



# **Cardiovascular Disease Fellowship Training Program**

## **University of Pennsylvania Health System**

## **University of Pennsylvania School of Medicine**

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**The Cardiovascular Disease Fellowship for the University of Pennsylvania Health System, University of Pennsylvania Program**, is designed to prepare cardiologists in training for careers as leaders in academic cardiology by being outstanding clinical cardiologists, clinician investigators or basic scientists. The fellowship program is three years in duration, unless you enter our program as a short track fellow interested in basic science research. Short track fellows are obligated to 5 years of training, as required by the ABIM. Fourth year positions are available to those trainees desiring additional research training and/or clinical training on one of our ACGME approved subspecialty programs (clinical electrophysiology, heart failure and transplantation and interventional cardiology).

Clinical training is provided by three major teaching hospitals, all within 15 minutes of the University of Pennsylvania campus. The first two years of the fellowship consists of a core curriculum in clinical cardiology, including consultative cardiology, diagnosis and management of cardiac patients in the critical care units, cardiac catheterization, noninvasive imaging, exercise physiology, heart failure and transplantation, clinical electrophysiology, vascular medicine, risk assessment and cardiac rehabilitation. Each clinical rotation is designed to provide individual instruction, in addition to daily teaching sessions and weekly seminars for data review and literature updates. The third year of training is tailored to meet the individual needs of our fellows. This year can be devoted to mentored clinical or basic research activities, including sub-specialization in cardiac catheterization and interventional cardiology, electrophysiology, non-invasive imaging, heart failure, basic laboratory research or clinical epidemiology and biostatistics. The last year of the fellowship is designed for intensive exposure to a clinical and/or basic research area, with the specific aim of presenting research at national scientific meetings and publications in peer reviewed journals.

Throughout the academic year, fellows are exposed to a wide range of clinical and basic research endeavors of the cardiology faculty. Multidisciplinary clinical research programs are designed to enable collaborative studies with other departments, including Cardiovascular Surgery, the Institute for Medicine and Engineering, the Center for Experimental Therapeutics, the Pennsylvania Muscle Institute, the Department of Physiology, the Department of Clinical Epidemiology and Biostatistics, and Pediatric Cardiology. For fellows interested in pursuing basic laboratory science research training, there are opportunities within the Penn Cardiovascular Institute, the Wistar Institute, as well as training programs in affiliated basic science departments.

It is the mission of the Cardiovascular Disease Fellowship Program of the University of Pennsylvania Health System to:

- Develop a nationally recognized, state of the art cardiology fellowship program that provides a mentored scholarly environment that enables fellows to become expert clinical cardiologists, independent clinical researchers, or basic science investigators.
- Teach cardiology fellows to deliver optimal clinical care to patients with cardiac and vascular diseases, guided by up-to-date precise knowledge of the most efficient use of diagnostic investigations and cost-effectiveness.
- Train cardiology fellows to become academic cardiologists (clinical educators and clinician scientists), to be recognized nationally as leaders and innovators in their respective fields, able to successfully compete for outside sources of funding, to become expert consultants and procedural specialists who will play a prominent and important role in the health care delivery system of the future.

To achieve these aims, the program has selected the best clinical educational opportunities at three tertiary care hospital facilities (Hospital of the University of Pennsylvania - HUP, Presbyterian Medical Center – PMC, and the Veterans Affairs Medical Center – VAMC, as described under Training Institutions). The basic cardiovascular research laboratories and their respective collaborations with the Penn Cardiovascular Institute, the Department of Cell Biology, Clinical Therapeutics, the Wistar Institute, the Pennsylvania Muscle Institute and the Department of Clinical Epidemiology and Biostatistics provides an integrated thematic educational experience for all fellowship trainees.

We participate in ERAS (the Electronic Residency Application Service <http://www.aamc.org/eras>). We participate in the National Medical Specialties Matching Program, and adhere to their published deadlines. Interviews are by invitation only and are conducted during prearranged dates from February to April. When necessary, interviews can be arranged on unscheduled days. Your application, curriculum vitae, personal statement, 3 letters of reference (one from your current Program Director), and a copy of your Medical School Dean's letter should be submitted to ERAS by the end of December in order to be considered for an interview. Please contact our Fellowship Administrator, Gwynne Katzenbach, at [gwynne.katzenbach@uphs.upenn.edu](mailto:gwynne.katzenbach@uphs.upenn.edu) with questions, or call her at 215-662-2884.

## **TRAINING INSTITUTIONS**

The three core hospitals of the fellowship training program, the Hospital of the University of Pennsylvania, the Presbyterian Medical Center and the Philadelphia VA Medical Center, provide comprehensive exposure to all aspects of clinical cardiology, clinical research and basic research to all fellows in training.

**Hospital of the University of Pennsylvania (HUP):** HUP is the primary teaching hospital of the University of Pennsylvania School of Medicine, and is a 782 bed facility with both primary and tertiary care functions. The Founders Pavilion houses the Coronary Care and Step-Down units, Surgical Intensive Care, a new Heart Failure and Transplantation unit, and Interventional Cardiology and Electrophysiology Laboratories. There are seven state-of-the-art digital Catheterization and Electrophysiology Laboratories.

The Penn Heart and Vascular Center is located in the new Ruth and Raymond Perelman Center for Advanced Medicine and houses the cardiac ambulatory care outpatient practices, including the Heart Failure/Transplantation and Cardiac Risk Intervention Programs. The Noninvasive Imaging Center accommodates echo, exercise and nuclear facilities.

Over 3,800 cardiac catheterizations are performed annually at this facility. This includes diagnostic studies, angioplasties and intracoronary stents, atherectomies and valvuloplasties. In addition, we perform 1752 cardiac biopsies annually. There are approximately 2,200 electrophysiology procedures and close to 1310 major cardiac surgical procedures performed at HUP annually. The noninvasive laboratory performs approximately 19,000 transthoracic echocardiograms, 2,200 transesophageal echocardiograms, 420 Holter ambulatory electrocardiograms, and 75,000 computerized electrocardiograms a year. The Division's Clinical Services consult on or directly manage more than 43,000 cardiac patients per year. There is an active heart failure assessment and cardiac transplantation program, which performs over 50 heart transplants per year.

**The Presbyterian Medical Center (PMC):** PMC is part of the University of Pennsylvania Health System and is an essential component of the cardiovascular fellowship training program. PMC is a 331 bed tertiary care facility located less than a mile from HUP, and is covered entirely by University of Pennsylvania Medicine housestaff. It provides most cardiovascular services, including state of the art digital catheterization and electrophysiology laboratories, a heart failure inpatient unit, vascular laboratories, noninvasive facilities including echocardiography, stress exercise and nuclear labs. Most important, this facility provides experience in the management of post-operative care of the cardiovascular surgical patient.

Cardiac procedures at this training site include 7,700 transthoracic echos, 575 transesophageal echos, 120 holter monitors 585 stress tests (nuclear and echo), 1,300 peripheral vascular disease evaluations, and approximately 4,200 diagnostic catheterizations, PTCAs, atherectomies, stents and percutaneous aortic valve replacements. Approximately 1,300 electrophysiology procedures and 583 major surgical procedures are performed annually. The Cardiovascular Division faculty is assigned to teaching rotations at this training site, and University of Pennsylvania House staff and fellows rotate between HUP and the Presbyterian Medical Center. Fellows participate on the CCU/consult rotation, and actively participate in the perioperative management of patients undergoing major cardiovascular procedures.

