The mandate of the Associate Chair, Research is to promote and facilitate research within the Department. To meet this mandate, the Associate Chair has focused on the following activities: (1) ensuring the success of junior faculty involved in research activities, (2) updating the scoring system that was implemented to quantify research output of faculty for purposes of remuneration and promotion and tenure, (3) ensuring that adequate departmental resources are earmarked for research, and (4) facilitating the internal peer review of tri-council grant submissions.

The Associate Chair, Research meets all new recruits to provide feedback to the Department Chair regarding their research potential. Those selected for faculty appointments meet with the Associate Chair on a regular basis in the research stream for mentorship and advice regarding grant applications, funding and career planning. The Associate Chair also provides advice to department members regarding new funding opportunities and research strategies.

The Associate Chair, Research serves as a member of the Departmental Executive, Research Executive, Promotion and Tenure and Alternate Funding Plan Committees. The role of the Associate Chair on these committees is to advise and advocate for research. A standardized scoring system has been developed to quantify research output.

The Department of Medicine Internal Career Awards for new faculty members have a tenure of up to three years and are granted on a competitive basis. Awards are available for both research and education and are aimed at fostering the next generation of researchers and educators. Funding from this source can be used to offset clinical expenses, thereby increasing protected time for research. The Associate Chair, Research is a member of the committee that reviews and prioritizes the application for Internal Career Awards.

The Department of Medicine continues to be a major contributor to the research productivity of McMaster University. The amount of research funding for 2013-14 was maintained at the level of the previous year; that is approximately $50 million. The majority of this funding is from peer-reviewed sources. In fact, 40% is from tri-council, 15% from National Centres of Excellence, 4% from the Heart & Stroke Foundation of Canada and 4% from disease-specific funding agencies. Members of the Department of Medicine also received a considerable amount of funding from industry. These funds are normally mainly administered through the hospitals. These accomplishments are all the more noteworthy given the increasing emphasis on clinical productivity and the competitive nature of the grant review process.
Total research funding dollars obtained this year

$49,849,551

PERSONAL AWARDS BY TYPE
$2,254,000
- Studentships – 6%
- Career Awards – 61%
- Fellowships – 12%
- Other Faculty Support – 21%

RESEARCH FUNDING BY TYPE
$49,849,551
- Operating Grants – 63%
- Collaborative / Partnerships – 29%
- Personnel Awards – 4%
- Equipment and Other – 4%

PERSONAL AWARDS BY SOURCE
$2,254,000
- Canada Research Chairs – 49%
- Heart and Stroke Foundation of Canada/Ontario – 16%
- Canadian Institutes of Health Research – 11%
- Other – 7%
- Regional – 17%
The Population Health Research Institute (PHRI) was established in 1999, having evolved from the highly successful Preventive Cardiology and Therapeutics Research Program that was initiated in 1992 by Dr. Salim Yusuf. The primary objective of PHRI is to lead international health research focused on the causes of chronic diseases and their prevention or treatment. The PHRI also plays an active role in the education of individual researchers and in building capacity internationally for the development of global research programs. Dr. Salim Yusuf was re-appointed as Executive Director for PHRI effective July 2014 for his third five year term.

PROGRAM AREAS

PHRI continually reviews our programs to ensure our research is relevant in the current clinical and scientific environments. With that, we continue to conduct research in our core areas as well as developing new expertise.

Core and Maturing Expertise

- CVD Prevention and Treatment
- Arrhythmia
- Acute Coronary Syndromes
- Global Health
- Perioperative Ischemia
- Diabetes
- Stroke
- Thrombosis
- Neglected Diseases (Chagas, TB pericarditis)
- CV Surgery

Emerging and Developing Expertise

- Obesity and Bariatric surgery
- Population Genomics
- Cardio-Oncology
- Acute kidney injury
- Environmental impact on chronic diseases
- Health systems/CVR Knowledge Translation
- Early life influences on CVD
- Chronic kidney diseases
- Epidemiology of chronic obstructive airways disease

PHRI scientists also collaborate extensively with other research groups in Hamilton and the world.

TOP

1%

of most cited publications

Stuart Connolly, John Eikelboom, Janice Pogue, Koon Teo, Salim Yusuf

NETWORKS

PHRI has also developed expertise in establishing and coordinating research networks nationally and internationally. Over the last 22 years, PHRI has created and established a well-respected international network in which we conduct our research and support development of research capacity. More recently, PHRI has been very successful in establishing several national networks. Starting with the inception of CANNeCTIN in 2008 (completed in 2013), PHRI also leads the CVCD Alliance (2012-2017), C-SPIN (Canadian Stroke Prevention Intervention Network) (2013-2023) and SPOR (2013-2018).

In its first year, the C-SPIN network has successfully launched several studies in the PIaFF and C-CuSP programs, held two major meetings and has established their website as a communication platform. The CVCD Alliance was created to understand the role of socio-environmental and health system factors on individual CV risk factors, subclinical vascular disease, and clinical CV events. It has been successful in moving ahead with the collaborations with the CFTP cohorts as well as PURE cohort and starting recruitment for the aboriginal cohort. PHRI is one of 12 members that comprise the Ontario SPOR support unit (OSSu). With this investment PHRI will create a multi-institutional collaborative network in Ontario that will bring together Ontario researchers to undertake transformative research and train and mentor future Ontario research leaders. PHRI will also support the OSSu in linking with SPOR SUPPORT units and networks in other provinces to leverage funding and conduct multi-province and pan-Canadian studies.

NEW STUDIES

Several new clinical trials started this year. They include:

ARTESIA

Led by Jeff Healey, this is a randomized double-blind phase IV multi-center study to determine if treatment with apixaban, compared with aspirin, will reduce the risk of stroke and systemic embolism in patients with device-detected sub-clinical atrial fibrillation (SCAF) and additional risk factors for stroke. 4000 patients from approximately 100 sites in Canada, USA, and Europe. Estimated mean follow-up time is three years.

ANDEXANET AlFA

Led by Stuart Connolly, this is an open-label, prospective, multi-center study to evaluate the hemostatic efficacy of andexanet in patients receiving a FXa inhibitor presenting with acute major bleeding and reduced FXa activity and to demonstrate the decrease in anti-FXa activity following andexanet treatment.

HIP-ATTACK

Led by Mohit Bhandari and PJ. Devereaux, to determine the effect of accelerated medical clearance and accelerated surgery compared to standard care on the 30-day risk of a major perioperative complication (i.e., a composite of mortality, nonfatal myocardial infarction, nonfatal pulmonary embolism, nonfatal pneumonia, nonfatal sepsis, nonfatal stroke, and nonfatal life-threatening and major bleeding).

HOPE-4

Led by Salim Yusuf and JD Schwalm, this study is an open-label, cluster randomized study to develop, implement and evaluate an evidence-based, contextually appropriate program for cardiovascular disease (CVD) risk assessment, treatment and control involving: (1) simplified algorithms implemented by non-physician health workers (2) single pill, fixed dose, combination therapy (Policap) and (3) treatment supporters and e-health technology to optimize long-term medication and lifestyle adherence. This programme has the potential to reduce risk of CV events and CV events by 35% over approximately 6 years, as compared to usual care.

IVVE

Led by Mark Loeb and Hisham Dokainish this study is a randomized, placebo-controlled multi-center study to assess the feasibility of randomizing heart failure (HF) patients to either inactivated influenza vaccine or to placebo to assess whether influenza vaccine can reduce adverse vascular events in this population. The primary outcome for the
eventual trial will be a composite of major adverse vascular events, including cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.

**NAVIGATE ESUS**

Led by Robert Hart, this is a randomized double-blind double dummy multi-center study to evaluate whether rivaroxaban is superior to aspirin in reducing the risk of recurrent stroke, systemic embolic events, and myocardial infarction in patients with a recent ESUS (Embolic Stroke of Undetermined Source). The study is event-driven and thus, all patients will be treated (or followed-up in case of premature discontinuation of study medication) until the required approximately 585 confirmed primary efficacy outcomes are expected to have occurred.

**PACT-HF**

Led by Harriette Van Spall, this is to test its effectiveness in a multi-center stepped wedge cluster RCT that introduces the intervention to 16 Ontario hospitals in a randomized sequence over a number of time-periods. Our primary aim is to determine the effectiveness of PACT-HF in improving (1) 30 day all-cause readmissions and (2) the six-month composite all-cause emergency department (ED) visits, readmissions and deaths in patients being discharged with HF. Our secondary aim is to determine the effectiveness of PACT-HF in (1) improving the patient-centered outcomes of Discharge Preparedness and Health-related Quality of Life (HRQOL), and (2) reducing 6-month system health costs in patients being discharged with HF.

**MAJOR DISCOVERIES IN 2013–2014**

PHRI continues to be a leader in publications in high impact journals such as JAMA, Lancet, and Circulation with 281 publications in 2013 on research findings by PHRI scientists.

**SUMMARY:**

The scientific productivity and impact of the PHRI has grown significantly with the expansion of existing programs and the development of new areas for research. PHRI is one of the world’s most impactful health research institutes and we are proud to have contributed locally (McMaster University and Hamilton Health Sciences), nationally and globally. We are also grateful to the Hospital, the University and the broader Hamilton community for their support.

The Thrombosis & Atherosclerosis Research Institute (TaRAI), occupies three floors of the David Braley Research Building at the Hamilton General campus. This state-of-the-art research institute has facilitated the melding of basic and clinical research, thereby enabling a seamless “bench to bedside and back again” approach to complex health care problems. Our laboratories have enabled new collaborations that extend to all hospital sites as well as national and international research collaborations. TaRAI remains focused on its mission to reduce death and disability from thrombosis diseases by conducting research into the pathogenesis, prevention, diagnosis and treatment of thrombosis and vascular disease.

Dr. Jeffrey Weitz, Executive Director, continues to provide leadership to the core research programs at TaRAI which include:

- **Experimental Thrombosis and Atherosclerosis (ETA) Program**, which under the directorship of Dr. Weitz conducts fundamental research on the interplay among thrombosis, atherosclerosis, diabetes, obesity, cancer, and inflammation.

- **Clinical Thromboembolism Program (CTP)**, is led by Dr. Sam Schulman and performs research that informs optimal prevention, diagnosis and treatment of patients with thrombotic problems, as well as research in knowledge translation aimed at optimal transfer of this information to the bedside and the community. This city-wide program includes all Hamilton Health Sciences hospital sites as well as St. Joseph’s Healthcare and provides clinical care to patients in the hospital and in the community who have, or are at risk for, thrombotic disorders.

- **Comparative Medicine Program**, which is under the directorship of Dr. Shawn Petrik and focuses on the translation of basic research findings into clinically relevant models prior to evaluation in humans.

- **Biometrics Group**, which is led by Professor Robin Roberts and provides biostatistical support for all faculty and students in the various TaRAI programs. Professor Roberts also leads the statistical core for the Neonatal Research Program, which is led by Dr. Barbara Schmidt.

Consistent with the recommendation following a 10-year external review, a strategic planning retreat which included the four programs was held in May 2014. The retreat provided a venue to identify strengths, weaknesses, opportunities and threats of TaRAI. The Director has built a “consensus-building” process in which to identify strengths, weaknesses, opportunities and threats for the Research Institute. The retreat also provided an opportunity to develop 5-year priorities for the Thrombosis & Atherosclerosis Research Institute. These priorities include (a) creating translational research centers to foster collaboration between basic and clinical researchers, (b) targeted recruitment to build critical mass, (c) create an Endowed Chair as a vehicle for succession planning, (d) explore new avenues of funding to build collaborations and to diversify research investments, and (e) expand training opportunities by creating a Royal College of Physicians of Canada Certificate of Special Competence in Adult Thromboembolism.

