

Cardiovascular Disease Fellowship Training Program University of Pennsylvania Health System University of Pennsylvania School of Medicine

*Michael S. Parmacek, MD* Herbert C. Rorer Professor of Medical Sciences Chief, Cardiovascular Division Director, Cardiovascular Institute *Frank Silvestry, MD* Associate Professor of Medicine Director, Cardiovascular Fellowship Program

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, clinical investigators or basic and translational scientists. The fellowship program is three years in duration, unless you enter our program through the ABIM-designated clinical investigator program (CIP) which is designed to foster careers in basic and translational research investigation. Fellows enrolled in the clinical investigator program are obligated to five years of cardiology fellowship training, including three years of dedicated research, as required by the ABIM. Fourth year positions are available to those trainees desiring additional research training and/or clinical training in one of our ACGME approved subspecialty programs (clinical electrophysiology, advanced heart failure and transplantation and interventional cardiology). In addition, standard track cardiology fellows may apply for two additional years of research training through one of several NIH-sponsored T32 training programs.

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, advanced heart failure and transplantation, clinical electrophysiology, vascular medicine, adult congenital heart disease 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 cardiac imaging, advanced heart failure, adult congenital heart disease and transplantation, basic laboratory research or clinical epidemiology and biostatistics. Additional years of fellowship training, which are covered via NIH sponsored training programs, are designed for preparing trainees for academic careers focused in the areas of clinical, translational and/or basic research, 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, the Division of Cardiothoracic Surgery, the Department of Cell and Developmental Biology, the Department of Physiology and Pediatric Cardiology. For fellows interested in pursuing basic laboratory and translational investigation, there are opportunities within the Penn Cardiovascular Institute, the Institute for Translational Medicine and Therapeutics (ITMAT), the Institute for Diabetes, Obesity and Metabolism (IDOM), the Center for Clinical Epidemiology and Biostatistics, 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 and translational 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, Penn Presbyterian Medical Center –PPMC, and the Philadelphia Veterans Affairs Medical Center –PVAMC, as described under Training Institutions). The basic cardiovascular research laboratories and their respective collaborations with the Penn Cardiovascular Institute, the Department of Cell and Developmental Biology, the Center for Clinical Therapeutics Epidemiology and Biostatistics, the Institute for Translational Medicine and Therapeutics and the Pennsylvania Muscle Institute.

We participate in ERAS (the Electronic Residency Application Service (<u>http://www.aamc.org/eras</u>). 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 in October. 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 August in order to be considered for an interview. Please contact our Fellowship Administrator, Gwynne Katzenbach, at 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 Penn-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 Perelman School of Medicine at the University of Pennsylvania, 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, the Heart Failure and Transplantation unit, and Interventional Cardiology and Electrophysiology Laboratories. There are seven state-of-the-art digital Catheterization and Electrophysiology Laboratories.

The nationally recognized Penn Heart and Vascular Center is located in the Ruth and Raymond Perelman Center for Advanced Medicine and houses the cardiac ambulatory care outpatient practices, including the Heart Failure/Transplantation practice, Penn Cardiac Electrophysiology practice, the Philadelphia Adult Congenital Heart Disease program, the Pulmonary Hypertension Program and Preventive Cardiology Programs. The Noninvasive Imaging Center accommodates echo, cardiac MRI, cardiac CT and exercise and nuclear facilities cardiology imaging modalities.

Over 2,000 cardiac catheterizations are performed annually at this facility. This includes diagnostic studies, angioplasties and intracoronary stents, atherectomies and valvuloplasties The cath lab performs approximately 700 therapeutic procedures annually, including >500 PCIs and >150 structural interventions (balloon valvuloplasty, alcohol septal ablation, PFO and ASD closure, mitraclip repair, left atrial appendage occlusion, and others). In addition the heart valve team has performed >600 TAVR procedures with a current pace of close to 200 per year. In addition, we perform 1,600 cardiac biopsies annually. There are approximately 2,800 electrophysiology procedures and close to 1,650 major cardiac surgical procedures performed at HUP annually. The noninvasive laboratory performs approximately 18,500 transthoracic echocardiograms, 2,700 transesophageal echocardiograms, and 93,000 computerized electrocardiograms a year. The Division's Clinical Services consult on or directly manage more than 47,000 cardiac patients per year.

