



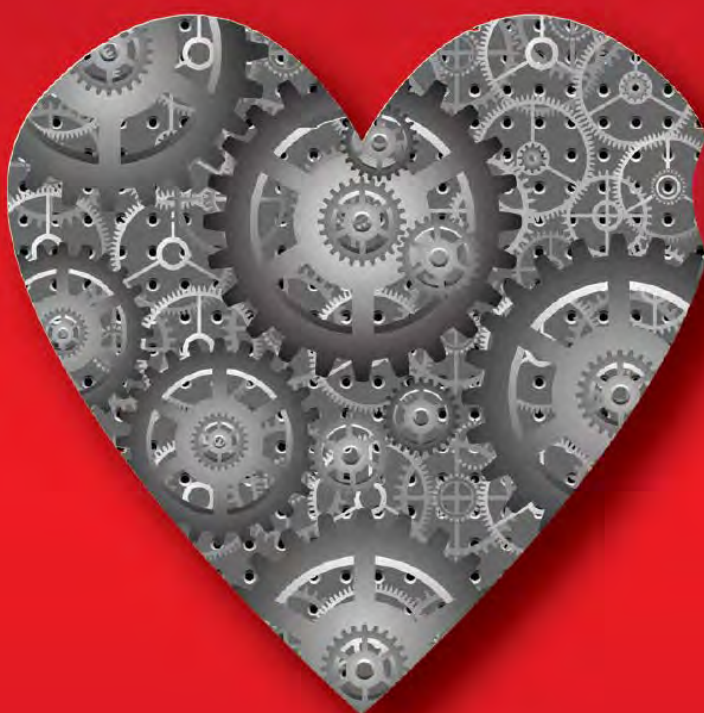
Heart & Stroke | Richard Lewar

Centre of Excellence in Cardiovascular Research

HSRLCE Self-Study Report

Period: 2013-2017

External Review: September 14-15, 2017



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HSRLCE INTRODUCTION

BACKGROUND:

In 1988, Dr. Michael Sole founded the Centre for Cardiovascular Research (CCR) as a joint venture between the Toronto General Hospital, Mount Sinai Hospital and the University of Toronto Faculty of Medicine to bring together interdisciplinary talent in the cardiovascular sciences. The CCR developed integrated bench-to-bedside programs in heart failure, atherosclerosis and arrhythmias and established a clinical trials unit. It offered start-up funds for new investigators and support programs for fellows and students. The CCR established an annual Cardiovascular Scientific Day and a Distinguished Visiting Professor Lecture Series to support cardiovascular education.

In 1999, with support from the Heart and Stroke Foundation and the Richard Lewar family, the Heart and Stroke/Richard Lewar Centre of Excellence in Cardiovascular Research (HSRLCE) was established to continue the CCR's success at a University-wide level and foster excellence in cardiovascular research and education at UofT. HSRLCE is a self-funded extra-departmental unit (EDU) of the Faculty of Medicine, University of Toronto. The HSRLCE expanded its collaborative infrastructure and brought together more than 129 researchers in basic science, clinical investigation and community health.

Today, the HSRLCE builds upon a solid foundation to strengthen its network and international impact. The HSRLCE brings together a consortium of university and hospital research centres in the heart of the city to deliver a comprehensive research program that spans the entire cardiovascular system. With an increased commitment to education, the HSRLCE brought the established Collaborative Cardiovascular Sciences Program (CSCP) under its umbrella to be the educational arm of HSRLCE. Looking abroad, the HSRLCE pursues an exciting internationalization strategy to increase its impact by attracting global talent, ideas, funding and new academic and industrial partners.

Leadership

HSRLCE's inaugural Director was Dr. Peter Liu who served until 2006. Dr. Mansoor Husain succeeded him as Director and served from 2007 to 2012. Dr. Michael Farkouh was appointed Director of the Centre on a five-year term starting January 1, 2013.

Vision & Mission Statements

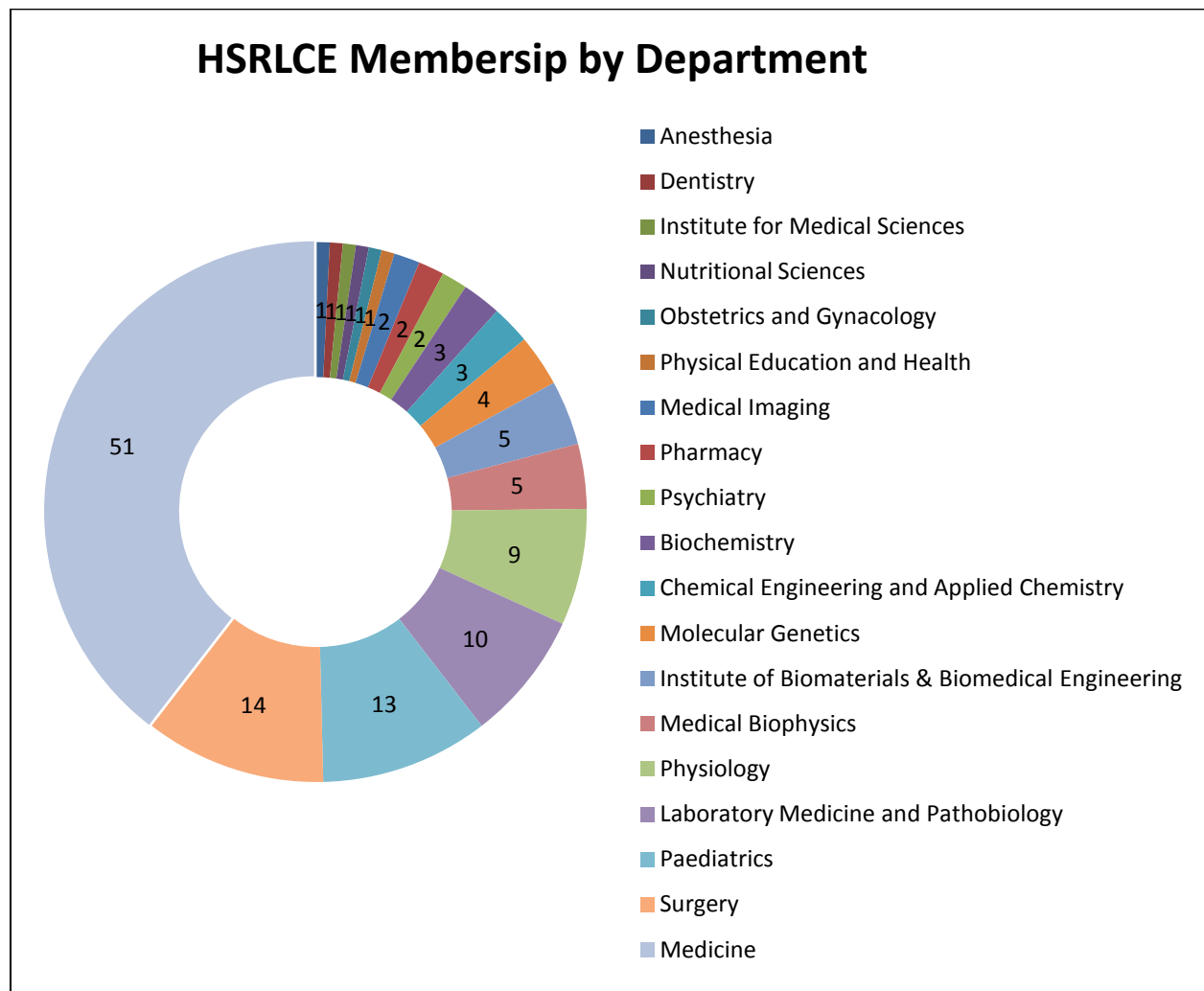
The Centre's mission is: *To foster a collaborative research and educational environment, locally and internationally, that transforms cardiovascular health.*

The Centre's vision is: *To conquer cardiovascular disease through research and education.*

We also introduced a tagline to go with the vision and mission statements: *Leading the fight against cardiovascular disease.*

Membership

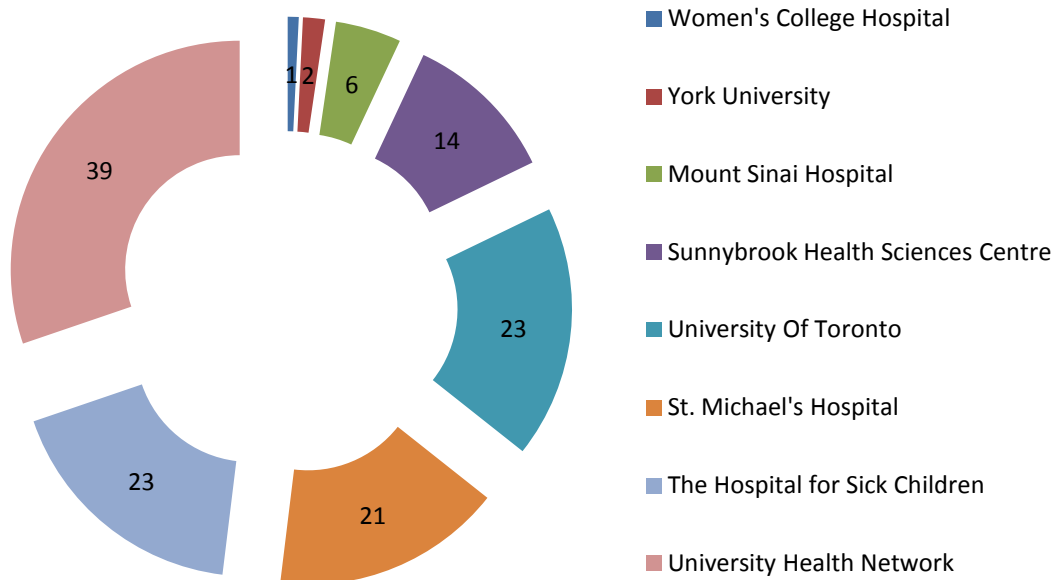
HSRLCE is a cross-departmental, multi-sited, inter-disciplinary academic unit that seeks to coordinate and accelerate cardiovascular research and training throughout our basic science and allied health campuses.



