During 2015, the Board of Directors of the Cardiovascular Research Institute of Vermont (CVRI) developed a five-year strategic plan. The Board used a retreat to review cardiovascular research at the University of Vermont and advance a strategy designed to further our mission of fostering cardiovascular research.

The Board noted that the University of Vermont is internationally recognized for research in vascular biology (including thrombosis) and cardiac muscle. A key element of the strategic plan is to enhance cross-disciplinary and cross-departmental research that encompasses the translation of basic and clinical research into improved care of patients.

To that end, the Board established two sections – vascular biology and cardiac muscle. Co-leaders of each section were identified whose combined expertise would span the translation of basic and clinical research. For vascular biology, the section leaders are Marilyn Cipolla, Ph.D., and Ira Bernstein, M.D. For cardiac muscle, the section leaders are David Warshaw, Ph.D., and Peter VanBuren, M.D. Each section will develop focused strategic plans that include process metrics. Both the plans and the metrics of success will be reviewed annually by the Board of Directors.

As you will see from the pages that follow, the section leaders are working from a position of strength as they seek to enhance cardiovascular research at the University of Vermont. Our annual report highlights research accomplishments including publications and actively funded research projects during 2015. Because collaboration can yield synergistic advances, a key focus of the CVRI is to connect cardiovascular researchers both within the University of Vermont as well as in the broader scientific community.

David J. Schneider, M.D., F.A.C.C., F.A.H.A.
Director
Cardiovascular Research Institute of Vermont
Professor of Medicine
University of Vermont College of Medicine
Director of Cardiovascular Services
University of Vermont Health Network
Cardiovascular Research News

**TRACY RECEIVES AHA DISTINGUISHED SCIENTIST AWARD**

Bruce Leavitt, M.D., with a patient during a surgical mission.

Bruce Leavitt, M.D., during a surgical mission.

Un Expected health discovery leads to stroke research gift

A chance occurrence involving philanthropy workshop presenter Joe Golding, CEO of Advancement Resources, Yael Friedman, a major gift officer for Academic Health Sciences at UVM, and Mary Cushman, M.D., M.Sc., director of the UVM Thrombosis and Hemostasis Program and CVRI Board of Directors member, led to a $25,000 gift for research.

Following his presentation to UVM faculty and health providers, Friedman noticed Golding suffering leg pain. Wary it could be a blood clot, and knowing that Cushman would be at Golding’s next presentation, she had Cushman examine Golding’s leg when she arrived.

“His leg looked terrible,” said Cushman, who arranged for an ultrasound that afternoon, which found no blood clot.

The scan showed a mass in Golding’s chest, which was later diagnosed as lymphoma upon his return home to Iowa.

Cushman’s work on blood vessel malfunctions in the brain also informs her study of ischemic strokes.

Bruce Leavitt, M.D.

Bruce Leavitt, M.D., received the New England Surgical Society’s 2015 Nathan Smith Distinguished Service Award in fall 2015.

The award is named in honor of Rehoboth, Mass. native and Upper Connecticut Valley surgeon Nathan Smith, who was born in 1762 and helped develop the specialty of surgery and was instrumental in the establishment of the country’s first medical schools, including the UVM College of Medicine and Dartmouth Medical School.

Smith also served as a surgeon and faculty member at the then-named Yale Medical School.

After earning his medical degree at UVM, Leavitt completed residencies in general surgery at Maine Medical Center and in cardiothoracic surgery at SUNY Health Sciences Center in Syracuse, NY, and joined the UVM faculty in 1988. He has served as vice chairman of the UVM Medical Group Board, as president of the Vermont Chapter of the American College of Surgeons and as Vice President of the New England Surgical Society.

In addition to teaching in the College of Medicine’s Foundations level and Surgery Clerkship and mentoring surgery majors and residents, Leavitt has been instrumental in translational multisector studies involving all the major medical centers in the region and also engaged in several translational multidisciplinary UVM research projects.

A member of the Northern New England Cardiovascular Research Consortium, he has been on eight surgical missions, including trips with Team Heart Cardiac Surgery to Rwanda, and with Doctors Without Borders to Sri Lanka and Nigeria.