TaRAI has been referred to as an “education engine”. Consistent with its academic mission of providing an excellent environment for learners, during 2013-14, TaRAI faculty has trained 15 M.Sc. students, 10 Ph.D. Students and 9 postdoctoral fellows. In addition, the faculty also has provided many undergraduate students with a site to conduct their four-year thesis projects. During 2013-14, TaRAI received approximately $5.3 million in external research support. Hamilton Health Sciences and McMaster University continue to provide valuable support to help fund faculty and students, as well as operational funding for infrastructure and funding for endowed chairs.

**2013-14 RESEARCH FUNDING BY SOURCE**

<table>
<thead>
<tr>
<th>Source</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricouncil/ Federal</td>
<td>41%</td>
</tr>
<tr>
<td>Industry</td>
<td>9%</td>
</tr>
<tr>
<td>Regional</td>
<td>11%</td>
</tr>
<tr>
<td>OHSF / O</td>
<td>19%</td>
</tr>
<tr>
<td>CIHR</td>
<td>2%</td>
</tr>
<tr>
<td>McMaster</td>
<td>1%</td>
</tr>
</tbody>
</table>

The Hamilton Health Sciences Foundation and McMaster University provided an opportunity to develop 5-year priorities for the Thrombosis & Atherosclerosis Research Institute. These priorities include (a) creating translational research centers to foster collaboration between basic and clinical researchers, (b) targeted recruitment to build critical mass, (c) create an Endowed Chair as a vehicle for succession planning, (d) explore new avenues of funding to build collaborations and to diversify research investments, and (e) expand training opportunities by creating a Royal College of Physicians of Canada Certificate of Special Competence in Adult Thromboembolism.
The Firestone Institute for Respiratory Health (FIRH) has been a world-renowned centre for the investigation and treatment of respiratory diseases for more than four decades. FIRH scientists and clinicians have and continue to contribute to groundbreaking respiratory research with global impact. FIRH faculty members have been at the center of developing the Aerochamber for inhaled drug delivery to the respiratory system, the methacholine challenge test to assist in the diagnosis of asthma, and the exploration of sputum eosinophilia as biomarker for asthma management.

FIRH provides comprehensive inpatient and outpatient respiratory care as the regional respiratory centre for the City of Hamilton and the Hamilton Niagara Halton Brant Local Health Integrated Network. FIRH has a unique Chest Program that encompasses the spectrum of respiratory medicine together with affiliated head-and-neck and thoracic surgery services; all are located at one site.

Clinical, research and educational activities are integrated and collaborative within FIRH. The intent is to provide exemplary clinical care, in tandem with basic and translational research inquiry, while educating and mentoring health care professionals to treat, research, teach, and lead. The strength of FIRH continues to be its focus on improving patient outcomes.

FIRH’s patient-centred focus on care is achieved through the tremendous efforts of allied health care professionals, including nurses, respiratory therapists and technicians, and through the efforts of FIRH’s administrative staff. In 2013-2014, FIRH had 43,388 registrations including 10 full-time graduate students (candidates for Masters and for PhD) along with 4 postdoctoral fellows.

In addition, FIRH hosted numerous placements for nursing students, respiratory therapist students, undergraduate and post-secondary work placements, as well as countless hours of high school students earning mandatory community service hours.

FIRH conducts research to increase understanding of respiratory health and disease across the life cycle through collaborative basic and clinical investigations with the expectation of improving patient care. The proximity of research teams to clinical services has allowed conduct of highly relevant and well-powered clinical studies, and ensured rapid incorporation of new knowledge into the care of patients. This integration also strongly influences the education of physicians and allied health care professionals.

FIRH research is wide-ranging, from studies of smooth muscle physiology and intracellular signalling through experimental disease models to clinical trials and extends to population health and policy. The research productivity of FIRH is attested to by the high quality and impact of the peer-reviewed publications. In 2013, FIRH faculty were listed as authors on 167 peer-reviewed publications, including several in high-impact international publications. Since 2009, current FIRH faculty were listed as an author on over 400 peer-reviewed publications and presented their research at over 100 conferences and events throughout the world.

Faculty have been very successful in obtaining major CIHR operating grants. Dr. Malcolm Sears was successful in obtaining a 5-year $1.022M grant to the Canadian Healthy Infant Longitudinal Development study (CHILD) which is now beginning evaluation of the cohort at age 5 years for the primary outcome of childhood asthma. Dr. Martin Kolb was awarded a 5-year $701,000 grant to study the role of abnormal matrix in the progression of pulmonary fibrosis and Dr. Luke Janssen was successful in obtaining a 5-year, $695,000 grant to study calcium-signalling and gene expression human fibroblasts. Dr. Parameswaran Nair is a Co-PI in a randomized controlled trial of oseltamivir in outpatients with chronic pulmonary disease. Dr. Nair’s study received a 1-year $218,000 grant. Several other international, national and local team projects in interstitial lung disease (Drs. Labiris and Kolb), pulmonary fibrosis (Drs. Janssen, Ask and Kolb) and smoke cessation (Dr. McIvor) are currently developed under the leadership and active participation of FIRH faculty members.
Providing leadership and strategic direction for the Firestone Institute in 2013-2014 were Dr. Paul O’Byrne, Executive Director; Dr. Stewart Pugsley, Clinical Director; and Dr. Martin Kolb, Research Director. Members of the FIRH faculty hold important administrative posts locally, including Dr. Paul O’Byrne, Chair of the Department of Medicine at McMaster University; Dr. Martin Kolb, Division Director of Respiratory Medicine; Dr. Lori Whitehead, Program Director for Adult Respiratory residency training at McMaster University.

Faculty and staff wish to acknowledge and thank those who continue to support the efforts of the Institute. In particular, we thank St. Joseph’s Healthcare and its Foundation and the many people who contributed to support our clinical, research and educational initiatives this past academic year.

AllerGen NCE INC.

Helping Canadians address the challenges of living with asthma and allergic disease is at the core of AllerGen’s integrated research program.

AllerGen NCE Inc. (AllerGen), the Allergy, Genes and Environment Network, is a national research network with the mission to reduce the morbidity, mortality and socioeconomic impacts of allergy, asthma, anaphylaxis and related immune diseases.

AllerGen was established in 2004 by Industry Canada through the Networks of Centres of Excellence (NCE) Program. Hosted at McMaster University, AllerGen is led by Scientific Director and CEO, Dr. Judah Denburg, Professor of Medicine and Director, Division of Clinical Immunology and Allergy.

AllerGen acknowledges, with appreciation, ongoing support from McMaster University and especially Dr. John Kelton, Dean and Vice-President, Faculty of Health Sciences and the Michael G. DeGroote School of Medicine; Dr. Mo Elbestawi, Vice-President, Research and International Affairs; Dr. Stephen Collins, Associate Dean, Research; and Dr. Patrick Deane, President and Vice-Chancellor, and Board of Directors member of AllerGen.

Led by internationally recognized Canadian researchers with expertise across almost 50 disciplines, AllerGen’s 47 active research projects and strategic initiatives employ cross-sectoral, multidisciplinary approaches to accelerate the development of new diagnostic tests, better medications, accessible patient education tools and effective public policies relevant to allergic disease.

In 2013–2014, AllerGen engaged 93 Network Investigators and collaborators, 354 students, new professionals, research associates and technicians, and collaborated with 136 partner organizations across academia, industry, not-for-profit and government agencies.

Since its inception, AllerGen has provided education, training and capacity-building opportunities to over 1,200 students, trainees and new professionals, and awarded $2.3 million in trainee awards, grants and fellowships.

AllerGen research focuses its discovery, commercialization and knowledge mobilization efforts on:

THREE LEGACY PROJECTS
- The Canadian Healthy Infant Longitudinal Development (CHILD) Study;
- The Clinical Investigator Collaborative (CIC); and
- The Canadian Food Allergy Strategic Team (CanFaST).

THREE ENABLING PLATFORMS
- Gene-Environment Interactions;
- Biomarkers and Bioinformatics; and
- Patients, Policy and Public Health.

Research Impact

Led by professor Susan Waserman, researchers are evaluating a pilot project where security guards at Hamilton’s Jackson Square carry epinephrine auto-injectors. The team will look at the efficacy of the training, use of stock epinephrine auto-injectors during the pilot program, and the knowledge of consumers at risk of anaphylaxis and foodservice staff.
The Canadian Healthy Infant Longitudinal Development (CHILD) Study

Led by Dr. Malcolm Sears, Professor, Department of Medicine, McMaster University

The CHILD Study is a national birth cohort study that explores the role and interplay of environmental and genetic factors in the development of asthma, allergy and other chronic immune/inflammatory diseases.

Launched in 2008 with $12 million from AllerGen and the Canadian Institutes of Health Research (CIHR), the CHILD Study looks at how the environment that a child is exposed to during pregnancy and in the first few years of life can interact with genetics to cause allergies, asthma and other chronic diseases.

The CHILD Study has recruited over 3,600 pregnant mothers and is carefully assessing each child and its respective environment by collecting detailed housing, dietary and socioeconomic information, dust from homes, and biological samples such as breast milk, blood from parents and children, and children’s urine, feces and nasal secretions.

CHILD Study researchers are using the data to examine many potential effects on health, including the impacts of: the infant microbiome, household phthalate exposure, maternal stress and anxiety, maternal and infant diet, living with pets, numbers of siblings, environmental exposures in and outside the home, and antibiotic use on the development of childhood allergies and asthma.

Additional CHILD Study participants from McMaster University include Drs Judah Denburg, Paul O’Byrne, Sonia Anand and Joseph Macri.

Early findings from research using CHILD Study data have linked cesarean sections, breastfeeding and antibiotic use to changes in the infant gut microbiome.

The Clinical Investigator Collaborative (CIC)

Led by Dr. Paul O’Byrne, Professor and Chair, Department of Medicine, McMaster University

The CIC is a multi-centre Canadian-based Phase II clinical trials group enhancing drug discovery for allergic diseases from proof-of-concept to use in patient populations.

The CIC has placed Canada at the forefront of related diagnostics and therapeutics, leading the discovery, development and commercialization of new tests and treatments for the benefit of Canadians suffering from allergic airways diseases.

With the addition of severe asthma and allergic rhinitis to its existing expertise in allergic asthma, the CIC offers biotechnology and pharmaceutical companies an opportunity to evaluate promising new drug molecules for the treatment of allergic diseases in both the upper and lower airways.

The CIC conducts clinical trials in Canada and Sweden and is launching new international sites in the Netherlands and the UK.

Researchers and McMaster University faculty involved in the CIC include Drs Gail Gauvreau, Mark Larché, Parameswaran Nair, Susan Waserman and Helen Neighbour.

The Canadian Food Allergy Strategic Team (CanFAST)

CanFAST is a national, multi-centred, transdisciplinary food allergy research consortium that translates knowledge of food allergy into clinical and public health practices.

In 2009, AllerGen’s CanFAST team generated first-ever, reliable prevalence data for peanut, tree nut, fish, shellfish and sesame allergies and found that approximately 7.5% of Canadians reported at least one food allergy and that prevalence differed across socioeconomic groups and geographic regions.

The results contributed to a national food labeling reform in 2011.

In 2014, CanFAST researchers published the first nationwide study to estimate the prevalence of food allergy among vulnerable Canadians.

This research will improve the clinical management of food allergies and help to identify food safety thresholds that inform public health standards, regulations and food industry guidelines.

The study concluded that Canadians with lower education and new Canadians (individuals who immigrated to Canada within the last 10 years) have fewer food allergies than the general population.
The Farncombe Institute was formed in January 2009, building on the success of the Intestinal Disease Research Program. The Institute is an integrated group of clinical and basic scientists dedicated to understanding the impact of digestive health and nutrition on disease across the life span. It is focused on developing new strategies for the diagnosis, treatment and prevention of intestinal diseases such as Crohn’s disease and ulcerative colitis, which will have global benefits. However, the focus of research in the Institute is not limited to digestive diseases; rather, it includes diseases of many other organ systems that may be caused and/or profoundly influenced by digestive health and nutrition.