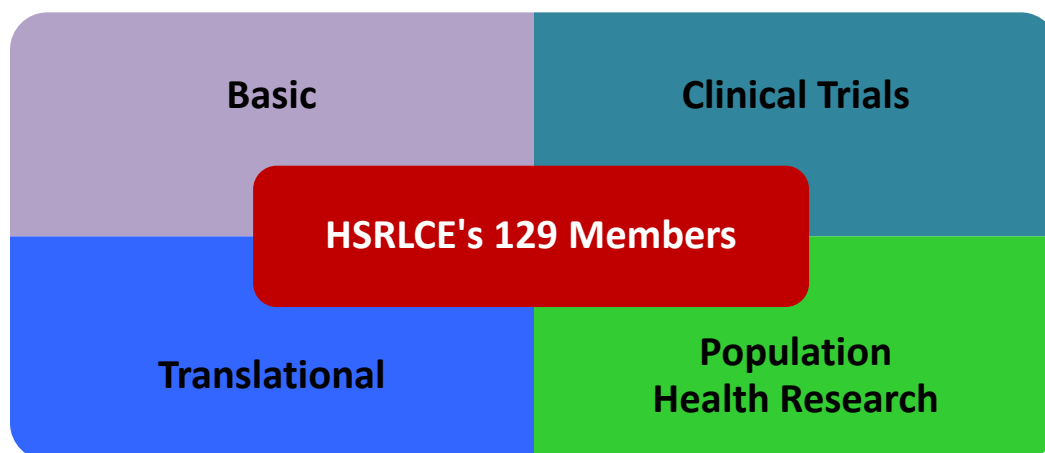
HSRLCE currently has 129 members representing 19 departments and situated across seven campuses, including the St. George campus of the Faculty of Medicine (UofT Campus), University Health Network (UHN), Mount Sinai Hospital (MSH), Sunnybrook Health Sciences Centre (Sunnybrook), The Hospital for Sick Children (HSC or SickKids), St. Michael's Hospital (SMH or St. Michael's), and Women's College Hospital (WCH), with affiliate members from York University.

**The list of members is included in the appendix section.*

HSRLCE Membership by Site



Our membership spans across four pillars: basic, clinical, translational and population health research.



Brochure: Please see the HSRLCE brochure that gives an overview on The Centre's activities.

The Centre's website is: <http://hsrlce.utoronto.ca/>

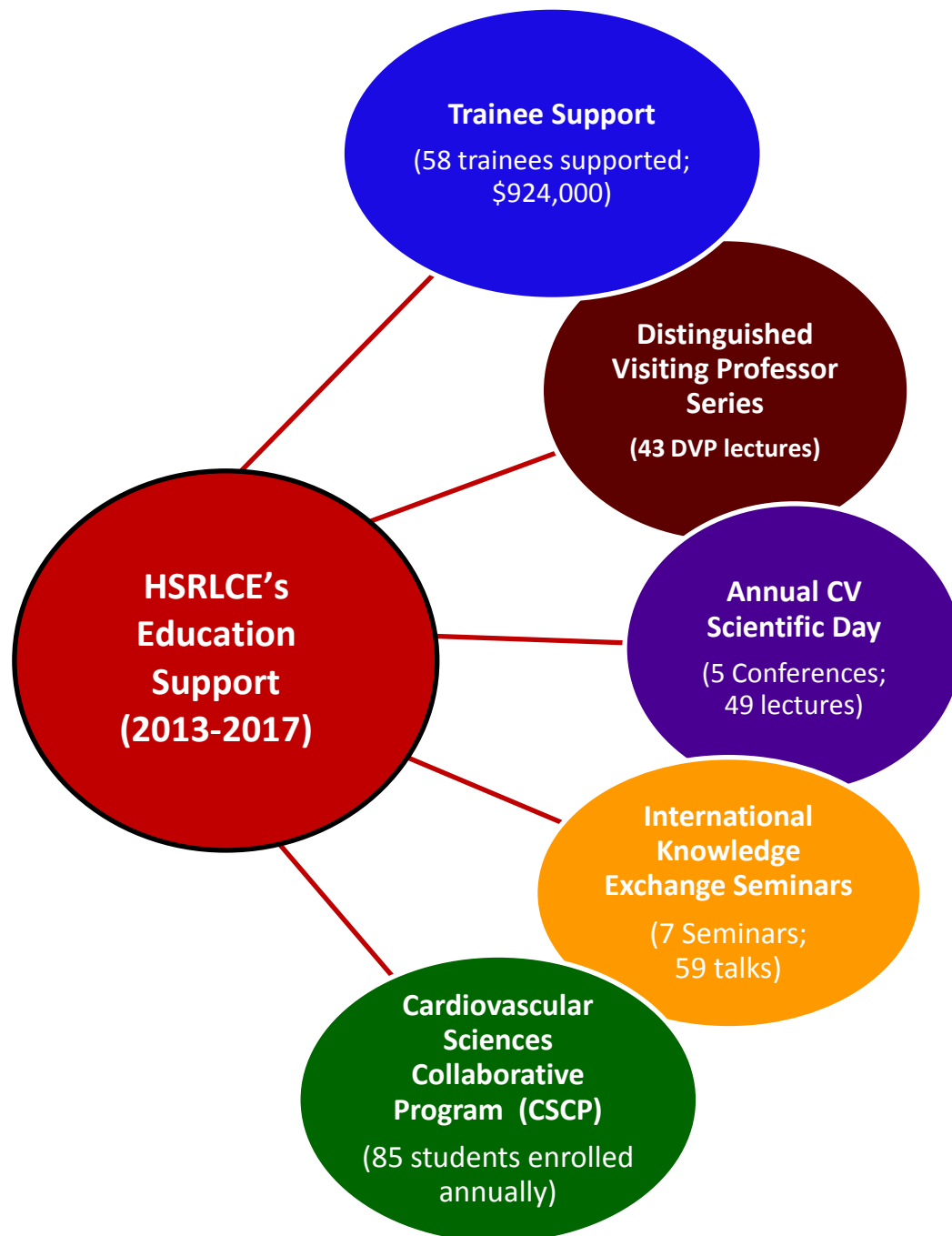
EDUCATION

EDUCATION OVERVIEW:

HSRLCE invests in education by:

1. Providing **stipend awards** to its member's trainees at the undergraduate, graduate, and postdoctoral levels;
2. Hosting **Distinguished Visiting Professors** that meet with trainees and faculty and give a talk on the research projects they are involved in;
3. Organizing an annual **Cardiovascular Scientific Day** where international experts, local faculty and trainees engage in knowledge exchange; and
4. Hosting one-day **knowledge exchange and clinical trials collaboration seminars** with its national and international partners. These seminars are held in conjunction with major cardiology conferences (CCC, AHA, ACC, & the ESC) – typically the meetings are held the day before the major conference commences. These seminars serve to advance HSRLCE's internationalization and collaboration strategies.
5. Partnering with the **Cardiovascular Sciences Collaborative Program (CSCP)**; HSRLCE's educational arm. CSCP was established in 1992 and has developed into a popular program that promotes exemplary linkages between teaching and research at the University of Toronto. The CSCP is a co-operative, interdisciplinary and inter-departmental graduate teaching program that brings together university departments and partnering hospitals to offer a strong curriculum and a unique learning experience.

Five-Year Educational Investment Snapshot (2012/13 to 2016/17)



1. TRAINEE AWARDS

Undergraduate Awards

In partnership with HSBC, HSRLCE offers two to three summer Undergraduate awards in the amount of \$4,500 to enable students to work alongside scientists in cardiovascular research laboratories. This award program was established in 2013. To-date 12 students have been funded.

Studentship Awards

HSRLCE offers up to six Studentship awards annually in the amount of \$15,000. The awards are intended to support individuals in the initial phase of their training (MSc or PhD) who wish to pursue a career in cardiovascular science. To-date (2017) 88 students have been funded.

Fellowship Awards

HSRLCE offers up to six Fellowship awards annually in the amount of \$25,000. The awards are intended to support individuals pursuing a career in cardiovascular science who are still considered “in training” but have completed a PhD, MD, BM, DVM or equivalent degree. To-date (2017) 102 students have been funded.

Award recipients: see the list of award recipients in the appendix section of this report.

2. HSRLCE DISTINGUISHED VISITING PROFESSOR SERIES

HSRLCE organizes a Distinguished Visiting Professors Series with sponsorship acquired through industry (Amgen, AstraZeneca, Merck, and Servier). Through this series, a forum is provided whereby external experts performing cutting edge research in priority areas are invited to speak and interact with Centre’s members and in turn, the activities of the Centre are profiled to the world’s opinion leaders. The Centre regularly collaborates with University of Toronto Departments and teaching hospitals. Faculty, clinicians, and students are encouraged to attend.

Visiting Professors: please see the list of professors and talk titles in the appendix section.

3. MICHAEL J. SOLE ANNUAL CARDIOVASCULAR SCIENTIFIC DAY (ACvSD)

HSRLCE hosts the ACvSD every April/May; averaging around 220 delegates. Local, national and international experts share their knowledge with the Centre’s trainees, faculty, industry, and other healthcare professionals. Each year we focus on a different theme. The Day also sees us host a trainee poster competition with three prizes (worth \$1,000, \$500 and \$250) given to the top three students. We also have a lecture given by the Dr. Subhash C. Verma Young Investigator’s Award recipient. The Award was established in 2006 by the HSRLCE. It is funded by the family of the late Dr. S. C. Verma. The award recognizes exceptional achievement in the

cardiovascular sciences and is open to HSRLCE members who have not been principal investigators for more than seven years. The themes in the past five years have been as follows: Atrial Fibrillation; Diabetes and Heart Disease; Innovation and International Partnerships; Vascular Medicine and Therapeutics; and Innovation in Devices, Research and Novel Partnerships

ACvSD details: please see the program details in the appendix section of this report.

4. NATIONAL & INTERNATIONAL KNOWLEDGE EXCHANGE SEMINARS

As part of HSRLCE's commitment to education as well as national and international collaboration, the HSRLCE hosts one-day knowledge exchange and clinical trials collaboration seminars with its national and international partners. These seminars are held in conjunction with major cardiology conferences (CCC, AHA, ACC, & the ESC). Typically the meetings are held the day before the major conference commences.

We run two versions of these seminars:

1. Canadian-centric seminars:

The seminars provide a forum for key experts from across Canada to share best practices and discuss clinical challenges in coronary syndromes. Data from clinical trials is presented and an opportunity to discuss and debate the implications of these data for clinical practice is provided. Seminars held are:

- i. CCC Seminar – Toronto – October 2015
- ii. ACC Seminar – Chicago – April 2016
- iii. AHA Seminar – New Orleans – November 2016

2. International-focused seminars:

In 2015, HSRLCE Director, Dr. Michael Farkouh founded the Worldwide Network for Innovation in Cardiovascular Clinical Research (WNICR); an ambitious initiative to connect and coordinate leading cardiologists and cardiovascular scientists on an international level by using the combined resources of its members. The consortium's goal is to facilitate the conduct of high quality clinical trials and translational research under the guidance and leadership of an international collaborative of world class cardiovascular clinical investigators from member institutions. WNICR's administration is handled by the HSRLCE office. To-date the following WNICR knowledge-exchange seminar have been held:

- i. AHA Seminar – Orlando – November 2015
- ii. ACC Seminar – Chicago – April 2016
- iii. ESC Seminar – Rome – August 2016
- iv. AHA Seminar – New Orleans – November 2016

Seminar details: please see the program details in the appendix section of this report.