**The Penn- Presbyterian Medical Center (PPMC):** PPMC is part of the University of Pennsylvania Health System and is an essential component of the cardiovascular fellowship training program. PPMC 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 interventional cardiology 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, 730 transesophageal echos, 150 holter monitors, 900 stress tests (nuclear and echo), 1,600 peripheral vascular disease evaluations, and approximately 3,700 diagnostic catheterizations, PTCAs, atherectomies, stents and percutaneous aortic valve replacements. Approximately 1,800 electrophysiology procedures and 600 major surgical procedures are performed annually. The Cardiovascular Division faculty members are assigned to teaching rotations in the PPMC CCU, and University of Pennsylvania House staff and fellows rotate between HUP and the Penn 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 (PVAMC):** The PVAMC is an integral part of the teaching programs of the University of Pennsylvania and includes a 145 bed acute care tertiary hospital and a 135-bed community living center. Adjacent to the University, cardiovascular fellows rotate between HUP and the PVAMC. The PVAMC serves as a regional referral center for the surrounding VA Medical Centers. It provides a complete range of state-of-the-art clinical facilities and services including intensive care units, cardiac catheterization and electrophysiology laboratories, transthoracic and transesophogeal echocardiography, nuclear medicine, CTA and MRI. Cardiovascular Division faculty and fellows of the University of Pennsylvania Health System 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. Fellows are integrally involved in doing procedures in the echo lab and on the catheterization and electrophysiology rotations in the respective laboratories.

**Children's Hospital of Philadelphia (CHOP):** CHOP is recognized as the national leader in Pediatric acute cardiac care. This 472-bed pediatric hospital is located on the University of Pennsylvania medical campus has 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 services 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 and Transplant Services and Adult Congenital Heart Disease. All fellows participate in outpatient clinic one half day per week during their first three years of fellowship training. Senior fellows may elect to participate in subspecialty clinics, in addition to the Cardiology Fellows' Clinic in their second and third year 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 PVAMC cardiology clinics. Annual awards are presented to fellows for outstanding teaching and research achievement.

#### **Cardiovascular Fellowship Rotations**

| ROTATION                | 1ST YEAR                             | 2ND YEAR         | ROTATION                              | 1ST YEAR | 2ND YEAR           |
|-------------------------|--------------------------------------|------------------|---------------------------------------|----------|--------------------|
| Cardiac Care Unit (CCU) | VA 4-8<br>weeks<br>PPMC 4-6<br>weeks | HUP 6-8<br>weeks | Electrophysiology                     | 4 weeks  | 4 weeks            |
| Cardiac Catheterization | 8 weeks                              | 8 weeks          | Exercise/Nuclear                      | 6 weeks  | 2-3 weeks optional |
| Cardiac Consults        | 6-8 weeks                            |                  | Heart Failure and<br>Transplant/Rehab | 4 weeks  | 2-4 weeks          |
| Echocardiography        | 2 months                             | 2 months         | Vacation /meetings                    | 1 month  | 1 month            |
| Vascular                | 2 weeks                              | 1-6 weeks        | Adult Congenital                      | 2 weeks  |                    |

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 19 different departments in the Smilow Center for Translational Research (SCTR) 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 2012, NIH support to cardiovascular research programs at Penn exceeded \$69,000,000. 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. 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.

The Penn CVI is located in the newly constructed SCTR (SCTR) and is home to 19 faculty members in the Cardiovascular Medicine and CT Surgery Divisions. The Penn CVI contains integrated 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 Penn CVI contains three conference rooms that are used for Cardiology Grand Rounds, the weekly Penn CVI Seminar Series and weekly lab meetings. Separate space has been set aside for students and post-doctoral fellows. 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 10th floor of the SCTR building immediately adjacent to the Penn CVI. Dr. Garret FitzGerald, MD, FRS, a cardiologist who chairs the Department of Pharmacology, serves as director of the ITMAT. Dan Rader, of the Division of Human Genetics and Translational Therapeutics 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 Genomics and Proteomics Core Facilities. In addition to providing core resources for translational 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 has one of the largest advanced heart failure and transplantation (HF/T) programs in the United States. The 10 full-time physicians in this program reflect a mix of professional emphasis including individuals predominantly involved with clinical practice and others who lead clinical and/or translational research efforts in addition to their clinical responsibilities. The academic interests among the HF/T faculty are likewise diverse and together provide expertise and mentoring for a wide representation of topics. Within this framework, the assets of the HF/T clinical and translational research programs are highlighted below.