A donation of more than $18 million from the Farncombe family has allowed for the development of state-of-the-art metagenomics laboratory run by Dr. Michael Surette and the only gnotobiotic facility in Canada run by Dr. Elena Verdú. The Farncombe family donation has also enabled the building of a spectacular atrium, and extensive renovations to the office and laboratory area on the 3rd floor of the McMaster University Medical Centre. We welcomed Dr. Walter Reinisch to the Farncombe Family Digestive Health Research Institute as the first recipient of the Audrey Campbell Chair in Ulcerative Colitis Research in 2013.

Dr. Stephen Collins has been appointed Director of the Institute in 2014. The 13 full members of the Farncombe Institute and their trainees and staff have published over 80 peer-reviewed articles and abstracts in 2013-2014 that have been cited over 300 times according to the Web of Knowledge.

The following Institute members received distinguished honours in 2013-2014:

- Dr. Stephen Collins has been appointed as a Fellow to the Royal Society of Canada
- Dr. David Armstrong was appointed President elect of the Canadian Association of Gastroenterology 2013-2014

The objectives of the CRC are:

1) To provide a stimulating environment to create new research collaborations which culminate in acquiring peer review grants, industry funding and private/corporate funding;
2) To provide core faculty with infrastructure to acquire and analyze their data, and;
3) To promote mentoring and training of students at all levels including undergraduate, graduate, and post-doctoral fellows.

Faculty Members who participate in centre research include: Dr. Sonia Anand (Director, Department of Medicine and Epidemiology), Dr. Joseph Bayene, Dr. Russ des Souza, and Dr. David Meyre (Department of Epidemiology), Dr. Guillaume Pare (Department of Pathology), Dr. Zena Samaan (Department of Psychiatry).

Associated Faculty include: Dr. Judah Denburg (Medicine), Dr. Mark Loeb (Pathology and Molecular Medicine), Dr. Andrew Mente (Epidemiology), Dr. Malcolm Sears and Dr. Mike Surette (Medicine), Dr. Gita Wahi (Pediatrics).

Current Projects: In 2013-14, faculty within the CRC supervised over two junior faculty, nine post-doctoral fellows, 19 PhD, 12 Master’s and 29 undergraduate students, 22 of whom are in formal graduate training programs. CRC faculty have received 23 grants from peer review sources, private donors, and industry totaling over $8,000,000. Current projects include the Aboriginal Birth Cohort (ABC), Canadian Alliance for Healthy Hearts & Minds (CVCD Alliance), Diet and Gene Interaction Study (DIGEST), GENOA (Genetics of Addiction), Dengue Population Genomics study, South Asian Heart Risk Assessment Project (SAHARA), South Asian Birth Cohort (START), and the Nutrition and Genetic Interactions Birth Cohort (NutriGen) Alliance.

Global Health Research Award: In addition to their generous gift for the Centre, the Chanchlani Global Health Research Award was created by the Chanchlani Family and McMaster University in 2012 to recognize a leading scholar in the area of Global Health. The Scholar is selected based on their scholarly contributions to Global Health. Each year a discipline within Global Health (i.e. Determinants of Health, Policy Development, Innovative Solutions) will be chosen, and an internal review committee at McMaster will review leading candidates. In 2012, the first Global Health Award Lecture recipients were Drs. Nitika Pai and Madhukar Pai from McGill University, and in 2014 the award recipient is Professor Hans Rosling, Professor of International Health from the Karolinska Institute.

The Chanchlani Research Centre (CRC) was established in 2011 after a generous donation made by Vasu and Jaya Chanchlani to McMaster University. The Chanchlani Research Centre pursues research studies seeking to add to the collective knowledge in the areas of genetics, genomics, and environmental risk factors for chronic diseases across the life course, with special emphasis on high risk groups including ethnically-diverse populations, those of low socioeconomic status and women.
Dr. Alfred Cividino’s focus for the Chair position continues to be the expansion of awareness and education about Rheumatic Diseases to physicians, residents, students and patients.

Dr. Cividino received peer-reviewed funding from CIORA (Canadian Initiative for Outcomes in Rheumatoid Arthritis) totaling $75,000 for a project ‘Training the rheumatologists of tomorrow’. This is the first Pan-Canadian study to identify what rheumatology faculty, administrators and learners identified as effective means and messages to attract future learners. This first phase of a three phase project was completed in May 2014 in collaboration with Dr. Lynne Lohfeld and Diane Crawnshaw with additional support from the chair funds. The results have been presented at national and international meetings and have been submitted for publication.

Dr. Cividino has assumed the Head of Human Resources Committee for the Canadian Rheumatology Association. In that role, with support from the CRA, phase two of the project will be implemented. The goal is to utilize the knowledge from phase one and capitalize on the existing engagement with the post graduate programs across the country to develop and test novel tools to inform and attract new trainees to rheumatology.

Physician manpower resources in Rheumatology remain static leaving most areas of the country underserviced. The chair’s current thrust is to facilitate enhanced recruit in rheumatology training programs.

In conjunction with Dr. John O’Neill as editor, the Division of Rheumatology has published a textbook ‘Essential Imaging in Rheumatology’. This is a first for a Canadian Rheumatology training program. Dr. Cividino’s contribution was writing the chapter on Osteoarthritis.

Dr. Jonathan D. Adachi

The Alliance for Better Bone Health Chair in Rheumatology has been used to further our research interests in the effective transfer of guidelines to practice and to further our research in osteoporosis through the support of George Ioannidis and a PhD graduate student, Andy Kin On Wong in their research endeavors in rheumatology.

Dr. George Ioannidis has continued his work with CaMos, GLOW, and ViDOS (Vitamin D and Osteoporosis in long-term care) and osteoporosis guidelines in long-term care projects. In the past year, he has been part of a team, led by Dr. Alexandra Papaioannou, which has examined osteoporosis care in the long-term care setting, the impetus for the development of guidelines. They have published on the care gap, attitudes about osteoporosis in front care givers and vitamin D and pharmacologic therapy in long-term care and the impact that ViDOS has had in improving the care of patients at risk for fractures. In addition to his research, Dr. Ioannidis has contributed to the education of interns, residents, undergraduate as well as graduate students.

Dr. Richard C. Austin

Dr. Austin is a Professor of Medicine in the Division of Nephrology, McMaster University and St. Joseph’s Healthcare Hamilton. He is a Career Investigator of the Heart and Stroke Foundation of Ontario and holds the Amgen Canada Chair in Nephrology. Currently, Dr. Austin holds grant-in-aid funding from the Heart and Stroke Foundation of Canada and Canadian Institutes of Health Research. Dr. Austin is also Director of the Hamilton Centre for Kidney Research (HCKR). The overall goal of the HCKR is to identify and characterize novel therapeutic targets and strategies aimed at decreasing chronic kidney disease and its complications, including cardiovascular disease. Dr. Austin has recently discovered several new genetic factors that influence the development of vascular calcification, the underlying cause of cardiovascular disease in patients with renal disease. Dr. Austin has been awarded a grant from the American Heart Association to investigate the role of TGF-β signaling in vascular calcification. This research has been published in the Journal of the American Society of Nephrology.

Andy Kin On Wong, a Vanier award winner, has focused his research work on bone structure and, more recently, on the effects of muscle and fat on bone structure and fractures. Andy has been responsible for the successful CIHR grant on bone quality that was awarded to our group. His work has focused on improving the reliability of pQCT-derived muscle area and density measures using a watershed algorithm for muscle and fat segmentation. A trimodality comparison of volumetric bone imaging technologies using pQCT, HRpQCT and PMRI was conducted. Short-term precision and validity, 1 yr change, long-term precision, and least significant change were established and their association with fragility fractures has been published.

Dr. Alfred Cividino

The Alliance for Better Bone Health Chair in Rheumatology has been used to further our research interests in the effective transfer of guidelines to practice and to further our research in osteoporosis through the support of George Ioannidis and a PhD graduate student, Andy Kin On Wong in their research endeavors in rheumatology.

Dr. George Ioannidis has continued his work with CaMos, GLOW, and ViDOS (Vitamin D and Osteoporosis in long-term care) and osteoporosis guidelines in long-term care projects. In the past year, he has been part of a team, led by Dr. Alexandra Papaioannou, which has examined osteoporosis care in the long-term care setting, the impetus for the development of guidelines. They have published on the care gap, attitudes about osteoporosis in front care givers and vitamin D and pharmacologic therapy in long-term care and the impact that ViDOS has had in improving the care of patients at risk for fractures. In addition to his research, Dr. Ioannidis has contributed to the education of interns, residents, undergraduate as well as graduate students.

Andy Kin On Wong, a Vanier award winner, has focused his research work on bone structure and, more recently, on the effects of muscle and fat on bone structure and fractures. Andy has been responsible for the successful CIHR grant on bone quality that was awarded to our group. His work has focused on improving the reliability of pQCT-derived muscle area and density measures using a watershed algorithm for muscle and fat segmentation. A trimodality comparison of volumetric bone imaging technologies using pQCT, HRpQCT and PMRI was conducted. Short-term precision and validity, 1 yr change, long-term precision, and least significant change were established and their association with fragility fractures has been published.

Dr. Richard C. Austin

Dr. Austin is a Professor of Medicine in the Division of Nephrology, McMaster University and St. Joseph’s Healthcare Hamilton. He is a Career Investigator of the Heart and Stroke Foundation of Ontario and holds the Amgen Canada Chair in Nephrology. Currently, Dr. Austin holds grant-in-aid funding from the Heart and Stroke Foundation of Canada and Canadian Institutes of Health Research. Dr. Austin is also Director of the Hamilton Centre for Kidney Research (HCKR). The overall goal of the HCKR is to identify and characterize novel therapeutic targets and strategies aimed at decreasing chronic kidney disease and its complications, including cardiovascular disease. Dr. Austin has recently discovered several new genetic factors that influence the development of vascular calcification, the underlying cause of cardiovascular disease in patients with renal disease. Dr. Austin has been awarded a grant from the American Heart Association to investigate the role of TGF-β signaling in vascular calcification. This research has been published in the Journal of the American Society of Nephrology.

Andy Kin On Wong, a Vanier award winner, has focused his research work on bone structure and, more recently, on the effects of muscle and fat on bone structure and fractures. Andy has been responsible for the successful CIHR grant on bone quality that was awarded to our group. His work has focused on improving the reliability of pQCT-derived muscle area and density measures using a watershed algorithm for muscle and fat segmentation. A trimodality comparison of volumetric bone imaging technologies using pQCT, HRpQCT and PMRI was conducted. Short-term precision and validity, 1 yr change, long-term precision, and least significant change were established and their association with fragility fractures has been published.
The Andrew Bruce Douglas Chair in Neurology was established in March 2006 to further the clinical, educational, and research aspects of Amyotrophic Lateral Sclerosis (ALS) at McMaster. With respect to clinical activities, we have established and maintained a position as a premier clinical site in Canada for the treatment of ALS, and patients come to the clinic from South Central Ontario, and indeed, all Ontario and beyond. We remain grateful to Hamilton Health Sciences for their ongoing support of the clinic. The ALS team is multi-disciplinary, and includes respiratory technology, speech and language support, social work, seatng and mobility support, equipment loans (with the ALS Society of Ontario), and is ably coordinated by Ms. Jane Allan. Ms. Shelley Curry provides the logistic and secretarial support, and Ms. Joan Martin is the research coordinator. We have close collaborations with Dr. Bruno Salena and Dr. John Cunnington for gastrointestinal and resprirological issues, respectively. With respect to education, medical students and neurology residents rotate through the clinic. Also, staff from ALS Canada and ALS Ontario have often come to the clinic to gain a clearer appreciation into ALS issues, as well as, over the years, interested federal and provincial politicians, and many health science and medical students and residents. With respect to research, we participated in one research trial sponsored by CytoKinetix, and I am on the Independent Drug Monitoring Committee of another ALS trial sponsored by GSK that is ongoing. We have undertaken two in-house trials looking at the activity of certain compounds in CSF from ALS patients and controls, and a genetic mutational analysis of ALS patients. Our basic research continues to evolve. It seems highly likely that a firmer understanding of sporadic ALS will arise in the next two years, and thereafter useful therapies may appear and we fully hope to play a significant role in these developments.

