Annual Meeting of the North American Section
of the International Academy of Cardiovascular Sciences

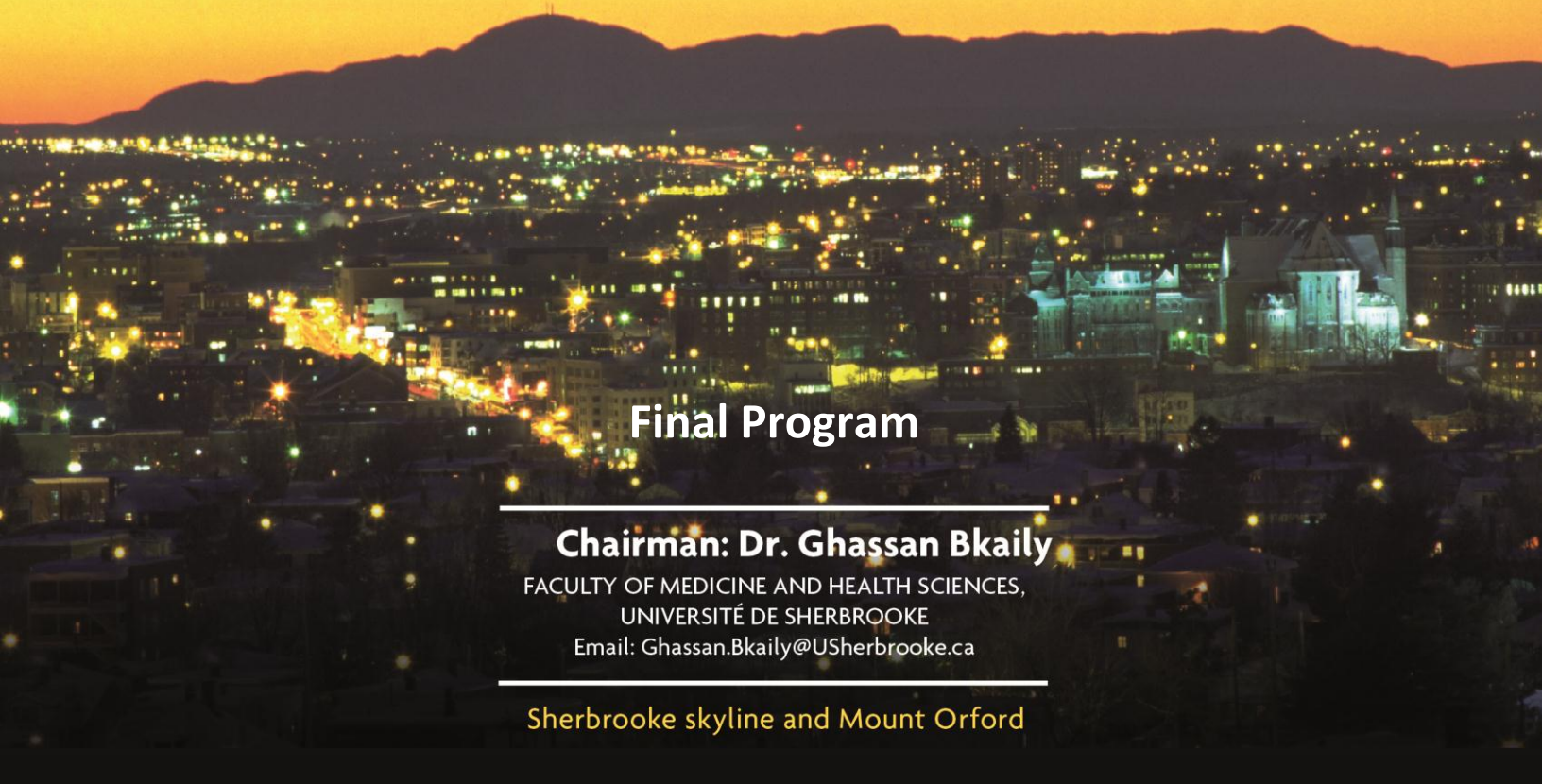
4th Cardiovascular Forum for Promoting Centres of Excellence and Young Investigators

September 22 - 24, 2016
Sherbrooke, Quebec, Canada

UNIVERSITÉ DE SHERBROOKE

4TH ANNUAL MEETING IACS NORTH AMERICAN SECTION 2016
International Academy of Cardiovascular Sciences
Education • 1996 • Research

4th Cardiovascular Forum for Promoting Centres of Excellence and Young Investigators
FACULTY OF MEDICINE AND HEALTH SCIENCES



Final Program

Chairman: Dr. Ghassan Bkaily
FACULTY OF MEDICINE AND HEALTH SCIENCES,
UNIVERSITÉ DE SHERBROOKE
Email: Ghassan.Bkaily@USherbrooke.ca

Sherbrooke skyline and Mount Orford

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Message from the Forum Chair

Dear Colleagues,

On behalf of the local organizing committee, I would like to welcome you all to the 4th Cardiovascular Forum for Promoting Centers of Excellence and Young Investigators.

This meeting is very special in that it coincides with Dr. Naranjan S. Dhalla's 80th birthday and the 20th anniversary of the International Academy of Cardiovascular Sciences. I would like to acknowledge the remarkable contribution of Dr. Dhalla in promoting cardiovascular research worldwide and in his pursuit of innovation and excellence. His relentlessness in promoting cardiovascular research is a model to be followed by all young scientists.

The meeting brings together international para-clinical and clinical scientists with first class young investigators in cardiovascular research. Cardiovascular research ensures the future of new knowledge and gets us closer each day to better treatments for cardiovascular diseases. Therefore, the conference puts particular emphasis on enriching the experience of our young scientists by exposing them to cutting-edge science from the bench to the bedside. At the same time, this meeting will give them center stage to present their latest discoveries and further expand their knowledge, through their discussions with senior scientists in the field, in order to better understand and treat patients for a better healthy growth and aging for people all around the world.

I would like to thank all our generous sponsors and supporters which made our meeting possible.

We welcome you to beautiful Sherbrooke and the Eastern townships of Quebec and we hope that you get the best scientific forum. Please enjoy our French-Canadian hospitality.

Bienvenue au Québec, bienvenue and welcome to Canada.

Dr. Ghassan Bkaily

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www.heartacademy.org

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Dr. Naranjan S. Dhalla
Executive Director,
IACS

Dr. Grant Pierce
President,
North Amercian
Section

UNIVERSITÉ DE SHERBROOKE

Message from President Luce Samoisette

Bienvenue!

Our university community is very pleased to welcome you to this wonderful forum of the International Academy of Cardiovascular Sciences.

In helping to bring together these talented and experienced researchers and those who follow in their footsteps in cardiovascular research, we are extremely proud to be promoting scientific dialogue and exchanges among passionate people. It goes without saying that pooling your efforts, sharing your work and developing your expertise are a source of hope for your patients and for our entire society.

The Université de Sherbrooke is located in the heart of one of Quebec's three major research hubs. Known for its spirit of innovation, the Université de Sherbrooke is a key partner of senior and regional governments in the promotion of economic, cultural, and social development. It has a well-earned reputation thanks to the strong growth in its research activities in recent years, its successes in technology transfers, as well as its initiatives in entrepreneurship and open innovation in collaboration with industry and social milieus.

Our Faculty of Medicine and Health Sciences (FMSS) stands out as an exceptional place to work or study. From the very outset, the FMSS brought together a faculty of medicine and university hospital at one location. Today, the FMSS offers programs of study in Sherbrooke, Longueuil and Saguenay in Quebec, and in the Moncton area of New Brunswick, tied to the needs of the communities where it has a presence. Despite this remarkable growth, the Faculty has been able to maintain a degree of flexibility that promotes innovation in both teaching and research. The FMSS hosts more than 140 researchers whose research impact attracts growing numbers of students to its graduate programs.

I would like to offer my thanks and congratulations to the team from our Department of Anatomy and Cellular Biology for organizing this far-reaching event, which has helped, through its dynamism and dedication, to put the Université de Sherbrooke and the Ville de Sherbrooke on the world research map.

Dans le cadre enchanteur de notre magnifique région des Cantons-de-l'Est, nous vous souhaitons des rencontres inspirantes ainsi que des échanges fructueux qui donneront lieu à des collaborations encore plus prometteuses!

Prof. Luce Samoisette
President
Université de Sherbrooke

UNIVERSITÉ DE SHERBROOKE

Faculty of Medicine and Health Sciences

Message from Dean Pierre Cossette

The Faculty of Medicine and Health Sciences of University of Sherbrooke is proud to host the 4th Cardiovascular Forum of the International Academy of Cardiovascular Sciences. This fall semester has a special meaning for us, because 50 years ago our Faculty welcomed its first medical class of 26 students. Since 1966, over 15 000 students have graduated from our Faculty.

Many people worked relentlessly in making this Faculty a place where knowledge is shared while critical thinking and creativity are encouraged for the well being of our society. Over the years, our establishment was able to develop its research capacity and more than a 100 academic programs. Our researchers are at the center of our mission and it is with great pleasure that we support their networking and involvement in the organisation of this scientific meeting. We are delighted that Sherbrooke has become a scientific destination for this important Forum.

It is an honour for us to welcome you here. Furthermore, fall in Quebec's Eastern Townships is definitively the place to be for its colored scenery at this time of year. I sincerely hope that you will enjoy your stay and will benefit on a professional and a personal level from these few days spent with us.

Dr. Pierre Cossette
Dean, Faculty of Medicine and Health Sciences
Université de Sherbrooke

Office of the Mayor of Sherbrooke

It is a great pleasure to welcome you to Sherbrooke for this major scientific conference.

As a university city and a city of knowledge, Sherbrooke frequently has the opportunity to host major scientific gatherings, to welcome scientists and researchers from across the country and around the world working in such specialized fields.

We are indeed privileged by the presence of a university hub (le Pôle universitaire de Sherbrooke) that is very active on the international stage, and of which the Université de Sherbrooke is a part.

This educational institution plays a key role in training a new generation that is exceptionally well prepared to take on the challenges of the future, and it is a tremendous asset to Sherbrooke and the Eastern Townships community.

With these few words, I sincerely hope that you will enjoy your stay in Sherbrooke and our picturesque region, and that you will have an opportunity to discover some of the many attractions and activities that our city has to offer during this beautiful time of the year.

Once again let me say that it is a genuine honour to welcome you and thank you for having chosen Sherbrooke as the site for this major conference.

Bernard Sévigny
Mayor of Sherbrooke

4TH CARDIOVASCULAR FORUM FOR PROMOTING CENTERS OF EXCELLENCE AND YOUNG INVESTIGATORS

Sherbrooke, Quebec, Canada – September 22-24, 2016

Local Organizing Committee

Chair: Ghassan Bkaily, Professor, Faculty of Medicine, Université de Sherbrooke
Honorary Chair: Naranjan S. Dhalla, Distinguished Professor, University of Manitoba

André Carpentier, Professor, Department of Medicine
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Pedro D'Orléans-Juste, Professor, Department of Pharmacology
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Paul Farand, Professor, Department of Medicine
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Danielle Jacques, Professor, Department of Anatomy and Cell Biology
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Michel Nguyen, Professor, Department of Medicine
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Serge Lepage, Professor, Department of Medicine
Faculty of Medicine and Health Sciences, Université de Sherbrooke
Lucien Bergeron Jr., Scientific coordinator, CMDO, CRCHUS, Université de Sherbrooke

International Organization Committee:

Devendra Agrawal, Omaha
Madhu Anand-Srivastava, Montreal
Peter Backx, Toronto
Patrick Burgon, Ottawa
Mohamed Chahine, Quebec
Michael Czubryt, Winnipeg
James Gilchrist, Winnipeg
Fernand Gobeil Jr., Sherbrooke
Susan Howlett, Halifax
Morris Karmazyn, London, Ontario
Abdelouahed Khalil, Sherbrooke
Madhu Khullar, Chandigarh
Frantisek Kolar, Prague
Ren-Ke Li, Toronto
Vincenzo Lionetti, Pisa
Gary Lopaschuk, Edmonton
Sheldon Magder, Montreal
Nilanjana Maulik, Farmington
Dennis McNamara, New Orleans
Martin Morad, Charleston
Moni Nader, Riyadh
Bohuslav Ostadal, Prague
Sampath Parthasarathy, Orlando
Grant Pierce, Winnipeg
Tanya Ravingerova, Bratislava
Domenico Regoli, Ferrara
Delfin Rodriguez-Leyva, Winnipeg
Stephen Schaffer, Mobile
Adel Schwertani, Montréal
Pawan K. Singal, Winnipeg
Dinender Singla, Orlando
Jan Slezak, Bratislava
Ashok Srivastava, Montreal
Saadeh M. Suleiman, Bristol
Balwant Tuana, Ottawa
Jeffrey Wigle, Winnipeg
Carin Wittnich, Toronto

Secretariat:

Mrs. Mélanie Roy, Department of Anatomy and Cell Biology, Faculty of Medicine and Health Sciences Université de Sherbrooke, Sherbrooke, QC, Canada J1H 5N4, Email: Melanie.Roy9@USherbrooke.ca, Tel: 1-819-821-8000, ext. 70147.

General Information

Forum Hotel

Delta (Future Marriott) Sherbrooke Hotel and Conference Centre
2685 King Street West
Sherbrooke, QC J1L 1C1
Tel: 1-819-822-1989

The hotel is located on the main street in Sherbrooke and is within a 10-minute walking distance from the shopping mall. The hotel reservation website is http://cwp.marriott.com/yscdr/iacsmedsherb. The special meeting rate for room reservation is available until August 29, 2016 (Group code: MS1MS1A). Please make your hotel reservation as soon as possible in order to benefit from the low price of the meeting rate. After this date, we do not guarantee a room or a special rate. Please note that before the meeting date, Delta will be changed into Marriott.

Shuttle Information

A free shuttle from the Montreal airport to the conference site (Delta Sherbrooke Hotel) will be available for all delegates on Thursday September 22 and back to Montreal airport on Sunday September 25. Three shuttles will be available with departure from Montreal airport at 1:00 PM, 3:30 PM and 5:30 PM. The delegates will be asked to indicate their arrival time as well as the airline and flight number. Departure from the conference site to the Montreal airport will take place at 7:00 AM and 9:00 AM on September 25. It is also encouraged to rent a car at the Montreal airport. Driving is very easy and pleasant to the Eastern Townships (approximately a 90-minute drive from the airport, please see details in the preliminary program). Parking at the hotel is free of charge. City bus passes for delegates will also be provided free of charge by the City of Sherbrooke.

Registration

Registration fee includes all meals (except Friday evening free time dinner) and entertainment as well as complementary shuttle from and to Montreal airport. A French breakfast will be available for all participants at 7:00 AM at the Foyer hall (facing the conference rooms).

Early Bird Registration Start-Deadline and Fee

May 25, 2016 extended to July 25, 2016
Students and postdoctoral fellows: 450 $ US includes hospitality
Regular attendee: 550 $ US includes hospitality

Late Registration Fee

Following July 25, 2016
Students and postdoctoral fellows: 550 $ US includes hospitality
Regular attendee: 650 $ US includes hospitality

Registration Desk (Foyer Lower Level)
September 22: 4:00 PM to 7:00 PM
September 23: 8:00 AM to 5:00 PM
September 24: 8:00 AM to 4:00 PM

Abstract Submission Process & Deadlines

- Abstract submission starts on May 25, 2016. The submission deadline for abstracts to be published and presented at the forum has been extended to July 25, 2016.
- To submit your abstract without registration, please click here https://www.fourwav.es/view/280/registration/, select Submit abstract and register later and then click Join conference. Then go to Submission section in the menu.
- Abstracts can also be submitted after registration as part of the online registration process.
- If you have a problem submitting your abstract online, please send it to danielle.jacques@usherbrooke.ca, and we will take care of it.
- If your abstract is not fully prepared, we still encourage you to register. There is no abstract submission fee. However, in order to be eligible for award nomination and competitions, it is mandatory to register at the same time of abstract submission.

Formatting requirements for abstracts are as follows:

- Abstract title section (maximum 25 words);
- For the Authors' names and Affiliations section, please follow the indications in the submission section;
- Abstract section :
    - Abstract length limit is 250 words and do not include the title, authors' names and affiliations.
    - Rich text formatting and special characters are permitted.
    - The abstract body [structured or free form styles are both permitted].
    - Acknowledgements *Please do not include author titles or credentials in the abstract itself.

Regular Invited Speaker Oral Presentations
Speakers are allocated 20 minutes for presentations and questions.

Award Competition Posters (Grant Pierce, James Willerson, Gary Lopaschuk and Roberto Bolli awards)
The aim of this new category of presentation is to increase the contact and exchange between young investigators, young faculty and senior scientists. For the award competitions, the speakers are allocated 20 minutes for a PowerPoint presentation including the question period. The poster part of this new category is to prepare a poster (based on the oral presntation) that will be exposed, as other

poster categories, throughout the duration of the conference. The poster will be part of the combined poster session but will not be judged or be eligible for the Morris Karmazyn and Margaret Moffat Poster awards.

Poster Oration

The aim of this new category of presentation is to increase the contact and exchange between young investigators, young faculty and senior scientists and make the speakers eligible for the poster awards. For the oration part, the speakers are allocated 20 minutes for a PowerPoint presentation including the question period. The poster part of this new category is to prepare a poster (based on the oration) that will be exposed, as other poster categories, throughout the duration of the conference. The poster will be judged during the combined poster session for the Morris Karmazyn and Margaret Moffat Poster awards.

Poster Oral Presentations

This category of poster presentation gives the opportunity for the participant to give a 5 minutes PowerPoint presentation without a question period. This permits the participant and more particularly young investigators to improve their skill as orators. Participants should also prepare a poster that will be exposed throughout the duration of the conference .The poster will be judged during the combined poster session for the Morris Karmazyn and Margaret Moffat Poster awards.

Poster Only

Presenters should prepare a poster that will be exposed throughout the duration of the conference and be part of the combined poster session. The poster will be judged during the combined poster session for the Morris Karmazyn and Margaret Moffat Poster awards.

Speaker Ready Room

Please provide your talk on a USB memory stick to the Speaker Ready Room (Lac Orford Room) at least 30 minutes prior to your session. You may make minor edits and review your talk at this time; however, access to the Ready Room PC is limited. Our staff will transfer your talk to the computer in your presentation room.

Please note that no personal computers are allowed for presenting.

Poster Presentations

Posters (4' x 4' or 121 cm x 121 cm) should be mounted on the appropriate numbered poster boards before 9:00 AM on Friday, September 23. The posters should be displayed until 5:00 PM on Saturday, September 24. We are not responsible for any posters remaining in the Poster Room after 5:00 PM on Saturday, September 24.

Exhibition Displays (Foyer Lower Level Hall)

Hospitality

All invited guests and registered participants have access to the following events:

1. French Breakfast
2. Coffee Breaks
3. Lunches
4. Reception
5. Dinners/Entertainment

Lecture Rooms

Three lecture rooms (Grand Salon Sherbrooke A, B and C) located on the main level below the lobby will be used simultaneously for the symposium sessions. Each symposium session room will be identified. A floor plan inside the back cover of the Program Book can be used for orientation purposes.

Websites

www.fourwav.es/IACSNA2016 (registration)
www.heartacademy.org
http://www.destinationsherbrooke.com/en/conventions-and-meetings/organization-committee-support/event-promotion/international-academy-of-cardiovascular-sciences-iacs
http://www.destinationsherbrooke.com/en/conventions-and-meetings/organization-committee-support/event-promotion/iacs-offers

Conference Administration:

Conference Coordinator

Dr. Lucien Bergeron Jr.; Email: lucien.junior.bergeron@rrcmdo.ca; Tel.: 819-346-1110, ext. 12703

Chair of Hospitality, Accommodations and Audiovisual

Dr. Johny Al-Khoury; Email: Johny.Al.Khoury@USherbrooke.ca; Cell: 819-212-1005
Mr. Marc Chamoun; Email: Marc.Chamoun@USherbrooke.ca; Cell: 819-919-0950

Registration Team

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Ms. Maram Alshahrani; Email: Maram.Alshahrani@USherbrooke.ca; Cell: 873-200-4794

Publication of the Proceedings of the Meeting in the Canadian Journal of Physiology and Pharmacology: Invited editors, Dr. Danielle Jacques (Sherbrooke) and Dr. Morris Karmazyn (London, Ontario).

Original papers:

Abstracts of all oral and poster presentations will be published in a special issue of the Canadian Journal of Physiology and Pharmacology (CJPP). All attendees are welcome to submit a full original manuscript based on the material presented at the conference. The submitted papers for original work, following the peer review process, will be published in the first special issue.

Review papers with 25% original data:

A second issue will be devoted to review manuscripts from invited speakers including some original unpublished data (25%).

Note: It is highly recommended to prepare your manuscript before the meeting. We guarantee a two week review period which accelerates the publication of the proceedings. Hence, be ready to submit your original article and your review paper.

Awards

Dr. Grant Pierce Travel Awards
Based on the excellence of their abstract, ten graduate students and trainees will receive travel awards in the amount of $500 provided by IACS North American Section President Dr. Grant Pierce. In order to be eligible for this award, it is mandatory to register at the same time of abstract submission.

Young Investigator Awards
As is the tradition, several competitions will take place during our meeting to promote young investigators. This includes:
Four oral sessions:
The Grant Pierce Young Investigator Award Competition in Cardiovascular Science for Graduate Students. Four speakers will be selected for presentation. The abstracts of other applicants will be considered for Poster Oral Award Session.
The James Willerson Young Investigator Award Competition in Cardiovascular Medicine: Residents and Postdoctoral Fellows. Four speakers will be selected for presentation. The abstracts of other applicants will be considered for Poster Oral Award Session.
The Gary Lopaschuk Young Faculty Award Competition in Cardiovascular Biomedical Sciences. Four faculty members (within 10 years of appointment) will be selected for presentation. The other applicants will be considered for oral presentation.
The Roberto Bolli Young Faculty Award Competition in Cardiovascular Medicine. Four faculty members (within 10 years of appointment) will be selected for presentation. The other applicants will be considered for oral presentation.

Selected nominees will receive complimentary accommodation and/or registration and hospitality in addition to a plaque and a major cash prize. We therefore kindly invite you to nominate an outstanding junior faculty member and/or a trainee to be considered for these various awards. The information required for these nominations includes the name of the nominee, contact information, a two-page CV and an abstract (250 words maximum).

Established Investigator Awards
Furthermore, Established Investigator Awards will be given to four worthy recipients from the list of invited speakers, who will be chosen for the Howard Morgan Award, Norman Alpert Award, Naranjan Dhalla Award and a Special Award. Each awardee will receive a major cash prize and a plaque.

Two poster oral sessions
The Margaret P. Moffat Award in Biomedical Sciences
Two individuals from this Poster Oral Presentation Session will be selected. Each awardee will receive $500 and a certificate.
The Morris Karmazyn Award in Translational Medicine.
Two individuals from this Poster Oral Presentation Session will be selected. Each awardee will receive $500 and a certificate.

Two poster sessions

The Margaret P. Moffat Award in Biomedical Sciences.

Two individuals from this Poster Session will be selected. Each awardee will receive $500 and a certificate.

The Morris Karmazyn Award in Translational Medicine.

Two individuals from this Poster Session will be selected. Each awardee will receive $500 and a certificate.

FINAL SYMPOSIUM PROGRAM

THURSDAY, SEPTEMBER 22

1:00 to 7:00 PM *Registration (Foyer Lower Level)*

6:00 to 6:40 PM **Welcome Remarks**
Room: Salon Sherbrooke B
Chair: ***Dr. Ghassan Bkaily,*** Chair of the Annual Meeting of IACS-North American Section, Sherbrooke, Quebec

- **Dr. Pierre Cossette**, Dean, Faculty of Medicine and Health Sciences, Université de Sherbrooke representing the president of Université de Sherbrooke, **Prof. Luce Samoisette**
- **Mr. Bernard Sevigny** , Mayor of the City of Sherbrooke represented by **Mr. Robert Pouliot**, Acting Mayor
- **Dr. Grant Pierce,** President, IACS North American Section
- **Dr. Danielle Jacques**, Secretary, 4th Cardiovascular Forum, Sherbrooke, Canada: Program Highlights

Accreditation for Medical Fellows: 45 min (Conference 45 min)
Learning Objectives - At the end of this conference, participating medical fellows will be able to: 1) Identify last advances in the cardiovascular field and 2) Apply recent knowledge in daily practice.

6:40 to 7:40 PM ***Inaugural Address Dedicated to Dr. Naranjan S. Dhalla on his 80th Birthday***
Room: Salon Sherbrooke B
Chair: ***Dr. Grant Pierce,*** Professor and President of IACS – North American Section
University of Manitoba, Winnipeg, Canada

6:40 to 6:55 PM **Dr. Bohuslav Ostadal:** Presentation of Dr. Naranjan S. Dhalla: 20 years from the foundation of the International Academy of Cardiovascular Sciences.

6:55 to 7:40 PM **Dr. Andras Varro:** An address and conference in the honour of Dr. Naranjan S. Dhalla

7:40 to 9:30 PM ***Meet and Greet Reception***
Room: Foyer Lower Level

FRIDAY, SEPTEMBER 23

8:00 to 9:00 AM *Registration (Foyer Lower Level)*

8:00 to 9:00 AM *French Breakfast (Foyer Lower Level) and Networking*

9:00 to 10:20 AM ***1. Thematic Symposium: Cardiovascular Dysfunction in Chronic Diabetes***

Room: Salon Sherbrooke A
Chairs: Dr. Gary Lopaschuk and Dr. Andre Carpentier

9:00 AM to 9:20 AM **Madhu Khullar:** Role of fibrosis associated transcription factors in hyperglycemia induced endothelial to mesenchymal transition (EndMT).

9:20 AM to 9:40 AM **Andre Carpentier:** Molecular imaging of fatty acids to assess cardiometabolic interventions.

9:40 AM to 10:00 AM **Vincenzo Lionetti:** Maspin-enriched exosomes released from sulforaphane-treated fibroblasts prevents hypertrophy in angiotensin II induced HL-1 cardiomyocytes.

10:00 AM to 10:20 AM **Gary Lopaschuk:** Acetylation control of cardiac fatty acid β-Oxidation and energy metabolism in obesity and diabetes.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives: At the end of this program, participants will be able to: 1) Review the link between diabetes and cardiovascular problems and 2) Describe available treatments and their mechanisms.

2. Dr. Grant Pierce Young Investigator Award Competition in Cardiovascular Science: Graduate Students

Room: Salon Sherbrooke B
Chairs and Judges: Dr. Adriana Adameova and Dr. Stephen Schaffer
Judges: Dr. Dinender Singla, Dr. Danielle Jacques and Dr. Mohamed Chahine

9:00 AM to 9:20 AM: **Heidi Shoulders:** BMP-7 treatment induces monocyte to M2 macrophage differentiation and improves blood flow velocity in atherosclerosis.

9:20 AM to 9:40 AM: **Stephanie LeBlanc:** Carotid versus coronary atherosclerosis burdens in acute compared to chronic symptomatic coronary artery disease.

9:40 AM to 10:00 AM: **Jonathan Weldrick:** Identification and characterization of a miRNA cohort initiated transitional program that controls cell cycle arrest of the perinatal heart.

10:00 AM to 10:20 AM: **Jaroslav Hrdlicka:** Effect of moderate exercise training and continuous normobaric hypoxia on postinfarction heart failure in rats.

3. Gary Lopaschuk Young Faculty Award Competition in Cardiovascular Biomedical Sciences

Room: Salon Sherbrooke C

Chairs and Judges: Dr. Jan Slezak and Dr. Saadeh Suleiman

Judges: Dr. Sheldon Magder, Dr. Ashok Srivastava and Dr. Ren-Ke Li

9:00 AM to 9:20 AM: **Jin O-Uchi:** Post-translational modification of mitochondrial Ca^{2+} uniporter mediates mitochondrial Ca^{2+} overload and cell death in the heart.

9:20 AM to 9:40 AM: **Levon Avedanian:** Role of nuclear T-tubules in human vascular smooth muscle cell function and disease.

9:40 AM to 10:00 AM: **Sanjiv Dhingra:** Prostaglandin E2 mediated secretion of chemokines prevents rejection of implanted allogeneic mesenchymal stem cells and restores post-infarction ventricular function

10:00 AM to 10:20 AM: **Hao Wang:** Cardiomyocyte-specific deletion of the G-protein-couled estrogen receptor (GPER) leads to left ventricular dysfunction and adverse remodeling: a sex-specific gene profiling.

10:20 to 10:40 AM *Coffee Break (Foyer Lower Level)*

10:40 AM to 12:00 PM

4. Thematic Symposium: Arrhythmias and Heart Failure in Hereditary Cardiovascular Diseases

Room: Salon Sherbrooke A

Chairs: Dr. Ghassan Bkaily and Dr. Naranjan S. Dhalla

10:40 AM to 11:10 AM: **Martin Morad:** Pacemaker mechanisms in human iPSC-derived cardiomyocytes: A step closer to tissue-based pacemakers.

11:10 AM to 11:35 AM: **Ghassan Bkaily:** Sodium-hydrogen exchanger blocker for the treatment of heart and vascular failures in Becker and Duchenne muscular dystrophy.

11:35 AM to 12:00 PM: **Ren-Ke Li:** Conductive polymer hydrogel improves electrical conduction velocity in the injured heart.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Cite hereditary arrhythmic cardiovascular diseases and 2) Propose adequate investigations.

5. Thematic Symposium: Age and Cardiovascular Disease

Room: Salon Sherbrooke B

Chairs: Dr. Frantisek Kolar and Dr. Dinender Singla

10:40 AM to 11:00 AM: **Susan Howlett:** Impact of age and frailty on cardiac function in a mouse model.

11:00 AM to 11:20 AM: **Carin Wittnich:** Does young age really put the heart at risk?

11:20 AM to 11:40 AM: **Bohuslav Ostadal:** Impact of perinatal hypoxia on cardiac tolerance to ischemia/reperfusion injury in adults.

11:40 AM to 12:00 AM: **Mohamed Chahine:** Induced pluripotent stem cells derived cardiomyocytes.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able

to: 1) Recognize the importance of aging in cardiovascular disease and 2) Choose therapeutic targets.

6. James Willerson Young Investigator Award Competition in Cardiovascular Medicine: Residents and Postdoctoral Fellows

Room: Salon Sherbrooke C

Chairs and Judges: Dr. Michel Nguyen and Dr. Tanya Ravingerova

Judges: Dr. Madhu Anand-Srivastava, Dr. James Gilchrist and Dr. Fernand Gobeil

10:40 AM to 11:00 AM:	**Martin Lewis:** Age related differences in the cardiac proteome of proteins involved in signalling and response to Ischaemia.
11:00 AM to 11:20 AM:	**Alice E. Kane:** Influence of ACE inhibitors on frailty and cardiac function in middle-aged female C57BL/6 mice**.**
11:20 AM to 11:40 AM:	**Ayelen Rodriguez-Portelles:** Use of high resolution Doppler ultrasound for the diagnosis of endothelial dysfunction in young adults exposed to tobacco.
11:40 AM to 12:00 PM:	**Denis Blondin:** Does TAG/FA cycling contribute significantly to cold-induced thermogenesis? Determining the metabolic fate of oversupplied fatty acids during a mild cold exposure in humans.

12:00 to 1:10 PM *Lunch Break (Lac Memphrémagog Hall, 2nd Floor)*

12:00 to 1:10 PM **IACS-North America Executive Committee Business Meeting (President: Dr. Grant Pierce)**
Room: Lac Orford

1:10 to 2:30 PM ***7. Thematic Symposium: Oxidants and Anti-oxidants in Heart Health and Diseases***

Room: Salon Sherbrooke A

Chairs: Dr. Martin Morad and Dr. James Gilchrist

1:10 PM to 1:30 PM: **Jan Slezak:** Radiation induced heart disease and amelioration of X ray toxic effect with selected substances and H2.

1:30 PM to 1:50 PM: **Stephen Schaffer:** Taurine deficient heart exhibits mitochondrial oxidative stress, apoptosis and impaired ATP generation.

1:50 PM to 2:10 PM: **Frantisek Kolar:** Cardioprotection conferred by chronic hypoxia combined with regular exercise in rats.

2:10 PM to 2:30 PM: **Madhu Anand-Srivastava:** Nitric oxide and regulation of blood pressure.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Examine the role of oxidative events in cardiovascular problems and 2) Identify ways to modify the oxidative balance.

8. Dennis B. McNamara Symposium: Vascular Disease and Atherosclerosis

Room: Salon Sherbrooke B

Chairs: Dr. Dennis B. McNamara and Dr. Vincenzo Lionetti

1:10 PM to 1:35 PM: **Sampath Parthasarathy:** Novel ways to lipid load cells to study macrophage functions.

1:35 PM to 2:00 PM: **Ashok Srivastava:** Stromal interaction molecule-1 and orai1 channel mediate angiotensin-II-induced expression of early growth response protein-1 (Egr-1) in vascular smooth muscle cells.

2:00 PM to 2:25 PM: **Dinender Singla:** Increased anti-inflammatory M2 macrophages prevents cardiac diseases.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Review the last knowledge about atherosclerosis development and 2) Describe new therapeutic targets.

9. Thematic Symposium: Nutrition and Prevention of Cardiovascular Disease

Room: Salon Sherbrooke C

Chairs: Dr. Delfin Rodriguez-Leyva and Dr. Morris Karmazyn

1:10 PM to 1:30 PM: **Devendra Agrawal:** Epicardial adipose tissue and vitamin D in the immunomodulation of coronary artery disease.

1:30 PM to 1:50 PM: **Karmin O:** Nutritional regulation of non-alcoholic fatty liver disease (NAFLD) and its impact on cardiovascular disease (CVD).

1:50 PM to 2:10 PM: **Morris Karmazyn:** Ginseng for the treatment of cardiovascular disease.

2:10 PM to 2:30 PM: **Grant N. Pierce:** The unique technical challenges that natural health products pose as a therapeutic intervention in a clinical trial.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Recognize the role of nutrition in the development of cardiovascular problems and 2) Sketch a nutrition plan for prevention of cardiovascular diseases.

2:30 to 2:50 PM *Coffee Break (Foyer Lower Level)*

2:50 to 4:10 PM ***10. Kern Wildenthal Symposium: New Approaches for the Therapy of Cardiac Diseases: Novel Devices***

Room: Salon Sherbrooke A

Chairs: Dr. Paul Farand and Dr. Devendra Agrawal

2:50 PM to 3:10 PM: **Tanya Ravingerova:** Novel "conditioning" approaches to mend the broken heart: a potential for clinical application?

3:10 PM to 3:30 PM: **Serge Lepage:** Roles of B-type Natriuretic Peptide (BNP) in decision making and follow up of heart failure patients.

3:30 PM to 3:50 PM: **Delfin Rodriguez-Leyva:** Wearable devices in modern cardiology.

3:50 PM to 4:10 PM: **Michel Nguyen:** High-sensitivity troponin for diagnosis, prognosis stratification and definition of myocardial infarction.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Discuss

new approaches for therapies for cardiac diseases and 2) Identify the more promising avenues of therapeutic approaches.

11. Karl Weber Symposium: Molecular Basis for Heart Disease

Room: Salon Sherbrooke B

Chairs: Dr. Pawan Singal and Dr. Nilanjana Maulik

2:50 PM to 3:10 PM:	**Adriana Adameova:** Necroptosis in diseased heart.
3:10 PM to 3:30 PM:	**Patrick Burgon:** Deletion of muscle-enriched A-type lamin-interacting protein (MLIP) leads to cardiac hyperactivation of Akt/mTOR and impaired cardiac adaptation.
3:30 PM to 3:50 PM:	**Nilanjana Maulik:** New molecular targets of VEGF signaling in cardiovascular disease.
3:50 PM to 4:10 PM:	**Jeffrey Wigle:** Transcriptional control of cardiac fibroblast activation.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Identify certain molecular problems associated with cardiovascular problems and 2) Describe available therapeutic targets.

12. Stephen Vatner Young Investigator Orations in Cardiovascular Medicine: Graduate Students

Room: Salon Sherbrooke C

Chairs: Dr. Madhu Anand-Srivastava and Dr. Susan Howlett

2:50 PM to 3:10 PM:	**Jennifer Major:** Deregulation of the E2F pathway in post-natal myocardium impacts metabolic control and dilated cardiomyopathy.
3:10 PM to 3:30 PM:	**Thierry Chénard:** Modulation of human adipocyte metabolism for the prevention of type 2 diabetes.
3:30 PM to 3:50 PM:	**Lionel Tastet:** Impact of higher ApoB/ApoA-1 ratio on the hemodynamic progression of aortic stenosis - Results from the PROGRESSA study.
3:50 PM to 4:10 PM:	**Laetitia Guillemette:** Prenatal exposure to gestational and pre-gestational diabetes impairs cardiac relaxation in youth with type 2 diabetes.