**Philadelphia Veterans Affairs Medical Center (VAMC):** The VAMC is a 277 bed primary and tertiary care facility which is an integral part of the teaching programs of the University of Pennsylvania, and is adjacent to the University. The Philadelphia VAMC serves as a regional referral center for the surrounding VA Medical Centers. Cardiovascular Division faculty of the University of Pennsylvania Health System are assigned to the VA service and rotate on the Coronary Care Unit and Consultative Cardiology Service, and on the Diagnostic and Interventional Cardiac Catheterization and Electrophysiology Services, and their respective laboratories. Cardiovascular fellows rotate between HUP and the VA Medical Center. The VA provides a complete range of state-of-the-art clinical facilities and services including intensive care units, cardiac catheterization and electrophysiology laboratories, transthoracic and transesophageal echocardiography, nuclear medicine, CTA and MRI.

**Children's Hospital of Philadelphia (CHOP):** CHOP is a 472 bed University affiliated pediatric hospital adjacent to HUP, with an internationally renowned program in cardiovascular diseases. Several joint programs are in place between the adult and pediatric programs. Opportunities are available for cardiovascular fellows to participate in clinical and research activities at CHOP, including a combined Adult Congenital Heart Program at CHOP and HUP.

**University of Pennsylvania School of Veterinary Medicine:** Established in 1884, the University of Pennsylvania School of Veterinary Medicine is the only veterinary school in the nation to be developed in association with a medical school and is one of only two private veterinary schools in the nation. Its mission is teaching, service and research. In the past there has been a long standing collaboration between the electrophysiology service of the two Cardiovascular Divisions. Fellows may elect to develop research projects with our associated faculty at the Veterinary School.

### **ORGANIZATION OF THE FELLOWSHIP**

The Cardiovascular Fellowship consists of two years of clinical core curriculum that conforms to the American College of Cardiology and COCATS recommendations', and an additional one or two years of advanced clinical sub-specialization and/or basic science research training.

#### **Clinical Core Curriculum**

The clinical rotations that comprise the 24-month core curriculum include Cardiac Catheterization, Electrophysiology, Noninvasive Imaging (including Transesophageal and Stress Echocardiography, Nuclear Stress Testing and Imaging, Vascular and Magnetic Resonance Imaging), Clinical Cardiovascular Services (including medical and surgical consultations), Coronary Care and Heart Failure, Rehabilitation and Transplant Services. All fellows participate in outpatient clinic one half day per week during their fellowship. Senior fellows may elect to participate in subspecialty clinics, in addition to the Cardiology Fellows' Clinic in their second and third of training. These clinics include the Arrhythmia Evaluation Center, Adult Congenital Heart Disease Clinic, Heart Failure and Cardiac Transplant Clinic, and the Lipids and Preventive Medicine Clinic. Fellows provide long-term continuous care of their own patients and are supervised by designated faculty members at the Hospital of the University of Pennsylvania and the VA Medical Center cardiology clinics. Annual awards are presented to fellows for outstanding teaching and research achievement.

#### **Cardiovascular Fellowship Rotations**

<b>ROTATION</b>	<b>1ST YEAR</b>	<b>2ND YEAR</b>	<b>ROTATION</b>	<b>1ST YEAR</b>	<b>2ND YEAR</b>
<b>Cardiac Care Unit (CCU)</b>	---	<b>3 months</b>	<b>Electrophysiology</b>	<b>1 month</b>	<b>1 month</b>
<b>Cardiac Catheterization</b>	<b>2 months</b>	<b>2 months</b>	<b>Exercise/Nuclear</b>	<b>2 months</b>	---
<b>Cardiac Consults</b>	<b>3 months</b>		<b>Heart Failure and Transplant/Rehab</b>	<b>1 month</b>	<b>Optional</b>
<b>Echocardiography</b>	<b>2 months</b>	<b>2 months</b>	<b>Vacation /meetings</b>	<b>1 month</b>	<b>1 month</b>
<b>Elective</b>	---	<b>3 months</b>			

The schedule above is a typical schedule for the first two years of training. There may be some variation to first and second year rotations, depending on number of fellows and individual needs. ECG interpretation is part of the Exercise rotation. Cardiac Rehabilitation and Risk Prevention is part of the Heart Failure rotation. Third and fourth year training in clinical or basic research is planned according to the specific interests of the cardiac fellow.

### **Research Training**

Opportunities are available for fellows to obtain in-depth research experience in clinical investigation or basic science research, both within and outside the Cardiovascular Division. Programs are individually designed and extend over at least a 24 month period. Several NIH sponsored training grants provide support for fellows during this period of investigative training. Described in detail below is an aggregate of research programs and activities that fellows can participate in during their fellowship training.

#### **University of Pennsylvania Cardiovascular Institute (CVI)**

The University of Pennsylvania CVI was established in January 2005 to promote multi-disciplinary cardiovascular research and discovery across schools, institutes, centers, departments and divisions at the University of Pennsylvania. The Penn CVI is now home to over 180 investigators based in 17 different departments on the campus of the University of Pennsylvania (<http://www.med.upenn.edu/cvi>). It is directed by Dr. Michael S. Parmacek, Herbert C. Rorer Professor of Medical Sciences and Chief of the Division of Cardiovascular Medicine. Dr. Jonathan Epstein, a cardiologist, who is Chairman of the Department of Cell and Developmental Biology, is the Scientific Director of the Penn CVI. The Penn CVI is an umbrella structure over all cardiovascular research and clinical programs on the Penn medical campus. In 2009, NIH support to cardiovascular research programs at Penn exceeded \$60,000,000. The CVI will leverage this strong foundation in cardiovascular research by promoting collaboration across entities, providing additional infrastructure for translational research, and perhaps most importantly, identifying and breaking down barriers between basic scientists, translational researchers, clinical investigators and faculty members involved primarily in delivery of patient care.

The Penn CVI is organized into multi-disciplinary programmatic units including basic, translational and patient-oriented research faculty members in key strategic areas including: cardiovascular development/congenital heart disease, vascular biology/atherosclerosis, myocyte biology/heart failure, channel biology/electrophysiology, and molecular imaging and bioengineering. Each unit is directed by a nationally recognized NIH-funded physician-scientist (or scientists) performing translational cardiovascular research. These include CV Development/Congenital Heart Disease, Vascular Biology/Atherosclerosis, Myocyte Biology Heart Failure, Channel Biology/EP, Thrombosis and Haemostasis, Pulmonary Vascular Disease and Bioengineering/Imaging. The program unit leader is responsible for organizing monthly meetings of working group faculty members performing basic, translational and patient-oriented cardiovascular research. These meetings are designed to facilitate discussions on multidisciplinary approaches in strategic areas of cardiovascular research. In addition, the Penn CVI sponsors a weekly seminar series highlighting internal scientists and nationally recognized experts performing translational cardiovascular research. All trainees are required to attend the monthly programmatic unit meeting as well as the weekly seminar series.

