turnout of both existing community members and external heart failure clinicians and scientists coming together at the Toronto Public Library. The energy from all those involved was palpable, and it was encouraging to see the groundbreaking advances made in heart failure research even during this challenging time, providing much confidence in the direction our Centre is heading. Many of these remarkable achievements are highlighted throughout this report, including:

CHF QBP Demonstration Project

- The TRCHR's Comprehensive Program in Heart Function was selected as one of six Ontario Health Teams (OHT) to create an innovative new model of care for heart failure. Using Medly as a digital-based tool to provide high-quality care in an efficient manner, this key project will help inform the average cost of holistically treating a patient with heart failure in Ontario.

Tmem65

- Drs. Anthony Gramolini and Robert Hamilton made a significant breakthrough on their work examining how the structure of the heart plays a role in abnormal heart rhythms. Using mice models, their work showed that a protein known as Tmem65 in the intercalated disc is imperative for a healthy heartbeat, with a goal of one day being able to screen patients for Tmem65 abnormalities before severe heart symptoms develop.

Cardiac Genome Clinic

- Dr. Raymond Kim and his team at the Cardiac Genome Clinic at SickKids were able to provide a diagnosis and path forward for a family that had been searching for answers to their neurological and cardiac symptoms for decades, uncovering a never-before-seen connection between the *MYBPC1* gene and a cardiac condition. This new association may help inform future screening measures for patients presenting with similar symptoms.

All of this would not have been possible without the generous support of the Rogers Foundation, and we continue to be grateful for the historic second gift received in 2021. With this renewed focus and energy, we finalized and launched our updated strategic framework for this next chapter in the Ted Rogers Centre for Heart Research history. Detailed in pages 6-7 of this year's report is an overview of our new strategic framework and objectives, developed by engaging patients and staff across all three partner sites to set big goals for what we'll accomplish in the years ahead. Our overarching objectives of increasing patient and caregiver engagement; increasing diversity, equity, and accessibility; and leveraging artificial intelligence are pillars on which our strategic priorities are anchored, which can be seen woven throughout the highlights of this year's report.

Building off the momentum of the previous seven years, we're excited to continue to work collaboratively to improve heart failure with our engaged, motivated, and growing community. We're confident that we will continue setting and exceeding our ambitious goals of understanding, treating, and eventually eradicating heart failure for all those in Canada and beyond. Thanks to the ongoing support and generosity of the Rogers Foundation, we continue to attract top talent, educate future leading researchers, and establish TRCHR as a global leader on our mission to transform and dramatically improve the future of heart health in Canada and around the world.

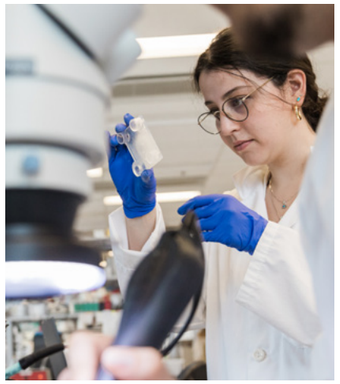


Dr. Mansoor Husain
Professor of Medicine, University of Toronto
Executive Director, Ted Rogers Centre for Heart Research

Looking Ahead: Our Refreshed Strategic Framework

Over the last decade, the Ted Rogers Centre for Heart Research has played a pivotal role in reshaping the landscape of heart health for individuals in Canada and beyond. Through collaborative endeavors spanning the University of Toronto, University Health Network, and SickKids, significant strides have been made in diverse fields of cardiac research, such as precision diagnostics, targeted therapies, and personalized care. This impactful work has not only contributed to advancing our understanding of cardiovascular health but has also translated into life-changing benefits for children, adults, and families. Following the historic milestone of a generous second gift from the Rogers Foundation, the TRCHR Executive Committee embarked on a journey to refresh the Centre's strategic plan and chart a course for the next chapter of groundbreaking advances in heart health.

To develop the plan, we leveraged the five-year internal assessment and external review that were previously conducted, identifying areas of strength and pulling insights to inform key future objectives. As part of this process, a reflection of existing and planned objectives across each program and partner took place to create an initial draft. These proposed goals and objectives were refined with the



Scientific Leads of the TRCHR, each of whom led discussions with their respective program team to seek input, align existing projects, and identify the need for new objectives.

Our next step was to involve the wider TRCHR family—including staff, trainees, and patient partners. We formed working groups with representation from each partner institution to further brainstorm around and sharpen our objectives. Each group was tasked with suggesting specific, measurable, achievable, relevant, and time-bound (SMART) goals to break down objectives into individual steps. They also identified gaps or opportunities that might have been missed. Patient partners were crucial in this phase as part of our goal of increasing patient engagement in research, from the very beginning stages throughout dissemination, a priority for both TRCHR and our partner institutions.

The community working groups offered valuable feedback on the new strategic plan. The next step involved the Directorate and Executive Committee going back to the proposed goals and objectives, incorporating the feedback received at each stage of the process. This led to a set of refined goals and objectives, which were then shared with the institutes. The institutes collaborated with their teams to align their program- and lab-specific initiatives with the overall objectives.

With the refined goals and objectives in place, the last phase involved drafting the official strategic plan. This document was reviewed by the Scientific Advisory Panel and key external partners, culminating in final approvals from the Executive Committee and the President's Steering Committee. The collaborative effort and extensive feedback received throughout this process have shaped a comprehensive guide that lays the groundwork for the TRCHR to continue delivering innovative and groundbreaking solutions to improve the heart health of Canadians and beyond.

Our Strategic Framework

OUR MISSION
Transform and dramatically improve the future of heart health for children, adults, and families across Canada and around the world, through an integrated program of outstanding research, education, and clinical care

OUR VISION
Create a world free of heart failure through groundbreaking collaborative research

OUR OVERARCHING GOALS



Increase patient and caregiver engagement



Increase inclusion, diversity, equity, and accessibility

Our Strategic Goals



Foster and promote world-class talent
Train, develop, and promote a diverse leadership of scientists, clinicians, engineers, patient partners, and entrepreneurs in collaborative approaches to HF research discovery and application



Target causes and progression of heart failure
Address biological, genomic, social, and environmental factors to prevent congenital and acquired heart failure at every stage of disease



Create precise and predictive digital health solutions
Empower heart failure patients, caregivers, and providers with accessible solutions that enable data-driven, person-centred, and personalized care



Enable equitable access to high-quality person-centred care
Implement and evaluate solutions to address inequities in access to quality heart failure care across settings through collaboration, partnership, and co-creation



Accelerate the application of discovery and innovation
Drive timely translation of research discoveries to practice through patient and caregiver engagement, knowledge mobilization, technology development, health policy, and commercialization

Integrated Program for Excellence in Heart Function

The Excellence in Heart Function Program at the Ted Rogers Centre for Heart Research comprises a coordinated suite of initiatives within UHN to deliver heart failure care, improve outcomes, and perform groundbreaking research.