<u>Clinical Research</u>: As one of the nine regional centers in the NHLBI-funded Heart Failure Clinical Research Network, the Penn HF/T program has access to the Network's novel proof-of-concept trials. Penn is currently the lead center in the Network's trial evaluating the impact of GLP-1 agonist treatment for patients with advanced heart failure. These trials and the Network's growing databases and biorepositories allow particularly rich opportunities for trainee research projects through ancillary studies. Penn HF/T faculty also lead and participate in a variety of investigator-led and extramurally-funded clinical trials originating outside the HF Network, including studies utilizing pharmaceuticals, devices and novel biologics. Led by Dr. Tom Cappola, the HF/T clinical research enterprise employs three full-time research nurses and several research assistants who assist with trial activation and regulatory processes, screening/enrollment, and study execution. Ongoing clinical trials and observational studies within the HF/T research enterprise include studies involving novel remodeling strategies using gene therapy, ultrafiltration, remote disease-monitoring straties, LVAD-associated recovery, sleep-disordered

breathing, HF with preserved ejection fraction, pulmonary hypertension and anti-rejection strategies for heart transplant recipients. Complementing interventional clinical trials are growing observational cohorts and biobanks of genotyped patients with advanced heart failure, chemotherapy-induced cardiotoxicity and hereditary cardiomyopathies. These clinical cohorts empower association studies, hypothesis-generating inquiries, and clinical biomarker development.

<u>Translational Research</u>: The HF/T Research laboratories include over 1,800 square feet of modern laboratory space on the 11th floor of the new Smilow Center Translational Research (SCTR). The HF/T translational research program is directed by Dr. Ken Margulies who is nationally recognized for research focused on myocardial mechanics and remodeling. Active areas of inquiry include studies focusing on integrative genomics enabling novel myocardial target identification, inquiries using cardiac tissue engineering for mechanistic inquiries and drug screening, and studies of endogenous cardiac repair. Versatile core capabilities within the HF/T translational program include the cardiac myocyte core lab, cell and tissue culture facilities, advanced microscopy capabilities, high-throughput quantitative PCR screening, and a large human cardiac tissue repository including samples from hundreds of patients with advanced heart failure and from non-failing controls. Close proximity to the labs of other Penn Cardiovascular Institute investigators on 11 SCTR and CVI core labs (mouse physiology core, iPSC core, histology core) further enhance 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 has a 40 year history of producing pioneering research in cardiac electrophysiology. Currently, Dr. Francis Marchlinski, who directs the program, and the team of 16 PENN EP faculty members are internationally recognized for their studies demonstrating the efficacy of radiofrequency catheter ablation to treat, and in many patients cure, ventricular and atrial tachyarrhythmias. Each year, Penn EP faculty members publish 20-30 peer-reviewed manuscripts in leading Cardiology journals, many of which are authored by Penn cardiology and EP subspecialty fellows. In addition, Penn cardiology and EP fellows present at national and international EP conferences including the annual meeting of the Heart Rhythm Society, the National AHA and ACC Conferences. For over a generation, PENN EP faculty members have helped train investigators for careers in academic electrophysiology at many of the major medical centers in the U.S. In addition, Vickas Patel, MD, PhD established a translational research program in channel biology/mouse electrophysiology. He has mentored several trainees interested in academic careers in basic cardiac electrophysiology have access to the Mouse Cardiac Electrophysiology Core laboratory and the large animal Experimental Electrophysiology Laboratory located on the 7<sup>th</sup> floor of the SCTR.

#### **Clinical and Translational Research Center (CTRC)**

The Penn CTRC (formerly the General Clinical Research Center-GCRC) is a multidisciplinary research facility founded in 1962 with a NIH grant, is located in the Hospital of the University of Pennsylvania. With the award of the Clinical and Translational Science Award (CTSA) in 2006, the GCRCs at both Penn and CHOP integrated to form the CTRC. The CTRC is a core facility for patient related clinical research at the Penn Medicine and Children's Hospital of Philadelphia. It is co-directed by Thomas Cappola, MD, Associate Professor of Medicine and Carole Marcus, MBBCh, Professor of Pediatrics. The CTRC 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 CTRC has state-of-the-art software and databases designed to store, protect and analyze research data. The CTRC 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 Adult or Pediatric CTRC.