**CIPOLLA AND ADES NAMED 2015-16 UNIVERSITY SCHOLARS**

Mary Cipolla, Ph.D. and Philip Ades, M.D.

Professor of Medicine Philip Ades, M.D., and Professor of Neurological Sciences Marilyn Cipolla, Ph.D., were honored as University Scholars for 2015-16 by the University of Vermont.

Both professors have led extensive studies involving all the major medical centers in the region and also engaged in several translational multidisciplinary UVM research projects.

Ades is a CVRI Distinguished Investigator and Cipolla is a member of the CVRI Board of Directors.

Bruce Leavitt, M.D., with a patient during a surgical mission.

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A member of the Northern New England Cardiovascular Research Consortium, he has been on eight surgical missions, including trips with Team Heart Cardiac Surgery to Rwanda, and with Doctors Without Borders to Sri Lanka and Nigeria.
Marilyn Cipolla, Ph.D., professor of neurological sciences, along with Isabella Canavero, M.D., a neurology resident from Pavia, Italy, and Helene Sherburne, a Dartmouth College student, investigated how those substances might affect the blood vessels in the brain that were not directly impacted by the stroke and elsewhere in the body. The results of their research, published in January 2016 in the journal Translational Stroke Research, found that healthy blood vessels became more constricted when filled with serum from the blood of ischemic stroke patients.

“It is a very simple idea of asking these very simple questions about circulating factors in post-stroke patients,” says Cipolla, “yet nobody’s done this before.”

The researchers used serum obtained from three subtypes of ischemic stroke patients: those with large vessel disease; those with large vessel disease with high blood pressure; and those with cardioembolic stroke – a type of ischemic stroke in which the clot originates in the heart and migrates to the cerebral vessels – as well as high blood pressure. Serum that was taken at 24 hours post-stroke was perfused into healthy rat blood vessels. The effect of serum from these different stroke patients was compared between blood vessels from the brain (cerebral) and gut (mesenteric). Serum from all three types of stroke patients – compared against a control of a normal saline solution – caused the cerebral arteries to constrict or increase in tone, which could potentially reduce blood flow. Brain vessel tone increased the most with the serum from the patients with cardioembolic stroke. To a lesser degree, tone increased in the gut vessels with serum from the patients with cardioembolic stroke and large vessel disease without hypertension.

The significance of the vasoactive effect of stroke serum in non-ischemic vessels is unknown. Cipolla believes further research should explore the characteristics of the serum that cause the increase in tone and whether it negatively impacts outcome. Scientists also could look at the significance of this change, how these circulating factors affect blood flow in the other regions of the brain unaffected by the stroke, and perhaps uncover ways to minimize that effect. “If a vasoconstricting agent is being produced,” Cipolla says, “we could probably inhibit it with therapies.” Whether these factors are detrimental due to reducing blood flow in normal tissues, or beneficial due to helping in the repair process is not known, but may be important to understand for future therapies.

The circulatory system of the human body is the setting for many disease conditions that can benefit from research into the vessels themselves, and the clotting that can occur within them.

**Vascular Biology and Thrombosis**

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TO NEW HYPER TENSION THERAPY

PATENTED MOLECULE COULD LEAD TO NEW HYPERTENSION THERAPY

Sometines serendipity can play a role in research. That was the case with UVM Professor of Pharmacology Wolfgang Dostmann, Ph.D., and colleagues, in a project that led to the discovery of a molecule that rescues damaged blood vessels, yet preserves healthy vessels. The work, which was published in December 2015, has the potential for the average person, since about 30 percent of people develop hypertension or cardiovascular disease in their lifetime," says Nelson. "We’re now making very significant inroads.”

