1. **Course Description:**

The cardiovascular system is a complex system. In this course, the class sessions focus on selected topics of current research and provide an opportunity for the student to delve in depth into some of the molecular events and mechanistic processes governing heart and vascular function in health and disease. Prerequisites: Physiology 3120, 3130y and 3140a.

2. **General Objectives of the Course:**

   a. To build on the general understanding of the mechanisms governing heart and vascular function with in-depth integration of contemporary knowledge of cardiovascular physiology and patho-physiology.

   b. To increase your knowledge of the mechanistic basis and molecular events associated with physiological adaptation of the heart and vascular system to the evolution of cardiovascular pathogenesis.

   c. To consider in some depth current concepts of heart function in health and disease, and to critically assess research publications in these fields.

   d. To gain experience in scientific presentation and discussion.

3. **Evaluation**

   a. Weekly presentation of research paper 15%
   b. Participation in weekly in class discussions 5%
   c. Mid-term examination (short answer and essay format) 25%
   d. Assignment – topics and deadline to be discussed with class 5%
   e. Final examination (short answer and essay format) 50%

**NOTE THAT:**

(i) YOU MUST WRITE THE MID-TERM EXAMINATION TO SIT FOR THE FINAL EXAMINATION

(ii) MINIMUM 80 % ATTENDANCE IN THE WEEKLY DISCUSSION SESSIONS IS REQUIRED TO WRITE THE FINAL EXAMINATION

4. **Weekly Research Paper Presentation/Discussion Session**

Each session will consist of a brief overview (~30 min) of the "Research Topic of the Day” by the faculty instructor, presentation of material from two research papers by students (presentation
time: 20 min for each paper), and a discussion period (~10-15 min) following each research paper presentation. Presentation of each research paper will be the responsibility of a single student, or the joint responsibility of two students, as dictated by the number of students enrolled in the course. Evaluation will be based on each participating student’s knowledge and performance. Two students (in addition to the presenters) will be selected to serve as “Discussion Leaders” for each research paper presented; they will initiate and lead the discussion of the paper with active participation from all students in the class. \textit{ALL students are expected to have read the papers BEFORE class and to participate in discussions.} The lectures and research paper presentations for the current academic year are listed under item #6 of this document. \textit{The Research Paper Presenters and Discussion Leaders for each classroom session will be randomly assigned and posted on the class schedule on OWL.}

\*\textbf{Calculation of Presentation Marks:} \begin{tabular}{ll}
Knowledge of topic & 40 \% \\
Presentation of material & 40 \% \\
Responses to Questions & 20 \% \\
\end{tabular}

\textbf{Calculation of Participation Marks:} \begin{tabular}{ll}
Performance as Discussion Leader & 80 \% \\
(knowledge of topic, originality and quality of questions) & \\
Contribution as classroom participant & 20 \% \\
\end{tabular}

\*Note: All students (including the presenter) can participate in marking the presentations by students. The marks from students will be collected by the faculty instructor on each day after the presentations. For each presentation, marks from students deviating by not more than 3\% \textit{(plus or minus)} from that given the faculty instructor, will be included in averaging the presentation mark. Marks from students showing more than 3\% deviation \textit{(plus or minus)} will not count. This peer participation in marking is optional.

\begin{center}
\begin{tabular}{llll}
\textbf{Participating Faculty} & \textbf{Office} & \textbf{Telephone} & \textbf{E-mail Address} \\
Dr. Robert Gros & RRI4282 & 519-931-5777 x 24429 & rgros@robarts.ca \\
( Instructor & Course Manager) & & & \\
Dr. Marlys Koschinsky & RRI2260 & 519-931-5777 x 24389 & mlk@robarts.ca
\end{tabular}
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5. Time and Location of Lectures: Friday, 9:30 – 11:20 a.m. DSB 3008

6. Class Schedule, Lectures and Research Paper Presentations for the Academic Year Lectures/Presentation Dates and Faculty Supervisor


Jan. 19 Dr. Robert Gros: Vascular Function in Health and Disease: Regulation of Blood Vessels via GPCRs.
Jan. 26 Dr. Robert Gros: Vascular Function in Health and Disease: Regulation of Blood Vessels via GRKs.

Feb. 2 Dr. Robert Gros: **No Class – Start work on assignment**

Feb. 9 Dr. Robert Gros: Vascular Function in Health and Disease: Regulation of Blood Vessels via Myogenic Tone.

Feb. 16 **Mid – Term Examination in Class (Jan. 19– Feb. 9 Topics – Dr. Gros’ Lectures)** (Feb 19– 23 Reading Week – No Classes)

Mar. 2 Dr. Robert Gros: Vascular Function in Health and Disease: Regulation of Blood Vessels via Steroid Hormones.

Mar. 9 Dr. Marlys Koschinsky: The Role of HDL in Cardiovascular Disease: Good, Bad, or Both?