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

The CCEB was established in 1993 on the University of Pennsylvania medical campus. Harold Feldman, MD, MSCE, Professor of Medicine and Professor of Biostatistics and Epidemiology is the Interim Center Director. Dr. Stephen Kimmel, Professor of Medicine (Cardiology) and Epidemiology is Acting Director of the Epidemiology Division and Director of the Center for Therapeutic Effectiveness 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 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 (MSCE.), a PhD degree program in Epidemiology, M.S. and PhD programs in Biostatistics, and combined MD/MSCE. and MD/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, and 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 <u>http://www.med.upenn.edu/cvi/education.shtml</u>, <u>http://www.cceb.upenn.edu/education/epi-degree/msce.php</u>, and <u>http://www.med.upenn.edu/mshp</u>, 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. Additionally, there is a weekly fellows clinical conference series, conferences in adult congenital heart disease, vascular medicine, and multimodality cardiovascular imaging, all designed for fellows. 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   |  |  |
| 7:30-8:30                | Catheterization Core Curriculum, 9 Gates Conference Room  |  |  |
| 7:15-8:30                | EPS Research Conference, 9 Founders Conference Room   |  |  |
| 8:00-8:30                | CCU/HF Service Core Curriculum, 8 Founders Conference Room  |  |  |
| 12:00-1:00               | Medical Grand Rounds, Flyers/Sixers Auditorium  |  |  |
| 12:00-1:00               | Consultants Rounds Lecture Series, 9 Gates Conference Room *  |  |  |
|                          | (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 *  |  |  |
| 7:30-8:30                | PPMC Clinical Management Conference – 2nd Wednesday   |  |  |
| <b>- - - - - -</b>       | Philadelphia Heart Institute, 1st Floor-PHI106  |  |  |
| 7:30-8:30                | HF Fellows Conference, Oval conference room on 11-TRC   |  |  |
| 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),   |  |  |
| 12.00 1.00               | Every 4th Wednesday (subject to conflict changes), Perelman 2E Cardiology Conference Room<br>ECG Conference, 9 Founders Conference Room * |  |  |
| 12:00-1:00<br>12:00-1:00 | VA Medical Center Grand Rounds, 7th Floor LVA Auditorium  |  |  |
| 4:00-5:00                | Penn Cardiovascular Institute Seminar Series, 11-146 SCTR   |  |  |
| 4.00-5.00                | Thursday  |  |  |
| 7:15-8:30                | EPS Case Presentation Conference, 9 Founders Conference Room  |  |  |
| 7:30-8:30                | Cardiology Grand Rounds (includes Morbidity & Mortality Conference one week every other month), 11-                                       |  |  |
|                          | 146 SCTR  |  |  |
| 7:30-8:30                | PPMC Catheterization Conference, 1st Thursday – Philadelphia Heart Institute, 1st Floor-PHI106  |  |  |
| 7:30-8:30                | PPMC CV Surgery Conference, 2nd Thursday – Philadelphia Heart Institute, 1st Floor-PHI106   |  |  |
| 7:30-8:30                | PPMC Cardiology Grand Rounds, 3rd Thursday – Philadelphia Heart Institute, 1st Floor-PHI106   |  |  |
| 7:30-8:30                | PPMC CV/CT M & M Conference, 4th Thursday – Philadelphia Heart Institute, 1st Floor-PHI106  |  |  |
| 8:00-8:30                | CCU/HF Service Core Curriculum, 8 Founders Conference Room  |  |  |
| 12:00-1:00               | Fellows Noninvasive Conference, 9 Gates*  |  |  |
|                          | 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 Film Review, 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 (First Friday of the Month)  |  |  |
| 12:00-1:00               | Vascular Medicine Conference, 9 Gates Conference Room, every other week   |  |  |
| 12:00-1:00               | Multimodality Imaging Conference, 9 Gates Conference Room – every other week  |  |  |
|                          | Vascular Medicine and Multimodality Imaging Conferences are on alternating Friday's   |  |  |

\* Mandatory fellow attendance

#### Adult Congenital Heart Disease Program

HUP Yuli Kim, MD (Director)

TITID

Alex Davidson, MD

Richard Donner, MD

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.