The 10-person team’s research is supported by a Transatlantic Networks of Excellence grant worth about $6 million from Fondation Leducq, an organization based in Paris that supports efforts to combat cardiovascular and neurovascular diseases. Nelson met the work of the laboratory in Paris, and his longtime collaborator at the University of Paris, Anne Joutel, M.D., Ph.D., directs their research team, which is currently generating peptide libraries for first-in-class PKG-targeted therapies could lead to treatments for more diseases than just high blood pressure, because the target α1cGMP-dependent PKG has been shown to be relevant in cancer, obesity, chronic obstructive pulmonary disorder (COPD) and all forms of cardiovascular disease, and the signaling pathway involved in this mechanism has historically been a target for drug development.

An additional surprise the group uncovered: only small arterial vessels were affected by these molecules if the tissue lining the blood side was damaged - what is known as arterial dysfunction. Atherosclerosis, a condition marked by plaque buildup in the arteries, is a more common example of arterial dysfunction. The peptides rescue the damaged vessels, but they have no effect on the healthy vessels,” says Dostmann. The team is currently generating peptide libraries for further study and intends to collaborate with medicinal and computational chemists to screen compound libraries to gain leads on how to develop more potent activators.

This therapeutic pathway has huge potential for the average person, since about 30 percent of people develop hypertension or cardiovascular disease in their lifetime,” Dostmann says.

The researchers determined that when applied directly to arteries harvested from animal models, s-tides activated critical biological signaling components related to PKG activation, which in turn led to a prevention of the pressure-induced constriction of the vessels that causes high blood pressure. Dostmann explains that drugs like nitroglycerine and Viagra – the latter was originally developed to treat blood pressure - all act on this signaling pathway and are designed to keep intracellular cGMP molecules at an elevated level. In contrast, he adds, s-tides do not change the endogenous level of cGMP. The group’s development of first-in-class PEG-targeted therapies could lead to treatments for more diseases than just high blood pressure, because the target α1cGMP-dependent PKG has been shown to be relevant in cancer, obesity, chronic obstructive pulmonary disorder (COPD) and all forms of cardiovascular disease, and the signaling pathway involved in this mechanism has historically been a target for drug development.

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A POTENTIAL TREATMENT TARGET FOR A DEADLY CARDIAC MUTATION

New research by Chair of Molecular Physiology and Biophysics David Warshaw, Ph.D., and Assistant Professor Michael Previs, Ph.D., moves a step closer to a possible new treatment to address the underlying root cause of familial hypertrophic cardiomyopathy, an inherited disease that causes the heart muscle to thicken and struggle to pump blood. Their study, published recently in the Proceedings of the National Academy of Sciences, provides insight into what happens structurally in the heart when there is a mutation in a protein critical to the heart’s pumping process.

Warshaw and Previs examined the function of cardiac myosin-binding protein C (cMyBP-C), one of the key controls of the heart’s contraction and relaxation functions, and found that phosphorylation – or the addition of phosphate at a key link in the cMyBP-C protein chain – alters the protein’s structure and ensures that it effectively facilitates heart-pumping.

In cases of hypertrophic cardiomyopathy (hCM), a frequent cause of sudden death in young athletes, cMyBP-C lacks phosphorylation, though it is not clear why this is the case. Without phosphorylation, cMyBP-C becomes overactive; it allows the heart muscle to contract too vigorously, such that it then cannot relax and fill with blood – a condition known as diastolic dysfunction. Using a car engine analogy, the researchers describe cMyBP-C as the driver’s foot, regulating the speed by stepping on the gas pedal to rev up the mechanism that makes the heart contract. Specifically, it enhances the presence of calcium inside the trillions of microscopic cells that make up the heart muscle.

In each of those cells, calcium allows one protein – myosin, the heart’s molecular motor – to move another protein – actin – to make the heart contract. As soon as the calcium level is high enough to trigger contraction, cMyBP-C switches its role to put on the brakes, forcing myosin to release the actin, which slows down the heart’s engine so that it can refill with blood.

Warshaw and Previs’s new research shows structurally what happens: Phosphorylation changes the shape of cMyBP-C, from an elongated string of molecules to a bended, or “closed,” chain. The cMyBP-C is elongated when it wee up and is closed when it brakes.