4:10 to 6:00 PM **Wine and Cheese Combined Poster Session**
Room: Foyer Lower Level

All posters will be judged in a single session. Cheese, crackers and beverages will be available during this session.

13. Translational Medicine (Morris Karmazyn Award)
Judges: Nilanjana Maulik, Tanya Ravingerova, Balwant Tuana, Jeffrey Wigle, Antoinette Blackman.

Accreditation for Medical Fellows: 110 min (interactions between participants). Learning Objectives - At the end of this program, participants will be able to: 1) Identify optimal ways for successful collaborations, 2) Integrate collaborative initiatives in faculty priorities and 3) Illustrate beneficial collaborative avenues between paraclinical and clinical scientists.

14. Biomedical Sciences (Margaret P. Moffat Award)
Judges: Patrick Burgon, Michael Czubryt, Abdelouahed Khalil, Madhu Khullar, Adel Schwertani.

Accreditation for Medical Fellows: 110 min (interactions between participants). Learning Objectives - At the end of this program, participants will be able to: 1) Implement successful approaches in practice and 2) Criticize the current knowledge about genesis of cardiovascular diseases.

6:00 PM *Free Evening for Networking*

SATURDAY, SEPTEMBER 24

8:00 AM to 4:00 PM *Registration (Foyer Lower Level)*

8:00 to 9:00 AM *Breakfast and Networking*

9:00 to 10:20 AM ***15. Management of Cardiovascular Diseases***

Room: Salon Sherbrooke A
Chairs: Dr. Serge Lepage and Dr. Sheldon Magder

9:00 AM to 9:20 AM: **Domenico Regoli:** Rational bases of modern therapies for cardiovascular diseases.

9:20 AM to 9:40 AM: **Fernand Gobeil:** Criteria for the choice of ACE-inhibitors as drugs in the treatment of cardiovascular diseases.

9:40 AM to 10:00 AM: **Adel Schwertani:** Role of lipoprotein A in aortic valve calcification

10:00 AM to 10:20 AM: **Paul Farand:** Economic evaluation of heart failure management by specialized clinics in Quebec.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) List the different types of management of cardiovascular diseases and 2) Use the more efficient approaches in treatments.

16. Otto F. Schanne Young Investigator Orations

Room: Salon Sherbrooke B

Chairs: Dr. Danielle Jacques and Dr. Balwant Tuana

9:00 AM to 9:20 AM: **Glen Lester Sequiera:** Differential passage of mesenchymal stem cells introduces variability in their immunoprivilege – an "Omic"-al perspective.

9:20 AM to 9:40 AM: **Louisane Desbiens:** Cardiovascular pharmacology of vasoactive factors revisited in the non-anesthetized mouse.

9:40 AM to 10:00 AM: **Christophe Noll:** Seven-day overfeeding decreases myocardial dietary fatty acid partitioning in healthy subjects.

10:00 AM to 10:20 AM: **Johny Al-Khoury:** Angiotensin II receptors modulation of calcium homeostasis in human vascular endothelial cells.

Accreditation for Medical Fellows: 80 min (Conference 60 min– Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Discuss recent developments in the field of stem cells and dietary fatty acids 2) Identify patients who could benefit from these therapies.

17. Eric Olson Symposium: Cardiovascular Health and Disease

Room: Salon Sherbrooke C
Chairs: Dr. Bohuslav Ostadal and Dr. Andras Varro

9:00 AM to 9:20 AM: **Naranjan S. Dhalla:** Role of protease activation in cardiac dysfunction due to ischemia-reperfusion injury to the heart.

9:20 AM to 9:40 AM: **Saadeh Suleiman:** Cardiopulmonary bypass & cardiac injury during coronary surgery.

9:40 AM to 10:00 AM: **Peter Backx:** The role of exercise in atrial fibrillation.

10:00 AM to 10:20 AM: **Antoinette Blackman:** Clinical importance of grade I left ventricular diastolic dysfunction.

10:20 to 10:40 AM *Coffee Break (Foyer Lower Level)*

10:40 AM to 12:00 PM ***18. Roberto Bolli Young Faculty Award Competition in Cardiovascular Medicine***

Room: Salon Sherbrooke A
Chairs and Judges: Dr. Ren-Ke Li and Dr. Bohuslav Ostadal
Judges: Dr. Vincenzo Lionetti, Dr. Frantisek Kolar and Dr. Sampath Parthasarathy

10:40 AM to 11:00 AM: **Samarjit Das:** Role of miR-181 family in the heart: A tale of two intracellular compartments.

11:00 AM to 11:20 AM: **Moni Nader:** Striatin is a novel risk gene for human dilated cardiomyopathy that regulates cardiomyocyte response to adrenergic stimuli.

11:20 AM to 11:40 AM: **Sarah Cohen:** Exposure to low-dose ionizing radiation from cardiac procedures and risk of malignancy in adults with congenital heart disease.

11:40 AM to 12:00 PM: **Delfin Rodriguez-Leyva:** Serious new concerns for patients with peripheral arterial disease.

19. Jawahar Mehta Symposium: New Approaches in Management of Cardiovascular Diseases

Room: Salon Sherbrooke B

Chairs: Dr. Madhu Khullar and Dr. Patrick Burgon

10:40 AM to 11:00 AM: **Pawan Singal:** Role of toll-like receptors in innate signaling in heart failure.

11:00 AM to 11:20 AM: **Balwant Tuana:** New mechanisms leading to DCM.

11:20 AM to 11:40 AM: **Abdelouahed Khalil:** HDL functionality, or HDL quality versus HDL quantity.

11:40 AM to 12:00 PM: **Michael Czubryt:** Novel approaches to treating cardiac fibrosis.

Accreditation for Medical Fellows: 80 min (Conference 60 min– Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Criticize certain new approaches in management of cardiovascular diseases and 2) Select the more appropriate treatment.

20. Thematic Symposium: Endothelium and Cardiovascular Disease

Room: Salon Sherbrooke C

Chairs: Dr. Antoinette Blackman and Dr. Peter Backx

10:40 AM to 11:05AM: **Sheldon Magder:** Cross talk between the heart and peripheral circulation: potential role of cardiac and peripheral endothelium.

11:05 AM to 11:30 AM: **Pedro D'Orleans-Juste:** New indications for endothelin antagonists in cardiovascular diseases.

11:30 AM to 12:00 PM: **Danielle Jacques:** Crosstalk between the NPY and ET-1 systems in human endocardial endothelial cells.

Accreditation for Medical Fellows: 80 min (Conference 60 min– Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Review the role of endothelial dysfunction in pathogenesis of cardiovascular diseases and 2) Describe new therapeutic approaches targeting the endothelium.

12:00 to 1:10 PM *Lunch Break (Lac Memphrémagog Hall, 2nd Floor)*

12:00 to 1:10 PM **IACS Executive Committee Business Meeting (Presidents: Dr. Naranjan S. Dhalla and Dr. Bohuslav Ostadal).**
Room: Lac Orford

1:10 to 2:30 PM ***21. Bruce McManus Young Investigator Orations: Graduate Students, Biomedical Sciences***

Room: Salon Sherbrooke A
Chairs: Dr. Jeffrey Wigle and Dr. Carin Wittnich

1:10 PM to 1:30 PM: **Gauri Akolkar:** Cardioprotective role of Vitamin C in Doxorubicin-induced cardiomyopathy via mitigation of oxidative/nitrosative stress.

1:30 PM to 1:50 PM: **Estelle Rolande Simo Cheyou:** Increased levels of intracellular cAMP attenuate Angiotensin-II-induced expression of the early growth response protein-1 (Egr-1) in vascular smooth muscle cells (VSMC).

1:50 PM to 2:10 PM: **Taha Rehmani:** The cardiac specific isoform of tail anchored membrane protein SLMAP1 enhances GLUT4 levels by directing endosomal size and recycling.

2:10 PM to 2:30 PM: **Thomas Hedley:** Involvement of heat shock protein-60 in vascular smooth muscle cell proliferation through a modulation of nuclear protein Import.

22. Nick Sperelakis Postdoctoral Young Investigator Orations

Room: Salon Sherbrooke B
Chairs: Dr. Michael Czubryt and Dr. Pedro D'Orleans-Juste

1:10 PM to 1:30 PM: **Chian Ju Jong:** Leptin-induced cardiomyocyte hypertrophy is associated with enhanced mitochondrial fission.

1:30 PM to 1:50 PM: **Fawaz Bardooli:** Early changes in circulating miRNA 133a are indicative of cardiac remodelling after 3

	months in patients presenting with acute ST elevation myocardial infarction.
1:50 PM to 2:10 PM:	**Kanta Chechi:** Characterization of the oxidative potential and its relationship with the adipose tissue physiology in fat depots surrounding human heart.
2:10 PM to 2:30 PM:	**Balazs Ordog**: MiRP2 rescues cardiac slow delayed rectifier K^+ channel (IKs) function in long QT syndrome 5.

Accreditation for Medical Fellows: 80 min (Conference 60 min – Questions 20 min). Learning Objectives - At the end of this program, participants will be able to: 1) Identify the different markers of heart disease.

23. Combined Poster Oral Presentations: Translational Medicine (Morris Karmazyn Award) and Biomedical Sciences (Margaret P. Moffat Award)

Room: Salon Sherbrooke C

Chairs: Dr. Moni Nader and Dr. Fernand Gobeil

1:10 PM to 1:15 PM	**Ayelen Rodriguez-Portelles:** Effect of daily dietary supplementation with flaxseed on exercise capacity and cardiac electrical activity in patients with peripheral arterial disease.
1:15 PM to 1:20 PM	**Sara Almajdoob:** Resveratrol attenuates hyperproliferation of vascular smooth muscle cells from spontaneously hypertensive rats: Role of ROS and ROS-mediated signalling.
1:20 PM to 1:25 PM	**Aleksandra Stamenkovic:** Oxidized phosphatidylcholine (OxPC) induces cell death through the ferroptotic pathway in isolated adult cardiomyocytes.
1:25 PM to 1:30 PM	**Maxime Gagnon:** Potentiation of bradykinin B2R activity by heterologous expression of a newly-identified protein coded by an alternative ORF of the B2R mRNA.

1:30 PM to 1:35 PM	**Marek Zalesak:** Molecular hydrogen facilitates beneficial effect of hypoxic postconditioning on ischemia-reperfusion injury.
1:35 PM to 1:40 PM	**Branislav Kura:** Modulation of cardiac specific miRNAs in irradiated rat myocardium after treatment with selected drugs.
1:40 PM to 1:45 PM	**Raghu Sundaresan Nagalingam:** Scleraxis is a direct transcriptional regulator of MMP-2 gene expression.
1:45 PM to 1:50 PM	**Jan Neckar:** Selective replacement of mitochondrial DNA reduces the sensitivity of mitochondrial permeability transition pore to opening in chronically hypoxic hearts of spontaneously hypertensive rats.
1:50 PM to 1:55 PM	**Olivier Kamtchueng Simo:** Paraoxonase 1 promotes cholesterol efflux from macrophages by stimulating the PPARγ-LXRα-ABCA1 pathway.

Accreditation for Medical Fellows: 80 min (interactions between participants). Learning Objectives - At the end of this program, participants will be able to: 1) Identify optimal ways for successful collaborations, 2) Integrate collaborative initiatives in faculty priorities and 3) Illustrate beneficial collaborative avenues between paraclinical and clinical scientists.

2:35 to 6:00 PM *Free Time*

6:00 to 10:00 PM ***IACS Awards Banquet and Closing Reception***

Room: Salon Sherbrooke B-C
Chair: Dr. Ghassan Bkaily

6:00 PM to 6:20 PM:	**Closing Remarks** **Dr. Pierre Cossette**, Dean, Faculty of Medicine and Health Sciences, Université de Sherbrooke **Mr. Bernard Sevigny**, Mayor of the City of Sherbrooke
6:20 PM to 6:40 PM:	**Announcement and Presentation of IACS Awards**

Chairs: Dr. Grant Pierce, Dr. Gary Lopaschuk and Dr. Frantisek Kolar

- Grant Pierce Travel Awards
- Grant Pierce Young Investigator Award (Graduate Students)
- James Willerson Young Investigator Award (Residents and Postdoctoral Fellows)
- Roberto Bolli Young Faculty Award (Cardiovascular Medicine)
- Gary Lopaschuk Young Faculty Award (Cardiovascular Biomedical Sciences)

Chairs: Dr. Morris Karmazyn, Dr. Danielle Jacques and Dr. Jan Slezak

- Margaret Moffat Poster Award (Biomedical Sciences)
- Morris Karmazyn Poster Award (Translational Medicine)

Chairs: Dr. Naranjan S. Dhalla, Dr. Bohuslav Ostadal and Dr. Andras Varro

- Howard Morgan, Norman Alpert and Naranjan S. Dhalla Awards (to recognize distinguished scientists)
- IACS Lifetime Achievement Award
- IACS Distinguished Leadership Award

6:40 PM to 6:45 PM Vote of Thanks by **Dr. Ghassan Bkaily**

6:45 PM to 6:50 PM Introduction of 2017 Annual Meeting of the IACS-North American Section by Dr. Dinender Singla

6:50 PM to 7:20 PM Cultural Program (Organizer: Dr. Lucien Bergeron Jr.)

7:20 PM to 10:00 PM Banquet Dinner

Travel Awardees

Gauri Akolkar (Winnipeg, Canada)
Sara Almajdoob (Montreal, Canada)
Fawaz Bardooli (Bristol, United Kingdom)
Vijayan Elimban (Winnipeg, Canada)
Thomas Hedley (Winnipeg, Canada)
Branislav Kura (Bratislava, Slovakia)
Jennifer Major (Ottawa, Canada)
Balasz Ordog (Szeged, Hungary)
Lionel Tastet (Quebec City, Canada)
Marek Zalesak (Bratislava, Slovakia)

Special Thanks

Dr. Lucien Bergeron Jr., CMDO, CRCHUS
Dr. Johny Al-Khoury, University of Sherbrooke
Mrs. Helene Beaudet, Audiovisual, Faculty of Medicine, University of Sherbrooke
Mrs. Anick Bouchard, Audiovisual, Faculty of Medicine, University of Sherbrooke
Mrs. Amelie Bourque, Delta Sherbrooke
Mrs. Catherine Arguin, Delta Sherbrooke
Mrs. Julie Nadeau, Destination Sherbrooke
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Poster Only

P1 - Alpha Linolenic Acid Decreases the Production of Pro-Apototic Oxidized Phospholipids over time in Cardiomyocytes After Ischemia/Reperfusion.
Riya Ganguly, Devin Hasanally, Thane G. Maddaford, Rakesh Chaudhary, Grant N. Pierce, Amir Ravadi (Winnipeg, Canada)

P2 - Role of Endothelin-1 and its receptors, ET_A and ET_B in the survival of human vascular endothelial cells.
Rana Semaan, Mariane Mikhail, Huda Alajlan, Yanick Simon, Danielle Jacques, Ghassan Bkaily (Sherbrooke, Canada)

P3 - Diastolic dysfunction after estrogen loss is linked to cardiac chymase in WKY but not SHR rats.
Hao Wang, Jacqueline da Silva, Daniele Gabriel-Costa, Safaraz Ahmad, Xuming Sun, Marina Lin, Roberto T. Sudo, Jasmina Varagic, Carlos Ferrario, Gisele-Zapata Sudo, Leanne Groban (Winston-Salem, USA and Rio de Janeiro, Brazil)

P4 - Early effect of bariatric surgery (Sleeve gastrectomy (SG) vs Biliopancreatic Diversion with Duodenal Switch (BPD-DS) on postprandial fatty acid inter-organ partitioning.
Anne-Marie Carreau, Christophe Noll, Frédérique Frisch, Lucie Bouffard, Serge Phoenix, Brigitte Guérin, Denis Richard, Laurent Biertho, Éric Turcotte, André Tchernof, André Carpentier (Serbrooke, Canada and Quebec City, Canada)

P5 - Effect of extra virgin olive oil supplementation on the quality of HDL in health subjects.
Roua Walha, Hicham Berrougui, Olivier Kamtchueng Simo, Abdelouahed Khalil (Sherbrooke, Canada)

P6 - Effects of ovarian estrogens on local RAS activity in cardiomyocytes and non-cardiomyocytes.
Xuming Sun, Sarfaraz Ahmad, Marina Lin, Gisele Zapata Sudo, Cheping Cheng, Jasmina Varagic, Carlos Ferrario, Hao Wang, Leanne Groban (Winston-Salem, USA and Rio de Janeiro, Brazil)

P7 - Increased Blood Flow by CO2-enriched Water Bath Treatment in Diabetic Rats with Peripheral Ischemia.
Vijayan Elimban, Yan-Jun Xu, Hideo Kumamoto, Hiroaki Hasebe, Naranjan S. Dhalla (Tokyo, Japan and New York, USA)

P8 - Integrin alpha-M beta-2 (MAC-1, CD11b/CD18) interacts with SIRPalpha (MFR) during macrophage fusion.
Marketa Hlavackova , Nathaly P. Podolnikova, YiFei Wu, Ivan S. Yermolenko, Tatiana P. Ugarova (Prague, Czech Republic and Tucson, USA)

P9A - High blood pressure awareness campaign in Winnipeg.

Stephanie PB Caligiuri, J. Alejandro Austria, S. Brian Penner, Grant N. Pierce (Winnipeg, Canada)

P9B - ET_A and ET_B receptors contribute to neuropeptide Y-induced secretion of endothelin-1 in right but not left human ventricular endocardial endothelial cells.
Cynthia Jubinville-Leblanc, Dima Abdel-Samad, Alexandre Normand, Ghassan Bkaily, Danielle Jacques (Sherbrooke, Canada)

P9C - Effects of TNF-α on cytosolic and nuclear calcium in cells of the human cardiovascular system
Marc Chamoun, Wassim Najibeddine, Alexandre Normand, Rana Semaan, Danielle Jacques, Ghassan Bkaily (Sherbrooke, Canada)

Poster Oral Presentation

P10 - Effect of daily dietary supplementation with flaxseed on exercise capacity and cardiac electrical activity in patients with peripheral arterial disease.
Ayelen Rodriguez Portelles, Delfin Rodriguez-Leyva, Randy Guzman, Grant N. Pierce (Winnipeg, Canada)

P11 - Modulation of cardiac specific miRNAs in irradiated rat myocardium after treatment with selected drugs.
Branislav Kura, Chang Yin, Rakesh C. Kukreja, Jan Slezak (Bratislava, Slovakia and Richmond, USA)

P12 - Molecular hydrogen facilitates beneficial effect of hypoxic postconditioning on ischemia-reperfusion injury.
Marek Zálešák, Ján Graban, Branislav Kura, Dezider Pancza, Tatiana Ravingerová, Ján Slezák (Bratislava, Slovakia)

P13 - Oxidized phosphatidylcholine (OxPC) induces cell death through the ferroptotic pathway in isolated adult cardiomyocytes.
Aleksandra Stamenkovic, Kimberley A. O'Hara, David C. Nelson, Grant N. Pierce, Amir Ravandi (Winnipeg, Canada)

P14 - Paraoxonase 1 promotes cholesterol efflux from macrophages by stimulating the PPARγ-LXRα-ABCA1 pathway.
Olivier kamtchueng Simo, Souade Ikhlef, Hicham Berrougui, Abdelouahed Khalil (Sherbrooke, Canada)

P15 - Resveratrol Attenuates Hyperproliferation of Vascular Smooth Muscle Cells from Spontaneously Hypertensive Rats: Role of ROS and ROS-Mediated Signalling.
Sara Almajdoob, Ekhtear Hussain, Yuan Li, Madhu B. Anand-Srivastava (Montreal, Canada)

P16 - Scleraxis is a direct transcriptional regulator of MMP-2 gene expression.
Raghu Sundaresan Nagalingam, Hamza A. Safi, Rushita A. Bagchi, Michael P. Czubryt (Winnipeg, Canada)

P17 - Potentiation of bradykinin B2R activity by heterologous expression of a newly-identified protein coded by an alternative ORF of the B2R mRNA.
Maxime Gagnon, Martin Savard, Xavier Roucou, Fernand Gobeil (Sherbrooke, Canada)

P18 - Selective replacement of mitochondrial DNA reduces the sensitivity of mitochondrial permeability transition pore to opening in chronically hypoxic hearts of spontaneously hypertensive rats.
Jan Neckář, Anna Chytilová, Zdeněk Drahota, Petra Alánová, Michal Pravenec, František Kolář (Prague, Czech Republic)

Poster Orations

P19 - Angiotensin II receptors modulation of calcium homeostasis in human vascular endothelial cells.
Johny Al-Khoury, Maud Kamal, Maram Alshahrani, Danielle Jacques, Ghassan Bkaily (Sherbrooke, Canada)

P20 - Cardioprotective role of Vitamin C in Doxorubicin-induced cardiomyopathy via mitigation of oxidative/nitrosative stress.
Gauri Akolkar, Danielle da Silva Dias, Prathapan Ayyappan, Katia de Angelis, Davinder Jassal, Pawan Singal (Winnipeg, Canada and Sau Paulo, Brazil)

P21 - Characterization of the oxidative potential and its relationship with the adipose tissue physiology in fat depots surrounding human heart.
Kanta Chechi, Pierre Voisine, Patrick Mathieu, Denis Richard (Quebec City, Canada)

P22 - Deregulation of the E2F Pathway In Post-Natal Myocardium Impacts Metabolic Control and Dilated Cardiomyopathy.
Jennifer Major, Aaraf Dewan, Maysoon Salih, Balwant S. Tuana (Ottawa, Canada)

P23 - Early changes in circulating miRNA 133a are indicative of cardiac remodelling after 3 months in patients presenting with acute ST elevation myocardial infarction.
Fawaz Bardooli, M-Saadeh Suleiman, Elisa McAlindon, Ben Littlejohns, Chiara Bucciarelli-Ducci, Andreas Baumbach (Bristol, United Kingdom)

P24 - Impact of Higher ApoB/ApoA-1 Ratio on the Hemodynamic Progression of Aortic Stenosis - Results from the PROGRESSA Study.
Lionel Tastet, Romain Capoulade, Mylène Shen, Marie-Annick Clavel, Nancy Côté, Patrick Mathieu, Marie Arsenault, Élisabeth Bédard, Jonathan Beaudoin, Mathieu Bernier, Jean-G. Dumesnil, Jean-Pierre Després, Philippe Pibarot (Quebec City, Canada)

P25 - Increased levels of intracellular cAMP attenuate Angiotensin-II-induced expression of the early growth response protein-1 (Egr-1) in vascular smooth muscle cells (VSMC).
Estelle Rolande Simo Cheyou, Viktoria Youreva, Ashok Srivastava (Montreal, Canada)

P26 - Involvement of Heat Shock Protein-60 in Vascular Smooth Muscle Cell Proliferation through a Modulation of Nuclear Protein Import.
Thomas E. Hedley, Justin F. Deniset, Markéta Hlaváčková, Elena Dibrov, Mirna N. Chahine, Grant N. Pierce (Winnipeg, Canada)

P27 - Leptin-induced cardiomyocyte hypertrophy is associated with enhanced mitochondrial fission.
Chian Ju Jong, Justin Yeung, Emily Tseung, Morris Karmazyn (London, Ontario, Canada)

P28 - MiRP2 rescues cardiac slow delayed rectifier K+ channel (IKs) function in long QT syndrome 5.
Balázs Ördög, Teodóra Hartai, Szilvia Déri, László Virág, Norbert Jost, István Baczkó, András Varró (Szeged, Hungary)

P29 - Modulation of human adipocyte metabolism for the prevention of type 2 diabetes.
Thierry Chénard, André Carpentier, André Tchernof, Rafael Najmanovich (Sherbrooke, Canada and Quebec City, Canada)

P30 - Prenatal Exposure to Gestational and Pre-Gestational Diabetes Impairs Cardiac Relaxation in Youth with Type 2 Diabetes.
Laetitia Guillemette, Allison Dart, Vernon W. Dolinsky, Davinder Jassal, Elizabeth Sellers, Todd Duhamel, Jonathan McGavock (Winnipeg, Canada)

P31 - The cardiac specific isoform of tail anchored membrane protein SLMAP1 enhances GLUT4 levels by directing endosomal size and recycling.
T. Rehmani, A. Dewan, M. Salih, C. Triggle, H. Ding, BS Tuana (Ottawa, Canada and Doha, Quatar)

P32 - Cardiovascular pharmacology of vasoactive factors revisited in the non-anesthetized mouse.
Louisane Desbiens, Modou LO, Hanène Touil, Martin Houde, Joseph Mauban, Withrow Gil Weir, Pedro D'Orléans-Juste (Sherbrooke, Canada and Baltimore, USA)

P33 - Differential passage of mesenchymal stem cells introduces variability in their immunoprivilege – an "Omic"-al perspective.

Glen Lester Sequiera, Niketa Sareen, Vikram Sharma, Ejlal Abu El-Rub, Saravanan Sekaran, Rakesh Chaudhary, Meenal Moudgil, Subir Roy Chowdhury, Paul Fernyhough, Amir Ravandi, Sanjiv Dhingra (Winnipeg, Canada and Plymouth, United Kingdom)

P34 - Seven-day overfeeding decreases myocardial dietary fatty acid partitioning in healthy subjects.
Christophe Noll, Margaret Kunach, Frédérique Frisch, Lucie Bouffard, Stéphanie Dubreuil, Serge Phoenix, Stephen CUNNANE, Brigitte Guérin, Eric Turcotte, Martine Laville, André Carpentier (Sherbrooke, Quebec and Lyon, France)

Award Competition Posters

P35 - Age related differences in the Cardiac Proteome of proteins involved in Signalling and Response to Ischaemia.
Martin Lewis, M.S Suleiman (Bristol, United Kingdom)

P36 - BMP-7 Treatment Induces Monocyte to M2 Macrophage Differentiation and Improves Blood Flow Velocity in Atherosclerosis.
Heidi Shoulders, Dinender Singla (Florida, USA)

P37 - Cardiomyocyte-specific deletion of the G protein-coupled estrogen receptor (GPER) leads to left ventricular dysfunction and adverse remodeling: a sex-specific gene profiling analysis.
Hao Wang, Xuming Sun, Jeff Chou, Marina Lin, Gisele Zapata-Sudo, Carlos M Ferrario, Leanne Groban (Winston-Salem, USA and Rio de Janeiro, Brazil)

P38 - Carotid versus coronary atherosclerosis burdens in acute compared to chronic symptomatic coronary artery disease.
Stéphanie LeBlanc, Karine Bibeau, Valérie Lévesque, Béatrice Deschênes-Saint-Pierre, Philippe Pibarot, Jean-Pierre Després, Eric Larose (Quebec City, Canada)

P39 - Does TAG/FA cycling contribute significantly to cold-induced thermogenesis? Determining the metabolic fate of oversupplied fatty acids during a mild cold exposure in humans.
Denis Blondin, Frédérique Frisch, Serge Phoenix, Brigitte Guérin, Éric E. Turcotte, Denis Richard, François Haman, André Carpentier (Sherbrooke, Canada and Ottawa, Canada)

P40 - Effect of moderate exercise training and continuous normobaric hypoxia on postinfarction heart failure in rats.

Jaroslav Hrdlicka, Jan Neckář, Frantisek Papousek, Jana Vasinova, Petra Alanova, Frantisek Kolar (Prague, Czech Republic)

P41 - Exposure to low-dose ionizing radiation from cardiac procedures and risk of malignancy in adults with congenital heart disease.
Sarah Cohen, Aihua Liu, Michelle Gurvitz, Eva Goossens, Liming Guo, Judith Therrien, Ariane Marelli (Montreal, Canada and Boston, USA and Flanders, Belgium)

P42 - Identification and characterization of a miRNA cohort initiated transitional program that controls cell cycle arrest of the perinatal heart.
Jonathan Weldrick, Patrick G. Burgon (Ottawa, Canada)

P43 - Influence of ACE inhibitors on frailty and cardiac function in middle-aged female C57BL/6 mice.
Alice E. Kane, Kaitlyn M. Keller, Susan E. Howlett (Hallifax, Canada)

P44 - Post-translational modification of mitochondrial Ca^{2+} uniporter mediates mitochondrial Ca^{2+} overload and cell death in the heart.
Jin O-Uchi (Providence, USA)

P45 - Prostaglandin E2 mediated secretion of chemokines prevents rejection of implanted allogeneic mesenchymal stem cells and restores post-infarction ventricular function.
Sanjiv Dhingra (Winnipeg, Canada)

P46 - Role of miR-181 Family in the Heart: A Tale of Two Intracellular Compartments.
Samarjit Das, Mark Kohr, Brittany Dunkerly, Djahida Bedja, Oliver Kent, Anthony Leung, Jorge Henao-Mejia, Richard Flavell, Charles Steenbergen (Baltimore, USA and New Haven, USA and Toronto, Canada)

P47 - Role of nuclear T-tubules in human vascular smooth muscle cell function and disease.
Levon Avedanian (Beirut, Lebanon)

P48 - Striatin is a novel risk gene for human dilated cardiomyopathy that regulates cardiomyocyte response to adrenergic stimuli.
Moni Nader, Shahd AlOtaibi, Ebtihal Alsolame, Rahmah Alsomali, Nduna Dzimiri (Riyadh, Kingdom of Saudi Arabia)

P49 - Use of high resolution Doppler ultrasound for the diagnosis of endothelial dysfunction in young adults exposed to tobacco.
Ayelen Rodriguez Portelles, Delfin Rodriguez-Leyva (Holguin, Cuba and Winnipeg, Canada)

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Poster Abstracts

P1

Alpha linolenic acid decreases the production of pro-apototic oxidized phospholipids over time in cardiomyocytes after ischemia/reperfusion.

Riya Ganguly[1,2,3], Devin Hasanally[1,3], Thane G. Maddaford[1,2,3], Rakesh Chaudhary[1], Grant N. Pierce[1,2,3], Amir Ravadi[1,3,4]
[1]Institute of Cardiovascular Sciences, [2]Canadian Center for Agri-food Research in Health and Medicine (CCARM), [3]St. Boniface Hospital Research Center and the Department of Physiology and Pathophysiology, [4]Internal Medicine, Faculty of Health Sciences, University of Manitoba, Winnipeg, Canada

Alpha linolenic acid (ALA) is a plant derived omega-3 fatty acid, found in high levels within flaxseed, and when ingested is thought to elicit cardiovascular benefits. Although ALA is suggested to be cardioprotective during an ischemic insult, the mechanism(s) by which this protection occurs is unknown. In this study, primary cultured rat cardiomyocytes were exposed to media with or without ALA for 24 hours and then were subjected to 60 minutes of non-ischemic control conditions (CTR), simulated ischemia (ISCH) for 60 minutes or 60 minutes of simulated ischemia and reperfusion conditions (IR). Pre-treating the cells with ALA resulted in significant incorporation of ALA within cardiomyocyte phosphatidylcholine (PC). There was an increase in cell death after ISCH and IR. The-pro-apoptotic oxidized phospholipids (OxPC), 1-palmitoyl-2-(5'-oxo-valeroyl) sn-glycero-3 phosphocholine (POVPC) and 1-palmitoyl-2-glutaryl-sn-glycero-3-phosphocholine (PGPC) were significantly increased in ISCH and IR. Pre-treating cardiomyocytes with ALA significantly reduced cell death after ISCH or IR. Treatment of cells with ALA resulted in significantly less apoptosis after ISCH and IR as demonstrated by the reduced the number of tunel-positive myocytes and activated caspase-3/7 activity. ALA pre-treatment significantly decreased the rise of resting Ca^{2+}during ischemia and reperfusion, however there was little change to the transient Ca^{2+}. Pre-treatment with ALA significantly decreased the production of PGPC and POVPC after ISCH or IR. These results suggest that ALA elicits protection to cardiomyocytes by inhibiting the production of pro-apoptotic OxPC species. This research was supported by grants from CIHR, ARDI, Western Grains Research Foundation and the Heart and Stroke Foundation of Canada.

P2

Role of Endothelin-1 and its receptors, ET_A and ET_B in the survival of human vascular endothelial cells.

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Recently our laboratory showed the presence of endothelin-1 (ET-1) receptors, ETA and ETB, in human vascular endothelial cells (hVECs). Moreover, we showed that the ETB receptor (ETBR) seems to play a role in the survival of human vascular smooth muscle cells (hVSMCs). In this study, we wanted to test the hypothesis that ETBR can also play an important role in survival of hVECs.

We used the annexin V technique coupled to real 3D confocal microscopy as well as the ISEL (in situ Tunel) technique coupled to fluorescence microscopy to perform survival experiments of hVECs following apoptosis induced by genistein. Our results suggest that treatment of hVECs with ET-1 (10-7 M) seems to prevent apoptosis induced by genistein, an effect that is mimicked by treatment with ETBR specific

agonist IRL1620. Furthermore, our results indicate that blockade of ETBR with the selective ETBR antagonist A192621 prevents the anti-apoptotic effect of ET-1 in hVECs. However, activation of ETA receptor alone does not seem to contribute to the anti-apoptotic effect of ET-1. In addition, our results show that the anti-apoptotic effect of ETBR is mediated via nhibition of caspase 3 activation. Furthermore, our results demonstrate that the protective role of ETBR does not depend on the density of this receptor.

In conclusion, our results show that ET-1 possesses an anti-apoptotic effect in hVECs and that this effect is mediated, to a great extent, via the activation of ETBR. This study allows a better understanding of the role of ET-1 in the survival of hVECs. (Granted by CIHR and NSERC)

P3

Diastolic dysfunction after estrogen loss is linked to cardiac chymase in WKY but not SHR rats

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Left ventricular diastolic dysfunction (LVDD) develops in response to hypertension and estrogen (E2) loss and is consequent to heart failure in women. To understand the mechanisms underlying the development of LVDD as a result of the interaction between E2 loss and the cardiac renin-angiotensin-system (RAS), we compared the relationships of LV tissue RAS components and E/e¢ between adult SHR (n=13) and WKY (n=9) female rats after ovariectomy (OVX) or sham surgery (intact). In intact rats, E/e¢ was higher in SHR vs. WKY rats ($P<0.05$ strain effect) and after OVX, the diastolic phenotype of WKY's mimicked that of intact SHR counterparts (Figure). While relationships between RAS enzymatic activities and E/e¢ were not significant in SHRs with respect to estrogen status (data not shown), OVX-induced increases in E/e¢ were significantly linked to increases in chymase gene expression and enzymatic activity in the WKY strain (Figure). These data indicate that 1) the altered diastolic function in SHR is relatively insensitive to loss of estrogen while the opposite is true in WKY rats, and 2) OVX-induced LVDD in WKY is directly related to increases in cardiac chymase activity. Further elucidation of the interplay between an activated cardiac chymase-mediated RAS metabolism and LVDD following estrogen loss in normotensive subjects is warranted.

P4

Early effect of bariatric surgery (Sleeve gastrectomy (SG) vs Biliopancreatic Diversion with Duodenal Switch (BPD-DS) on postprandial fatty acid inter-organ partitioning (P4)

Anne-Marie Carreau[1], Christophe Noll[1], Frédérique Frisch[1], Lucie Bouffard[1], Serge Phoenix[1], Brigitte Guérin[1], Denis Richard[2], Laurent Biertho[2], Éric Turcotte[1], André Tchernof[2], André Carpentier[1]

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Introduction: Insulin resistance and obesity are associated with an increase in circulating fatty acids (FA) and changes in myocardium fatty acid uptake and oxidation leading to myocardial lipid accumulation. Results from our laboratory showed that subjects with impaired glucose tolerance have an increase in myocardium dietary FA uptake and impaired myocardial function, which is improved by lifestyle changes and modest weight loss. **Objective:** To determine myocardial and organ-specific postprandial FA uptake and partitioning in severely obese type 2 diabetics (T2D) before and 12 days after BPD-DS or SG, two bariatric surgeries that improve early hepatic insulin resistance and hyperglycemia in T2D patients before weight loss. **Methods:** 14 T2D subjects undergoing SG or BPD-DS will undergo a 6-hour postprandial metabolic protocol before and 12 days after surgery. Standard meal containing [U-13C]-palmitate, [^{2}H]-glucose will be ingested at time 0, with an IV perfusion [^{3}H]-glucose and [7,7,8,8-2H]-palmitate, allowing quantification of glucose absorption, endogenous glucose production, lipolysis from adipose tissue and dietary FA spillover. A gel capsule containing ^{18}F-thia-6-heptadecanoid acid (^{18}FTHA) will be administered with the meal. ^{18}FTHA is a positron-emitting long chain FA analog that is absorbed and metabolized as a dietary FA, allowing the quantification of organ-specific dietary FA metabolism using positron emission tomography coupled to computed tomography. **Results:** Preliminary results from 2 subjects before and after SG and 1 subject before and after BPD-DS suggest a decrease in myocardium dietary FA partitioning and an increase in visceral adipose tissue partitioning.