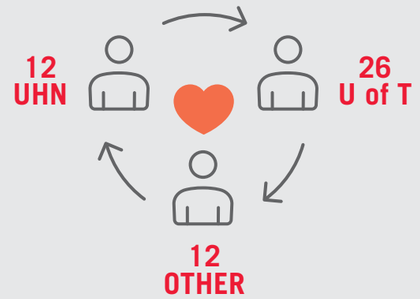
COMPREHENSIVE PROGRAM IN HEART FUNCTION

The Comprehensive Program in Heart Function is dedicated to improving clinical outcomes, patient education, quality of life, research, and trainee education, including the remote and digital heart failure monitoring program, Medly. Serving as a vital referral and resource hub for Ontario hospitals, inpatient and outpatient clinical services are supplemented by initiatives such as The Heart Hub—a go-to patient and caregiver online resource of expert-curated information on living with heart failure.

In Year 2022/23, the Comprehensive Program in Heart Function was selected as one of six Ontario Health Teams (OHT) demonstration sites to innovate new models of care for congestive heart failure. An OHT is a group of healthcare providers and organizations that deliver a seamlessly coordinated range of care services to a specific geographic population, in this case the Mid-West Toronto (MWT) region. Co-led by Dr. Heather Ross with partners from Women's College Hospital and Sinai Health, as well as two community health centres and involvement of patient partners, Medly's digital platform is now part of new integrated care pathways currently being tested within the MWT OHT. The focus on digital health–and Medly–seeks to reduce hospitalizations, refer patients directly from emergency departments to heart function clinics, and introduce remote management so patients can have their medications optimized. Early results show great promise, and aspects of this model are being considered in other OHTs across Ontario.

YEAR 2022/23 HIGHLIGHTS

- Dr. Douglas Lee, Ted Rogers Chair in Heart Function Outcomes, was a recipient of a Heart-Brain Connection IMPACT award totaling $3M for his project UNEARTH CVD, together with a national team of over 50 collaborators from TRCHR and beyond. This four-year project will investigate novel approaches for early recognition of transient ischemic attack, heart failure, and connections with vascular dementia to improve patient care and outcomes in Canada.



- Dr. Lee published the results of the Comparison of Outcomes and Access to Care for Heart Failure (COACH) Trial in the *New England Journal of Medicine*, a study examining the impact of a hospital-based strategy to determine which patients required rapid follow-up after visiting emergency care with acute heart failure. The trial showed that using the Emergency Heart Failure Mortality Risk Grade (EHMRG) calculator, developed in partnership with ICES and TRCHR, led to a lower risk of death from any cause or additional hospitalization after 30 days compared to the standard of care. Results are being applied in the MWT OHT's demonstration project with positive patient outcomes.

PETER MUNK CARDIAC CENTRE CARDIOVASCULAR BIOBANK

The Peter Munk Cardiac Centre Cardiovascular BioBank, supported by the TRCHR, is a centralized collection of de-identified patient samples and medical data from a diverse cardiovascular disease population. These samples are then used to empower translational research nationally and internationally.

In Year 2022/23, Dr. Phyllis Billia, a cardiologist and researcher at UHN, made great strides with a new diagnostics platform, CHI Diagnostics, which utilizes biomarkers to improve patient care for individuals with heart failure. In 2022, CHI Diagnostics discovered a new biomarker to help identify which patients will need continued intense surveillance following receiving a heart transplant and which do not. This biomarker has the potential to reduce the risk of complications, improve patient and family experience following a transplant, and reduce healthcare costs by decreasing hospitalizations and medical resources. A patent was filed for this novel biomarker in 2022 and commercialization of the venture is underway, with a Canada-wide prospective randomized clinical trial comparing the CHI Diagnostics platform against the standard of care beginning in October 2023.

YEAR 2022/23 HIGHLIGHTS

- The Biobank consented 3,959 patients and banked 45,338 specimens (plasma, serum, buffy coats, frozen surgical tissue, and extracted gDNA), growing the total number of consented patients to 20,826 and total number of stored specimens to 320,578.

- A total of 8,452 (+1,801 from previous year) biospecimens have been distributed from the Peter Munk Cardiac Centre CV Biobank for 54 study requests to support 28 unique studies.

- The biobank made significant strides in advancing accessibility and user engagement through the successful launch of the new website, pmccbiobank.ca. This innovative platform not only enhances interoperability but also establishes a centralized point of contact, providing researchers with a seamless and consistent method to query the biobank and learn about the range of services available.

CARDIOTOXICITY PREVENTION

Through research studies and clinical trials, the Cardiotoxicity Prevention program ensures cancer patients receive optimal cancer therapy while working to avoid heart failure, a potentially life-threatening side effect. UHN's program is a global leader, developing methods to diagnose and treat the harmful side effects of chemotherapy, including new immunotherapies, to ensure more patients benefit from these agents.

In October 2022, the TRCHR co-hosted the Global Cardio-Oncology Summit with the Canadian Cardiac Oncology Network and the InternationalCardiOncology Society. The conference saw over 500 international, interdisciplinary healthcare professionals share the latest research on the prevention, management, and treatment of cardiac complications related to oncology therapy. Additionally, the Cardiotoxicity Program co-authored the first European Society of Cardiology 2022 Guidelines on Cardio-Oncology. These guidelines set a new standard, helping healthcare professionals who provide care to oncology patients before, during, and after treatments with respect to their cardiovascular health and wellbeing. With such international leadership, the Cardiotoxicity Prevention program is a go-to expert in cardiotoxicity for clinical advancements and research breakthroughs.

YEAR 2022/23 HIGHLIGHTS

- Dr. Paaladinesh Thavendiranathan and his team explored whether using a heart function measure called global longitudinal strain (GLS) to guide cardioprotection (CPT) would result in less heart dysfunction in cancer survivors treated with potentially harmful chemotherapy compared to standard care. The results showed that both groups had similar improvements in heart function, and using GLS to guide CPT did not significantly differ from standard care in preventing heart dysfunction.

- Dr. Oscar Calvillo was awarded the Young Investigator Award at the Global Cardio-Oncology Society meeting for their work in cardio-oncology in Sudbury Ontario, and Dr. Pavithra Jeyadeva won the Best Research Award for the Canadian Society of Echocardiography Meeting for their work on the impact of cancer therapy on the heart in women with breast cancer. Additionally, Dr. Flora Huang won the Ursula Banks Research Day Award for their work on describing diastolic dysfunction in patients receiving breast cancer therapy.



HEART FAILURE TRAINING AND EDUCATION

Dr. Michael McDonald, Martha Rogers Chair in Heart Failure Training and Education, had an impressive year with his team, where he focused on training new researchers and improving care for patients living with heart failure. In 2022/23, Dr. McDonald chaired the updated Canadian Cardiovascular Society/Canadian Heart Failure Society Guidelines on Heart Failure with Reduced Ejection Fraction (HFrEF). In HFrEF, the left ventricle becomes weakened and cannot contract with enough force to adequately pump blood, resulting in decreased blood flow to the body. These guidelines are transforming pharmacologic treatment for patients with HFrEF.

YEAR 2022/23 HIGHLIGHTS

- TRCHR's Heart Hub team created *"Heart Failure Medications: A Guide for Patients and Caregivers"*. This collaboration with the Canadian Cardiovascular Society (CCS), Canadian Heart Failure Society, and HeartLife explains complex heart failure medications and supports patients in getting the right doses and combinations for their condition. A panel of clinicians, people with lived experience, and other experts collaborated to create this national education resource.