Phosphorylation helps the protein accelerate and decelerate smoothly so, when it’s in high gear, it won’t brake too quickly and make a hard stop or jerky movement. Without phosphorylation, it’s a bumpy ride, with the heart not functioning as well.

Many hCM cases stem from cMyBP-C mutations where phosphorylation levels are low. The new study shows that, even if the protein is normal, the lack of phosphorylation leads to the same problem – the heart never relaxes and struggles to fill with enough blood to pump adequately.

These findings support a possible new therapy, a chemical way to provide phosphorylation and, essentially, keep the engine tuned. Pharmaceutical companies are now paying attention to cMyBP-C, Warshaw says.

The team’s next step is to determine the reason why phosphorylation changes the structure of cMyBP-C. “To just say that it happens isn’t enough,” Warshaw says. “We want to know why.”

From left: David Warshaw, Ph.D., and Michael Previs, Ph.D.
The origin of a common abnormality in heart failure patients called diastolic dysfunction remains a mystery, and cardiologists have no current therapies to treat it. Professor of Medicine Martin LeWinter, M.D., and Associate Professor of Medicine Peter Van Buren, M.D., are working to change this situation.

Diastolic dysfunction, marked by the left ventricle’s inability to relax properly and adequately fill with blood before it pumps, primarily occurs in patients with a history of high blood pressure. In a recent Circulation study coauthored by LeWinter and Van Buren, they examined the effects of high blood pressure and other factors contributing to this problem by comparing those groups of patients — those with high blood pressure with and without heart failure and those with neither high blood pressure nor heart failure.

“We looked at the mechanisms of why the heart stiffens or fails to relax normally in these patients,” says LeWinter, who is internationally known for his work in heart failure. “It turns out it’s a really complicated business.” Some of these patients are elderly, have high blood pressure and occasionally consume too much salt, leading to acute heart failure. “Others suffer from severe trouble breathing, says Van Buren.

Other patients have metabolic syndrome — a combination of overweight, diabetes and high blood pressure. In a recent study coauthored by LeWinter and Van Buren, they examined the effects of high blood pressure and other factors contributing to this problem by comparing three groups of patients — those with high blood pressure with and without heart failure and those with neither high blood pressure nor heart failure.

By obtaining heart biopsies in patients undergoing coronary bypass surgery, the researchers identified, for the first time, molecular indicators of left ventricular stiffness in human subjects with high blood pressure.

This work enhances the UVM Medical Center’s reputation as a leader in treatment of heart failure. A 2015 U.S. News & World Report hospital rankings report ranked UVM Medical Center as “high performing” in heart failure care, following an evaluation of more than 500 U.S. institutions. UVM’s low rates of readmission and infections were strengths. Only 10 percent of the hospitals earned this rating.

UVM’s success in cardiology, LeWinter says, has even more to do with making sure patients get appropriate treatment with the right medications in the right amounts.

By obtaining heart biopsies in patients undergoing coronary bypass surgery, the researchers identified, for the first time, molecular indicators of left ventricular stiffness in human subjects with high blood pressure, confirming previous studies in animal models. The study suggests the potential for early diagnosis and intervention to reduce long-term mortality.

“If we are both lucky and good, we will receive a grant to effectively treat these people,” LeWinter says, who wrote a proposal with colleague Philip Aides, M.D., director of UVM’s cardiac rehabilitation program. The researchers hope to examine the benefits of a sustained exercise and diet program for reducing diastolic dysfunction in patients with high blood pressure — before they develop heart failure.

DAUERMAN TEAM FINDS TAVR PROVIDES MARKED IMPROVEMENT FOR PATIENTS

Early findings from CoreValve® Pivotal Trial-related research conducted by CVRI board member Harold Dauerman, M.D., UVM professor of medicine and interventional cardiologist, and colleagues was presented at a moderated poster session during the American College of Cardiology Scientific Sessions and Expo held in Chicago, Ill. in April 2016.

This new research, which examined a group of aortic stenosis patients with reduced left ventricular (LVEF) ejection fraction who were treated with Transcatheter Aortic Valve Replacement (TAVR) technology, a therapy that received FDA approval in June 2015, was presented at the American Heart Association’s Annual Scientific Sessions Expo held in Chicago, Ill. in November 2015.