ASTRAZENECA CHAIR IN RESPIRATORY EPIDEMIOLOGY
Dr. Malcolm Sears

Dr. Sears directs the Canadian Healthy Infant Longitudinal Development (CHILD) Study, a large national longitudinal epidemiological study involving some 40 investigators across Canada. The study was initiated in 2008 with funding by CIHR and the Allergy, Genes and Environment (Allergen) Network of Centres of Excellence. After recruiting 3,624 pregnant mothers, 3,542 infants, who met inclusion and exclusion criteria at birth, are being followed to age 5 years. CHILD was designed as an intensive investigation of factors responsible for development of allergy and asthma, with a particular emphasis on gene-environment interactions. A very broad definition of the environment including not only indoor and outdoor air, but psychosocial environment including maternal stress, infections and nutrition, has allowed expansion of the scope of the study to include the early origins of obesity, metabolic diseases including diabetes, and cardiovascular disease. The CHILD cohort is now a solid platform for multidisciplinary research into the Developmental Origins of Health and Disease (DOHaD). Several novel CIHR-funded studies have been added to the core CHILD study, including a study of sleep in infants and consequent neurodevelopment, studies of the infant microbiome and immune development, and a multi-cohort study examining nutrition, environment and epigenetics as risk factors for chronic non-communicable diseases. A recent CIHR application to study the effects of specific environments in modulating high and low genetic risks for developing allergies and asthma received the highest ranking of all applications assessed by the Respiratory Committee, providing much needed funding to allow analysis of some of the biobanked samples. Mentoring of the younger leadership of the study, who are critical to the longitudinal continuation (anticipated beyond age 5 years) and success of the CHILD study, is a high priority.

Dr. Sears also continues his involvement in respiratory assessments in another major epidemiological study now running for 42 years, the Dunedin Multidisciplinary Health and Development Research Study in New Zealand. Collaborating with geneticists and epidemiologists both in Dunedin and at Duke University, a Genetic Risk Score was recently developed for asthma, which was predictive in identifying those likely to have persistent asthma from childhood into mid-adulthood. Longitudinal analyses also highlighted the key role of childhood atopy as a determinant of persistent asthma, especially among those developing incompletely reversible airflow obstruction in adulthood.

AUDREY CAMPBELL CHAIR IN ULCERATIVE COLITIS RESEARCH
Dr. Walter Reinisch

Dr. Reinisch has a longstanding clinical research interest into diagnostics, treatment and monitoring of patients with Inflammatory Bowel Disease (IBD). He conducted multiple clinical trials in patients with Crohn’s disease and ulcerative colitis. More recently, the potential of therapeutic drug monitoring has been revealed as a tool to optimize the outcome of patients with IBD treated with monoclonal antibodies directed against TNF-alpha, a key cytokine mediating the chronic inflammation. The aim of treating patients with IBD is to stop the inflammatory cascade and as a consequence to induce mucosal healing in the intestinal tract. Dr. Reinisch performed studies in patients with Crohn’s disease and ulcerative colitis showing associations of mucosal healing with increasing serum concentrations of the anti-TNF-alpha antibody infliximab. These studies published in 2014 emphasize the relevance of therapeutic drug monitoring and the need for treatment strategies including this concept. He is working on a model predicting serum concentrations of anti-TNF agents in order to treat predefined cut-off levels.
In collaboration with Dr. Susan Kahn (PI) from McGill University, we were key contributors to the “SoX” study, a recently completed RCT of over 800 patients with DVT who were randomly allocated to receive graduated compression stockings or placebo for the prevention of the post-thrombotic syndrome (PTS). The results of this study were presented at the American Society of Hematology and published in Lancet. There has been a number of sub-studies of the “Lancet” SoX study that have shown the over-utilization of stockings in patients with DVT and that PTS is not a homogeneous disease, but rather caused by one of a number of mechanisms. We continue to perform studies in women with suspected PE and expect to author the results of this pivotal study shortly.

Over the last year, I have become very involved with Drs. Eikelboom, Hirsh and Weitz in regular discussions where Dr. Eikelboom’s research fellows’ work is discussed. This group of 3-4 senior investigators discusses the projects, largely thinking “outside the box” and spark creative thinking among the group and with research fellows. This group has been very productive.

1. Chan WS, Spencer FA, Lee AV, Chunilal S, Douketis JD, Rodger M, Ginsberg JS. Safety of withholding anticoagulation in pregnant women with suspected deep vein thrombosis following negative serial compression ultrasound and iliac vein imaging. CMAJ 2013 PMID 23319405

I have been very fortunate to hold the Boris Family Chair in Education and Internal Medicine since February 2014. In addition to being appointed as the first recipient of this Chair, I was also appointed as inaugural Medical Director of The Boris Clinic which is located at McMaster University Medical Centre.

Over the last few months, I have been actively involved in the visioning, strategic direction and planning of The Boris Clinic. I am happy to say that Phase I of the construction of The Boris Clinic was completed in June 2014. The second phase of The Boris Clinic will be completed in May 2015.

The Boris Clinic brings all medical specialties under one roof resulting in more efficient, timely, and coordinated care for patients presenting with multiple complex medical problems. The Boris Clinic is based on three pillars of excellence: best clinical care, education, and research.

Phase I of the clinic offers two multidisciplinary clinics, Endocrinology & Diabetes Care and Research Program and a General Internal Medicine Rapid Assessment Clinic (GIMRaC). Phase II of the clinic will have all the other subspecialties of Internal Medicine. The Boris Clinic will also house the first Internal Medicine Ambulatory Clinical Teaching Unit, which will provide a structured educational environment for learners of all levels to gain the skillset to manage complex medical patients in an out-patient setting.

As the inaugural Medical Director of the clinic, and as holder of the Boris Chair, I have been involved in assembling and implementing the governance and management for this innovative clinic. As this is a joint initiative, I have been working closely with Hamilton Health Sciences administration and McMaster University administration. We have an effective Executive Committee, which I chair, and an active Physician Advisory Group (PAG), which I also chair. The PAG is made up of all Division Directors of all the subspecialties in the Department of Medicine. I have been working very closely with HHS administrative leadership in the operational, financing, and budgeting of the clinic.

The Boris Clinic has also introduced an electronic medical health record, one of a kind system that ensures that patient information is shared among those in his or her circle of care. As a central component of the clinic, this paperless record would be accessed by many caregivers throughout the region and allows physicians to communicate with each other. In putting this electronic system in place, I have been working with all healthcare professionals, including physicians, to get used to working in the paperless system.

In preparation for Phase II of The Boris Clinic, I have been involved in multiple meetings with divisions from different subspecialists of medicine and organizing the room allocation, patient flow, setting appointments, and staffing. This has been a very educational experience for me.
Dr. Papaioannou is a Professor in the Department of Medicine, McMaster University and a Geriatrician at Hamilton Health Sciences at St. Peter’s Hospital. She is the Scientific Director for the GERaS Centre (Geriatric Education and Research in Aging Sciences Centre) at St Peter’s – HHS. She has a joint appointment in the Division of Rheumatology, and is an associate Member in the Department of Clinical Epidemiology and Biostatistics. She is faculty in the Medical Sciences Program and supervises PhD and Masters students in Medical Sciences and Health Research Methodology Programs at McMaster University. Dr. Papaioannou has received a number of awards including the Department of Medicine Graduate Medical Education Teaching award for teaching graduate students at McMaster university, the Lindy Fraser Award by Osteoporosis Canada, the YWCa Women of Distinction award and the Ontario College of Family Physician’s Certificate of Recognition award. She is a member of Osteoporosis Canada and the International Osteoporosis Foundation (IOF) Committee of Scientific Advisors (Elected). She has led a number of knowledge translation strategies since leading the Osteoporosis Guidelines for Canada. She is a member (Elected) of the Canadian Patient Safety Institute, Falls and Falls Injury Prevention Faculty, and a member of the Ontario Osteoporosis Strategy, Strategy Review Working Group. Dr. Papaioannou is Research Director, Division of Geriatric Medicine, McMaster University. She has 230 publications and has been invited to speak at both national and international meetings.

Dr. Papaioannou is the lead investigator for the Ontario Ministry of Health-funded Ontario Osteoporosis Strategy for Fracture Prevention in Long-term Care. Dr. Papaioannou is primary investigator for a CIHR-funded grant “A knowledge to action intervention in long term care - A feasibility study focusing on the uptake of osteoporosis and fracture prevention best practices”. She is co-investigator of the TAPESTRY grant led by the Department of Family Practice and the CIHR-funded grant “The development of bone quality parameters for assessing osteoporosis using peripheral quantitative computed tomography”. She is also a co-investigator of a CHF-funded grant “A randomized double-blind-placebo-controlled trial for the evaluation of a polypill, a low dose aspirin and vitamin D supplementation in primary prevention to reduce cardiovascular disease (CVD) outcomes – The international polycap study 2 (TIPS-2)”. One of the major objectives of The Boris Clinic is that we will create innovative models of care in education. The Boris Clinic will also be a hub of critical research in exploring and researching different models of healthcare delivery.

I continue to be the Division Director of General Internal Medicine at McMaster University and have been actively involved in the recruitment of academic Internal Medicine specialists, who in addition to doing in-patient activities on the Clinical Teaching Unit, would be involved in out-patient teaching activities in the new Ambulatory CTU at The Boris Clinic. One of the gaps in the Internal Medicine training program has been out-patient training for our learners and we believe The Boris Clinic would be an ideal hub to train and educate learners in management of ambulatory and out-patient patients.

I am happy to inform you that since the opening of Phase I of The Boris Clinic, we have had visits from healthcare professionals, both out of the city and out of the country, to see the layout and the functioning of the clinic. We are receiving positive feedback from patients who have visited The Boris Clinic. The areas that people have positively commented on are the general ambiance and structure of the clinic, friendliness of the staff and the efficiency and team approach in patient care.

I am actively involved in the physician resource planning and recruitment of clinician educators and clinician researchers for the Division of General Internal Medicine and for the Department of Medicine, and I am happy to inform that we have been fortunate in recruiting highly trained academic internists who will be working in The Boris Clinic. I should also mention that our Ambulatory CTU is the first of its kind in the country and we have already submitted a paper describing the concepts and the structure of the clinic to a medical journal.

In my capacity as the GIM Division Director, I have been involved in organizing a large Internal Medicine Review Course which was held in April 2014 and had 750 physicians from across the country and internationally attending the three day event. This was our 6th Review Course and we have planned our 7th Annual Internal Medicine Review Course, which will occur in March 2015.

Since being appointed as the holder of the Boris Family Chair in Education and Internal Medicine, I have been extremely busy in multiple areas of clinical care, education, and administration.

I look forward to the next 12 months and will be happy to report the successes of the initiatives in my next year’s report.
**ELI LILLY CANADA/MAY COHEN CHAIR IN WOMEN’S HEALTH**

**Dr. Shannon Bates**

I am very honored to have been appointed the Eli Lilly Canada/May Cohen Chair in Women’s Health. Dr. Cohen, a former Associate Dean and Professor in the Faculty of Health Sciences well known for her leadership in the field of women’s health and contributions to gender equality within the medical profession, is an important role model for me and for other women in medicine. The Eli Lilly Canada/May Cohen Chair in Women’s Health was established in 1998 with funding from Eli Lilly Canada Inc. The Chair is responsible for developing an awareness of the current activities in women’s health that are in place in the broader academic and health network and for the promotion of McMaster as a leader in women’s health. The Chair will make contributions to the education arena of the faculty, remain a leader in the field and, where appropriate, be involved in clinical work that informs the research agenda.

