

THE 2016 ANNUAL REPORT
CARDIOVASCULAR RESEARCH
INSTITUTE OF VERMONT

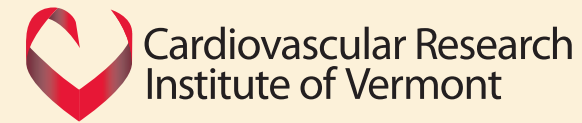


THE CARDIOVASCULAR RESEARCH INSTITUTE OF VERMONT is dedicated to reducing the incidence, morbidity, and mortality of heart and vascular diseases through improving prevention, diagnosis, and treatment.

By fostering collaborations among departments at The University of Vermont and The University of Vermont Medical Center, the Cardiovascular Research Institute of Vermont encourages the critical thinking that challenges assumptions and promotes excellence in clinical practice.

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MESSAGE FROM THE DIRECTOR

2016 was marked by important achievements that will enable the CVRI to support its core mission of fostering cardiovascular research. While it is important to highlight accomplishments of senior investigators, the challenges associated with establishing and maintaining funding has led the CVRI to focus on supporting early career investigators. During the past year, the CVRI has expanded internal funding opportunities and under the guidance of its early career advisory committee has developed opportunities to enhance collaboration.

This year Dr. Martin Bloomfield, a UVM alumnus, has enabled the CVRI to expand its support of early career investigators through philanthropy. Dr. Bloomfield endowed an early career award that will provide financial support for a junior faculty member for two to three years. He also endowed a fund that will support in perpetuity the Burton E. Sobel and the Norman R. Alpert visiting professorships. Charitable donations by Mark Ray in honor of his father have enabled us to expand this program. Another CVRI program focused on early career investigators that is supported by a gift from Paul Millman/Chroma Technologies provides funding for summer research projects that are proposed by first year medical students, expanding an existing program of the Larner College of Medicine. The early career advisory committee of the CVRI hosted a series of networking events during the past year. What began as a social opportunity designed to introduce cardiovascular researchers from different disciplines has transitioned into short scientific exchanges designed to foster new collaboration.

The Philip Ades, M.D. Professor of Cardiovascular Disease Prevention was endowed during 2016 and Dr. Ades was installed as the first professor. This professorship honors the significant impact of the cardiac rehabilitation and disease prevention work performed by Ades over his more than 30-year career at UVM.

We are proud of the accomplishments achieved in cardiovascular research at the University of Vermont. Thank you for taking the time to learn about these accomplishments in the pages that follow.



David J. Schneider, M.D., F.A.C.C., F.A.H.A.

Director
Cardiovascular Research
Institute of Vermont

Professor of Medicine
The Robert Larner, M.D. College of Medicine
at The University of Vermont

Director of Cardiovascular Services
University of Vermont Health Network

Cardiovascular Research News

CUSHMAN NAMED EDITOR-IN-CHIEF OF NEW INTERNATIONAL JOURNAL



Mary Cushman, M.D., M.Sc., editor-in-chief of the new *Research and Practice in Thrombosis and Haemostasis* journal.

In January 2017, the International Society on Thrombosis and Haemostasis (ISTH), in partnership with John Wiley and Sons, Inc., announced the launch of the Society's new

open access journal, *Research and Practice in Thrombosis and Haemostasis* (RPTH), with its inaugural issue publishing in conjunction with the meeting of the ISTH 2017 Congress in Berlin, Germany, in July

Mary Cushman, M.D., M.Sc., professor of medicine at the Larner College of Medicine, director of the thrombosis and hemostasis program at the University of Vermont Medical Center, and a CVRI Board of Directors member, will lead the launch of the journal as its inaugural Editor-in-Chief. The editorial team represents all areas of the world.

Complementing the Society's flagship journal, the *Journal of Thrombosis and Haemostasis* (JTH), RPTH will provide an innovative new open access platform for science and discourse among researchers,

clinicians and patients. It will publish a broad array of article types covering the widest possible spectrum of topics in thrombosis, hemostasis and related areas. Studies by multidisciplinary research groups, from emerging areas of research and from under-represented regions of the world, will be of particular interest.

"RPTH epitomizes the current era of inter-disciplinary scientific discovery and new methods of knowledge dissemination," says Cushman. "Capitalizing on its open access and online-only format, RPTH will provide unrestricted access to scientific results from around the globe as a 'living journal,' serving as an important catalyst for digital discussion. In so doing, it will also provide the public with ease of access to research findings."

BERNSTEIN INDUCTED AS 2016-17 UNIVERSITY SCHOLAR

Larner College of Medicine faculty member Ira Bernstein, M.D., was named as one of four 2016-17 University Scholars. Led by the UVM Graduate College, the University Scholars program recognizes "sustained excellence in research, creative and scholarly activities." He delivered his University Scholar Lecture in February 2017 on "Pregnancy and Preeclampsia: Insights into Women's Health."

Bernstein is professor and John Van Sicklen Maeck Chair of Obstetrics, Gynecology and Reproductive Sciences, medical director of Women's Health Care Services at the UVM Medical Center, and a member of the Board of Directors of the CVRI. A 1983 alumnus of the College

of Medicine, he graduated as an Alpha Omega Alpha medical honor society member, completed a residency in obstetrics and gynecology at George Washington University Hospital, and then joined the UVM faculty in 1987, completing a maternal fetal medicine fellowship here in 1990.

Bernstein has served as director of maternal fetal medicine (MFM) and MFM fellowship training, as well as senior associate dean for research at the College of Medicine. His primary research focuses on human integrative physiology and its pathophysiologic variations during the course of pregnancy. Bernstein's honors include the Distinguished Academic Achievement Award from the College and research awards from the New

England Perinatal Society, the Society for Maternal Fetal Medicine and the Society for Reproductive Investigation. He currently serves on the medical advisory board for the Preeclampsia Foundation and is a member of the Executive Board of the Vermont Oxford Neonatal Network.



Ira Bernstein, M.D., with a patient.



Professor of Medicine Peter Spector, M.D., in the UVM Medical Center Cardiac Catheterization Lab.

SPECTOR PUBLISHES BOOK ON "UNDERSTANDING CLINICAL CARDIAC ELECTROPHYSIOLOGY"

Electrophysiologist **Peter Spector, M.D.**, has uncovered a wealth of new information about why the heart's electrical system works the way it does – or goes awry. His 2016 book – titled *Understanding Clinical Cardiac Electrophysiology: A Conceptually Guided Approach* and published by Wiley-Blackwell – comes out of his nearly 25 years of experience studying the electric signals and flow of electrical current that spurs the heart to pump.

Spector is a Larner College of Medicine professor of medicine and director of electrophysiology at the UVM Medical Center. As a specialist in atrial fibrillation (A-fib), the most common form of heart rhythm disorder, he has developed a deep understanding of this process so that he can better treat patients, he says.

Spector calls it a cohesive approach to a complex system. "Electrophysiology is not a linear system, in which one change or action leads to the next change, which leads to the next – a chain reaction." In a complex system, one change leads to multiple changes in multiple directions, and those changes in turn cause multiple reactions in multiple places.

"I put this all together in a way that makes sense to me," Spector says. "The book is trying to tell the complex story of the mechanisms of the heart."

SPEES' NIH GRANT EXPANDS STUDY OF NOVEL POST-HEART ATTACK THERAPY

A heart attack continues to harm cardiac muscle even after the immediate problem – a blocked artery – is fixed, but Larner College of Medicine Associate Professor of Medicine **Jeff Spees, Ph.D.**, and a team of researchers have developed a new biologic drug that can preserve blood vessels critical to the body's blood-pumping system.

When an artery in the heart is clogged, toxic substances from cardiac tissue that has been deprived of oxygen and nutrients build up in the blood, similar to how the water that pools in front of a dam collects dirt and debris. When a stent is surgically inserted to open the blocked blood vessel, there can be a negative side effect: a cascade of blood filled with built-up toxins flowing into the smaller downstream blood vessels. This damages the sensitive endothelial cells that line the microvasculature and capillaries.

Ultimately, this activity causes additional heart tissue to die and is commonly referred to as "reperfusion injury." It's collateral damage that's nearly impossible to avoid, and the body doesn't naturally restore the resulting dead or dying tissue, says Spees.

Spees and his colleagues have developed a therapy called VasaPlex – a protein complex that rescues some of the blood vessels and surrounding tissue at risk in animal models of heart attack. The National Heart, Lung and Blood Institute of the National Institutes of Health this year awarded Spees a \$1.2 million R01 research grant to continue to test this invention.