P5

Effect of extra virgin olive oil supplementation on the quality of HDL in health subjects

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Cardiovascular diseases (CVD) are the leading cause of death in Canada and worldwide. Although the inverse relationship between plasma levels of high-density lipoprotein (HDL) and

cardiovascular disease has been largely demonstrated, many observations have suggested that the quality of HDL is a more relevant parameter than their quantity for protection against CVD. Objective: We aim in this study to determine the effect of consumption of extra virgin olive oil (EVOO) on the quality and quantity of HDL in young and elderly healthy subjects. Methods: 86 subjects were recruited and divided into two groups: 27 young (<25 years) and 56 older (65-85 years). All subjects were asked to consume 25 ml / day of EVOO for 3 months. HDL quality was determined by measuring the particle size and the distribution of different HDL subclasses by using the Quantimetrix® Lipoprint system. Results: Our results show that the % and the concentration of small HDL were higher ($p < 0.05$) while the % of large HDL was lower in older subjects compared to the young subjects ($p < 0.05$). EVOO supplementation decreases significantly the % of small HDL ($p < 0.05$) in the elderly group. Thus, HDL size distribution (quality) becomes comparable to that of young subjects. Discussion: Our results show that HDL quality deteriorates during aging and that EVOO consumption permits its improvement. These results suggest a new pathway by which olive oil may exert its beneficial effect. Conclusion: The Mediterranean diet improves the HDL atheroprotective potential during aging.

P6

Effects of ovarian estrogens on local RAS activity in cardiomyocytes and non-cardiomyocytes

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The relatively low efficacy of ACE-I's in the treatment of heart failure in women after estrogen (E2) loss may be due to their inability to reach the intracellular sites at which Ang II is generated and/or the existence of cell-specific mechanisms in which ACE is not the essential processing pathway for Ang II formation. We compared the metabolic pathway for Ang II formation in cardiomyocytes (CMs) and non-cardiomyocytes (NCMs) isolated from gonadal-intact and ovariectomized (OVX) adult WKY and SHR rats. Circulating levels of angiotensinogen were higher in WKY vs. SHR and E2 loss augmented this effect in WKY (WKY OVX: 1,169 ± 66 vs. SHR OVX: 625 ± 41 pg/mL). Correspondingly, plasma Ang II levels were higher in WKY vs. SHR, independent of OVX. Chymase activity was nearly 40-fold higher in NCMs compared to CMs, and for the NCMs, activities were highest in cells from WKY vs. SHR and OVX vs. intact rats (Figure). Neither strain nor gonad status influenced ACE activity found in both NCMs and CMs. In contrast, ACE2 activity in CMs and NCMs was higher in cells from WKY vs. SHR, independent of E2 status. We conclude that NCMs from WKY and SHR express significantly higher levels of chymase, ACE, and ACE2. E2 loss leads to selective changes in the activity of chymase, but not ACE, in NCMs. The significance of these novel findings is that targeted cell-specific chymase rather than ACE inhibition may have a greater benefit in the management of HF in women after menopause.

P7

Increased blood flow by CO2-enriched water bath treatment in diabetic rats with peripheral ischemia

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Chronic diabetes is associated with peripheral artery disease as a consequence of reduced blood flow to the limbs from narrowed arteries. Earlier we have reported an increase in blood flow and angiogenesis in the ischemic hind limb by CO_2-enriched water bath (CEWB) therapy in rats. Since the effect of CEWB therapy in diabetes is not known, we investigated its actions on diabetic animals with and without peripheral ischemia. Diabetes was induced by streptozotocin for 4 weeks, whereas peripheral ischemia was induced by femoral artery occlusion. Diabetic rats were treated with or without CEWB at 37°C for 6 weeks (30 min/day; 5 days/week) starting 2 weeks after femoral artery occlusion. CO_2 treatment increased blood flow in both diabetic and diabetic ischemic groups as measured by Pulse Wave Doppler Ultrasound technique. There were no significant difference in blood lipids, glucose and creatine kinase levels after CEWB treatment. MDA concentration was significantly reduced in diabetic group after CEWB, whereas Ox-LDL was significantly reduced in diabetic ischemic group. Morphological examination of the skeletal muscle revealed increase in small artery numbers in diabetic ischemic group after CEWB treatment. It is suggested that beneficial action of CO_2 therapy in diabetic animals may be due to the formation of new blood vessels in the ischemic skeletal muscle.

P8

Integrin alpha-M beta-2 (MAC-1, CD11b/CD18) Interacts with SIRPalpha (MFR) during microphage fusion

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Inflammation is a crucial factor in the etiology of a plethora of diseases, including cardiovascular disease. The inflammatory response of leukocytes is partially conveyed by integrin alpha-M beta-2, also called macrophage-1 antigen (Mac-1), which plays numerous roles during the inflammatory response. We have recently discovered a new function of Mac-1. In particular, we found that Mac-1 is involved in macrophage fusion (1), a salient feature of chronic inflammation in many diseases, including atherosclerosis and other vascular pathologies. Deficiency of intercellular adhesion molecule 1, a counter-receptor for Mac-1, did not alter the macrophage fusion rate. These results suggested that other Mac-1 ligands are involved. Therefore the aim of this study was to define a counter-receptor(s) of Mac-1 involved in macrophage fusion. Search for potential Mac-1 ligands according structural and functional properties, recombinant techniques, cell adhesion assays and immunofluorescent staining were used. We have found that macrophage fusion receptor (MFR/SIRPalpha), a receptor up-regulated on the surface of fusing macrophage, interacts with Mac-1. The adhesion of Mac-1 over-expressing HEK293 cells to MFR was completely blocked by pre-incubation of cells with anti-Mac-1 antibody and partially inhibited by pre-incubation of cells with soluble extracellular MFR truncated protein. Adhesion of mouse macrophages to MFR was partially blocked by anti-Mac-1 antibody and the adhesion of Mac-1 knockout mouse macrophages to MFR was significantly lower than that of wild type cells. Moreover, Mac-1 co-localized with MFR in macrophage membrane fusion areas. These results suggest MFR as Mac-1 ligand partner during macrophage fusion.

P9A

High blood pressure awareness campaign in Winnipeg

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A mobile hypertension awareness campaign was created to: 1) determine the prevalence of hypertension in Winnipeg, Manitoba, Canada, 2) increase hypertension awareness, and 3) identify reasons for lack of therapy adherence. Locations for the clinic included: shopping malls, workplaces, hospitals and community centres. One thousand ninety-seven participants participated in the hypertension awareness campaign. Fifty percent of the participants presented with high blood pressure. Additionally twenty-nine percent of the participants were previously diagnosed with hypertension yet exhibited uncontrolled blood pressure (> 140/90 mmHg). Two percent exhibited a hypertensive urgency/emergency. Two-thirds of these individuals reported they had been diagnosed previously with hypertension but were no longer taking anti-hypertensive medications. The remaining one-third of the 2% were <40 years of age with no prior diagnosis of hypertension. Characteristics of these young individuals indicated secondary hypertension. Reasons for lack of therapy adherence included: denial, being unaware of health consequences and proper management of hypertension. Approximately 25% of those with a hypertensive urgency/emergency dismissed the results and the advice they were given during the appointment. The prevalence of high blood pressure and particularly hypertensive emergencies was higher than expected. A public mobile hypertension clinic may provide a strategy for awareness of impending medical need and for knowledge translation to the public. These hypertension awareness clinics should be implemented across Canada to prevent the impact of hypertension on our society.

Supported by CIHR, Western Grains Research Foundation, ARDI, and Sask Flax.

P9B

ET_A and ET_B receptors contribute to neuropeptide Y-induced secretion of endothelin-1 in right but not left human ventricular endocardial endothelial cells

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Our recent work showed that neuropeptide Y-induced secretion of endothelin-1 (ET-1) in left and right human ventricular endocardial endothelial cells (hLEECs or hREECs respectively) via the activation of neuropeptide Y2 or Y5 receptors depending on the cell type. The aim of this study was to verify whether hLEECs or hREECs secretion of ET-1 induced by NPY is due, in part, to the activation of ETA and/or ETB receptors by the secreted ET-1. Using the technique of indirect immunofluorescence coupled to real 3-D confocal microscopy, as well as ELISA, our results show that in hREECs, the NPY-induced release of ET-1 seems to be due, in part, to the activation of both ETA and ETB receptors. On the other hand, in hLEECs, ETA and ETB receptors do not contribute to the ET-1 released by NPY. Therefore, our results suggest that the NPY-

induced release of ET-1 in EECRs is due to NPY receptor activation and the subsequent activation of the ETA and ETB receptors by the released ET-1. However, the release of ET-1 by NPY in hLEECs is mainly due to NPY receptor activation. Furthermore, this secretory process of ET-1 is different between the right and left ventricular cells and highlights the important tuning roles that right and left ventricular EECs possess as well as their contribution to the physiological and pathophysiological states of the underlying heart muscle. (Granted by CIHR, NSERC and HSFC)

P9C

Effects of TNF-α on cytosolic and nuclear calcium in cells of the human cardiovascular system

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It is well known that TNF-α is implicated in intracellular calcium modulation, however, there is no information about whether the TNF-α calcium-induced response occurs in the cytosol and/or the nucleus, and whether this response is dependent on the density of TNFR1 at the levels of the plasma membrane and the nuclear membranes (NMs). In this study we investigated the effects of TNFR1 in human cells of the cardiovascular system. Our results showed that TNFR1 is present at the levels of the plasma membrane (including the cytosol) and mostly at the level of the NMs (including the nucleoplasm).The distribution of the receptor is different between cell types, however, it seems that the density is significantly higher at the nuclear level in all four cell types. The density of the receptor was the highest in contractile cells including the cardiomyocytes and VSMCs, compared to endothelial cells including endocardial endothelial and vascular endothelial cells. Furthermore, the cytokine induced a sustained calcium increase in both compartments in all four cell types. This increase was more significant at the nuclear level, mainly in endothelial cells. In conclusion, TNFR1 is present at the level of the NMs in the cells of the cardiovascular system and may contribute to the pathogenesis of autoimmune diseases such as rheumatoid arthritis. Therefore, this receptor could be a target for a new generation of pharmacological antagonists. (Granted by CIHR)

P10

Effect of daily dietary supplementation with flaxseed on exercise capacity and cardiac electrical activity in patients with peripheral arterial disease

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Patients with peripheral artery disease (PAD) are at an increased risk for cardiovascular events and a susceptibility to arrhythmias may be involved. The objectives of this study were to determine whether consumption of a diet rich in flaxseed has any effect in the prevalence of cardiac arrhythmias as well as in the physical status of patients with PAD. We included 110 patients from FLAX-PAD, a double blinded, randomized controlled clinical trial that examined the effects of 30g of milled flaxseed (or placebo) per day in PAD individuals. Prevalence of cardiac arrhythmias was considered a secondary endpoint. Variables from cardiac stress test were compared at different time intervals during one year. At baseline, the prevalence of arrhythmias in the flaxseed group was 48% and in the placebo group was 32%. After 1 year, cardiac arrhythmias in the flaxseed group decreased by 2%. Although it increased by 12% in the placebo group (NS). Electrocardiographic variables (P, PR, QRS, QT, QTc) did not change in either group during the trial. Patients from both groups improved initial and absolute claudication distances but this was also not statistically significant. Patients with PAD have a high incidence of cardiac arrhythmias that are concerning. The prevalence of cardiac arrhythmias trended in a positive direction but were not statistically significant for patients ingesting flaxseed suggesting a larger sample size may be required. Similarly, either a larger sample size or a longer intervention with flaxseed may be required to show changes in physical capacity compared to placebo.

P11

Modulation of cardiac specific miRNAs in irradiated rat myocardium after treatment with selected drugs.

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Accidental irradiation of heart and vessels during radiotherapy in mediastinal region may cause alteration of heart and vessels function (radiation-induced heart disease). MiRNAs are known to be involved in many cardiovascular disorders. Their manipulation may be an important tool for modulation of heart diseases including diseases caused by radiotherapy.

This study examined the expression levels of cardiac specific miRNAs (miR-1, -15b, -21) in rat hearts irradiated by 25 Gy in a single dose (dose rate 6-7 Gy/min). Changes in miR levels were measured by RT-qPCR after treatment with selected drugs (Atorvastatin, acetylsalicylic acid - ASA, Tadalafil, Enbrel) for six weeks after irradiation.

MiR-1 was shown to be downregulated in many cardiac diseases. In our experiments, it was downregulated by radiation and reversed by Enbrel, which increased miR-1 level in irradiated hearts up to the level of non-irradiated untreated group.

Increase of miR-15b expression is pro-apoptotic. After irradiation, miR-15b was suppressed by more than 26%. ASA treatment exerted the most marked effect, which increased miR-15b to its value in non-irradiated group.

Upregulation of miR-21 was observed in many cardiac diseases. After irradiation, miR-21 was increased nearly 2-fold compared to controls. Our results demonstrated that Tadalafil had the most pronounced effect on miR-21 (reduction about 40% compared with that in untreated group).

Our results suggest that administration of selected drugs can modulate levels of examined miRs. Based on this, Tadalafil and Enbrel can be protective and mitigate the damaging effects of irradiation.

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P12

Molecular hydrogen facilitates beneficial effect of hypoxic postconditioning on ischemia-reperfusion injury

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Molecular hydrogen (H_2) is considered as a selective antioxidant able to react with strong oxidants and preserve cell signaling mediated by NO and superoxide radicals. This study aimed to verify whether H_2 can potentiate protective effect of hypoxic postconditioning (HpostC) against ischemia-reperfusion (I/R) injury. Isolated rat hearts perfused with Krebs-Henseleit buffer (KHB) were exposed to 30-min global ischemia/120-min reperfusion. HpostC was induced by 4 cycles of 1-min perfusion with oxygen-free KHB intercepted by 1-min perfusion with normal KHB, while in H_2+HPostC group, oxygen-free KHB was enriched with H_2. Severity of I/R injury was evaluated by measurement of infarct size (IS) within the area at risk (AR) (IS/AR, TTC staining) and recovery of function. IS/AR was markedly reduced in HpostC group to 24.6 ± 0.9% compared with 38.7 ± 1.4% in non-conditioned controls, and even more significantly in H_2+HPostC group (16.6 ± 0.8%; $P<0.05$ vs. both, controls and HPostC). Post-I/R recovery of systolic function (LVDP) was improved in both postconditioned groups (HpostC: 46 ± 11%, H_2+HpostC: 53 ± 11% vs. 23 ± 1.6% in controls). However, this difference reached the level of significance ($P<0.05$) only in the H_2-enriched group. End-diastolic pressure (LVEDP) was decreased in both conditioned groups to a similar level (HpostC: 22.1 ± 5.9 mmHg, H_2+HpostC: 28.6 ± 5.6, both $P<0.05$ vs. 55.2 ± 6.9 mmHg in controls). Application of H_2 potentiated the beneficial antiinfarct effect of HpostC, and exerted a significant antistunning effect. Molecular mechanisms behind remain to be elucidated.

Grants: VEGA SR 2/0201/15, 2/0021/15, APVV-0102-11, APVV-0241-11, APVV-15-0376.

P13

Oxidized phosphatidylcholine (OxPC) induces cell death through the ferroptotic pathway in isolated adult cardiomyocytes

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Background: Phosphatidylcholine (PC) is a class of membrane phospholipid susceptible to oxidation (OxPC). Myocardial ischemia/reperfusion (I/R) injury is followed by cardiomyocyte loss and a large production of OxPCs. Ferroptosis is an iron dependent accumulation of lipid oxidation products involved in I/R injury. It is unknown whether OxPCs induce cardiomyocyte cell death and which mechanisms are involved.

Objective: Our objective was to determine the effects of various OxPCs on cardiomyocyte viability, and to examine the role of the ferroptotic pathway in cell death.

Methods: Adult rat cardiomyocytes were treated with 1-palmitoyl-2-oxovaleroyl-*sn*-glycero-3-phosphocholine (POVPC), 1-palmitoyl-2-(5'-oxo-valeroyl)-sn-glycero-3-phosphocholine (PONPC), 1-palmitoyl-2-glutaroyl-*sn*-glycero-3-phosphocholine (PGPC), 1-palmitoyl-2-azelaoyl-sn-glycero-3-phosphocholine (PAzPC), 1-palmitoyl-2-(5-keto-6-octene-dioyl)-sn-glycero-3-phosphocholine (KOdiA-PC), 1-palmitoyl-2-(4-keto-dodec-3-enadioyl)-sn-glycero-3-phosphocholine (KDdiA-PC) and 1-

palmitoyl-2-stearoyl-sn-glycero-3-phosphocholine (PSPC) at concentrations of 0.1µM, 1µM, 5µM, and 10µM. Following a 1 h treatment, Live/Dead™ assays were performed to determine cellular viability. Ferrostatin-1, an inhibitor of ferroptosis, was added together with an OxPC.

Results: *In vitro*, several oxPC species as well as PC exhibited no cardiotoxic effect when incubated with isolated cardiomyocytes. However, five of the seven tested OxPCs (POVPC, PONPC, PGPC, PAzPC and KDdiA-PC) induced a decrease in cell viability at higher concentrations ($p<0.001$). Two OxPCs (POVPC and PONPC) induced significant cytotoxic effects at low µM concentrations. The cardiotoxic effects were dependent upon the duration of incubation with the cells. The addition of ferrostatin-1 with POVPC blocked the cardiotoxic effects of POVPC on its own ($p<0.001$).

Conclusion: These data demonstrate the cardiotoxic effects of OxPCs in cardiomyocytes and suggest a new therapeutic target for preventing cell loss in myocardial I/R injury.

P14

Paraoxonase 1 promotes cholesterol efflux from macrophages by stimulating the PPARγ-LXRα-ABCA1 pathway

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The aims of the present study were thus to investigate the mechanism by which PON1 may modulate cholesterol efflux and to elucidate the impact of PON1 on the regulation of cholesterol homeostasis. Our results showed that pre-treating oxLDL with PON1 (oxLDL-PON1) contributes to the formation of LysoPC. Purified LysoPC stimulated macrophage-derived cholesterol efflux in a LysoPC concentration-dependent manner. Incubating J774 macrophages with oxLDL pre-treated with PON1 increased cholesterol efflux by more than 47% ($p<0.0001$) compared to oxLDL alone. This effect was significantly reduced in the presence of DIDS, an ABCA1 inhibitor. oxLDL-PON1 also significantly increased ABCA1 and ABCG1 protein expression (58.51% ($p<0.0001$) and 51.80% ($p<0.0001$), respectively) and RNA expression byJ774 macrophages as well as PPARg and LXRa protein and RNA expression compared to oxLDL alone. The stimulatory effect of oxLDL-PON1 was lower in the presence of ABCA1, PPARg and LXRa inhibitors (DIDS, GW9662 and GGPP, respectively). Pre-treating [^{3}H]-labeled J774 macrophages with oxLDL-PON1 or LysoPC before injecting the macrophages into the peritoneal cavities of C57/BL6 mice significantly increased [^{3}H]-cholesterol levels in the plasma and liver compared to control mice. Pre-treating the macrophages with oxLDL-PON1 or LysoPC also increased the fecal elimination of macrophage-derived cholesterol by more than 64.39% ($p<0.005$) and 84.46% ($p<0.044$), respectively, compared to control mice. Our results suggest that PON1 stimulates cholesterol efflux and regulates the RCT process via a mechanism that involves the capacity of PON1 to hydrolyze oxidized phospholipids.

P15

Resveratrol attenuates hyperproliferation of vascular smooth muscle cells from spontaneously hypertensive rats: Role of ROS and ROS-mediated signalling

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Resveratrol, a natural polyphenolic compound found in grapes is implicated in several vasculo-protective effects. Resveratrol has also been reported to attenuate the blood pressure; however, the molecular mechanism underlying the anti-hypertensive effect of resveratrol is still unclear. Vascular remodeling due to hyperproliferation of vascular smooth muscle cells (VSMC) is central in the development of the hypertension. VSMCs from spontaneously hypertensive rats (SHR) exhibit hyperproliferation and overexpression of cell cycle proteins. We earlier showed that the enhanced oxidative stress through c-Src, growth factor receptor transactivation, MAP kinase (MAPK/PI3K) signaling and overexpression of Giα proteins contribute to the excessive proliferation of VSMC from SHR. The present study was undertaken to investigate if resveratrol could attenuate hyperproliferation of VSMC and explore the underlying molecular mechanisms. For these studies, aortic VSMC from 14-week-old SHR and Wistar-Kyoto (WKY) rats were used. The proliferation of VSMC was determined by [^{3}H] thymidine incorporation and the levels of proteins were determined by Western blotting. VSMC from SHR exhibited hyperproliferation which was significantly attenuated by resveratrol. In addition, overexpression of cyclin D1, cyclin E, cyclin dependent kinase 2 (cdk2), Giα, Nox2/Nox4 and P^{47}phox proteins, enhanced phosphorylation of retinoblastoma protein (pRb), ERK1/2, AKT, EGF-R and the increased production of superoxide anion, NAD(P)H oxidase activity in VSMC from SHR were attenuated by resveratrol. These results suggest that resveratrol through the inhibition of ROS and ROS-mediated transactivation of EGF-R, and MAPK/PI3K, attenuates the overexpression of Giα and cell cycle proteins and results in the attenuation of hyperproliferation of VSMC from SHR.

P16

Scleraxis is a direct transcriptional regulator of MMP-2 gene expression

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In the heart, the extracellular matrix (ECM) is a crucial structural component that provides mechanical support. During cardiac fibrosis, ECM synthesis and degradation are altered due in part to increased expression of remodeling enzymes including the Matrix Metalloproteinases (MMPs). Cardiac fibroblasts and myofibroblasts express the transcription factor scleraxis, which we reported is a crucial regulator of ECM proteins, including collagen 1α2, fibronectin, and α-smooth muscle actin, by binding to E-box consensus sequences located in target gene promoters. MMP-2 hydrolyzes ECM components to govern the mechanical characteristics of the matrix, and contributes to cardiac remodeling during fibrosis. We show here that the MMP-2 gene promoter is directly transactivated by scleraxis, which is similarly up-regulated in cardiac fibrosis. We identified several E-boxes in the MMP-2 promoter to which scleraxis binds, and confirmed promoter transactivation by scleraxis using luciferase reporter assay. Studies in NIH-3T3 fibroblasts demonstrated that MMP-2 expression mirrored scleraxis expression. Gain and loss of function of scleraxis in primary adult rat cardiac proto-myofibroblasts confirmed these results at the mRNA and protein levels: scleraxis induced MMP-2 expression, while scleraxis loss resulted in down-regulation of MMP-2. Intriguingly, MMP-2 expression in scleraxis-null cardiac proto-myofibroblasts could be rescued by scleraxis over-expression. Our data demonstrates that scleraxis directly governs the expression of MMP-2, and provides the first description of the underlying mechanism. Our results further highlight the importance of scleraxis in controlling multiple processes that contribute to fibrosis, including ECM expression, remodeling and fibroblast to myofibroblast conversion.

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P17

Potentiation of bradykinin B2R activity by heterologous expression of a newly-identified protein coded by an alternative ORF of the B2R mRNA

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Background: The GPCR bradykinin B2 receptors (BK/B2R) are thought to play a protective role in cardiovascular diseases, in part demonstrated by the substantial therapeutic benefits of ACE-inhibitors in these diseases. Our recent functional/proteomic studies in eukaryotes predicted the possibility of translation of alternative open reading frames (AltORFs) in mature GPCR mRNAs (~95%), leading to expression of very different proteins of unknown functions in addition to the annotated GPCRs. Such prediction also encompasses the B2R.

Hypothesis: The human B2R mRNA can code for an alternate protein (AltB2R), which in turn can modulate B2R activities.

Methods: Expression and co-localisation of AltB2R with B2R were investigated in the human B2R-expressing HeLa cell line using FACS, confocal microscopy, bi-molecular fluorescence complementation (BiFC) and co-IP. Modulatory effects of AltB2R on BK-induced Ca^{2+} intracellular mobilisation and activation of p42/p44 MAPK were demonstrated by confocal microscopy using Fluo-3AM and by western blotting using phospho-specific antibodies, respectively.

Results: Total and surface B2R expression remained unchanged after AltB2R stable infection compared to Mock controls. Both B2R and AltB2R were found to co-localize at the plasma membrane and at intracellular sites, mostly the endoplasmic reticulum. Furthermore, heterologous expression of AltB2R protein significantly potentiated the B2R agonist-induced Ca^{2+} mobilisation and activation of p42/p44 MAPK through phosphorylation.

Conclusion: Our results indicate that AltB2R is a novel interaction partner and positive regulator of B2R signalling. Future studies should thoroughly investigate the roles of AltB2R with respect to B2R-mediated mechanisms of protection in cardiovascular diseases. (Work supported by CIHR).

P18

Selective replacement of mitochondrial DNA reduces the sensitivity of mitochondrial permeability transition pore to opening in chronically hypoxic hearts of spontaneously hypertensive rats.

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Effects of adaptation to continuous normobaric hypoxia (CNH; 10% O_2, 3 wks) on mitochondrial functions [respiration,

cytochrome c oxidase (COX) activity, sensitivity of mitochondrial permeability transition pore (MPTP) to opening] and myocardial infarct size were analyzed in spontaneously hypertensive rats (SHR) and in conplastic SHR-mt^{BN} strain characterized by the selective replacement of the mitochondrial genome of SHR with that of more ischemia-resistant Brown Norway strain. In mitochondria isolated from left ventricles, respiration and COX activity were measured using Oxygraph-2k. The sensitivity of MPTP opening was assessed spectrophotometricaly as Ca^{2+}-induced swelling. Myocardial infarct size was analyzed in anesthetized open-chest rats subjected to 20-min coronary artery occlusion and 3-h reperfusion. The infarct size reached 68±3.0% and 65±5% of the area at risk in both normoxic strains. CHN decreased myocardial infarction to 46±3% in SHR. In hypoxic SHR-mt^{BN}, infarct size reached 33±2% and was significantly smaller compared with that of hypoxic SHR. Mitochondria isolated from hypoxic hearts had increased stimulated COX activity and were less sensitive to MPTP opening. Maximal swelling rate was significantly lower in hypoxic SHR-mt^{BN} compared with hypoxic SHR and positively correlated with myocardial infarction in all experimental groups. In conclusion, mitochondrial genome of SHR modulates infarct size-limiting effect of adaptation to CNH by a mechanism involving COX and MPTP.

P19

Angiotensin II receptors modulation of calcium homeostasis in human vascular endothelial cells (P9)

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Angiotensin II (Ang II) plays an important role in the regulation of vascular contractility. Most of the functions of Ang II in the vascular system are attributed to AT_1 receptor activation. There is no information whether both AT_1 and AT_2 receptors are present in human aortic endothelial cells and whether AT_1 and/or AT_2 receptors in this type of human cells undergo internalization and regulate intracellular calcium. Using human isolated cultured aortic endothelial cells (hVECs) and western blots, our results showed that both AT_1 and AT_2 receptors are present in hVECs. Using real 3-dimension confocal microscopy imaging, our results showed that both AT_1 and AT_2 receptors were present at both the cell membrane and the nuclear envelope membrane and that only AT_1 receptors but not AT_2 receptors undergo internalization and nuclear translocation. Using real 3-D Ca^{2+} imaging technique, our results showed that Ang II induced increase of cytosolic and nuclear Ca^{2+} via activation of AT1 receptors.

These results demonstrate that both AT_1 and AT_2 receptors are present in hVEC and that only AT_1 receptors seem to undergo transcellular trafficking and modulate hVEC Ca^{2+} homeostasis. However, the role of AT_2 receptor in modulation of hVEC function remains to be determined. This work is supported by CIHR and NSERC grants to Dr. G. Bkaily.

P20

Cardioprotective role of Vitamin C in Doxorubicin-induced cardiomyopathy via mitigation of oxidative/nitrosative stress

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Background: Oxidative/nitrosative stress is being linked as a key event in the development of various cardiovascular diseases including doxorubicin (Dox)-induced heart failure. The present study aims to understand the role of a potent antioxidant, vitamin C (Vit C), on cardiac function, oxidative/nitrosative stress in an animal model of Dox-induced cardiomyopathy.

Methods and Results: Adult male Wistar rats were treated with Vit C (50 mg/ kg bw orally daily for 6 weeks) or Dox (15mg/kg bw given intraperitoneally in six equal doses for three weeks) or combination treatment of Vit C+Dox. Vit C co-treatment showed an increase in survival (93%) and cardiac function in animals in comparision to Dox alone. Cardiac tissue of Dox treated animals showed increased oxidative stress as indicated by the formation of protein carbonyls, superoxide anions and lipid peroxidation along with compromised antioxidant enzyme activities of superoxide dismutase and glutathione peroxidase. These Dox mediated effects were found to be reduced by Vit C. Dox treatment caused loss of cardiomyocytes by the activation of various pro-apoptotic proteins which was observed to be prevented in Vit C treated animals. An increased level of Nitric oxide, Nitric oxide synthase (NOS) activity and its protein expression (inducible NOS) as well as protein nitrosylation were observed in the heart of Dox treated rats. These effects were significantly blocked by Vit C.

Conclusion: Based on these results, it is suggested that attenuation of major triggers of Dox-induced cardiotoxicity by Vit C would be beneficial in protecting the heart from adverse effects of chemotherapy.

P21

Characterization of the oxidative potential and its relationship with the adipose tissue physiology in fat depots surrounding human heart

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Background: We, and others, have previously reported that human epicardial adipose tissue (eAT) expresses uncoupling protein 1 (UCP1), a marker of brown adipocytes, at both mRNA and protein levels.

Objective: To characterize the molecular and oxidative properties of UCP1-expressing adipocytes in the fat depots surrounding human heart, and assess their relationship with the markers of adipose tissue physiology.

Methods: Samples of eAT, mediastinal- (mAT) and subcutaneous- fat (sAT) were collected from patients (n=53) undergoing heart surgeries, and utilized for primary cell culture, gene expression and histological analysis.

Results: A higher expression of UCP1 in eAT relative to mAT and sAT was verified in the current cohort. However, a closer look at the data revealed significant variation in UCP1 expression across fat depots and individuals. Functionally, both eAT and mAT derived primary adipocytes exhibited higher capacity for enhancing uncoupled respiration upon stimulation. Screening for specific markers identified both eAT and mAT to be beige in nature, with mAT exhibiting a stronger white phenotype than eAT. Cluster analysis revealed UCP1 associating with beige-specific gene markers in eAT and mAT. Patient stratification based on this cluster analysis further revealed a positive association between beige phenotype and fibrotic and anti-inflammatory markers in eAT.

Conclusion: UCP1 expression, its presumptive activity and a beige phenotype is detectable in both eAT and mAT. An association between beige phenotype and fibrotic and inflammatory markers in these fat depots points towards a physiological relevance for UCP1. RNA sequencing and proteomic analyses are currently underway to probe this question further.

P22

Deregulation of the E2F pathway in post-natal myocardium impacts metabolic control and dilated cardiomyopathy

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The E2F/Rb pathway regulates metabolism in numerous cell types and cancers, but its role in cardiac metabolism remains to be defined. We expressed the transcriptional repressor, E2F6- which is believed to repress E2F independently of Rb, to achieve a dominant negative model of the E2F pathway in post-natal myocardium. E2F6 expression caused dose dependent dilated cardiomyopathy in transgenic (Tg) mice and activation of E2F responsive genes, attributed to interference with E2F/Rb which normally represses E2F responsive genes in post-natal myocardium. The Seahorse method was utilized to measure metabolism in neonatal cardiomyocytes isolated from Wt and Tg mice. Basal glycolysis, as measured by the extracellular acidification rate following the addition of glucose, was decreased by ~20% in Tg cardiomyocytes. Analysis of the cardiac glucose transporter, Glut4, revealed a ~30% reduction in protein, and analysis of the regulator of glucose homeostasis, Akt2, revealed a ~50% decrease in its activation which may account for the depression of glycolysis in Tg cardiomyocytes. Fatty acid metabolism, as measured by the oxygen consumption rate following the addition of free fatty acids, was not altered in Tg cardiomyocytes, thereby suggesting it was not increased to compensate for the reduced glycolysis. Analysis of the regulator of ketone metabolism, BDH1, revealed its transcriptional activation and early induction of protein in Tg pup myocardium suggesting that ketone metabolism could be activated in E2F6-Tg myocardium. This study reveals that appropriate regulation of the E2F pathway is required for the normal coordination of cardiac metabolism and substrate choice in post-natal myocardium.

P23

Early changes in circulating miRNA 133a are indicative of cardiac remodelling after 3 months in patients presenting with acute ST elevation myocardial infarction

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Background

MicroRNAs (miRNA) are small non-coding RNAs that regulate gene expression by interacting with multiple mRNAs. They can be released from cardiac tissue as a consequence of damage. Whether they can also predict long term cardiac remodeling after reperfusion injury, is not presently known.

Purpose

Plasma miRNAs levels were monitored in patients presenting with acute ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI) to establish whether they would reflect long term cardiac remodeling.

Methods

Four miRNAs linked to cardiac injury and cardiac remodeling (miRNA-133a, miRNA-208b, miRNA214 &miRNA-194) were measured in plasma of patients (n=50) upon admission (baseline), 24 hours and 3 months after reperfusion. Cardiac MRI was performed during admission and at 3 months. MiRNAs were measured using Taqman primers and miRNA levels assessed using quantitative PCR and normalized using cel-miR-39-3p(000200).Early changes in miRNA (24hours - baseline) were tested for correlation with clinical parameters measured acutely and after 3 months using pearson correlation (SPSS software).

Results

miRNA133a was the only miRNA to show significant correlation (-0.397,P=0.025) with change of infarct size (in grams) over 3 months period where the higher the elevation during the initial 24hrs, the more positive (survival) remodeling outcome in 3 months.

Conclusion

Early changes in miRNA133a may predict the degree of myocardial remodeling after 3 months in patients presenting with STEMI undergoing PPCI

P24

Impact of higher ApoB/ApoA-1 ratio on the hemodynamic progression of aortic stenosis - Results from the PROGRESSA study.

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BACKGROUND: Aortic stenosis (AS) is a chronic and multifactorial disorder that involves lipid-mediated inflammation similar to what occurs in atherosclerosis. Apolipoprotein B/Apolipoprotein A-I (ApoB/ApoA-I) ratio reflects the balance of atherogenic and antiatherogenic lipoproteins. This study examines the contribution of the ApoB/ApoA-I ratio to the hemodynamic progression of AS in younger versus older patients.

METHODS: 159 consecutive patients (66±13 years, 73% male) with AS were prospectively recruited in the PROGRESSA study. Hemodynamic progression of AS was assessed by the change in peak aortic jet velocity (V_{peak}) measured by echocardiography between baseline and 2-year follow-up. Blood sample was collected at baseline to measure plasma levels of ApoB and ApoA-I.

RESULTS: AS progression rate was similar between younger (age ≤69 y.o. [median age for the cohort]; n=80) versus older patients (V_{peak}: +0.26±0.33 vs. +0.24±0.29 m/s; p=0.86). There was a significant interaction (p=0.007) between age and baseline ApoB/ApoA-I ratio with respect to effect on AS progression. Higher ApoB/ApoA-I ratio was significantly associated with faster AS progression in younger patients (r=0.39; p=0.0003) but not in older patients (p=0.63). After multivariable adjustment, higher ApoB/ApoA-I ratio remained independently associated with faster AS progression in younger patients (standardized β=0.40; p=0.001). Higher ApoB/ApoA-I also remained associated with faster AS progression in younger patients after further adjustment for baseline levels of lipoprotein (a) [Lp(a)] and low-density lipoprotein corrected for cholesterol content in Lp(a) (p<0.05).

CONCLUSION: These findings suggest that the lipid-mediated processes may have an important role in the pathogenesis of AS in younger but not in older patients.