The support of the Eli Lilly Canada/May Cohen Chair in Women’s Health will be instrumental in allowing me to pursue my interests related to women’s health. My clinical and academic work focuses on women’s issues in thrombosis and anticoagulant therapy, especially as they relate to pregnancy, assisted reproduction, and hormonal therapy. My goal is to enhance the care of women in these settings through physician and patient education, development and dissemination of evidence-based practice guidance, advocacy, and participation in related research.

This year, I had the opportunity to present educational sessions on thrombosis and women's reproductive issues at annual meetings of the American Society of Hematology, the American Society of Clinical Oncology, the North American Society for Pediatric and Adolescent Gynecology, and Thrombosis Canada. I worked with the latter organization to update their Clinical Guidelines on venous thromboembolism prophylaxis in pregnancy and treatment of venous thromboembolism during pregnancy and to revise their diagnosis of deep vein thrombosis document to include guidance specific to diagnosis in pregnant women. I also undertook a video interview with Thrombosis Canada publicizing venous thromboembolism as a woman’s health issue and providing information for patients about venous thrombosis and pregnancy. I continued to serve on the Medical Advisory Committee of the Foundation for Women and Girls with Blood Disorders.

My co-investigators (including Dr. Gordon Guyatt) and I completed our PSI Foundation-funded international multicenter cross-sectional interview study examining women’s willingness to receive low molecular prophylaxis during pregnancy to prevent recurrent venous thromboembolism and the determinants of that decision. We are currently preparing two manuscripts and are planning a follow-up study to explore the discrepancies in responses we received in our first study.

**GLAXOSMITHKLINE CHAIR IN GASTROENTEROLOGY**

**Dr. Stephen Collins**

The laboratory of Dr. Stephen Collins and Dr. Premysl Bercik is supported by two CIHR operating grants and a research contract from the Nestle Research Centre in Switzerland. Our work focuses on the role of the intestinal resident bacterial population (known as the microbiota or microbiome) on gut and brain function in health and disease. The gut-brain axis is an important component of many GI disorders ranging from functional to inflammatory bowel diseases and the Collins-Bercik lab has pioneered work that integrates the microbiome into this axis. We, and others, have shown that the behavioural profile and brain chemistry differs from that seen in normal (bacteria-containing) mice, and that colonizing germ free mice within a limited time frame after birth restores normality. We have also shown that transient colonization with a single bacterial strain (monocolonization) is sufficient to normalize behaviour in germ free mice. Our recent results indicate that this is mediated via activation of the innate, but not the adaptive immune system, and current work is aimed at identifying the responsible mediators. Our laboratory was the first to show that components of behavioural phenotype can be transferred between organisms via the fecal microbiota. This observation has generated considerable interest given the use of fecal transplants in the management of patients with refractory and recurrent Clostridium difficile infection. It raises issues regarding donor selection for fecal transplantation. This finding has also been exploited in our investigation of the role of the intestinal microbiota in the expression of the Irritable Bowel Syndrome (IBS) – the most common GI problem in our society. A substantial number of IBS patients also exhibit psychiatric co-morbidity. While it is known that the microbial composition of the gut is altered in IBS, it is not known whether this is simply a result of changes in gut physiology or whether it drives gut and possibly the behavioural abnormalities that so often accompany IBS. We therefore developed a model in which germ free mice are colonized with human microbiota from IBS patients with co-morbid anxiety, or healthy controls. We found that the IBS microbiota induces gut dysfunction and immune activation reminiscent of IBS. We also found that the fecal microbiota of those IBS patients with high levels of anxiety also induced anxiety like behaviour in recipient mice. In contrast, microbiota from IBS patients without anxiety induced changes in gut function but not in behaviour. These novel findings justify the use of microbiota-directed therapies, such as probiotics, in managing both intestinal and behavioural manifestations of IBS. Indeed, our preliminary analysis of a placebo controlled trial indicates that a selected probiotic improved both intestinal and behavioural symptoms in IBS patients with psychiatric co-morbidity.
The endowed professorship has permitted continued productivity in the neuromuscular disease clinic this past academic year. Inherited peripheral neuropathy (IPn) continues to be the focus of my research. We have published a paper describing the effects of type 2 diabetes on patients with CMT1A. We found that a special measure of distal nerve conduction (the terminal latency index) provides the best estimate of whether these individuals have superimposed carpal tunnel syndrome. Through the use of whole exome sequencing (WES) a novel mutation in Valosin-Containing Protein (VSP) was identified. This represents the second case identified in a CMT kindred when the gene was previously associated with a form of hereditary myopathy and ALS. WES has also been employed to discover compound heterozygous mutations in 2 genes which each have DNA helicase activities and appear to have synergized to cause a novel dysmyelinating IPn. We have also submitted manuscripts reporting cases of CMTX and CMT4C. Continued investigation into the effects of exercise on CMT is planned including the role of balance training.

I continue to serve as a medical advisor to Dr. Stuart Phillips’ laboratory. His laboratory has maintained a very productive schedule publishing numerous manuscripts on the complex genetics of skeletal muscle hypertrophy. We have recently published a manuscript in the Canadian Journal of Neurological Sciences defining, for the first time, a pathophysiologic spectrum connecting statin-induced inflammatory myopathy with necrotizing myopathy. Dr. S. Verno and I published a report describing the first case of transient neonatal autoimmune autonomic ganglionopathy. This appeared in the journal, Neurology: Neuroimmunology & Neuroinflammation. Finally, I continue to serve as an associated editor for Muscle & Nerve and am on the medical advisory board of the Canadian GBS/CIDP Society.
Dr. Anand received the Heart and Stroke Foundation / Michael G. DeGroote Chair in Population Health Research at McMaster University in 2008, and it was renewed in 2013. The mandate of this Chair is to improve research in population health as it relates to cardiovascular disease. Dr. Anand’s research focuses on understanding the contribution of environmental and genetics factors on the development of cardiovascular risk factors and cardiovascular disease. She has a particular interest in conducting intersectoral research including ethnicity, sex/gender, and social factors. Dr. Anand is currently: 1) investigating the role of genetic and epigenetic factors and type 2 diabetes and MI risk in various ethnic populations, 2) evaluating the effectiveness of culturally-tailored multimedia intervention to modify risk factors for cardiovascular disease in the South Asian population (SAHiRA trial), and 3) has initiated two birth cohort studies in the South Asian and Aboriginal communities in Ontario to determine the early life determinants on the development of adiposity and related metabolic factors in high risk populations. Recently, Dr. Anand has teamed up with Dr. Jack Tu (ICES) and Dr. Matthias Friedrich (Montreal Heart Institute) to lead the Canadian Alliance of Healthy Hearts and Minds Study funded by the Canadian Partnership against Cancer and the Heart and Stroke Foundation. This study aims to recruit 9,700 adults from across Canada to understand the community and individual level determinants of cardiovascular disease and cancer including a new Aboriginal Cohort.

Dr. Kearon’s research focuses on clinical trials designed to optimize the diagnosis and treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), which are collectively referred to as venous thromboembolism (VTE).

Two ongoing CIHR-funded diagnostic studies are evaluating new ways to use D-dimer blood tests to help rule out DVT and PE, with the goal of reducing the number of ultrasound and CT pulmonary angiogram examinations that are required. Instead of using the same cut-off value to categorize D-dimer results as positive or negative, these studies are testing the safety of ruling-out thrombosis using a higher D-dimer value when clinicians decide that the clinical suspicion for thrombosis is low. These studies also use a very high D-dimer level to decide which patients need to return for repeat testing after a week.

A CIHR-funded study is testing if D-dimer levels can be used to decide which patients with an unprovoked VTE need to stay on anticoagulant therapy for life because they have a high risk of recurrent thrombosis, and which patients can safely stop anticoagulants after 3 months. A HSF-funded substudy is exploring if subclinical inflammation is contributing to recurrent thrombosis in these patients. An NIH-funded trial is comparing removal of DVT using a catheter with just using anticoagulant therapy, hoping to show that active removal of thrombosis reduces the risk of patients being left with a chronically sore and swollen leg. A third study is determining if one of the new and very convenient anticoagulant drugs is an effective way to treat superficial vein thrombosis.

Dr. Kearon also collaborates with the "perioperative medicine" research group, and leads an international panel that is developing guidelines for the treatment of VTE. He is program director for McMaster’s Clinician Investigator Program.
LEO PHARMA CHAIR IN THROMBOEMBOLISM RESEARCH

Dr. Mark Crowther

Dr. Crowther’s research focus is on studies designed to improve the quality of anticoagulant care. Dr. Crowther holds a Career Investigator Award from the Heart and Stroke Foundation of Ontario. He is the Vice-President of Research at St. Joseph’s Healthcare, Hamilton and Chair of the Department of Pathology and Molecular Medicine at McMaster University. He is principal investigator on a Heart and Stroke Foundation of Canada-funded project examining whether rivaroxaban reduces the risk of recurrent thrombosis in patients with antiphospholipid antibodies. He chairs the American Society of Hematology’s (ASH’s) Quality Committee and is overseeing ASH’s guideline development program. Working closely with Dr. Wendy Lim and other collaborators, Dr. Crowther continues to lead systematic reviews and meta-analyses examining various aspects of anticoagulant care and control. His work also extends to other areas of benign hematology including evaluation of patients with immune mediated hematologic disorders and porphyria. Dr. Crowther has more than 310 peer-reviewed publications with an H-factor of 81, and more than 400 invited national and international speaking opportunities.
Dr. Mark Loeb has been focusing his research on viral infections that include influenza and dengue. His research includes understanding how influenza virus is transmitted through communities and is studying genetic variants that underlie susceptibility to severe complications. Dr. Loeb has completed the second year of a large CIHR-funded randomized controlled trial in the Hutterite community comparing live influenza vaccine to inactivate vaccine in order to assess the effect of herd immunity. He was asked to present preliminary findings of the trial to the U.S. CDC and the APIC Influenza Working Group to inform on recommendations for influenza vaccination. Dr. Loeb was also asked by the World Health Organization to present his findings at a meeting in live influenza vaccine in Geneva to better understand vaccine effectiveness. Dr. Loeb presented preliminary findings of his dengue genetics study to a panel at the NIH. He has been conducting a pilot study to assess if randomizing children in Vietnam to Vitamin D or placebo will reduce respiratory infections. The pilot study has demonstrated feasibility. In 2013-2014 academic year, Dr. Loeb received the Jonas Salk award from the March of Dimes. Dr. Loeb has taken on the role of Taskforce Lead of the WHO Working Group on Pregnancy and Influenza.

Dr. Loeb continues to lead a large NIH study to assess genetic variants associated with severe dengue infection. This study is being conducted in nine countries in central and south America as well as in southeast Asia. In 2014, Dr. Loeb awarded a CIHR grant for a clinical trial to assess whether oseltamivir can prevent complications in a high risk population. Dr. Loeb received three contracts from the WHO for systematic reviews of influenza in pregnancy, herd immunity, and pediatrics over the 2013-2014 academic year. Over the past year, Dr. Loeb assumed the role of Chair of the Data Safety and Monitoring Board of an important NIH vaccine trial on influenza H7N9 which was first reported to infect humans in March 2013. He was an invited speaker at an NIH meeting on population genetics.

Dr. Loeb was also asked by the World Health organization to present his findings at an NIH meeting on population genetics. H7n9 which was first reported to infect humans in March 2013. He was an invited speaker at an NIH meeting on population genetics.

Endowed Chairs

Michael G. DeGroote Chair in Infectious Diseases
Dr. Mark Loeb

The 3 Wishes Project is a feasible, portable, scalable intervention that fosters dying with dignity. It integrates palliative care and spiritual care into critical care practice. This individualized approach to end-of-life care offers conversational frameworks that support more authentically connected clinicians. Encouraging behaviours that cue the emotional support valued by patients and fostering personal acts of engagement may help to create therapeutic encounters that aid in the terminal transitions of care, particularly for physicians-in-training. Our findings underscore the drive that we all have to search for meaning, memories and closure in anticipation of death, while helping to create preparedness, comfort and connections during the dying process.