A critical component of the Penn CVI is that faculty members performing cardiovascular research will be geographically aggregated (whenever possible) into adjacent spaces that will serve as cardiovascular centers-of-excellence on the Penn medical campus. Trainees will have access to an extensive array of core laboratories located within the CVI including: Histology/Imaging, Transgenic/ES cell, Mouse Cardiovascular Physiology and Myocyte Function, Mouse Electrophysiology, Penn Laboratory for Preclinical Cardiology, and Cardiovascular Genetics and Genomics. Cardiovascular research programs and collaborations located outside these spaces also fall under the Penn CVI umbrella including on-going collaborations with investigators in the Departments of Genetics and Cell and Developmental Biology, the Institute for Medicine and Engineering and the Abramson Cancer Institute. Each of these institutes and departments has a strong focus in basic and/or translational cardiovascular research and will provide trainers for this program.

#### **Molecular Cardiology Center (MCC)**

The Penn MCC was established in 1999 to promote interdepartmental collaborations and to facilitate scientific interactions among investigators with interests in the molecular and cellular biology of the cardiovascular system. The program is currently directed by Dr. Jonathan A. Epstein. The MCC is located in 16,000 square feet of space on the 9<sup>th</sup> floor the Biomedical Research Building II/III, and is home to ten faculty members in the Cardiovascular Medicine and CT Surgery Divisions. The MCC contains integrated Transgenic/ES cell, Molecular Biology and Molecular Imaging and Mouse Physiology Core Laboratories that are partially subsidized by the Penn CVI and a restricted endowment for cardiovascular research from the Commonwealth of Pennsylvania. The MCC contains a central conference room/library (seating capacity approximately 60) that is used for lab meetings, as well as the weekly research seminar series, journal club and outside speaker series. Separate space has been set aside for students and post-doctoral fellows. One of the major purposes of this room is to foster collaborative interactions between students and fellows from different laboratories. MCC

activities relevant to this training program include a monthly Molecular Cardiology seminar series at which pre- and postdoctoral fellows must present their recently- or near-completed research projects to the Molecular Cardiology faculty, fellows and students. In addition, pre- and post-doctoral fellows organize a weekly journal club to promote critical reading of the literature. Each session is supervised and mentored by a Molecular Cardiology faculty member. The MCC and faculty members have, and will, serve as mentors for many trainees in the basic research track (see below).

### **The Institute of Translational Medicine and Therapeutics (ITMAT)**

Trainees in the translational/patient-oriented research track will have access to faculty members and core laboratories located in the ITMAT which is located on the 8<sup>th</sup> floor of the BRBII/III building immediately adjacent to the Penn CVI. Dr. Garret FitzGerald, M.D., Ph.D., a cardiologist who chairs the Dept. of Pharmacology serves as director of the ITMAT. Dan Rader, of the Division of Cardiovascular Medicine serves as Associate Director of the ITMAT. The Institute fosters translational and clinical research designed to identify new targets for therapeutic intervention by the study of human pathophysiology, to elucidate the mechanisms of drug action and the factors that contribute to differences among individuals in their responses to drugs. Center resources include a mass spectrometry and bioanalytical facility, a clinical investigational unit, a DNA Genomics Unit. The ITMAT is home to Genetics/Genomics and Proteomics Core Facilities. In addition to providing core resources for translational research, the ITMAT provides an internal framework for students and fellows wishing to pursue careers in patient-oriented research. Cardiology fellows may enroll in the Masters of Science in Translational Research degree program, or complete the Translational Medicine Core Curriculum which are organized through the ITMAT or a Center for Clinical Epidemiology and Biostatistics (CCEB)-sponsored degree or certificate program (these programs are described under the Curriculum section).

### **Heart Failure and Transplantation Research Program**

The University of Pennsylvania is one of the five busiest heart failure and transplantation programs in the United States. The Heart Failure and Transplantation Translational Research Program is directed by Dr. Ken Margulies who is nationally recognized for his translational heart failure research focused on human cardiac myocyte physiology. Penn transplant cardiologists now follow over 800 patients post-transplantation and Dr. Margulies has established a large human cardiac tissue repository from patients with cardiomyopathy. The Heart Failure Translational Research Center is located in approximately 7,000 square feet of space. Drs. Tom Cappola and Dan Dries lead a nationally renowned program in the Genetics and Genomics of Heart Failure and Transplantation are also located in this space. Established and directed by Dr. Cappola, the Penn Heart Study is a database including extensive clinical profiles, biochemical indices, DNA and RNA on approximately 2000 heart failure patients. The Heart Failure and Transplantation program provides a relatively unique environment for physician-scientists interested in obtaining postdoctoral training in translational heart failure and transplantation research.

### **Cardiac Electrophysiology Research Program**

The University of Pennsylvania is internationally recognized for the pioneering research programs in the area of cardiac electrophysiology. Dr. Marchlinski is internationally recognized for his studies demonstrating the efficacy of radio-frequency catheter ablation and devices to treat and in some cases cure ventricular and atrial tachyarrhythmias. Penn EP faculty members have a longstanding record of academic productivity and of training investigators for careers in academic electrophysiology. In addition, Vickas Patel, M.D., Ph.D., established a translational research program in channel biology/mouse electrophysiology. He has mentored several trainees interested in academic careers in basic cardiac electrophysiology research. Trainees interested in channel biology/cardiac electrophysiology have access to the Mouse Cardiac Electrophysiology Core laboratory and the large animal Experimental Electrophysiology Laboratory located as part of the Penn Medicine Innovations program.

### **Penn Laboratory for Preclinical Cardiology**

To facilitate preclinical research in interventional cardiology and acute coronary syndromes, a GLP-certified Experimental Interventional Cardiology Laboratory was established as part of the Penn Medicine Innovations program in Glenolden, PA (accessible via a shuttle bus). This laboratory is directed by Dr. Robert Wilensky, an interventional cardiologist with expertise in intra-coronary drug and gene delivery. The focus of the laboratory is to translate discoveries in vascular biology into new therapies for atherosclerosis and its complications. Through this laboratory and the Molecular Cardiology Center, fellows have the opportunity to obtain expertise in molecular biology, vascular biology and biochemistry as well as in large animal models of myocardial infarction, valvular heart disease and heart failure.

### **General Clinical Research Center (GCRC)**

The Penn GCRC is a multidisciplinary research facility founded in 1962 with a NIH grant, is located in the Hospital of the University of Pennsylvania. The GCRC is a core facility for patient related clinical research at the Penn Medical Center. It is directed by Dan Rader, Professor of Medicine and Pharmacology. The GCRC houses eight in-patient beds and five out-patient bays and includes a metabolic kitchen staffed by a dietician and a highly sophisticated cardiac monitoring system. The GCRC has state-of-the-art software and databases designed to store, protect and analyze research data.

The GCRC is utilized by faculty members in the Center for Clinical Epidemiology and Biostatistics (CCEB) and the Institute for Translational Medicine and Therapeutics (ITMAT) to provide practical training for students and postdoctoral fellows enrolled in degree granting programs. Trainees, under the mentorship of a trainer, have the opportunity to perform clinical protocols in the Penn GCRC.