P25

Angiotensin-II-induced expression of the early growth response protein-1 (Egr-1) in vascular smooth muscle cells (VSMC)

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Aberrant VSMC proliferative responses contribute to the development of intimal lesion. Cyclic adenosine monophosphate (cAMP) is believed to inhibit VSMC proliferation. Vascular diseases have been associated with impairment in cAMP-induced responses involving two signaling effectors, the protein kinase A (PKA) and the exchange protein directly activated by cAMP (Epac). Since an up regulation of Egr-1 expression has been linked with atherosclerosis and intimal hyperplasia, we recently investigated the effect of angiotensin-II (Ang-II) on Egr-1 expression and demonstrated that Ang-II regulates this transcription factor via a mechanism involving Ca^{2+}/ERK1/2-mediated cAMP-response element binding protein (CREB) activation. However, whether Ang-II-induced signaling leading to Egr-1 expression is a target of cAMP-dependent activity remains unexplored. Therefore, in the present studies, we have examined whether elevation of cAMP in VSMC could modify the signaling cascades underlying Ang-II-induced expression of Egr-1 and investigated the respective contributions of PKA and Epac. Both forskolin (FSK), an adenylate cyclase activator, as well as dibutyryl-cAMP, a cAMP analog, attenuated Ang-II-induced Egr-1 expression in a dose-dependent fashion. BNZ-cAMP and CPT-cAMP, activators

of PKA- and Epac-mediated pathways respectively exerted a similar effect. Moreover, FSK suppressed Ang-II-induced phosphorylation of PKB, ERK1/2, and CREB in a dose-dependent fashion. In addition, pharmacological blockade of PKA and Epac abolished FSK-mediated inhibition of Ang-II-induced signaling and resulted in a potentiation of Egr-1 induction. In summary, PKA- and Epac-mediated suppression of Ang-II-induced Egr-1 expression and phosphorylation of PKB, ERK1/2, and CREB may be among the mechanisms by which cAMP exerts its vasoprotective effects. (Supported by CIHR).

P26

Involvement of heat shock protein-60 in vascular smooth muscle cell proliferation through a modulation of nuclear protein import

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Heat shock protein (Hsp) 60 is a proposed mediator of stress-induced vascular smooth muscle cell (VSMC) proliferation. Nuclear protein import (NPI) regulates cell growth and division by controlling translocation of transcription factors into the nucleus. This study examined whether Hsp60 can mediate cell proliferation through an NPI-dependant mechanism.

Hsp60 with or without a mitochondrial targeting sequence ($AdHsp60^{mito-}$) was overexpressed in primary rabbit VSMCs. Rat VSMCs were treated with well-established stress-stimuli, oxidized low-density lipoprotein (oxLDL). Rat VSMCs were also treated with oxLDL following Hsp60 siRNA treatment.

Both AdHsp60 and $AdHsp60^{mito-}$ increased Hsp60 expression, VSMC proliferation, and rate of NPI with respect to control. Both AdHsp60 and $AdHsp60^{mito-}$ induced an up-regulation of the cytosolic nuclear transport proteins Importin-a, Importin-b and Ran compared to control. OxLDL treatment stimulated VSMC proliferation and induced increases in Hsp60 and Ran expression compared to control. However, after oxLDL treatment, Hsp60 siRNA treatment decreased the expression of Hsp60 and eliminated any of the increases in Ran expression. Furthermore, knockdown of Hsp60 prevented stimulation of NPI by oxLDL treatment. Heat shock, AdHsp60 and $AdHsp60^{mito-}$ treatments all produced co-immunoprecipitation of Ran and HSP60.

Therefore, nuclear protein import has an important role in VSMC proliferation, which can be modulated via an Hsp60-dependent cytosolic mechanism involving Ran.

P27

Leptin-induced cardiomyocyte hypertrophy is associated with enhanced mitochondrial fission

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Leptin, a 16-kDa appetite-suppressing protein secreted primarily but not exclusively by adipocytes, has shown to induce cardiomyocyte hypertrophy. In hypertrophy, there is an imbalance in mitochondrial fission and fusion, which alters both mitochondrial and cellular functions. This study determined whether the hypertrophic response to leptin is related to mitochondrial fission or fusion. Cardiomyocytes treated for 24 hours with 3.1-nM leptin (50-ng/ml), a concentration representing elevated plasma levels in obese individuals, were hypertrophic as demonstrated by larger surface area and increased beta-myosin heavy chain expression. Mitochondrial staining showed elongated structures in control cells (average length 4.5-µm) while mitochondria in leptin-treated myocytes were smaller and shorter in a time-dependent manner. The hypertrophic response to leptin was associated with increased protein levels of the mitochondrial fission protein dynamin-related protein1 (Drp1) although its gene expression was unaffected, suggesting post-translational modifications of Drp1 by leptin. Indeed, leptin treatment decreased the phosphorylated Drp1 levels and increased Drp1 translocation to the mitochondria thereby demonstrating a pro-fission effect of leptin. Leptin-induced mitochondrial fission was dependent on leptin receptor activation and calcineurin activity since either a highly specific leptin receptor antagonist or the calcineurin inhibitor FK506 inhibited leptin-induced mitochondrial fission and the accompanying dysfunction. In conclusion, our data show that leptin-induced cardiomyocyte hypertrophy is associated with enhanced mitochondrial fission which likely contributes to mitochondrial dysfunction via a calcineurin-mediated pathway. The ability of leptin to stimulate mitochondrial fission may be important in understanding its role in cardiac pathology especially that related to mitochondrial dysfunction. (This study was supported by CIHR)

P28

MiRP2 rescues cardiac slow delayed rectifier K^+ channel (IKs) function in long QT syndrome 5

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Long QT syndrome (LQTS) is a congenital cardiac rhythm disorder that is caused by mutations affecting ion channel

function and is associated with the incidence of cardiac arrhythmias and sudden cardiac death. An unexpectedly large number of LQTS mutation carriers exist without manifest symptoms but carrying the risk of life threatening arrhythmias. LQTS5 is caused by mutations in the gene encoding for minK, an important regulator of the cardiac slow delayed rectifier potassium current (I_{Ks}). An LQTS5 variant of minK, carrying the G52R mutation suppresses I_{Ks}, resulting in decreased current amplitude *in vitro*. A transgenic rabbit model of LQTS5 that is based on the cardiac specific over-expression of G52R-minK has recently been developed. I_{Ks} amplitudes were unchanged and I_{Ks} deactivation was accelerated in LQTS5 transgenic cardiomyocytes compared to wild type cells. In this study, we demonstrate that MiRP2 interacts with I_{Ks} channels and prevents the reduction of current amplitudes in the presence of G52R-minK, but accelerates current deactivation, partially rescuing the LQTS5 phenotype. These effects are in line with the observations made on I_{Ks} in the LQTS5 transgenic model. Our findings suggest that MiRP2 may play a critical role in the regulation of I_{Ks} channels and contribute importantly to the repolarization reserve. As such, MiRP2 may represent a novel, previously unrecognized mechanism for the low penetrance of mutations in LQTS5.

P29

Modulation of human adipocyte metabolism for the prevention of type 2 diabetes

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Experimental evidence in humans and animal models support that overexposure of lean tissues to fatty acids (FA) is critical in the development of type two diabetes (T2D). Adipose tissues also play a central role in buffering FA fluxes. Limited FA storage in adipocytes has been associated with increased circulating levels of free FA occurring early in the development of T2D. More specifically, hypertrophic adipose tissue expansion, associated with dyslipidemia, inflammation and insulin resistance, is a recognized contributor to T2D.

We used a systemic bioinformatics analysis of adipocyte metabolism to identify genes coding for enzymes affecting adipose tissue expansion mechanisms (adipocyte hypertrophy and/or hyperplasia).

We performed an in-silico gene deletion analysis on our adipocyte metabolic network, iTC1389adip, using flux balance analysis. This analysis permitted the prediction of gene deletion on optimal production of lipid droplets and biomass as representation of adipose hypertrophy and hyperplasia respectively. 27 genes in the network were predicted as having a larger effect on lipid droplet with a small effect on biomass production, which is an indication that such deletion could result in decreased adipocyte hypertrophy. Some of the identified genes, including LCAT and DGAT1, have experimental results supporting the predicted effect in adipocytes while others, such as FAR2 and HSD17B12, could serve as new potential targets in adipose tissue remodeling and diabetes treatment if their role is validated.

These results will guide in-cellulo and ex-vivo studies to validate new therapeutic targets which could affect the development of T2D.

P30

Prenatal exposure to gestational and pre-gestational diabetes impairs cardiac relaxation in youth with type 2 diabetes

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At least one Canadian child per class of 20 was prenatally exposed to type 2 diabetes (T2D) or gestational diabetes (GDM) and is therefore at a greater risk of T2D and its cardiovascular complications. Objective: To determine if these exposures are associated with adverse cardiac changes in adolescence.

We performed cross-sectional comparisons of echocardiography-derived cardiac morphology and function in 82 Indigenous adolescents stratified per mother-reported prenatal diabetes status: T2D (n=37), GDM (n=13) or normoglycemia (n= 32). Main outcomes were left ventricular (LV) mass, hypertrophy, and diastolic and systolic function.

The groups were similar for confounders: sex (62 vs 43 vs 71% female), age (~15 years), duration of diabetes (~3.0 years), adiposity (30-33% body fat), and blood pressure load (45 [22-74] vs 42 [24-53] vs 33 [19-61]% of wear time). We observed smaller LV mass (137 [112-174] vs 150 [130-183] vs 168 [140-190] g; p=0.02) and impaired LV relaxation (early-to-late tissue relaxation: 1.9 [1.6-2.3] vs 1.8 [1.6-2.3] vs 2.3 [1.8-3.0]; p=0.03) in those exposed to T2D and GDM compared to controls. No differences were observed in LV hypertrophy (eg, interventricular septal wall thickness: 10.4 [9.4-11.6] vs 10.6 [9.7-12.0] vs 11.0 [10.2-12.5] mm; p=0.2). Ejection fraction was reduced after exposure to GDM (61.3 [57.0-64.2]%; p=0.02), but not to T2D (64.3 [62.0-67.3]%) or normoglycemia (64.3 [62.0-65.7]%).

Adolescents with T2D exposed to T2D or GDM exhibit smaller LV size and impaired LV relaxation in the absence of LV hypertrophy. Exposure to prenatal diabetes may be associated with cardiomyopathy in adolescents with T2D.

P31

The cardiac specific isoform of tail anchored membrane protein SLMAP1 enhances GLUT4 levels by directing endosomal size and recycling

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SLMAP1, Sarcolemmal Membrane Associated Protein isoform 1, is a tail anchored membrane protein that belongs to a family of membrane proteins involved in fusion and vesicle transport. A transgenic mouse (tg) with gain of function of SLMAP1 in cardiomyocytes leads to increased GLUT4 levels and enhanced glucose uptake and metabolism [1]. Enlarged membrane vesicles were noted in tg myocardium and were identified as GLUT4 vesicles [1,2]. Further tg myocardium was found to contain upregulated levels of SNARE protein complex (SNAP23, Syntaxin-4, VAMP2) and early endosomal tethering protein, EEA1 [3]. The increased levels of these vesicle proteins mostly likely enhanced fusion events resulting in the notable enlarged early endosomes [3]. Immunofluorescence analysis indicated that early endosome traffic is being redirected to the ERC (endosomal recycling complex) through Rab11, Rab5 and its effecter protein Rabaptin-5. Further, SLMAP1 was found in complex with Myosin VI, a molecular motor involved in vesicle transport to the plasma membrane. This data implicates a role for SLMAP1 in vesicle transport with a particular impact on GLUT4 recycling. In order to further establish a role for SLMAP in vesicle biology trafficking an *in-vivo* loss of function model, aMHC-MERCreMER-Lox mouse model is being generated. This modified Cre enzyme allows control of spatial and temporal SLMAP in mouse myocardium. Genotyping and Western blot data reveals a 50% reduction in SLMAP in heterozygous-floxed 5-week-old mouse hearts. The data generated from these animal models should position SLMAP as a novel player in vesicle biology and associated disease conditions.

P32

Cardiovascular pharmacology of vasoactive factors revisited in the non-anesthetized mouse

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Despite close to 300 publications associated with telemetry monitored changes of blood pressure in conscious mice, it is surprising that no studies, to our knowledge, have yet assessed the responsiveness of the cardiovascular system in a non-anesthetized murine model.

Using a single bolus intravenous administration protocol, we determined the effects on blood pressure parameters of Endothelin-1 (ET-1) , Angiotensin II (Ang II), Methoxamine, L-NAME and Bradykinin, in non-anesthetized or anesthetized mice (C57Bl/6). In a second series of experiments, two-photon microscopy analyses of changes of calcium or diameter to Ang II (intraperitoneal) were performed in conscious or isoflurane anesthetized ExMLCK mice.

Our main results show a 6 log units leftward shift of the dose-dependent responses, in conscious versus anesthetized mice, to all agents stated above. For example, apparent affinities of ET-1 or Ang II were experimentally calculated at 0,01781 or 0,2786 fmol/kg in conscious versus 1,2 or 0,4750 nmol/kg in anesthetized congeners [independently of the type of anesthesia used (ketamine/xylazine, avertin or isoflurane) or strained used (C57Bl/6 or CD-1)]. Interestingly, nitric oxide synthase inhibition associated with hypertensive responses can be attained at doses of L-NAME a million time lower in conscious versus anesthetized mice. Finally, Ang II increases calcium and reduced diameter of singly monitored ear vessels at doses 100,000 lower in conscious versus anesthetized ExMLCK mice.

It is concluded that the pharmacodynamics characteristics of vasoactive agents currently reported in the mouse model should be revisited in freely moving/conscious mice.

P33

Differential passage of mesenchymal stem cells introduces variability in their immunoprivilege – an "Omic"-al perspective

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Bone-marrow derived allogeneic MSCs have found promising applications in regenerative therapies. Even though immunoprivileged at first, MSCs provoke immune response in recipient heart and are rejected after transplantation. Our observations revealed that cell-surface oxidized phospholipids (ox-PCs) modulate allogeneic immune cell response, which in turn are affected by regular passage. This study attempted to address the variability in immunogenicity that is imparted owing to passage of MSCs in the in vitro setup. MSCs isolated from SD rats were collected at different passages - 3, 5 and 7 (P 3, 5 and 7). Immunoprivilege of MSCs was assessed by mixed-leukocyte-reaction assay. Leukocyte-mediated cytotoxicity (LDH) and apoptosis (Bax/Bcl-xl ratio) in MSCs was assessed after co-culture. Proliferation of leukocytes was assessed by flow-cytometry. MSCs were also analyzed by LC/MS/MS - "lipidomic platform" for cell surface ox-PCs levels and LC/MS based "proteomic platform" for total cellular proteins. Cellular bioenergetics for each of the passages was performed through SeaHorse Analyses. Lymphocyte-mediated cytotoxicity and apoptosis decreased in MSCs at P5 and7 compared to P3. Levels of immunomodulatory ox-PCs increased in MSCs at P5 and P7. Inhibition of ox-PCs correlated with loss of immunoprivilege of MSCs. Proteome analyses revealed ox-PCs interacted with downstream intracellular proteins. Candidates related to intracellular immune response, lipid metabolism and mitochondrial dynamics registered significant changes. Associations between cell surface ox-PCs and intracellular proteins involved in immune modulation is being studied through combining all the omic data. This is the first study utilizing membrane lipidomics with intracellular proteins to assess immunogenicity of MSCs (supported by CIHR).

P34

Seven-day overfeeding decreases myocardial dietary fatty acid partitioning in healthy subjects

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Subjects with impaired glucose tolerance have increased myocardial dietary fatty acids (DFA) partitioning after a 7-day caloric and saturated fat restriction associated with a decrease in left ventricular function. The aim of the present study is to determine the effect of a 7-day hypercaloric diet (+50 % kcal/d from "junk food") high in saturated fat (~10 % of energy) (HIGHCAL study) vs. isocaloric with low saturated fat (~7 % of energy) diet (ISOCAL) on DFA metabolism in healthy subjects. Organ-specific DFA partitioning and cardiac and hepatic DFA fractional uptake rates were measured in 12 IGT subjects (6M/6F) using the oral 18-Fluoro-6-thia-heptadecanoic acid positron emission tomography method ([^{18}F]-FTHA) after 7 days of ISOCAL vs. HIGHCAL diet using a randomized crossover design. HIGHCAL led to an increase in weight (+1.0 ± 0.3 kg, P < 0.02) and an increase in fasting plasma insulin level (+44.8 ± 13.2 %, P < 0.002). We found a significant decrease in myocardial DFA partitioning over 6 hours after HIGHCAL vs. ISOCAL (2.1 ± 0.2 vs. 2.4 ± 0.2 SUV, P < 0.04). However, early (90 to 120 min) myocardial DFA fractional uptake was unchanged after HIGHCAL (0.053 ± 0.013 vs. 0.059 ± 0.033 min^{-1}, P > 0.6). We found a negative correlation between change in myocardial DFA partitioning and change in dietary fibers intake per 1,000 kcal/d (ρ=-0.690, P < 0.07). Our preliminary results show that an increase in caloric intake is associated with a decrease in myocardial dietary fatty acids partitioning in healthy subjects.

P35

Age related differences in the cardiac proteome of proteins involved in signalling and response to ischaemia

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Introduction

It is clear that there is an age related variation in vulnerability to ischaemic and reperfusion injury during the postnatal period which occurs with a characteristic pattern rising towards 14-days postnatal before falling towards adulthood.

The reasons for this are unclear. We hypothesised that variations in the protein expression in key functions may account for some of these differences, and surveyed these families for developmental changes in abundance.

Methods

Hearts were excised from male Wistar rats at 7 (n=4), 14 (n=8), 28 days post-natal (n=8) and adults (n=7). Tissue was homogenised and protein extracted, then analysed by Mass Spectrometry- Tandem Mass Tagging. Peptide fragments were identified and parent proteins identified; those with a confidence level < 0.05 excluded. We identified over 10,800 unique proteins. Subsets of the proteins were identified including ion exchange, calcium handling, redox proteins and signalling molecules.

Results

Across all subsets we found significant alterations in protein abundance that match the pattern of ischaemic vulnerability, with an over two- fold increase seen between seven and fourteen days of age before falling towards adulthood. This

was seen in NCX, LTCC, RyR, SERCA, PLC, and Catalase amongst other species.

Conclusions

A correlation between observations of whole organ tolerance of ischaemia and abundance of significant cardiac proteins has been observed. The functional roles of these during ischaemia and reperfusion is unclear. In many cases the changes seen may be inconsequential but these data suggest avenues for functional study of selected targets, developmental variation in which is previously unknown.

P36

BMP-7 treatment induces monocyte to M2 macrophage differentiation and improves blood flow velocity in atherosclerosis

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We have previously shown that treatment with bone morphogenetic protein-7 (BMP-7) affects the presence of macrophage subtypes *in vitro* and *in vivo* at an early stage of atherosclerosis; however, it remains unknown whether BMP-7 treatment affects development and progression of atherosclerosis at a mid-stage of the disease. We therefore performed a Day 28 (D28) study to examine BMP-7's potential to affect monocyte differentiation. Atherosclerotic plaque formation was developed using our standard method and ApoE$^{-/-}$ mice were sacrificed at D28. Animals were treated with IV injections of BMP-7 at 200ug/kg of bodyweight. Immunohistochemical staining was performed to determine BMP-7's effect on inflammatory M1 (iNOS) and anti-inflammatory M2 (CD206, Arginase-1) macrophages, and monocytes (CD14) present within the arterial area. BMP-7 significantly reduced inflammatory macrophage presence and significantly increased the presence of anti-inflammatory macrophages ($p<0.05$). Western blot analysis confirms a significant increase in pro-survival kinase ERK and a significant reduction in pro-inflammatory kinases p38 and jnk in BMP-7 treated mice ($p<0.05$). ELISA analysis showed a significant reduction in pro-inflammatory cytokines (IL-6, MCP-1, and TNF-α) and a significant increase in anti-inflammatory cytokine (IL-1ra) in BMP-7 treated mice ($p<0.05$). In summary, our data indicates BMP-7 treatment induces monocyte to M2 macrophage differentiation, increases anti-inflammatory cytokine levels (IL-1ra and IL-10), and improves blow flow velocity ($p<0.05$) compared to untreated animals. The mechanisms of macrophage differentiation are mediated by the p38, jnk, and ERK pathways indicating BMP-7 is capable of reducing the inflammation associated with atherosclerosis and slowing progression of the disease.

P37

Cardiomyocyte-specific deletion of the G protein-coupled estrogen receptor (GPER) leads to left ventricular dysfunction and adverse remodeling: a sex-specific gene profiling analysis

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Activation of G protein-coupled estrogen receptor (GPER) by its agonist, G1, protects the heart from stressors such as pressure-overload, ischemia, a high-salt diet, estrogen loss, and aging, in various male and female animal models. Due to nonspecific effects of G1, the exact functions of cardiac GPER cannot be concluded from studies using systemic G1 administration. Moreover, global knockdown of GPER affects glucose homeostasis, blood pressure, and many other cardiovascular-related systems, thereby confounding interpretation of its direct cardiac actions. We generated a cardiomyocyte-specific GPER knockout (KO) mouse model to specifically investigate the functions of GPER in cardiomyocytes. Compared to wild type mice, cardiomyocyte-specific GPER KO mice exhibited adverse alterations in cardiac structure and impaired systolic and diastolic function, as measured by echocardiography. Gene deletion effects on left ventricular dimensions were more profound in male KO mice compared to female KO mice. Analysis of DNA microarray data from isolated cardiomyocytes of wild type and KO mice revealed sex-based differences in gene expression profiles affecting multiple transcriptional networks. Gene Set Enrichment Analysis (GSEA) revealed that mitochondrial genes are enriched in GPER KO females, whereas inflammatory response genes are enriched in GPER KO males, compared to their wild type counterparts of the opposite sex. The cardiomyocyte-specific GPER KO mouse model provides us with a powerful tool to study the functions of GPER in cardiomyocytes. The gene expression profiles of the GPER KO mice provide foundational information for further study of the mechanisms underlying sex-specific cardioprotection by GPER.

P38

Carotid versus coronary atherosclerosis burdens in acute compared to chronic symptomatic coronary artery disease

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Purpose. Prediction of coronary events remains elusive. Carotid atherosclerosis may be a surrogate for coronary risk, as carotid and coronary disease occur simultaneously - albeit at times with a weak association - depending on clinical presentation. We investigated coronary and carotid atherosclerosis in men with newly discovered coronary artery disease (CAD) presenting with acute ST-segment elevation myocardial infarction (STEMI) *vs.* long-standing chronic stable angina (CSA) referred for coronary artery bypass graft surgery.

Methods. Bilateral carotid artery and three-vessel coronary artery atherosclerosis burdens were measured within 1 month, respectively by 3D volumetric carotid magnetic resonance imaging (MRI) and coronary angiography-derived modified CASS-50 score.

Results. Men with new-onset acute STEMI (*n*=50) and long-standing CSA (*n*=50), matched for age, were prospectively enrolled (58.6 ± 8.8 years). The prevalence of hypertension (*p*=0.013), dyslipidemia (*p*=0.013), and history of cardiovascular disease in a first-degree relative (*p*<0.001) were greater in CSA *vs.* STEMI. All symptomatic CAD participants had presence of carotid atherosclerosis on MRI. Coronary burden was greater in CSA *vs.* STEMI (modified CASS-50 score: 3 *vs.* 1, *p*<0.0001), while carotid burden was greater in STEMI *vs.* CSA (wall volume: 201.25 ± 43.44 *vs.* 173.11 ± 46.80mm^3/4mm, *p*=0.018). Normalized wall index of internal carotid was associated with modified CASS-50 in STEMI (*rho*=0.398, *p*=0.022).

Conclusions. Carotid atherosclerosis was observed in all patients of our sample with symptomatic CAD of either acute or chronic course. However, the burden of atherosclerosis is greater in the *coronary* arteries of long-standing CSA, but greater in the *carotid* arteries of new-onset acute STEMI.

P39

Does TAG/FA cycling contribute significantly to cold-induced thermogenesis? Determining the metabolic fate of oversupplied fatty acids during a mild cold exposure in humans

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Cold exposure triggers cold-defence responses and mobilizes substrates to fuel the thermogenic processes. In particular, exposure to cold stimulates white adipose tissue lipolysis 2-fold, thereby increasing the appearance rate of fatty acids (FA) into the circulation. With FA supply reaching levels that are double the demand, the metabolic fate of these FA is unclear. We propose that if these FA are not oxidized, they must necessarily be stored through re-esterification, thereby increasing the thermogenic contribution of the triglyceride-FA (TAG/FA) cycle to whole body heat production during cold exposure. Using stable isotope methodologies and PET with ^{18}F-fluoro-thiaheptadecanoic acid, the aim of this study was to monitor the metabolic fate and kinetics of non-esterified FA and glycerol in cold-exposed humans. Non-acclimated men with well-controlled type 2 diabetes, age-matched control subjects and young lean control subjects took part in acute cold exposure studies. Our findings demonstrate that total TAG/FA cycling increased 2-3 fold during cold exposure in all three groups (from 925 ± 148 µmol.min^{-1} to 1938 ± 216 µmol.min^{-1}, *P* = 0.0002). The energy cost of this recycling therefore increased 2-fold (from 0.6 ± 0.5 kJ.min^{-1} to 1.2 ± 0.7 kJ.min^{-1}, *P* < 0.0001). Ingesting nicotinic acid, an inhibitor of intracellular lipolysis, during cold exposure completely abolished this cold-induced increase in TAG/FA cycling. With some concerned that the cold-induced rise in FA and triglycerides may pose unintended risks in atherosclerotic plaque development or instability, the present findings suggest that much of these fatty acids are stored for subsequent hydrolysis.

P40

Effect of moderate exercise training and continuous normobaric hypoxia on postinfarction heart failure in rats

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Adaptation to continuous normobaric hypoxia (CNH) and exercise training (ET) are known to protect the heart against acute ischemia/reperfusion (I/R) injury. Much less is known about potential therapeutic effect of these interventions on myocardial infarction (MI). The aim of this study was to find out whether CNH (12% O_2) or ET (treadmill; 60 min/day for 5 days/wk) can attenuate the progression of postinfarction heart failure. MI was induced by coronary artery occlusion in 2-month-old male rats. Animals were assigned to six groups: i) sham-operated, ii) MI sedentary normoxic controls, iii) CNH for

3 wks before MI, iv) CNH for 3 wks since day 7 after MI, v) ET (30 m/min) for 2 wks before MI, and vi) ET (15 m/min) for 3 wks since day 7 after MI. Echocardiographic examination of the left ventricle (LV) was performed before and 7, 14 and 28 days after MI. Invasive LV pressure measurement was then performed and hearts were collected for histology. MI resulted in LV scar circumference of 38%, gradual increase in systolic and diastolic LV diameter and markedly decreased fractional shortening compared to sham group. CNH before MI reduced mortality from 55% in normoxic controls to 26%. Postinfarction exposure to CNH attenuated LV dilatation. ET before or after MI had no effect on analyzed parameters. Our data suggest that preventive adaptation to CNH reduces acute mortality during I/R insult. Therapeutic exposure to CNH has certain potential to attenuate the progression of unfavorable changes in ventricular geometry induced by post-ischemic heart failure.

P41

Exposure to low-dose ionizing radiation from cardiac procedures and risk of malignancy in adults with congenital heart disease

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We showed that congenital heart disease(CHD) patients were exposed to increasing number of low-dose ionizing radiation(LDIR) from cardiac procedures between 1990 and 2005. We also showed an increase in prevalence of cancer among the adults with CHD(ACHD) in Quebec relative to the general population. We aimed to measure the association between LDIR exposure and cancer incidence in ACHD.

We performed a nested case-control study using the Quebec CHD Database. Incident cancer cases were identified from 1995 to 2010 (5-year wash-out period). Each case was matched on age, sex and calendar year with 4 controls. LDIR exposure was measured as lifetime cumulative number of LDIR cardiac procedures (cardiac catheterization, CT scans, nuclear medicine and arrhythmia-related) prior to incident cancer diagnosis for each case-control pair.

A total of 2690 cases were matched with 10748 controls. Genitourinary, digestive, respiratory, breast and hematological cancers were accounted for 88.2% of cancers. In a restricted population of 2052, 18-65 year olds (median age=53), each additional LDIR procedure exposure was associated with 1.12-fold (95%CI: 1.073-1.166) increase in cancer risk. The impact of LDIR exposure as a categorical variable using conditional logistic regression is shown using patients with ≤1 procedures as reference. A sensitivity analysis in those with hematological cancers revealed an 6.3-fold (95%CI: 1.9-21.1) increase in cancer incidence related to ≥6 procedures.

We demonstrated an association between increase in exposure to LDIR-cardiac procedures and incident cancer risk in this population-based ACHD cohort. Studies are required to further understand this possible risk and to confirm these important findings in additional data sources.

P42

Identification and characterization of a miRNA cohort initiated transitional program that controls cell cycle arrest of the perinatal heart

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During fetal and early perinatal development the myocardium undergoes a period of hyperplastic growth resulting in an exponential increase in the number of cardiomyocytes that will constitute the adult heart. Soon after birth, cardiomyocytes proceed through a final round of cell division in the absence cytokinesis that results in binucleation of >95% of adult cardiomyocytes. All subsequent increase in myocardial mass is accomplished by myocardial hypertrophy. Fetal heart genes are re-activated with the onset of pathological hypertrophic or dilated cardiomyopathies, yet there is no evidence of cardiomyocyte re-entry into cell cycle. Despite the importance of this phenomenon, little is known about the molecular basis for the transition from hyperplastic to hypertrophic-based myocardial growth. **We hypothesize a specific perinatal heart gene program is necessary for the normal transition from a fetal heart gene program to an adult heart gene program**. To identify molecular mechanisms and pathways involved in cardiac myocyte differentiation during the perinatal transition, cardiomyocyte gene expression and micro-RNA profiles during the perinatal period were determined. Our analysis revealed a down regulation of mitotic cell cycle pathways (p=1.38E-44) with an up-regulation of cell cycle arrest markers (p=0.00279) between E19 and 5 days post-birth. Also, 63 cell cycle genes are collectively down regulated (p=4.3x10-4) between 5 days and 10 days post-birth. We identified 131 genes that are

transiently up regulated at 5 days compared to E19 and 10D. The data generated from this study provide new insight into the molecular mechanisms by which cardiomyocytes regulate and permanently exit the cell cycle.

P43

Influence of ACE inhibitors on frailty and cardiac function in middle-aged female C57BL/6 mice

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ACE inhibitors improve exercise capacity in functionally impaired older adults without cardiovascular disease and improve physical performance in aged rodents. We hypothesised that chronic treatment with ACE inhibitors may attenuate frailty through changes in cardiac function. To explore this, female C57BL/6 mice (12 months old) were given an ACE inhibitor (enalapril; 40 mg/kg/day; n=10) or control (n=10) for 3 months. At baseline, and after 3 months, frailty was quantified as deficit accumulation with the mouse clinical frailty index (FI). Blood pressure (BP) was measured with a tail-cuff and *in vivo* cardiac function was measured using echocardiography. After 3-4 months, contractile function and calcium homeostasis (fura-2) were measured simultaneously in field-stimulated cardiomyocytes (2 Hz), isolated from the mice. FI scores were significantly lower in the enalapril group when compared to control mice (0.14 ± 0.01 vs 0.21 ± 0.03, $p<0.05$) after 3 months. BP, heart structure and systolic and diastolic contractile function were not significantly different between the enalapril and control groups. Cardiomyocytes obtained from enalapril-treated mice, compared to control mice, showed increased cell shortening (1.6 ± 0.2 vs 3.0 ± 0.5 %, $p<0.001$) and increased velocity-to-peak contraction (0.068 ± 0.005 vs 0.133 ± 0.016 µm/ms, $p<0.001$) and ½ relaxation (0.044 ± 0.005 vs 0.100 ± 0.016 µm/ms, $p<0.001$), with no changes in underlying calcium transients. These results show that ACE inhibitors attenuate frailty in middle-aged animals, even in the absence of cardiovascular disease, and suggest that ACE inhibitor treatment may enhance cellular contractile function independent of effects on calcium homeostasis.

P44

Post-translational modification of mitochondrial Ca^{2+} uniporter mediates mitochondrial Ca^{2+} overload and cell death in the heart

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Mitochondrial Ca^{2+} uptake via the mitochondrial Ca^{2+} uniporter (MCU) is important for the cardiomyocyte survival and death. Basal tyrosine phosphorylation (P-Y) of MCU was reported from mass spectroscopy of human and mouse tissues. However, it is still not clear whether the post-translational modifications of MCU such as phosphorylations modulate its channel properties as well as mitochondrial functions in cardiomyocytes. Here we showed that P-Y of MCU activates mitochondrial Ca^{2+} uptake and induces mitochondrial Ca^{2+} overload, followed by mitochondrial superoxide (mSO) overproduction and cell death signaling activation n cardiomyocytes. alpha$_1$-adrenoceptor (alpha$_1$-AR) signaling activated mitochondrial matrix-localized tyrosine kinase named Pyk2 and enhanced the interaction between Pyk2 and MCU, which subsequently increased P-Y of MCU and mitochondrial Ca^{2+} uptake in rat cardiomyocytes. We confirmed that two tyrosine sites that showed an increase of phosphorylation levels in response to a_1-AR stimulation *in situ*. In addition, the overexpression of dephospho-mimetic mutants of MCU failed to increase mitochondrial Ca^{2+} uptake in response to cytosolic Ca^{2+} elevation, whereas wild-type MCU overexpression dramatically accelerated mitochondrial Ca^{2+} uptake compared to control cells. Finally, persistent alpha$_1$-AR stimulation increased mSO generation, cytochrome C release, and cardiomyocyte death. These effects were abolished by the overexpression of a dominant-negative mutant of MCU in cardiomyocytes. In conclusion, MCU contains Pyk2-specific phosphorylation site(s) and P-Y of MCU activates its channel function. Persistent P-Y of MCU induces mitochondrial Ca^{2+} overload, mSO generation and apoptosis in cardiomyocytes.

P45

Prostaglandin E2 mediated secretion of chemokines prevents rejection of implanted allogeneic mesenchymal stem cells and restores post-infarction ventricular function

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The unique immunoprivileged nature of bone marrow derived allogeneic mesenchymal stem cells (MSCs) makes them excellent candidate cell type for clinical applications. Outcome of preclinical studies and initial clinical trials suggested that after transplantation to the infarcted heart, MSCs were able to improve cardiac function. However the long term fate of transplanted cells in these studies was not determined. We recently reported that allogeneic MSCs improved heart function after transplantation in the infarcted heart. However, late after implantation, cells lost their immunoprivilege, and were rejected. We started investigations to study the mechanisms of rejection. We found that MSC immunoprivilege

is mediated by prostaglandin E2 (PGE2)-induced endogenous secretion of two critical chemokines, CCL12 and CCL5. These chemokines induced T cell chemotaxis toward MSCs, suppressed T cell proliferation, and increased T regulatory cell number. Myogenic differentiation of MSCs was associated with decreased PGE2 levels and loss of immunoprivilege. Treatment of differentiated MSCs with PGE2 maintained the levels of CCL12 and CCL5 and preserved their immunoprivilege. In a rat myocardial infarction (MI) model, allogeneic MSCs (3×10^6 cells/rat), with or without a biodegradable hydrogel that slowly released PGE2, were injected into the infarct region. Five weeks later, MSCs were rejected in the control group, in PGE2 group significant number of cells survived and heart function was significantly improved. Therefore, immunoprivilege of MSCs was maintained by PGE2-induced secretion of CCL12 and CCL5. MSC differentiation resulted in decreased PGE2 levels and loss of immunoprivilege. Maintaining PGE2 levels preserved immunoprivilege and improved cardiac function after an MI.

P46

Role of miR-181 family in the heart: A tale of two intracellular compartments (P46)

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Background. MicroRNA (miR) are a type of non-coding RNA that can repress the expression of target genes through post-transcriptional regulation. In addition to numerous physiologic roles for miRNAs, miRNAs play an important role in pathophysiologic processes affecting cardiovascular health. Previously, we reported that nuclear encoded miR-181c is present in heart mitochondria, and importantly overexpression affects mitochondrial function by regulating mitochondrial gene expression.

Methods and Results. To investigate further how the miR-181 family affects the heart, we suppressed miR-181 using a miR-181-sponge containing ten repeated complimentary miR-181 "seed" sequences, and generated a set of stable-H9c2 cells by transfecting either a scrambled or the miR-181-sponge sequence. Sponge-H9c2 cells showed a decrease in ROS production and reduced basal mitochondrial respiration, and protection against doxorubicin-induced oxidative stress. We found that miR-181a/b targets PTEN, and the sponge expressing stable cells had increased PTEN activity and decreased PI3K signaling. Protection against doxorubicin is augmented in sponge-H9c2 expressing cells treated with siRNA against PTEN. In addition, we have used miR-181a/b$^{-/-}$ and miR-181c/d$^{-/-}$ knockout mice and subjected them to ischemia-reperfusion injury. Our results suggest divergent effects of different miR-181 family members. miR-181a/b targets PTEN in the cytosol, resulting in an increase in infarct size in miR-181a/b$^{-/-}$ mice due to increased PTEN signaling whereas miR-181c targets mt-COX1 in the mitochondria, resulting in decreased infarct size in miR-181c/d$^{-/-}$ mice.

Conclusions. The miR-181 family alters the myocardial response to oxidative stress, notably with detrimental effects by targeting mt-COX1 (miR-181c), or with protection by targeting PTEN (miR-181a/b).