- Dr. McDonald was appointed to lead knowledge translation for the CCS National Active Surveillance Study of Myocarditis and/or Pericarditis following mRNA COVID-19 Vaccination (MYCOVACC) Registry, which is a national registry evaluating long-term outcomes in patients with COVID vaccine-related myocarditis and pericarditis, which are types of inflammation in specific areas of the heart.

- Dr. Mena Gewarges co-founded the Diversity and Inclusion in Cardiology Education (DICE) program within the Division of Cardiology at UHN/Sinai Health and the Black and Indigenous Medical Society (BIMS) program within the Department of Medicine at the University of Toronto. Her leadership, supported by the TRCHR Outcomes program, helps mentor and empower underrepresented undergraduate, medical, and post-graduate students and garnered more than $60,000 in funding for in-person workshops, training, and research opportunities.

LORETTA ROGERS CHAIR IN IMMUNOBIOENGINEERING

Dr. Slava Epelman, Loretta Rogers Chair in Immunobioengineering and Clinician-Scientist at the Peter Munk Cardiac Centre, continues to take significant strides toward the goal of unraveling how the immune system contributes to heart damage and how to facilitate its repair. During his five-year tenure as a Chair at TRCHR, his team utilized mouse model macrophages to achieve considerable milestones. Notably, a 2022 paper in *Immunity* explored recent advancements in the field of macrophages, specifically focusing on the diversity of macrophages in the heart, where they come from, and what they do under normal conditions and after the heart is injured. The team then categorized the functions of these resident heart macrophages based on whether they directly affect the heart's functioning or if they indirectly influence it by coordinating communication between different types of cells in the heart. This will help inform how each type of macrophage could be used to repair damage in the heart after a cardiac event.

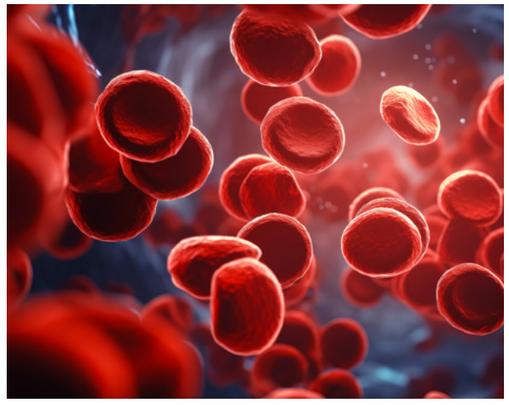
In a key 2023 paper published in *Nature*, Dr. Epelman and team shared "A cardioimmunologist's toolkit: genetic tools to dissect immune cells in cardiac disease". This paper examined real-life examples showing how the choice of tools can impact the quality and interpretation of data, particularly for cardiovascular biologists who may not be as familiar with the field of immunology. This inclusive approach, covering topics such as bone marrow chimeras, lineage-specific gene deletion, and transcriptional profiling of human cardiac immune and non-immune cells, is essential for educating newer clinicians and scientists in this evolving field. Through these efforts, the Epelman lab has solidified itself as a trailblazer in immunoengineering, establishing the "state-of-the-art" in this interdisciplinary field of cardiac research.

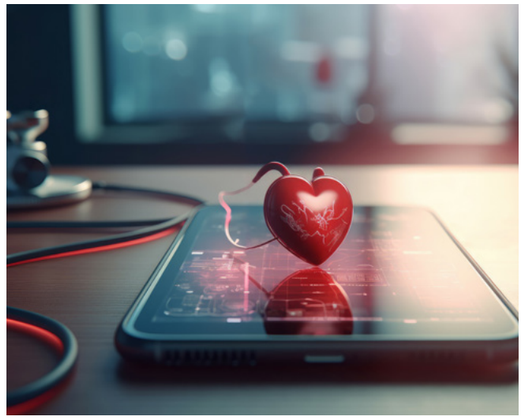
YEAR 2022/23 HIGHLIGHTS

- Dr. Epelman was recognized as a Web of Science Highly Cited Researcher, a prestigious award given to the top 1 per cent of researchers by citation in a specific field and publication year.

- The Epelman lab was awarded over $2M in funding this past year, including three CIHR grants for work on cardioprotection during hypertensive heart disease, exploring the role type 1 interferon plays in cardiac adaptation to stress and preventing heart failure, and analysis of monocyte-derived macrophages in viral cardiomyopathy.

- Under Dr. Epelman's leadership, six PhD candidates, three scientific associates, and two postdoctoral researchers focused on understanding the role myeloid cells (monocytes, macrophages, and dendritic cells) play within the myocardium during steady-state and following tissue injury.





PROGRAM IN HEALTH TECHNOLOGY ASSESSMENT AND DATA SCIENCE

The program in Health Technology Assessment (HTA) and Data Science was created alongside the Ted Rogers Computational Program (TRCP) and the Peter Munk Digital Cardiovascular Health Platform (DCHP) to combine leading data science, machine learning, and traditional statistical methods to improve research and patient outcomes. With an emphasis on quality improvement projects and quantifying the impact of research funding, the program provides novel and traditional analytical and methodological expertise to help complement the range of research projects currently underway across TRCHR.

In Year 2022/23, Dr. Valeria Rac, a senior researcher at UHN, and her team were pivotal members of the MAS-AI Framework, a project to develop the first HTA framework for artificial intelligence (AI)-powered technologies in Canada. With AI becoming increasingly used in health research and applications, this framework aims to assess the value of different AI-powered heart failure technologies to ensure relevance, safety, and technical and cost effectiveness. Initially developed within a Danish context and now validated in Canada, Dr. Rac and the MAS-AI team will look to expand validation of the tool in other international areas, such as Italy and Spain, in 2024 and beyond.

YEAR 2022/23 HIGHLIGHTS

- The HTA team had over 15 high-impact publications on topics such as evaluating programs in health equity in underserved communities, empiric model evaluation in 1-year mortality in patients with heart failure with reduced left ventricular ejection fraction, and the creation of a model for assessing the value of AI in medical imaging.

- The TRCP team were primary statisticians or lead authors in 37 publications, including six high-impact publications in the *Circulation* journal and the *Journal of American College of Cardiology*.

- Comprehensive data management and statistical trainings were conducted by the TRCP team to educate UHN cardiology fellows, UHN transplant fellows, and SickKids cardiovascular surgery fellows on advanced data science methods for future research.

- The Ted Rogers Computational Program is the first Canadian site in the Cath PCI (percutaneous coronary intervention) Registry of the National Cardiovascular Disease Registry in the American College of Cardiology. The CathPCI Registry evaluates the features, treatments, and results of patients with cardiac diseases undergoing diagnostic catheterization and/or PCI procedures.



Dr. Heather Ross Wins UHN's Inventor of the Year



(L to R) Dr. Brad Wouters, UHN's Executive Vice President of Science and Research, Dr. Heather Ross, Dr. Joseph Cafazzo, and Mr. Mark Taylor, Director of Commercialization at UHN. (Photo: UHN StRIDe Team)

Year 2022/23 was a big one for our Scientific Lead! Dr. Heather Ross, Division Head of Cardiology at the Peter Munk Cardiac Centre, was awarded UHN's Inventor of the Year Award. This is the first time a TRCHR Scientific Lead has received this prestigious award.

Presented by UHN Commercialization, the Inventor of the Year Award acknowledges an individual or team whose invention has significantly contributed to creating a healthier world. For Dr. Ross, the recognition was given for her ongoing work building and commercializing the Medly remote management program for heart failure.