Aortic stenosis is a condition in which the heart’s aortic valve narrows, or does not fully open, causing decreased blood flow and increased work for the heart, often leading to chest pain and ultimately, heart failure. Approximately one-third of patients suffer from symptomatic aortic stenosis have reduced left ventricular ejection fraction (LVEF). The TAVR procedure involves attaching an artificial aortic valve to a wire frame, which is then guided by a thin, flexible tube — a catheter — to the heart. When it gets to the appropriate location in the heart, the wire frame expands, allowing the new aortic valve to open and begin to pump blood.

The researchers studied 156 patients from the CoreValve extreme risk/high risk trials who had an LVEF measurement of 40 percent or less. Via cardiac ultrasound, patients were assessed at baseline, post-TAVR procedure, at discharge, and 30 days, six months and one year post-procedure. The team found that early LVEF recovery, which was defined as “an absolute increase of 20 percent or more in LVEF,” occurred in more than 62 percent of the patients, generally prior to discharge, and was sustained throughout the first year in 70 percent of the trial participants.

Dauerman and his team concluded that “Nearly two-thirds of patients with reduced LVEF will have a marked early improvement after TAVR. Early LVEF recovery is associated with improved clinical outcomes and is most likely among patients with higher baseline aortic valve gradients.”
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

September 22, 2015
Mysteries of the Endothelium, More Secrets Unveiled
GAUTAM CHAUDHURI, M.D., Ph.D.
Professor and Chair, Department of Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles

October 2, 2015
In Vivo Diagnosis of Plaque Erosion: Insights from Optical Coherence Tomography
IK-KYUNG JANG, M.D., Ph.D.
Professor of Medicine at Harvard Medical School and Interventional Cardiologist, Division of Cardiology, Massachusetts General Hospital

February 5, 2016
Translating Effective Lifestyle Interventions into Practice: Lessons from the Hopkins-Healthways Collaboration
LAWRENCE APPEL, M.D., M.P.H.
The C. David Molina, M.D., M.P.H. Professor of Medicine, Epidemiology, Nursing, and International Health and Director of the Welch Center for Prevention, Epidemiology and Clinical Research at The Johns Hopkins University School of Medicine

April 24-25, 2016
Genetics of Cardiomyopathies
ALLAN J. MARIAN, M.D.
Professor and Director, Center for Cardiovascular Genetic Research, The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases, University of Texas Health Science Center at Houston

May 13, 2016
Optimizing Cardiac Rehabilitation Participation
RANDAL THOMAS, M.D.
Professor of Medicine, Cardiovascular Diseases at Mayo Clinic and Vice-Chair, Clinical Cardiology Council, American Heart Association

Spring 2016
Multiscale Computational Modeling of Cardiac Electrophysiology
GUNNAR SEEMANN, DR.-ING.
Associate Professor, Institute of Biomedical Engineering, Karlsruhe Institute of Technology, Germany

2015-2016 SOBEL VISITING PROFESSOR
Honoring Burton E. Sobel, M.D., Founding Director of the CVRI
May 23-25, 2016
Genetic Forms of Heart Failure; Genetic Screening; and Small Molecule Therapies Targeted to Contractile Proteins
CHRISTINE SEIDMAN, M.D.
The T.W. Smith Professor of Medicine & Genetics and Director of the Brigham & Women’s Cardiovascular Genetics Center

2015-2016 ALPERT VISITING PROFESSOR
Honoring Norman Alpert, Ph.D., Professor and Chair of the UVM Department of Molecular Physiology and Biophysics from 1966 to 1995
April 24-25, 2016
Multiscale Computational Modeling of Cardiac Electrophysiology
GUNNAR SEEMANN, DR.-ING.
Associate Professor, Institute of Biomedical Engineering, Karlsruhe Institute of Technology, Germany