P47

Role of nuclear T-tubules in human vascular smooth muscle cell function and disease (P47)

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Utilizing various organelle detecting probes and 3D confocal microscopy, our studies demonstrate the presence of two kinds of nuclear structures in human vascular smooth muscle cells (hVSMCs). First, an ER-like nuclear structure, which is a resident nuclear entity and possesses Glucose-6-phosphatase activity. It is endowed by Ca^{2+}-ATPases, IP_3 and Ryanodine receptors. Second, nuclear tubular structures, which appear to be invaginations of the nuclear envelope membranes into the nucleoplasm, possess nuclear pores and bear Ca^{2+}-ATPase pumps. They seem to contain Ca^{2+} and to date exhibit a GPCR, the AT_2 receptor of Ang-II. These nuclear tubular invaginations seem to be dynamic in nature and are absent from isolated nuclei.

Taking into consideration the fact, that cytosolic and perinuclear Ca^{2+} transients can propagate to the nucleus, and because spontaneous and pharmacologically induced Ca^{2+} sparks, puffs and waves can occur in isolated nuclei bathed in cytosolic medium, we can conclude that cytosolic Ca^{2+} seems to be important in regulation of nuclear Ca^{2+} homeostasis. However, on the other hand, since nuclear Ca^{2+} transients and sub-nuclear Ca^{2+} oscillations could be generated in zero cytosolic Ca^{2+} conditions, this suggests that nuclear Ca^{2+} can possess the ability to regulate itself independently of cytosolic Ca^{2+}.in addition, our results showed that hypertrophy is associated to a decrease in NTTs number. In conclusion, nuclear Ca^{2+} can be regulated both dependently and independently of cytosolic Ca^{2+} and the newly identified nuclear structures have the potential of playing an important

role in this regulation as well as markers of hypertrophy. (Granted by CIHR and NSERC)

P48

Striatin is a novel risk gene for human dilated cardiomyopathy that regulates cardiomyocyte response to adrenergic stimuli

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Mounting evidence implicates striatin (STRN), a scaffold protein originally found in AC rich fraction, in the pathogenesis of cardiomyopathies. We screened 96 samples of patients with idiopathic dilated cardiomyopathy (DCM) and found 277 novel heterozygous variants, within the STRN gene, with two hot spots (50% in exon 17, and 33% in exon 2). Western blot revealed downregulation of STRN proteins in human DCM vs normal ventricle samples (post-mortem). *In vitro* studies, using cultured cardiomyocytes (rat), showed that knockdown of STRN reduced their rate of spontaneous contraction by almost 45%. Surprisingly, isoproterenol challenge failed to induce positive chronotropy in cells with reduced STRN expression, thus phenotypically mimicking end stage heart failure. Moreover, the amplitude of intracellular calcium increase in KCl-depolarized cardiomyocyte was lower in STRN knockdown cells when compared to controls. In contrast, the overexpression of striatin increased the rate of contraction (~ 4 fold) of cultured cardiomyocyte indicating that striatin is involved in regulating their contraction. Collectively, our data show that STRN emerges as a novel marker for human cardiac failure and it regulates intracellular calcium and cardiomyocyte response to adrenergic stimuli.

This work is supported by a KACST operating grant (#13-BIO1452-20) to MN.

P49

Use of high resolution Doppler ultrasound for the diagnosis of endothelial dysfunction in young adults exposed to tobacco

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Background: High resolution ultrasonography diagnoses endothelial dysfunction noninvasively. Endothelial dysfunction is an early event in the genesis of atherosclerosis. Smoking is the most important modifiable coronary risk factor. The purpose of this study was to determine the endothelial function in young adults exposed and unexposed to tobacco smoke and the effects of acute exposure to it.

Method: A study of cases and controls that included 30 volunteers was done. Students from third year of medical school in Holguin under acute exposure to cigarettes were included as cases and students unexposed to cigarettes were considered as controls. Brachial artery diameter and brachial artery flow velocity were measured at baseline, after reactive hyperemia and post sublingual administration of nitroglycerin.

Results: Average age of the participants was 21 years old. Male was the predominant gender. Smokers were smoking for 5 years. Smokers showed significant endothelial dysfunction compared to non-smokers. Arterial dilatation mediated by the endothelium was significantly higher in non-smokers than in smokers (p=0.005). Non-endothelium mediated arterial dilatation was significantly impaired in smokers compared to non-smokers (p=0.02). After reactive hyperemia there was a significant increase in blood flow in non-smokers (+ 61%) than in the smokers group (+29%). After acute exposure to cigarette smoke, arterial dilatation and brachial flow velocity were lower than those achieved in the abstinence phase (p=0.005).

Conclusions: Endothelium-dependent arterial dilation is impaired in young smokers and it worsens even after acute exposure to cigarette smoke. Endothelial dysfunction can be detected at early stages of smoking and at young ages.

Invited Speaker Abstracts

Necroptosis in diseased heart

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The death of cardiomyocytes induced by various damaging stimuli can result in several forms of heart dysfunction. Because of a low capability of cardiomyocytes to regenerate and renew the loss of cardiac cells might be a rate-limiting step in the development of adverse cardiac remodeling, and disturbances in contractile function. Until recently, apoptosis and necrosis have traditionally been believed to be responsible for the significant loss of cardiomyocytes. In our study, the existence and relevance of necroptosis, a regulated form of necrosis, has been proposed to participate in the pathogenesis of acute myocardial ischemia-reperfusion injury as well as heart failure after myocardial infarction. Necroptosis has also been evidenced in other forms of failing hearts. Although the expression of the most terminal component in the necroptosis pathway was higher in dilated cardiomyopathy there was no correlation with main markers of tissue injury. Interestingly, the adaptation to short ischemic episodes lowered infarct size without affecting the levels of major pro-necroptotic proteins. A pharmacological inhibition of necroptosis produced neither additive nor synergistic effects with cardioprotection associated with ischemic preconditioning with respect to excitation-contraction coupling and the extent of necroptosis. In the presented work, the evidence of necroptosis in certain models of cardiac injury will be provided and the underlying pathologic mechanisms will be discussed. *Supported by grants APVV-15-607, VEGA 1/0271/16 and Slovak Society of Cardiology.*

Epicardial adipose tissue and vitamin D in the immunomodulation of coronary artery disease

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Objective: Epicardial adipose tissue (EAT) is present in close proximity to the adventitia of coronary arteries and the underlying myocardium. We examined if obesity-induced inflammatory phenotype of EAT is exacerbated by vitamin D(VD)-deficiency and enhanced intimal hyperplasia and restenosis following coronary intervention.

Methods: Yucatan microswine were fed with high fructose high cholesterol (HFHC) diet. Atherosclerotic animals were subjected to angioplasty and intravascular stenting in coronary arteries. Coronary stenosis was examined by angiography and OCT followed by histopathological and immunohistochemical examination of the EAT and coronary arteries. Preadipocytes of EAT were examined for the underlying molecular mechanisms.

Results: Swine fed HFHC diet developed obesity and many signs of metabolic syndrome, and developed intimal hyperplasia and restenosis following intervention of the atherosclerotic coronary arteries. There was significant infiltration of CD68+ cells, mild CD206 immunostaining (M2-macrophages), which was increased in the adipocytes of VD-supplemented swine. VD-deficiency was associated with increased infiltrates and decreased SOCS3 expression in EAT. In preadipocytes, VD inhibited NF-kB activation and reduced importin-?3 levels through increased VDR expression. VD-deficiency caused extensive progression in coronary artery disease and advanced atherosclerotic plaques, which are linked to increased importin-?3 and nuclear NF-kB in EAT.

Conclusions: HFHC diet accelerates coronary artery lesions and develops inflammatory phenotype of EAT, which is enhanced by VD-deficiency. VD attenuates NF-?B activation by targeting importin-?3. VD-deficiency accelerates CAD progression through enhanced chronic inflammation of EAT by upregulation of importin-?3, which enhances NF-kB activation. Thus, VD supplementation could be beneficial in the prevention and treatment of coronary artery disease. (Supported by research grants from NIH-NHLBI R01HL116042 and R01HL120659)

Nitric oxide and regulation of blood pressure

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Nitric oxide (NO) donors are used as promising therapeutic agents for the treatment of cardiovascular diseases such as angina pectoris, myocardial infarction and congestive heart failure. However, its role in the regulation of blood pressure (BP) is not clear. We previously showed that nitric oxide (NO) donor, SNAP, decreased the enhanced expression of Giα proteins and associated functions in aortic vascular smooth muscle cells (VSMC) from spontaneously hypertensive rats (SHR). Since the enhanced expression of Giα proteins is implicated in the pathogenesis of hypertension, the present study was undertaken to investigate the effect of *in vivo* treatment of SHR with NO donor; sodium nitroprusside (SNP) on the development of high BP and to explore molecular mechanisms responsible for this response. 8 week-old SHR and Wistar-Kyoto (WKY) rats were intraperitoneally injected with

SNP (0.5mg/kg body weight) twice a week for two weeks. SNP treatment attenuated the high BP by about 50 mmHg without affecting the BP in WKY rats. In addition, increased production of superoxide anion, peroxynitrite, NAD(P)H oxidase activity, overexpression of NAD(P)H oxidase subunits, Giα proteins, AT1 receptor, increased phosphorylation of growth factor receptors, c-Src, and ERK1/2 in VSMC from SHR were attenuated by SNP treatment. Furthermore, the hyperploliferation of VSMC from SHR was also inhibited by SNP treatment. These results suggest that *in vivo* treatment of SNP attenuates the high BP in SHR through the inhibition of enhanced levels of Giα proteins, oxidative stress, c-Src and growth factor receptors activation and MAPK signaling pathways (Supported by CIHR).

Sodium-hydrogen exchanger blocker for the treatment of heart and vascular failures in Becker and Duchenne muscular dystrophy

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Cardiomyopathy is defined as a cardiac muscle disease that is characterized by necrosis, followed by hypertrophy associated with a progressive development of heart failure, which eventually leads to premature sudden death. Hereditary cardiomyopathy in the hamster, more specifically the UM-X7.1 colony, provides a unique possibility for studying the pathology and clinical course of primary congestive cardiomyopathies. Using this animal model, it was reported that heart failure is associated with an intracellular calcium overload. However, treatment with calcium blockers did not give the expected beneficial effects. In this study, we showed that an intracellular sodium overload takes place before the appearance of any visible pathological markers of cardiomyopathy. The early development of the sodium overload was associated with an increase in the density of the sodium-hydrogen exchanger. This took place in both the cardiac and vascular systems and led to hypertrophy, heart failure and eventually premature death. However, blockade of the NHE1 prevented sodium overload as well as all signs of heart failure and prevented early death. This work is supported by the Canadian Institutes of Health Research (CIHR).

Clinical importance of grade I left ventricular diastolic dysfunction

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Introduction: Grade I Diastolic dysfunction is related to abnormalities of ventricular relaxation. QT dispersion, an electrical phenomenon, is associated with increased risk of severe arrhythmias and sudden cardiac death. Objective: To evaluate the circadian variation of QT dispersion and prevalence of arrhythmia in patients with grade I left ventricular diastolic dysfunction. Method: Observational, transversal study. Assessed 44 ambulatory patients: Group I, 26 patients with grade I left ventricular diastolic dysfunction, mean age 55.7± 5.8, 34% arterial hypertension, 7% type II diabetes, 27% sedentary, 12% smokers, and 20% did not diagnosed cardiac disease. Group II, 18 healthy, mean age 47.4 ± 6.9. Underwent 12 lead-Holter. Measured QT dispersion in the morning, afternoon, evening and at night, during sleep, and evaluated prevalence of arrhythmias. Results: Average heart-rate-corrected QT dispersion in Group I was 71.7 ± 13.3 in the morning, 69.1 ± 9.9 in the afternoon, 68.2 ± 9.6 in the evening, and 65.1 ± 9.6 ms during sleep. In Group II, the average were 66.9 ± 7,9, 66.8 ± 8.6 , 67 ± 5,2 and 61.4 ± 7.5 ms, respectively. The comparison between the two groups did not present any statistically significant difference (p= 0,2016; p= 0,4379; p= 0,6588 and p= 0,2189, respectively). In 30.8% of Group I (62.5% arterial hypertension and 37.5% without cardiac disease) mean heart-rate-corrected QT dispersion >80ms (cut-off 71ms) and 3.8% presented ventricular extrasystole higher than 10 /h. Conclusion: The study evidencedIncreased QT dispersion ≥ 80ms in patients without cardiovascular symptoms, with grade I left ventricular diastolic dysfunction.

Deletion of muscle-enriched A-type lamin-interacting protein (MLIP) leads to cardiac hyperactivation of Akt/mTOR and impaired cardiac adaptation

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Aging and diseases generally result from tissues inability to maintain homeostasis through adaptation. The adult heart is particularly vulnerable to disequilibrium in homeostasis as its regenerative abilities are limited. Here, we report that Muscle enriched A-type lamin interacting protein (MLIP), a unique protein of unknown function, is required for proper cardiac adaptation. Mlip$^{-/-}$ mice exhibited normal cardiac function despite myocardial metabolic abnormalities and cardiac-

specific over activation of Akt/mTOR pathways. Cardiac-specific MLIP overexpression led to an inhibition of Akt/mTOR, providing evidence of a direct impact of MLIP on these key signalling pathways. Mlip$^{-/-}$ hearts showed an impaired capacity to adapt to stress (isoproterenol-induced hypertrophy), likely due to deregulated Akt/mTOR activity. Genome Wide Association Studies showed a genetic association between *Mlip* and early response to cardiac stress, supporting MLIP's role in cardiac adaptation. Together, these results revealed that MLIP is required for normal myocardial adaptation to stress through integrated regulation of the Akt/mTOR pathways.

Biophysical, molecular and pharmacological characterization of Nav channels from induced pluripotent stem cells derived cardiomyocytes

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The ability to differentiate patient specific hiPSC into cardiac myocytes (hiPSC-CM) offers exciting perspectives for cardiovascular research. A monolayer-based differentiation protocol based on the modulation of wnt signalling was used to generate functional hiPSC-CM from a healthy human subject. Cardiomyogenesis was assessed using both cardiac-specific immunofluorescence staining and patch-clamp recordings. Distinct electrophysiological features indicated that three hiPSC-CM subpopulations were generated and exhibited action potential shapes and durations consistent with nodal-, auricular-, and ventricular-like cells. hiPSC-CM displayed spontaneous electrical activity as well as a sarcomer-like organization of contractile proteins (troponin T, myosin light chain 2v). Electrophysiological, pharmacological and molecular characterization revealed that in addition to the principal Nav1.5 channels, neuronal tetrodotoxin (TTX) sensitive Nav1.7 channels were also significantly expressed in hiPSC-CM accounting for ~20% of Na+ current The majority of the Na+ current was resistant to block by micromolar concentrations of TTX while therapeutic concentrations of lidocaine, a class I antiarrhythmic, also blocked INa in a use-dependent manner. Nav1.5 and Nav1.7 protein expression and maturation profiles appeared to be highly comparable between hiPSC-CM and native human cardiac tissues as opposed to stably expressing cell lines. The four Navb regulatory subunits were found to be all expressed in hiPSC-CM with b3 as the preponderant subtype. Similarly to the human heart, hiPSC-CM expressed several Nav1.5 splice variants, including neonatal and adult forms.

All together, our data propose hiPSC-CM as a valuable and reliable model to study developmental and pathogenic processes in human cardiomyocytes and to develop novel relevant therapeutics for cardiac Na^+ channels.

Novel approaches to treating cardiac fibrosis

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Cardiac fibrosis remains a clinical conundrum: despite playing a significant pathological role in heart failure and arrhythmogenesis, leading to increased patient morbidity and mortality, fibrosis lacks any kind of primary treatment. This gap in patient care stems from both an incomplete understanding of the underlying mechanism and from a lack of specific therapeutic targets. We have identified the transcription factor scleraxis as a novel core regulator of fibrosis that shows tremendous potential for direct intervention as a means to prevent or attenuate disease progression. We found that scleraxis is induced in cardiac fibrosis and myocardial infarct scar, and in turn up-regulates a host of extracellular matrix components that contribute to fibrosis, particularly fibrillar collagen. The induction of myofibroblasts is a key pathological contributor to fibrosis, and we reported that scleraxis directly regulates mesenchymal cell phenotype, including induction of epithelial-to-mesenchymal transition and the conversion of cardiac fibroblasts to pro-fibrotic myofibroblasts. Scleraxis works synergistically with Smad transcription factors downstream of pro-fibrotic TGFβ, and is required for normal pro-fibrotic signaling by TGFβ, AngII, CTGF and mechanical stretch. Knockdown or knockout of scleraxis strongly reduces extracellular matrix gene expression, fibroblast to myofibroblast conversion and TGFβ/Smad signaling. Hearts of scleraxis null mice exhibit a 50% loss of cardiac extracellular matrix and fibroblasts, and conditional scleraxis gene deletion attenuates pressure overload-induced fibrotic gene up-regulation. A scleraxis dominant-negative mutant completely attenuated fibrillar collagen expression in primary cardiac myofibroblasts. Together, these results identify scleraxis as a potent and novel target for fibrosis therapy development.

Role of protease activation in cardiac dysfunction due to ischemia-reperfusion injury to the heart

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Since the activities of several proteases such as calpain and metallomatrix protease (MMP-2) are increased due to ischemia-reperfusion (I/R) injury, we examined their role and

mechanisms during the development of cardiac dysfunction in the isolated rat heart preparations. The activation of both calpain and MMP-2, impairment of cardiac performance and depression in sarcolemmal Na^+-K^+ ATPase as well as sarcoplasmic reticular Ca^{2+}-uptake and Ca^{2+}-release activities in the I/R hearts were found to be dependent upon the duration of ischemic insult. These I/R-induced alterations in protease activation, subcellular activities and cardiac function were simulated upon subjecting the heart to hypoxia-reoxygenation as well as perfusion with H_2O_2 or a mixture of xanthine plus xanthine oxidase. The I/R-induced changes in cardiac function, protease activation and subcellular activities were attenuated by ischemic preconditioning of the heart. Perfusion of the heart with antioxidants such as N-acetylcysteine and mercaptopropionyl glycine was observed to depress the I/R-induced alterations in cardiac function, protease activation and subcellular activities. The increase in both calpain and MMP-2 activation, decrease in Na^+-K^+ ATPase, Ca^{2+}uptake and Ca^{2+}-release activities as well as changes in cardiac function in the I/R hearts were attenuated by treatments with protease inhibitors such as leupeptin, MDL 28170 and doxycycline. These results suggest that the activation of both calpain and MMP-2 due to I/R may induce cardiac dysfunction as a consequence of subcellular defects. Furthermore, oxidative stress may play a critical role in the activation of both calpain and MMP-2 due to I/R injury.

Economic evaluation of heart failure management by specialized clinics in Quebec

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BACKGROUND: Heart failure (HF) prevalence is on a constant rise. The purpose of this study is to evaluate if multidisciplinary clinics are cost-effective on a local and provincial level.

METHOD: Our retrospective study evaluates the HF clinics in the Sherbrooke regional hospital and in the province of Quebec in 2014. We estimate the costs of the clinics and the consumption of resources by patients suffering of heart failure. One actual model considers that some of the patients were followed by an HF clinic and another factual model considers the absence of such clinic. In the actual model, we considered that the followed patients experience a reduction in their length of stay of 49% and 40% during admissions and readmissions respectively and a reduction of 40% in their admissions/readmissions rate. We also considered a 71% reduction in their emergency room consultation rate. Those numbers come from several studies and reports made in the province of Quebec.

RESULTS: The local HF clinic tested in the model is cost-effective. On a provincial level, we did not have the exact proportion of admissions, readmissions and emergency consultations attributed to followed patients, but the model become cost-effective if a minimal number of all visits for heart failure were attributed to patients followed by an HF clinic.

CONCLUSION: The study showed that HF clinics in a public funded health system are cost effective.

Criteria for the choice of ACE-inhibitors as drugs in the treatment of cardiovascular diseases

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Recent studies indicate that not all angiotensin-converting enzyme inhibitors (ACEIs) are optimal for the treatment of cardiovascular diseases (CVDs). New criteria emerge related to the chemical, pharmacodynamic and pharmacokinetic properties of each compound. A clinical profile for the choice of the ACEIs should include: lipophilicity, ACE binding duration, affinity for bradykinin (BK) binding site, half-life, increased BK availability, clinical impact and toxicity. By applying these criteria, two compounds, Perindopril and Ramipril, emerged as the best therapeutic tools for fulfilling the three basic criteria namely, reduction in blood pressure, morbidity and mortality, actually used to assess their therapeutic value. Compounds of the second category, Enalapril. Transdolapril, and Quinapril, did not show any clinical benefits with respect to placebo. However, the therapeutic evaluation of these last compounds suffered of limitations due to the short duration of trials and use of low dosage (as for Enalapril). This is been validated by selective clinical trials (*e.g.*, Europa (Perindopril) and HOPE (Ramipril)) and recent meta-analyses based on large numbers of trials.

Among the new therapeutic approaches is represented by the single compound LCZ-696, a combination of a Sartan (Valsartan) and a neutral endopeptidase (NEP) inhibitor (Sacubitril). This compound is intended to block the Angiotensin AT1 receptor and to inhibit the degradation of the atrial natriuretic peptide (ANP). Through these actions, the compound has shown therapeutic value in CVDs by reducing blood pressure and heart rate (through Valsartan) and acting as a vasodilator and natriuretic.

Impact of age and frailty on cardiac function in a mouse model

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Frailty is a state of increased vulnerability to adverse health outcomes for older adults of the same age. Importantly, frail patients with cardiovascular disease experience worse outcomes and higher mortality than non-frail patients, although why this occurs is unclear. We have quantified frailty in naturally ageing mice with novel "frailty index" (FI) tools based on the concept that frailty can be measured as the accumulation of health deficits. We have used these tools to investigate the relationship between frailty and cardiac structure and function in aged C57BL/6 mice. Hemodynamic function was measured in Langendorff-perfused hearts from aged mice and hypertrophy was evaluated by comparing heart weight to tibia length (HW:TL) ratios. Cellular morphology and contraction were measured in isolated ventricular myocytes. Results showed that aged mice (28-30 mos) had higher FI scores than young (<12 mos) and middle-aged (≈19 mos) animals, indicating they are more frail. Interestingly, left ventricular developed pressure (LVDP) and the rates of pressure development (+dP/dt) and decay (-dP/dt) declined dramatically as FI scores increased. By contrast, age itself was not correlated with changes in LVDP, +dP/dt, or -dP/dt. Furthermore, HW:TL ratios increased with frailty but not age. Similar changes were seen in isolated myocytes. Cellular hypertrophy increased as FI scores increased, while peak contractions declined with frailty. These results suggest that cardiac contractile dysfunction and hypertrophy are more closely linked to frailty than chronological age. As these age-dependant changes are maladaptive, our findings strongly suggest that frailty increases susceptibility to cardiovascular disease in the aging heart.

Crosstalk between the NPY and ET-1 systems in human endocardial endothelial cells

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The aim of this study was to test the hypothesis that a crosstalk may exist between the neuropeptide Y (NPY) and ET-1 systems. In order to verify this hypothesis, we used human left and right ventricular endocardial endothelial cells (hLEECs or hREECs, respectively) and verified whether NPY-induced secretion of ET-1 is mediated at least in part through stimulation of ETA and/or ETB receptors by their ligand, ET-1. Using the technique of indirect immunofluorescence coupled to quantitative 3-D confocal microscopy, as well as ELISA, our results showed that in hREECs, the NPY-induced release of ET-1 seems to be partly due to the activation of both ETA and ETB receptors. However, in hLEECs, this crosstalk either did not take place or contributed slightly to ET-1 secretion. Thus, our work highly suggests that the NPY-induced release of ET-1 in EECRs is partly due to NPY receptor activation as well as subsequent stimulation of the ETA and ETB receptors by the released ET-1. In contrast, the release of ET-1 by NPY in hLEECs is primarily due to NPY receptor activation and more specifically Y2 and Y5 receptors. These results support the concept that secretion of ET-1 could depend on the endothelial cell type and that right ventricular EECs play a role in releasing ET-1 into the right ventricle, whereas left ventricular EECs tune the level of ET-1 prior to its release into the arterial circulation. This work also highlights the importance of the secretory process of EECs. Supported by the CIHR and the HSFC.

Ginseng for the treatment of cardiovascular disease

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Ginseng is a herb which has been used for thousands of years in Asian societies for the treatment of a large number of clinical disorders. Ginseng can contain up to 200 active ingredients depending on ginseng type, among these being polysaccharides, polyacetylenes, peptides and amino acids. However, the major active components in ginseng are the ginsenosides identified in various parts of the ginseng plant including root, leaves, flower buds and seeds although key ginsenosides exerting biological effects are most abundant in the ginseng root. Many cardiovascular benefits attributed to ginseng include cardioprotection against ischemia, antihypertensive effects, attenuation of myocardial hypertrophy and heart failure, reduced hyperlipidemia as well as anti-atherogenic effects. Although results from animal studies with ginseng are generally robust, clinical evidence of efficacy is not as convincing, likely owing primarily to the paucity of well designed, randomized and controlled clinical trials. Adding to the complexity in understanding the cardiovascular effects of ginseng is the fact that each ginseng variety possesses distinct cardiovascular properties, due to their respective constituents, particularly ginsenosides, rendering it difficult to assign a general, common cardiovascular effect to ginseng. Additional challenges include identification of mechanisms (likely multifaceted) accounting

for the effects of ginseng and determining which ginsenoside(s) or other constituents, mediate these cardiovascular properties. These concerns notwithstanding, the potential cardiovascular benefits of ginseng are worthy of further studies in view of its possible development as a cardiovascular therapeutic agent, particularly as adjunctive therapy to existing medications.

(Studies were supported by the Canadian Institutes of Health Research)

HDL functionality, or HDL quality versus HDL quantity

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It has long been recognized that the concentration of plasma high-density lipoproteins (HDL) is inversely related to the risk of cardiovascular diseases. However, the results of recent pharmacological interventions resulted in a shift of concept. Rather than HDL levels, the functionality of HDL particles is increasingly regarded as potentially clinically important. The above developments have led to a redesign of the HDL hypothesis to a different and more subtle concept, namely the HDL function hypothesis.

The functionality of HDL corresponds to their ability to exert their anti-atherogenic activities, *i.e.*, antioxidant and anti-inflammatory activities, and to mediate reverse cholesterol transport (RCT), which is believed to be the main anti-atherogenic function of HDL.

Paraoxonase-1 (PON1) is a HDL-associated serum enzyme thought to make a major contribution to the antioxidant and anti-inflammatory capacities of HDL. Recent studies from our laboratory also shown that PON1 modulates the capacity of HDL to maintain cellular cholesterol homeostasis and to mediate RCT. PON1 activity decreases in several pathologies associated with atherosclerosis and this decrease affects significantly the functionality of HDL and their capacity to protect against the atherosclerosis process. Our results show that PON1 activity is significantly decreased with aging and also in acute coronary syndrome patients. The reduction of PON1 activity in the presence of risk factors for cardiovascular diseases may affect the anti-atherosclerotic properties of HDL. Therefore, the elucidation of the mechanisms by which PON1 regulates HDL functionality constitutes a new avenue for the prevention of the atherosclerosis process and cardiovascular complications.

Role of fibrosis associated transcription factors in hyperglycemia induced endothelial to mesenchymal transition (EndMT)

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Recent studies suggest that endothelial cells may transition into active fibroblasts through endothelial to mesenchymal transition and thus contribute to fibrosis. During EndMT endothelial cells lose epithelial characteristics and acquire mesenchymal phenotype.

We studied the effect of hyperglycemia on the mesenchymal transitioning of cardiac microvascular endothelial cells and potential involvement of transcription factors MRTF-A and ATF-3 during that transition.

Significant EndMT features observed after high glucose treatment such as decrease in epithelial markers, gain of mesenchymal markers, cytoskeletal actin remodelling and increased migration of cardiac microvascular endothelial cells. High glucose treatment increased the transcriptional activities of both the transcription factors, also induced nuclear localization of ATF-3. Immunohistochemistry of the myocardial tissues of streptozotocin treated diabetic rats also show nuclear localization of MRTF-A in the endothelial as well as cardiac myocytes, in parallel with an increase in interstitial collagen deposition. Induction of ATF-3 was also observed in microvessels of diabetic hearts.

These results suggest that high glucose is a potent stimulus of cardiac microvascular endothelial to mesenchymal transition and fibrosis associated transcription factors MRTF-A and ATF-3 appear to mediate this transition but need further investigation.

Cardioprotection conferred by chronic hypoxia combined with regular exercise in rats

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It is well established that chronic hypoxia and regular exercise training result in a sustainable improvement of myocardial tolerance to lethal ischemia/reperfusion (I/R) injury. As molecular mechanisms of these cardioprotective stimuli are not fully understood, it is unknown whether their combination can result in a synergetic effect. We, therefore, examined myocardial ischemic tolerance in adult male Wistar rats that exercised (treadmill; 30 m/min, 1 h/day) under conditions of

continuous normobaric hypoxia (CNH; FiO_2=0.12; 3 weeks). The animals were randomly assigned to one of following groups: normoxic (FiO_2=0.21) sedentary, normoxic trained, hypoxic sedentary, and hypoxic trained. Infarct size was assessed in open-chest rats subjected to I/R insult. Separate groups were used to quantify components reflecting myocardial inflammatory and redox status. Both CNH and exercise in normoxia reduced infarct size but exercise in hypoxia provided the same degree of protection as CNH alone. Treatment with antibody against tumour necrosis factor-α (TNF-α) abolished the infarct size-limiting effect of CNH. Unlike exercise alone, CNH increased TNF-α and interleukin-6 levels and the expression of TNF-α type 2 receptor, nuclear factor-κB, inducible nitric oxide synthase (iNOS), cytosolic phospholipase A_2α, cyclooxygenase-2, manganese superoxide dismutase (MnSOD) and catalase. Exercise in hypoxia abolished or attenuated these CNH-induced responses, except for iNOS and MnSOD upregulation. In conclusion, exercise training does not amplify the cardioprotection conferred by CNH. High ischemic tolerance of CNH hearts persisting after exercise can be likely attributed to the maintenance of increased myocardial antioxidant capacity regardless the suppression of TNF-α-dependent protective mechanism.

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Conductive polymer hydrogel improves electrical conduction velocity in the injured heart

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Coronary heart disease is the leading cause of death in the world and new treatments are required to prevent progressive heart failure after a myocardial infarction (MI). Cardiomyocyte necrosis after injury results in scar formation and myocardial fibrosis delays electrical impulse propagation, inducing dys-synchronous cardiac activation and uncoordinated contraction. We generated an injectable biocompatible conductive polymer that not only stabilized the infarct region, but also facilitated electrical signal propagation across scar tissue to enhance synchronous ventricular contraction.

Using a polymerization technique, we conjugated polypyrrole to chitosan and hydrogels were created by glutaraldehyde crosslinking. Electrical conductivity was measured by two-probe cyclic voltammetry. The conductive biomaterial had significantly greater conductivity compared to chitosan control. Improved electrical propagation was demonstrated when neonatal rat cardiomyocytes were cultured on the conductive biomaterial and the biomaterial had significantly higher Ca^{2+} transient propagation velocity evaluated by optical mapping. When the conductive biomaterial was employed for *in vivo* studies using an MI model, we found that control hearts showed disrupted propagation patterns and significantly reduced conduction velocities, while conductive biomaterial-treated hearts had higher conduction velocities that were similar to healthy controls. The research data suggest that this new biomaterial may be a potential new therapy to synchronize cardiac contraction.

Maspin-enriched exosomes released from sulforaphane-treated fibroblasts prevents hypertrophy in angiotensin II induced HL-1 cardiomyocytes

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Introduction: The communication between fibroblasts and cardiomyocytes underlies hypertrophic response of the heart to stressors, such as angiotensin-II (AngII). Fibroblast-derived exosomes (F-Exo), smallest nanosized extracellular vesicles, are mediators of such cross-talk. However, the control F-Exo's release is currently unknown. Sulforaphane (SFN), a class I histone deacetylase (HDAC1) inhibitor extracted from cruciferous vegetables, prevents AngII-induced cardiomyocytes hypertrophy. We tested whether SFN induces the release of anti-hypertrophic F-Exo, in vitro.

Methods: Murine fibroblasts were treated with non-toxic dose of SFN (3μM/7 days) or vehicle. Intact F-Exo were isolated by differential centrifugation and quantified by Nanosight Nanoparticle Tracking Analysis, and Western blot using anti-CD63. Hypertrophy of HL-1 cardiomyocytes was induced by AngII (100nM/12h). Cell surface area, an indicator of cell hypertrophy, was measured after 24h-incubation with 30μg exosomes isolated from SFN-treated (SFN-F-Exo) or untreated (F-Exo, control) fibroblasts. Uptake by HL-1 of DiA-labeled exosomes was measured under rest or AngII. Exosomal content of Maspin, a protease inhibitor with function of HDAC1 inhibitor, and acetyl-Histone H4 levels were assessed by Western blot.

Results: SFN increased acetyl-Histone H4 levels and induced the release of F-Exo with higher content of Maspin. Stressed HL-1 treated for 24h with SFN-F-Exo displayed cell surface area similar to resting cells, but not those treated with F-Exo.

Stressed HL-1 exhibited a ~3-fold increase in SFN-F-Exo uptake rather than F-Exo.
Summary/conclusion: SFN induces the release of Maspin-enriched F-Exo which prevent AngII-induced cardiomyocytes hypertrophy. Maspin-enrichment due to higher SFN-F-Exo uptake by stressed HL-1 may represent a novel mechanism of epigenetically-driven adaptive response to AngII.

Acetylation control of cardiac fatty acid β-Oxidation and energy metabolism in obesity and diabetes

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Alterations in cardiac energy metabolism are an important contributor to the cardiac pathology associated with obesity, diabetes, and heart failure. High rates of fatty acid β-oxidation with cardiac insulin resistance represent a cardiac metabolic hallmark of diabetes and obesity, while a marginal decrease in fatty acid oxidation and a prominent decrease in insulin-stimulated glucose oxidation are commonly seen in the early stages of heart failure. Alterations in post-translational modification of energy metabolic processes have recently been identified as an important contributor to these metabolic changes. In particular, lysine acetylation of non-histone proteins, which controls a diverse family of mitochondrial metabolic pathways, contributes to the cardiac energy derangements seen in obesity, diabetes, and heart failure. Lysine acetylation is controlled both via acetyltransferases (GCN5L1) and deacetylases (sirtuins), as well as by non-enzymatic lysine acetylation due to increased acetyl CoA pool size or dysregulated nicotinamide adenine dinucleotide (NAD^+) metabolism (which stimulates sirtuin activity). An important mitochondrial acetylation target are the fatty acid β-oxidation enzymes, with increased acetylation in obesitiy and diabetes leading to an increase in myocardial fatty acid ß-oxidation. This results in an excessvie use of fatty acids as a source of energy, which can ultimately lead to heart failure. As a result, pharmacological targeting of either cardiac mitochondrial acetylation (i.e inhibiting GCN5L1) or deacetylation (stimulating sirtuin activity) is a potential therapeutic approach to normalizing cardiac energy metabolism and preventing the development of heart failure in obesity and diabetes.

Cross talk between the heart and peripheral circulation: potential role of cardiac and peripheral endothelium

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Studying baroreceptor regulation of peripheral circulation in response to hypotension, we found that co-release of neuro-peptide (NPY) in peripheral circulation is responsible for decreasing vascular capacitance and increasing vascular stressed volume. We showed that decreasing baroreceptor tone increases plasma NPY but does not change endothelin (ET-1). However, a decrease in blood volume with a constant baroreceptor pressure increased ET-1 but not NPY, indicating endothelial release of ET-1 in response to a decrease in vessel stress. Subsequent studies in cardiac endocardial endothelial cells raise the potential for cross-talk between the heart and circulation. To test this we studied patients following cardiac surgery who had catheters across the right heart so that samples could be taken from the right atrium (RA), pulmonary artery (PA) and a systemic artery (ART) before and after the application of end-expiratory airway pressure (PEEP) to reduce the return of blood to heart and reduce heart size. The initial NPY concentration was high after surgery but there was significant increase in blood concentration from PA to ART indicating likely release of NPY from the left heart and possible uptake by the right heart. The concentration of ET-1 decreased from PA to ART indicating uptake of ET-1 by the pulmonary circuit or left heart and possibly some uptake by the right heart. The application of PEEP reduced the uptake by the right heart and increased peripheral release of NPY and ET1. These results suggest that cardiac endocardial endothelial cells can modulate circulatory levels of humeral signals from the periphery.