The Medly program, a hallmark invention of TRCHR and the Centre for Digital Therapeutics at UHN, has transformed patient outcomes over the past eight years. This digital app allows patients to input real-time health updates, keeping track of data and analyzing trends. A sophisticated algorithm calculates the likelihood of a negative cardiac event, communicating directly with the healthcare team for remote monitoring and updated treatment plans, with no in-person visit required. Medly enables one nurse to monitor up to 250 heart failure patients simultaneously, surpassing the capacity of in-person care. In 2020, research showed that Medly reduced rehospitalizations by 50 per cent and all-cause admissions by 24 per cent for people with heart failure while improving their self-care and quality of life, becoming the first telemonitoring system to be designated a Class II medical device by Health Canada.

SPECIAL HIGHLIGHT

"We are often still overly focused on treating patients once they become acutely ill and end up in hospital," says Dr. Ross. "Leveraging the incredible power of artificial intelligence and predictive analytics, Medly provides a more proactive, scalable and affordable solution to managing the epidemic of heart failure – and research is continually ongoing to enhance it."

Medly's reach now extends far beyond the Greater Toronto Area, thanks to an ongoing partnership with Weeneebayko Area Health Authority (WAHA) and a Health Innovation Challenge grant from Ontario Health and Boehringer Ingelheim. Dr. Ross is bringing the Medly program to remote communities along the James and Hudson Bay coasts in Northern Ontario to support WAHA in providing optimum healthcare as close to home as possible. By the end of year 2022/23, Dr. Ross and her team exceeded their target enrollment of WAHA patients by 33 per cent, with over 85 per cent of patients reporting that they were satisfied with the care Medly provided. In addition to WAHA, Dr. Ross's team is working in collaboration with Yale University to adapt Medly for rural and remote communities in Uganda thanks to a five-year National Institutes of Health (NIH) grant valued at almost three million dollars.

It was this momentum that caught the attention of the judging panel for UHN's Inventor of the Year award, and ultimately secured the win for Dr. Ross amongst many other excellent innovations. Congratulations, Dr. Ross and team!



Dr. Heather Ross has spearheaded the Medly Program since its inception in 2015.

Translational Biology and Engineering Program

The Translational Biology and Engineering Program (TBEP) is a multi-disciplinary collaboration of engineers, scientists, and clinicians from the University of Toronto's Faculty of Applied Science and Engineering, Temerty Faculty of Medicine, and Faculty of Dentistry.

The TBEP team investigates the genetic, molecular, and cellular physiology and pathology underpinning heart failure to uncover new strategies to diagnose and treat cardiovascular disease and regenerate heart tissue. By working closely with clinical and industry partners, TBEP paves the way for translational research and technology development. This collaborative effort ensures that new ideas, tools, and technologies that start in the research lab make their way to having a positive impact on patients' lives.

YEAR 2022/23 HIGHLIGHTS

- TBEP attracted 69 trainees (40 PhD and 20 MSc candidates and nine postdoctoral researchers) and 16 full-time research staff from nine departments across the University of Toronto.

- TBEP trainees held over $775,000 in scholarships and awards and contributed to 49 peer-reviewed publications in high-impact journals. Of those, 37 per cent included cross-collaborations with other members of the TRCHR.

- The TBEP Undergraduate Summer Research Program (USRP) provides training for undergraduate students for up to 16 weeks alongside TBEP investigators on interdisciplinary research projects focused on cardiovascular disease and heart failure, with 12 students recruited for the summer of 2022.

- TBEP principal investigators held $11,471,789 in internal and external grants ($10,894,396 for operating and equipment) and industry research contracts ($577,393) that supported interdisciplinary and collaborative research projects, establishing new or fortifying past partnerships within the TRCHR (making up 46 per cent of the grant proposals). Of those, $9,591,789 were from sources external to TRCHR and the University of Toronto.

With a New Frontiers in Research Fund (NFRF) grant and a Natural Sciences and Engineering Research Council Idea 2 Innovation (NSERC I2I) grant, collectively valued at $265,000 over two years, TBEP principal investigator, Dr. Michelle Bendeck, in collaboration with Dr. Paul Santerre, a fellow TBEP investigator, developed a novel peptide nanoparticle delivery system to treat vascular disease. When blood vessels are blocked, common treatments involve angioplasty and/or stenting procedures, which can sometimes lead to the narrowing of the blood vessels (restenosis) and blood clotting (thrombosis). Current drugs used to prevent restenosis can be toxic to vascular cells, delaying the healing of the inner lining of the blood vessels (the endothelium) and potentially leading to in-stent thrombosis. To address this problem, Dr. Bendeck's research team developed a novel protein-targeting substance that effectively prevents the unwanted migration of vascular cells that contribute to restenosis, while allowing endothelium repair. When applied to injured blood vessels in rats, the peptide delivery system reduced vessel thickening without negatively impacting vascular cells and hindering the repair process. This work demonstrates the potential of using targeted peptide therapies to prevent the unwanted issues caused by angioplasty and stenting procedures in patients with vascular disease.

Dr. Paul Santerre, TBEP principal investigator and Baxter Chair in Health Technology and Commercialization at UHN, and his lab made significant headway in Year 2022/23 towards their work on regenerating vascular tissue using adipose tissue from humans. Adipose tissue—or fat tissue—is abundant, easy to acquire, and largely dispensable, making it an excellent source for creating artificial blood vessels for patients who have damaged or diseased vessels. Dr. Santerre's research team focused on studying the composition of human fat tissue and its resident cells to identify cell types that have the greatest potential for regenerating artificial blood vessels. In their most recent findings, they were successful in identifying two cell populations, one with the ability to regenerate the inner lining of a blood vessel and the second with the potential capacity to support the maturation of the vessel lining through the assembly of a support structure. The Santerre lab also developed a new method using magnets to selectively and reproducibly isolate specific cell populations from fat tissue. In addition to being a less expensive, simpler, and more reproducible alternative to existing methods, this two-staged protocol yielded cell populations with high purity and the capacity to be grown and maintained in the lab for long periods. This exciting work is helping to investigate treatment options for patients with damaged blood vessels in a way that is both accessible and cost-effective.

TED ROGERS CHAIR IN CARDIOVASCULAR ENGINEERING

Dr. Daniel Franklin, TBEP principal investigator and Ted Rogers Chair in Cardiovascular Engineering, and his lab had multiple notable highlights in Year 2022/23. In particular, his lab led several high-impact publications, including an article demonstrating racial bias and inaccuracies in pulse oximetry measurements in individuals with darker skin tones. A patient monitoring tool using non-invasive measurement of blood oxygen saturation, pulse oximetry has been recognized as a powerful and essential technology to improve patient safety with increased applications for remote monitoring and in wearables. Dr. Franklin and his team, in collaboration with Dr. Heather Ross (Scientific Lead at UHN), are working on strategies to mitigate bias, improve the accuracy of pulse oximetry across skin tones, and enhance its clinical use across a diverse population.

YEAR 2022/23 HIGHLIGHTS

- Dr. Franklin and his team were finalists in the Open Oximetry Competition in 2022 with newly developed wearable sensors that quantify skin constituents and improve pulse oximeter accuracy across skin tones.