Associate Professor of Medicine Jeffrey Spees, Ph.D., in his laboratory.

A Road Map for Saving Lives through Cardiac Rehab

A strategy explored by Philip Ades, M.D., could save 25,000 lives and prevent 180,000 hospitalizations annually

More than two million Americans experience some type of a cardiac event every year. Whether they've had a heart attack or coronary revascularization procedure, such as bypass surgery or coronary stent placement, physicians typically recommended these patients participate in Cardiac Rehabilitation (CR) as outpatients. However, despite the proven benefits of increased longevity and reduced hospitalizations with CR, only 20 to 30 percent of eligible patients actually participate.

Why are the rates for this comprehensive secondary prevention program so low? And how can they be improved?

An article published in November in the Mayo Clinic Proceedings by lead author **Philip Ades, M.D.**, professor of medicine at The Larner College of Medicine at the University of Vermont, associate director of the Vermont Center on Behavior

and Health, and a CVRI Distinguished Investigator, offers answers and solutions. Written by participants of the Cardiac Rehabilitation Collaborative (CRC), a group of experts convened by Million Hearts, the U.S. Department of Health and Human Services initiative, the paper identifies ways to increase participation rates to at least 70 percent among eligible patients – an outcome that, if adopted nationwide, could save 25,000 lives and reduce hospitalizations by 180,000 annually.

According to the report, two steps are necessary to substantially increase CR participation: First, the systematic referral of eligible patients needs to be increased and, second, the successful enrollment and adherence of those who are referred to CR needs to be optimized.

“While there are many reasons that individuals do not attend CR, including

geographic availability of a program, the primary reason – and one that is modifiable – is that doctors and caregivers do not recommend it strongly enough,” says Ades.

“Referral and enrollments would be substantially improved if the hospital electronic discharge process required the physician to address CR referral, such that appropriate patients leave the hospital with a CR appointment scheduled for a week or so after hospital discharge,” Ades says, adding that a “liaison” should be assigned to meet with each patient to introduce the concept of CR and help coordinate the referral process.

The authors of the paper found that automatic electronic medical record referrals combined with the use of a liaison led to referral rates of 86 percent and participation rates of over 70 percent compared to 32 percent in controls who received neither intervention.



Participation rates would skyrocket, say Ades and his colleagues, if CR referral was considered to be a “quality of care indicator,” like aspirin and statin use after a heart attack. The authors reference a study done using the American College of Cardiology’s National Cardiovascular Data Registry that documented a referral rate to “over 80 percent in hospitals participating in quality improvement activities.”

The Cardiac Rehabilitation Collaborative (CRC) is an open forum of individuals and organizations committed to improving the utilization of cardiac rehabilitation. Co-led by the Centers for Disease Control and Prevention and the Centers for Medicare & Medicaid Services to prevent 1 million heart attacks and strokes by 2017, Million Hearts

“While there are many reasons that individuals do not attend CR... one that is modifiable – is that doctors and caregivers do not recommend it strongly enough.”
– Philip Ades, M.D.

supports cardiac rehabilitation as a life-saving and life-enhancing intervention.

“We are thrilled the members of CRC have banded together to boost participation in this important program,” said Janet Wright, M.D., F.A.C.C., and executive director of Million Hearts. “We know cardiac rehabilitation is vastly underutilized by eligible patients – and particularly among women, older Americans, people of color and those living in rural communities. Getting more eligible patients into cardiac rehab can save lives, and result in better health and quality of life for thousands of Americans each year.”

Dr. Ades can be seen explaining the study results on the YouTube channel of “Mayo Proceedings.”

UVM HOLDS INVESTITURE OF FIRST PHILIP ADES, M.D. PROFESSOR OF CARDIOVASCULAR DISEASE

In December 2016, University of Vermont President Tom Sullivan and Larner College of Medicine Dean Frederick Morin, M.D., invested **Philip Ades, M.D.**, professor of medicine, director of cardiac rehabilitation and preventive medicine, and a CVRI Distinguished Investigator, as the inaugural Philip Ades, M.D. Professor of Cardiovascular Disease Prevention. The ceremony, hosted by the UVM Foundation, took place in the Hoehl Gallery in the Health Science Research Facility.

The Ades Professorship in Cardiovascular Disease – UVM’s 105th endowed professorship – honors the significant impact of the cardiac rehabilitation and disease prevention work performed by Ades over his more than thirty-year-long career at UVM. Dedicated to improving the lives of thousands of patients with heart conditions, Ades has conducted world-class research on the important role exercise can play in rehabilitation after a heart attack and the benefits of weight loss in obese coronary heart disease patients.

The new professorship, designed to ensure that Ades’ legacy continues, is to be held by the director of cardiac rehabilitation in the Division of Cardiovascular Medicine at the UVM Medical Center. The endowment will allow the Cardiac Rehabilitation and Prevention Program to continue to grow and evolve to meet the needs of patients,

as well as continue to conduct leading-edge research. The Ades Endowed Professorship was made possible thanks to donations from Ades and his wife, Deborah Rubin, M.D., as well as grateful patients, family members and a gift from the estate of alumna Harriet Dustan, ’42, M.D.’44, a cardiologist and pioneer in the detection and treatment of hypertension.

Ades, who also serves as associate director of the Vermont Center on Behavior and Health, received his M.D. from the University of Maryland School of Medicine and completed an internship and residency in internal medicine at McGill University in

Montreal, Canada and a fellowship in cardiovascular disease at University of Colorado Health Sciences.

At the December event, Ades dedicated his endowed professorship to his late father, who passed away at a young age due to cardiovascular disease, and added “I have admiration for first, our patients, and second, my wife Deborah Rubin . . . I wouldn’t be standing here without her.” Of his career in his field, Ades added that “the best thing is that mean people don’t do cardiac rehab and only nice people work at cardiac rehab.”



Philip Ades, M.D., presenting his work to a participants in the 2016 CVRI Cardiovascular Community Clerkship.



Dr. Ades is congratulated by Larner College of Medicine Dean Rick Morin and UVM President Tom Sullivan after receiving his endowed professorship medallion at the December ceremony.

Supporting the Full Spectrum of Research Careers

Bloomfield Helps Early Career Investigators, Visiting Professors

For **Martin Bloomfield, M.D.**, a member of the UVM College of Medicine Class of 1960, giving back in recognition of the financial support he's received earlier in his life was always part of the plan.

"I was a fully-supported scholarship student," he explains. Growing up in Cranston, R.I., the son of a schoolteacher, money was always tight. "I knew early on that the only way I was going to go to college was to find a place that would offer me scholarship help." That place was the University of Vermont, where Bloomfield matriculated as an undergraduate in the fall of 1952. In 1956 he entered the College of Medicine, also on scholarship.

At the College of Medicine, Bloomfield became interested in cardiology. "I liked the discipline of physiology," he explains. "And cardiac physiology at that time was the most exciting to me."

That excitement helped spark a distinguished career for Bloomfield as a pioneer in the field of nuclear cardiology, and a decades-long affiliation with Lenox Hill

Hospital in New York City as a researcher, clinician, and teacher.

Now Dr. Bloomfield has provided two grants to the CVRI. The gifts - one to support creative careers in research and the other to bring leading cardiovascular thinkers to campus - honor both his lifetime of work at the front lines of heart health and the CVRI's mission to reduce the incidence, morbidity, and mortality of heart and vascular diseases through improving prevention, diagnosis, and treatment.

A \$1 million bequest will create an endowment to support early career investigators as they work to build a research program. The Bloomfield CVRI Early Career Award in Cardiovascular Research is unique in its focus on faculty who are at the beginning stages of their career. In an increasingly competitive funding environment, this early support can be pivotal as faculty establish themselves and secure grant funding. The two-year award goes to a researcher at the assistant professor level and within the first

five years of faculty appointment. Bloomfield has generously decided to provide the current funding of his future bequest, thus allowing the CVRI to bestow this \$45,000 award on a junior investigator in 2017.

A \$250,000 gift from Bloomfield supports two existing visiting professorships that honor beloved faculty connected to the CVRI. The Sobel Visiting Professorship pays tribute to Burton E. Sobel, M.D., the founding director of CVRI, and the Alpert Visiting Professorship is named for Norman Alpert, Ph.D., professor and chair of UVM's Department of Molecular Physiology and Biophysics from 1966 to 1995. Both professorships bring world-renowned researchers to campus for a distinguished lecture and multi-day series of interactions with trainees and junior investigators.