New molecular targets of VEGF signaling in cardiovascular disease

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Therapeutic angiogenesis is a promising approach to the treatment of ischemic injury. Angiogenesis is a global highlight in the medical field. Many angiogenesis related factors are involved in the development of vessels, in response to physiological or pathological stimuli. VEGF modulates the complex process of angiogenesis and other various aspects of endothelial cell function through either of its two tyrosine kinase receptors, VEGFR1/Flt-1 or VEGFR2/Flk1/KDR via its target protein MAPKinase 2. VEGF mediated angiogenesis signaling is widely accepted however relatively little is known regarding VEGF mediated downstream signaling through Flt-1 and/or Flk-1. The use of Affymetrix gene chip technology in Flk-$1^{+/-}$ knockout (KO) mice allowed us first time to identify several target genes in ischemic preconditioned myocardium. By chip

analysis we demonstrated first time down regulation of Pellino-1(Peli1) after ischemic insult to the Flk-$1^{+/-}$KO mice. Our study showed that overexpression of Peli1 by adeno-Peli1 gene therapy (Ad-Peli1) significantly increased angiogenic effect, increased ejection fraction and reduces ventricular remodeling in myocardial infarction (MI) model. Western blot analysis 24 h after MI revealed increased phosphorylation of Akt, eNOS and MAP Kinase 2 with Ad-Peli1 treatment compared to Ad-LacZ. Immunohistochemical analysis with picrosirius red staining exhibited a decrease in collagen deposition in Ad-Peli1MI group as compared to Ad-LacZMI. Vascular density and connexin-43, a major ventricular gap junction protein was found to be increased in Ad-Peli1MI group compared to Ad-LacZMI. Collectively, our study documents Peli1 as a promising molecule in the treatment of myocardial infarction, which could potentially lead to new therapeutic target.

Pacemaker mechanisms in human iPSC-derived cardiomyocytes: A step closer to tissue-based pacemakers.

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Electronic battery-powered pacemakers, universally used in treatment of bradycardia, sick sinus syndrome, and Atrial fibrillation, often require battery and lead replacement, imposing significant psychological and financial burdens on patients.

Human fibroblast-derived cardiomyocytes (hiPSC-CM), with electrophysiological and pharmacological properties comparable to mature cardiomyocytes, can potentially be engineered to serve as cell-powered and immunologically compatible pacemaker devices. HiPSC-CMs pace spontaneously by releasing and sequestering Ca^{2+}, activating inward NCX currents cyclically that contribute to diastolic depolarization (DD). Spontaneous pacing was independent of holding potential, activation of "funny-current" (I_f), and I_f -blocking drugs. TIRF and confocal imaging of cells infected with genetically engineered probes targeted to mitochondrial matrix showed that Ca^{2+}-cross signaling between mitochondria and SR was critical in triggering pacing activity of hiPSC-CMs.

Since I_f is specifically expressed in Sino-atrial node but activates at voltages negative to DD range, *we hypothesized that I_f is expressed to protect the SA-nodal cells from hyperpolarizing currents generated by atrial electrical sink (-90mV).* In support of this idea, I_f generates large slowly developing inward currents only negative to DD, thereby *functionally insulating* the SA-nodal cells from the atrial electrical drag. Using "*sleeping beauty*" transposon construct of HCN4, we generated hiPSC-CM cell line expressing ~4x larger I_f. Even in such cells, expression of spontaneous pacing did not correspond to the magnitude of I_f, but depended on density of Ica and cyclic release and uptake of Ca^{2+}. Sleeping-beauty HCN4-transposed myocytes express both the "*Ca^{2+}-oscillator*" and "*functional insulating*" mechanisms critical for a dependable tissue-based pacemaker device.

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Nutritional regulation of non-alcoholic fatty liver disease (NAFLD) and its impact on cardiovascular disease (CVD)

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Non-alcoholic fatty liver disease (NAFLD) has emerged as a serious global health issue. It is strongly associated with obesity, type-2 diabetes and cardiovascular disease. The primary cause of death in NAFLD patients is cardiovascular disease (CVD). NAFLD covers a broad spectrum of disorders that range from simple hepatic lipid accumulation (steatosis) to oxidative stress and inflammation (steatohepatitis). Chronic consumption of energy dense diets (i.e. high-fat) is one of the most common causes for NAFLD. The aim of our research was to investigate the impact of dietary intervention on NAFLD pathophysiology, systemic oxidative stress and inflammatory response. Feeding mice with a high-fat diet for 5-12 weeks stimulated rapid body weight gain and induced NAFLD phenotype. Chronic consumption of high-fat diet also caused hepatic lipid accumulation, hyperglycemia, oxidative stress and proinflammatory cytokine expression in the liver. Elevated *de novo* cholesterol synthesis contributed to hepatic lipotoxicity. NAFLD-associated hyperlipidemia, hyperglycemia, chronic oxidative stress and chronic inflammatory response had adverse effects on the cardiovascular system. Supplementation of micronutrients (i.e. folic acid) alleviated lipotoxicity, oxidative stress and hyperglycemia. Such beneficial effects were mediated, in part, through restoration of hepatic AMPK activation, regulation of endogenous lipid biosynthesis, balance of homocysteine and hydrogen sulfide metabolism as well redox status. Our results suggest that dietary intervention may have important clinical implications in NAFLD management and CVD prevention.

Impact of perinatal hypoxia on cardiac tolerance to ischemia/reperfusion injury in adults

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Perinatal period is critical for the normal cardiac development. Epidemiological and experimental studies have suggested a possible link between perinatal hypoxia and increased sensitivity to ischemia/reperfusion (I/R) injury in adults. However, the mechanisms are not yet been satisfactorily clarified. It has been suggested that chronic hypoxic exposure during early development may cause *in utero* or neonatal programming of several genes which can play an important role in the increased susceptibility of the adult heart to I/R injury. Furthermore, it has been observed that late myocardial effects of hypoxia may be sex-dependent. Unlike in males, perinatal exposure to chronic hypoxia significantly increased cardiac tolerance to acute I/R injury in adult rat females, expressed as the lower incidence of ischemic arrhythmias, decreased infarct size, decreased cardiac enzyme release, and increased postischemic recovery of left ventricular function. It was suggested that sex-dependent changes may be due to differences in fetal programming of PKCε gene expression and in part by the greater expression of estrogen receptors in the heart of female fetuses. These results would have important clinical implications: (i) cardiac sensitivity to oxygen deprivation in adult patients may be significantly influenced by perinatal hypoxia; (ii) the observed sex differences suggest that the management of the diseased human male and female heart should be different.

Novel ways to lipid load cells to study macrophage functions

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Generation of foam cells, an essential step for studying the reverse cholesterol transport (RCT). Currently available methods use the technique of receptor dependent macrophage loading with radiolabeled acetylated Low Density Lipoprotein (Ac-LDL). In this study, we used the ability of a biologically relevant detergent molecule, Lysophosphatidylcholine (Lyso PtdCho), to form mixed micelles with cholesterol or cholesteryl ester (CE) to generate macrophage foam cells. Fluorescent or radiolabelled cholesterol / Lyso PtdCho mixed micelles were prepared and incubated with RAW 264.7 or mouse peritoneal macrophages. The micelles were stable and could be used for a long periods of time with consistent and reproducible results.

Macrophages incubated with cholesterol or CE (unlabeled, fluorescently labeled or radiolabeled) / Lyso PtdCho mixed micelles accumulated CE as documented by microscopy, lipid staining, labeled oleate incorporation, and by thin layer chromatography (TLC). The cytotoxic Lyso PtdCho was very efficiently converted by macrophages to innocuous PtdCho. Such foam cells unloaded cholesterol when incubated with high density lipoprotein (HDL) and not with oxidized HDL (Ox-HDL). We propose that stable cholesterol or CE / Lyso PtdCho micelles would offer advantages over existing methods.

Using this technique, we demonstrated that such macrophages mimicked biological properties attributed to cholesterol loaded macrophages. Earlier, we had used similar technique to enrich cells with beta carotene. We suggest that this novel technique of delivering macromolecules to the cells could be further manipulated to deliver other hydrophobic large molecular cargos to the cells.

Taurine deficient heart exhibits mitochondrial oxidative stress, apoptosis and impaired ATP generation

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Myocardial taurine deficiency leads to the development of unique dilated cardiomyopathy, characterized by diminished systolic and diastolic function, impaired ventricular compliance, decreased ventricular wall thickness and reduced cell size. To help clarify the basis underlying the development of the taurine deficient cardiomyopathy, we examined two mechanisms that could alter taurine deficiency-mediated heart failure. First, taurine deficiency is associated with inhibition of complex I of the respiratory chain, initiation of mitochondrial fragmentation and onset of mitochondrial oxidative stress. The generation of reactive oxygen species by the taurine deficient heart leads to apoptosis, as evidenced by the activation of caspase 9. Second, we proposed that taurine deficiency mediates a reduction in ATP production, which also interferes with normal contractile function. The primary effect of taurine deficiency on ATP generation is inhibition of the respiratory chain. Although the normal heart preferentially utilizes fatty acids for the generation of ATP, taurine deficiency specifically reduces ATP generation by fatty acids. However, glucose metabolism is also a poor source of ATP in the taurine deficient heart. This relates to the reduction in glucose oxidation, as pyruvate is converted to lactate rather than being converted to acetyl CoA. The energy deprived, taurine deficient heart exhibits the characteristic decrease in the creatinine phosphate/ATP ratio. In conclusion, taurine deficiency adversely affects contraction by causing

mitochondrial changes, which result in oxidative stress and diminished ATP generation, which together alter muscle contraction.

The unique technical challenges that natural health products pose as a therapeutic intervention in a clinical trial.

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The vast majority of clinical trials use drugs as the intervention of choice to improve health. Although many may initially think that using a natural health product instead of a drug as the clinical trial intervention would offer no differences with regard to the challenges facing the trial organizers, there are conversely many unique technical differences that will confront the Principal Investigator. These challenges are found in each of the three distinct phases of a trial: the initial organization, the collection of the data and the completion of the trial, and finally, the dissemination of the data obtained from the trial. Each one presents very different issues that will limit the conclusions of the trial if not properly addressed before, during and after the trial is successfully completed. A careful planning of the trial taking into consideration twelve important technical parameters that are identified in this manuscript can insure that the data are significant and lead to reliable conclusions, every bit as valuable as those obtained in drug trials. Supported by CIHR, ARDI, Western Grains Research Foundation, SaskFlax and St Boniface Hospital Foundation.

Novel "conditioning" approaches to mend the broken heart: a potential for clinical application?

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Although ischemic preconditioning (PC) is the most robust form of endogenous cardioprotection, it is blunted by comorbidities and aging, and its application in humans is limited. Other forms (e.g. "remote" PC, RPC) started to be used in patients with acute myocardial infarction, albeit with controversial results. As shown previously, transcription factors PPAR are involved in response to ischemia/reperfusion (IR) in normal and diseased (diabetes, post-irradiation) hearts, and PPAR-α agonists (hypolipidemics) confer PC-like cardioprotection.

We assessed the efficiency of non-invasive RPC in younger (3-months) and mature (6-months) adult normotensive and hypertensive (SHR) rats, and explored a role of PPAR-α in cardioprotective mechanisms.

RPC was applied on a hind limb of animals using three cycles of 5-min pressure cuff inflation (200 mmHg)/5-min deflation with or without PPAR-α antagonist MK886. Infarction size (IS), functional recovery (LVDP) and occurrence of ventricular tachyarrhythmias (VT) were evaluated in Langendorff-perfused hearts exposed to 30-min global ischemia/120-min reperfusion. In parallel groups, LV tissue was sampled for examination of PPAR-α gene expression (RT-PCR) and PKCε protein levels (WB).

RPC significantly reduced IS, VT severity and enhanced LVDP recovery in hearts of younger and mature normotensive rats. Protection was retained in SHR groups of both ages. All cardioprotective effects as well as RPC-induced up-regulation of PPAR-α and PKCε were abrogated by MK.

The results suggest the role of PPAR-α as one of potential cardioprotective mechanisms of RPC. RPC appears as a cost-effective and easily performed intervention with a potential clinical relevance. Grants VEGA 2/0201/15, APVV-0102-11, APVV 15-0607, APVV-15-0119, APVV-15-0376, APVV-SK-CZ-2013-0075.

Rational bases of modern therapies for cardiovascular diseases

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Cardiovascular (CV) homeostasis is maintained by the opposite actions of the Renin-Angiotensin-Aldosterone System (RAAS) and Kallikrein-Kinin System (KKS). RAAS mainly acts through its biologically active component, the Angiotensin II (Ang II), which promotes vasoconstriction and sodium retention (via aldosterone release). When RAAS is abused by excess of risk factors of modern life, the extremely dangerous pathological factor Ang II causes and sustains hypertension, severe CV diseases in non-diabetic and diabetic patients. The KKS, through the two kinins (Lys-BK and BK), is the most potent, multifactorial integrative vasodilatory system, which confers efficient protection for the heart and peripheral vessels. In the endothelium and in the lung, the protease Angiotensin-

Converting Enzyme (ACE) promotes the formation of Ang II and inactivates the kinins. Inhibition of ACE is therefore the best rational approach to restore CV homeostasis. Numerous ACE inhibitors (ACE-Is) have been prepared, tested in many clinical trials and extensively used in the clinic for treating CV diseases and the cardiovascular complications of diabetes. The therapeutic value and safety of ACE-Is can today be evaluated by meta-analyses and the therapeutic validity of single compounds of this drug class can be assessed by modern criteria introduced recently in clinical practice.

Wearable devices in modern cardiology.

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Wearable technology is changing our lives. Wearable devices *or 'body-borne computers' are devices that can be worn by users* and *are intended to interact with the wearer without punching keys or other manipulation*. They can *perform real time calculations and information processing. The wearable technology consists of two parts, the sensors and the information aggregators and analysers. A* comprehensive overview of existing wireless cardiac monitoring devices is presented. Main areas of cardiac technology include: comprehensive vital sign monitoring, blood pressure monitoring, intermittent electrocardiographic monitoring, applications for heart failure patients and new portable ultrasound devices. Main cardiac variables in current devices include: heart rate, R-R interval, heart rate variability, respiratory rate and volume, VO_2 Max, body position and posture, emotions, emotional eating, arrhythmias analysis, long term ECG monitoring, fluids levels, transthoracic impedance, body weight, radial artery waveforms and ultrasound images. Potential for cardiac research and translation is reviewed.

Role of toll-like receptors in innate signaling in heart failure

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We and others have reported that heart failure subsequent to myocardial infarction is associated with an increase in tumor necrosis factor-α (TNF-α) and a decrease in interleukin-10 (IL-10). In isolated cardiomyocytes, it was shown that IL-10 antagonizes the pro-apoptotic effect of TNF-α. We have now studied the differential role of Toll-like Receptors (TLR4 and TLR2) and their downstream signals in adult cardiomyocytes under stressful conditions: Il-$10^{-/-}$ and ischemia/reperfusion (I/R). In IL-10 stimulated cardiomyocytes, TLR4 expression followed the upregulation of myeloid differentiation primary gene 88 (MyD88). Its activation led to IRF3 dimerization and phosphorylation which augmented IL-1β translational activity. In IL-$10^{-/-}$ hearts there was an increase in TLR2 activity indicating its negative regulation by IL-10. Circulating and myocardial levels of TNF-α were higher in IL-$10^{-/-}$ hearts. The ex-vivo I/R in the rat hearts caused a marked upregulation of TLR2. However, 40min reperfusion with IL-10 triggered an increase in TLR4 expression. Increase in interleukin-1 receptor-associated kinase-M (IRAK-M) and IRAK-2 activity during I/R injury suggested their role in TLR2 signaling. Inhibition of MyD88 modulated IL-10 induced expression of TLR4, IRF3-dependent IL-1β production and NFκB p65 phosphorylation and translocation. These data suggest that IL-10 through TLR4 activation and suppression of TLR2, may be a key molecule in restoring heart health under stressful conditions. (Supported by CIHR)

Increased anti-inflammatory M2 macrophages prevents Cardiac Diseases

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Inflammation plays a monumental role in the development and progression of cardiac diseases is a current area of investigation. This is completely unknown whether infiltrated monocytes differentiate into what kind of macrophage phenotypes such as pro-inflammatory M1 or anti-inflammatory M2. Moreover, their role in developed cardiac diseases is still unknown. We will demonstrate data on inflammation induced cell culture and in vivo models to demonstrate the increase in M1 macrophage phenotypes present and their role in the development and progression of cardiac diseases. Furthermore, we will provide alternative strategies to regulate monocyte differentiation into anti-inflammatory M2 macrophages. The increased M2 macrophages release anti-inflammatory cytokines that reduces inflammation, adverse cardiac disorders and improve heart function. We will also discuss the involvement of SMAD pathway in the regulation of M2 macrophage differentiation.

Radiation induced heart disease and amelioration of X ray toxic effect with selected substances and H2.

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Therapeutic doses of chest irradiation in oncological patients represent a significant source of cardiovascular morbidity and mortality. Irradiation of normal tissues leads to intracellular signaling and altered cell function, resulting in organ dysfunction and ultimate failing of the heart. This process can be modulated by therapies directed at mitigating the cascade of events resulting from normal tissue injury.

The aim of the study was to explore the effects of a single dosage radiation (25 Gy) applied to the mediastinal area of normal adult Wistar rats on the heart functional parameters, selected molecular markers and the effects of selected drugs that might be involved in molecular mechanisms of tissue radiation injury.

Morphological examination revealed increased ultrastructural signs of both, endothelial cell degeneration/regeneration, microthrombi, activated fibroblasts, mast cells and monocytes. Gene expression of PPARα was significantly lower in left ventricular tissue of irradiated rats, while expression of microRNA-21 in these hearts was increased nearly 10-fold. Myocardial Cx43 was upregulated via reduced miRNA-1. miRNA-15b was downregulated almost by 42% and Bax protein decreased, indicating triggered adaptive mechanism. Activities of circulating 72kDa MMP-2 was significantly increased. As compared to untreated control groups, irradiation caused a significant decrease in TNF-α. Enbrel and ASA decreased the level of TNF-α, however, in the Sildenafil group, there was an increase in the TNF-α levels.

These results suggest possible protective action of Enbrel and Tadalafil on the heart damaged by irradiation as demonstrated by changes in miRNAs and TNF-α levels.

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Stromal interaction molecule-1 and orai1 channel mediate angiotensin-II-induced expression of early growth response protein-1 (Egr-1) in vascular smooth muscle cells.

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Egr-1 is a zinc finger transcription factor that has been suggested to regulate the expression of genes linked with inflammation and cell cycle regulation. An up-regulation of Egr-1 expression has been reported in models of atherosclerosis and intimal hyperplasia. Various vasoactive peptides and growth promoting stimuli have been shown to induce the expression of Egr-1 in VSMC. Angiotensin-II (Ang-II) is a critical vasoactive peptide implicated in the pathogenesis of vascular diseases. Ang-II elevates the intracellular level of calcium through activation of store-operated calcium entry involving inositol-3-phosphate receptor (IP3R)-coupled depletion of endoplasmic reticular calcium and stromal interaction molecule 1 (STIM-1)/Orai 1 channel. However, an involvement of IP3R/STIM-1-/Orai 1-induced calcium pathway in Ang-II-induced Egr-1 expression remains unexplored. Therefore in the present studies we have examined the role of Ang-II-induced calcium release in Egr-1 expression in VSMC and investigated the contribution of STIM-1/Orai1 in this process. Pharmacological blockade of IP3R with 2-aminoethoxydiphenyl borate (2-APB) decreased Ang-II-induced calcium release and attenuated Ang-II-induced enhanced expression of Egr-1 protein and mRNA levels. Activation of ERK1/2 pathways was essential to trigger Ang-II-induced expression of Egr-1 since its inhibition by U 0126 suppressed Egr-1 expression and 2 APB-induced reduction in Egr-1 expression was associated with a decreased phosphorylation of ERK1/2 and CREB. Furthermore, silencing of STIM-1 or Orai 1 via RNA interference resulted in an attenuation of Ang-II-induced Egr-1 expression as well as phosphorylation of ERK1/2 and CREB. Our data demonstrate that Ang-II-induced Egr-1 expression is mediated by STIM-1/Orai 1-dependent signaling pathways in VSMC. (Supported by CIHR).

Cardiopulmonary bypass & cardiac injury during coronary surgery

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It is widely assumed that reperfusion of arrested and globally ischaemic heart during coronary artery bypass surgery is responsible for cardiac injury and subsequent remodelling leading to heart failure. However, whether cardiopulmonary bypass (CPB) is also a significant contributor to cardiac injury remains controversial. CPB is associated with significant inflammatory response and oxidative stress which can trigger cardiac remodelling/injury.

To identify deleterious cardiac effects associated with CPB, off-pump surgery and miniaturised CPB (mCPB) have been investigated. Known benefits of mCPB include attenuated cytokine release and neutrophil activation and improvement in cardiac index compared to conventional CPB (cCPB). This work represents a secondary objective of randomised controlled trial in patients undergoing primary elective CABG at the Hammersmith Hospital and was powered to detect ischaemic stress/cardiac injury but not to detect clinical outcome (n=36). Bypass surgery involved using intermittent cross clamp fibrillation (ICCF). Ventricular biopsies were collected prior to and after arrest/surgery. Ischaemic stress and cardiac injury were assessed.

ICCF was associated with ischaemic stress (drop in energy rich phosphates) and increased sensitivity to reperfusion injury which was similar for both mCPB and cCPB. However, cardiac injury was reduced when using mCPB compared to cCPB. Unlike surgery using CPB, off-pump surgery was associated with little global ischemic stress and reduced cardiac injury. In conclusion, this work shows that in low risk group of CABG patients, ICCF is associated with ischaemic stress and that mini-pump reduces cardiac injury. Off pump (beating heart) CABG surgery is associated with metabolic preservation and reduced cardiac injury.

The mode dependent effect of NCX inhibition on contractility and Ca-handling in cardiac ventricular myocytes

Andras Varro[1,2]
[1]MTA-SZTE Division of Cardiovascular Pharmacology, Hungarian Academy of Sciences, Szeged, Hungary., [2]Dept. of Pharmacol., University of Szeged, Szeged, Hungary.

In the present work the effects of ORM-10962, a novel highly selective NCX inhibitor were studied on the cardiac NCX current and Ca-handling. The selectivity of the drug on various transmembrane ionic currents was also investigated.

ORM-10962 significantly reduced both the inward and outward NCX currents with the estimated EC50 values of 55nM and 67nM, respectively. The compound, even at the high concentration (1µM), did not change significantly the amplitude of various other ionic currents. The effect of ORM-10962 on Ca-handling and contractility was mode dependent. ORM-10962 did not alther Ca-handling and contractility at normal ”physiological” condition. However if forward-mode was augmented it increased amplitude of Ca-transient and contractility. If reverse-mode was enhanced the ORM-10962 decreased the amplitude of the Ca-transient and contractility. The amplitude of pharmacologically induced delayed afterdepolarizations was significantly decreased by 1µM ORM-10962 in canine Purkinje fibres. ORM-10962 (0.3mg/kg) pre-treatment significantly delayed the development of ouabain induced ventricular extrasystoles or ventricular tachycardia in anesthetised guinea pig.

The present study provides evidence for the highly selective NCX-inhibitory activity of ORM-10962. In addition it suggested that specific inhibition of the NCX current influences Ca-handling and contractility in a mode dependent manner and also contributes to the prevention of DAD based arrhythmias in vivo.

Transcriptional control of cardiac fibroblast activation

Jeffrey Wigle[1]
[1]university of manitoba

Following cardiac injury, fibroblasts become activated and convert into myofibroblasts. These cells are key players in extracellular matrix (ECM) remodeling and fibrosis, which is a primary contributor to heart failure. There is no effective therapy available to specifically target cardiac fibrosis. We previously showed that Meox2, a homeobox transcription factor, may partially block fibroblast activation via downregulation of expression of α-smooth muscle actin (α-SMA) and ED-A fibronectin, two markers of the myofibroblastic phenotype. We now show that Zinc Finger E Box-Binding Homeobox 2 (Zeb2), a repressor of Meox2, plays a critical role during myofibroblast phenoconversion. Zeb2 overexpression in primary rat cardiac fibroblasts is associated with significantly increased expression of embryonic smooth muscle myosin heavy chain (SMemb), ED-A fibronectin and α-SMA. Western blotting indicates that Zeb2 is highly expressed in myofibroblast nuclei but not in fibroblast nuclei. Moreover, ectopic Zeb2 expression in myofibroblasts results in a significantly less migratory and more contractile phenotype, characteristic of mature myofibroblasts. We observed that Zeb2 overexpression repressed Meox2 expression in endothelial cells suggesting that Zeb2 has the potential to inhibit the anti-fibrotic Meox2 pathway and thus potentially promote cardiac fibrosis. Our current findings add to our understanding of the mechanisms behind fibroblast-to-myofibroblast phenoconversion and provide the basis for development novel anti-fibrotic therapies for treatment of diseases associated with cardiac fibrosis.

Does young age really put the heart at risk?
Carin Wittnich[1]
[1]University of Toronto

Despite significant advances in the management and treatment of heart disease in adults and children, there continue to be patients who have worse outcomes than might be expected. A number of risk factors have been identified that could be responsible and evidence based findings will be reviewed that could contribute to this. Specifically, whether young age and/or reduced body weight exacerbate these responses will be clarified. For example, newborn children undergoing congenital cardiac surgery are known to have worse outcomes than older children. This presentation will further discuss our research program exploring reasons for this including that newborn hearts tolerate ischemia less well than adults, develop irreversible injury sooner and exhibit at risk metabolic profiles. Our research has shown that elevations in free fatty acids occur during CPB; which can have detrimental effects on the heart. What exactly is the cause of this elevation, whether this is affected by oxygen levels, heparin administration, and age will be discussed. Furthermore myocardial energetic state has also been suggested to impact outcomes. Evidence will be provided that newborn children suffering from congenital heart disease with lower body weights also have lower myocardial energetic state. Clinical data will show that in newborn children, lower body weight correlated with lower myocardial energetics, longer post operative ventilatory support and a trend to longer ICU stay, implying that unfavorable myocardial metabolic profiles could contribute to their burden of post operative complications. Potential causes for these unfavorable profiles, explored using animal models, will be presented.

Brief Biosketches of Invited Speakers and Chairs

DR. ADRIANA ADAMEOVA

Comenius University in Bratislava, Faculty of Pharmacy, Department of Pharmacology and Toxicology.

Received master (Mgr.) degree in Pharmacy in 2002, doctoral degree (PharmD.) in 2003 and Ph.D. degree in Pharmacology in 2006 from the Comenius University in Bratislava, Slovakia. As a part of postdoctoral study, she was trained in The Hatter Institute, University of London, Faculty of Medicine, London, U.K. and at the Division of Cardiovascular Sciences, St. Boniface Research centre, Faculty of Medicine, Winnipeg, Canada (2008). She received training from Basic Cardiology by European Society of Cardiology, Nice, France (2009).
Served as an Assistant Professor at Comenius University in Bratislava from 2005-2013. Currently, she is an Associate Professor (2014-) and serves as a Co-gestor of Ph.D. program form Pharmacology.
She has been a member of European Agency for Medicine, Efficacy working Party, London, U.K., (2007-2010) and a member of Committee on Generic Drugs (assessment of bioequivalence), State Institute for Drug Control, Slovakia (2009-).
She has published 29 full-length papers in peer-reviewed journals indexed in PubMed, 7 bookchapters and 105 abstracts. Her work has attracted over 200 citations registered in WOS database with h-index 10 (according to Google Scholar more than 400 citations with h-index 15).
She is the editor of 1 book from Pharmacology entitled General Pharmacology for Pharmacists: Principles and Applications.
She has been actively engaged in studying mechanisms of ischemia-reperfusion injury in diseased hearts (diabetic, hypercholesterolemic), mainly those leading into the abolishment of preconditioning-induced cardioprotection. Furthermore, she has described some non-lipid, pleiotropic beneficial effects of statins, and studied their association with PPAR receptors. Her current projects are focused on studying of CaMKII in health and diseased heart (heart failure and ischemic/reperfused heart) and a role of necroptosis in myocardial tissue.
She serves on the Editorial Boards for 3 international journals, Molecular and Cellular Biochemistry, Current Research Cardiology and CV Network and is a regular reviewer for Physiological Research.
Received a Scientific qualification degree from Slovak Academy of Sciences (2010), Rector's Award for Excellence in Teaching and Research Supervision (2012), and Award ESF JPD 3 2005/1-049 - Promotion of research activities of young investigators at the Faculty of Pharmacy, Comenius University (2007 and 2008).

DR. DEVENDRA K. AGRAWAL, FAAAAI, FAHA, FAPS, FIACS

Professor and Chairman
Department of Clinical & Translational Science
The Peekie Nash Carpenter Endowed Chair in Medicine
Senior Associate Dean for Clinical & Translational Research

Dr. Devendra K. Agrawal earned M.Sc. (Chemistry) in 1973 and Ph.D. (Biochemistry) in 1978 from Lucknow University, India. Following his services as a Clinical Biochemist at King George's Medical College, Lucknow, India, Dr. Agrawal moved to Canada and earned Ph.D. (Medical Sciences) in 1984 from McMaster University, Canada (Advisor-Professor Edwin E. Daniel) followed by a Postdoctoral Fellowship at the University of British Columbia, Vancouver, Canada (Advisor-Professor John McNeill). In 1985, he was appointed as an Assistant Professor at Creighton University School of Medicine, Omaha, Nebraska, USA where he rose to the rank of Full Professor in 1997. Dr. Agrawal also earned MBA in 2004 and MS (ITM) in 2005 from Creighton University, Omaha, Nebraska, USA. He founded the Center for Clinical & Translational Research at Creighton University, which is recently developed into an independent Department.

Dr. Agrawal is a member of the Alpha Omega Alpha Honor Medical Society and is a Fellow of the American Academy of Allergy, Asthma and Immunology, Fellow of the American Heart Association, Fellow of the American Physiological Society, and Fellow of the International Academy of Cardiovascular Sciences. Creighton University recognized and honored Dr. Agrawal with many awards, including Young Investigator Award, Distinguished Research Career Award, Distinguished Professor Award, Distinguished Faculty Service Award, University Research Award and Distinguished Mentor Award at Creighton. In 2001, the Midwest Chapter of American Association of Physicians of India recognized Dr. Agrawal for his contribution as a teaching professor, researcher and mentor. The India Association of Nebraska recognized him with the Man of the Year award in 2000 and Award of Excellence in appreciation of outstanding service and contribution to Nebraska Community at large in 2013. Recently, the International Academy of Cardiovascular Sciences recognized Dr. Agrawal with the Professor Bohuslav Ostadal Award for Excellence in Cardiovascular Sciences and Distinguished Leadership Award. Dr. Agrawal has been an invited speaker to many prestigious national and international scientific meetings.

Dr. Agrawal has served on many grant review panels, including VA Merit Review, NIH-CSR, DoD, NIH-NIAID, NIH-NHLBI, MRC-UK and US-Israel BSF Grant Review Committees, Science Foundation Ireland, Austrian Science Fund, British Lung Foundation, Swiss NSF, and Asthma Research Foundation of Western Australia. Dr. Agrawal has served/is serving on editorial board of several journals, including J. Immunology, American Journal of Respiratory Cell and Molecular Biology, Canadian Journal of Physiology and Pharmacology. Dr. Agrawal has authored/co-authored >320 original papers in peer-

reviewed journals and book chapters. He has co-edited three books in the area of Allergy, Asthma and Immunology. His major research interests have been in the area of cellular, molecular and immunobiology of pulmonary and vascular diseases. NIH funds his research projects. In collaboration with clinical scientists, Dr. Agrawal has developed active and productive research projects in many fields, including bariatric surgery, esophageal diseases, rotator cuff injury, osteoarthritis, traumatic brain injury, spinal cord injury, malignant melanoma, ulcerative colitis, Crohn's disease, lung cancer, keloids and hypertrophic scar. He has trained about 48 postdoctoral fellows and 52 MD-PhD/PhD/M.S. students in cellular, molecular, and immunobiology of clinical diseases. At Creighton University, Dr. Agrawal has been developing multidisciplinary/ interdisciplinary approaches and new perspectives in the advancement of Clinical & Translational Science, mentoring and training new generation of translational researchers.

DR. MADHU ANAND-SRIVASTAVA, FIACS

Dr. Madhu B. Anand-Srivastava is Professor, Department of Molecular and Integrative Physiology, University of Montréal. The main theme of her research is directed towards understanding the mechanisms that underlie the cellular and molecular basis of hypertension. She is an Internationally recognized expert in the field of G protein and hypertension and atrial natriuretic peptide receptor-C (NPR-C), cell signalling and cell function and has made significant contributions in these areas. Her work is highly cited. She has published more than 150 papers, 29 book chapters and 215 abstracts and edited 3 books. She has trained more than 50 students and post-doctoral fellows and has been invited to several National and International conferences and Academic Institutions to present her work. She was also awarded Vincenzo Panagia Distinguished Lecture Award from Institute of Cardiovascualr Science in 2004. She is a fellow of International Academy of Cardiovascular Sciences and Indian Society of Hypertension. She has served or is currently on the different committees of CIHR and Heart and Stroke Foundation of Canada and also on the Editorial board of scientific publications including Journal of Molecular and Cellular Cardiology and Molecular and Cellular Biochemistry.

DR. PETER BACKX

Dr. Peter Backx received his B.Sc., M.Sc. and DVM from the University of Guelph in biophysics, chemistry and veterinary medicine. He subsequently completed his Ph.D. from the University of Calgary in cardiac physiology. After receiving postdoctoral training at Johns Hopkins University, Peter joined the Department of Medicine at Johns Hopkins University as an Assistant Professor in 1991. In October 1993, Dr. Backx moved to the Department of Medicine at the University of Toronto as an Assistant Professor and a Staff Scientist at the University Health Network (Toronto General Hospital). Peter remained at the University of Toronto until December 2015 when he retired from the Departments of Physiology and Medicine. He is now an Emeritus Professor at the University of Toronto. Currently, Dr. Backx is a Senior Scientist at the University Health Network and a Professor of Biology at York University where he also holds the Canada Research Chair in Cardiovascular Biology.

Dr. Backx is a Fellow of the Royal Society of Canada and the American Heart Association. He served as the Chair of the Scientific Research Committee at the Heart and Stroke Foundation of Canada (HSFC) until 2014 where he oversaw the peer-review programs (Grants-in-Aid and strategic grants) and as well as the National Strategic Research Funds. Peter received a Career Investigator Award for 12.5 years of funding (1999 2011) as well as the Lowell Langille Mentorship Award from the Heart & Stroke Foundation of Ontario. Peter also received a Merit Award, Heart & Stroke Foundation of Canada and the John Foester Distinguished Lecture Award from St Boniface Hospital Research Institute.

Dr. Backx is a recognized expert in cardiac mechanics, heart failure and arrhythmias. His research focuses on the role of ion transport, ion channels and myocardial signaling in the initiation and progression of heart disease with a particular interest in atrial fibrillation. He holds a patent on tissue specific drug delivery and has published over 190 peer reviewed articles, many in the top tier journals like Cell, Nature, Nature Medicine, Journal of Clinical Investigation and Circulation Research. His work has been cited over 13,000 times, with over 5600 in the last 5 years. Dr. Backx has delivered over 150 distinguished invited lectures at the national and international level. Dr. Backx has received more than $14M in research funding as a principal investigator or co-investigator within the last ten years, including 3 CFI awards. He has also supervised 26 graduate students (13 PhD and 13 MSc) and 17 post-doctoral fellows. Many of his trainees hold academic and industry positions worldwide.

DR. GHASSAN BKAILY, FIACS

Dr. Ghassan Bkaily received his Ph.D. in Biophysics in 1982 from the University of Sherbrooke. He then undertook his post-doctoral training in Physiology at the University of Virginia and the University of Cincinnati. In 1984, Dr. Bkaily joined the Department of Physiology and Biophysics of the Faculty of Medicine of the University of Sherbrooke as a Professor. In 1996, he was appointed Chairman of the Department of Anatomy and Cell Biology at the same institution.

Dr. Bkaily' s research work in molecular cardiology currently focuses on healthy and non-healthy aging in the crosstalk between plasma and nuclear membrane receptors and ionic transporters in cells of the human cardiovascular system. He has held several positions, more specifically as Director of the CIHR Group on Cardiovascular Interactions and Director of the FRQNT Team on Nuclear Membrane GPCR Receptors. He also serves as Associate Editor of several scientific journals and he was recently appointed Co-Editor of the Canadian Journal of Physiology and Pharmacology, beginning January 1, 2016.