Michael G. DeGroote Chair in Stroke Prevention
Dr. Robert G. Hart

Established in 2003 with a generous gift from Mr. Michael G. DeGroote and subsequently converted to a Chair with funds from the Department of Medicine, the goal of the Michael G. DeGroote Chair in Stroke Prevention is to contribute significantly to the body of scholarship in the area of stroke prevention. One area of special research focus is silent brain ischemia: that is, strokes that are unrecognized because they do not cause weakness or trouble with speech, but still cause serious brain problems. Silent brain ischemia accounts for at least one-third of thinking and memory decline in middle-aged and elderly people, presenting a growing public health concern to an aging population. Currently, there are no proven treatments to prevent silent brain ischemia. Recently, our group has initiated two clinical trials (COMPASS MIND MRI, NAVIGATE ESUS MRI) to test interventions to prevent silent brain ischemia.

In 2014, we proposed a new clinical entity called “embolic strokes of undetermined source” (ESUS). This has garnered international attention and prompted the organization of a large international randomized clinical trial called NAVIGATE ESUS led by the McMaster Stroke Program, sponsored by Bayer Healthcare, to be carried out at 450 international stroke research centers in 30 countries. This new paradigm is likely to revolutionize management of cryptogenic stroke, comprising about one-quarter of all strokes due to blocked arteries and has brought McMaster into the international spotlight as leading innovative stroke research.

It has been a successful year for the McMaster Stroke Program. We have recruited talented new faculty and stroke fellows, and we are now the largest stroke program in Ontario. The NAVIGATE ESUS international trial is underway (described above), bringing international research prominence to the Program. I have continued to publish regularly in the peer-reviewed stroke literature, including several invited commentaries on major issues in stroke management and research.

During the coming year, I will be developing an ambitious proposal for a large clinical trial to test new anticoagulants in patients with cerebral vascular atherosclerosis (“hardening of the arteries”). I will continue to devote considerable time and effort mentoring our junior stroke research faculty and stroke fellows to foster their skills in grant writing and publications.
Dr. Paul M. O’Byrne has had a longstanding research interest into the causes and treatment of asthma. In particular, his research is focused on the roles of environmental allergens in causing airway inflammatory responses and the associated changes in physiological responses of the airways, which are a hallmark of asthma. These studies have demonstrated mechanisms by which the airways signal the bone marrow to increase production of eosinophils, which then traffic into the airway to participate in allergen-induced responses. Eosinophils and other airway cells, including mast cells, release a group of mediators known as cysteinyl leukotrienes, which Dr. O’Byrne’s research group has demonstrated to be critical mediators for a number of allergen-induced responses including bronchoconstriction, the further influx of inflammatory cells, and the trafficking of dendritic cells, which are the professional antigen-presenting cells in the airways. In addition to this, Dr. O’Byrne’s laboratory has used the clinical models of allergen-induced airway responses and airway inflammation as a mechanism to study the potential efficacy of new drugs in asthma, as well as the mechanisms by which established drugs work. Recently, the first documented evidence of anti-sense treatment to inhibit the production of cytokine receptors was shown to be beneficial in this clinical model. Other studies have focused on humanized monoclonal antibodies directed against a number of cytokines thought to be possible mediators of allergic inflammation. This included the first study with an anti-IL-5 monoclonal antibody to show benefit in severe asthma. Finally, research in his laboratory has identified a pivotal role for Th2 cytokines such as IL-4, IL-5, IL-13 and TSLP in inducing airway responses and a possible role for interferon-γ in inhibiting allergen-induced airway inflammation.
This chair was established to increase the clinical component of the Farncombe Family Digestive Health Research Institute and strengthen population-based gastroenterology research as well as evidenced-based medicine within the Institute. Dr. Paul Moayyedi has held the Chair since 2004. He has published over 270 papers that have been cited approximately 8,000 times. He was appointed Director of the Division of Gastroenterology in 2006 and the Division has continued to thrive under his leadership. He was appointed Acting Director of the Farncombe Family Digestive Health Research Institute in 2012. He also has been re-appointed as joint Editor-in-Chief of the American Journal of Gastroenterology in 2012. This is the world’s highest impact factor general clinical gastroenterology journal and he is the first person not to reside in the U.S. to be appointed to this prestigious position.

Dr. Moayyedi is responsible for the Cochrane Upper Gastrointestinal and Pancreatic Diseases (uGPD) Review Group moving from the University of Leeds, U.K. to McMaster University. The uGPD group has received funding from CIHR for 2010-2015 through a $9.6 million grant to Cochrane Canada. The uGPD group is responsible for commissioning all Cochrane systematic reviews relating to the upper GI tract and annually updating these reviews on the Cochrane Library. This provides evidence on the most effective health care interventions to doctors and patients worldwide. The systematic reviews that he has conducted have informed guidelines that will better serve the needs of patients with gastro-esophageal reflux disease, dyspepsia and H. pylori infection. This work has also had an international impact and been a major feature of guidelines in Canada, the U.S., and the U.K. His systematic review work on H. pylori eradication to prevent gastric cancer has also been central to IARC/WHO Working Group Report on the prevention of gastric cancer, which has the potential to save 600,000 lives each year.

He was the first to conduct a randomized trial evaluating the efficacy of fecal transplants in ulcerative colitis with Drs. Lee and Surette. This showed that this therapy could be effective in a proportion of ulcerative colitis patients and could pave the way for a new therapy after further study. He was involved in an NIH trial to evaluate antidepressant therapy in functional dyspepsia and is the deputy or Principal Investigator the world’s two largest randomized trials in Barrett’s esophagus assessing how to prevent the development of esophageal cancer. He has published over 300 peer-reviewed papers and his work has been cited over 9,500 times with an h index of 53 according to Thomson Reuters (June 10, 2015). He is in the top 10 most cited gastroenterologists according to Google Scholar.

The Salim Yusuf Chair in Cardiology supports the activities of the Director of the Division of Cardiology at McMaster University, currently Dr. Stuart Connolly.

Clinical Activities:
The Cardiology Training Program continues to flourish under the leadership of Dr. Nicholas Valettas. Currently, we have 12 trainees in the program and we are hoping to increase to 13 to be able to provide a uniformed and consistent level of training on all three of our cardiology teaching services. Having completed our internal review last year, we are anticipating a successful external review in the spring 2015.

Research Activities:
The cardiology division continues to flourish in the realm of research with a wide variety of strong programs. The Division Director has played a role in supporting many programs.

As Dr. Stuart Connolly’s second term draws to a close, he will be stepping down from the role of Division Director and relinquishing the Chair in Cardiology. He expresses his gratitude for the support he has received over the past 10 years.
In Dr. Samir Sinha’s report “Living Longer, Living Well” (January 2013), he emphasized the need for mandatory core geriatric training programs for students. With this in mind, the Chair has remained committed to the promotion of innovative and sustainable educational, research, and clinical models of care that enhanced the provision of health care and fostered the independence and quality of life for our growing aging population.

During the past year, the highly successful inter-professional education program, 4th Annual Update in Geriatrics Day and Life Long Achievement Award had over 350 participants. This year’s theme was “Balancing Priorities in Chronic Disease Management: When is Enough, Enough?” We were honoured to have Dr. Audrey Chan, Associate Professor Geriatrics and Palliative Medicine Mt. Sinai Hospital, and Director at the Martha Stewart Center for Living and Vice-Chair for Clinical Programs in the Department of Geriatrics and Palliative Medicine in New York, as our keynote speaker. Her presentation, “Aging is Not for Sissies: Frailty and its Implications for Clinical Care” highlighted the complexity of our seniors and the need to prevent frailty. Other internationally renowned speakers included Drs. Paul O’Byrne, Hertzel Gerstein, and Alexandra Papaioannou.

The Life Long Achievement Award, established by the Chair and Regional Geriatric Program Central (RGPc), was presented in November 2013 to Mr. Charles and Mrs. Margaret Juravinski who have contributed selflessly to the building of caring communities through their generous philanthropic contributions to McMaster University and community hospitals. Their contributions have improved the quality of life of citizens in our community and have helped to ensure that our future health care professionals provide the best care through innovative and ground-breaking research and lifelong learning.

In 2013, a consortium of expert geriatric care educators and clinicians launched the Geriatric Certificate Program (GCP) with support from the Chair and RGPc. The GCP consortium developed an integrated, evidence-based and inter-professional educational certificate program. There are over 180 clinicians registered, and 19 clinicians have successfully graduated from the GCP. The GCP consortium will invest in the development of e-learning modules on common geriatric problems, which will be disseminated nationally and internationally. At the recent “Ontario Summit for Seniors” meeting supported by the Council of Ontario Universities and funded by the MOHLTC, the GCP was highlighted as an innovative educational program. It was described as ‘virtual’ educational program in the sense that it draws on and combines existing, best-in-class educational material. The courses have been sourced from multiple, leading educational partners and the whole is informed by a set of core competencies (Baronikian H, 2014).

Research projects to improve care, self-management, social interactions and health behaviours for our seniors within the community and acute care hospitals are supported by the Chair, including the “iLearn, iLive Well” study which has the goal of teaching older adults how to confidently use an iPad by completing a training program, using volunteers, and to reduce social isolation and loneliness that some seniors may be experiencing. Above all, the main objective is to improve the wellbeing of older adults through mentorship and the use of technology. Another research project supported and developed by the Chair and the RGPc is the “Seniors and caregivers perspectives on transitions from the emergency department (ED) and the community” study. Information from patient and caregiver surveys and telephone interviews will provide valuable information to better understand patient and caregiver perspectives of their ED visit, discharge planning and experiences upon return to the community.

The Chair has continued to support researchers such as Dr. George Ioannidis, a member of Dr. Papaioannou’s research team, who has taken on a senior lead role in the “Gaining Optimal Osteoporosis Assessments in Long Term Care” and “Diabetes and Fracture” risk studies. In recognition of Dr. Christopher Patterson’s research accomplishments in aging, primary care diagnosis and management of patients with dementia, the “Dr. Christopher Patterson Internal Medicine Resident Research Grant in Seniors Care” has continued. This grant will foster interest in the care of frail seniors and promote the development of clinical and research expertise within the field of geriatrics in postgraduate trainees in the core Internal Medicine Program at McMaster University.

During the coming year the goal of St. Peter’s/McMaster Chair of Aging will be to identify and disseminate key capacity building programs and innovative research findings to a broader spectrum of health care providers, seniors, and community at large nationally and internationally. The Chair will promote and develop evidence-based, accessible and novel educational programs that improve functional independence, social isolation, and quality of life of our seniors. With our growing aging population, health care providers with geriatric expertise are essential and key to ensuring quality care for our frail seniors. However, despite this need less than two per cent of medical students will pursue a career in geriatrics. The Chair will promote and support research endeavours to promote geriatrics as a specialty in our future health care professionals and projects.

The Chair has been very grateful for the generous support and leadership of the following: St. Peter’s Hospital Foundation / Hamilton Health Sciences, Rebecca Repa, Dr. John Kelton, Dr. Paul O’Byrne, Kevin Sulewski, Dr. Alexandra Papaioannou, Lynn Pacheco, David Jewell, Anisha Patel, Lily Consoli, RGPc and Ryan Liddell.
I would like to thank Mr. Gary W. DeGroot and Mr. Michael H. DeGroot for their generous gift in support of the William J. Walsh Chair in Medical Education and to express my continued appreciation to Drs. John Kelton, Paul O’Byrne and Akbar Panju for their ongoing personal and professional support.