The knowledge that his philanthropy will be put to work without delay is particularly satisfying to Bloomfield. "There's an immediacy which I might not feel if I had done some other avenue of giving," he says. "I'm very pleased to see that."



Left: Martin Bloomfield, M.D., center, with members of the CVRI Board of Directors.



Christine Seidman, M.D., Professor of Genetics and the Thomas W. Smith Professor of Medicine, Harvard Medical School, Director of the Cardiovascular Genetics Center, Brigham and Women's Hospital and a Howard Hughes Medical Institute Investigator lecturing as part of the Burton E. Sobel Visiting Professor Seminar.

Scholarly Events

The Cardiovascular Research Institute of Vermont (CVRI) brings outstanding scientists in cardiovascular medicine to the University of Vermont as Visiting Professors. These visits include a major lecture and a series of interactions with trainees and junior investigators.

CVRI RESEARCH SEMINARS

June 14, 2016

TRP Channels as Potential Therapeutic Targets for Cerebrovascular Disease
SCOTT EARLEY, PH.D.

Professor of Cellular and Molecular Pharmacology and Physiology, Department of Pharmacology, University of Nevada School of Medicine

September 7, 2016

Effects of Cardiac Heterogeneity: Insights from Computational Models

GUNNAR SEEMANN, DR.-ING.
Associate Professor, University Heart Center, Freiburg - Bad Krozingen and the Albert-Ludwigs University - Freiburg's Institute for Experimental Cardiovascular Medicine Computational Modeling Group

September 30, 2016

"Statin Myopathy"

PAUL D. THOMPSON, M.D.
Professor of Medicine, University of Connecticut School of Medicine; Director of the Division of Cardiology and Director of The Athletes' Heart Program, Hartford Hospital

BURTON E. SOBEL VISITING PROFESSOR SEMINAR

Honoring Burton E. Sobel, M.D., Founding Director of the CVRI

May 25, 2016

"Cardiomyopathies: Mutations, Mechanisms, and Therapeutics"

CHRISTINE SEIDMAN, M.D.
Professor of Genetics and the Thomas W. Smith Professor of Medicine, Harvard Medical School; Director, Cardiovascular Genetics Center, Brigham and Women's Hospital; Howard Hughes Medical Institute Investigator

NORMAN R. ALPERT VISITING PROFESSOR SEMINAR

Honoring Norman Alpert, Ph.D., Professor and Chair of the UVM Department of Molecular Physiology and Biophysics from 1966 to 1995

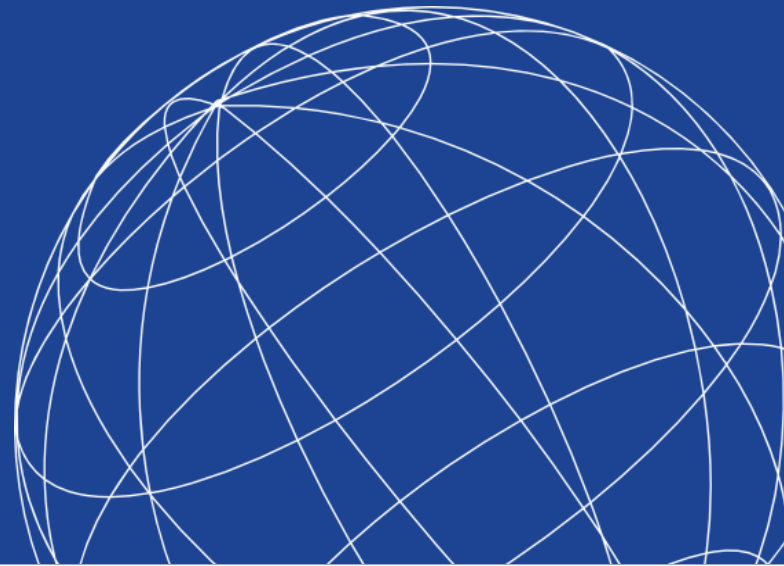
October 6, 2016

Ca²⁺ Signaling in Cardiac Ventricular Myocytes and Mitochondria

W. JONATHAN LEDERER, M.D., Ph.D.
Professor of Physiology and Director of the Center for Biomedical Engineering and Technology, University of Maryland

Connecting Our Scholars

The Cardiovascular Research Institute of Vermont encompasses the full range of scholarship, from young scientists and physicians at the start of their careers to our Distinguished Investigators with decades of notable work to their credit. Through travel awards, research seminars, and an Early Career Advisory Committee available to them, junior investigators who are affiliated with the CVRI have plenty of rich opportunities to interact and learn from their more experienced colleagues.



CVRI TRAVEL AWARDS

Biophysical Society – 60th Annual Meeting Los Angeles, CA – February 2016

Michael J. Previs, MD

Assistant Professor, Department of Molecular Physiology and Biophysics

POSTER AND ORAL PRESENTATIONS: Phosphorylation and calcium antagonistically tune myosin-binding protein C's molecular structure and function

Society for Reproductive Investigation 63rd Annual Scientific Meeting

Montreal, Canada – March 2016

Erica Hammer, MD

Fellow, Maternal Fetal Medicine

ORAL PRESENTATION: Gestational expression and activity of P-glycoprotein at the blood-brain barrier in rats: The potential role of efflux transporters in seizures in pregnancy

Kylie Cooper, MD

Fellow, Maternal Fetal Medicine

POSTER PRESENTATION: The interaction of fetal sex and maternal cardiovascular adaptation

Abbie Johnson, PhD

Postdoctoral Associate, Department of Neurological Sciences

POSTER PRESENTATION: Inhibition of efflux transporters at the blood-brain barrier induces spontaneous seizure in pregnant rats
AWARD: Best New Investigator Poster Award

American Heart Association Epidemiology and Prevention, Lifestyle and Cardiometabolic Health 2016 Scientific Sessions

Phoenix, AZ – March 2016

Nels Olson, PhD

*Postdoctoral Fellow, Laboratory for Clinical Biochemistry Research
Department of Pathology and Laboratory Medicine*

POSTER PRESENTATION: Evaluation of a novel coagulation biomarker, activated coagulation factor VII-antithrombin complexes (FVIIa-AT) in the Cardiovascular Health Study: associations with single nucleotide polymorphisms in the F7/F10 locus and risk of cardiovascular disease mortality

American College of Cardiology 2016 – 65th Annual Scientific Sessions

Chicago, IL – April 2016

Mark Lee, MD

Fellow, Electrophysiology, Department of Medicine – Cardiology

POSTER PRESENTATION: Predictors of pacemaker dependency after transcatheter aortic valve replacement

Keystone Symposium on “Positive Strand RNA Viruses”

Austin, TX – May 2016

Iwona Buskiewicz, PhD

Assistant Professor, Department of Pathology and Laboratory Medicine

POSTER PRESENTATION: Novel interaction of toll like receptor 4 and decay accelerating factor promotes autophagy induction during Cocksackie virus B3 infection

American Association of Cardiovascular and Pulmonary Rehabilitation 31st Annual Meeting

New Orleans, LA – September 2016

Diann Gaalema, PhD

Assistant Professor, Department of Psychiatry

ORAL PRESENTATION: Patient characteristics predictive of failure to complete a cardiac rehabilitation program

International Society for the Study of Hypertension in Pregnancy 20th World Congress

Sao Paulo, Brazil – October 2016

Abbie Johnson, PhD

Postdoctoral Associate, Department of Neurological Sciences

ORAL PRESENTATION: Decreased dilation of hippocampal arterioles in a rat model of preeclampsia
AWARD: Received “Best Oral Presentation” award

American Heart Association’s Annual Scientific Session

New Orleans, LA – November 2016

Abraham Abernethy, MD

Cardiology Fellow, Department of Medicine

POSTER PRESENTATION: Inflammatory biomarkers in heart failure with preserved ejection fraction: Stable versus acutely decompensated patients

Elisabeth Runte, MD

Postdoctoral Associate, Cardiology, Department of Medicine

POSTER PRESENTATION: Relaxation and calcium cycling in isolated contracting myocardium from patients with hypertensive heart disease and heart failure with preserved ejection fraction

American Society of Hematology 58th Annual Meeting

San Diego, CA – December 2016

Christina Cahill, MPH

Medical Student, COM Class of 2018

POSTER PRESENTATION: Sickle cell trait and risk of cognitive impairment in African Americans: The Reasons for Geographic And Racial Differences in Stroke (REGARDS) cohort

SCHOLARLY ACTIVITY: PRESENTATIONS AT NATIONAL AND INTERNATIONAL MEETINGS Cardiac Muscle

Markus Meyer, M.D.