Mar. 16 Dr. Marlys Koschinsky: New Perspectives on the Contribution of Smooth Muscle Cells to Atherosclerosis.

Mar. 23 Dr. Robert Gros: Cardiac Function in Health and Disease: Physiological versus Pathological Hypertrophy of the Heart.

Mar. 30 **Good Friday – No Classes.**

Apr. 6 Dr. Robert Gros: Cardiac Function in Health and Disease: Novel Cardiac Macrophages.

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**Research Paper Presentations/Assignments Schedule**

**January 12, 2018:** Introduction and Overview, Rules & Guidelines for Research Paper Presentation (Dr. Gros)

Heart is the first organ to be formed during embryogenesis and the manifestation of life begins with the heart beat. Indeed, the ability to generate the heart beat at regular intervals (heart rhythm) is intrinsic to the heart and needs no input from any other organ, including the brain and nervous system. Cessation of the heart beat marks the end of life. Besides its automaticity, the
heart has a striking ability to respond to neuro-humoral signals (acute and chronic) so as to adjust heart rate, contractile force and cardiac output, and thus maintain circulatory homeostasis in accordance with varying physiological demands. Not surprisingly, pathology of the heart and vasculature has major consequences for survival, and cardiovascular disease remains the “number one killer” of people world-wide. As a result of intensive research in several laboratories, new insights and novel concepts regarding the mechanisms governing the (a) origin and regulation of the heart beat and cardiac contractile function, as well as (b) pathogenesis of systolic and diastolic dysfunction leading to heart failure, have emerged. Being a fourth year honours course, this “current topics” offering will provide the students the opportunity to explore in depth, some of these topics with the faculty instructor and lead the discussion with their peers on the papers designated for each day. This introductory session will be to introduce you to the topics for discussion this year and develop the course material, which will be used.

Will also provide information and guidelines aimed to develop and enhance students’ scientific communication skills. In addition, general principles to be followed while undertaking critical review and assessment of research publications will be outlined.

January 19, 2018: Vascular Function in Health and Disease: Regulation of Blood Vessels via GPCRs (Dr. Gros)

G-protein-coupled receptors (GPCRs) represent the largest family of integral membrane proteins and play a crucial role in the regulation of vascular tone and hence peripheral resistance, which reflects the net balance between vasoconstrictor and vasodilator mechanisms. Regulation of vascular tone is complex and involves many different GPCR agonists some of which are the classical, well-established activators and some that are known as emerging GRCR activators. A better understanding of the role of these emerging GPCR agonist in regulating vascular function may lead to the discovery of novel therapeutic treatments for cardiovascular diseases.

Recommended review article:

Maguire JJ, Davenport AP  Regulation of vascular reactivity by established and emerging GPCRs. Trends Pharmacol Sci. 2005 Sep;26(9):448-54
http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T1K-4GR8MS8-4&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=8fb449dab255723e3692426726cd9d9c

Papers for presentation and discussion:

http://circres.ahajournals.org/cgi/reprint/103/3/315

Presenter (RPP): Mokshal Porwal
Discussion Leader (DL): Alexander Xiao

**Presenter (RPP): Gregory Robinson**  
**Discussion Leader (DL): Kevin Krysiak**

**January 26, 2018: Vascular Function in Health and Disease: Regulation of Blood Vessels via GRKs. (Dr. Gros)**

The regulation of GPCR activity in the vasculature represents a delicate but coordinated balance between receptor signalling and molecular mechanisms that govern receptor desensitization and re-sensitization. The desensitization of most GPCRs if affected by G-protein-coupled receptor kinases (GRKs), which mediate GPCR phosphorylation. Alterations in the expression and/or activity of GRKs has been associated with cardiovascular diseases such as hypertension.

**Recommended review article:**


**Papers for presentation and discussion:**


**Presenter (RPP): Kevin Krysiak**  
**Discussion Leader (DL): Christina Lam**

[http://ajpheart.physiology.org/content/305/8/H1111](http://ajpheart.physiology.org/content/305/8/H1111)

**Presenters (RPP): Jin Grace and Tabitha Mcguire**  
**Discussion Leader (DL): Matthew Ryckman**

**February 2, 1018 – No Class – Start Work on Assignment.**
February 9, 2018: Vascular Function in Health and Disease: Regulation of Blood Vessels via Myogenic Tone. (Dr. Gros)

The regulation of vascular tone under both physiological and pathological conditions is complex. In addition to the vascular responses to circulating and/or locally produced hormones acting on a variety of receptors (including GPCRs), some vascular beds have the unique ability to mediate vascular constriction or vasodilation in response to changes in intraluminal/intravascular pressure. This is known as the myogenic response, a phenomenon described over a 100 years ago, which is critical to the regulation blood flow, responsible for the constant maintenance of steady perfusion pressure and the prevention of possible tissue damage. Alterations in myogenic tone have been associated with various cardiovascular diseases including hypertension.