CARDIOVASCULAR SCIENCES COLLABORATIVE PROGRAM

*Heart & Stroke/Richard Lewar Centre of Excellence(HSRLCE)
Faculty of Medicine, University of Toronto*

April 2017

FitzGerald Bldg., 150 College Street, Room 83E, Toronto ON M5S 3E2
Tel: 416/978-0746 Fax: 416/946-5713 E-mail: cv.program@utoronto.ca
Web site: www.cscp.utoronto.ca

SUMMARY

Below is provided a short summary highlighting the Cardiovascular Sciences Collaborative Program's (CSCP) activities and accomplishments as the educational arm of the Heart & Stroke/Richard Lewar Centre of Excellence (HSRLCE). Specifically, HSRLCE member students were highly competitive for both awards and studentships; HSRLCE members were featured faculty speakers and lab tours for our Open Labs program; and our summer CSI program has included a focus on HSRLCE members. As well, the CSCP developed a new Microvascular Medicine JCV course, not only popular with the students at this university, but was designed to support the new international initiatives of the HSRLCE. With this partnership, it is anticipated that the critical full funding support needed to administer and expand the education efforts will be forthcoming. If so, the CSCP will be positioned to successfully deliver its award winning full education package as part of the overall HSRLCE mission - thereby sharpening that profile for the HSRLCE. This initiative creates a unique stand alone feature that will be highly sought after and appealing to local, national and international consumers wanting the whole package. This consists of world class university quality education (CSCP) combined with world class research (HSRLCE) at the highly valued and respected University of Toronto. Additionally, this further develops excellence in cardiovascular education at the University of Toronto across all Faculties and departments.

As you read through this summary of our education initiatives, it should be immediately apparent that the CSCP does the extra to ensure that our efforts dovetail with those of the HSRLCE and our participating Faculties, Departments and Institutes/Centres to optimize our trainees' experiences. This enhances both our efforts and all those of our participating units and especially the HSRLCE, providing trainees with outstanding exposure to cardiovascular sciences, making the University of Toronto, the place for graduate training in this field.

In 2014, the CSCP underwent a successful 7-year review and was lauded as a well-established collaborative program with steady sustained program enrolment and positive student feedback. The report summarized that the CSCP was a truly interdisciplinary collaborative program with a definite focus that draws together a large and diverse number of participating units from across the campus. They praised the strong research foundation provided by core faculty members (many are HSRLCE members), who are clearly invested in student development and offer unique learning opportunities. Annual student enrollment in the CSCP has been steadily increasing yearly, despite significant numbers of students graduating each year. The last few years has averaged around 85 students. There has also been a steady increase in the numbers of PhD students who are enthusiastically participating, such that currently 50% of our students are PhD trainees.

Continued high level of student satisfaction with the CSCP is confirmed during their annual meeting with the Student Affairs Committee Chair and the exit surveys routinely conducted. It continues to be true that today's discerning student is well aware that it is not enough to just fulfill their department's degree requirements if they hope to succeed post graduation. Even those who chose to enter professional degree programs know that a specialist certification, such as that issued upon successful completion of the CSCP, is a statement of excellence that provides them with an edge. All our students benefit from personal contact with our faculty, who are top University of Toronto cardiovascular scientists from across the campus, including the HSRLCE. Our faculty are involved with the CSCP at every level from administration to teaching to supervision. This has given the CSCP trainee exposure to the diversity of excellence we have both on campus and at our teaching hospitals and research centres. In the progressively more

difficult financial times we face, clearly any time taken from the research done by the student could be viewed as lessening the productivity for the supervisor, yet participation in the CSCP is promoted. This is a testimonial to the value and quality offered by the CSCP to the cardiovascular research community and its' trainees.

Details on the CSCP activities can be found below in this summary and on the HSRLCE website under education. The flagship event, the Student Research Day, is where students are able to network with other students across the campus in the many differing disciplines. This event is organized by the students and includes sessions not only on their research but on career guidance and other valued skills such as resume writing and interviewing skills. Another CSCP activity is 'Open Labs- Innovative Techniques in Cardiovascular Research', which consist of visits to the different research locations of our diverse faculty. This allows the students to experience current and ongoing projects in the cardiovascular arena and appreciate the varied techniques used in these labs. Then the summer CSI series includes practical visits to facilities such as Toronto Rehabilitation Centre and the Surgical Skills Laboratory to further expand the awareness of the breadth and depth in the cardiovascular sciences. Our flagship graduate course JCV3000 series, made up of 5 modules each worth .5 FTE, includes a recent addition of a Microvascular Medicine module (JCV3064). As well, the addition of the JCV1060 module on Developmental Cardiovascular Physiology now means we have 6 highly evaluated modules available for our trainees and will also meet future needs of the HSRLCE international initiatives,

Finally, it is also worth a mention that the CSCP is a unique collaborative program as it yearly allocates more than \$153,000 of student support including scholarships, bursaries and awards with funds raised by the CSCP. The CSCP is pleased to be able to provide this tangible monetary benefit for our HSRLCE partner and graduate units as one of the many compensations for their involvement and support.

Future efforts include the expansion of the CSCP to include all cardiovascular post doctoral trainees at the University of Toronto. This initiative would provide a more uniform, structured and rich training experience for this very important cohort of trainee, preparing them for their careers as cardiovascular scientists!

In closing, the CSCP is dedicated to continue delivering the highest quality education that will be the envy of all in the cardiovascular field, making the University of Toronto the chosen location for cardiovascular training.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Dr. Carin Wittnich', with a stylized, flowing script.

*Dr. Carin Wittnich, O.Ont.; Northrop Frye Scholar
Director, CSCP
Professor of Surgery & Physiology*

CSCP MISSION STATEMENT

“The Cardiovascular Sciences Collaborative Program, approved by the University and Ontario Council on Graduate Studies in 1992, and listed in the calendar of the School of Graduate Studies, exists to give formal, organized expression to cardiovascular studies and research at the graduate level. It builds on the strengths of all participating academic units, and other agencies, to enhance the visibility of cardiovascular studies and to facilitate collaborative, interdisciplinary training and research.”

The above mission is achieved by advertising and promoting the importance of, and opportunities in, cardiovascular studies, by making known the results of such studies, by recruitment of excellent students, and by coordinating the graduate collaborative program in cooperation with the academic units in which they are registered. Students in this collaborative program must fulfill the requirements of their home units as well as the Program. Upon graduation the notation “Specialization in Cardiovascular Sciences” will appear on the student’s academic transcript and the Program will present the student with a certificate and gift.

CSCP COLLABORATING FACULTIES

Applied Science and Engineering
Dentistry
Kinesiology and Physical Education
Medicine
Leslie Dan Faculty of Pharmacy

CSCP COLLABORATING GRADUATE UNITS

Biomaterials and Biomedical Engineering
Chemical Engineering & Applied Chemistry
Dentistry
Exercise Sciences
Laboratory Medicine and Pathobiology
Medical Biophysics
Medical Science
Pharmaceutical Sciences
Pharmacology and Toxicology
Physiology
Rehabilitation Science

CSCP SUPPORTING CLINICAL DEPARTMENTS

Anesthesia
Medical Imaging
Medicine
Surgery

COMMITTEES

Executive

The Executive Committee consists of the CSCP Director and 4 members of the Program Committee representing as wide a range of disciplines as possible. Each member also acts as a Chair of one of the various subcommittees which provide student counseling, screens applicants, oversees academic standards including course reviews and provides advice and acts as a Steering Committee.

Program

The Program Committee consists of a representative from each collaborating department as well as two student representatives. It administers the Program, selects the Director, and generally has conducted much of its business through e-communications which optimized the use of everyone's time and allowed critical issues to be handled in a timely and efficient manner, with face-to-face meetings held only when absolutely required. Many members of this committee are also members of the HSRLCE.

CARDIOVASCULAR COURSES OFFERED

** Core Courses for PhD Trainees (2 of 6 modules required); JCV denotes joint listing with most of our collaborating departments.*

JCV1060H*	Developmental Cardiovascular Physiology
JCV3060H*	Advanced Topics in Cardiovascular Sciences – Molecular Biology & Heart Signal Transduction
JCV3061H*	Advanced Topics in Cardiovascular Sciences – Hormones
JCV3062H*	Advanced Topics in Cardiovascular Sciences – Heart Function
JCV3063H*	Advanced Topics in Cardiovascular Sciences – Vascular
JCV3064H*	Advanced Topics in Cardiovascular Sciences – Microvascular Medicine

CSCP PROGRAM SPONSORED ACTIVITIES

ANNUAL STUDENT RESEARCH DAY

The Annual Cardiovascular Sciences Collaborative Program (CSCP) Student Research Day is held in April each year. As part of the CSCP requirements, all students must present their research once during their graduate training. The event provides a platform for students to express their scientific ideas and encourages them to push the boundaries of current scientific paradigms in the field of cardiovascular research. In addition, 2 of our faculty are invited yearly to share their advice on developing a career and balancing academic and personal lives - always well appreciated by our students. The awards ceremony held during this event, include certificates of completion as well as the other annual awards given by the CSCP including prizes given to students who were judged to have given the best oral presentation and most innovative presentations. Students further socialize and network during the complimentary lunch. Workshop on various topics relevant to student career development (eg: preparing an academic CV) also form part of the day. This event provides trainees an opportunity to present their research to their peers in a welcoming environment promoting discussion and the free flow of ideas.

CARDIOVASCULAR SUMMER INITIATIVE (CSI)

The CSI program consists of field trip experiences run during the summer where students are given the opportunity to go and learn more about various areas of cardiovascular research and potential alternative career paths. Field trips have included the MRI/CT Imaging Centre at St. Michael's Hospital, the Toronto Cardiac Rehabilitation outpatient centre, tour of an exercise physiology Lab, tour a pharmaceutical research division, tour a retinal blood flow lab, and a tour of the Surgical Skills Centre at Mt. Sinai Hospital, to name a few. This activity provides the graduate cardiovascular student community, as well as invited undergraduate summer students, a more inclusive feel for the cardiovascular field. It gives them a broader frame of reference than just the lab experience and offers them chances to delve into areas they might not have otherwise considered.

CIRCULATION SEMINARS

These sessions highlight world respected visiting cardiovascular scientists hosted by our participating and partner units. They are often acceptable for respective departmental seminar credits with the appropriate documentation and verification. Full information on this activity can be found on our web site at www.cscp.utoronto.ca.