Relaxation and the Role of Calcium in Isolated Contracting Myocardium from Patients with Hypertensive Heart Disease and Heart Failure with Preserved Ejection Fraction.

American Heart Association Scientific Sessions, November 2016, New Orleans, La.

David Warshaw, Ph.D.

Cardiac Myosin Binding Protein-C: Stepping on the Gas and Brake to Modulate Cardiac Contractility.

Keystone Symposia: Heart Failure. Genetics, Genomics, and Epigenetics, April 2016, Snowbird, Utah

Cardiac Myosin Binding Protein-C: Stepping on the Gas and Brake to Modulate Cardiac Contractility.

Gordon Research Conference: Cardiac Regulatory Systems, June 2016, New London, N.H.

Cardiac Myosin Binding Protein-C: Stepping on the Gas and Brake to Modulate Cardiac Contractility.

Mechanical Forces in Biology and Disease, November 2016, Madrid, Spain

Harold Dauerman, M.D.

TAVR: From Low Risk to Expanded Use.

American College of Cardiology: Northern New England Chapter Annual Meeting, 2016

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SCHOLARLY ACTIVITY (continued)

Vascular Biology/Thrombosis

Harold Dauerman, M.D.

Oral and Intravenous Antiplatelet Therapy for PCI.
American College of Cardiology Interventional Board Review Course,
August 2016, Amelia Island, Fla.

Genetics and Drug Interactions in PCI Pharmacology.
American College of Cardiology Interventional Board Review Course,
August 2016, Amelia Island, Fla.

Is There Still a Role for Fibrinolysis in STEMI?
Westchester Cardiovascular Symposium, September 2016, Rye Brook, NY.

Marilyn Cipolla, Ph.D.

*Leptomeningeal Vasoconstriction during Hypertension: Targeting
Pial Collaterals in Stroke Treatment.*
AHA International Stroke Conference, February 2016, Los Angeles,
Calif.

Targeting Brain Arterioles for Acute Stroke Treatment.
AHA International Stroke Conference, February 2016, Los Angeles,
Calif.

Targeting Brain Arterioles for Acute Stroke Treatment.
Neurological Sciences Basic Lecture Series, February 2016, University of
Vermont

Time is Brain! Novel Treatments for Acute Ischemic Stroke.
Community Clerkship Lecture series, February 2016, University of
Vermont

*Role of Peroxynitrite in Vasoconstriction of Brain Parenchymal
Arterioles during Postischemic Reperfusion.*
Experimental Biology '16, April 2016, San Diego, Calif.

Targeting Brain Arterioles for Acute Stroke Treatment.
Neurology Grand Rounds, Cedars-Sinai, April 2016, Los Angeles, Calif.

Mechanisms of Seizure During Pregnancy and Preeclampsia.
OB/GYN Didactic Lecture Series, Cedars-Sinai, Los Angeles, CA, April
2016

*Vascular Protection for Stroke: Targeting Brain Arterioles for Acute
Stroke Treatment and Role of the BBB in Seizure During Pregnancy*

and Preeclampsia.
University of Maastricht Research Seminar, June 2016, Maastricht, The
Netherlands
Targeting Brain Arterioles for Acute Stroke Treatment.
Center for Cerebrovascular Research Seminar, Harvard/MGH, July
2016, Boston, Mass.

*Hypertension Decreases the Number and Duration of Collateral
Openings during Middle Cerebral Artery Occlusion (MCAO) and
Impairs Reperfusion.*
Society for NeuroInterventional Surgery (SNIS) annual meeting, July
2016, Boston, Mass.

Mechanisms of Seizure During Pregnancy and Preeclampsia.
Neurology Grand Rounds, April 2016, University of Vermont

Vascular Biology in Pre-eclampsia: An Update.
International Society for the Study of Hypertension in Pregnancy,
October 2016, Brazil

Mary Cushman, M.D., M.Sc.

Racial Differences in Stroke and Cognitive Decline in the US
Visiting Professor, Leiden University Medical Center, Jan. 2016, Leiden,
Netherlands

*Epidemiology of VTE - the Scope of the Problem and Post Thrombotic
Syndrome - the Gift That Keeps on Giving*
AHA Scientific Sessions, Nov. 2016, New Orleans, La.

Venous Thrombosis and Stroke in Pregnancy.
American Society of Hematology Annual Meeting, Dec. 2016, San
Diego, Calif.

Friederike Keating, M.D.

Patient Centered Imaging: Role of the Protocol Nurse (Abstract)
ASNC Scientific Sessions, Sep. 2016, Boca Raton, Fla.

Mark Nelson, Ph.D.

*Capillary inward rectifier potassium channels and TRPV4 channels
differentially sense neuronal activity to regulate local cerebral blood
flow.*
Cutting Edge Concepts in Molecular Pharmacology: GPCR's -
G-Proteins - TRP Channels, Feb. 2016, Berlin, Germany

*Capillaries as decoders of the neural rhythm of the brain: Translating
thought into blood flow*
Paul M. Vanhoutte Distinguished Lecturer in Vascular Pharmacology"

Sponsored by ASPET at Experimental Biology
2016, April 2016, San Diego, Calif.

*Ion Channel Networks in Control of Cerebral
Blood Flow.*
Gordon Research Conference on Ion
Channels, July 2016, Mount Holyoke College,
South Hadley, Mass.

*Potassium channelopathy-like defect
underlines early-stage cerebrovascular
dysfunction in a genetic model of small
vessel disease.*
General Physiologists 70th Annual Meeting
and Symposium on Genetic & Animal Models
for Ion Channel Function in Physiology
and Disease, Sep. 2016, Marine Biological
Laboratory, Woods Hole, Mass.

*Capillaries as decoders of the neural rhythm
of the brain: Translating thought into blood
flow.*
British Pharmacological Society Meeting, Sep.
2016, Magdalen College, Oxford, UK

*Potassium sensing by capillary KIR channels
initiates retrograde electrical signaling to
regulate cerebral blood flow.*
North American Vascular Biology
Organization, 19th International Vascular
Biology Meeting, Nov. 2016, Boston, Mass.

Ira Bernstein, M.D.

Vascular Stiffness and Preeclampsia.
AJP Heart and Circulation podcast: June 2016

*Sympathetic Responsiveness and Subsequent
Hypertension in Pregnancy.*
With Supple J, McBride C, Badger G, Morris E.
Society for Maternal-Fetal Medicine, Jan. 2016,
Atlanta, Ga.
Multiple presentations at the Society for
Reproductive Investigation, March 2016,
Montreal, QC:

*Factors Contributing to the Increased
Birth Weight in Pregnancies Following*

Preeclampsia.
With Chase V, Hammer E, Badger G, Howe L.

*The Effect of Pregnancy Interval on
Subsequent Pregnancy Blood Pressure
Following Preeclampsia.*
With Howe L, Hammer E, Badger GJ.

*Effect of Maternal Smoking Cessation on
Blood Pressure During Pregnancy.*
With Brown A., Skelly JM, Heil SH, Higgins S.

*Reduced Uterine Blood Flow in the Non-
Pregnant State Contributes to Subsequent
Early Pregnancy Loss..*
With McBride CA, Badger GJ, Morris EA.

*Low Prepregnancy Plasma Volume and
Increased Blood Pressure are Associated with
Increased Risk of Small for Gestational Age
Infants in Subsequent Pregnancy.*
With Morris EA, McBride CA, Badger GJ.

*Women with a History of Early Pregnancy
Loss Have Enhanced Cardiovascular
Response to Subsequent Pregnancy.*
With McBride CA, Badger GJ, Morris EA.

*The Interaction of Fetal Sex and Maternal
Cardiovascular Adaptation.*
With Cooper K, McBride C, Badger G.

*Pre-pregnancy Adiposity is associated with
the Development of Preeclampsia.*
With Mann S., McBride C, Magness R.

*Remodeling of the Maternal Aorta in
Pregnancy Involves Down Regulation of
TET Genes and Epigenetic Modification of
Vascular Smooth Muscle.*
With Brown L, Osol G, Brown S.

Distinguished Investigators

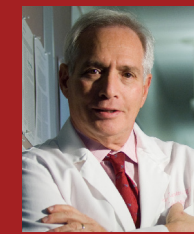
CVRI has recognized six University
of Vermont faculty as Distinguished
Investigators, acknowledging the
long-term high impact of their work in
cardiovascular research. Distinguished
Investigators are appointed for a
period of five years.