The CVRI presented its first Cardiovascular Medicine Community Clerkship in the College of Medicine’s Lerner Team-Based Classroom on February 1, 2016. This event showcased to several dozen community leaders the ways that cardiovascular patients in the Vermont community and beyond are being better served by advances in treatment, and presented a broad view of some of the leading-edge research taking place in UVM laboratories and at the bedside in the UVM Medical Center.
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

The International Society on Thrombosis and Haemostasis 61st Annual Congress
Toronto, Canada – June 2015

Osama Harraz, Ph.D.
Postdoctoral Fellow, Laboratory for Clinical Biochemistry Research, Department of Pathology and Laboratory Medicine

Poster: Regulation of endothelial TRPV4.

9th Annual Meeting and Symposium
Woods Hole, MA – September 2015

Kathleen M. Trybus, Ph.D.
Professor of Pharmacology

Poster: Extracellular histones activate endothelial calcium signals.

Heart Failure Society of America
19th Annual Scientific Assembly
National Harbor, MD – September 2015

Russell Tracy, Ph.D.
Professor of Pharmacology

Poster: Extracellular histones activate endothelial calcium signals.

SCHOLARLY ACTIVITY

Biophysical Society 59th Annual Meeting
February 2015 – Baltimore, MD

Fabrice Dubétrand, Ph.D.
Assistant Professor, Department of Pharmacology

Poster: Novel intact extracellular vesicles differ in structural and functional properties.

Experimental Biology 2015
April 2015 – Boston, MA

André E. Reudys, M.D., Ph.D.
Novel Method for Investigating Impaired Blood Pressure Regulation Following Subarachnoid Hemorrhage in Conscious Rat Models.

Japanese Circulation Society
April 2015 – Osaka, Japan

Mary Cushman, M.D., M.Sc.
Diabetes and Heart Failure in the United States.

Brain 2015
June 2015 – Vancouver, BC

Marilyn J. Cipolla, Ph.D.
Increased Tone of Brain Arterioles during Early Post-ischemic Reperfusion.

American Society for Preventive Cardiology
Annual Cardiovascular Disease Prevention Conference
July 2015 – Boca Raton, FL

Mary Cushman, M.D., M.Sc.
Is it Time to Take on Inflammation?

Transcatheter Cardiovascular Therapeutics – TCT 2015
October 2015 – San Francisco, CA

Harold L. Dauerman, M.D.
Antithrombins for PCI in Acute Coronary Syndromes and Pharmacology for PCI and TAVR.

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. Appointed for a period of five years, the inaugural group was named in April 2014.

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15 www.uvm.edu/medicine/cvri
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, which represents a significant portion of the $85 million in funding received by the College of Medicine in 2015. 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

General Overview

Awards

- PI: Peter VanBuren, M.D.
- PI: Martin leWinter, M.D.
- PI: Markus Meyer, M.D.
- PI: David M. Warshaw, Ph.D.
- PI: Kathleen Trybus, Ph.D.
- PI: Matthew Watkins, M.D.
- PI: Mark T. Nelson, Ph.D.
- PI: saulius Butenas, Ph.D.
- PI: Kenneth Mann, Ph.D., and Mark T. Nelson, Ph.D.
- PI: Mary Cushman, M.D., M.Sc.
- PI: Steven Higgins, Ph.D.
- PI: Erica Hammer, M.D.
- PI: David J. Schneider, M.D.
- PI: Harold Dauerman, M.D.
- PI: Majid Ahmed, M.B., B.Chir., M.D., and Joseph Yorio, M.D.

Blandimere Endowment

- PI: Joseph Blandimere, M.D.

Boston Scientific

- Local PI: Matthew Watkins, M.D.

AstraZeneca

- Local PI: Mark T. Nelson, Ph.D.

Medtronic

- Local PI: Matthew Watkins, M.D.

Janssen Pharmaceuticals, LLC

- Local PI: Mathias Winkel, M.D.

Cerebrovascular Research

- North American Coordinator: Mark Underwood, M.D., Ph.D., M.S.