### **The Center for Clinical Epidemiology and Biostatistics (CCEB)**

The CCEB was established in 1993 on the University of Pennsylvania medical campus. Brian L. Strom, MD, MPH, Professor of Biostatistics and Epidemiology, Professor of Medicine and Pharmacology is the Center Director. Dr. Stephen Kimmel, Associate Professor of Medicine (Cardiology) is Director of Cardiovascular Research at the CCEB. The CCEB is an inter-disciplinary and inter-departmental program. Its mission is to improve the health of the public by linking epidemiology, biostatistics, and clinical medicine, bringing epidemiologic research methodology to clinical medicine. The educational programs offered by the Center for Clinical Epidemiology and Biostatistics (CCEB) are designed for health care professionals and respond to the individual needs of the trainees. These programs include a Master of Science in Clinical Epidemiology degree program (M.S.C.E.), a PhD degree program in Epidemiology, M.S. and PhD programs in Biostatistics, and combined M.D./M.S.C.E. and M.D./PhD degree programs. In addition, a Clinical Research Certificate program is available to those trainees who envision careers as clinician investigators. This program provides didactic course work, but does not require preparation of a thesis project. Over the past decade many Cardiology fellows, with the support of our NIH training program, have elected to obtain advanced degrees in the CCEB.

### **The Clinician-Investigator Pathway**

Clinician-Investigator Pathway is designed as a training program to teach the fundamentals of clinical research to fellows wishing to pursue academic careers as collaborators in clinical studies. The Clinician-Investigator Pathway has three objectives: 1) to obtain clinical expertise in a subspecialty of cardiology, 2) to gain background training in the vocabulary of clinical epidemiology and biostatistics, and 3) to attain practical experience through development and execution of a clinical research project. Fellows who wish to pursue a research-based career in which they take the lead in clinical studies should enroll in the Masters of Science in Clinical Epidemiology program for clinical epidemiology research, the Masters of Science in Translational Research program for translational research, or the Masters of Science Program in Health Policy Research for health policy research.

Courses are offered through Penn's Clinical Research Certificate Program or the Clinical Research Training Program. Fellows may choose from courses including epidemiology, biostatistics, critical appraisal of the medical literature, database management and clinical trials. Fellows may take a minimum of one and a maximum of four courses during their third and fourth years of fellowship.

Information is available at <http://www.med.upenn.edu/cvi/education.shtml>, <http://www.cceb.upenn.edu/education/epi-degree/msce.php>, and <http://www.med.upenn.edu/mshp>, respectively.

### **Conferences**

A major strength of the program is the frequency and breadth of the teaching conferences held by the Cardiovascular Division, Department of Medicine, and Medical School. The Cardiovascular Medicine Division and Cardiothoracic Surgery Division hold a joint Cardiac Diseases conference each week to discuss patient management issues. There are also weekly Cardiovascular Grand Rounds where clinical and basic science research topics are discussed by faculty from Penn and other institutions. Other weekly conferences include a Journal Club with participation by both fellows and faculty, and conferences held by Cardiovascular Imaging, Heart Failure Transplant and Rehabilitation, Interventional Cardiology and Electrophysiology groups. In addition to the Cardiovascular Division Conferences, there are a variety of clinical and research conferences held throughout the medical center which cardiovascular fellows are encouraged to attend.

### Cardiovascular Conferences

#### *Monday*

- |            |  |
|------------|--|
| 7:15-8:30  | EPS Case Presentation Conference, 9 Founders Conference Room |
| 8:00-8:30  | CCU/HF Service Core Curriculum, 8 Founders Conference Room   |
| 12:00-1:00 | Journal Club, 9 Gates Conference Room *                      |

#### *Tuesday*

- |            |   |
|------------|---|
| 7:00-8:00  | Cardiac Transplant Conference (by invitation), Perelman 2E Cardiology Conference Room   |
| 7:15-8:30  | EPS Research Conference, 9 Founders Conference Room   |
| 7:30-8:30  | Catheterization Film Review, 9 Gates Conference Room  |
| 8:00-8:30  | CCU/HF Service Core Curriculum, 8 Founders Conference Room  |
| 12:00-1:00 | Medical Grand Rounds, Medical Alumni Hall, Ground Maloney   |
| 12:00-1:00 | Consultants Rounds Lecture Series, 9 Gates Conference Room *<br>(Basics of ACHD, Cardiomyopathies and Preventive Cardiology/Vascular Disease) |

#### *Wednesday*

- |            |  |
|------------|--|
| 7:15-8:30  | EPS Core Curriculum, 9 Founders Conference Room  |
| 7:30-8:30  | Mechanical Circulatory Support Conference, Perelman 2E Cardiology Conference Room  |
| 7:30-8:30  | Combined CV/Cardiac Surgery/Cardiac Anesthesia, Flyers/Sixers Surgical Theater, Ground White *   |
| 8:00-8:30  | CCU/HF Service Core Curriculum, 8 Founders Conference Room   |
| 12:00-1:00 | Advance Heart Failure & High Risk Cardiovascular Surgery Cases (with Lancaster General Hospital),<br>Every 4th Wednesday (subject to conflict changes), Perelman 2E Cardiology Conference Room |
| 12:00-1:00 | ECG Conference, 9 Founders Conference Room *   |
| 12:00-1:00 | VA Medical Center Grand Rounds, 7 <sup>th</sup> Floor LVA Auditorium   |
| 4:00-5:00  | Penn Cardiovascular Institute Seminar Series, 253 BRB II/III   |

#### *Thursday*

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|------------|--|
| 7:30-8:30  | Cardiology Grand Rounds, Medicine Conference Room, 5 Maloney *   |
| 7:30-8:30  | Cardiology Morbidity & Mortality Conf, 5 Maloney (1 wk every other month during Cardiology Grand Rounds) |
| 7:30-8:30  | PMC Cardiology Grand Rounds, Philadelphia Heart Institute 1 <sup>st</sup> Floor                          |
| 7:30-8:30  | PMC Catheterization Conference, Philadelphia Heart Institute 1 <sup>st</sup> Floor                       |
| 7:30-8:30  | PMC CV Surgery Conference Philadelphia Heart Institute 1 <sup>st</sup> Floor                             |
| 8:00-8:30  | CCU/HF Service Core Curriculum, 8 Founders Conference Room   |
| 12:00-1:00 | Fellows Noninvasive Conference, 9 Gates*   |
| 12:00-1:00 | Radiology/Cardiology Lecture Series, CV Imaging Working Group, 9 Founders Conference Room                |
| 12:00-1:30 | Cardiology Basic Science Meeting, 8 Stellar Chance Conference Room                                       |

#### *Friday*

- |             |  |
|-------------|--|
| 7:00-8:00   | Vascular Surgery Conference, 4 Silverstein                                   |
| 7:15-8:30   | EPS Case Presentation Conference, 9 Founders Conference Room                 |
| 7:30-8:30   | Catheterization Core Curriculum, 9 Gates Conference Room                     |
| 8:00-9:00   | Nuclear Cardiology Conference, Every other week, Ground Perelman or 1 Donner |
| 8:00-8:30   | CCU/HF Service Core Curriculum, 8 Founders Conference Room                   |
| 11:30-12:30 | Vascular Medicine Conference, Perelman 2E Cardiology Conference Room         |

\* Mandatory fellow attendance

## Advanced Clinical Training (Years 3-4)

Fellows may spend one to two years in advanced clinical training in any of the following areas.

**Cardiac Catheterization/Interventional Cardiology:** Diagnostic catheterization, PTCA, rotational atherectomy, intracoronary stents, valvuloplasty, and atrial septal device closure. Fellows are expected to participate in clinical or translational research.