Philip Ades, M.D.
Professor of Medicine



Joseph E. Brayden, Ph.D.
Professor of Pharmacology



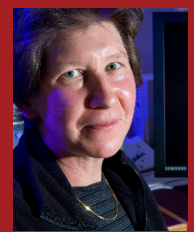
Martin M. LeWinter, M.D.
Professor of Medicine



George Osol, Ph.D.
Professor of Obstetrics,
Gynecology and
Reproductive Sciences



Russell Tracy, Ph.D.
Professor of Pathology



Kathleen M. Trybus, Ph.D.
Professor of Molecular
Physiology and Biophysics

Research Funding: 2016 Highlights

Understanding the causes and consequences of cardiovascular disease, from the molecule to the patient to populations to policy, drives a robust research enterprise at the University of Vermont, and represents a significant portion of the \$85 million in funding received by the Larner College of Medicine in 2016. Grant funding comes from Federal, State, Corporate and Non-Profit sources; below is a sampling of recent awards.

Cardiac Muscle

National Institutes of Health Funding

NIH/Renova Therapeutics 13761
Adenovirus Vector Type 5 (Ad5.hAC6o) Expressing Human Adenylyl Cyclase Type 6 Administered via Intracoronary Catheterization
PI: Matthew Watkins, M.D.
\$26,000

NIH/NIA Ro1 AG033547
Muscle Disuse and Contractile Dysfunction in the Elderly
PI: Michael Toth, Ph.D.
NCE

NIH 5Ro1 HL122744
Sarcolemmal Calcium Extrusion Defect in Patients with Diastolic Dysfunction
PI: Markus Meyer, M.D.
\$1,800,000

NHLBI U1o HL110342
Heart Failure Research Network - Vermont, New York and Quebec Regional Clinical Center
PI: Peter VanBuren, M.D.
\$1,150,000

NHLBI Ro1 HL118524
Myofilament Based Mechanisms of Diastolic Dysfunction in HFpEF
PI: Martin LeWinter, M.D.
\$1,044,000

Ro1 HL126909-01
Cardiac Myosin-Binding Protein C: Molecular Modulation Actomyosin Function
PI: David M. Warshaw, Ph.D.
\$1,216,000

Ro1 AR067279
Skeletal Myosin-Binding Protein C: Molecular Structure and Function
PI: David M. Warshaw, Ph.D.
\$950,000

Ro1
Mutational Studies of Processive Myosin Motors
PI: Kathleen Trybus, Ph.D.
\$349,562

R21 AI117476
Reconstitution of the Class XIV Myosin Glideosome from the Malaria Parasite
PI: Kathleen Trybus, Ph.D.
\$234,000

Ro1 HL078888
Genomics and Pharmacodynamics of Statin-Related Rhabdomyolysis
Subcontract PI: Russell Tracy, Ph.D.
\$292,734

No1 HC95170
Jackson Heart Study - Specimen Repository
Subcontract PI: Russell Tracy, Ph.D.
\$403,919

NIH PPG - University of Texas (Houston) Health Science Center
Mutations in Smooth Muscle Contractile Proteins: Pathways to Vascular Diseases Project 1: Molecular Mechanisms of ACTA2 Missense Mutations
PI: Kathleen Trybus, Ph.D.
\$390,444

Ro1 HL127028
Transition for Risk Factors to Heart Failure: Prevalence, Pathogenesis, and Phenomics
Subcontract PI: Russell Tracy, Ph.D.
\$164,438

UO1 HL084904
Heart Failure Network
Subcontract PI: Russell Tracy, Ph.D.
\$916,735

Clinical Trials/Industry Support

Medtronic
SURTAVI: TAVR vs Surgical AVR for Patients at Intermediate Risk
Local PI: Harold Dauerman, M.D.
\$200,000

Pacing-Induced Remodeling in a Swine Model of Left Ventricular Hypertrophy III
PI: Markus Meyer, M.D.
\$50,000

Pacing-Induced Remodeling in Patients - A Safety and Feasibility Study
PI: Markus Meyer, M.D.
\$65,000

CoreValve® Expanded Use and Continued Access Transcatheter Aortic Valve Replacement Registries
Local PI: Harold Dauerman, M.D.
\$873,500 for 92 patients

CoreValve® Transcatheter Aortic Valve Replacement in Patients at Low Risk for Surgical Aortic Valve Replacement
Local PI: Harold Dauerman, M.D.
Core Valve funding is \$631,600 for 23 patients

AdaptResponse Clinical Trial
Local PI: Joseph F. Winget, M.D.
\$67,550

Product Surveillance Registry 09-167 Registry Study: Patients who have received specific leads in the past 30 days, examining the longevity of the system/leads once implanted
PI: Robert Lobel, M.D.
\$250,000

Capricor, Inc.
Randomized, Double-Blind, Placebo-Controlled Phase I/II Study of the Safety and Efficacy of Intracoronary Delivery of Allogeneic Cardiosphere-derived Cells in Patients with an Anterior Myocardial Infarction and Ischemic Left Ventricular Dysfunction (ALLSTAR)
Local PI: Matthew Watkins, M.D.
\$326,000

St. Jude Medical
Quadripolar Pacing Post Approval Study
PI: Daniel Lustgarten, M.D., Ph.D.
\$17,250

Boston Scientific
Evaluation of the WATCHMAN LAA Closure Device In Patients with Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL)
Local PI: Daniel Lustgarten, M.D., Ph.D.
\$168,613

Quadripolar CRT-D on Currently Approved Lead SystemS (CROSS X4)
Local PI: Joseph F. Winget, M.D.
\$250,000

Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device In Patients with Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL) and Continued Access to PREVAIL (CAP2)
Local PI: Daniel Lustgarten, M.D., Ph.D.
\$250,000

Actelion
Eisenmenger Quality Enhancement Research Initiative (ES-QuERI)
PI: William Hopkins, M.D.
\$33,500

Vascular Biology/Thrombosis

National Institutes of Health Funding

Ro1 1HL121706
Regulation of Myoendothelial Function by Signaling Microdomains in Hypertension
PI: Mark T. Nelson, Ph.D.
\$1,923,375

T32 HL007594
Thrombosis and Hemostasis Program for Academic Trainees
PI: Robert J. Kelm, Jr., Ph.D.
\$320,958

Ro1 HL131181-01
K+ Sensing and Electrical Signaling by Kir Channels in Brain Vasculature
PI: Mark T. Nelson, Ph.D.
\$475,887

Ro1 NS093289-01
Targeting Parenchymal Arterioles in Acute Stroke Treatment
PI: Marilyn J. Cipolla, Ph.D.
\$1,653,665

NIH/NINDS/NIGMS Ro1 NS073815
Control of Reactive Astrocytes by Notch1 and Amyloid Precursor Protein
PI: Jeffrey Spees, Ph.D.
\$1,250,000

NIH/NHLBI PO1 HL095488-01
Calcium Signaling in the Cerebrovascular Unit in Health and Disease
PI: Mark T. Nelson, Ph.D.

Project 1 and Administrative Core
PI: Mark T. Nelson, Ph.D.
\$7,831,664

Project 3: Cerebrovascular Function During Ischemia and Reperfusions
PI: Marilyn J. Cipolla, Ph.D.
\$1,900,000

UM1 HL120877
Analysis and Characterization of Trauma-Induced Coagulopathy

Project 1: Mechanism and Extent of Thrombin Generation in TIC
PI: Kenneth Mann, Ph.D.

Project 2: The Role of Factor Xla in TIC
PI: Saulius Butenas, Ph.D.

Project 6: The Coagulation and Fibrinolysis Interface
PI: Kathleen Brummel-Ziedins, Ph.D.

Project 12: Effects of Histones, Polyphosphates (polyP) and Thrombin on Native Endothelium in Trauma
PI: Mark T. Nelson, Ph.D.