OPEN LAB: INNOVATION IN CARDIOVASCULAR TECHNIQUES

The CSCP student body organizes and runs this event which highlights the diverse nature of research carried out by our faculty. Formerly known as Circulation Rounds, these academic site visits rotate through the various research centers at the University of Toronto and each event is hosted by a faculty member where their research focus is the topic of the day. The goal of this event is to provide graduate students, post-doctoral fellows, research associates, undergraduates and project/summer students with an interest in cardiovascular sciences with the chance to develop an appreciation of the vast range of excellent research being conducted in our widespread community. The students do a great job organizing these events. In 2016 host labs were from Drs Jason Fish, Clint Robbins, and Jacques Belik. Full information on this activity can be found on our web site at www.cscp.utoronto.ca.

STUDENT FORUM

This event is an excellent opportunity for new students of the CSCP to meet one another and for senior students to catch up with old friends, and develop relationships with the up and comers. Discussions range from basic research, laboratory trials and triumphs, to future academic /career directions. Connections for research collaboration, as well as friendships are developed, and all those in attendance thoroughly enjoy a festive dinner and the chance to meet other students. Due to limited funding we have recently been unable run this event but we hope to resume this event in 2017.

AWARDS

MEDTRONIC TRAVEL AWARD

Two competitions are held (spring and fall) for the Medtronic Travel Award. This award, established in 1995, helps to defray costs of travel for Program students presenting their research work at recognized scientific meetings.

BIGELOW BOOK PRIZE

This prize was established in 1995 to recognize and honor a pioneer clinician and scientist in the field of cardiovascular sciences. The award is given in every year that a qualified student is identified. Qualifications include sustained academic scientific excellence, innovative experimental approaches, original discoveries and good scientific productivity. Some weight is given to work that has recognizable clinical relevance, especially that which promises to improve patient care. The Bigelow Book Prize consists of a book written by Dr. W.G. Bigelow entitled "Mysterious Heparin" and a keeper plaque created to honor Dr. Bigelow. Appropriate candidates are identified and the final decision is made by the Program Committee with the award presented at the Annual Student Research Day.

LORNE PHENIX GRADUATE AWARD

This award was made possible by a generous donation in the memory of Mr. Lorne Phenix by Mrs. Geraldine Phenix. It is her hope that this will focus attention on the issue women who have heart problems and encourage trainees to pursue this area of research to address this particular problem. It is awarded to a graduate student in the Faculty of Medicine on the basis of research and academic excellence. This consists of a cash prize and certificate and is presented to the recipient at the Annual Student Research Day. Appropriate candidates are identified and a winner is selected by the Awards Subcommittee. The award is given in every year that a qualified student is identified and presented at the Annual Student Research Day.

FINANCIAL SUPPORT TO STUDENTS

ONTARIO STUDENT OPPORTUNITY TRUST FUNDS (OSOTF) AWARD

The OSOTF award refers to a class of awards that have resulted from the Ontario government's "matching" program. Under the program every dollar of donation received for student assistance has been matched by the government as well as the university on a dollar-for-dollar basis. There are two major conditions for all OSOTF awards; recipients must be Ontario residents and demonstrate financial need. However, the CSCP has additional eligibility criteria that must be adhered to, including excellence in science and academic performance. One competition is held per academic year. The applications are handled centrally through the Office of the Associate Dean, Inter-Faculty and Graduate Affairs. Applications pertaining to the CSCP are sent to us and are then adjudicated by a subcommittee chaired by Dr. Margaret Rand. Committee recommendations are then forwarded to the OSOTF Awards Committee (Faculty of Medicine).

QEII – GSST (GRADUATE SCHOLARSHIPS IN SCIENCE & TECHNOLOGY)

The QEII program is designed to encourage excellence in graduate studies in science and technology. The program is supported through funds provided by the Ministry of Training, Colleges and Universities and by funds raised by the University of Toronto and the Heart & Stroke Foundation of Ontario. To be awarded to graduate students at the University of Toronto who are pursuing cardiovascular/stroke research. Students must have maintained an overall A-average over the last two years of study at the post-secondary level and exhibit research ability/potential, good communication skills and interpersonal/leadership abilities.

HSRLCE'S INVESTMENT IN RESEARCH

OVERVIEW: INVESTMENT IN PEOPLE

The HSRLCE has played a major role in partnering with various University of Toronto Departments and University Hospitals to recruit cardiovascular investigators. In the last five years, HSRLCE has supported the recruitment of six researchers.



Recruit	Support Term	Support Amount
Phyllis Billia	July 2013 - June 2016	\$75,000 (\$25K for 3 years)
Brian Courtney	November 2014 - October 2017	\$75,000 (\$25K for 3 years)
Slava Epelman	January 2015 - December 2017	\$75,000 (\$25K for 3 years)
Michael Laflamme	August 2015 - July 2018	\$75,000 (\$25K for 3 years)
Clinton Robbins	September 2012 - August 2014	\$250,000 (\$125K for 2 years)
Idan Roifman	January 2016 - December 2018	\$75,000 (\$25K for 3 years)

OVERVIEW: INVESTMENT IN PROGRAMS (LOCAL)

As part of its commitment to advancing collaborative cardiovascular research, The HSRLCE is proud to support the following research initiatives across University of Toronto and the teaching hospitals.

Initiative	Support Term	Support Amount
PMCC Cardiovascular Biobank	2012 to 2015	\$255,000
Cardiovascular Data Management Centre	2012 to 2017	\$465,000
Sunnybrook Large Animal Facility	2009 to 2017	\$360,000
Toronto Centre for Microvascular Medicine	2012 to 2015	\$250,000
Centre for Microvascular Medicine, Munich	2013 to 2016	\$364,000
Transgenic Physiology Lab	2012 to 2017	\$237,000
Athlete's Heart Laboratory	2017	\$20,000
Toronto Stroke Research Network	2016	\$50,000



Local: HSRLCE is integrated with every teaching hospital engaged in cardiovascular research at University of Toronto. We have established support nodes in:

- **Large Animal Models Facility:** Focuses on the integration of large animal models of cardiovascular diseases with novel imaging modalities. Research at the clinic includes various forms of vascular disease (chronic total occlusions and atherosclerosis) and myocardial damage.
- **Toronto Centre for Microvascular Medicine:** TCMM combines basic science and clinical medicine to advance new microvascular knowledge and technologies with promising translational and clinical applications. With a multidisciplinary approach, the TCMM hopes to illuminate the microvascular system's importance and relevance to major health and disease states. In doing so, the TCMM will attract attention and resources to prioritize microvascular research in the cardiovascular sciences.
- **Cardiovascular Data Management Centre:** Serves the cardiovascular disease community by forging linkages between databases, and by providing access to the data for researchers and clinicians, risk adjusted reports for clinical quality improvement initiatives, and statistical services to participants.
- **Cardiovascular Biobank:** Mission: to establish and maintain a standardized approach to human specimen accrual, management, distribution and use for research purposes. Objective: to improve researchers' accessibility to blood and tissue specimens from patients suffering from cardiac and vascular disease and to create a framework that promotes appropriate standards of quality and security.
- **Transgenic Physiology Laboratory:** Mandates of the platform are to provide mouse cardiac physiological assessment of mice, to generate mouse models of disease, and to allow acute genetic manipulation of mice as well as mouse tissues/cultures using viral-based gene transfer methods.
- **Athlete's Heart Laboratory:** The general objectives of the Athlete's Heart Group are to examine the impact of long-standing, excessive endurance exercise on cardiac remodeling, providing the basis for a long-term follow-up study to identify specific factors contributing to development of atrial fibrillation in middle-aged endurance athletes. A broader goal for the Group is to secure significant funding to fully develop an Athlete's Heart Centre that includes a sports cardiology clinic, national registry and a core program of research focused on cardiac remodeling, arrhythmia risk and primary/secondary prevention.
- **Toronto Stoke Research Network:** The Network combines the expertise, strengths and patient populations of 3 University of Toronto Stroke Centers (St. Michael's Hospital, Sunnybrook Health Sciences Centre, and University Health Network) and Stroke researchers across the Greater Toronto Area with the aim of becoming an international leader in stroke clinical practice, research and education.

OVERVIEW: INVESTMENT IN PROGRAMS (INTERNATIONAL)

International: HSRLCE's International research initiatives:

- **Worldwide Network for Innovation in Clinical Research:** NICR Birthed from a University of Toronto initiative to conduct single and multicentre trials under the leadership of the University's cardiovascular clinical investigators. This vision was then expanded to include international partners – and WNICR was formed. WNICR's membership includes biomedical researchers, clinician scientists, cardiologists, experts in diabetes and cardiometabolic disorders, nutritional scientists and epidemiologists. WNICR's program is focused on: research, clinical trials, education, and clinical impact.



- **Centre for Microvascular Medicine Munich:** The CM³ aims to bring together much needed resources to advance the microvascular field. To achieve this, they have designed four integrated programs to pilot new paradigms in basic microvascular research, biomedical graduate and postdoctoral education, platform development and innovation management. The CM³ will also serve as the European node for WNICR's global clinical trials network. Munich's rich biotech sector and central location in Europe positions the CM³ to access global talent, ideas, funding and industry. We have invested \$364,000 into this program.

OVERVIEW: INVESTMENT IN RESEARCH COLLABORATIONS

Cardiovascular/Diabetes Grant

HSRLCE, Banting & Best Diabetes Centre, UofT Faculty of Medicine, and AstraZeneca partnered to fund a grant in cardiovascular/diabetes research. A total of \$1.5 Million was raised to fund this initiative. The purpose of this funding program is to: foster bench to bedside translational research with a focus on innovation and first-in man clinical trials; foster the training of graduate students across disciplines and research institutes; establish the University of Toronto as an international leader in the study of diabetes and heart disease; and encourage collaboration between the BBDC and the HSRLCE. To-date), five awards of up to \$250,000 have been given to researchers investigating diabetes and cardiovascular disease.