- The Franklin lab was part of several key funding awards, including a Canadian Foundation for Innovation (CFI) Grant ($17.6M), a Natural Sciences and Engineering Research Council of Canada Collaborative Research and Training Experience (NSERC CREATE) Grant ($1.65M), and the Heart & Stroke Foundation and Brain Canada IMPACT award for UNEARTH CVD ($2.9M) with co-investigator Dr. Douglas Lee (Ted Rogers Chair in Heart Function Outcomes).

- Several of Dr. Franklin's trainees took home significant awards in 2022, including the Best Presentation Award at the Cardiovascular Sciences Collaborative Specialization Annual Student Research Day and first place in the inaugural ECHO Discovery Pitch Competition.



Dr. Daniel Franklin (top left) with his lab.

ECHO

Entrepreneurship for Cardiovascular Health Opportunities (ECHO) is a 12-month national training program supporting cardiovascular research commercialization through education, mentorship, networking, and funding. Led by a diverse network of experts, ECHO fosters successful startups in cardiovascular health, culminating in an annual pitch competition (ECHO PITCH) offering up to $250,000 in funding. Since 2018, ECHO has engaged 86 mentors, held 107 workshops, hosted 23 webinars, trained 81 team members, and launched 37 ventures in the cardiovascular health space.

YEAR 2022/23 HIGHLIGHTS

Up to and including Year 2022/23, ECHO has held four pitch competitions and awarded $1M in funding to support five promising cardiovascular ventures, ensuring more life-changing technologies and promising innovations reach patients. Since their graduation from ECHO and leveraging the program's resources, the winning ventures have continued to grow and have made significant progress. On a financial level, in addition to the ECHO funds, ventures in the program have cumulatively raised ~$3.7M of external funding, 44 per cent ($1,620,000) in investments and 56 per cent ($2,076,708) in non-dilutive funds.

In its eighth year ECHO awarded $250,000 to Vitreosonic, a startup venture led by Dr. Gary Yau (University of Toronto) and Dr. Kullervo Hynynen (Sunnybrook Hospital). Vitreosonic is developing the only non-surgical solution to treat sudden vision loss from intraocular hemorrhage, a leading cause of blindness in heart failure patients.

In Year 2022/23, ECHO launched the national Discovery Program through a partnership between TBEP and the TRANSFORM HF initiative. ECHO Discovery is a six-month foundational education program intended specifically for those who are interested in exploring ideation, research translation, and entrepreneurship within the cardiovascular health sector but do not yet have an innovation. Within its inaugural year, ECHO Discovery enrolled and trained a diverse population of 30 trainees from across Canada, including four undergraduate and 22 graduate students, three clinical and postdoctoral fellows and a clinician. While 70 per cent of the trainees were from U of T and affiliated hospitals, the remaining 30 per cent were from other Canadian universities and research institutions.

ECHO Discovery culminated with a public virtual pitch competition where Panaroma Health, with a team of five trainees, won $500 to put towards launching their idea. Panaroma Health is proposing an app that integrates daily data from wearable devices with AI-generated prompts to engage and encourage positive behavioural change and reduce smoking, which is a major risk factor for cardiovascular disease.



SPECIAL HIGHLIGHT

TRANSFORM HF

This partnership of TRCHR and the University of Toronto is committed to empowering collaboration and patient-driven, technology-powered equitable care, with the ultimate goal of improving the lived experience for patients with heart failure. TRANSFORM HF co-leads Dr. Craig Simmons, Scientific Lead for TRCHR's Translational Biology and Engineering Program, and Dr. Heather Ross, Scientific Lead for TRCHR's Excellence in Heart Function Program, drive the initiative's vision of digital innovation. In Year 2022/23, TRANSFORM HF saw strong growth, increased patient engagement in research, and significant advancements in digital technologies for equitable access to personalized heart failure care.

YEAR 2022/23 HIGHLIGHTS

- The TRANSFORM HF team entered a new phase in its partnership with Weeneebayko Area Health Authority (WAHA) and communities along James and Hudson Bay. A May 2022 sharing circle in Moosonee with more than 20 community members informed the design of the team's activities as they strive to provide equitable access to high-quality heart failure care as close to home as possible. Guided by a local Cree Elder, results were published as a graphic report as well as in an academic journal, ensuring community members could validate and affirm the team's work and interpretations.
- Membership increased 56 per cent, and TRANSFORM HF members now hold over $10M+ in leveraged funding, including a six-year NSERC Collaborative Research and Training Experience (CREATE) grant valued at $1.65M to develop the Translating Cardiovascular Remote Diagnostic & Monitoring Technologies for Health Equity (CaRDM Eq) training program over six years with partner contributions, with a goal of developing a $4M program and training 120+ highly qualified personnel.



56% Membership Increase | **$10M+ Leverage Funding** | **6 Year Collaborative Research and Training**

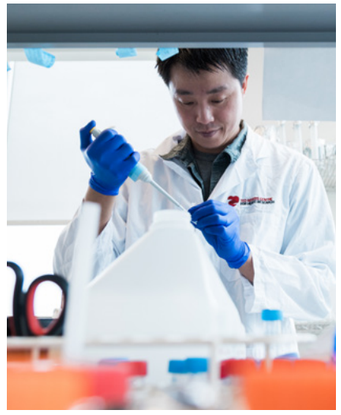
GOAL: $4M Program and Training 120+ Highly Qualified Personnel

- Across TRANSFORM HF's internal funding competitions, including seed grants, trainee awards, and collaboration starter grants, there were eight funding competitions, 49 unique applicants, 97 unique collaborators, and over $490,000 of research funding awarded.
- The team at TRANSFORM HF reimagined TRCHR's patient education site, The Heart Hub, guided by input from more than 300 UHN patients and caregivers, and overseen by an advisory committee of people with lived experience and clinicians.
- In May 2022, TRANSFORM HF launched its first On-the-Land Indigenous Education Program, a cultural safety training for clinicians, engineers, and trainees. Learning from Elders and Knowledge Keepers, members embark on a journey to equity and justice in heart failure care, education, and research.

Tmem65 Breakthrough Yields New Insights in Cardiac Health

For Dr. Anthony Gramolini and his team of researchers at TBEP, 2022 was a big year that was almost a decade in the making. Dr. Gramolini's research focuses on cell surface proteins in the heart which are known for cell-cell communication and possess great therapeutic potential. Thanks to funding from the TRCHR and the CIHR, this work culminated in an impactful discovery—the role of Tmem65, a cell membrane protein found in intercalated discs (ICDs), which are complex structures in the heart muscle critical for synchronized heart beats.

While the team discovered Tmem65 as a top candidate of 500 cell membrane proteins back in 2015 using new protein purification methods and mass spectrometry, it was not immediately clear what role Tmem65 played in a healthy, functioning heart. A few years later, Dr. Allen Teng joined the project in the Gramolini lab and set out to learn more about Tmem65. This scientific investigation was a collaborative effort with another TRCHR investigator, Dr. Robert Hamilton, a Clinician-Scientist at SickKids



Dr. Allen Teng joined the Gramolini lab and set to work exploring Tmem65.

whose research focuses on heart rhythm disorders.