#### **Cardiac Catheterization Laboratory**

| HOP<br>Howard C. Herrmann, MD (Director)<br>John W. Hirshfeld, Jr., MD | Saif Anwaruddin, MD.<br>Daniel M. Kolansky, MD | Jay Giri, MD<br>Robert L. Wilensky, MD |
|--|--|--|
| РМС  |  |  |
| Gene Chang, MD   | Craig A. Frankil, DO                           | Christine M. Gasperetti, MD            |
| William C. Groh, MD  | Robert H. Li, M.D                              | William H. Matthai, Jr. MD             |
| Alan S. Moak, MD .   |  |  |

Several clinical research objectives are pursued in the cardiac catheterization laboratory. These include both pharmacologic and device interventions for patients with coronary artery disease, structural and valvular heart disease, and hypertension. A major theme is the evaluation of devices for interventional non-coronary cardiac procedures for structural and valvular heart disease. These include the Sapien and Corevalve transcatheter aortic valve replacement, Mitraclip mitral valve repair, left atrial appendage occlusion, Amplatzer and Helex devices for PFO and ASD closure, and alcohol septal ablation for HOCM. Faculty in the lab have been leaders in transcatheter aortic valve replacement, percutaneous repair for mitral regurgitation, renal denervation for resistant hypertension, and stem cell therapy for myocardial regeneration. Other research projects are directed at understanding and modifying the course of thrombosis in patients with unstable angina, acute myocardial infarction, and in patients undergoing interventional coronary procedures.

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 SIMPLICITY, PARTNER, EVEREST, COAPT, ACP, REDUCE, 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.

#### **Clinical Cardiology**

#### HUP

| Andrew J. Litwack, MD (Interim Director) |                            |                         |
|--|----------------------------|-------------------------|
| Marietta Ambrose, MD, MPH                | Helene Glassberg, MD       | Jonathan Gomberg, MD    |
| David M. McCarthy, MD                    | William O'Donnell, MD, PhD | Frank E. Silvestry, M.D |
| Michael B. Simson, MD                    |                            |                         |

#### PPMC

Alan K. Askenase, MD Norman Feinsmith, MD William C. Groh, MD Robert H. Li, MD William J. Untereker, MD Gene Chang, MD Terry D. Friedman, MD Douglas Jacoby, MD William H. Matthai, Jr., M.D Gary J. Vigilante, MD Theodhor Diamanti, MD Christine Gasperetti, MD Neil Levin, MD Kelly Anne Spratt, DO Richard L. Weiss, MD 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 the 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.

#### Electrophysiology

| HUP                                 |                       |                           |
|-------------------------------------|-----------------------|---------------------------|
| Frank E. Marchlinski, MD (Director) | Rupa Bala, MD         | David J. Callans, MD      |
| Rajat Deo, MD                       | Sanjay Dixit, MD      | Andrew Epstein, MD        |
| David Frankel, MD                   | Fermin Garcia, MD     | Mathew D. Hutchinson, MD  |
| David Lin, M.D                      | Vickas Patel, MD, PhD | Michael P. Riley, MD, PhD |
| Michael B. Simson, M.D              | Gregory Supple, MD    | Robert Schaller, DO       |
| Ralph J. Verdino, MD                |                       |                           |
|                                     |                       |                           |
| DDMC                                |                       |                           |

#### PPMC

TITID

John R. Bullinga, MD (Director)

Charles Leng, MD

Joshua Stern, MD

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 five 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.

#### **Advanced Heart Failure and Cardiac Transplantation Program**

#### HUP

Lee Goldberg, MD, M.P.H. (Director) Mariell L. Jessup, MD Anjali Owens, MD Anjali Vaidya, MD

Susan C. Brozena, MD Kenneth B. Margulies, MD J. Eduardo Rame, MD Joyce Wald, DO Thomas P. Cappola, MD, ScM Rhondalyn McLean, MD Richard P. Shannon, MD

PPMC

| Stephen | Chrzanowski, | MD |
|---------|--------------|----|
|---------|--------------|----|

Brian M. Drachman, MD

Ross R. Zimmer, MD

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.