European Union Horizon 2020

- Project 1: Molecular Mechanisms of EGF Receptor Activation
- Project 2: The Role of Factor Xla in TIC Dysregulation
- Project 3: Targeting Microvascular Arteries in Acute Stroke Thrombolysis
- Project 4: Analyses of 100 Patients in the ALLSTAR Study
- Project 5: Targeting Key Enzymes in Vascular Coagulation
- Project 6: The Coagulation and Fibrinolysis Interface
- Project 7: Randomized, Double-blind, Placebo-controlled Study of U26682 in Patients with Acute Myocardial Infarction and Thoracic Left Ventricular Dysfunction (ALLSTAR)
Cardiac Muscle

Atherosclerosis


Research Publications:

Head and Neck


Vascular Biology/Thrombosis

Aslman A, Kleinman NC,先进单位, 155:53-97.

Ades PA. A lifestyle program of exercise and weight loss is effective in preventing recurrent type 2 diabetes mellitus in individuals at high risk. J Am Coll Cardiol. 2015;65:129-37.


levels of monocyte activation markers are
pulmonary arterial hypertension. Ann Am
Perivascular adipose tissue: a novel
Research Publications: A Sampling (continued)
Pappas AC, Koide M, Wellman GC.
Elevated biomarkers of inflammation
dependent protein kinase Iα. Chem Biol.
cGMP-independent activators of cGMP-
tomography. Eur Heart J Cardiovasc
and Racial Differences in Stroke study. J
pulmonary hypertension. In: UpToDate;
Winters JP, Callas PW, Cushman M, Repp
and Racial Differences in Stroke study. J
pulmonary hypertension. In: UpToDate;
models of the vascular smooth muscle
transcriptomic profiles of aging
C, Divers J, Siscovick D, Burke G, Post W, Moses EK, Kent JW, Curran JE, Johnson

36x148]

36x115]

36x124]

36x166]

36x198]

36x237]

36x284]

36x320]

36x355]

36x374]

36x414]

36x500]

36x554]

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36x1944]

36x1980]

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36x2160]

36x2196]
Dr. Alpert attended both Wesleyan and Columbia Universities. He received his Ph.D. in Biophysics from Columbia University in 1951. He then joined the Department of Physiology at the University of Illinois where he ascended in rank from assistant professor to full professor by 1965. In 1966 he moved to the University of Vermont to become chair of the Department of Physiology and Biophysics. During his tenure as chair, he created one of the pre-eminent departments of cardiovascular and muscle physiology.

Dr. Alpert published 140 articles ranging from respiratory metabolism to the step size of a single cardiac myosin molecule. Scientifically, his contributions to understanding the molecular compensatory mechanisms associated with cardiac hypertrophy were significant. In collaboration with Louis Mulieri, Ph.D., he developed an elegant thermopile system to investigate the relationship between energy utilization and contractility of cardiac muscle. This ingenious system utilized sensors coated with antimony and bismuth to accurately measure energy utilization as best production when a cardiac muscle strip was electrically stimulated. The device proved an important tool in differentiating and quantifying the rates of energy utilization during crossbridge cycling (actomyosin ATPase activity) and Ca2+ cycling by the sarcoplasmic reticulum (Ca2+ ATPase activity). These pioneering studies were the basis for the present understanding of the physiology of crossbridge and Ca2+ cycling kinetics in normal and failing hearts.

Dr. Alpert always felt it important that a scientist give back to the scientific community by being an involved citizen, and he held an important role in the growth of several organizations, such as the International Society for Heart Research (ISHR), for which he served as president (1993-1995). He was also vice president of the International Academy of Cardiovascular Sciences, and founding member of the Vermont Academy of Science and Engineering. He was a co-organizer of the first International Conference of Muscle Energetics, held in Burlington, Vermont in 1992, where it returned in 1994 and 2001. Dr. Alpert also organized one of the most successful ISHR meetings, which was held in Burlington, Vermont in 2004. He also served as the editor of the Journal of Molecular and Cellular Cardiology (1994-1998) and as an associate editor of American Journal of Physiology-Heart and Circulation (1981-1987).

—David M. Warshaw, Ph.D.