TACTIC Repository
PI: Russell Tracy, Ph.D.
\$23,769,600

Ro1 NS045940-10
The Role of the Blood-brain Barrier in Seizure during Pregnancy and Preeclampsia
PI: Marilyn J. Cipolla, Ph.D.
\$1,667,970

Ro1 HL071944-06
Pre-pregnancy Phenotype and Predisposition to Preeclampsia
PI: Ira Bernstein, M.D.
\$1,881,250

HHS N2682015000031
Multiethnic Study of Atherosclerosis (MESA)
Task 1 and 3 Repository Maintenance
Subcontract PI: Russell Tracy, Ph.D.
\$589,117

Task 2
Subcontract PI: Russell Tracy, Ph.D.
\$462,940

Uo1 AG050499
Enabling Reduction of Low-grade Inflammation in Seniors (ENRGISE)
Subcontract PI: Russell Tracy, Ph.D.
\$605,472

NIDA/USFDA P5o DAO36114
Tobacco Centers of Regulatory Science
PI: Steven Higgins, Ph.D.
\$2,961,410

Ro1 HL120854
T-cell Subsets as Risk Factors for CVD in CHS and Mesa
Subcontract PI: Russell Tracy, Ph.D.
\$1,506,234

Ro1 HL125032
Immune Function and the Risk of Cardiovascular Disease among HIV+ and Uninfected Veterans
Subcontract PI: Russell Tracy, Ph.D.
\$1,338,871

Ro1 HL126542
Targeting Hypercoagulation to Reduce Inflammation in Treated HIV Disease
Subcontract PI: Russell Tracy, Ph.D.
\$372,595

Ro1 HL126543
Role of Innate Immunity in HIV related Vascular Disease: Biomarkers and Mechanisms
Subcontract PI: Russell Tracy, Ph.D.
\$74,185

HHSN268201600006P
CHS Biorepository Support Services
\$182,816

UM1 HL120877
Analysis and Characterization of Trauma-Induced Coagulopathy
Subcontract PI: Russell Tracy, Ph.D.
\$280,607

Uo1 HL130114
CHS Research Resources for the Cardiovascular Health of Older Adults
Subcontract PI: Russell Tracy, Ph.D.
\$82,551

Ro1 HL133860
Tissue Sodium, Inflammation and Blood Pressure in MESA
Subcontract PI: Russell Tracy, Ph.D.
\$98,345

Ro1 AG053325
Non-esterified Fatty Acids and Cardiometabolic Disease in Older Adults
Subcontract PI: Russell Tracy, Ph.D.
\$327,580

1UH2NS100605
Microglial, Inflammatory and Omics Markers of Cerebral Small Vessel Disease in the CHARGE Consortium
Subcontract PI: Russell Tracy, Ph.D.
\$1,953,792

NINDS NS041588
Etiology of Geographic and Racial Differences in Stroke Mortality
Subcontract PI: Mary Cushman, MD, MSc
\$4,759,000

NHLBI HL59367
Epidemiology of Venous Thrombosis and Pulmonary Embolism
Subcontract PI: Mary Cushman, MD, MSc
\$788,773

P2o GM109098
Effects of Perfluorooaklyl Chemicals on Stroke Incidence and Mortality
Subcontract PI: Mary Cushman, MD, MSc
\$10,288

Ro1 N5080850
Impact of Disordered Mineral Metabolism on Stroke and Cognitive Impairment
Subcontract PI: Nancy Jenny, Ph.D.
\$486,408

Ro1 HL093009
Mediators of Atherosclerosis in So. Asians Living in America
Subcontract PI: Nancy Jenny, Ph.D.
\$195,036

Ro1 HL132264 NIH/NHLBI
Vascular Protection by HGF/IgG Protein Complexes that Activate RYK
PI: Jeffrey Spees, Ph.D.
\$1,619,373

BARDA: Biomedical Advanced Research and Development Authority
Establishment of a Minipig Model of Ionizing Radiation-induced Thrombocytopenia, Coagulopathies and Measures of Associated Vascular and Organ Injury
Subcontract PI: Kathleen Brummel-Ziedins, Ph.D.
\$271,800

American Heart Association Funding
Founders Affiliate Grant-in Aid 16GRNT31160006
Role of PURB in Controlling the Phenotypic Plasticity of Vascular Smooth Muscle Cells
PI: Robert J. Kelm, Jr., Ph.D.
\$154,000

Mechanisms of EGF Receptor Activation Leading to Decreased Cerebral Blood Flow after Subarachnoid Hemorrhage
PI: Masayo Koide, Ph.D.
\$308,000

Funding from Other Agencies
Naval Health Research Center
NHRC BAA 13-001

Complex Systems Approachs to Characterizing Trauma Induced Coagulopathy
PI: Kathleen Brummel-Ziedins, Ph.D.
\$2,613,270

European Union 666881 Horizon 2020
Small Vessel Disease in a Mechanistic Perspective: Targets for Intervention - Affected Pathways and Mechanistic Exploration for Prevention of Stroke and Dementia
PI: Mark T. Nelson, Ph.D., for WP1; Co-PI for WP2, WP3, WP4, WP5
\$616,909

British Heart Foundation
Imaging Small Artery Endothelial Calcium Signals in Human Obesity: Does Damage to TRPV4 Channel Function Explain Endothelial Dysfunction? Clinical Research Training Fellowship at UVM for Majid Ahmed.
Co-PIs: Adam S. Greenstein, Ph.D., and Mark T. Nelson, Ph.D.
£164,006

Fondation Leducq
Pathogenesis of Small Vessel Disease of the Brain
North American Coordinator: Mark T. Nelson, Ph.D.
\$6,000,000

Totman Medical Research Trust
Cerebrovascular Research
PI: Mark T. Nelson, Ph.D.
\$150,000

Clinical Trials/Industry Support

Medtronic
SIMPLICITY HTN-3: A randomized trial of renal denervation versus maximal medical therapy for severe hypertension
Local PI: Harold Dauerman, M.D.
\$100,000

Abbott Vascular
ABSORB 3: A Randomized Trial Comparing a Fully Bioresorbable Drug Eluting Poly(lactid Acid) Polymer Coronary Stent Versus a Permanent Everolimus Eluting Coronary Stent
Local PI: Harold Dauerman, M.D.
\$44,500

Bayer Healthcare
GALILEO: A Randomized Trial of Antiplatelet versus Antithrombotic Strategy with Riviroxiban to Improve Outcomes after TAVR
Local PI: Harold Dauerman, M.D.
\$783,500 for 100 patients

Research Publications: 2016 Highlights

Across our academic medical center campus, throughout the region, and around the world, teams of physicians and scientists are dedicated to reducing the incidence, morbidity, and mortality of heart and vascular diseases through improving prevention, diagnosis and treatment. We are pleased to present a sampling of publications from our University of Vermont colleagues engaged across a wide range of cardiovascular research.

Cardiac Muscle

Ades PA. Exercise in chronic heart failure: Anything left to learn? *J Card Fail.* 2016 Jul;22:498-500.

Brutsaert EF, Biggs ML, Delaney JA, Djousse L, Gottdiener JS, Ix JH, Kim F, Mukamal KJ, Siscovick DS, Tracy RP, de Boer IH, deFilippi CR and Kizer JR. Longitudinal assessment of N-terminal pro-B-type natriuretic peptide and risk of diabetes in older adults: The cardiovascular health study. *Metabolism.* 2016;65:1489-97.

Carrick RT, Benson BE, Bates JH, Spector PS. Prospective, tissue-specific optimization of ablation for multiwavelet reentry: Predicting the required amount, location, and configuration of lesions. *Circ Arrhythm Electrophysiol.* 2016 Mar;9(3):pii: e003555.

Cushman M, Callas PW, McClure LA, Unverzagt FW, Howard VJ, Gillett SR, Thacker EL, Wadley VG. N-terminal pro-B-type natriuretic peptide and risk of future cognitive impairment in the REGARDS cohort. *J Alzheimers Dis.* 2016;54:497-503.

Dauerman HL, Reardon MJ, Popma JJ, Little SH, Cavalcante JL, Adams DH, Kleiman NS, Oh JK. Early recovery of left ventricular systolic function after CoreValve transcatheter aortic valve replacement. *Circ Cardiovasc Inter.* 2016;9:pii: e003425.

Hammond HK, Penny WF, Traverse JH, Henry TD, Watkins MW, Yancy CW, Sweis RN, Adler ED, Patel AN, Murray DR, Ross RS, Bhargava V, Maisel A, Barnard DD, Lai NC, Dalton ND, Lee ML, Narayan SM, Blanchard DG, Gao MH. Intracoronary gene transfer of adenylyl cyclase 6 in patients with heart failure. *JAMA Cardiol.* 2016;1:163-71.

Kamel H, Kleindorfer DO, Bhavne PD, Cushman M, Levitan EB, Howard G, Soliman EZ. Rates of atrial fibrillation in black versus white patients with pacemakers. *J Am Heart Assoc.* 2016;12:pii:e002492.