2014 Recipient:

PI:	Ravi Retnakaran (BBDC)
Co-Applicants:	Candice Silversides (HSRLCE); Philip Connelly (BBDC/HSRLCE)
Research Site:	Mount Sinai Hospital
Project:	A Randomized Controlled Trial to Evaluate Exenatide and Insulin Glargine Combination Therapy for the Preservation of Pancreatic Beta-cell Function and Endothelial Function in Early Type-2 Diabetes
Award:	\$249,340

2014 Recipient:

PI:	Kim Connelly (HSRLCE/BBDC)
Co-Applicants:	Richard Glibert (BBDC); Andrew Advani (BBDC); Howard Leong-Poi (BBDC/HSRLCE); David Cherney (BBDC); Darren Yuen (BBDC/HSRLCE)
Research Site:	St. Michael's Hospital
Project:	CD34+ Cell Therapy for Diabetic Cardio-Renal Disease
Award:	\$250,000

2015 Recipient

PIs:	Graham A. Wright & Idan Roifman (HSRLCE)
Co-Applicants:	Kim Connelly (HSRLCE/BBDC), Michael Farkouh (HSRLCE/BBDC), Nilesh Ghugre, Andrew Crean, Harindra Wijeyesundera (HSRLCE), Anna Zavodni (HSRLCE)
Research Site:	Sunnybrook Health Sciences Centre
Project:	The impact of Diabetic Microvascular Dysfunction on Late Major Adverse Cardiac Events Post Non-ST Elevation Acute Coronary Syndrome
Award:	\$247,225

2016 Recipient

PI:	Rulan Parekh (HSRLCE)
Co-Applicants:	Jason Fish (TGRI), David Cherney (UHN), Mansoor Husain (UHN)
Research Site:	Toronto General Research Institute/ SickKids/ UHN
Project:	Novel Biomarkers of Vascular Dysfunction in Diabetes and End-stage Renal Disease
Award:	\$224,790

2017 Recipient

PI:	David Cherney (HSRLCE/BBDC)
Co-Applicants:	John Parker (MSH/UHN), Susanna Mak (MSH/UHN), Mansoor Husain (UHN), Bruce Perkins (MSH/UHN), John Floras (MSH/UHN), Jacob Udell (UHN/WCH), Daniel Drucker (MSH)
Research Site:	Toronto General Hospital, Renal Physiology Laboratory
Project:	iNcretin And Treatment with Inhibition of sodium-glucose cotransporter-2 combination In Congestive Heart Failure Preserved Ejection Fraction Trial ("NATRIURETIC-pEF")
Award:	\$249,863

Innovation Grant

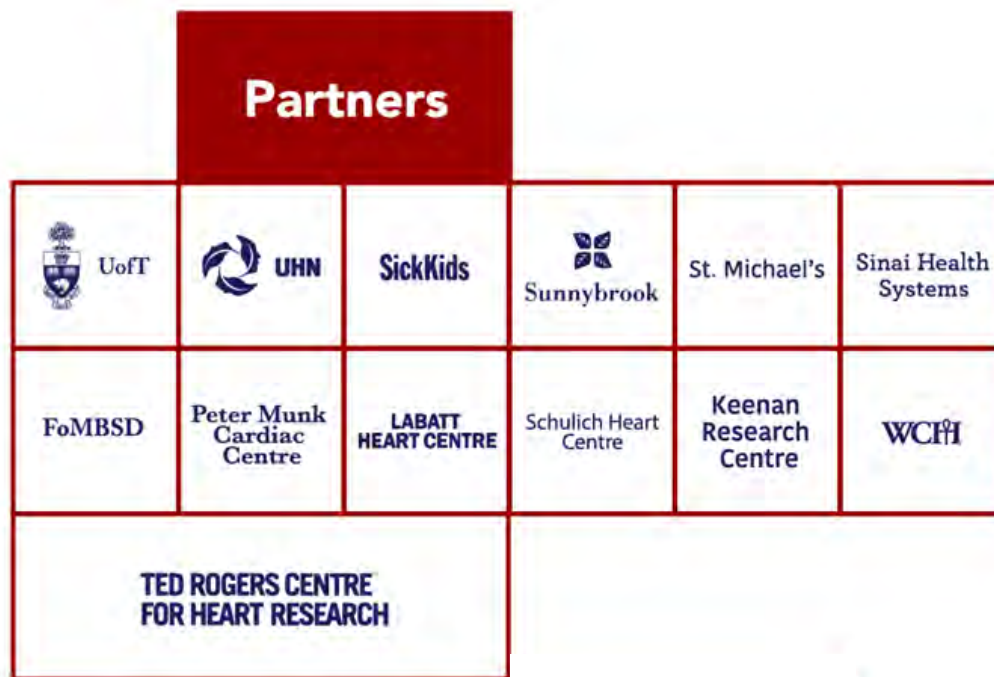
In collaboration with the HSRLCE, the academic/teaching hospitals from the Toronto Central Local Health Integration Network (TCLHIN) (i.e. St. Michael's Hospital, Sunnybrook Health Sciences Centre, University Health Network, and Women's College Hospital) hosted the inaugural Cardiac and Vascular Collaborative Innovation Competition in 2017. The goal is to spur innovation and collaboration between institutes with the aim of improving quality of care within cardiac and vascular programs. The purpose of the award is to provide seed funding for novel ideas aimed at cardiovascular disease management, emphasizing collaborative research and development at multiple sites within the TCLHIN. Available funding is up to \$250,000 annually.

Criteria for selection are: *novelty of innovation; commercialization potential; cardiovascular disease target; and multi-site collaboration.*

2017 Recipient

<i>PI:</i>	Andrew Dueck
<i>Co-Applicants:</i>	Graham Wright (Sunnybrook), Trisha Roy (UofT), Thomas Forbes (UHN), Mark Wheatcroft (SMH)
<i>Research Site:</i>	Sunnybrook Research Institute
<i>Proposal:</i>	Development of a novel image analysis software program to plan peripheral vascular interventions (PVI) for patients with peripheral arterial disease (PAD)
<i>Award:</i>	\$150,000

OVERVIEW: PARTNERSHIPS



Partnership with the Ted Rogers Centre for Heart Research

In November 2014 the Ted Rogers Centre for Heart Research (TRCHR) formed, enabled by an unprecedented gift from the Rogers family and jointly conceived by SickKids, UHN and U of T. The Centre represented a major investment in basic science, translational and clinical research, innovation, and education in regenerative medicine, genomics, and clinical care of pediatric and adult heart disease. TRCHR's vision is to provide the world with new diagnoses, treatments, and tools to help people prevent, manage, and survive the devastating consequences of heart failure; and to provide global leadership in the cardiac field and be a magnet for research and clinical talent.

HSRLCE has a collaborative relationship with the TRCHR in terms of personnel, educational programming, and research support. TRCHR's leadership and team members are also members of the HSRLCE. In terms of programming, where in the past the HSRLCE would have had heart failure-focused lectures and visiting professorships, we now partner with TRCHR and publicize their activities to our membership. The two Centres are also currently in talks to explore how we can combine our Annual Scientific Days to take advantage of our joint expertise to offer outstanding programming to our common stakeholders. The two Centres also jointly support the key research programs such as the Cardiovascular Data Management Centre (CVDMC) and the Peter Munk Cardiac Centre Biobank.

OVERVIEW: RESEARCH PRODUCTIVITY

PERIOD ASSESSED: 2011- 2016

The research data below represents 113 of the 129 HSRLCE members. The 108 are active, full-time members of our Centre who are primarily appointed in the Faculty of Medicine, hold the rank of Professor (Assistant, Associate, or Full), and are cross-appointed to our Centre. Tenure-stream, clinical, and status only professorial appointments have been captured.

It should be noted also that HSRLCE membership does not include all investigators engaged in cardiovascular research at UofT or its allied teaching hospitals. There are many investigators in the Departments of Medicine, Surgery, Paediatrics, and other basic and applied science departments who directly or indirectly engage in cardiovascular research but are not members of the Centre. As such, the research productivity of the HSRLCE noted below under-represents the full breadth and depth of cardiovascular science at UofT.

Global Comparisons:

HSRLCE research productivity was measured against that of five other academic institutions: Harvard University, University of California Los Angeles, University College London, University of British Columbia, and McGill University.

We were evaluated based on three web of science categories:

1. Cardiac and cardiovascular system,
2. Peripheral vascular disease, and
3. Urology and nephrology

Totals Global Comparisons 2011-2016						
Subject Area: All (Cardiac & Cardiovascular Systems, Peripheral Vascular Disease, Urology & Nephrology)	Web of Science Documents	Times Cited	% Docs Cited	Journal Normalize d Citation Impact	% Internati onal Collabor ations	Citation Impact
Harvard University	11765	173814	79.11	1.21	41.05	14.77
University of Toronto	4772	57411	77.51	1.31	49.90	12.03
University of California Los Angeles	3135	40152	81.28	1.26	33.46	12.81
University College London	2975	37779	78.52	1.25	53.34	12.70
University of British Columbia	1851	28659	78.01	1.42	49.59	15.48
McGill University	1604	23978	81.17	1.50	55.11	14.95

**** Please see the appendix for complete details and charts**

Bibliometrics:

- Web of Science Documents: 5,181
- Times Cited: 69,421
- Percentage of Documents Cited: 81.41%
- Journal Normalized Citation Impact: 1.03
- Percentage of International Collaborations: 44.09%
- Citation Impact: 13.40

***** Please see the appendix for complete details and charts***

Patents:

For the 2011 to 2016 period, HSRLCE members had 149 patents:

- 2011: 10
- 2012: 21
- 2013: 32
- 2014: 30
- 2015: 33
- 2016: 23

***** Please see the appendix for complete details and charts***

OVERVIEW: RESEARCH FUNDING

PERIOD ASSESSED: MAY 2012 - APRIL 2016

In the four year period between 2012 and 2016, HSRLCE members received a total of 3,194 awards totaling close to \$270 million. The awards sources were: tri-council (CIHR, NSERC and SSHRC), industry, CFI and other sources. Majority of the grants were given for operations purposes; and the largest funding source was industry.

By Amount

YEAR	FUNDING SOURCES				TOTAL
	Tri-Council	Industry	CFI	Other	
2012/13	\$15,573,143	\$46,855,194	\$5,738,630	\$5,927,582	\$74,094,549
2013/14	\$16,044,687	\$35,770,224	\$5,169,172	\$2,025,797	\$59,009,881
2014/15	\$17,131,162	\$37,689,193	\$5,978,270	\$4,394,111	\$65,192,735
2015/16	\$17,399,343	\$46,915,383	\$4,660,172	\$2,144,006	\$71,118,905
	\$66,148,336	\$167,229,994	\$21,546,245	\$14,491,495	\$269,416,070

By Number of Awards

YEAR	FUNDING SOURCES				TOTAL
	Tri-Council	Industry	CFI	Other	
2012/13	169	519	81	13	782
2013/14	162	524	79	9	774
2014/15	186	567	89	16	858
2015/16	161	537	68	14	780
	678	2147	317	52	3194

Funding by Grant Administration Site

Grant Administration Site	Grants Amounts
University Health Network	\$84,372,240
University of Toronto	\$63,500,573
St. Michael's Hospital	\$44,864,251
Hospital for Sick Children	\$27,850,078
Sunnybrook Health Sciences Centre	\$26,281,071
Mount Sinai Hospital	\$22,299,755
Women's College Hospital	\$248,101

REPORT OF LEARNERS

We asked some of the trainees who have received HSRLCE trainee awards to let us know how getting an HSRLCE Undergraduate/Studentship/Fellowship award has impacted their research. Below are their testimonies.