#### Cardiovascular Imaging and Echocardiography HUP

| 1101                     |                        |                                |
|--------------------------|------------------------|--------------------------------|
| Victor A. Ferrari, MD    | Dinesh Jagasia, M.D    | Maren E. Jeffery, M.D          |
| James P. Kirkpatrick, MD | Bonnie Ky, MD          | Emile R. Mohler, MD            |
| Muredach Reilly, MD      | Frank E. Silvestry, MD | Martin G. St. John Sutton, M.D |
| Yuchi Han, MD, M.M.Sc.   |                        |                                |
|                          |                        |                                |
| PPMC                     |                        |                                |

Jignesh Bhavsar, MD David Schwartz, M.D Terry Friedman, MD Gary Vigilante, MD Neil Levin, M.D Richard L. Weiss, MD

#### PVAMC

Julio Chirinos, MD

This very busy clinical program focuses on the use of quantitative Doppler echocardiographic analysis to assess left ventricular remodeling post-myocardial infarction and 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 human and experimental animal models. Transesophageal echocardiographic evaluation of valvular repair and replacements (TAVR, etc.), and complex aortic surgery in collaboration with Cardiothoracic Surgery and Anesthesiology is ongoing. Other research interests include gender differences in the diagnosis and treatment of cardiovascular disease, and right ventricular function and metabolism in pulmonary hypertension. Two large important trials involve extensive collaboration with CRIC and the Penn Heart Failure Study investigators.

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

| Scott Akers, MD, Ph.D         | William Boonn, MD | Julio Chirinos, MD     |
|-------------------------------|-------------------|------------------------|
| Benoit Desjardins, MD, Ph.D   | Kevin Duffy, MD   | Victor A. Ferrari, M.D |
| Yuchi Han, MD, M.M.Sc         | Saurabh Jha, M.D  | Harold Litt, MD, PhD   |
| Martin G. St. John Sutton, MD |                   |                        |

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 seven clinical 1.5 Tesla scanners, two 3 Tesla high field scanners, and a seven Tesla ultra-high field system available for studies in humans. In addition, a dedicated 3T cardiac system is available for large animal research at the SCTR. Ongoing research includes quantitative assessment of regional wall motion and myocardial mechanics, and 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.

Novel approaches to 4D flow assessment, diffuse myocardial fibrosis evaluation, and right ventricular function and metabolism in pulmonary hypertension are areas of active investigation.

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 area of strong interest is the small animal imaging program—a collaborative effort with the Molecular Cardiology and Molecular Imaging groups. We have developed imaging protocols, coils, and tagging methods for studying rodents at 4.7 and 9.4 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.

Cardiac 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 and the Philadelphia VA Medical Center 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.

#### Nuclear Cardiology/PET Imaging/Exercise Physiology

#### HUP

David M. McCarthy, MD (Director)

Andrew Litwack, MD

PPMC

Alan D. Askenase, MD

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.

# Preventive Cardiovascular Medicine and Lipid Clinic

| Daniel J. Rader, MD (Director) | Emil M. deGoma, MD  | Kristen Dilzell, C.G.C.       |
|--------------------------------|---------------------|-------------------------------|
| Richard L. Dunbar, MD, M.S.T.R | Emile R. Mohler, MD | Muredach P. Reilly, MD, MSCE. |
| Daniel Soffer, MD              |                     |                               |

#### PPMC

Doug Jacoby, MD

Arthur Topoulos, MD

The Preventive Cardiovascular Program is an interdisciplinary program dedicated to the comprehensive systematic assessment of cardiovascular risk and risk reduction. Cardiologists and general 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, and alternative and complementary approaches to cardiovascular risk. The program places a major emphasis on cardiovascular risk assessment using state-of-the-art technologies including advanced laboratory testing and noninvasive imaging of atherosclerosis.

One of the longest-running comprehensive lipid management programs in the country, the Preventive Cardiovascular Program cares for a large cohort of patients with genetic dyslipidemia, including familial hypercholesterolemia. The program maintains one of the largest LDL-apheresis centers and participates in numerous trials of novel lipid-lowering therapies. The clinic was one of the first to utilize coronary artery calcium scanning for cardiovascular risk refinement, as well as one of the pioneering centers to provide genetic counseling for inherited cholesterol disorders.

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; and 4) Clinical trials of novel LDL/triglyceride-lowering agents, HDL-targeted therapies, and direct anti-atherogenic medications.