Drs. Teng and Hamilton wanted to learn how Tmem65 contributed to heart function. Their research showed that Tmem65 was required for ICD structural integrity, coordinating contractions of neighboring cardiac muscle cells, and maximizing heart function. Applying a heart-specific gene-silencing approach, the team was able to remove 90 per cent of Tmem65 protein from mouse hearts compared to a control group. The decrease in Tmem65 led to a 60 per cent reduction in the amount of blood pumped out of the heart per minute as determined by high-resolution echocardiography, resembling what can happen in severe forms of human heart failure. Additionally, there was a decrease in electrical signals within the heart, as observed through optical recording and electrocardiograms (ECGs). Specifically, the optical recording showed a delay in heart signal conduction and a reduction in the ability of the heart to contract. Seven weeks after the Tmem65 silencing, all mice in the experimental group succumbed to heart failure and arrhythmia-related sudden death. This association between Tmem65 and arrythmias had never been observed before, and as a result was published in the prestigious journal *Nature Communications* in October 2022. These findings have since been replicated by other members of Dr. Gramolini's team in donated human hearts.

SPECIAL HIGHLIGHT



(L to R) Dr. Anthony Gramolini, Ms. Michelle Di Paola, Dr. Allen Teng, and Ms. Wenping Li all helped to discover how Tmem65 contributes to heart function.

According to Dr. Teng, this novel discovery has the potential for far-reaching implications. "If there isn't enough Tmem65 present, our work has shown that ICDs are negatively impacted across the board. This makes us believe that genetic screening for Tmem65 in the future may enable us to identify people at risk of arrhythmia so clinical support can be implemented." Although there is still plenty of work needed to translate these findings into a clinical context, Dr. Gramolini echoes Dr. Teng's optimistic outlook on the impact their work may have on people living with heart failure. "Our fascination in cardiac biology has thus far revealed many unchartered territories, which, we envision, will capture patients who are at the risk of conduction defects and sudden death". Thanks to this work, the team is one step closer to understanding new cardiac structures and the role ICDs play in keeping hearts healthy and functioning as they should.



Ms. Michelle Di Paola and Dr. Allen Teng working in the Gramolini lab at the Translational Biology and Engineering Program.

Cardiac Genome Clinic

The Cardiac Genome Clinic (CGC), led by Dr. Raymond Kim, one of the Centre's Scientific Leads and an Associate Professor of Medicine at the University of Toronto and Medical Geneticist at SickKids, is a clinical research program utilizing comprehensive genetic testing, known as Whole Genome Sequencing (WGS), to identify the genetic origins of heart conditions like heart failure in both individuals and their families. The program is designed to tailor treatment options for patients and their family members and facilitate the integration of research findings into clinical care. Findings are categorized into four levels: primary, which explain the genetic origins of their heart condition; secondary, which are medically actionable results unrelated to the heart condition; pharmacogenomic, which inform an individual's response to specific drugs; and research candidates used for further gene discovery work. These findings collectively enhance medical care and contribute to the identification of other family members at risk for the same condition. A collaborative team of medical geneticists, cardiologists, genome data analysts, genetic counselors, and bioinformaticians work together to improve health outcomes for both patients and their families.

YEAR 2022/23 HIGHLIGHTS

- Since inception, the program has received referrals from 94 healthcare providers from seven sites across Ontario, positioning itself as a cardiovascular genetics program of significant importance in the province.
- The team has cumulatively performed WGS on 1,100 individuals from 400 families.
- Four families received a new primary genetic finding explaining their cardiac diagnosis, and three had secondary findings conferring risks for other actionable genetic conditions.
- The program has clinically validated 130 pharmacogenomic findings for return to individuals and their care teams.

In addition to facilitating genome sequencing for individuals and families, the Cardiac Genomic Clinic is also focused on sharing how genetic testing in cardiology has proven to be instrumental in improving patient and family management. WGS has emerged as a powerful tool within precision medicine, enhancing genetic discoveries, diagnostics, and personalized care. However, there are challenges in seamlessly integrating WGS into cardiology, including the need for better genomic literacy, ongoing data interpretation, and managing communications with patients. In Year 2022/23, the Cardiac Genome Clinic shared details about how they use a multidisciplinary model to integrate genomics with cardiac care so that other cardiology departments can use a similar strategy to incorporate WGS into pediatric cardiology. The study was published in the *Canadian Journal of Cardiology* and led by Ms. Kaitlin Stanley, a genetic counselling student at the University of Toronto and Clinical Research Project Coordinator with the Cardiac Genome Clinic along with two Cardiac Genome Clinic-affiliated genetic counsellors, Ms. Eriskay Liston and Ms. Kelsey Kalbfleisch. Their work provides data demonstrating WGS' ability to support new diagnoses, identify medically actionable secondary findings, and enhance medication management.

While targeted genetic testing is currently initiated in certain clinical scenarios, WGS, with its comprehensive and non-targeted approach, offers a promising alternative by improving results, reducing the need for multiple tests, and contributing to gene discovery with broad applications. The multidisciplinary model presented includes genetic counselors, geneticists, cardiologists, bioinformaticians, and pharmacogenetic specialists working together to create informed treatment plans for patients. The Cardiac Genome Clinic is hopeful this work will provide a blueprint for other cardiac departments looking to implement WGS to improve overall patient outcomes.



(L to R) Dr. Raymond Kim and Dr. Rebekah Jobling of the Cardiac Genome Clinic.

Cardiac Precision Medicine Program

The Cardiac Precision Medicine Program develops personalized treatments and preventative strategies based on the unique biological, clinical, and lifestyle characteristics for children with heart disease. Using a biobank, next-generation sequencing, and characterization of tissue- and patient-derived induced pluripotent stem cells, along with the testing of novel therapies, the program has made significant strides towards understanding the causes of heart disease and finding better ways to treat it.

YEAR 2022/23 HIGHLIGHTS

- The program's Heart Centre Biobank recruited over 100 new participants at SickKids, bringing the total number of consented individuals to 10,623.

- The program identified genetic variants known to cause or relate to cardiac conditions in 78 individuals and communicated these findings for disclosure.

Building off the program's work in precision medicine for cardiomyopathies and remote monitoring, Dr. Seema Mital, the SickKids Scientific Co-Lead of TRCHR, and Dr. Aamir Jeewa, a TRCHR-affiliated Scientist, were awarded the Canadian Heart Function Alliance (CHFA) CIHR Network Team Grant as pediatric team leads. The team, as part of a pan-Canadian alliance, will develop an AI-based model to diagnose diastolic heart failure, implement remote physiological monitoring using smart textiles, and launch a digital peer-to-peer self-management program for adolescents and transitioning patients across Canada. The CHFA is a $5M CIHR award leveraging an additional $27.2M from industry and academia through cash and in-kind contributions. The project involves collaboration with 30 hospitals across nine provinces and one territory, with participation from over 40 patient partners.

With genome sequencing completed in 1,397 cardiomyopathy patients and families within the program supervised by Dr. Mital, a team of researchers published an article in 2022 in the *Journal of Cardiovascular Translational Research* highlighting age and sex differences in the genetics of cardiomyopathy. Cardiomyopathy is a group of diseases impacting the heart's ability to pump blood effectively through the body which makes it the leading cause of sudden death in adolescents. This study contributes information to guide family screening for this disease in clinical practice. Findings suggest that the gene affected, the location of the mutation within the gene, and the features of its inheritance are predictive of when the disease will manifest and its severity, which is valuable for predictive counseling and targeted treatment for families at risk.