Throughout his career, Dr. Bkaily has published numerous papers and book chapters and has edited several books. His work received several awards and honors, such as the Most Outstanding Pharmacology Research Paper of the Pharmacological Society of Canada (2004), the Merck-Frosst-FRSQ Research Chair, and very recently the Ramesh K. Goyal oration award in cardiovascular sciences (International Academy of Cardiovascular Sciences, India section), the Ken Bowman Research Achievement Award for excellence in cardiovascular research from the Institute of Cardiovascular Sciences (University of Manitoba) and Fellow of the International Academy of Cardiovascular Sciences. He was also appointed as the President of the 4th Annual meeting of the North American section of the International Academy of Cardiovascular Sciences to be held in Sherbrooke, Canada in September 2016. Dr. Bkaily's research is supported by the CIHR, NSERC, HSFQ and FRQNT. Some of his discoveries include the slow sodium channel, potassium channel openers, and the R-type calcium channel. More recently, he reported the presence and role of nuclear T-tubules, GPCRs, and ionic transporters in nuclear membranes and their implication in the regulation of nuclear ionic homeostasis and cardiovascular pathology. His work in hereditary cardiomyopathy has led to the approval and treatment with a sodium-hydrogen exchanger blocker in heart failure of Duchenne Muscular Dystrophy. He is also the President of a R&D biotechnological company, GBBC Medica Inc., specializing in the development of a new class of calcium blockers for treatment of cardiovascular diseases.

DR. ANTOINETTE OLIVEIRA BLACKMAN

Dr. Blackman received her doctoral degree in medicine from the Cardiovascular Foundation St. Francis of Asisi – ServCor, Belo Horizonte Brazil in the year 2015 under the guidance of Prof. Dr. Otoni Moreira Gomes and co-advisor: Prof. Dr. Melchior Luiz Lima. The research was about evaluating QT dispersion in patients with grade I Left Ventricular Diastolic Dysfunction. Received her master degree in Medical Sciences from the Brasilia University – UNB – Brazil,i in the year 1995 with the advisor Prof. Dr. Luiz Fernando Junqueira Júnior studying the QT interval dispersion EKG in patients with Acute Myocardial infarction –three first days treated of not by thrombolysis. Universitary Brasília Hospital - HUB-UNB, Brasilia, Brazil.

Specialization - Medical Residence in Cardiology in the Army Forces Hospital – HFA, Brasilia, Brazil and Intensive Care Medicine – HUB/UNB- Brasilia, Brazil.

Undergraduation in Medicine of Federal University of Espirito Santo – UFES, Vitória, Espírito Santo, Brazil.

Member associated of Brazilian Cardiovascular Society, Image Cardiovascular Department and Brazilian Society of Arrhythmias. Member associated of Brazilian Cardiovascular Society. Vice-president of Cardiovascular and Respiratory Physiology Department of SBC.

Medical professor of Faculty of Education and Health – FACES - UniCEUB, Brasilia, - Federal District – Brazil.

She guided medical residents in the Intensive care unit from Base Hospital of Federal District – HBDF, Brasilia, Brazil. Her current workplace is in the emergency room in public services.

Received Ricardo Gelpi Award for Excellence in Cardiovascular Sciences, in November 2015.

Current clinical research interest include left ventricular diastolic dysfunction, cardiac arrhythmias, QT dispersion, electrocardiography ambulatory and arterial hypertension. She had been disseminating their results to the general, scientific, and medical communities.

DR. PATRICK BURGON, FAHA

Principal Investigator & Director of Molecular Signaling Laboratory
University of Ottawa Heart Institute

Patrick Burgon earned a BAppSc degree in Biochemistry and Microbiology in 1989 from the Royal Melbourne Institute of Technology and a Ph.D. degree in 1996 from Monash University, Melbourne, Australia. Dr. Burgon received his post-doctoral training at Harvard University and Harvard Medical School, initially under Drs. Ernest Peralta and Eva Neer (regulation of G-protein coupled receptor signaling), and then under Dr. Christine Seidman and Dr. Jon Seidman (cardiovascular genetics). Dr. Burgon joined the University of Ottawa Heart Institute in 2005. Dr. Burgon's research program is focused on defining the molecular basis for the transition from hyperplastic to hypertrophic-based myocardial growth that occurs during normal perinatal cardiac development. His research program is supported by grants from CIHR and HSFC. Dr. Burgon was a finalist in the 2013 Eric Olson Orations in Cardiovascular Science from the International Academy of Cardiovascular Sciences. He was awarded the Top 5 Abstract from Canada, at the 2011 American Heart Association conference. Dr. Burgon has patented his Muscle Lamin A/C Interacting Protein in the United States (Patent Appln No. 60/956,533).

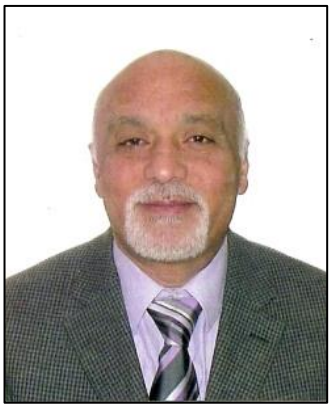
DR. ANDRÉ CARPENTIER, FCAHS

Dr. Carpentier is the recipient of the GSK Research Chair in Diabetes of Université de Sherbrooke and professor, endocrinologist-lipidologist and clinician scientist in the Departments of Medicine, Faculty of Medicine at the *Université de Sherbrooke*. He is also the director of the university's *Centre de recherche sur le diabète, l'obésité et les complications cardiovasculaires* and the director of the Province of Quebec Research Network on Cardiometabolic Health, Diabetes and Obesity.

Dr. Carpentier's research interests include: 1) the role of postprandial fatty acid metabolism in the development of type 2 diabetes and cardiovascular diseases (funded by CIHR funded since 2001); 2) the investigation of brown adipose tissue metabolism in diabetes (funded by CDA then CIHR since 2010); and 3) the anti-diabetic mechanisms of bariatric surgery (funded by CIHR then CDA since 2009). He is also involved in translational research in collaboration with private partners using *in vivo* investigations techniques his laboratory develops to help advance diagnostic and treatment of diabetes and lipid disorders. For example, he is the PI of the postprandial chylomicron metabolism international multicenter trials program of UniQure for the development of gene transfer therapy (alipogene tiparvovec) for lipoprotein lipase deficiency. His work contributed to the regulatory approval of this therapy in Europe. His clinical interest is focused on diabetes, lipid disorders and preventive cardiovascular medicine.

Dr. Carpentier has been a member of numerous scientific panels for granting agencies including the CDA, CIHR, FRSQ and HSFC. He has published more than 300 peer-reviewed abstracts and communications and 111 peer-reviewed manuscript publications. He is the recipient for multiple awards, including the 2011 Diabetes Young Investigator Award of the Canadian Society of Endocrinology and Metabolism, the CDA/CIHR Young Investigator Award in 2012 and the Canadian Lipoprotein Conference Physician-Scientist Award in 2014.

DR. MOHAMED CHAHINE



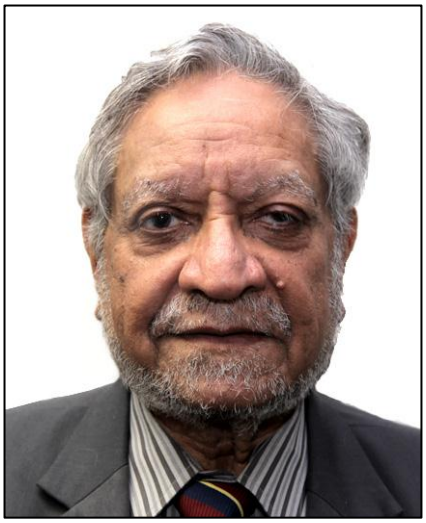
Dr. Chahine is a Professor in the Department of Medicine at Laval University in Quebec city, Canada. His expertise is in channel structure-function studies and mutagenesis studies at both molecular and biophysical levels. Specifically, his expertise is in ion channelopathies, using techniques such as side directed mutagenesis and confocal microscopy. He has published many paper related to long QT syndrome, Brugada syndrome and cardiac arrhythmias in general. Honors include appointment as Senior Investigator at the Joseph C. Edwards Foundation, Montréal, Canada; Invited Professor at the Institut de Physiologie et Biologie, Cellulaires, Université de Poitiers, Poitiers, France; Invited Scientist at the National Institute for Physiological Sciences Okazaki, Japan; a Junior2 fellowship at the Fond de la recherché en santé du Québec (FRSQ), Canada; and a Research Scholar at the Heart and Stroke Foundation of Canada (HSFC) Canada. He is an Associate Editor for Frontiers in Pharmacology of Ion Channels and Channelopathies and sits on the editorial board of the Canadian Journal of Cardiology, World Journal of Cardiology, and the KBM Journal of Cardiovascular Research. Dr. Chahine is a present member of the Biophysical Society, the Society of Neurosciences, and the American Heart Association. He currently receives research support from the Canadian Institute of Health Research and the National Institutes of Health, and has completed research projects for the Canada Foundation for Innovation and a NIH consortium grant.

DR. MICHAEL CZUBRYT, FCVS, FAHA

Dr. Michael Czubryt earned his Ph.D. in Cardiovascular Physiology from the University of Manitoba in 2000 under the guidance of Dr. Grant Pierce. Following a postdoctoral fellowship under Dr. Eric Olson at the University of Texas Southwestern Medical Center at Dallas, Dr. Czubryt established the Molecular Pathophysiology Laboratory at the St. Boniface General Hospital Research Centre in late 2003. He is currently appointed as a tenured Professor of Physiology and Pathophysiology in the College of Medicine, Faculty of Health Sciences, University of Manitoba. Dr. Czubryt was the 2004 recipient of the McDonald Scholarship from the Heart and Stroke Foundation of Canada, awarded annually to the highest ranked New Investigator in Canada, and the 2006 Young Investigator Award from the Canadian Cardiovascular Society.

Dr. Czubryt's research expertise is the control of gene activation and repression in the heart, providing insight to both how disease arises and how it may be treated effectively. His current focus is on cardiac fibrosis – a condition in which the heart tissue stiffens over time in response to stresses such as heart attack, high blood pressure, diabetes and natural aging. Fibrosis reduces the effectiveness of both the pumping and refilling stages of the heartbeat, contributing to heart failure. Despite being relatively common, fibrosis currently lacks treatments – a deficit that Dr. Czubryt hopes to correct. His research has identified a powerful regulator of the fibrosis process – a gene regulatory protein called "scleraxis" – that he has shown can be targeted to reduce fibrosis. Dr. Czubryt's team is actively working to translate this exciting basic science discovery into a first-of-its-kind treatment for fibrosis in not only the heart, but also other tissues such as the lungs and kidneys.

DR. NARANJAN S. DHALLA, CM, OM, FRSC, FIACS



After obtaining MS degree at the University of Pennsylvania and PhD degree at the University of Pittsburgh, as well as serving as Assistant Professor at the St. Louis University for 2 years, Dr. Naranjan S. Dhalla joined the University of Manitoba in Winnipeg in 1968. He progressed through academic ranks and was appointed as Professor in 1974 and Distinguished Professor in 1995. He has been investigating the cardiovascular pathophysiology and pharmacology and has published 617 full length papers in referred journals and 177 review articles in books and monographs. His research work has been cited more than 22,637 times in the literature with an h-index of 71. Dr. Dhalla was one of the first investigators in the world to identify membrane defects during the development of heart disease. By employing different experimental models such as genetic cardiomyopathy, catecholamine cardiomyopathy, infective cardiomyopathy, diabetic cardiomyopathy and ischemic cardiomyopathy, he provided evidence for the occurrence of subcellular remodeling in heart failure and for establishing the concept regarding the subcellular and molecular basis of cardiac dysfunction. Dr. Dhalla carried out seminal research work to reveal the role of oxidative stress and intracellular Ca2+-overload in inducing ischemia-reperfusion injury. He was first to demonstrate the presence of Ca2+-Mg2+ ectoATPase in cardiac cell membrane and suggested its function in eliciting intracellular Ca2+-overload in heart disease. He has also shown the involvement of oxidation products of catecholamines in the genesis of cardiac dysfunction, myocardial cell damage and cardiac arrhythmias due to stress induced heart disease. Dr. Dhalla has trained 59 MSc and PhD students, 50 postdoctoral fellows and 37 visiting scientists in the field of experimental cardiology. They are actively engaged in cardiovascular research, education and administration at various levels all over the world. He is known for his dedication to inspire young investigators and promote their professional careers. In view of his excellent record in cardiovascular research and training, St. Boniface Hospital Research Foundation has established Naranjan Dhalla Chair in Cardiovascular Sciences. The first Centre of Excellence in Heart Research by the Medical Research Council of Canada was established in 1978 under his direction. He served as Founding Director of the Institute of Cardiovascular Sciences (formerly known as Division of Cardiovascular Sciences) at the St. Boniface Hospital Research Centre for 19 years during 1987-2006. He established endowments for 10 awards to be given annually for promoting cardiovascular education and research. He recruited several highly talented investigators for building a multidisciplinary program in research and education in Winnipeg, which is recognized as one of the premier institutes in biomedical sciences. Dr. Dhalla has given 349 symposia talks at various national and international conferences on the pathogenesis and therapeutics of heart disease. He has also been invited to deliver 146 lectures at different institutions in the world to promote the scientific basis for the practice of cardiovascular medicine. He has always emphasized the importance of translational research and need for newer approaches for the prevention of heart disease. In order

to enhance the profile of the Canadian cardiovascular community, Dr. Dhalla in his capacity as Chairman, organized 12 cardiovascular conferences in Winnipeg, which were attended by 300 to 2,000 participants each. In addition, he served as member of the organization committees or advisory boards for 134 international conferences in biomedical sciences. He also edited 52 books on the pathophysiology and therapy of heart disease for the benefit of young investigators and scientists in the developing world. He is the longest serving Editor-in-Chief of an international journal "Molecular and Cellular Biochemistry" for the past 29 years. He built this 600 page quarterly journal into a 3600 page publication (13 issues per year) by Springer, New York. He, as Associate Editor for 26 years, also played a critical role in development of the Canadian Journal of Cardiology, which is now the official journal of the Canadian Cardiovascular Society. He promoted the development of the International Society for Heart Research (formerly known as the International Study Group for Research in Cardiac Metabolism) for the exchange of scientific information and to promote research collaborations throughout the world. He served this organization in his capacity as Secretary General for 15 years and then as President-Elect, President and Past-President for 9 years. He established the Richard Bing Award for Young Investigators and the Peter Harris Award for Senior Scientists in this Society, which awards have become highly prestigious. Dr. Dhalla founded the International Academy of Cardiovascular Sciences for the promotion of cardiovascular education and prevention of heart disease. Since 1996, he has been serving as Executive Director of the Academy, which has membership based under seven regions namely North American, South American, European, Indian, Japanese, Russian and Chinese sections. The Academy recognizes the achievements of distinguished scientists by bestowing Medals of Merit, several Named Awards and Fellowships in addition to holding different young investigator award competitions as well as poster award competitions throughout the world annually. His academic and professional achievements as well as services to cardiovascular community have been recognized by 186 honours and awards from various organizations and institutions around the globe. In particular, he is a member of the Order of Canada, Order of Manitoba and Fellow of the Royal Society of Canada. He has been awarded Honorary Doctorate Degree from 6 universities and Honorary Professorship from 4 universities. He has been inducted into the Citizens Hall of Fame in Winnipeg and he is recipient of the Life-time Achievement Award of the Canadian Cardiovascular Society as well as Medal of Honour of the Canadian Medical Association.

DR. PEDRO D'ORLÉANS-JUSTE

Dr. D'Orleans-Juste received his Ph.D. in Pharmacology from the University of Sherbrooke in 1987 under the supervision of Pr. Domenico Regoli. He then undertook his post-doctoral training in the cardiovascular pharmacology of endothelins at the William Harvey Research Institute in London, UK (Supervisor: late Sir John Vane, FRS, Nobel of Medicine (1982)). He is currently a Professor in the Department of Pharmacology and Physiology at the University of Sherbrooke where he initiated his career in 1990. He was appointed Chairman of his Department in 1999 until 2004.

Funded uninterruptedly by Federal or Provincial funding agencies throughout his career, Dr. D'Orleans-Juste has authored or co-authored hundreds of peer-reviewed articles, 15 book chapters and one monograpy on ACE inhibitors. His work has focused for close to 35 years on the cardiovascular pharmacology of endothelial derived factors namely prostanoid, nitric oxide and endothelins. Currently, his main research interests address the contribution of mast cell derived serine proteases in the production of endothelins in cardiovascular and neurovascular diseases such as atherosclerosis, cardiac infarct and multiple sclerosis. Dr D'Orleans-Juste has successfully trained over 30 undergraduate, 25 MSc, 15 PhD and 7 post-doctoral students during his career. Dr D'Orleans-Juste was also the chairman, co-organizer and host of two International Conferences on Endothelin-1 (Montreal, 1999 and 2009).

Dr D'Orleans-Juste has received the Merck Frost Young Investigator Award in Cardiovascular Sciences (1995), has been identified among the top 100 most cited pharmacologists worldwide (2002) and has obtained numerous provincial and national recognitions. Dr D'Orleans-Juste was the first director of the Bachelor degree in Pharmacology at the University of Sherbrooke (the first French speaking undergraduate program in that discipline in North America). He was also the Director of the Québec Cardiovascular Research Network (2000-2005), the director of the Centre Universitaire d'Enrichissement de la Formation à la Recherche (2009-2015), a scientific councillor at the Fonds de la Recherche en Santé du Québec (1997-2007), the President of the Heart and Stroke Foundation of Quebec, the President of the New Brunswick Health Research Foundation Young Investigator Competition (2014-2016) and acted a vice-president of a R&D biotechnological company, GBBC Medica Inc., specializing in the development of a new class of calcium blockers for treatment of cardiovascular diseases.

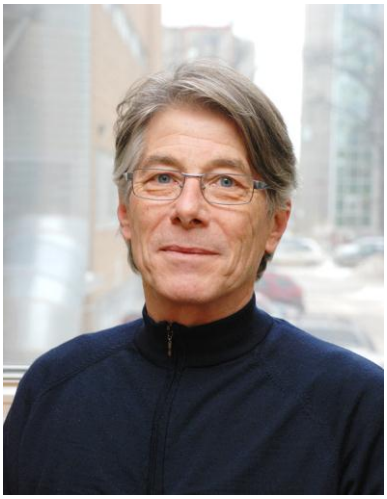
DR. PAUL FARAND

Dr. Farand joined the Faculty of Medicine of the University of Sherbrooke in 2006 where he is now Associate Professor in Cardiology. In 2004, he received his Certificate of specialist in Internal Medicine and in 2006, he received his Certificate of specialist in Cardiology, both from University of Sherbrooke. He received a MSc in pharmacology from University of Sherbrooke in 2004 and completed a training in cardiovascular magnetic resonance at Quebec Heart and Lung Institute (IUCPQ) in 2010.

Since 2012, he was appointed head of the Division of cardiology of the Sherbrooke University Hospital (CHUS) and he's the actual head of the Division of imaging of the CIUSSS-CHUS.

Dr. Farand's research work currently focuses on the assessment of the safe use of investigations and cardiovascular therapies in order to improve the quality of the medical act, usually from retrospective studies in synergy with doctors in training.

DR. JAMES GILCHRIST



Dr. James Gilchrist is a Professor from the College of Dentistry at the Rady Faculty of Health Sciences of the University of Manitoba in Winnipeg, Manitoba. Following undergraduate Sport Science interests at John Moores University in Liverpool, he pursued initial research interests in muscle adaptations to exercise in his M.Sc. program at the University of Alberta. In his doctoral program at UBC, he investigated mechanisms regulating the calcium dependence of ryanodine receptor activation and inactivation in cardiac and skeletal muscle. As a Principal Investigator at the St. Boniface Research Centre, Dr. Gilchrist's research program was focussed upon structure-function studies of nuclear calcium regulation of cardiac and vascular smooth muscle cells. Dr. Gilchrist now actively pursues focussed interests in science education and enrichment for youth as Director of the Biomedical Youth Program at the University of Manitoba.

DR. FERNAND GOBEIL

Fernand Gobeil is a Professor at the Faculty of Medicine and Health Sciences at the Université de Sherbrooke (UdeS) and a former chercheur-boursier Senior of the Fonds de recherche du Québec-Santé (FRQS). Born in Montreal, he obtained a Ph.D. in Pharmacology from the UdeS where he specialized in the field of kinin peptides. His current research interests include the development synthetic kinin peptides with long duration of action as high-valued pharmacological tools and for diagnostic/therapeutic purposes against cardiovascular disease, neurological disorders, diabetes and some cancers. Notably, some of these peptides are used worldwide to elucidate functions of kinin receptors in animal models of health and diseases. The molecules are the subject of an in vitro screening and classical ex vivo assays, followed by the demonstration of proof of concept in vivo using animal models of human diseases. His multidisciplinary research has been funded by the Canadian Institutes for Health Research (CIHR), the Heart and Stroke Foundation of Canada (HSFC), the Canadian Diabetes Association (CDA), the Canada Foundation for Innovation (CFI), Movember-Prostate Cancer Canada, Fonds québécois de la recherche sur la nature et les technologies (FQRNT) and the FRQS. He is author and co-author of more than 115 peer-reviewed papers, some in high-impact journals such as Circulation Research, Nature Medicine, Hypertension, Pharmacology & Therapeutics, and Journal Biological Chemistry. He also holds several patents on kinin analogues and their therapeutic applications in various diseases. Moreover, he has been expert-consultant in pharmacology for several companies. In addition, Pr Gobeil is actively involved with national and international granting agencies (FRSQ, CIHR, HSFC, NSERC, Wellcome Trust (UK)) and served as an expert reviewer for many scientific journals.

DR. SUSAN HOWLETT

Dr. Susan Howlett is a Professor of Pharmacology and Geriatric Medicine in the Faculty of Medicine at Dalhousie University in Halifax, Nova Scotia, Canada. She also holds an Adjunct Appointment in the Department of Cardiovascular Sciences at the University of Manchester in the UK. Originally from Montreal, she completed her PhD in Experimental Medicine at Memorial University, and a Postdoctoral Fellowship in Pharmacology at the University of Alberta, before moving to Dalhousie in 1989.

Continuously funded by the Canadian Institutes of Health Research and its predecessor the Medical Research Council throughout her career, Dr. Howlett is well known for her work on cardiac excitation-contraction coupling. A leader in the exploration of calcium homeostasis in heart cells, Dr. Howlett has discovered profound differences in the way that male and female heart cells function and how this changes with age. These findings may lead to the discovery of sex-specific heart disease treatments for older adults and even preventive therapies based on the effects of sex hormones. Most recently her laboratory has pioneered the measurement of frailty in naturally aging animal models. She has used concepts developed in clinical medicine to quantify animal frailty with a "frailty index" based on deficit accumulation. The ability to quantify frailty in animal models is a major advance that promises to accelerate the effort to translate basic mechanisms of cellular dysfunction in aging into meaningful clinical interventions.

DR. DANIELLE JACQUES

Dr Danielle Jacques obtained her Ph.D. in physiology in 1995 from University of Sherbrooke. She then spent three years postdoctoral training in neuropharmacology at McGill University (Dr Rémi Quirion). In 1998, Dr Jacques joined the department of anatomy and cell biology, Faculty of medicine and health sciences of University of Sherbrooke where she is full professor since 2008. She obtained several awards including the Alfred B. Grossman Award from the EJLB Foundation (Heart and Stroke Foundation of Quebec) and the George Fodor Feature Symposium Award from the Canadian Institutes of Health Young Investigator Forum. She was editor-in-chief of «Revue Medicine Sciences Amerique» and she is an Associate editor for the Canadian Journal of Physiology and Pharmacology. During the course of her career, Dr Jacques published many papers and book chapters and two of her papers are among the 10 most cited in the field of endothelin-1 and Angiotensin II. She is highly implicated in the medical curriculum renewal at her institution. She is supported by the Canadian Institute of Health Research, Natural Sciences and Engineering Research Council of Canada and the Heart and Stroke Foundation of Canada and «Fonds de recherche du Québec- nature et technologies». Dr Jacques's research interests are in the implication of the peptides and their specific receptors in cardiac pathophysiology to elucidate endothelial dysfunctions in general and more specifically of the endocardial endothelium in hypertrophy and heart failure.

DR. MORRIS KARMAZYN, FIACS

Professor Karmazyn was born in Poland and obtained his MSc degree in Animal Science from Macdonald College of Montreal's McGill University and his PhD degree in Physiology from McGill under the supervision of the late Dr David F Horrobin. These were followed by postdoctoral training at the University of Manitoba in Winnipeg under the supervision of Professor Naranjan S Dhalla. He was also a visiting scientist at the Weis Center for Research of the Geisinger Clinic in Danville, Pennsylvania working in the laboratory of the late Dr James R Neely. Dr Karmazyn's first faculty position was at the Department of Pharmacology, Dalhousie University in Halifax, Nova Scotia which he joined in 1981 and he then joined the University of Western Ontario in 1989 where he currently is a Full Professor in the Department of Physiology and Pharmacology and a Tier 1 Canada Research Chair in Experimental Cardiology. He has previously held a Career Investigator Award from the Heart and Stroke Foundation of Ontario (HSFO) and was the recipient of the Merck Frosst Award from the Pharmacological Society of Canada, the Vincenzo Panagia Award from the Institute of Cardiovascular Sciences at the St Boniface General Hospital Research Center in Winnipeg as well as the Dean's Award of Excellence for Research at the University of Western Ontario. He is also an elected Fellow of the International Academy of Cardiovascular Sciences and has also been recognized by the Academy as a recipient of the Naranjan Dhalla Award for Innovative Investigators in Cardiovascular Sciences, the Suresh K Gupta Oration Award for Excellence in Cardiovascular Sciences and the Howard Morgan Award for Distinguished Achievements in Cardiovascular Research. He is the former Director of the Program in Heart Failure supported by the HSFO. Professor Karmazyn has served as a member of many grant review panels for the Heart and Stroke Foundation of Canada, the Canadian Institutes of Health Research (CIHR) and the National Institutes of Health in the United States and has also served as Chair of the CIHR Cardiovascular A committee for nearly five years. He has served or continues to serve on the Editorial Boards of numerous journals. Professor Karmazyn has for many years held a strong interest in the area of cardiac protection against myocardial ischemia and reperfusion injury and his laboratory has pioneered research related to the role of the sodium-hydrogen exchanger in this type of injury. His primary area of research today involves studying the mechanisms of cardiac hypertrophy and heart failure and the development of novel therapeutic strategies, funded both by the Heart and Stroke Foundation of Canada and the CIHR. Among current studies are those involving the role of leptin in heart failure, the potential benefit of ginseng and other natural products for treating heart failure and the role of cardiac JAK2 in the development of hypertrophy and heart

failure using genetically modified mouse models. Professor Karmazyn has published nearly 220 peer-reviewed papers and has delivered more than 200 invited lectures in Canada and abroad. He is listed in American Men & Women of Science and Canadian Who's Who. He has held uninterrupted research funding from the CIHR for more than 30 years. In his spare time he enjoys cooking, reading and is an avid listener of Classical music.

DR. ABDELOUAHED KHALIL

Prof. Abdel Khalil obtained a Ph.D. in Biochemistry of lipoproteins from the Faculty of Medicine René-Descartes (University of Paris V, Paris, France) in 1995 and a Master in radiobiology from the National Institute of Nuclear Sciences and Techniques in 1991. Prof. Khalil joined later (1995 to 1999) the Research Center on Aging at the University of Sherbrooke to complete a postdoctoral training and was recruited at the University of Sherbrooke as assistant professor (2000-2005), then associate Professor (2005-2010). He is currently full Professor at the department of medicine faculty of medicine, director of the research group on the biological mechanisms of aging and president of the Institutional Committee for the Care and Use of Laboratory animals at the University of Sherbrooke. He is a member of the steering committee of the Research Centre on Aging and member of the steering committee of the Quebec Network of Research on Aging. He directed the graduate training program in gerontology at the University of Sherbrooke from 2007 to 2016. Pr. Khalil received many awards and recognitions including the Postdoctoral training award and salary awards from the FRQS. He obtained several grants from Canadian Institutes of Health Research, the Heart and Stroke Foundation of Canada, of the University Agency of Francophonie. Prof. Khalil research interests focus on HDL biochemical changes that occur with age and are associated with the pathophysiology of atherosclerosis and Alzheimer's disease. This work has led to a hundred of publications in international journals and several training graduate students and postdoctoral fellows.

DR. MADHU KHULLAR, FIACS

Dr. Khullar is Professor in the Department of Experimental Medicine & Biotechnology, PGIMER, Chandigarh. She obtained her PhD from PGIMER, Chandigarh and obtained fellowship in Hypertension Research from Henry Ford Hospital, Detroit, USA. She is Fellow, National Academy of Medical Sciences, India, Fellow, International Academy of Cardiovascular Sciences, Fellow, International College of Clinical Nutrition. Her main research interest is in Cardiovascular diseases, Hypertension and diabetes. Her research work involves studying molecular mechanisms, genetics, epigenetics and functional genomics of Primary cardiomyopathies, Hypertension and Diabetic cardiomyopathies. She has published 168 papers in peer reviewed international and national journals. She is Chief editor, Editor and Editorial member of Several National and International Journals.

DR. FRANTISEK KOLAR, FIACS

Dr. Frantisek Kolar is a physiologist engaged in cardiovascular research. His university education started in 1972 at the Faculty of Science of the Charles University in Prague, where he graduated in 1977 and received PhD degree in 1985. He accepted a postdoctoral position at the Institute of Physiology, Czechoslovak Academy of Sciences in Prague, and then underwent research training in cardiovascular physiology and biochemistry at the St. Boniface Research Centre in Winnipeg, Canada, the University of Ottawa, Canada, the Catholic University of Louvain in Brussels, Belgium, and the University of Strathclyde in Glasgow, Scotland. In 2006, he was appointed Full Professor of Medical Physiology at the Charles University in Prague. He has been the Head of the Department of Developmental Cardiology at the Institute of Physiology, Czech Academy of Sciences since 2005.

Dr. Kolar is a member of several societies including the International Society for Heart Research (serving as a Secretary of the European Section in 1998-2003), the International Society for Chronic Hypoxia, the Society for Experimental Biology and Medicine, and the International Academy of Cardiovascular Sciences (Council Member of the European Section). He has been involved in committees of the Czech Science Foundation and co-organized several national and international scientific conferences. He is currently on Editorial Boards of Experimental Biology and Medicine and Physiological Research, and serves as Field Editor of Acta Physiologica and Associate Editor of Current Research: Cardiology. Dr. Kolar received awards from the Czechoslovak Cardiological Society, the

Czech Physiological Society, the Ministry of Health of the Czech Republic, the Slovak Academy of Sciences and the International Academy of Cardiovascular Sciences.
Dr. Kolar has published more than 160 peer-reviewed papers, reviews and book chapters and is a co-author of one monography. His early research concerned the role of skeletal muscle in catecholamine-induced thermogenesis. After joining the Institute of Physiology, his main research interest focused on early postnatal development of the heart with particular respect to cardiac contractile function, calcium handling and its humoral control. More recently, he became interested in myocardial tolerance to acute ischemia/reperfusion injury of normal and diseased hearts and, in particular, in the mechanisms of sustainable forms of cardioprotection induced by adaptation to chronic hypoxia and regular exercise.

Dr. Ren-Ke Li, FIACS

Dr. Ren-Ke Li, MD, PhD is a Professor of Medicine in the Department of Surgery, Division of Cardiac Surgery and a Full Member of the Institute of Medical Science. He is also cross-appointed as a Full Member in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. Dr. Li is a Senior Scientist at the Toronto General Research Institute, University Health Network working in the field of stem cell transplantation and tissue engineering. Dr. Li completed his M.D. at Harbin Medical University in China in 1983 and his M.Sc. and Ph.D. in Clinical Biochemistry at the University of Toronto in 1992. He became an Assistant Professor at the University of Toronto in 1993 and was promoted to Full Professor in 2002. He is the recipient of the Canada Research Chair in Cardiac Regeneration (Tier 1) of the Canadian Institutes of Health Research and a Career Investigator of the Heart and Stroke Foundation of Canada. Dr. Li has been on the forefront in the field of cell transplantation and tissue engineering. In 1996, he published the first demonstration that cells transplanted into myocardial scar tissue survived, differentiated into muscle tissue, and improved heart function. More recently, his group has defined optimal cell types for transplantation, and described the optimal conditions under which the transplanted cells can achieve the most efficient repair. Currently, his research group is attempting to determine the mechanisms by which transplanted cells exert their beneficial effects. Clarifying these mechanisms will allow them to develop the "next generation" of gene enhanced cells for transplantation (cell-based gene therapy). Dr. Li has published 159 peer-reviewed papers and his work has appeared in high impact journals including Journal of Clinical Investigation, Circulation, Circulation Research, the FASEB Journal and American Journal of Physiology. Dr. Li has been invited to contribute several commentaries and viewpoint articles and is an international opinion leader in his field.

DR. VINCENZO LIONETTI

Dr. Vincenzo Lionetti was born in 1973, graduated in Medicine at the University of Bari School of Medicine in 1999. He received the Specialization in Anethesiology and Intensive Care Medicine at the University of Turin School of Medicine in 2003 and the Ph.D. in Innovative Strategies in Biomedical Research at the Scuola Superiore Sant'Anna of Pisa, Italy (SSSUP) in 2007. From 2008 to 2014 he was Assistant Professor of Physiology at the Institute of Life Sciences, SSSUP. Since 2014 he is Associate Professor of Anesthesiology at the same academic institution.

His main interest is pathophysiology of heart failure, physiology of myocardial cross talk and development of anti-remodeling and pro-repair approaches of ischemic myocardium. He received the following awards: the "Trainee Abstract Award" in 2002 by the Council on Basic Cardiovascular Science of the American Heart Association (AHA), the "Young Investigator Award" in 2007 by the National Institute of Cardiovascular Research (Bologna, Italy), and the "Pfizer European Young Researcher Award" in 2010 by Pfizer-Europe. In 2010, the Council on Basic Cardiovascular Science elected him "International Fellow" of the AHA.

He serves SSSUP as Deputy Coordinator of the PhD Program in Translational Medicine, Director of the II level University Master Course in "Underwater and Hyperbaric Medicine" and Vice-President of the Center of Experimental Biomedicine (CNR, Pisa, Italy). He is Faculty member of the Postgraduate School in Anesthesiology and Intensive Care Medicine at University of Pisa, Italy. He also serves as anesthesiologist at Fondazione Toscana "G.Monasterio", Pisa, Italy. He currently serves: i) the Research Executive Agency of the European Commission as expert evaluator of the Marie Skłodowska-Curie Actions: Innovative Training Networks (ITN), ii) the Research Fund - Flanders (FWO) and JSC "National Centre of Science and Technology Evaluation" (Republic of Kazakhstan) as grant evaluator.

From 2001 to 2002 he was Research Fellow at the Department of Physiology, New York Medical College, USA. In 2011 he was Visiting Scholar at the Division of Cardiology, Department of Medicine, University of Maryland, Baltimore, USA. From 2008 to 2010 he was AHA mentee. He serves as consultant of AstraZeneca, Aboca SpA, Pastificio Attilio Mastromauro Granoro s.r.l. He has received several grants from National and European Institutions, has published over 75 refereed peer-reviewed papers as well as several chapters in international medical books. He is member of several italian and international scientific societies and ESC Working Groups on Myocardial Function and Cellular Biology of the Heart. He is Treasurer of the Italian Society of Cardiovascular Research (SIRC). He is member of the Editorial Board of the Am. J Physiol-Heart and Circulatory Physiology, PLoS ONE, Ultrasound Med and Biol, Frontiers in Physiol and Frontiers in Cardiovasc Med. He serves as Associate Editor of the Can J Physiol and Pharmacol and Academic Editor of PLoS ONE. He serves as reviewer for several peer review journals.

DR. SERGE LEPAGE

Dr. Serge Lepage is a professor in Cardiology at the University of Sherbrooke. He joined the Faculty of Medicine of the University of Sherbrooke in 1981 and received his M.D. in 1985. Since 1992, he is Director of Clinical Research in Cardiology, Centre Hospitalier Universitaire de Sherbrooke (CHUS). Dr. Lepage participated in more than 80 sponsored studies in heart failure, ACS, hypertension, AF, cholesterol. He was director of the Department of Cardiology, Centre Hospitalier Universitaire de Sherbrooke and President of CMDP. Founder of the heart failure clinic at CHUS. He is presently President of CMDP of CIUSSS of the Estrie-CHUS.