#### Vascular Medicine (Clinical) Research Program HUP

Emile R. Mohler, MD Emil deGoma, MD Daniel J. Rader, MD Muredach Reilly, MD

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 and vascular dysfunction is being assessed with diagnostic modalities such as, novel MR imaging to evaluate vascular function, ultrasound to assess vascular reactivity, and NIRS imaging to evaluate tissue oxygenation and blood flow.

Current clinical research studies include evaluation of vascular function via measurement of circulating endothelial progenitor cells and microparticles in a blood test named the "Vascular Health Profile." An NIH supported study is underway to evaluate the mechanisms leading to improved walking in response to exercise rehabilitation in patients with peripheral artery disease (PAD). Pharmaceutical-sponsored studies involving evaluation of novel drugs for treatment of claudication are also being conducted. A prospective registry of patients with PAD is being conducted, including collection of DNA and plasma samples and ultrasound imaging to evaluate the environmental and genetic causes of progression of atherosclerosis.

Another investigation is centered on the pathologic mechanisms involved in varicose vein development including genetic studies of patients with this condition.

Cardiovascular Epidemiology HUP Stephen E. Kimmel, MD, M.S.

Muredach Reilly, MD

Brian L. Strom, MD, M.P.H.

Edward Morrisey, PhD

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.

#### BASIC AND TRANSLATIONAL SCIENCE RESEARCH PROGRAM

Cardiology fellows may elect to spend 2-3 years of postdoctoral fellowship research training in the laboratory of one of the Penn CVI faculty members engaged in NIH funded research. To enter this program, Cardiology fellows are asked to identify a laboratory and faculty mentor during their first two years of clinical fellowship training. Fellows interested in this pathway then apply for a formal position on one of several institutional NIH sponsored T32 postdoctoral fellowship training grants. The Penn CVI training grant (Michael S. Parmacek, MD, PI) sponsors six postdoctoral fellows interested in performing basic and translational cardiovascular research. In addition, to establishing a research thesis project, trainees may enroll in didactic coursework related to their research project. Multiple trainees have obtained a Masters of Translational Research program through the Penn ITMAT-sponsored training program. The vast majority of trainees in this program apply for, and receive, NIH K08 or equivalent grants, during their second or third year of training which presents a bridge to a faculty position.

#### **Development of the Heart and Vascular System**

| Jonathan A. Epstein, M.D | Mark Kahn, MD            |
|--------------------------|--------------------------|
| Michael S. Parmacek, MD  | Vickas V. Patel, MD, PhD |

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.

#### Vascular Biology

Lawrence Brass, MD, PhD Garret A. Fitzgerald, MD Edward Morissey, PhD Muredach Reilly, MD Peter Davies, PhDJonathan Epstein, MDMark Kahn, MDEmile R. Mohler, MDMichael S. Parmacek, MD Daniel J. Rader, MDRobert L. Wilensky, 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, aortic aneurysm and dissection, diabetic vascular disease and peripheral vascular disease. Core facilities include the Penn CVI Histology and Mouse Physiology and Imaging Core Laboratories in the SCTR where mouse models of cardiovascular disease may be generated and characterized. Dr. Parmacek, Director of the Penn CVI, has a longstanding interest in understanding the transcriptional programs and signaling pathways that control vascular smooth muscle cell development and its relationship to atherosclerosis and aortic aneurysm and dissection. Dr. Epstein's research focuses on the contribution of the cardiac neural crest to the cardiac outflow tract and great arteries and its relationship to congenital heart disease. Dr. Epstein, Chairman of the Department of Cell and Developmental Biology, also has pioneered research in stem Dr. Kahn is nationally recognized for his expertise in platelet cells and regenerative therapies. function/thromobosis/hemostasis and development and physiology of the lymphatic system. Professor Morrisey is internationally recognized for his research examining development of the pulmonary vasculature. Dr. Rader, Chief78 of the Division of Translational Research and Genetics, is internationally recognized for his research interest in lipid metabolism (especially HDL) and its relationship to atherosclerosis. He is also recognized for his research in genetics of atherosclerosis and lipid metabolism. Dr. Reilly is recognized for his translational and genetic research studies in the area of vascular inflammation. Dr. Brass, Director of the Penn MD/PhD training program, examines the molecular mechanisms underlying thrombosis and hemostasis. Professor Peter Davies is recognized for his expertise in endothelial cell biology, shear stress 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. Dr. Wilensky, an interventional cardiologist is recognized for translational and clinical research in the area of vulnerable plaque and large animal models of atherosclerosis. Dr. Emile Mohler is recognized for his translational and clinical research in the area of vascular medicine and peripheral arterial disease.