In 2013/2014, I provided coverage for the Clinical Teaching Unit and ancillary General Internal Medicine services for approximately 32 weeks in addition to eight weeks of out-patient coverage. During my clinical activities, I taught students from the Michael G. DeGroote School of Medicine and trainees from several postgraduate programs. My non-clinical education contributions have included participation in the MD and Postgraduate Programs as a tutor, lecturer, clinical skills supervisor, retreat presenter and facilitator, and OSCE examiner. A significant portion of my time is spent on mentoring trainees within the core Internal Medicine and General Internal Medicine Programs and faculty members in the Division of General Internal Medicine and Department of Medicine. In addition, I continue to mentor several trainees who are pursuing additional training at other institutions and others who have started their careers at community hospitals while continuing to contribute academically.

My administrative contributions include Medicine Associate Chair (Education), Director of the Clinical Teaching Unit at the Juravinski Hospital, and Deputy Division Director for the Division of General Internal Medicine. At the hospital level, I am one of three Co-Chiefs of Medicine for the Juravinski site, the Physician Lead at the Juravinski Hospital for the Physician Assistant and Nurse Practitioner Programs for General Internal Medicine, and the Lead Physician for the Alternate Level of Care Unit.

I represent the Department of Medicine and the university on a national level as a Royal College of Canada examiner for Internal Medicine, Ontario Academic Representative for the Canadian Society of Internal Medicine and as a member of the National Council for the Society of Internal Medicine. I contributed as a Co-Chair and Planning Committee member for three national/international conferences: Canadian Anesthesia and Medicine Perioperative Conference, Canadian Society of Internal Medicine Annual Meeting and the McMaster University Annual Review Course in Internal Medicine.

Residents under my supervision for research have had multiple presentations at the Department of Medicine Research Day and at the annual meetings of the Canadian Society of Internal Medicine, Canadian Endocrine Society, National Conference on Residency Education, and at the American College of Physicians Ontario Chapter Meeting. In 2014, I was an author on four abstracts and on five peer-reviewed publications.

I am currently a site co-investigator for two multi-centre international trials: HIP ATACK and MANAGE. I am also a co-principle investigator on an End of Life Study, EXCEPT 360, and a study examining a nutritional intervention in hospitalized medical patients. Both these studies will start enrolling in 2015.

Dr. Patel has been a significant contributor to several multi-centre international trials and has contributed to several peer-reviewed publications.

Dr. Denburg has continued to be active in all three areas of academic internal medicine, achieving objectives for performance in clinical, educational and research endeavours. In the clinical arena, Dr. Denburg continues to attend one of the largest and most intensive specialist academic internal medicine practices in Canada, specifically in immune aspects of disease affecting many organ systems. He has continued his referral-based outpatient and inpatient activities, seeing patients almost all with complex medical problems. Additionally, he has continued involvement in clinical trials for some of these disorders.

His main research thrusts include examination of the mechanisms of allergic inflammation, with particular emphasis on hemopoietic cytokines and their role in activating the differentiation and recruitment of inflammatory cells such as eosinophils, basophils and mast cells. This includes an understanding of the growth and differentiation of human basophil and eosinophil precursors, with the development of in vitro assays to monitor clinically relevant fluctuations in these cells during allergic responses. The specific diseases studied have included allergic rhinitis, nasal polypsis and asthma. These studies have established the biological importance of hemopoietic mechanisms in allergic inflammation and emphasize important and now globally-recognized links among rhinitis, asthma and other allergic disease manifestations (“allergy as a systemic disease”). Findings have been published in high-impact journals, and are the subject of ongoing peer-reviewed and industrial grants.

As creator, Scientific Director and CEO of AllerGen NCE Inc., Dr. Denburg has overseen the continued development of this applied research and training network in allergy and asthma in Canada, now with global outreach in several continents. The Walsh Professorship has been a critically important asset in support of Dr. Denburg’s role in developing and maintaining AllerGen’s activities. For a summary of AllerGen’s major accomplishments over the past year, see the report included in this publication.
REPORTS: CANADA RESEARCH CHAIRS

CANADA RESEARCH CHAIR IN ETHNIC DIVERSITY AND CARDIOVASCULAR DISEASE

Dr. Sonia Anand

In April 2011, Dr. Anand received the Canada Research Chair in Ethnic Diversity and Cardiovascular Disease. The goal of the chair includes:

1. Identifying health behaviours (dietary and activity) and genetic determinants of abdominal obesity in related cardiometabolic risk factors in adults of diverse ethnic origin,
2. Evaluating interventions aimed at lowering CV and diabetes risk in high risk ethnic groups such as CIHR - funded SAHARA trial.
3. Investigating the impact of the in utero environment, maternal fetal-genetics and epigenetics together with early life behaviours on the development of cardiometabolic traits among South asian and Aboriginal people. In 2013, Dr. Anand and her colleagues received a grant from CIHR Institute of Nutrition, Metabolism and Diabetes aimed at understanding the early origins of chronic diseases by studying the nutritional, genetic, epigenetic, and microbiome associations with cardiometabolic phenotypes and allergic disorders among 5,500 newborns from the CHILD, FAMILY, START and ABC birth cohort studies.

CANADA RESEARCH CHAIR OF RESEARCH TRANSFER IN INTENSIVE CARE

Dr. Deborah Cook

My CRC report this year is focused on the 25th anniversary of the Canadian Critical Care Trials Group (CCCTG). The CCCTG is the oldest and most productive clinical ICU research consortium in the world - a group of Canadian critical care professionals from ICUs across the country. Collectively, we plan and implement innovative investigator-initiated, patient-focused, multicenter research. The dedication, shared expertise and spirit of collegiality that are embodied by the CCCTG have been replicated globally. The high impact research we conduct has helped to advance health care in Canada and around the world by changing the practice and improving the quality of care of the critically ill.

The academic home of the CCCTG was McMaster University from the beginning, and we continue to help lead, collaborate on, or support the most to practice-changing research in the country. This modus operandi has led to an uncommon depth of respected ICU scientists of all ages across the country who are now leading investigator-initiated research on the world stage.

Since the CCCTG was established in 1989, our membership has grown to over 100 clinical scientists, and we have published more than 200 articles including 15 in the New England Journal of Medicine. While scientific productivity today demands metrics, intangible ingredients of success that fuel a research group such as ours are seldom captured by bibliographic analyses.

A clear purpose, strong methods and shared values helped us to harmonize. We found that truly synergistic science requires empathetic listening and honouring different perspectives. At protocol presentation meetings, constructive critique has always been expected. A culture of egalitarianism quickly emerged, and remains. Through to the present day, although feisty discussions are not unusual, and provocative questions arise, everyone's input is respectfully delivered. Voices of junior colleagues have always been valued as much as mid-career and senior colleagues. Ideas are welcome from all corners – co-investigators, collaborators, new investigators, veterans and visitors. Concepts are developed and refined by community mentoring, which augments the individual mentoring that is so special in this country.

We had many transition points in our 25 year history. Early on, we branched out to embrace study designs beyond randomized trials. In collaboration with Research Coordinators, we conducted 'research on how we do research', creating new metrics for recruitment efficiency, clarifying models of informed consent for vulnerable critically ill patients, and creating co-enrolment principles that have been replicated worldwide. We pioneered research programs and establishing safety oversight principles suitable for investigator-initiated studies. We tried to be nimble to adapt to the challenging granting climate, creating economies of scale and hybrid funding models. We have engaged in international collaboration for 2 decades. The proverbial whole is so much greater than the sum of the parts!

Our most important achievement in 2014 was to obtain funding through the Community Development Program grant from CIHR. With the funding that we will receive over the next 5 years, we plan to expand our core infrastructure, enhance our first-class career mentorship further, and create renewed and new dedicated partnerships. These steps are sorely needed to accelerate improvements in the process and outcomes of critical illness, given our aging society and increasing demands on the healthcare system — starting in our own backyard and 'going global'.
Dr. Eikelboom's Canada Research Chair in Cardiovascular Medicine supports an ongoing program of research into the mechanisms of variable response to antithrombotic therapies, optimization of antithrombotic therapies for the prevention and treatment of thromboembolic disease and the relationship between bleeding, blood transfusion and risk of subsequent non-fatal and fatal cardiovascular events.

Premature graft failure following coronary artery bypass graft surgery is an independent predictor of myocardial infarction and death. The only proven effective treatment for prevention of premature graft failure is aspirin, but, despite its routine use, 40% of patients have at least one blocked graft within one year of surgery. An increased rate of platelet production following surgery resulting in a high proportion of uninhibited active platelets in the circulation during aspirin's 24 hour dosing interval may explain why aspirin fails to protect some patients against premature graft failure. Research supported by Dr. Eikelboom's Canada Research Chair has demonstrated that more frequent aspirin dosing provides more complete and sustained inhibition of platelets than once daily aspirin during the first week after surgery. Ongoing research is exploring whether more frequent aspirin dosing during this period will result in better protection against the risk of premature graft failure.

For the first time in more than 60 years, we have alternative oral anticoagulants to vitamin K antagonists. The major advantage of these non-vitamin K antagonist oral anticoagulants is that they offer effective, safe and more convenient treatment because they do not require routine laboratory monitoring. Concern about variable response to the non-vitamin K antagonist oral anticoagulants has prompted calls for routine monitoring and dose adjustment. Dr. Eikelboom's Canada Research Chair supports a series of studies to investigate variable response to dabigatran, rivaroxaban and apixaban. Preliminary results published during 2014 have shown that dose adjustment based on clinical characteristics provides predictable anticoagulant effects and that a single measurement of blood level does not reliably classify patients according to their expected response. These findings suggest that routine monitoring is unlikely to be beneficial unless serial testing is performed and even then it is unclear if that dose adjustment based on the results will yield benefit.

A new initiative that has been funded through peer-reviewed granting agencies during the past year will help to support a study examining predictors of bleeding and subsequent cardiovascular outcomes in patients with gastrointestinal bleeding. This study complements an ongoing international randomized controlled trial examining the effect of transfusing the freshest available compared with standard issue red blood cells on mortality in more than 30,000 hospitalized patients.

Dr. Eikelboom's program of research is funded by Canadian Institutes for Health Research, Heart and Stroke Foundation of Canada, Hamilton Health Sciences and industry and supports the education and training of Canadian and international fellows.
Inflammation is a key component of most airway diseases such as asthma and COPD. The CRC-funded research program established methods to measure airway inflammation in sputum. The methods helped identify the types of inflammation and are now leading to identifying specific therapies for the different types of inflammation. This has now been recommended by Canadian and international guidelines to treat asthma, chronic cough and COPD. The research also demonstrated that such treatment strategies are more effective and less expensive than the currently available strategies.

The program has identified new targets for drug development. Currently, we are exploring proteomic and genomic technologies to identify new biomarkers in sputum. The Chair, originally awarded in 2005 was renewed for five years in 2010.

The major impact of the research in the past year can be summarized as follows: 20 peer-reviewed publications in major scientific journals; 30 lectures at major universities or scientific societies in Europe, Asia and North America including the Canadian Thoracic Society, the American Thoracic Society, the American Academy of Allergy and Immunology, American College of Chest Physicians, and the European Academy of Allergy and Immunology Annual conferences and induction into the exclusive Collegium Internationale Allergologicum, and research grants of over one million dollars. This includes investigator initiated grants of $300,000 from pharmaceutical industry and a CIHR grant in collaboration with Dr Mark Loeb. A number of new research initiatives are being developed for potential funding through the Canadian Respiratory Research Network and the CIHR Strategy for Patient oriented Research Program. The research program has also trained 2 post-doctoral fellows, 1 masters student and 4 undergraduate students. The research program has supported a regional interdisciplinary severe asthma program that is serving the local LHIN and the province.

Research Impact

Gregory Steinberg, professor of medicine, was named to the Royal Society of Canada’s College of New Scholars, a national group that recognizes the country’s emerging academic leaders.