Both economic and scientific evidence are needed to inform policy for new diagnostic testing, such as whole genome sequencing, which the Cardiac Precision Medicine Program strives to make more readily available to families in need. Dr. Wendy Ungar and team, supported by both the Cardiac Precision Medicine Program and the Cardiac Genome Clinic, recently micro-costed trio genome sequencing for children with cardiac conditions. Trio genome sequencing involves sequencing a child and both parents, which helps to determine if conditions are passed down or new and can inform diagnosis and treatment decisions. The results of the study indicated that while the initial average cost for testing was higher for cardiac conditions compared to other developmental disabilities, the five-year estimated program cost for testing in these patient populations was nearly five times less than that for developmental disabilities. Higher costs per sample were due to increased interpretation time for the number and types of genes tested for cardiac conditions, whereas program costs were lower overall based on the number of families who met the criteria for testing. These results will help inform decision makers about cost and resource requirements to more broadly deploy this technology in practice.

SPECIAL HIGHLIGHT

Unraveling The Mystery of a Family's Heart Struggles

In 2022, the Ted Rogers Centre for Heart Research Cardiac Genome Clinic accomplished something extraordinary for the Jefferson* family, who had been grappling for decades with chronic muscle weakness, tremors, and multifocal non-ischemic myocardial fibrosis. Myocardial fibrosis is a condition that involves abnormal thickening and scarring of the heart muscle in multiple areas, affecting its structure and ability to function. The family had sought answers through a variety of specialists, but it was the team at the Cardiac Genome Clinic at SickKids who finally provided clarity.

The Cardiac Genome Clinic is a unique collaboration of clinical healthcare providers and researchers dedicated to using cutting-edge whole genome sequencing (WGS) to identify causes and potential treatment options for severe health concerns in children, adults, and families. WGS is a comprehensive genetic testing method that examines the complete DNA sequence, offering insights into genetic variations and mutations.

For the Jefferson family, their journey began with Mr. Jefferson experiencing muscle weakness and tremors from birth. Although his symptoms were always present, they began worsening in adulthood, where he experienced difficulties walking unassisted and developed new symptoms of chest pain. A cardiac MRI revealed thickening and scarring of the muscles in his heart, which was impacting his ability to function normally and resulting in chest pain. His daughter had faced similar challenges of muscle tremors and weakness since birth. When the family saw the adult genetics team at UHN in 2019, they ordered a type of comprehensive genetic testing called trio whole exome sequencing in Ms. Jefferson and both of her parents, but this testing did not identify the cause of their health struggles. The team at UHN then referred the family to the Cardiac Genome Clinic at SickKids to see if an answer could be uncovered. The Cardiac Genome Clinic, using advanced whole genome testing made possible by funding from the Ted Rogers Centre for Heart Research, identified a previously missed pathogenic variant in the *MYBPC1* gene.

MYBPC1, or Myosin Binding Protein C, Slow Type, is a gene that provides instructions for making a protein involved in muscle contraction, and issues with this gene can result in the muscles not being able to function normally, as was the case with the Jefferson family. The specific change in the *MYBPC1* gene wasn't noticed in the initial genetic testing report because, at that time, its connection to the family's health condition wasn't known, but it was able to be identified in 2022 thanks to advances in genomic research since 2019.

Dr. Raymond Kim was happy with the outcome from the CGC, "Our work goes beyond individual cases, unraveling genetic mysteries to provide not only answers for families like the Jeffersons but also contributing to a broader understanding of cardiac-related health conditions." He continued, "This work can potentially pave the way for faster and more accurate diagnoses in similar cases."

This groundbreaking discovery marked a new chapter for the Jefferson family by finally providing a diagnosis and insight into the right treatment plan, as well as the greater field of *MYBPC1* and genomic research. It marks the first time *MYBPC1* has been linked to heart muscle dysfunction, offering crucial insights that can contribute to faster diagnoses and treatments for patients showing similar symptoms. The Cardiac Genome Clinic team are confident that this discovery will help clinicians provide these patients with cardiac screening before *MYBCP1* can impact cardiac functioning.

*Names have been altered for patient privacy.

A Miniature Marvel: Pediatric Heart Solutions Through Innovation

With new treatments being devised for adults with heart conditions on an ongoing basis, is it possible that they could work equally well on children? That was the question Dr. James Ellis, a Senior Scientist at SickKids, and Dr. Seema Mital, Scientific Lead at the Ted Rogers Centre for Heart Research and Clinician-Scientist at SickKids, wanted to explore following their 2018 TRCHR Strategic Innovation Award. The sought-after award focuses on propelling great bench research, proof-of-concept development, and clinical assessment to move new innovations forward. Whereas major government grant competitions tend to be more risk averse, this award encourages lofty but achievable targets that include collaboration between at least two of the Centre's three partners.

With this funding, the team was able to investigate possible treatments for pediatric hypertrophic cardiomyopathy (HCM). Hypertrophic cardiomyopathy is a genetic disorder typically caused by variants in the *MYH7* and *MYBPC3* genes and is characterized by abnormal thickening of the heart muscle, which makes it harder for the heart to pump blood effectively. This condition can impact individuals of all ages but is the leading cause of heart failure and sudden cardiac death in children.



Lead author Dr. Caroline Kinnear at the Ellis Lab in the Peter Gilgan Centre for Research and Learning at SickKids.

Currently, the best treatments available include calcium channel blockers and beta-blockers, but they only provide symptom relief instead of treating the root cause. It was this issue that caught the attention of the team, and they decided to test if myosin-targeted drugs like myosin ATPase inhibitors that were recently approved or trialed in adults might also help children.

To explore this, Dr. Ellis and team generated induced pluripotent stem cells (iPSC)-derived cardiomyocytes, which are beating heart muscle cells created in the lab by reprogramming a patient's own skin cells, from four pediatric patients with HCM. As controls, cardiomyocytes were derived from the same stem cells after the genetic variants in *MHY7* and *MYBBPC3* were corrected by gene editing. The HCM and control cardiomyocytes were tested for their response to the myosin inhibitors compared to the existing standard-of-care drugs like calcium channel and beta-blockers. Dr. Mital's team looked at the effect of the drugs on cell contractility, relaxation, and other cardiac function abnormalities seen in HCM cells. When the experiment was completed, both inhibitors had reversed the abnormalities and were more effective than existing therapies. Moreover, when compared to cells in which the mutation had been corrected with gene editing, the drugs were as effective as genetic correction of the cells!

SPECIAL HIGHLIGHT

These results highlight the need for future myosin inhibitor drug trials in pediatric HCM patients to see if this might be a pathway to preventing heart failure and sudden cardiac death in children. For Dr. Ellis, the highlight of the study is that "it shows how stem cells can model pediatric disease in the lab and then advance precision medicine by identifying the optimal treatment for each child's genetic variant." According to Dr. Mital, "By investigating the efficacy of myosin ATPase inhibitors in pediatric patients, we're not just alleviating symptoms but targeting the underlying genetic causes of hypertrophic cardiomyopathy, potentially transforming the landscape of pediatric heart treatments."