Kavinsky CJ, Kusumoto FM, Bavry AA, Bailey SR, Ellenbogen KA, Hess PL, Lustgarten DL, Moussa ID, Spies C. SCAI/ACC/HRS institutional and operator requirements for left atrial appendage occlusion. *Heart Rhythm.* 2016;13:e241-50.

Kavinsky CJ, Kusumoto FM, Bavry AA, Bailey SR, Ellenbogen KA, Hess PL, Lustgarten DL, Moussa ID, Spies C. SCAI/ACC/HRS institutional and operator requirements for left atrial appendage occlusion. *J Am Coll Cardiol.* 2016;67:2295-305.

Kavinsky CJ, Kusumoto FM, Bavry AA, Bailey SR, Ellenbogen KA, Hess PL, Lustgarten DL, Moussa ID, Spies C. SCAI/ACC/HRS institutional and operator requirements for left atrial appendage occlusion. *Catheter Cardiovasc Interv.* 2016;87:351-62.

Klein FJ, Bell S, Runte KE, Lobel R, Ashikaga T, Lerman LO, LeWinter MM, Meyer M. Heart rate-induced modifications of concentric left ventricular hypertrophy: exploration of a novel therapeutic concept. *Am J Physiol Heart Circ Physiol.* 2016;311:H1031-9.

LeWinter MM. Commentary on "Hypertrophic cardiomyopathy from A to Z," with response from Dr. Baxi and colleagues. *Radiographics.* 2016;36:355-7.

Natriuretic Peptides Studies Collaboration. Natriuretic peptides and integrated risk assessment for cardiovascular disease: individual-participant data meta-analysis of 40 prospective studies. *Lancet Diabetes Endocrinol.* 2016;4:840-9.

O'Neal WT, Howard VJ, Kleindorfer D, Kissela B, Judd SE, McClure LA, Cushman M, Howard G, Soliman EZ. Interrelationship between electrocardiographic left ventricular hypertrophy, QT prolongation, and ischemic stroke: The REasons for Geographic and Racial Differences in Stroke Study. *Europace.* 2016;18:767-72.

Paz YMHL, Hazen SL, Tracy RP, Strohl KP, Auckley D, Bena J, Wang L, Walia HK, Patel SR, Mehra R. Effect of continuous positive airway pressure on cardiovascular biomarkers: the Sleep Apnea Stress Randomized Controlled Trial. *Chest.* 2016; 150:80-90.

Previs MJ, Mun JY, Michalek AJ, Previs SB, Gulick J, Robbins J, Warsaw DM, Craig R. Phosphorylation and calcium antagonistically tune myosin-binding protein C's structure and function. *Proc Natl Acad Sci U S A.* 2016;113:3239-44.

Rengo JL, Callahan DM, Savage PD, Ades PA, Toth MJ. Skeletal muscle ultrastructure and function in statin-tolerant individuals. *Muscle Nerve.* 2016;53:242-51.

Rumora AE, Ferris LA, Wheeler TR, Kelm RJ Jr. Electrostatic and hydrophobic interactions mediate single-stranded DNA recognition and Acta2 repression by purine-rich element-binding protein B. *Biochemistry.* 2016;55:2794-805

Sanchez OA, Lazo-Elizondo M, Zeb I, Tracy RP, Bradley R, Duprez DA, Bahrami H, Peralta CA, Daniels LB, Lima JA, Maisel A, Jacobs DR, Jr, Budoff MJ. Computerized tomography measured liver fat is associated with low levels of N-terminal pro-brain natriuretic protein (NT-proBNP). Multi-Ethnic Study of Atherosclerosis. *Metabolism.* 2016;65:728-35.

Skolnick M, Kremntsova EB, Warsaw DM, Trybus KM. Tropomyosin isoforms bias actin track selection by vertebrate myosin Va. *Mol Biol Cell.* 2016;27:2889-97.

Sladewski TE, Kremntsova EB, Trybus KM. Myosin Vc is specialized for transport on a secretory superhighway. *Curr Biol.* 2016;26:2202-7.

Spector, P. Understanding clinical cardiac electrophysiology: A conceptually guided approach (1st ed.). Hoboken, NJ: Wiley-Blackwell, 2016. ISBN: 978-1-118-90549-4.

Tang Q, Billington N, Kremntsova EB, Bookwalter CS, Lord M, Trybus KM. A single-headed fission yeast myosin V transports actin in a tropomyosin-dependent manner. *J Cell Biol.* 2016;214:167-79.

Teng AE, Lustgarten DL, Vijayaraman P, Tung R, Shivkumar K, Wagner GS, Ajijola OA. Usefulness of His bundle pacing to achieve electrical resynchronization in patients with complete left bundle branch block and the relation between native QRS axis, duration, and normalization. *Am J Cardiol.* 2016;118:527-34.

Toth MJ, Callahan DM, Miller MS, Tourville TW, Hackett SB, Couch ME, Dittus K. Skeletal muscle fiber size and fiber type distribution in human cancer: Effects of weight loss and relationship to physical function. *Clin Nutr.* 2016;35:1359-65.

Warsaw DM. HEART DISEASE. Throttling back the heart's molecular motor. *Science.* 2016;351:556-7.

Zipes DP, Neuzil P, Theres H, Caraway D, Mann DL, Mannheim C, Van Buren P, Linde C, Linderth B, Kueffer F, Sarazin SA, DeJongste MJ; DEFEAT-HF Trial Investigators. Determining the feasibility of spinal cord neuromodulation for the treatment of chronic systolic heart failure: The DEFEAT-HF Study. *JACC Heart Fail.* 2016;4:129-36.

Vascular Biology/Thrombosis

Ahnstedt H, McCullough LD, Cipolla MJ. The importance of considering sex differences in translational stroke research. *Transl Stroke Res.* 2016;7(4):261-73.

Ahnstedt H, Sweet J, Cruden P, Bishop N, Cipolla MJ. Effect of ischemia and reperfusion and tPA on cerebrovascular function, nitrosative stress and polymorphonuclear neutrophils in female rats. *Transl Stroke Res.* 2016;7(3):228-38.

Al-Naamani N, Palevsky HI, Lederer DJ, Horn EM, Mathai SC, Roberts KE, Tracy RP, Hassoun PM, Girgis RE, Shimbo D, Post WS, Kawut SM, Group A-SS. Prognostic significance of biomarkers in pulmonary arterial hypertension. *Ann Am Thorac Soc.* 2016;13:25-30.

Aleshnick M, Foley JH, Keating FK, Butenas S. Procoagulant activity in stored units of red blood cells. *Biochem Biophys Res Commun.* 2016 Jun;10;474(4):680-5.

Ali MY, Vilfan A, Trybus KM, Warsaw DM. Cargo transport by two coupled myosin Va motors on actin filaments and bundles. *Biophys J.* 2016 Nov;111(10):2228-40.

Ali Babi M, Al jerdi S, Gorman M, Clouser R, Allen G, Cipolla MJ, Commichau C. Ondansetron-related hemorrhagic posterior reversible encephalopathy syndrome (PRES) following gastric bypass. *SpringerPlus.* 2016;5:18.

Appiah D, Heckbert SR, Cushman M, Psaty BM, Folsom AR. Lack of association of plasma gamma prime fibrinogen with incident cardiovascular disease. *Thromb Res.* 2016;143:50-52.

Aroner SA, St-Jules DE, Mukamal KJ, Katz R, Shlipak MG, Criqui MH, Kestenbaum B, Siscovick DS, de Boer IH, Jenny NS, Budoff MJ, Ix JH, Jensen MK. Fetuin-A, glycemic status, and risk of cardiovascular disease: The Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis.* 2016 May;248:224-9.

Auer PL, Reiner AP, Wang G, Kang HM, Abecasis GR, Altschuler D, Bamshad MJ, Nickerson DA, Tracy RP, Rich SS, Project NGES, Leal SM. Guidelines for Large-Scale Sequence-Based Complex Trait Association Studies: Lessons learned from the NHLBI exome sequencing project. *Am J Hum Genet.* 2016;99:791-801.

Bahrami H, Budoff M, Haberlen SA, Rezaeian P, Ketlogetswe K, Tracy R, Palella F, Witt MD, McConnell MV, Kingsley L, Post WS. Inflammatory markers associated with subclinical coronary artery disease: The Multicenter AIDS Cohort Study. *J Am Heart Assoc.* 2016;5(6): e003371.