**Clinical Cardiology:** Inpatient service, outpatient clinic, cardiac surgery service, medical and surgical consult service. Training is tailored to prepare fellows for general consultative cardiology practice.

**Electrophysiology:** Diagnostic electrophysiology laboratory, arrhythmia mapping, RF ablation of atrial and ventricular tachycardias, pacemaker insertion and management, implantable defibrillators, pharmacologic management of arrhythmias. Fellows are expected to participate in clinical or translational research. At the end of a two year training period, fellows will be eligible to sit for Electrophysiology Subspecialty boards.

**Heart Failure/Cardiac Transplantation:** Inpatient and outpatient management of patients with heart failure, pretransplant evaluation and management, post-operative transplant management and immuno-suppression in one of the largest transplant programs in the country. Opportunities for experience with both bridging and destination ventricular assist devices (VADs) are numerous. The faculty can provide a number of research projects to interested fellows, and a specialized year of transplant fellowship is possible.

**Intensive Care Medicine:** Coronary care unit management including invasive physiologic monitoring, intra-aortic balloon insertion, thrombolytic therapy, arrhythmia monitoring and treatment, helicopter transport program for acute cardiac emergencies.

**Noninvasive Imaging:** Transthoracic and transesophageal echocardiography and Doppler, exercise and pharmacologic stress echo, intracardiac echocardiography, peripheral vascular laboratory, intraoperative echo, magnetic resonance imaging, ultrafast CT, stress thallium/MIBI imaging, gated blood pool studies, evaluation of new imaging agents, interpretation of exercise tests, certification in nuclear cardiology. Fellows are encouraged to initiate an independent research project under the mentorship of a faculty member.

**Vascular Medicine:** Level two training in Vascular Medicine requires twelve months exposure including training in catheter based evaluation and treatment of peripheral arterial and venous disease. The year also includes ongoing outpatient vascular clinic and rotations on the vascular surgery, interventional radiology and hematology clinical services as well as training in the noninvasive vascular laboratory.

## CLINICAL RESEARCH PROGRAM

### ADULT CONGENITAL HEART DISEASE PROGRAM

Alex Davidson, M.D.

Richard Donner, M.D.

Martin G. St. John Sutton, M.D.

The Philadelphia Adult Congenital Heart Center is a joint program with the Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania. Patients have a wide variety of congenital heart defects. Their needs are met by a multidisciplinary group including surgery, intensive care, diagnostic imaging, heart catheterization, maternal fetal medicine, electrophysiology, heart failure and transplantation, pulmonary hypertension and genetics. Our research efforts focus on the adult congenital heart disease multicenter research network.

### **Selected Publications**

Opatowsky AR, Landzberg MJ, Kimmel SE, Webb GD. Percutaneous closure of patent foramen ovale and atrial septal defect in adults: the impact of clinical variables and hospital procedure volume on in-hospital adverse events. *Am Heart J* 157(5):867-74, May 2009.

Cohen M, Plappert T, Novello R, St. John Sutton M. *Adult Congenital Heart Disease in Atlas of Echocardiography*, Solomon SD (editor), Braunwald E (Series Editor). Current Medicine Heart Disease Series. Current Medicine, 2008

*Congenital Heart Disease in Adults*, Popelova J, Oechslin E, Kaemmerer H, St. John Sutton, MG. Published Informa healthcare. 2008.

## **Cardiac Catheterization Laboratory**

### **HUP**

Howard C. Herrmann, M.D.

John W. Hirshfeld, Jr., M.D.

Daniel M. Kolansky, M.D.

Robert L. Wilensky, M.D.

Amr Bannan, M.D.

### **PMC**

Gene Chang, M.D.

Craig Frankil, D.O.

Christine Gasperetti, M.D.

William C. Groh, M.D.

Robert H. Li, M.D.

William H. Matthai, Jr. M.D.

Alan Moak, M.D.

William J. Untereker, M.D.

Several clinical research objectives are pursued in the cardiac catheterization laboratory. One series of research projects is directed at understanding and modifying the course of thrombosis in patients with unstable angina, acute myocardial infarction, and in patients undergoing interventional coronary procedures. Novel anticoagulants, antiplatelet agents and inhibitors of re-stenosis as well as new stents are of particular interest; these are being administered both systemically and with unique local delivery catheters. A second theme is the evaluation of devices for interventional non-coronary cardiac procedures. These include the Inoue mitral valvuloplasty balloon, new coronary stent designs, intracoronary and intracardiac ultrasound, hemostatic devices, ASD and PFO closure devices, distal embolization protection devices, percutaneous left ventricular assist devices and new devices for percutaneous valve repair and replacement.

There are numerous research opportunities in interventional cardiology in experimental animal vascular research and clinical research in humans. The focus of the animal laboratory is the vascular response to angioplasty-induced injury with special emphasis on modulating this response. Local drug delivery plays a central role in these research efforts. Clinical research efforts are directed to randomized, blinded clinical studies evaluating the role of new devices and pharmacologic agents during elective and emergent interventions.

Penn catheterization laboratory faculty have had a leadership role in a number of national trials including TARGET (IIb/IIIa), RACE (closure device), Laser photoangioplasty, FINESSE (acute MI), FREEDOM (sirolimus-stent), FIRE (Filterwire protection), ADVANCE-MI (facilitated PCI), CLOSURE (PFO device trial), EVEREST (percutaneous mitral valve repair), MIST (PFO closure for migraine headache), CoSTAR (Connor drug-eluting stent trial), SIRIUS (drug eluting stents) as well as NHLBI Dynamic Registry for interventional procedures. In addition, we are one of the highest enrolling centers in the US in the Partner Transcatheter Aortic Valve Implantation trial and have a large and robust research effort involving this novel device.

### **Selected Publications**

Schwartz RS, Virmani R, Edelman E, Farb A, Boam A, Riemenschneider W, Carter A, Granada J, Chronos NAF, Robinson KA, Waksman R, Weinberger J, Wilensky RL. Drug eluting stents in preclinical studies. Document A: Clinical and laboratory. Updated Consensus Recommendations for Evaluation. *Circ Cardiovasc Intervent*, 2008;1: 143-153.

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Peterson ED. ACCF/SCAI/STS/AATS/AHA/ASNC 2009 Appropriateness Criteria for Coronary Revascularization : a report of the American College of Cardiology Foundation Appropriateness Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and the American Society of Nuclear Cardiology. Endorsed by the American Society of Echocardiography, the Heart Failure Society of America, and the Society of Cardiovascular Computed Tomography. *Catheter Cardiovasc Interv.* 2009 Feb 15;73(3):E1-24.

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## **CLINICAL CARDIOLOGY**

### **HUP**

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Irving M. Herling, M.D.  
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Frank E. Silvestry, M.D.

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Terry D. Friedman, M.D.  
Douglas Jacoby, M.D.  
William H. Matthai, Jr., M.D.  
William J. Untereker, M.D.

Theodor Diamanti, M.D.  
Christine Gasperetti, M.D.  
Neil Levin, M.D.  
Kelly Anne Spratt, D.O.  
Richard L. Weiss, M.D.

### **PVAMC**

Amr Bannan, M.D.