UNDERGRADUATE AWARDS

Sara Brade

My name is Sara Brade, a second year undergraduate student in the Queen's University Accelerated Route to Medical School (QuARMS) program. At Queen's University, I devote my spare time to physical activity, tutoring high school students, and volunteering at a crisis pregnancy centre. I have spent the past four summers working as a summer student in Dr. Susanna Mak's cardiac catheterization research laboratory. I have contributed to a number of projects relating to improving quality of care for in-patients with heart failure and investigating the characteristics of pulmonary hypertension. This past summer, with the HSRLCE/ HSBC Undergraduate Award, I was able to gain a deeper understanding of different blood pressure measurements recorded using cardiac catheterization and applied this knowledge to research projects that will advance understanding of the relationship between pulmonary hypertension and heart failure. I will be entering medical school this September and I am looking forward to a career in medicine and research.

Shelly Chauhan

My name is Shelly Chauhan and I am in the final year of my undergraduate studies pursuing an Honours Bachelor of Science with a double major in Cell and Molecular Biology and Human Biology: Health and Disease at the University of Toronto. I completed a fourth year thesis project and spent the past summer working as a research student in Dr. Billia's lab investigating the role of specific tumour suppressor genes in allowing cardiac regeneration. This past summer, with the HSRLCE/ HSBC Undergraduate Award, I focused my research on a family of genes that may hold the answer for reactivating the cell cycle in cardiomyocytes, allowing hearts to regenerate and heal upon an injury. In the future, I aspire to become a Clinician-Scientist and combine my passion for the biological sciences and clinical care.

STUDENTSHIP AWARDS

Henry Cheng

My name is Henry Cheng and I am currently in year 7 of A PhD program with the department of Laboratory Medicine and Pathobiology at the University of Toronto. My thesis work under the supervision of Dr. Jason Fish explores the pathological relevance of microRNA-146a in the context of vascular inflammation, specifically in atherosclerosis. My career goal is to continue in biomedical research in the cardiovascular field. I am grateful for the financial support the HSRLCE studentship award had provided me, which allowed me to concentrate on my research. Furthermore, this recognition strengthens my CV for fellowship applications.

Eric Tawagi

My name is Eric Tawagi, a 2nd year PhD student working under the supervision of Dr. Paul Santerre at University of Toronto, Institute of Biomedical and Biomaterials Engineering. My research focus is on therapeutic revascularization strategies for cardiovascular disease.

Cardiovascular disease is one of the biggest health issues facing Canada today and with an aging population, the occurrence of cardiovascular diseases (CVD) in Canada is expected to continue increasing. As a scientist in the field of biomedical engineering, my goal is to help find treatments and therapies for patients that need them the most. I enrolled in a project in the cardiovascular field in order to help find solutions to the enormous health issue of CVD. Fortunately, my previous research training in Chemistry and Biology and my career goals are well fitted for the path that I embarked on. My long-term career goals are focused on working with an innovative start-up or established company in the field of tissue engineering to design life-changing technologies. The use of biomaterials in new applications is a field with tremendous potential that I'm particularly interested in. By designing a novel immunomodulatory microsphere with the idea of translating it to the clinic, I'll learn basic scientific research skills and translational skills pertinent to the cardiovascular field. In pursuing graduate studies in the cardiovascular field, I am able to help discover a solution that can aid the many patients with no current options.

I am grateful to the HSRLCE for helping to fund my research at UofT. These funds allow me to continue working on a project to find an innovative revascularization therapy to regrow blood vessels following cardiac failure. The additional funds left over from my supervisor were put towards purchasing the expensive proteins and protein assays that are necessary to validate our therapy in a high impact research paper. We greatly appreciate your help.

Xiahong Xu

My name is Xiahong Xu. I obtained my MD degree from China in 2011 and Master of Science degree from University of Toronto in 2015. I am currently a PhD candidate and research fellow in Dr. Heyu Ni's group at St. Michael's Hospital.

My research interest is to investigate the novel mechanisms of thrombosis, which is the major cause of heart attacks and stroke, and to develop new anti-thrombotic therapies. My project is to study the role of apolipoprotein A-IV (apoA-IV), a lipid binding plasma protein, on platelets and in thrombosis. In this study, apoA-IV is identified as a novel ligand of platelet $\alpha IIb\beta 3$ integrin and an endogenous thrombotic inhibitor, which establishes a new link between lipoprotein metabolism and platelets, both critical factors in cardiovascular diseases. The manuscript of my project is currently under revision by the journal Nature Medicine.

With the support from the HSRLCE studentship from 2014-2015 during my graduate study, my knowledge and skills in the field of cardiovascular diseases and stroke have been significantly improved. I also had the great opportunity to learn from the excellent scientists and network with peers as a trainee of the HSRLCE. In addition, I have presented my research at several

international meetings, such as 2014 and 2016 Platelets International Symposium, 2016 Congress of the Asian-Pacific Society on Thrombosis and Hemostasis, 2015 Gordon Research Conference, 2014 American Society of Hematology Annual Meeting and 2014 Annual meeting of Arteriosclerosis, Thrombosis and Vascular Biology. I also obtained several prestigious awards: Young-Investigator Award, Young-Investigator Merit Award, Abstract Achievement Award and First-Place Poster Prize. I have published 15 first-author papers and 9 co-author papers, including publications in Circulation Research, Diabetes, Blood, and Thrombosis Research, etc.

I would like to continue my research in cardiovascular diseases and to apply my findings to clinical medicine, which may be eventually beneficial to patients in future.

FELLOWSHIP AWARDS

Dr. M. Ahsan Siraj

My name is M. Ahsan Siraj. I am currently a 3rd year Postdoctoral Fellow in Mansoor Husain Lab at Toronto General Research Institute, Toronto. In collaboration with Drucker, Husain Lab has pioneered the concept that incretin, Glucagon-like peptide-1 (GLP-1), its metabolites and related drugs exert cardioprotective effects in distinct animal models of cardiovascular disease. Importantly, recent human clinical trials (LEADER & SUSTAIN-6) have also demonstrated that GLP-1 analogs reduce major cardiovascular events. I joined this exciting program in 2015. My Postdoctoral research project focuses on cardioprotective effects of GLP-1(28-36), a neutral endopeptidase (NEP) –derived metabolite of GLP-1. We identified that GLP-1(28-36) prevents cardiac ischemia reperfusion injury (IRI) *ex-vivo* in isolated mouse hearts and myocardial infarction (MI) *in-vivo* in mice. These effects do not require GLP-1R but depends on activation of soluble adenylyl cyclase (sAC).

I received a HSRLCE Fellowship Award in 2016-2017 on a research proposal designed to identify cellular and molecular mechanisms of sAC-dependent cardioprotective effects of GLP-1(28-36). With the overall limited grants availability, I believe that HSRLCE Fellowship award has allowed me to pursue this interesting project to identify mechanisms underlying benefits of GLP-1(28-38). Furthermore, this award has been instrumental to achieve my career goals to excel as cardiovascular researcher. It has not only provided the financial support but also the intellectual stimuli, research framework, collaborative environment to help me nurture into a world class scientist.

Dr. Guillaume Bastin

My name is Dr. Guillaume Bastin. I am in my fourth year of a postdoctoral fellowship in the laboratory of Pr. Scott Heximer at the University of Toronto in Ontario, Canada. I was awarded a one-year Heart & Stroke/ Richard Lewand Centre of Excellence Postdoctoral Fellowship (September 2016 – August 2017).

Cardiovascular disease is a leading cause of death worldwide, and causes a significant burden on global healthcare costs related to long-term care and hospitalization. In our laboratory, we are interested in the mechanisms that underlie ischemia reperfusion injury of the myocardium with the ultimate goal of identifying potential therapeutic strategies for its treatment and prevention in human patients.

Presently, I am working on a heterotrimeric G-protein signalling alpha subunit, GNAI3, which we believe plays an important role in the pathogenesis of ischemia reperfusion injury. Importantly, GNAI3 function has been strongly correlated with the size of a cardiac infarct following reperfusion. Deleting GNAI3 actually reduced the infarct size by 40%, but the mechanism through which it mediated these deleterious effects remains unknown. We postulated that GNAI3 may function via its ability to potently inhibit autophagy, a known protective pathway initiated by the heart during times of metabolic stress. Indeed, reduced autophagy has been linked to a large number of pathologies, including several cardiomyopathies and ischemia reperfusion injury. Thus we set out to determine whether GNAI3-mediated regulation of autophagy contributes to ischemia reperfusion injury. As part of this work I have identified key upstream signaling pathways that regulate the function of GNAI3. Interestingly, GNAI3 is activated by a number of surprising and non-canonical pathways (other than the classical G-protein coupled receptor). Indeed, GNAI3 was activated by growth factors (IGF and EGF) via AKT and inhibited by MTORC1. Although MTORC1 is predicted to be activated by growth factors and AKT, it is also inhibited by AMPK, a known downstream effector of hypoxic signals during ischemia. A second potent activator of AMPK is a reduction of the ATP/AMP ratio, such that a diminution of ATP during ischemia should strongly activate AMPK. It is known that the longer the duration of ischemia the more profound is the reduction of the ATP/AMP ratio such that reperfusion may introduce a dangerous time window where GNAI3 is active, but AMPK and mTORC1 are not to result in injurious myocardial signalling events.

Our discovery is unique because of the unconventional regulation of GNAI3 activity. This new knowledge has led to a better understanding of the cell physiology of GNAI3 and its potential application to *in vivo* data. Presently, and in part thanks to the funding support of the HSRLCE, I have made significant progress toward understanding the role of GNAI3 function during pathological condition in the heart. We have more recently established a role for GNAI3 function as a regulator of mitophagy (selective autophagy of the mitochondria). We have shown its ability to regulate several points of the stress signals that regulate mitochondrial health and biogenesis. Interestingly, we also found that ROS signaling switched from pro-apoptosis in wild type model to anti-apoptotic in GNAI3 knock out model. Importantly, strong ROS production during reperfusion is proposed to be the major cause of tissue apoptosis/necrosis. Together, our data suggest that the ability to regulate GNAI3 function may be an important strategy to prevent the damage induced by reperfusion. Interestingly, we have been able to link the latter to its capacity to regulate autophagy. The discoveries I have made this year show that our work is leading us toward understanding some of the key pathways that control ROS production and infarct size following ischemia reperfusion.

In summary, the Lewar Fellowship Award has played a critical role in my research and my career development. Based on presentation on these studies I have been tentatively offered a research position in a cardiology laboratory in Lille France. I am grateful for the training environment provided by the Lewar Centre in Toronto and the opportunity to: i) contribute new knowledge to field of ischemia reperfusion injury, ii) identify new dogmas related to intracellular signalling partners of GNAI3, and iii) gathering data that may connect basic and future clinical research.

Thanks again for the award, it truly contributed to the possibility to push this discovery further.