Obesity is strongly associated with non-alcoholic fatty liver disease (NAFLD), which has an estimated prevalence of ~25% in Canada. NAFLD is a major cause of both type 2 diabetes and hepatic cellular carcinoma. More than 2 million Canadians currently have type 2 diabetes, and hepatic cellular carcinoma is predicted to become the third most common cause of cancer related death. Despite the important clinical ramifications of NAFLD, the causes of NAFLD are not fully understood and lifestyle interventions involving weight loss are currently the only therapy.

In December 2013, we published findings (Fullerton, Galic et al. Nature Medicine 19(12):1649-54, 2013) which described the molecular pathway controlling the development of NAFLD. By generating and then characterizing mice with single nucleotide polymorphisms we identified that AMP-activated protein kinase (AMPK) regulation of liver fatty acid synthesis was vital for preventing NAFLD and pre-diabetes. These data indicate that finding new therapies that target the AMPK pathway may be vital for preventing and treating NAFLD. These studies also debunked well-established dogma that NAFLD was a consequence of liver insulin resistance and pre-diabetes.

Metformin is one of the most-widely prescribed medications in the world and is currently consumed as first-line therapy by over 120 million individuals with diabetes. Remarkably, despite its widespread use the mechanism by which metformin is chronically able to lower blood sugar were not well understood. We found that chronic metformin treatment (at clinical doses) reduces blood glucose by decreasing liver fatty acid synthesis and NAFLD through activation of the AMPK pathway. These pre-clinical studies establish that the use of metformin may prevent and help reverse the development of NAFLD. In addition, by understanding the molecular mechanisms by which metformin lowers blood sugar we hope to rationally design combination therapy that will optimize glucose control in individuals with type 2 diabetes. Lastly, these data suggest that metformin may be effective for preventing hepatic cellular carcinoma.

Infra-red imaging specifically and non-invasively detects brown adipose tissue thermogenesis (Crane et al. Molecular Metabolism 2014)

Representative thermal images of wild-type mice (Ucp1+/+) and mice that lack the thermogenic adipose tissue protein UCP1 (Ucp1−/−), illustrating robust changes in surface heat in response to brown adipose tissue stimulation. Mice were injected with saline or the β3-adrenergic agonist CL-316,243 to stimulate brown adipose tissue. This work demonstrates a simple, yet precise, non-invasive method to quantify the activity of brown adipose tissue in mice.

Steinberg lab
The human body is host to numerous complex microbial communities that comprise the human microbiome. These microbes and their dynamic interactions within these communities, and with the host, play critical roles in human development and health. Although considered primarily beneficial, bacteria within the microbiome also contribute to disease. The human microbiome is a reservoir of potential pathogens and antibiotic resistance genes, specific interactions of seemingly benign commensal organisms with pathogens in polymicrobial infections can enhance virulence, and changes in the composition of the microbiome (dysbiosis) contribute to chronic inflammatory disease. His research is supported by operating grants from CIHR, Cystic Fibrosis Canada and Crohn’s and Colitis Foundation of Canada. Dr. Surette has a highly collaborative research program leading a CIHR Emerging Team grant on the human microbiome and is a participant in eight other collaborative research grants. Dr. Surette’s research is focused on the microbiome of the gastrointestinal and respiratory tracts with specific projects investigating cystic fibrosis respiratory infections, asthma, allergy, pneumonia, sepsis, ulcerative colitis, rheumatoid arthritis and irritable bowel syndrome. Additional research is focused in characterizing the development of the microbiome in infants and changes that occur with aging. Dr. Surette is co-director of the McMaster Genome Center. He is chair of the Research Subcommittee of Cystic Fibrosis Canada and a member of the Steering Committee of the Genetics, Environment, Microbial (GEM) Project supported by the Crohn’s and Colitis Foundation of Canada.

While it is often stated that most of the microbiome is not accessible by laboratory culturing methods, the Surette lab has challenged this assumption and developed methods that allow for comprehensive culturing of the human microbiome with a focus on the respiratory and gastrointestinal tracts. This allows a greater depth of analysis in metagenomic studies and more importantly opportunities to explore the full therapeutic and pathogenic potential of the microbiome to modulate the host. A culture based approach is used to complement high throughput molecular methods for understanding respiratory infections particularly in cystic fibrosis and asthma, and has been effective in guiding therapeutic interventions in patients.

Dr. Eva Szabo started as an assistant professor in 2013 in McMaster University’s Departments of Medicine & Biochemistry and Biomedical Sciences. Dr. Szabo’s research laboratory is located within the Stem Cell and Cancer Research Institute (SCC-RI), a shared facility that allows utilization of cutting-edge technologies along with vast human stem cell expertise to ask questions about how human stem cell are regulated in a healthy and disease setting. Dr. Szabo’s prior research demonstrated the role of Wnt calcium signaling in human hematopoietic and adipocyte development from embryonic ESCs and induced pluripotent stem cells (iPSCs). Furthermore, her work on human iPSCs provided pioneering work for the field of directed reprogramming from human skin cells by demonstrating that fibroblasts can be directly converted to functional blood and neural progenitor and brown/beige adipocytes bypassing the need for a pluripotent state. Her current research focuses on understanding how human stem cells and metabolic shifts regulate development of obesity and downstream complication of type 2 diabetes (T2D) and peripheral neuropathy. Accordingly, Dr. Szabo’s program has three main avenues of research that are supported by CIHR, 2014 Maud Menten New Principal Investigator Prize (clinical stream), OCRiT (Global Leadership Round in Genomics & Life Sciences grant (GL2i) and Canada Foundation for Innovation (CFI) fund, which include:

1. modeling human adipocyte development in a disease and healthy setting by utilizing stem cells, where her group show that there are clear differences between the stem cells of healthy versus obese patients in regards to insulin responses and glucose and fatty acid processing;
2. development of phenotypic drug-screening platforms that allow identification of novel compounds that decrease lipid accumulation and/or increase energy expenditure in adipocytes;
3. to understand the underlying molecular mechanism that cause obesity and T2D-induced neuropathy and to identify drugs that can prevent damage or allow regeneration of peripheral neurons following metabolic insult.

Therefore, the overarching aim of Dr. Szabo’s research is to understand the development of obesity and downstream complications, such as T2D, as well as to establish alternative treatment strategies towards alleviating the burden of obesity and improve patients’ quality of life.
Dr. Verdu has had a long-standing interest in the pathophysiology of inflammatory and functional gastrointestinal disorders, with particular focus on host-microbial and dietary interactions. Her studies have identified gluten as a critical antigen in the development of enteropathy and insulitis in genetically predisposed mice. Dr. Verdu’s laboratory has demonstrated that gut dysfunction can be triggered by gluten in mice, even in the absence of enteropathy, leading to the concept of non-celiac gluten sensitivity. Gluten sensitivity may constitute one possible cause of irritable bowel syndrome that could be treated by a gluten-free diet or adjuvant therapies to gluten exclusion. Clinical trials are currently being conducted to functionally characterize these patients and identify mechanisms of gluten sensitivity in humans. Dr. Verdu’s lab is also working on the preclinical development of several adjuvant therapies to a gluten-free diet including permeability modulators (currently in phase III), and a novel gluten-binding polymer (currently in phase I) and immunomodulatory and barrier protecting molecules such as elafin (preclinical phase). The CRC in Inflammation, Microbiota and Nutrition has enabled Dr. Verdu to manage and direct McMaster’s large Avenir Gnotobiotic Unit (AGU). Her studies have shown that colonization of axenic mice with stable human-derived microbial ecosystems may prevent inflammatory and autoimmune conditions of the gastrointestinal tract. Humanized mouse models using gnotobiotic colonization with gut bacteria from patients with inflammatory bowel disease have identified proinflammatory pathways involved in the generation of colonic inflammation. During 2013-14, we investigated the role of elafin, an anti protease with immune modulatory and barrier enhancing effects, in celiac disease (CD). We found that elafin expression in the small intestinal epithelium was lower in patients with active CD compared to control patients. In vitro, elafin significantly slowed the kinetics of the deamidation of the 33-mer peptide to its more immunogenic form. Treatment of gluten-sensitive mice with elafin delivered by the L. lactis vector normalized inflammation, improved permeability and maintained ZO-1 expression. We proposed that decreased elafin expression in small intestine of patients with active CD, the reduction of 33-mer peptide deamidation by elafin, coupled to the barrier enhancing and anti-inflammatory effects observed in gluten sensitive mice, suggest this molecule may have pathophysiological and therapeutic importance in gluten-related disorders. The data was published in Am J Gastroenterol 2014 May;109(5):748-56 and has received considerable media attention. We investigated environmental factors that can influence risk to develop celiac disease (CD) in a genetically predisposed host. To investigate a potential influence of the microbiota on host responses to gluten, germ-free, clean specific pathogen free (SPF) and conventional SPF NOD/08 mice were sensitized with a gliadin digest and challenged with gluten. Clean SPF mice harbour a defined microbiota absent of opportunistic pathogens and Proteobacteria. Conventional SPF mice harbour a complex microbiota with opportunistic pathogens, including Helicobacter and Escherichia. Mice colonized with a clean SPF microbiota had attenuated responses to gluten compared to germ-free mice that developed increased intraepithelial lymphocyte (IEL) cytotoxicity. Clean SPF mice also had less severe gluten-induced responses compared to conventional SPF mice. Supplementation of clean SPF mice with E. coli EN5 CA15, isolated from CD patients, enhanced gluten-induced pathology. Finally, we disrupted the colonization process of conventional SPF mice using pernatal antibiotic therapy which resulted in increased Proteobacteria, and more severe gluten-induced pathology in adulthood. The results provide evidence that distinct changes in the microbiota can either ameliorate or worsen responses to gluten in genetically susceptible hosts. The data is currently in second revision in Mucosal Immunology for consideration for publication.

In addition to these projects, we participated in multiple collaborative studies some of which have been published and others have been submitted for consideration for publication.

SPF mice harbour a defined microbiota absent of opportunistic pathogens and Proteobacteria. Conventional SPF mice harbour a complex microbiota with opportunistic pathogens, including Helicobacter and Escherichia. Mice colonized with a clean SPF microbiota had attenuated responses to gluten compared to germ-free mice that developed increased intraepithelial lymphocyte (IEL) cytotoxicity. Clean SPF mice also had less severe gluten-induced responses compared to conventional SPF mice. Supplementation of clean SPF mice with E. coli EN5 CA15, isolated from CD patients, enhanced gluten-induced pathology. Finally, we disrupted the colonization process of conventional SPF mice using pernatal antibiotic therapy which resulted in increased Proteobacteria, and more severe gluten-induced pathology in adulthood. The results provide evidence that distinct changes in the microbiota can either ameliorate or worsen responses to gluten in genetically susceptible hosts. The data is currently in second revision in Mucosal Immunology for consideration for publication.

In addition to these projects, we participated in multiple collaborative studies some of which have been published and others have been submitted for consideration for publication.

CANADA RESEARCH CHAIR IN INFLAMMATION, MICROBIOTA AND NUTRITION

Dr. Elena F. Verdu

Dr. Verdu has held this Tier 1 chair since 2001; the chair was renewed in 2008 and again in 2015. This chair provides salary support for Dr. Verdu and has been used to fund his research program. In addition to the chair, the Canada Foundation for Innovation has twice provided funds to purchase state-of-the-art equipment that is used by Dr. Verdu and other investigators at the Thrombosis and Atherosclerosis Research Institute. Focusing on thrombosis, this chair prompted the successful Canadian Institutes of Health Research Team Grant in Venous Thromboembolism that was awarded to Dr. Verdu and the McMaster Thromboembolism Group in 2006. Providing $4.2 million over seven years, the Team Grant funded new initiatives in thrombosis research that span the spectrum from basic science, to clinical trials, to research in knowledge translation, and created new collaborations at Queen’s University, McGill University, the University of Toronto and the University of Michigan. These interactions have facilitated successful grant-in-aid applications to the Canadian Institutes of Health Research, the National Institutes of Health and the Heart and Stroke Foundation.