The Cardiovascular Fellowship provides an opportunity for fellows to be exposed to a diversity of cardiologic disease and assist in the diagnosis and management of both in-patients and out-patients treated within the University of Pennsylvania Health System. Formal rotations on the Consultation Service are under the supervision of full-time clinical faculty. This is supplemented by out-patient experiences in our new Penn Heart and Vascular Center, located in the Perelman Center for Advanced Medicine. At the completion of the fellowship, fellows will have acquired sophisticated cardiac physical diagnostic skills as well as the ability to utilize appropriate cardiovascular investigations for the diagnosis and management of patients with cardiovascular disease. Fellows contribute to the preparation and presentation at weekly clinical conferences throughout the year. It is anticipated that the clinical skills acquired by the fellow will provide a foundation upon which further growth will occur and stimulate the initiation of clinical investigation.

Fellows are encouraged to participate in research that includes both investigator sponsored single center studies and participation in large, national cooperative trials. There are a number of ongoing trials to assess the value of new pharmaceutical agents or interventional devices in the treatment of coronary artery disease, valvular disease and intracardiac shunts. New areas of investigation include percutaneous left ventricular assist devices, mitral valve repairs

and aortic valve replacement, as well as new therapies for limiting acute infarct size and subsequent left ventricular remodeling.

### **Selected Publications**

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Floyd T, Mohler E, Magland J, Langham M. Evaluation of Cuff-Induced Ischemia in the Lower Extremity by Magnetic Resonance Oximetry. *JACC*, 2009.

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Mohler ER 3rd, Doraiswamy V, Sibley A, Bernhardt BA, Pyeritz RE. Transillumination of the fingers for vascular anomalies: a novel method for evaluating hereditary hemorrhagic telangiectasia. *Genet Med*. 2009 May;11(5):356-8.

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Mohler ER 3rd, Ballantyne CM, Davidson MH, Hanefeld M, Ruilope LM, Johnson JL, Zalewski A; Darapladib Investigators. The effect of darapladib on plasma lipoprotein-associated phospholipase A2 activity and cardiovascular

biomarkers in patients with stable coronary heart disease or coronary heart disease risk equivalent: the results of a multicenter, randomized, double-blind, placebo-controlled study. *J Am Coll Cardiol*. 2008 Apr 29;51(17):1632-41.

### **ELECTROPHYSIOLOGY**

Frank E. Marchlinski, M.D.  
Joshua M. Cooper, M.D.  
Andrew Epstein, M.D.  
Edward P. Gerstenfeld, M.D.  
Vickas Patel, M.D., Ph.D.  
Ralph J. Verdino, M.D.

Rupa Bala, M.D.  
Rajat Deo, M.D.  
Lawrence H. Frame, M.D.  
Mathew D. Hutchinson, M.D.  
Michael P. Riley, M.D., Ph.D.

David J. Callans, M.D.  
Sanjay Dixit, M.D.  
Fermin Garcia, M.D.  
David Lin, M.D.  
Michael B. Simson, M.D.

The electrophysiology clinical research program focuses on the detailed characterization of the electroanatomic substrate and mechanisms responsible for atrial and ventricular tachyarrhythmias. New recording and imaging tools including magnetic electroanatomic mapping, magnetic resonance imaging and intracardiac ultrasound are used to facilitate this investigation. Techniques for optimally localizing appropriate target sites for catheter ablative therapy and defining endpoints for success are being investigated. Other areas of active investigation include: Evaluation of the role of the autonomic nervous system in the initiation, maintenance, and termination of arrhythmias, optimizing follow-up of patients with implantable defibrillators, optimizing biventricular pacing implantation and programming techniques and the development of new catheter ablation tools and techniques for the control of supraventricular and ventricular arrhythmias. Our large patient population and 5 state-of-the-art electrophysiology laboratories afford us an ample opportunity to investigate a number of issues that have a direct impact on the care of patients with arrhythmias. The basic science research program complements the clinical electrophysiology research program in developing a detailed understanding of the mechanisms responsible for arrhythmogenesis and the optimum ablation strategies for curing arrhythmias. Studies investigate experimental atrial and ventricular arrhythmia models using extracellular recordings, trans-membrane potential recordings, monophasic action potential recordings, and high density computer electrograms activation mapping. Engineered mouse models demonstrating WPW syndrome and embryonic cell lines that may predispose to atrial fibrillation are being actively evaluated. The cardiology fellow with an interest in experimental arrhythmia research is afforded a variety of opportunities with successful investigators.

### **Selected Publications**

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#### **HEART FAILURE AND CARDIAC TRANSPLANTATION PROGRAM**

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The Heart Failure and Cardiac Transplant Program is among the five largest programs in the United States with transplant outcomes that well exceed national averages. The Heart Failure Program is the core that provides referrals and support for the Transplant, Mechanical Assist, Pulmonary Hypertension, High Risk Cardiac Surgery and Translational Research Programs. The research efforts of this program are multi-disciplinary and integrated to further our understanding of the abnormalities in patients with left or right ventricular dysfunction and pulmonary hypertension. We are interested in predictors of survival in patients with heart failure with medical therapy, following surgery, and with mechanical assist device management. The Penn Heart Failure Study, a large NIH funded prospective clinical, neurohormonal and DNA database (molecular epidemiology) has been established to address such questions. In our translational laboratories, active studies utilizing human myocytes include integrated genetic, epigenetic and genomic inquiries designed to identify molecular mechanisms modifying disease susceptibility, preclinical pharmacologic assessments of novel therapeutics and multilevel characterization of recovery and repair process within human hearts. Our mechanical assist program is averaging more than 50 ventricular assist device implantations annually and we have a very robust myocardial recovery research program integrating the clinical, pharmacologic, imaging and molecular/translational disciplines to advance this exciting field.

## **Selected Publications**

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Failure in Adults. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2009 Apr;119(14):1977-2016.

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#### **CARDIOVASCULAR IMAGING AND DOPPLER ECHOCARDIOGRAPHY**

##### **HUP**

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James P. Kirkpatrick, M.D.

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Frank E. Silvestry, M.D.

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##### **PVAMC**

Julio Chirinos, M.D.

This very busy clinical program focuses on the use of quantitative Doppler echocardiographic analysis to assess left ventricular remodeling post-myocardial infarction and in heart failure and exploring the effects of pharmaceutical agents and device therapy on ventricular function. This program incorporates extensive experience and current involvement in numerous multicenter clinical trials including ACTION, BEST, INSYNC, MIRACLE, MIRACLE-ICD, BLOCK-HF, REVERSE, COMPASS and PEERLESS. There is a longstanding collaborative research program with Cardiothoracic Surgery in evaluating the impact of acute mitral regurgitation and aneurysm formation on ventricular geometry ventricular remodeling and function in man and experimental animal models. Transesophageal echocardiographic evaluation of valvular repair and replacements in collaboration with Cardiothoracic Anesthesiology is ongoing. Other research interests include gender differences in the diagnosis and treatment of cardiovascular disease. Two large important trials involve extensive collaboration with CRIC and the Penn Heart Failure Study investigators.

#### **Selected Publications**

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Medina-Lezama J, Morey-Vargas OL, Zea-Díaz H, Bolaños-Salazar JF, Corrales-Medina F, Cuba-Bustinza C, Chirinos-Medina DA, Chirinos JA. Prevalence of lifestyle-related cardiovascular risk factors in Peru: the PREVENCIÓN study. *Rev Panam Salud Publica*. 2008 Sep;24(3):169-79.