Following this exciting discovery, Drs. Ellis and Mital turned to their partner at the University of Toronto, Dr. Milica Radisic, Professor and Canada Research Chair of Functional Cardiovascular Tissue Engineering, to test the effect of myosin inhibitors in a 3D tissue model. Dr. Radisic's work showed that blocking the myosin ATPase consistently made the heart tissues behave more like normal tissues, confirming that the drug had the desired effect. "The results are very promising" commented Dr. Radisic, "We're hopeful that future testing with this patient population will build upon what we're seeing here." With a high-impact publication currently in the works, the team will begin looking at clinical trials in the coming year.





(L to R) Drs. James Ellis, Seema Mital, Milica Radisic, Phyllis Billia, and Craig Simmons showcase the collaborative nature of the TRCHR by representing all three partners with their 2018 Strategic Innovation Award.

Education Fund Award Recipients – 2022



Post-Doctoral Researcher (4)

Trainee:	**Ayodele Odutayo**
Project:	Expanding the Use of SGLT-2 Inhibitors to Improve Cardiorenal Disease
Supervisor(s):	Jay Udell
Institution(s):	U of T
Collaborator(s):	David Cherney
Trainee:	**Faisal Alibhai**
Project:	Development of a Synthetic Safety Switch to Control Graft Related Arrhythmias Following HPSC Transplantation Post-MI
Supervisor(s):	Michael Laflamme
Institution(s):	UHN
Collaborator(s):	Michael Garton, Kumaraswamy Nanthakumar. Christoph Haller
Trainee:	**Katheryn Rothenberg**
Project:	Discovering Talin Binding Partners During in Vivo Migration
Supervisor(s):	Rodrigo Fernandez-Gonzalez
Institution(s):	U of T
Collaborator(s):	Anthony Gramolini, Rajiv Chaturvedi
Trainee:	**Maelys Venet**
Project:	Variations in Right Ventricular Myocardial Stiffness According to Loading Conditions
Supervisor(s):	Olivier Villemain
Institution(s):	SickKids
Collaborator(s):	Mark Friedberg, Scott Heximer, Craig Simmons

PhD (6)

Trainee:	**Amika Shah**
Project:	Design and Evaluation of a Digital Mental Health Stepped Care Model for a Heart Failure Remote Monitoring Program
Supervisor(s):	Emily Seto
Institution(s):	UHN
Collaborator(s):	Robert Nolan, Sanjeev Sockalingam, Gillian Strudwick, Kathleen Sheehan
Trainee:	**Cori Lau**
Project:	Targeting the Microvasculature to Treat Diabetes-Induced Heart Failure with Preserved Ejection Fraction
Supervisor(s):	Jason Fish
Institution(s):	UHN
Collaborator(s):	Michael Wilson, Paul Delgado-Olguin, Omar Khan
Trainee:	**Elana Sefton**
Project:	modRNA as a Modular Tool for Improving Outcomes with Human Pluripotent Stem Cell-Derived Cardiomyocyte Transplantation
Supervisor(s):	Michael Laflamme
Institution(s):	UHN
Collaborator(s):	Omar Khan, Kumaraswamy Nanthakumar, Christoph Haller
Trainee:	**Moses Cook**
Project:	MRI Guidance for Cardiac Repair Therapy Outcomes in Myocardial Infarction
Supervisor(s):	Graham Wright
Institution(s):	U of T
Collaborator(s):	Michael Laflamme, Hai-Ling Margaret Cheng
Trainee:	**Sadi Loai**
Project:	Novel MR Imaging-based Early Diagnostics for Heart Failure in Diabetics
Supervisor(s):	Hai-Ling (Margaret) Cheng
Institution(s):	U of T
Collaborator(s):	Michael Laflamme, Sara Vasconcelos, Mansoor Husain
Trainee:	**Tao Wang**
Project:	Role of Coronary-Resident Progenitor Cell Function in Heart Failure
Supervisor(s):	Mansoor Husain
Institution(s):	UHN
Collaborator(s):	Paul Delgado Olguin

Research Productivity: 2017 – 2022

98

RESEARCHERS AT THE TED ROGERS CENTRE FOR HEART RESEARCH PUBLISHED



2,604 PUBLICATIONS

485

PAPERS IN TOP JOURNALS (IMPACT FACTOR >10)



764

PAPERS IN IMPACT JOURNALS (IMPACT FACTOR 5-10)

2,549

PEER-REVIEWED PAPERS



89

CONFERENCE PAPERS

>5

PAPERS PER RESEARCHER PER YEAR



LEAD AUTHOR ON >40% OF PUBLICATIONS

63,397

CITATIONS



22%

OF OUR PUBLICATIONS WERE AMONGST THE



MOST CITED WORLDWIDE

Productivity

MEASURING RESEARCH PRODUCTIVITY AND IMPACT

Common measures of productivity and impact for a research centre include a) the number of publications produced and b) the frequency with which these publications are referenced or cited by other researchers. The following seven metrics build upon these measures and provide insight into TRCHR's productivity and impact over the past five years (2018-2022).

METRICS

a. Number of researchers
TRCHR currently has 98 investigators, including 38 involved in discovery, 25 involved in personalized medicine and 35 involved in heart failure outcomes.

b. Number of publications
Our researchers published a total of 2,604 publications during the five-year period (2018-2022) or over 5 papers per researcher per year. Articles, reviews, proceedings papers, indexed in *Clarivate's Web of Science* with a TRCHR researcher in the author list were included in this count.

c. Number of citations
TRCHR 2,604 publications generated 63,397 citations or over 24 citations per publication on average. This is 1.8x the number of citations of the average paper published globally in the same field and year. Citation metrics are from *Clarivate's Web of Science* and are current as of November 30, 2023.

d. Number of articles in:
i top journals and
ii higher impact factor journals
Journal Impact Factor (JIF) is a numerical score based on the citations of the journal that a paper is published in and has been traditionally used to assess a journal's impact on the research community. JIF is often used as a proxy for the importance of a journal to its field and can range from a high of over 500 to a low of less than 1.

In journals classified as Cardiac & Cardiovascular Systems in *Clarivate's SCIE Journal Citation Report*, journals in the top 10th percentile have a JIF > ~10 ("Top Journals") while journals ranked between the 10th and 30th percentile have a JIF of ~5-10 ("Higher Impact Journals")

i. Number of articles in top journals
Our researchers published 485 articles in journals with an impact factor of greater than 10 during 2018-2022. This represents 18 per cent of our total papers and includes papers in *CA-A Cancer Journals for Clinicians* (IF 508.7); *New England Journal of Medicine* (IF 176.1); *Lancet* (168.9).

ii. Number of articles in higher impact factor journals
Our researchers have published 764 articles in journals with an impact factor between 5-10. This represents 29 per cent of our total papers and includes *Advanced Healthcare Materials* (IF 10.0); *Cell Reports* (IF 9.99); and *Cardiovascular Diabetology* (IF 9.95).

e. Highly cited publications
Of our 2,604 publications, 22 per cent were in the top 10th percentile of the most cited publications world-wide.

f. Type of publications
The majority of our 2,604 publications were peer-reviewed journal articles or reviews (2,549). The remaining publications were conference papers (89).

g. Senior author publications
In addition, our researchers were either first or last author on 43 per cent of the publications, indicating leadership and or oversight of the related research