### **Interventional – Cardiac Cath**

Herrmann, Howard C. - Dir. Anwaruddin, Saif Giri, Jay Hirshfeld, Jr., John W. Kolansky, Daniel M. Wilensky, Robert L.

## **Electrophysiology – EP**

Marchlinski, Frank E. - Dir. Bala, Rupa Callans, David J. Cooper, Joshua M. Deo, Rajat Epstein, Andrew E. Frankel, David Garcia, Fermin C. Hutchinson, Mathew D. Lin, David Riley, Michael Schaller, Robert Supple, Gregory Verdino, Ralph J.

# Heart Failure /

Cardiac Transplant Goldberg, Lee R. – Dir. Brozena, Susan C. - Radnor Cappola, Thomas P. Jessup, Mariell – Clin. Vice Chief Margulies, Kenneth B. McLean, Rhondalyn Owens, Anjali Rame, J. Eduardo Shannon, Richard P. – Dept. Chair Vadiya, Anjeli Wald, Joyce W.

# **Clinical Cardiology**

Ambrose, Marietta Carver, Joseph Chokshi, Neel Glassberg, Helene L. Gomberg, Jonathan D. *Litwack, Andrew J. – Interim Dir.* McCarthy, Dave M. O'Donnell, William Simson, Michael B.

# Noninvasive Cardiology – Echo – Nuclear Imaging

*Ferrari, Victor A. – Interim Dir.* Han, Yuchi Jagasia, Dinesh Jeffrey, Maren E. (Radnor) Kirkpatrick, James N. Ky, Bonnie Silvestry, Frank E. St. John Sutton, Martin

# VA Cardiology

*Epstein, Andrew E. – Chief (EP)* Chirinos, Julio Dixit, Sanjay (EP) Duffy, Kevin J. Frame, Lawrence H. Giri, Jay

# Molecular Core Laboratory

Epstein, Jonathan A. – Dir. Kahn, Mark L. Morrisey, Edward E. Parmacek, Michael S Patel, Vickas (EP)

# **Clinical Cardiology – PPMC**

Feinsmith, Norman Vigilante, Gary J. Spratt, Kelly Anne Diamanti, Theodhor Patterson, Brandy Madhavi, Reddy Reynolds, Carl Rodriguez, Raymond

# Lipids – Preventive Cardiology -Epidemiology

Rader, Daniel deGoma, Emil Reilly, Muredach P. Kimmel, Stephen E. (Epi)

## Vascular

Mohler, III, Emile R.

## PHI – Waxman Group

Waxman, Harvey L. - Chief Askenase, Alan D - Nuclear Bhavasar, Jignesh Bullinga, John – EP Chang, Gene – Interventional Chrzanowski, Stephen - HF Drachman. Brian M - HF Frankil, Craig - Intrv Friedman, Terry D – Echo Gasperetti, Christine - Intrv Groh, William C - Intrv Jacoby, Douglas S - Prev Leng, Charles T - EP Levin. Neil - Echo Li. Robert H – Intrv Matthai, Jr., William - Intrv Moak. Alan S – Intrv Schwartz, David S - Echo Stern, Joshua Topoulos, Arthur P – Vasc Untereker, William J - Assoc. Chief Volosin, Kent J - EP Weiss, Richard L - Echo Zhang, Janet (Yardley) Zimmer, Ross R – HF

# Adult Congenital Heart Center (ACHD)

*Kim, Yuli – Dir.* Chrisant, Maryanne R.K. – CHOP. Donner, Richard - CHOP Ferrari, Victor A. Fogel, Mark – CHOP Herrmann, Howard C. Hirshfeld, John Jessup, Mariell L. Kreutzer, Jacquelyn – CHOP Litt, Harold Rome, Jonathan – CHOP Shah, Maully J. – CHOP Spray, Thomas L. – CHOP St. John Sutton, Martin Shaddy, Robert – CHOP