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### **Cardiovascular Magnetic Resonance Imaging (CMR) and Cardiac Computed Tomography (CCT)**

Scott Akers, M.D., Ph.D.

William Boonn, M.D.

Julio Chirinos, M.D.

Benoit Desjardins, M.D., Ph.D.

Kevin Duffy, M.D.

Victor A. Ferrari, M.D.

Saurabh Jha, M.D.

Harold Litt, M.D., Ph.D.

Martin G. St. John Sutton, M.D.

The program focuses on advanced cardiovascular MR and CT imaging in adults, encompassing the full spectrum of cardiac disease including complex congenital and aortic disease. The CMR program involves a close collaboration between the Division of Cardiovascular Medicine and the Department of Radiology. There are 7 clinical 1.5 Tesla scanners and two 3 Tesla high field systems available for studies in humans. In addition, a dedicated 3T cardiac system is available for large animal research at the Glenolden Research Facility. Ongoing research includes quantitative assessment of regional wall motion and myocardial mechanics, the relationship between perfusion, function and metabolism. Recent work has focused on viability in reversibly injured myocardium using CMR. Therapeutic trials with novel pharmacologic agents for heart failure as well as stem cell infusions are being analyzed in regard to effects on mechanics and metabolism. New contrast agents have been tested for 3D MR angiography and to assess coronary circulation and myocardial perfusion.

We have a long standing interest in regional intramural and left ventricular (LV) chamber mechanics using myocardial tagging in hypertrophy and post-infarction remodeling. Effects of novel surgical and medical therapies on these parameters have been evaluated. High temporal resolution methods to assess the impact of hypertension and congestive heart failure on LV function are available. A further strong area of interest is the small animal imaging program—a collaborative effort with the Molecular Cardiology group. We have developed imaging protocols, coils, and tagging methods for studying rodents at 4.7 Tesla. These techniques permit the study of phenotypes of genetically altered murine models of cardiovascular disease, and aid in assessment of various anatomic and functional abnormalities.

CT research has focused on the potential for CCT to provide rapid disposition and improved cost-effectiveness in evaluating acute chest pain patients in the Emergency Department as compared with conventional treatment strategies. Clinical rotations in CMR and CCT at the Hospital of the University of Pennsylvania provide exposure to both technological and practical implantation of these techniques. Electives in pediatric CMR and CCT at the Children's Hospital of Philadelphia are available to all fellows.

### **Selected Publications**

Kramer CM, Budoff MJ, Favad ZA, Ferrari VA et al. and the ACCF/AHA/ACP Task Force on Clinical Competence and Training: SAIP; SCAI; SCCT; SCMR; SVMB. ACCF/AHA 2007 clinical competence statement on vascular imaging with computed tomography and magnetic resonance : a report of the American College of Cardiology Foundation/American

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Qiao H, Zhang H, Zheng Y, Ponde D, Shen D, Gao F, Bakken A, Schmitz A, Kung HF, Ferrari VA, Zhou R. Embryonic stem cell grafting in normal and infarcted myocardium: Serial assessment with MR imaging and PET dual detection. *Radiology* 2009;250:821-829.

#### **NUCLEAR CARDIOLOGY/PET IMAGING/EXERCISE PHYSIOLOGY**

##### **HUP**

Andrew Litwack, M.D.

David M. McCarthy, M.D.

Nehal Mehta, M.D.

##### **PMC**

Alan D. Askenase, M.D.

The research program in Nuclear Cardiology is exploring a variety of issues in the application of single photon imaging. Pharmacological stress testing with dipyridamole, dobutamine and adenosine is a primary interest, especially the comparison to other diagnostic modalities as well as the prognostic value of these techniques in patients with acute and chronic coronary disease. Studies include transmission-emission techniques utilizing triple-headed cameras with 360 degree SPECT acquisition. The PET Center is actively engaged in the evaluation of myocardial viability in patients who are being considered for cardiac transplantation as well as the cost-effective application of PET imaging in patients with chronic coronary artery disease. The exercise physiology laboratory maintains active clinical and research interests in the determinants of myocardial ischemia. In addition, novel investigations continue in the physiologic characterization of patients with congestive heart failure, including quantitation of lung water and assessment of the response to therapy.

#### **Selected Publications**

Eraso LH, Ginwala N, Qasim AN, Mehta NN, Dlugash R, Kapoor S, Schwartz S, Schutta M, Iqbal N, Mohler ER 3<sup>rd</sup>, Reilly MP. Association of lower plasma Fetuin-A levels with peripheral arterial disease in type-2 diabetes. *Diabetes Care* 2009; Nov. 12 (Epub ahead of print).

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**PREVENTIVE CARDIOVASCULAR MEDICINE AND LIPID CLINIC**  
**HUP**

Daniel J. Rader, M.D.  
Emile R. Mohler, M.D.

Nehal Metha, M.D.  
Muredach Reilly, M.D.

Emma Meagher, M.D.

Preventive Cardiovascular Medicine and the Lipid Clinic are interdisciplinary programs dedicated to the comprehensive systematic assessment of cardiovascular risk and risk reduction. Cardiologists, endocrinologists, geriatricians, and internists work together in the program. Each physician has specialized areas of clinical expertise, including lipid disorders, hypertension, obesity, metabolic syndrome, type II diabetes mellitus, vascular medicine, women's cardiovascular health, cardiovascular prevention in the elderly, and alternative and complementary approaches to cardiovascular risk. The programs place major emphasis on cardiovascular risk assessment using state-of-the-art technologies including advanced laboratory testing and noninvasive imaging of atherosclerosis.

Clinical research is a major focus and projects include: 1) Genetic studies of patients with lipid disorders and premature coronary disease; 2) Assessment of novel cardiovascular risk factors; 3) Use of non-invasive methods of quantitating subclinical atherosclerosis; 4) Clinical trials of novel lipid-lowering, HDL-raising, and direct anti-atherogenic therapies.

**Selected Publications**

Brown RJ, Rader DJ. When HDL gets fat...*Circ Res.* 2008 Jul 18;103(2):131-2.

Martin SS, Qasim A, Reilly MP. Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. *J Am Coll Cardiol.* 2008 Oct 7;52(15):1201-10.

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Airan-Javia SL, Wolf RL, Wolfe ML, Tadesse M, Mohler E, Reilly MP. Atheroprotective lipoprotein effects of a niacin-simvastatin combination compared to low- and high-dose simvastatin monotherapy. *Am Heart J.* 2009 Apr;157(4):687.1-8.

Brown RJ, Edmondson AC, Griffon N, Hill TB, Fuki IV, Badellino KO, Li M, Wolfe ML, Reilly MP, Rader DJ. A naturally occurring variant of endothelial lipase associated with elevated HDL exhibits impaired synthesis. *J Lipid Res.* 2009 May 3. [Epub ahead of print]

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Tanigawa H, Billheimer JT, Tohyama JI, Fuki IV, Ng DS, Rothblat GH, Rader DJ. Lecithin: Cholesterol Acyltransferase Expression Has Minimal Effects on Macrophage Reverse Cholesterol Transport In Vivo. *Circulation.* 2009 Jun 29. [Epub ahead of print]

#### **VASCULAR MEDICINE (CLINICAL) RESEARCH PROGRAM**

##### **HUP**

Emile R. Mohler, M.D.

Daniel J. Rader, M.D.