DR. GARY LOPASCHUK, FIACS

Dr. Gary D. Lopaschuk is a Distinguished University Professor of Pediatrics at the University of Alberta, Edmonton. He is a Cardiovascular Researcher whose research focuses on the regulation of fatty acid oxidation in the heart, and the mechanism by which high rates of fatty acid oxidation contribute to heart disease and heart failure. He is also examining how alterations in fatty acid metabolism contribute to cardiovascular disease in the diabetic. At a molecular level he has characterized a number of key enzymes important in the regulation of cardiac fatty acid oxidation. He is also developing a number of therapeutic strategies that involve optimizing energy metabolism in the heart that can be used to prevent the development of heart disease, and that can also be used to treat heart failure. His research has resulted in the publication of over 400 original research articles, and he has been recognized by awards such as the Canadian Cardiovascular Research Achievement Award and the International Academy of Cardiovascular Sciences Research Achievement Award.
Dr. Lopaschuk is an Alberta Innovates Health Solution Scientist, and is a Fellow of the Royal Society of Canada. He has served as Scientific Director of the Mazankowski Alberta Heart Institute, and has

previously served in a number of capacities with the Heart Stroke Foundation of Canada, including as Chair of the Scientific Review Committee and the Vice-Chair of the Research Planning and Priorities Committee. He serves on a number of journal editorial boards, including Circulation Research, Journal of Clinical Investigation, American Journal of Physiology, Cardiovascular Research, Journal of Molecular and Cellular Cardiology, Canadian Journal of Physiology and Pharmacology, Heart and Metabolism, and Cardiovascular Drugs and Therapy. He is also the President and CEO of a biotechnology company (Metabolic Modulators Research Ltd.), that is developing novel drugs to treat heart disease that optimize energy metabolism in the heart.

DR. SHELDON MAGDER

MD FRCP(C)

Sheldon Magder is a Professor of Medicine and Physiology at McGill University and a Senior Physician at the McGill University Health Centre. Dr Magder's specialty training was in Cardiology but his clinical practice is currently mainly in general critical care.

Dr Magder has both active basic science and clinical research programs. His initial research training was in exercise physiology and his clinical research is now primarily on the regulation of cardiac output and the interaction of the heart and venous return under normal and pathological conditions. He also has an interest in acid-base balance and the physical chemical approach hydrogen ion concentration. His basic science research is in the vascular biology field. A major focus of this work is on the role of nitric oxide and reactive oxygen species in the vascular abnormalities of sepsis. In this work he is studying how reactive oxygen species may not only cause harm to tissues but may act as signaling molecules that regulate intracellular events. He has also performed studies on the effects of estrogens on the vascular wall and their potential protective and harmful effects.

DR. NILANJANA MAULIK, FIACS

I (Nilanjana Maulik, PhD) am a Professor in the Department of Surgery at the University of Connecticut Health, Farmington, Connecticut, and the Principal Investigator of NIH funded research grants and an expert in the field of Redox Regulated Molecular Signaling related to Angiogenesis in theischemic heart disease. My laboratory has explored several molecules and pathways involving myocardial angiogenesis using various pre---clinical models. I have authored or co---authored 190 articles in peer reviewed journals in the areas of myocardial angiogenesis, diabetic heart failure, hypertension, ischemia/reperfusion injury, myocardial infarction, mono---or combination gene therapy, ischemic and/or pharmacological preconditioning in myocardial protection also published 30 book chapters and edited three books in the field of epigenetics, cardiovascular biology, nutrition and healthy heart. Currently, I serve on several NIH study sections including special emphasis panels. I have served as Editor---In---Chief of Molecular Biology Reports for the last three years. I continue to service on the Editorial Boards of several journals.

DR. DENNIS MCNAMARA, FIACS

DR. MARTIN MORAD, FIACS

Dr. Morad is Professor of Regenerative Medicine and Cell Biology at the Medical University of South Carolina (MUSC) and the University of South Carolina (USC) and Professor of Bioengineering at Clemson University. He is the Director of the Cardiac Signaling Center and holds the BlueCross Blue Shield of South Carolina Endowed Chair in Cardiovascular Health, which includes a unique three-way faculty appointment at the USC, MUSC and Clemson University.

Dr. Morad is an internationally recognized scientist in the field of cardiac electrophysiology and calcium signaling. He has pioneered many seminal findings and technologies in the fields of electrophysiology and Cardiac signaling. He has had over 300 original publications, 19 of which have appeared in Science and Nature, and has trained over 90 Graduate students and postdoctoral fellows, most of whom have leading academic positions in American, European, and Asian Universities. Dr. Morad's career is marked by an incessant drive to formulate new physiological and molecular concepts based on innovative technology and experimental approaches unique to his lab. He has had a distinguished scientific career as professor of Physiology and Medicine at University of Pennsylvania, Professor and Chair at Georgetown University, and now as an Endowed professor at the three leading universities of SC. He was awarded the German Government senior Scientist Alexander von Humboldt prize for his seminal work in cardiac electrophysiology. He was elected as a founding fellow of international society of heart research (ISHR) and a fellow of International cardiovascular academy.

Dr. Morad current research is focused primarily on the pathophysiology of heart failure and cardiac arrhythmias. Recently he has succeeded in developing beating heat cells from the skin biopsies of human volunteers that can be used to repair damaged hearts, using adult stem cell technology. Similar approach is now underway in his Center in Charleston to engineer biologically based pacemaker from patient's skin fibroblasts to correct the irregularities of heart rhythm. To this end he and his team are using genetically engineered probes to examine the calcium signaling nano-domains of proteins involved in the pacemaking in adult hearts as well as in stem cell derived and spontaneously beating cardiomyocytes. The possible creation of a biological pacemaker derived from genetically engineered cells will provide major therapeutic advances in treatment of cardiac arrhythmias.

DR. MONI NADER

Dr Moni Nader is an Assistant Professor of Physiology at Alfaisal Medical School (KSA). He also serves as an Adjunct Scientist at the Department of Genetics at KFSHRC. Dr Nader earned his MSc in physiology from the Lebanese University (Lebanon) and completed his PhD in Cell Biology from the University of Sherbrooke (Canada). He pursued a postdoctoral training in Molecular Cardiology at the University of Ottawa Heart Institute (Canada) where he was supported by the Heart and Stroke Foundation of Canada.

Dr Nader's laboratory is primarily focused on the role of membrane/scaffold proteins in regulating the excitation-contraction coupling in cardiomyocytes. His research team is dealing with fundamental aspects of calcium homeostasis and its role in cardiac disease and failure. He is exploring the dynamics of the scaffold protein Striatin during cardiac remolding and in ischemia-reperfusion injuries. His current work is supported by the national funding agency KACST. Dr Nader also serves as a reviewer for KACST and for international journals (JMCC, BioMed Res Int, CJPP, and 3-Biotech).

DR. MICHEL NGUYEN, FRCPC

Dr. Nguyen joined the Faculty of Medicine of the University of Sherbrooke in 1980 where receives his M.D. in 1984. He received his Certificate of Specialist in Cardiology and Internal Medicine from University of Montreal (1984-90). From 2000 to 2012, he was appointed as director of the Division of Cardiology and Cath Lab at the Faculty of Medicine and Centre Hospitalier Universitaire de Sherbrooke.

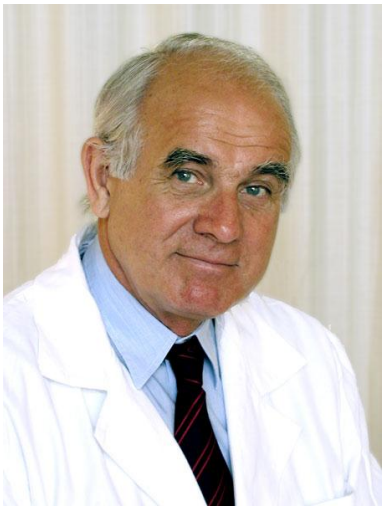
He is now Professor of Medicine at the Faculty of Medicine of University of Sherbrooke and Interventional Cardiologist at Centre Hospitalier Universitaire de Sherbrooke. His field of expertise cover Acute Coronary Syndrome and Interventional Cardiology

DR. KARMIN O

Dr. O is Professor in the Department of Animal Science, Department of Physiology and Pathophysiology, University of Manitoba and Principal Investigator in the CCARM, St. Boniface General Hospital, Canada. Her current research is focused on the regulation of oxidative stress and inflammatory response in cardio-metabolic disorders, kidney disease (AKI, CKD), NAFLD and health related effects of natural products and nutraceuticals.

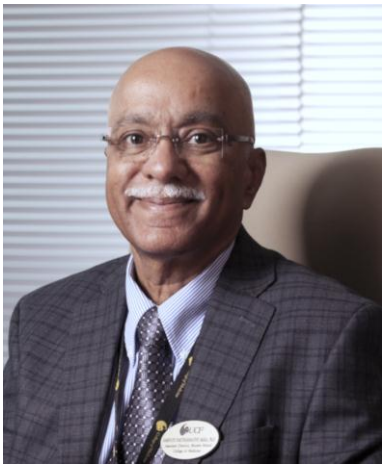
The research conducted in Dr. O's laboratory is funded by NSERC, Heart and Stroke Foundation, CIHR, Agriculture & Agri Food Canada. Dr. O has received the YMCA-YWCA Woman of Distinction Award for Research and Innovation.

DR. BOHUSLAV OSTADAL, FIACS



Professor Bohuslav Ostàdal, MD, DSc, a distinguished Czech cardiovascular physiologist, was born on January 28, 1940. His university education started in 1957 at the Faculty of Pediatric Medicine of the Charles University in Prague where he graduated in 1963. Since the very beginning, Ostàdal's main area of research has been focused on the ontogenetic development of heart structure and function. Already his early experimental studies on developing coronary circulation belong to landmark papers in the field that achieved well-deserved attention. His laboratory was among the first to demonstrate the important ontogenetic differences in cardiac sensitivity to various pharmacological agents. In a series of papers he investigated developmental changes in myocardial responses to acute oxygen deprivation, mechanisms of increased ischemic tolerance of the immature heart, and protective effects of preconditioning and chronic hypoxia. He has also been deeply concerned with late cardiovascular consequences of risk factors acting during early phases of ontogenetic development, the phenomenon known as fetal programming. Recently, he became particularly interested in differences of ischemic tolerance between hearts of males and females, the topic which appears to gain increasing attention of both experimental and clinical cardiologists.

DR. SAMPATH PARTHASARATHY



Dr. Sampath Parthasarathy, Ph.D., MBA is an internationally known cardiovascular scientist who holds the UCF College of Medicine's Florida Hospital Endowed Chair in Cardiovascular Sciences. He is also the Associate Dean for Research.

Before joining the college's Burnett School of Biomedical Sciences November of 2011, Dr. Parthasarathy held the Klassen Chair of Cardiothoracic surgery at Ohio State University.

Dr. Parthasarathy is a recognized expert in lipids and lipoproteins who is credited with the co-discovery of a major cardiovascular concept – the fact that oxidized LDL is involved in the initiation and progression of atherosclerosis. His areas of interest include atherosclerosis, diabetes, heart failure, Crohn's disease, Alzheimer's disease, and cardiovascular nutrition.

Dr. Parthasarathy has a breadth of research experience and has published over 250 original articles, including a single author monograph on "Modified Lipoproteins in the Pathogenesis of Atherosclerosis." He has won several meritorious awards and serves in numerous Editorial Boards. His work is extensively funded by the National Institute of Health (NIH) and AHA and he belongs to an elite group of the most highly cited authors worldwide in his field. He serves on numerous NIH committees.

Dr. Parthasarathy received his Ph.D. from the Indian Institute of Science and did post-doctoral training at Duke University and the University of Minnesota. In addition to The Ohio State, he has served as a faculty at the University of California, San Diego, Emory University and Louisiana State University. Dr. Parthasarathy also is an inventor and has a MBA degree in Technology Management.

DR. GRANT PIERCE, FACC, FAHA, FISHR, FAPS, FIACS

Dr Pierce completed postdoctoral training at UCLA before returning to Canada where he is Executive Director of Research at St Boniface Hospital and a Professor of Physiology and Pathophysiology at the University of Manitoba in Winnipeg. He has published over 200 peer reviewed research manuscripts and 7 textbooks on metabolism, nutrition and cardiovascular health. He has been cited over 8000 times with a Google Scholar H index of 53. He just completed a 13 year term as the Editor of the Canadian Journal of Physiology and Pharmacology. He recently received the Queen Elizabeth II Diamond Jubilee Medal for service to Canada and is an elected Fellow of the Royal Society of Canada, the highest distinction for a scientist in Canada.

DR. TANYA RAVINGEROVA, FIACS

Affiliation: Institute for Heart Research, Slovak Academy of Sciences, Bratislava, Slovakia

Current position: Chair of the Department of Cardiovascular Physiology and Pathophysiology, IHR SAS

Research interests: cardiac adaptation; innate cardioprotection under normal and pathological conditions and its molecular mechanisms; lifestyle-related cardiovascular disorders: diabetes, hyperglycemia, dyslipidemia, hypertension and their impact on cardiac ischemic tolerance.

Publication activity: cca 150 papers in extenso (mainly CC journals and book papers), cca 800 citations.

Membership and functions in scientific societies: IACS (Fellow and Vice-Prezident of the IACS-ES; ESC (Working Group on Pharmacology and Drug Therapy – council member); Czech-Slovak Working group on experimental cardiology - council member; Slovak Society of Physiology - council member; ISHR; Federation of European Physiological Societies (FEPS); European Academy of Sciences and Arts (member, Medical sciences).

DR. DELFIN RODRIGUEZ LEYVA, FRCPC, FAHA

Dr. Rodriguez Leyva received his MD from the University of Medicine of Santiago de Cuba in 1996 and followed with residences in Cardiology and Intensive Care Medicine at the University of Holguin. He obtained his PhD degree in Cardiovascular Research in 2004 from the High Institute of Medical Sciences of Havana. He was on faculty at Holguin University of Medical Sciences since 1997 as a Professor of Internal Medicine and Cardiology, serving also as Head of the Cardiovascular Research Division.

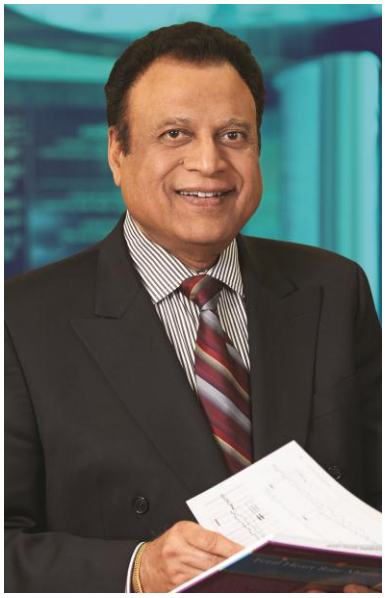
Dr. Rodriguez Leyva is the designer of the Cuban National Network of Cardiology. He has been internationally awarded with many scientific distinctions. His current clinical research interests include: omega-3 fatty acids, cardiac arrhythmias, hypertension, atherosclerosis and cardiac wearable devices. His work has been published extensively in high impact journals. Dr. Rodriguez has been appointed as associate professor in the Departments of Internal Medicine and Physiology and Pathophysiology at the University of Manitoba. He is certified in the specialties of Internal Medicine/Cardiology and Critical Care Medicine by the Royal College of Physicians and Surgeons of Canada becoming fellow of this institution. He is also an International Fellow of the American Heart Association.

DR. STEPHEN SCHAFFER, FIACS

Stephen Schaffer is presently a Professor of Pharmacology at the University of South Alabama. He received his PhD degree from the Department of Biochemistry at the University of Minnesota. His interest in the heart began during his postdoctoral training at the University of Pennsylvania, where he studied the effects of acidosis on the heart. He found that acidosis diminishes contractile function while dramatically altering energy metabolism. He began his professional career at Lehigh University and Hahnemann Medical School in Pennsylvania before joining the University of South Alabama School of Medicine. His work in Alabama initially focused on the effects of type two diabetes on heart function and metabolism. He was the first investigator to show that the type two diabetic heart develops a cardiomyopathy, characterized by defects in calcium transport, energy metabolism, protein phosphorylation and cell signaling. His present work has been directed at the study of the amino acid, taurine. Taurine, which is a beta-amino acid metabolite of cysteine, is of interest because it plays a central role in mitochondrial function Indeed, this function makes the beta-amino acid an essential nutrient in certain species, such as the cat. When cats are fed a taurine deficient diet they develop a cardiomyopathy, which can be fatal. Recent studies from his laboratory have shown that the conjugation of taurine with a Wobble position uridine in tRNALeu(UUR) alters the biosynthesis of a specific mitochondria encoded protein, ND6, which is an essential subunit of complex I of the respiratory chain. Thus, taurine deficiency leads to a decrease in respiration, generation of ATP and the availability of calcium for contraction. The taurine deficient cardiomyopathy is also associated with mitochondrial oxidative stress, which leads to apoptosis. The taurine deficient mouse serves as a model of the mitochondrial disease MELAS, which is one of the more widely studied mitochondrial diseases in humans, also develops a cardiomyopathy associated with impaired formation of the taurine - tRNALeu(UUR) conjugate. Taurine therapy has been shown to benefit the ischemic and failing hearts of animals and humans. Presently, taurine is approved as therapy against congestive heart failure in Japan. Moreover, a World Health Organization nutritional study has shown that elevations in taurine consumption are associated with improvements in cardiovascular health. The importance of taurine to heart health is beginning to be appreciated.

DR. ADEL SCHWERTANI

DR. PAWAN SINGAL, FIACS



Dr. Pawan Singal is a professor of Physiology and is Director of the Institute of Cardiovascular Sciences, St. Boniface Hospital and the University of Manitoba, Winnipeg, Canada. Dr. Singal completed his BSc Hons (1968) and MSc in Biophysics (1970) from Punjab University, India; PhD in Physiology in 1974 from the University of Alberta and his DSc degree in 1994 in Cardiovascular Pathophysiology. Dr. Singal joined the Physiology Department at the University of Manitoba as a lecturer, rose through the ranks and has been a professor since 1990. He served as Associate Dean for the Faculty of Graduate Studies, University of Manitoba. He is also holder of the Naranjan S. Dhalla Chair established by the St. Boniface Hospital Research Foundation.

Internationally known for his work on oxidative stress and heart failure, Dr. Singal has made significant contributions in our understanding of the sequeale of heart failure due to doxorubicin, chronic pressure overload as well as myocardial ischemia/reperfusion. He has published 270 papers, has co-edited 31 books and trained more than 100 students, fellows and visiting scientists. He has received more than 90 national and international recognitions. The University of Manitoba has established an award in his name called 'Pawan K. Singal Award for Graduate Students in Cardiovascular Sciences'. His name has been added to the Wall of Fame in the University Centre at the University of Manitoba recognizing his outstanding teaching skills and research.

DR. DINENDER SINGLA, FIACS

Dr. Dinender Singla received his B.Sc. and M.Sc. degrees from Punjabi University, Patiala, India and his Ph.D. from the the Post Graduate Institute of Medical Education and Research, Chandrigarh, India. He held post-doctoral fellowship positions in different Universities in Canada. He was joined as a tenure track Assistant Professor of Medicine at the University of Vermont. His current position at the University of Central Florida is a Professor and Head, Division of Metabolic and Cardiovascular Sciences, Burnett School of Biomedical Sciences in the College of Medicine at the University of Central Florida, Orlando, Florida. His major area of research is related to stem cells, heart failure, diabetes, inflammation and cardiac regeneration. Currently, he is exploring how to use the cutting edge technology on 3D printing in the pediatric and adult cardiac surgery. He is continuously serving to review the grants for various NIH, AHA, ministry of Italian health, and Hong Kong study sections. He is an Academic Editor for PLos one, Associate Editor for Canadian Journal of Physiology and Pharmacology as well as he is serving on the Editorial board member for different journals such as American Journal of Physiology: Heart and Circulatory. He is a chair, TPIG committee, American Physiology Society and also currently is a secretary North American section of the International Academy of Cardiovascular Sciences. He is a fellow international academy of cardiovascular sciences. He is a reviewer for different journals. He served as a chair for various scientific sessions throughout the world. He has also organized a scientific conferences. He is an author or coauthor for more than 70 peer reviewed papers.

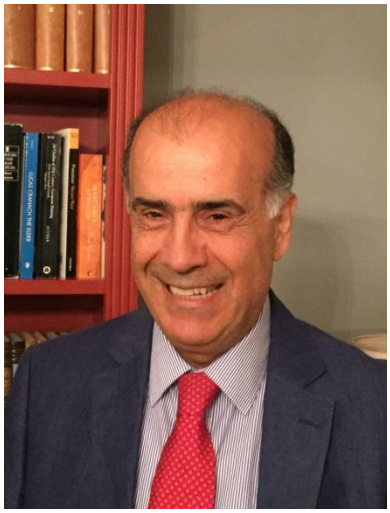
DR. JAN SLEZAK, FIACS

Professor Jan Slezak, MD, DSc., D.h.c. , Vice-rector of Slovak Medical University – a distinguished scientist and experimental cardiologist. After graduation al the Faculty of Medicine of the Comenius University in Bratislava-Slovakia in 1963, he joined the research team at Slovak Academy of Sciences (SAS)- the Institute for Heart Research (IHR) SAS. He got his Ph.D degree in 1968. He has been appointed as director of the IHR in 1988. He remained in this position until 1998 when he was elected a member of the Presidium of SAS and served as the First Vice-President of SAS until june 2009. In addition to his important positions in the research institutions, Prof. Slezak was always involved in teaching at the university and in 1986 he got the highest scientific degree DSc. He has been very active for more than 48 years teaching anatomy, histology, physiology and pathophysiology at the Faculty of Medicine of the Comenius University in Bratislava where he was appointed a Full Professor of Normal and Pathological Physiology in 1996. In 2008 he was awarded the degree of D.h.c. at the University of Zilina-Slovakia. The main area of his research interests has been focused on the topics of experimental cardiology and functional morphology, with particular regards to problematics of myocardial ischemia, cardiac heterogeneity and adaptability and, in particular, to subcellular mechanisms of myocardial adaptation and remodeling. He has been deeply involved in the studies investigating the role of reactive oxygen species in the mechanisms of cardiac in jury and some aspects of cardioprotective phenomena, e.g., ischemic preconditioning. During his life-long scientific career he has published more than 550 papers, 8 scientific books and 5 text-books. He has delivered many invited lectures at national and international conferences, universities and institutions, during his numerous study stays abroad (e.g., in Moscow, Leningrad, New York. Los Angeles, Winnipeg, Berlin, Bad Nauheim, Rotterdam, etc.). He was working as a visiting professor in the area of cardiac protection at UCLA, Mount Sinai Medical School New York and at the University of Manitoba for more than 4 years. He is a member of several scientific boards of research institutions and universities, and a member of Editorial Boards of 8 journals. Professor Slezak has been honored with the State Order of merit granted by the President of Slovakia and with numerous important awards and distinctions from the national and international scientific societies, academies and agencies in recognition of his achievements and services.

DR. ASHOK SRIVASTAVA

Dr. Ashok K. Srivastava is a Professor at the Department of Medicine, Université de Montréal, and Director of the Laboratory of Cell Signaling at the Research Center of the Centre hospitalier de l'Université de Montréal (CHUM). Dr Srivastava's laboratory is investigating the involvement of vasoactive peptide, growth factor and oxidant - induced signalling pathways in the pathogenesis of vascular abnormalities and diabetic complications.Dr. Srivastava has published more than 100 full-length papers and book chapters and has edited 4 books. He has contributed in the training of many graduate students and post-doctoral fellows. Dr. Srivastava is a member of the editorial boards of Molecular and Cellular Biochemistry, Recent Patents on Endocrine, Metabolic and immune Drug Discovery and Indian Journal of Biochemistry and Biophysics. He has also served as a guest editor of many journals such as Antioxidant and Redox Signaling, Canadian Journal of Physiology and Pharmacology, Cell Biochemistry and Biophysics and Molecular and Cellular Biochemistry. He has organized several International symposia and workshops, and also serves on the grant review panels of the Canadian Institutes of Health Research, the Heart and Stroke Foundation of Canada and the National Institutes of Health, USA.

DR. SAADEH SULEIMAN, FIACS



Professor Saadeh Suleiman (PhD, DSc) joined the University of Bristol, UK in 1988 after spending 8 years working at An-Najah University in Palestine. He currently holds the Chair of Cardiac Physiology at the Faculty of Medicine & Dentistry at Bristol. His ongoing academic activities include teaching clinical and biomedical sciences to undergraduate and postgraduate students in both Faculty of Medicine & Dentistry and Faculty of Medical & Veterinary Sciences. Professor Suleiman's current research is focused on investigating cellular mechanisms underlying the damaging effects of cardiac insults. Current clinical research includes investigating/designing novel cardio-protective interventions during adult and paediatric cardiac surgery and during angioplasty. Distinctions include being a member of the team that was awarded the UK Hospital Doctor Award for Team of the Year in Surgery and runners up for Cardiovascular Medicine, election to the executive committee of the British Society for Cardiovascular Research, elected as Fellow of both the International Academy of Cardiovascular Sciences and the Society of Biology. Has more than 250 scientific publications including papers, reviews, book chapters and peer reviewed abstracts. Successful at attracting significant funding with more than 70 grants (as PI or collaborator) totalling more than £15Million to support his research, students and staff. Professor Suleiman has organised and contributed as speaker to a large number of international meetings and has acted as a reviewer for national and international grant giving bodies and journals as well as acting as an external examiner/assessor for national and international academic institutions.

DR. BALWANT TUANA

Proessor at the Department of Cellular and Molecular Medicine Principal Scientist, University of Ottawa Heart Institute. Dr Tuana`s lab is focused on discovery science with view to define novel targets and pathways which control cell growth, death and differentiation. In particular the work has lead to the discovery of novel genes such as SLMAP and E2F6 as well as new splice variants of CaMKII and targeting partners. Cell based assays and genetically modified animal models have been generated and are being interrogated to decipher function and potential for therapeutic targeting of cardiac remodeling and heart failure.

DR. JEFFREY WIGLE

Dr. Jeffrey Wigle received his BSc(Honours) in Biochemistry from Queen's University and his PhD in Pharmacology from the University of Ottawa under the mentorship of Dr. Balwant Tuana. During his doctoral studies he cloned a new cardiac sarcolemmal protein- SLMAP. He then completed a PDF in the Department of Genetics at St. Jude Children's Research Hospital, Memphis before joining the Institute of Cardiovascular Sciences and the Department of Biochemistry and Medical Genetics, University of Manitoba. His postdoctoral fellowship was focused on the homeobox gene PROX1 and involved extensive use of mouse models. His work established for the first time the embryonic origin of the lymphatic vasculature. He was awarded a CIHR New Investigator Award and presently is an Associate Professor. His current research is directed at understanding the transcriptional programs used to control the growth and differentiation of cardiovascular cell types- endothelial cells (blood and lymphatic), vascular smooth cells and fibroblasts. He is currently interested studying how the interaction between Meox2 and Zeb2 transcription factorsi regulates the conversion of cardiac fibroblasts to myofibroblasts, which is an important step in cardiac fibrosis following myocardial infarction or in response to hypertension.

DR. ANDRAS VARRO, FIACS

Andras Varro graduated from the Szeged Medical University (Hungary) with an M.D. degree in 1978. He obtained his PhD degree in 1987. In 1998 he received the D.Sc. degree from the Hungarian Academy of Sciences. Between 1978 and 1990 he worked at The Cardiovascular Department of the Institute for Drug Research in Budapest and he was involved in various research projects applying in vivo and in vitro pharmacological methods to develop cardiotonic and antiarrhythmic drugs. Between 1991 and 2001 he was working at the Department of Pharmacology and Pharmacotherapy at the University of Szeged, Hungary with professor Julius Gy. Papp and András Varró succeeded him as chairman of the department in 2001. He was appointed as vice rector of the University of Szeged in 2011 supervising science and innovation. During his career, he spent 5 years in the USA, at the Kranner Institute of Cardiology, Indiana University with professor Borys Surawicz, and at the Department of Pharmacology and Cell Biophysics, University of Cincinnati, Ohio with professors Arnold Schwartz and David Lathtrop. He also spent more than 1 year (1991-1992) in the United Kingdom at the Department of Veterinary Preclinical Sciences, University of Liverpool, with professor David Eisner. His major research interests include physiology and pharmacology of cardiac potassium channels, cellular mechanisms of arrhythmias, antiarrhythmic and proarrhythmic drug actions. His research also focuses the genetical causes of LQT syndromes involving cellular (gene transfer) techniques and experimental in vivo (transgen models rabbit LQT approaches. His most important scientific achievements were contributing to the elucidation of the cellular mode of action of amiodarone (Eur. J. Pharmacol. 1985; 112:419), the role of the slow delayed rectifier potassium current (IKs) in cardiac repolarization and repolarization reserve (J Physiol, 2000; 523:67., Circulation, 2005; 112:1392.), characterization of the native human transmembrane potassium currents (Cardivasc Res, 1998; 40:508, 2001; 49:790.), and elucidation of the possible antiarrhythmic effect of the sodium calcium exchanger (NCX) (Br J Pharmacol. 2004; 143:827; Br J Pharmacol 2013;170:768)

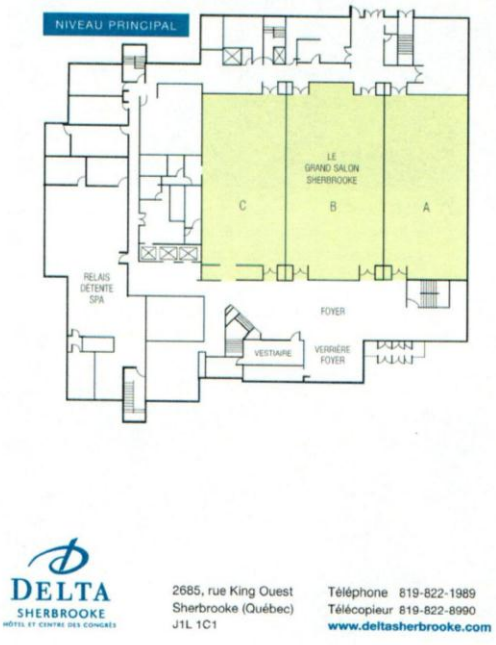
Between 1998 and 2002 he served as an editor for the British Journal of Pharmacology and since 2013 he is editor of Cardiovascular Research. He published more than 276 full length papers and 9 book chapters in English language which earned 7606 citations and resulted H index= 47. He was also involved in the development of several new cardioactive drugs which resulted 8 patent applications.

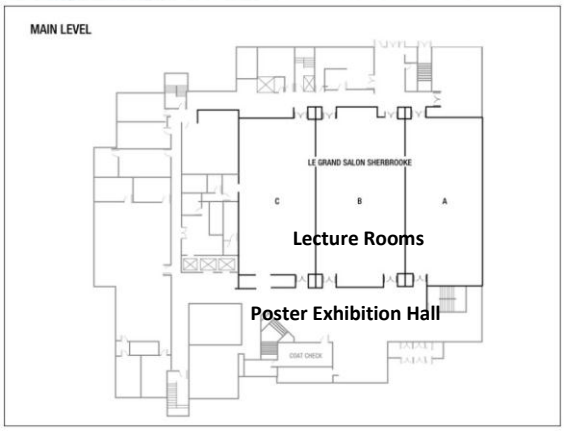
DR. CARIN WITTNICH

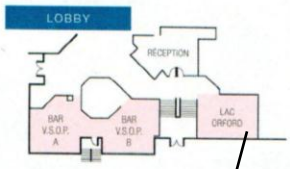
Dr. Wittnich is a tenured Full Professor in the Departments of Surgery and Physiology at the University of Toronto, and is the founding Director of the Cardiovascular Sciences Collaborative Program. As well, she is Staff in the Division of Cardiac Surgery at The Hospital for Sick Children and Division of Cardiology at The Toronto Hospital - General Division. She has held grants from the Heart & Stroke Foundation and MRC for work in newborn hearts response to stress and role of sex. As primary supervisor, she has trained over 13 MSc and 5 PhD students to date and continues to maintain an active research program, having published over 90 papers in peer reviewed journals. Outside of the University, she is a founding Director and Senior Scientist of the Oceanographic Environmental Research Society serves on a number of editorial boards for scientific journals and is Editor-in-Chief of the Journal of Marine Animals and Their Ecology (JMATE).

Dr. Wittnich was recognized by the Department of Surgery in 1991 with the George Armstrong Peters Prize for her outstanding initial research productivity and then in 1999 with the Lister Prize for her continuing Heart & Stroke Foundation of Ontario grant funded research of international stature. In 1996 the University of Toronto awarded her the prestigious “Northrop Frye Award” for her innovation and exemplary linking of teaching and research. The Faculty of Medicine continues to recognize her outstanding teaching contributions with the “Sustained Excellence in Graduate Teaching Award” (2005), Excellence in Life Science Teaching (2008) and Excellence in laboratory Undergraduate Teaching (2013). Outside the University of Toronto, in 2001 she was invested with the Order of Ontario for her work in promoting awareness and education of heart disease in women and children, and received the Queen's Jubilee Medals (Golden 2002, Diamond 2012). In 2006, she received the OVC Distinguished Alumni Award from her alma mater the University of Guelph for her outstanding contributions and successes in both academic and research fields. Her volunteer efforts are also well known and respected and she received the OVMA Recognition Award for her work with Hurricane Katrina relief efforts.

French **English**







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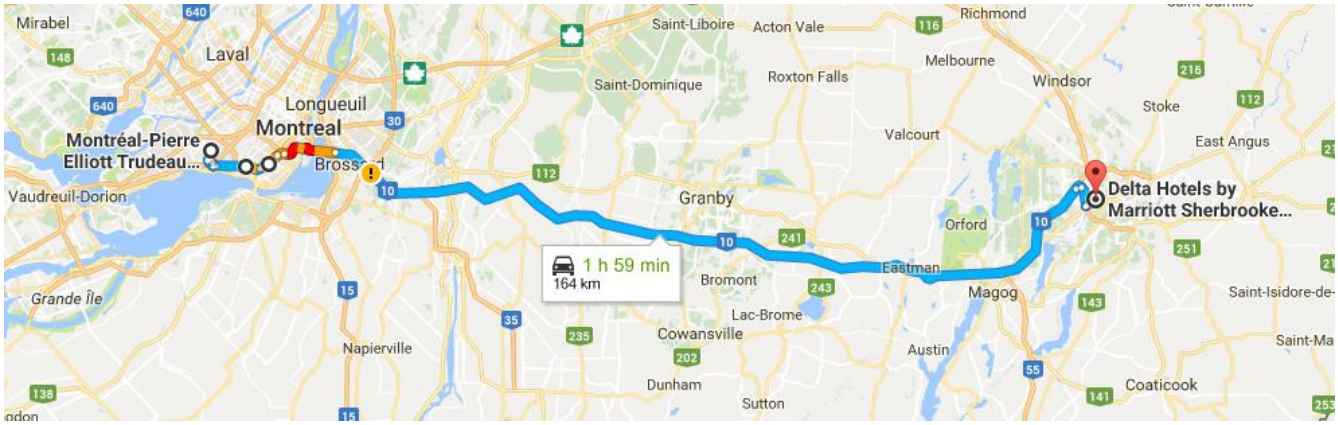
IACS-NA Executive Committee Business Meeting Room

Double Bedroom

Conference Rooms (Grand Salon Sherbrooke A+B+C)



Montréal-Pierre Elliott Trudeau International Airport
Québec

- Get on Autoroute 520 from Roméo-Vachon Blvd N/Roméo-Vachon Blvd North (Arrivals) and boul. Roméo-Vachon N
  4 min (1.7 km)
- Head north on boul. Roméo-Vachon N toward Roméo-Vachon Blvd N/Roméo-Vachon Blvd North (Arrivals)
  52 m
- Use the left 2 lanes to turn slightly left onto Roméo-Vachon Blvd N/Roméo-Vachon Blvd North (Arrivals)
  600 m
- Continue onto boul. Roméo-Vachon N
  700 m
- Keep right at the fork, follow signs for Autoroute 20/Montréal/Toronto and merge onto Autoroute 520
  400 m
- Take Autoroute 10 E to Rue King O/QC-112 E in Jacques-Cartier, Sherbrooke. Take exit 4E from Autoroute 410 E
  1 h 36 min (161 km)
- Merge onto Autoroute 520
  400 m
- At the roundabout, take the 3rd exit
  350 m
- Continue onto Boulevard Montréal-Toronto
  140 m
- Use the left lane to take the Autoroute 20 E ramp
  170 m
- Merge onto Autoroute 20
  10.8 km
- Take exit 68S for Autoroute 20 E/Autoroute 15 S toward Autoroute 10/Pont Champlain/U.S.A/Québec
  1.3 km
- Merge onto Autoroute 15 S/Autoroute 20
  9.0 km
- Continue onto Autoroute 10 E
  134 km
- Take exit 140 for Autoroute 410 toward Rue King Ouest
  1.1 km
- Continue onto Autoroute 410 E
  3.2 km
- Take exit 4E for Québec 112 E/Rue King Ouest toward Sherbrooke/Centre-Ville
  150 m
- Follow Rue King O/QC-112 E to your destination
  4 min (1.9 km)

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