Dr. Sri Nagarjun Batchu

My sincere thanks to The Heart & Stroke/Richard Lewar Centre of Excellence for awarding me a one year post-doctoral fellowship enabling me to conduct research in the field of kidney and cardiac disease at the Keenan Research Centre at St. Michael's Hospital under the guidance of Dr. Andrew Advani (Endocrinologist and clinician scientist) and Dr. Kim Connelly (Cardiologist and clinician scientist).

As a way of background, I conducted my undergraduate studies in pharmaceutical sciences in Hyderabad, India before moving to Canada in 2006. In 2011, I received my PhD from the University of Alberta in Pharmacy and Pharmaceutical sciences. Following my enthusiasm for research, I began my first post-doctoral fellowship at University of Rochester, USA. In 2014, I began my second post-doctoral fellowship at the Keenan Research Centre at St. Michael's Hospital under the supervision of Drs. Advani and Connelly who are both established researchers in kidney disease and heart disease. In July 2015, I was fortunate in being awarded the Heart & Stroke/Richard Lewar Centre of Excellence post-doctoral fellowship that enabled me to continue my training at St. Michael's Hospital.

Kidney disease is a common cause of illness in Canada. It also greatly increases the risk of heart disease. My career goal is to establish a research program aiming to improve quality of life for people with chronic kidney disease and heart disease. My objective is to significantly impact the lives of people with these disease conditions by focusing on understanding the underlying causes of kidney disease and heart disease and exploiting this knowledge, with the aim to translate these new findings into development of new treatments.

With the support of Heart & Stroke/Richard Lewar Centre of Excellence post-doctoral fellowship at St. Michael's Hospital, I had the opportunity to interact with other post-doctoral fellows, graduate students and technicians in our lab, as well as with other researchers who have an interest in kidney and heart disease and enabled me to develop skills necessary for running my own research program in the future. It also provided me with an outstanding opportunity to interact with the broader kidney and heart research community across Canada. I am in my 4th year of post-doctoral training and have actively pursuing for tenure faculty positions to establish my own lab. I strongly believe the training I have gained and relationships I have established during this period will definitely help me in enabling the translation of my

research findings into the development of new treatments that may ultimately improve the lives of people with kidney disease.

Research Outcomes:

During this period I have made progress in three interrelated projects.

HDAC6 in chronic kidney disease

In this project, I explored the role of an enzyme called HDAC6 (or histone deacetylase 6) in kidney and cardiac disease.

Research Outcome 1

We have discovered that inhibition of HDAC6 using a small molecule called Tubastatin A slows the development of both kidney disease and heart disease in rats. In the study, we demonstrated misfolded protein aggregates play a critical role in progression of chronic kidney disease and inhibition of HDAC6 activity decrease these misfolded protein accumulation by enhancing its clearance process, thus improving kidney functions in a disease setting. This work is currently under consideration (in revision) in a high impact journal called *Kidney International* (IF- 8.563).

Research Outcome 2

A graduate student working under my supervision presented these findings at the annual meeting of the Canadian Society of Nephrology in May of 2016.

Research Outcome 3

I have written an article reviewing the different roles that HDAC6 may have in disease and how HDAC6 inhibitors may be used to treat patients. It has been published in the *Clinical Science* (IF- 6.629) journal in June 2016.

IP receptor agonism in diabetic kidney disease

Research Outcome 4

Whilst conducting my research on HDAC6, I also conducted research on exploring a novel treatment for diabetic kidney disease (diabetes is the most common cause of kidney disease). In this study, I have discovered that stimulation of IP receptor reduces kidney disease in diabetic mice. It appears to do this by changing the way a kidney protein, called nephrin, works. Interestingly nephrin is also present in the insulin-producing cells of the pancreas and my work shows that this treatment also works to make pancreas cells produce more insulin. IP receptor agonism could be a new treatment for people with diabetes, working to lower blood sugar levels and separately protect the kidney from damage due to diabetes. I presented my findings at the 2015 meeting of the American Diabetes Association conference and a manuscript describing these findings (and acknowledging the generous support of the Heart & Stroke/Richard Lewar Centre of Excellence) was published in a high impact journal in field of diabetes (*Diabetes*, IF-8.784) in May of 2016.

JAK2 in diabetic kidney disease

Research Outcome 5

In this study, we are studying the role of a protein called JAK2 in diabetic kidney disease. Our initial findings were presented in December at the 2015 World Diabetes Congress meeting. Alongside, we have also published a manuscript describing the effect of JAK2 knock down on autophagy in specific renal epithelial cells called podocyte (*JASN*, IF-9.343). The kind support of Heart & Stroke/Richard Lewar Centre of Excellence was acknowledged in the manuscript.

In summary, I feel very fortunate to have been awarded the Heart & Stroke/Richard Lewar Centre of Excellence Post Doctoral fellowship. It enabled me to conduct important research into the causes of kidney disease which, to gain research training experience from leading experts in the field of cardiorenal disease at St. Michael's Hospital.

LIST OF HSRLCE MEMBERS

First Name	Last Name	Department	Institution
Lee	Adamson	Obstetrics and Gynecology	Mount Sinai Hospital
Khosrow	Adeli	Laboratory Medicine & Pathobiology	Hospital for Sick Children
Andrew	Advani	Medicine	St. Michael's Hospital
Cristina	Amon	Institute of Biomaterials & Biomedical Engineering	University of Toronto
Peter	Backx	Physiology	York University
Akshay	Bagai	Medicine	St. Michael's Hospital
Jacques	Belik	Paediatrics	Hospital for Sick Children
Denise	Belsham	Physiology	University Health Network
Michelle	Bendeck	Laboratory Medicine & Pathobiology	University of Toronto
Filio (Phyllis)	Billia	Medicine	University Health Network
Steffen-Sebastian	Bolz	Physiology	University of Toronto
Jagdish	Butany	Laboratory Medicine & Pathobiology	University Health Network
Christopher	Caldarone	Surgery	Hospital for Sick Children
Christopher	Chan	Medicine	University Health Network
Vijay	Chauhan	Medicine	University Health Network
David	Cherney	Medicine	University Health Network, TGRi and IMS
Angela	Cheung	Medicine	University Health Network
Eric	Cohen	Medicine	Sunnybrook Health Sciences Centre
John	Coles	Surgery	Hospital for Sick Children
Kim	Connelly	Medicine	St. Michael's Hospital
Philip	Connelly	Medicine	St. Michael's Hospital
Carolyn	Cummins	Pharmacy	University Of Toronto
Myron	Cybulsky	Laboratory Medicine & Pathobiology	University Health Network
Diego	Delgado	Medicine	University Health Network
Paul	Delgado Olguin	Molecular Genetics	Hospital For Sick Children
Michael	Domanski		University Health Network
Paul	Dorian	Medicine	St. Michael's Hospital
Daniel	Drucker	Medicine	Hospital For Sick Children
Vladimir	Dzavik	Medicine	University Health Network
Andrew	Emili	Donnelly Centre	University of Toronto
Slava	Epelman	Medicine	University Health Network
George	Fantus	Medicine	University Health Network
Michael	Farkouh	Medicine	University Health Network
Zhong-Ping	Feng	Physiology	University of Toronto

LIST OF HSRLCE MEMBERS

First Name	Last Name	Department	Institution
Jason	Fish	Laboratory Medicine & Pathobiology	University Health Network
John	Floras	Medicine	University Health Network
Thomas	Forbes	Surgery	University Health Network
Stephen	Fremes	Surgery	Sunnybrook Health Sciences Centre
Mark	Friedberg	Paediatrics	The Hospital for Sick Children
Adria	Giacca	Physiology	University of Toronto
Richard	Gilbert	Medicine	St. Michael's Hospital
Benjamin	Goldstein	Psychiatry	Sunnybrook Health Sciences Centre
Jack	Goodman	Physical Education and Health	University of Toronto
Shaun	Goodman	Medicine	St. Michael's Hospital
Avrum	Gotlieb	Laboratory Medicine & Pathobiology	University Health Network
Sherry	Grace	Psychiatry	University Health Network
Anthony	Gramolini	Physiology	University of Toronto
Gil	Gross	Paediatrics	Hospital for Sick Children
Lars	Grosse-Wortmann	Paediatrics	Hospital for Sick Children
Scott	Heximer	Physiology	University of Toronto
Aleksander	Hinek	Laboratory Medicine & Pathobiology	Hospital for Sick Children
Mansoor	Husain	Medicine	University Health Network
Robert	Jankov	Paediatrics	Sunnybrook Health Sciences Centre
Aamir	Jeewa	Paediatrics	The Hospital for Sick Children
Paul	Kantor	Paediatrics	Hospital for Sick Children
Frederick	Keeley	Biochemistry	Hospital for Sick Children
Rama	Khokha	Medical Biophysics	University Health Network
Thomas	Kislinger	Medical Biophysics	St. Michael's Hospital
Dennis	Ko	Medicine	Sunnybrook Health Sciences Centre
Wolfgang	Kuebler	Surgery	St. Michael's Hospital
Mary	L'Abbe	Nutritional Sciences	University of Toronto
Michael	Laflamme	Laboratory Medicine & Pathobiology	University Health Network
Patrick	Lawler		University Health Network
Douglas	Lee	Medicine	Sunnybrook Health Sciences Centre
Warren	Lee	Medicine	St. Michael's Hospital
Mathieu	Lemaire	Paediatrics	Hospital for Sick Children
Howard	Leong-Poi	Medicine	St. Michael's Hospital
Michelle	Letarte	Medical Biophysics	Hospital for Sick Children

LIST OF HSRLCE MEMBERS

First Name	Last Name	Department	Institution
General	Leung	Medical Imaging	St Michael's Hospital
Gary	Lewis	Medicine	University Health Network
Ren-Ke	Li	Surgery	University Health Network
Christoph	Licht	Paediatrics	The Hospital for Sick Children
Thomas	Lindsay	Surgery	University Health Network
Alexander	Logan	Medicine	Mount Sinai Hospital
Charmaine	Lok	Medicine	University Health Network
David	MacLennan	Biochemistry	University of Toronto
Susanna	Mak	Medicine	Mount Sinai Hospital
Muhammad	Mamdani	Pharmacy	St. Michael's Hospital
Philip	Marsden	Medicine	St. Michael's Hospital
Brian	McCrindle	Paediatrics	Hospital for Sick Children
Luc	Mertens	Paediatrics	The Hospital for Sick Children
Seema	Mital	Paediatrics	Hospital for Sick Children
Alan	Moody	Medical Imaging	Sunnybrook Health Sciences Centre
Tara	Moriarty	Dentistry	University of Toronto
Kumaraswamy	Nanthakumar	Medicine	University Health Network
Gary	Newton	Medicine	Mount Sinai Hospital
Heyu	Ni	Laboratory Medicine & Pathobiology	St. Michael's Hospital
Sara	Nunes de Vasconcelos	Institute of Biomaterials & Biomedical Engineering	University Health Network
Michael	Opas	Laboratory Medicine & Pathobiology	University of Toronto
Rulan	Parekh	Paediatrics	Hospital for Sick Children
John	Parker	Medicine	University Health Network
Thomas	Parker	Medicine	St. Michael's Hospital
Milica	Radisic	Chemical Engineering and Applied Chemistry	University of Toronto
Harry	Rakowski	Medicine	University Health Network
Vivek	Rao	Surgery	University Health Network
Clinton	Robbins	Laboratory Medicine & Pathobiology	University Health Network
Lisa	Robinson	Paediatrics	Hospital for Sick Children
Idan	Roifman	Medicine	Sunnybrook Health Sciences Centre
Heather	Ross	Medicine	University Health Network
Barry	Rubin	Surgery	University Health Network
Paul	Santerre	Institute of Biomaterials & Biomedical Engineering	University of Toronto