Muredach Reilly, M.D.

The goal of this research program is to investigate new diagnostic and therapeutic modalities for patients with vascular disease. The program is multidisciplinary and involves close collaboration with Vascular Surgery and Cardiovascular Radiology. A major research effort is directed at early detection and treatment of atherosclerosis. The presence of atherosclerosis is being assessed with diagnostic modalities such as electron beam CT imaging to detect vascular calcification, novel PET imaging to evaluate plaque stability, ultrasound to assess vascular reactivity, and MR imaging to evaluate carotid plaque morphology.

Current clinical research studies include evaluation of vascular reactivity in selected populations and studies of lipid treatment effects on carotid plaque morphology. An angiogenesis gene therapy-based program is ongoing and includes evaluation of animal models of hind-limb ischemia and clinical trials of cell therapy to promote collateral development in patients with claudication. Pharmaceutical-sponsored studies involving evaluation of novel drugs for treatment of claudication are also being conducted. A prospective collection of DNA and plasma samples of patients with atherosclerosis is underway to evaluate the genetic causes of atherosclerosis.

Basic science investigation is centered on the pathologic mechanisms involved in vascular calcification. There is a close collaboration with molecular orthopedic surgery to test vascular calcification pathways in animal and cell culture models.

##### **Selected Publications**

Mohler E, 3rd, Giri J. Management of peripheral arterial disease patients: comparing the ACC/AHA and TASC-II guidelines. *Curr Med Res Opin*;24:2509-2522, 2008.

Martin SS, Qasim A, Reilly MP. Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. *J Am Coll Cardiol.* 2008 Oct 7;52(15):1201-10.

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Wen-Chau W, Mohler E, Ratcliff SJ, Wehrli FW, Detre JA. Skeletal Muscle Microvascular Flow in Progressive Peripheral Artery Disease. *JACC* 2009; 53(25):2372-7.

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#### **CARDIOVASCULAR EPIDEMIOLOGY**

Stephen E. Kimmel, M.D., M.S.

Martin G. Keane, M.D.

Muredach Reilly, M.D.

Brian L. Strom, M.D., M.PH.

The Cardiovascular Epidemiology group focuses on the applications of epidemiologic methods, including observational studies and clinical trials, to the study of cardiovascular diseases. There is a wide range of ongoing research, with focuses in ischemic heart disease, coronary angioplasty, novel risk factors for cardiac disease, myocardial disease, anticoagulant therapies, and effects of non-cardiac drugs on cardiovascular outcome. Ongoing projects include studies of the genetic influences on clinical drug effects, genetic factors effecting preclinical coronary atherosclerosis, clinical trials of pharmacogenetics and adherence interventions, studies of novel biomarkers and novel risk factors to predict cardiac risk and ventricular remodeling.

#### **Selected Publications**

Frosch D, Kimmel SE, Volpp K. What Role Do Lay Beliefs about Hypertension Etiology Play in Perceptions of Medication Effectiveness. *Health Psychol* 27:320-326, 2008.

Hennessy S, Leonard CE, Newcomb C, Kimmel SE, Bilker WB. Cisapride and Ventricular Arrhythmia. *Br J Clin Pharmacol* 66(3):375-85, Sep 2008.

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Doshi JA, Zhu J, Lee BY, Kimmel SE, Volpp KG. Impact of a Prescription Copayment Increase on Lipid-Lowering Medication Adherence in Veterans. *Circulation* 119(3):390-397, Jan 2009.

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## BASIC SCIENCE RESEARCH PROGRAM

### DEVELOPMENT OF THE HEART AND VASCULAR SYSTEM

Michael S. Parmacek, M.D.

Peter Gruber, M.D., Ph.D.

Mark Kahn, M.D.

Jonathan A. Epstein, M.D.

Edward Morrissey, Ph.D.

Victor V. Patel, M.D., Ph.D

Research efforts in this program are aimed at defining the molecular events controlling embryonic development of the cardiovascular and pulmonary systems. Particular emphasis has been placed on defining the function of transcription factors and signaling pathways that regulate cell fate decisions and morphogenesis of the heart and vasculature. Stem cell biology and the application of cardiac stem cells for therapy is the focus of recent investigations. Transgenic and gene knock-out technologies are routinely employed. Specific areas of research focus include cardiac stem cells, genetics of congenital heart disease, lymphangiogenesis, pulmonary development and cardiac hypertrophy. The research training environment is facilitated by active collaborations and programmatic funding among these investigators and between these laboratories and those of adjacent basic science departments and institutes, including the Institute for Regenerative Medicine, the Department of Cell and Developmental Biology, the Cardiovascular Institute, the Institute for Translational Medicine, and the Institute for Diabetes, Obesity and Metabolism.

### **Selected Publications**

Cohen, E.D., K. Ihida-Stansbury, M.M. Lu, R.A. Panettieri, P.L. Jones, E.E. Morrissey, Wnt signaling regulates smooth muscle precursor development in the mouse lung via a tenascin C/PDGFR pathway. J Clin Invest, 2009. 119:2538-49.

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### **VASCULAR BIOLOGY**

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Jonathan Epstein, M.D.  
Emile R. Mohler, M.D.  
Muredach Reilly, M.D.

Lawrence Brass, M.D., Ph.D.  
Garret A. Fitzgerald, M.D.  
Ellen Puré, Ph.D.  
Robert L. Wilensky, M.D.

Peter Davies, Ph.D.  
Mark Kahn, M.D.  
Daniel J. Rader, M.D.

The overall goal of the research effort is the study of vascular biology at the cellular and molecular level with particular focus on understanding the pathogenesis of, and devising novel therapeutic strategies for vascular diseases including atherosclerosis, diabetic vascular disease and peripheral vascular disease. Core facilities include the Molecular Cardiology Core Laboratories where mouse models of atherosclerosis and vascular injury are generated, quantitatively assessed, imaged and histologically analyzed. Dr. Parmacek has a longstanding interest in understanding the transcriptional programs that control vascular smooth muscle cell differentiation and phenotypic modulation of the smooth muscle cell lineage. In addition, in collaboration with Drs. Mohler, Reilly, Wilensky and Lepore, they study the pathogenesis of diabetic vascular disease. Dr. Epstein's research focuses on the contribution of the cardiac neural crest to the heart and outflow tract. Both the Epstein and Parmacek laboratory also study angiogenesis and stem cell regenerative therapies. Dr. Rader has a longstanding interest in lipid metabolism (especially HDL) and its relationship to atherosclerosis. Dr. Pure, a Professor at the Wistar Institute, collaborates with Dr. Rader and investigates the process and mechanism by which vascular smooth muscle cells, T cells, macrophages and endothelial cells interact in early atherosclerosis. He also studies the genetics of atherosclerosis and lipid metabolism. Dr. Kahn's lab investigates signaling pathways in the development and function of blood and lymphatic vessels using mouse and zebrafish. Drs. Kahn and Brass both work on platelet signaling pathways involved in arterial thrombosis. Dr. Peter Davies, Director of the Institute of Medicine and Engineering, is internationally recognized for his expertise in endothelial cell biology and the cytoskeleton. Dr. Garret Fitzgerald, Director of the Center for Experimental Therapeutics, is internationally recognized for his work in the field of oxidant stress and vessel wall injury and applied molecular pharmacology.

### **Selected Publications**

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