Recommended review article:


Papers for presentation and discussion:


Presenter (RPP): Asha Kurup
Discussion Leader (DL): Nicholas Van Bilsen


Presenter (RPP): Monika Mielniczek
Discussion Leader (DL): Andrew Tran

February 16, 2018: In Class - Mid-term Examination (Jan. 19 – Feb. 9 Topics; Dr. Gros – 3 lectures only).

(February 19 – 23, 2018 Reading Week – No Classes)
March 2, 2018: Vascular Function in Health and Disease: Regulation of Blood Vessels via Steroid Hormones. (Dr. Gros).

The steroid hormones aldosterone and estrogen have been implication in the regulation of vascular tone. Some of these vascular effects are proposed to be mediated via the traditional steroid hormone receptors such as the mineralocorticoid (aldosterone) receptor and estrogen receptors, although more recently a novel GPCR (GPR30/GPER) has been identified as a possible mediator of the rapid vascular effects of these steroid hormones. A better understanding of the role of the different receptors involved in the steroid-mediated regulation of vascular tone under physiological and pathological conditions may lead to alternate therapeutic agents in the treatment of various cardiovascular diseases.

Recommended review articles:

Papers for presentation and discussion:


Presenter (RPP): TBA
Discussion Leader (DL): TBA


Presenter (RPP): TBA
Discussion Leader (DL): TBA

March 9, 2018: The Role of HDL in Cardiovascular Disease: Good, Bad, or Both? (Dr. Koschinsky).

HDL has been recognized as the “good” cholesterol compared to LDL, elevated levels of which have been associated with the development of coronary heart disease. In this regard, HDL has been shown to be a key player in the reverse cholesterol transport process, which removes excess cholesterol primarily from macrophages through the ATP-binding cassette transporter A1 (ABCA1) receptor. Consistent with its cardioprotective role, low levels of HDL have been associated with increased risk for cardiovascular disease. However, recent studies have shown that HDL is highly heterogeneous in terms of its proteome, which can influence its function and modifiable by systemic and vascular inflammation that in turn decreases its protective effects.
This is becoming a focus of study in order to identify pharmaceuticals that can recognize and target “dysfunctional” HDL.

**Recommended review article:**

**Papers for presentation and discussion:**

**Paper 1.**

**Presenter (RPP): TBA**  
**Discussion Leader (DL): TBA**

**Paper 2.** Paper for presentation and discussion.…  

**Presenter (RPP): TBA**  
**Discussion Leader (DL): TBA**

**March 16, 2018: New Perspectives on the Contribution of Smooth Muscle Cells to Atherosclerosis (Dr. Koschinsky).**

There have been conflicting views regarding the role of arterial smooth muscle cells in atherosclerosis, from accelerating the process due to their proliferation, to stabilizing atherosclerotic lesions due to their contribution to the formation of stable lesions through synthesis of extracellular matrix components. Seminal contributions to our understanding of VSMC biology and function have come from early studies highlighting the importance of phenotypic switching of these cells within lesions from a contractile to synthetic phenotype. VSMCs can undergo inflammatory activation, which contributes significantly to vascular disease. Recent studies have highlighted the importance of the embryological origin of VSMCs in their function and contribution to different stages of the atherosclerotic process.
Understanding the origin and behaviour of plaque VSMCs may provide interesting avenues for therapeutics useful in treating atherosclerosis.

Recommended review article:

Papers for presentation and discussion:


Presenter (RPP): TBA
Discussion Leader (DL): TBA


Presenter (RPP): TBA
Discussion Leader (DL): TBA

**March 23, 2018: Physiological versus Pathological Hypertrophy (Dr. Gros).**

The heart is able to respond to increasing workload by undergoing increasing the size of individual muscle cells, termed hypertrophy. This hypertrophy can result from both pathological signals as well as physiological stimuli. Recent findings suggest that these different stimuli utilize different downstream signal transduction pathways and this results in profoundly different forms of hypertrophy.

Recommended review article:

Papers for presentation and discussion:

Presenter (RPP): TBA
Discussion Leader (DL): TBA


Presenter (RPP): TBA
Discussion Leader (DL): TBA

March 30, 2018: GOOD FRIDAY – No Classes.

April 6, 2018: Novel Cardiac Macrophages (Dr. Robert Gros)
Macrophages are found both in the circulation and are resident within tissues. These are important cell types in protection against pathogens and also in repairing tissue after damage. Recently it has been found that not all macrophages arrive in a tissue through the circulation. Some macrophages arrive at a tissue, including the heart, early in embryogenesis and these tissue resident macrophages persist through adulthood and are capable of self-renewal. They also have different properties than the macrophages in circulation. We will examine the implications for these findings in cardiac disease.

Recommended review article:

Papers for presentation and discussion:


Presenter (RPP): TBA
Discussion Leader (DL): TBA

http://www.pnas.org.proxy1.lib.uwo.ca/content/111/45/16029.long

Presenter (RPP): TBA
Discussion Leader (DL): TBA

THE END