LIST OF HSRLCE MEMBERS

First Name	Last Name	Department	Institution
Gustavo	Saposnik	Medicine	St. Michael's Hospital
Ian	Scott	Molecular Genetics	Hospital for Sick Children
Michael	Sefton	Institute of Biomaterials & Biomedical Engineering	University of Toronto
Candice	Silversides	Medicine	Mount Sinai Hospital
Craig	Simmons	Mechanical and Industrial Engineering	University of Toronto
Krishna	Singh	Surgery	St. Michael's Hospital
Michael	Sole	Medicine	University Health Network
Bradley	Strauss	Medicine	Sunnybrook Health Sciences Centre
Hong-Shuo	Sun	Surgery	University of Toronto
Paaladinesh	Thavendiranathan	Medicine	Toronto General Hospital
Robert	Tsushima	Biology	York University
Jack	Tu	Medicine	Sunnybrook Health Sciences Centre
Michael	Tymianski	Surgery	University Health Network
Jacob	Udell	Medicine	Women's College Hospital
Subodh	Verma	Surgery	St. Michael's Hospital
Richard	Weisel	Surgery	University Health Network
Xiao-Yan	Wen	Medicine	St. Michael's Hospital
Duminda	Wijeysundera	Anaesthesia	University Health Network
Harindra	Wijeysundera	Medicine	Sunnybrook Health Sciences Centre
Michael	Wilson	Molecular Genetics	Hospital For Sick Children
Carin	Wittnich	Surgery	University of Toronto
Minna	Woo	Medicine	University Health Network
Graham	Wright	Medical Biophysics	Sunnybrook Health Sciences Centre
Andrew	Yan	Medicine	St. Michael's Hospital
Burton	Yang	Laboratory Medicine & Pathobiology	Sunnybrook Health Sciences Centre
Darren	Yuen	Medicine	St. Michael's Hospital
Peter	Zandstra	Institute of Biomaterials & Biomedical Engineering	University of Toronto
Anna	Zavodni	Medical Imaging	Sunnybrook Health Sciences Centre

HSRLCE TRAINEE AWARD RECIPIENTS (2012/3 TO 2016/7)

UNDERGRADUATE AWARDS

In partnership with HSBC, HSRLCE offers two to three summer Undergraduate awards in the amount of \$4,500 to enable students to work alongside scientists in cardiovascular research laboratories. This award program was established in 2013. To-date 12 students have been funded.

2013 Recipients

1. **Martha Carruthers**
 - Embryonic origins and localization of Soc2+progenitors in the adult murine aorta
2. **Sean Cai**
 - Elucidating the molecular mechanism behind DDR1-mediated aortic stenosis
3. **Amelia Fung**
 - Control of cardiomyocyte proliferation by Mdm2 and p53

2014 Recipients

1. **Maya Deeb**
 - Targeting Slit2-Robo4 Signaling as a New Treatment for Diabetic Renal Microvascular Injury
2. **Mery Deeb**
 - Understanding of Mechanisms where Calreticulin and Cell Adhesiveness Affect the Cardiomyogenic Fate of ES Cells
3. **Joshua Backx**
 - Studying the Role of Tmem65 in the Heart

2015 Recipients

1. **Mark Shafarenko**
 - Macrophages in heart disease
2. **Govind Krishna Kumar Nair**
 - Decreasing temporal variability of repolarization through renal sympathetic denervation

2016 Recipients

1. **Sara Brade**
 - Relationship Between Left Atrial Compliance and Right Ventricular Afterload in Heart Failure
2. **Shelly Chauhan**
 - The Role of p53 Family Members in the Regulation of Cardiomyocyte Proliferation

2017 Recipients

1. **Xavier Lee**
 - Degradation of Phospholamban Mutants in Cardiac Muscle Cells
2. **Nicholas Sequeira**
 - Using Wearable ECG Recording Device to Monitor Cardiac Structure and Function

STUDENTSHIP AWARDS

HSRLCE offers up to six Studentship awards annually in the amount of \$15,000. The awards are intended to support individuals in the initial phase of their training (MSc or PhD) who wish to pursue a career in cardiovascular science. To-date (2017) 88 students have been funded.

2012 Recipients

1. **Safina Ali**
 - Elucidating the role of the glucagon receptor in susceptibility to myocardial infarction in diabetes
2. **Petra Lucker**
 - Protein therapeutics for myocardial infarction: Induction of proliferation and maturation of cardiomyocytes in vitro and in vivo
3. **Mark Roufaiel**
 - Reverse transmigration of resident intimal dendritic cells in the normal murine arteries
4. **Allan Siu**
 - Resident intimal dendritic cells regulate inflammation in atherosclerosis
5. **Bilge Yoruk**
 - Defining a role for cerebral cavernous malformation 3 (Ccm3) gene in vascular development and disease
6. **Boyang Zhang**
 - Engineering of vascularized cardiac tissue using microfluidic and microfabrication approach

2013 Recipients

1. **Michelle Bergevin**
 - Microfluidics tools for deciphering the vascular dissemination mechanisms of a blood-borne pathogen
2. **Anton Mihic**
 - Functional electrical integration of cardiomyocyte-seeded patches in a rat model of MI
3. **Alexandra Mighiu**
 - Defining the role of RGS4 for atrial arrhythmia susceptibility
4. **Juarez Braga**
 - Prognostic impact of coronary artery disease in patients with heart failure
5. **Winnie Fung**
 - Discoidin domain receptor 1 inhibition screening in a vascular microenvironment
6. **Kathryn Lipsett**
 - Mass spectrometry identification of cell-specific protein markers in the heart

2014 Recipients

1. **Mark Blaser**
 - Role of C-type natriuretic peptide in aortic valve disease pathogenesis
2. **Jake Cosme**
 - Molecular mechanisms and biomarker discovery of human hypertrophic cardiomyopathy via proteomics

3. **Idan Roifman**
 - Temporal trends of non-invasive cardiac diagnostic test and downstream coronary angiography
4. **Nimalan Thavandiran**
 - A screening platform for the high content analysis of human pluripotent stem cell-derived cardiac tissue function
5. **Yun Xiao**
 - High-throughput perfusable cardiac biowires for cardiovascular drug screening
6. **Xiaohong Xu**
 - Apolipoprotein A-IV and platelet function: novel links with thrombosis, inflammation, and atherosclerosis

2015 Recipients

1. **Yuliya Lytvyn**
 - A deep phenotyping approach to assess the effect of uric acid lowering in patients with uncomplicated type 1 diabetes mellitus
2. **Songyi Xu**
 - N-cadherin regulation of vascular smooth muscle cells; role of Rho-GTPases and DDR1
3. **Jenna Usprech**
 - Screening environmental factors in 3D for MSC based heart valve tissue engineering
4. **Zhi Cui**
 - Injectable conductive polymer improve electrical propagation in injured heart
5. **Diana Buchsbaum**
 - Investigating function of Tmem65 ventricular protein through AAV9-mediated transduction in CD1 mice

2016 Recipients

1. **Ramadan Azza**
 - Role of autophagy in the pathogenesis and clinical course of aneurysms
2. **Henry Cheng**
 - Role of microRNA-146a in vascular inflammation and atherosclerosis
3. **Sarah Farr**
 - Role of GLP-1 bile acid signaling in regulating postprandial lipemia
4. **Marsel Lino**
 - The role of discoidin domain receptor 1 in vascular calcification and diabetes
5. **Eric Tawagi**
 - Adhesive and immunomodulatory microspheres as growth factor carries for enhanced revascularization

FELLOWSHIP AWARDS

HSRLCE offers up to six Fellowship awards annually in the amount of \$25,000. The awards are intended to support individuals pursuing a career in cardiovascular science who are still considered “in training” but have completed a PhD, MD, BM, DVM or equivalent degree.

To-date (2017) 102 students have been funded.

2012 Recipients

1. **Matthew Doyle**
 - Characterization of layer-specific anisotropic micromechanical properties of aortic valve tissue
2. **Andrew Lau**
 - Inflammatory roles of ASC in atherogenesis
3. **Allen Teng**
 - Investigation of degradation of phospholamban in cardiac cells

2013 Recipients

1. **Dang Lan**
 - Molecular determinants of endothelial cell fate specification and their implications in Ateriovenous Malformations
2. **Ya-Chi Huang**
 - Identification of a Novel Non-selective Cation Channel in mouse Sinoatrial Node
3. **Zachary Laksman**
 - Characterization of a familial and dilated cardiomyopathy using ips cells
4. **Guillaume Bastin**
 - RGS4 induced death in heart pressure overload mouse model in impairing autophagy
5. **Andrew Ramadeen**
 - Metabolic modulation to promote resuscitation from cardiac arrest

2014 Recipients

1. **Anastasiia Aleksandrova**
 - Investigation of regulatory networks underlying cardiac progenitor cell development and heart regeneration
2. **Gabriela Ghisi**
 - A randomized trial of cardiac rehabilitation in Brazil
3. **Jeffrey Kroetsch**
 - TNF-alpha Regulates the Circadian Rhythmicity of Myogenic Responsiveness and Blood Pressure
4. **Sachin Nayyar**
 - Age-mediated alterations to post-myocardial infarction macrophage mobilization

2015 Recipients

1. **Helena Petrosova**
 - Identifying Treponema pallidum endothelial adhesion determinants contributing to meningovascular and cardiovascular syphilis
2. **Anastasiia Aleksandrova**
 - Investigation of regulatory networks underlying the earliest steps of cardiac progenitor cell development
3. **Allen Teng**
 - Metformin increases degradation of phospholamban via autophagy in cardiomyocytes
4. **Sri Nagarjun Batchu**
 - HDA6 in cardiorenal disease

2016 Recipients

1. **Guillaume Bastin**
 - Defining New Therapeutic Strategies Toward Ischemia Reperfusion Injury
2. **Muhammad Ahsan Siraj**
 - Soluble adenylate cyclase dependent cardio-protective effects of GLP-1 (28-36)