Beheshtian A, Shitole SG, Segal AZ, Leifer D, Tracy RP, Rader DJ, Devereux RB, Kizer JR. Lipoprotein (a) level, apolipoprotein (a) size, and risk of unexplained ischemic stroke in young and middle-aged adults. *Atherosclerosis.* 2016;253:47-53.

Bell EJ, Agarwal SK, Lutsey PL, Cushman M, Heckbert SR, Folsom AR. Orthostatic hypotension and risk of venous thromboembolism in two cohort studies. *Am J Hyperten.* 2016;29:634-40.

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Bell EJ, Lutsey PL, Basu S, Cushman M, Heckbert SR, Lloyd-Jones DM, Folsom AR. Lifetime risk of venous thromboembolism in two cohort studies. *Am J Med.* 2016; 129:339.

Bernstein IM, Hale SA, Badger GJ, McBride CA. Differences in cardiovascular function comparing prior preeclampsia with nulliparous controls. *Pregnancy Hypertens.* 2016;6:320-6.

Blondon M, Cushman M, Jenny N, Michos ED, Smith NL, Kestenbaum B, de Boer IH. Associations of serum 25-hydroxyvitamin D with hemostatic and inflammatory biomarkers in the Multi-Ethnic Study of Atherosclerosis. *J Clin Endocrinol Metab.* 2016 Jun;101:2348-57.

Booth III JN, Colantonio LD, Howard G, Safford MM, Banach M, Reynolds K, Cushman M, Muntner P. Healthy lifestyle factors and incident heart disease and mortality in candidates for primary prevention with statin therapy. *Int J Cardiol.* 2016;207:196-202.

Bosetti F, Galis Z, Bynoe M, Charette M, Cipolla MJ, del Zoppo G, Gould D, Hatsukami T, Jones T, Koenig J, Lutty G, Maric-Balkan C, Stevens T, Tolunay E, Koroshetz W, Gibbons G. Small blood vessels: Big health problems?: Scientific recommendations of the NIH workshop. *J Am Heart Assoc.* 2016;5:pii:e004389.

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Capone C, Dabertrand F, Baron-Menguy C, Chalaris A, Ghezali L, Domenga-Denier V, Schmidt S, Huneau C, Rose-John S, Nelson MT, Joutel A. Mechanistic insights into a TIMP3-sensitive pathway constitutively engaged in the regulation of cerebral hemodynamics. *Elife.* 2016 Aug;5, doi 10.7554/eLife.17536.

Cipolla MJ, Sweet JG, Chan SL. Effect of hypertension and peroxynitrite decomposition with FeTMPyP on CBF and stroke outcome. *J Cerebr Blood Flow Metab.* 2016; 271678X16654158.

Chami N, Chen MH, Slater AJ, Eicher JD Cushman M, Ganesh SK, Auer PL, Johnson AD, Reiner AP, Lettre G. Exome genotyping identifies pleiotropic variants associated with red blood cell traits. *Am J Hum Genet.* 2016;99:8-21.

Chan S-L, Sweet JG, Bishop N, Cipolla MJ. Pial collateral reactivity during hypertension and aging: Understanding the function of collaterals for improved stroke therapy. *Stroke.* 2016;47:1618-25.

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Research Publications: A Sampling (*continued*)

CHARGE Consortium Hematology Working Group. Meta-analysis of rare and common exome chip variants identifies S1PR4 and other loci influencing blood cell traits. *Nat Genet.* 2016;48:867-76.

Chatterjee R, Zelnick L, Mukamal KJ, Nettleton JA, Kestenbaum BR, Siscovick DS, Ix JH, Tracy R, Hoofnagle AN, Svetkey LP, Edelman D, de Boer IH. Potassium measures and their associations with glucose and diabetes risk: The Multi-Ethnic Study of Atherosclerosis (MESA). *PLoS One.* 2016;11:e0157252.

Cipolla MJ. Models of Focal Ischemia. In: *Primer on Cerebrovascular Disease.* Lo, Yenari, Caplan, Biller, Leary, Thomas, Zhang, eds. 2016.

Cipolla MJ. The Cerebral Circulation. In: *Integrated Systems Physiology – from Molecule to Function.* Second Edition. Morgan & Claypool Life Sciences Publishers, San Rafael, CA, 2016.

Colantonio LD, Gamboa CM, Kleindorfer DO, Carson AP, Howard VJ, Muntner P, Cushman M, Howard G, Safford MM. Stroke symptoms and risk for incident coronary heart disease in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. *Int J Cardiol.* 2016;220:122-8.

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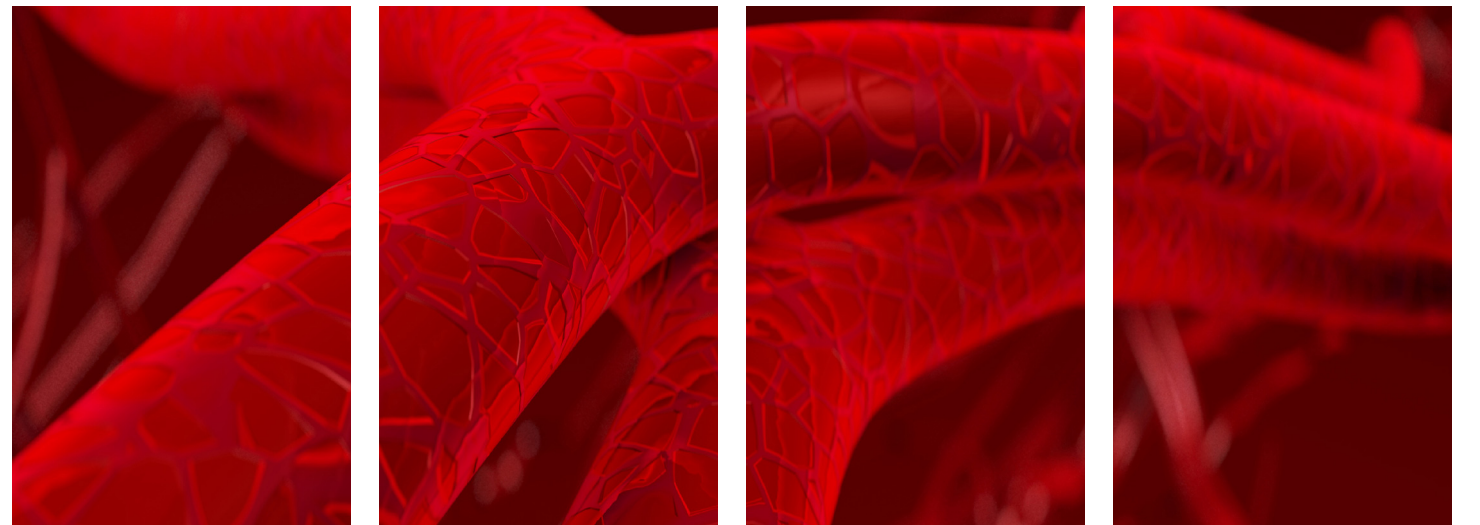
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2016 Patent Activity

Researchers associated with the CVRI have pursued innovations in a wide range of patentable areas concerning cardiovascular health, from devices and systems to new methods and research aids.

Ongoing activity

Peter Spector, M.D.

2013-03-15 129US7 #13_844753_(107283496): Catheter Systems and Related Methods for Mapping, Minimizing and Treating Cardiac Fibrillation

2013-03-15 129US3 #13_844600_(107283084): Methods and Systems for Mapping Cardiac Fibrillation

2013-03-15 129US4 #13_844623_(107283150): Optimizing Lesion Placement

Marilyn J. Cipolla, Ph.D.

#9,568,487: Oxidized LDL as a Biomarker for Brain Injury in Preeclampsia

Markus Meyer, M.D.

#13/030,740: Noninvasive Approach to Determine Cardiac Output
#14/387,971: Cardiac Pacemakers and Uses Thereof

David J. Schneider, M.D.

#14/403,337: Compositions and Methods for Assaying Platelet Reactivity and Treatment Selection

New patent awarded

Marilyn J. Cipolla, Ph.D.

#13/795,685 issued March 25, 2016: Methods of Treating Diseases Associated with PPAR



From left: Drs. Schneider, Dauerman, Cipolla, Warsaw, Nelson, Bernstein and Cushman.

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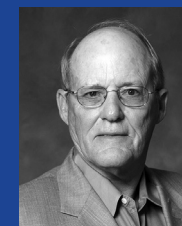
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