Facilities and Other Resources
HL007915: Training in Molecular Therapeutics for Pediatric Cardiology

THE CHILDREN’S HOSPITAL OF PHILADELPHIA

The Children’s Hospital of Philadelphia (CHOP) was founded in 1855 as the nation’s first pediatric hospital. Through its long-standing commitment to providing exceptional patient care, training new generations of pediatric healthcare professionals and pioneering major research initiatives, Children’s Hospital has fostered many discoveries that have benefited children worldwide. Its pediatric research program is among the largest in the country, ranking second in National Institutes of Health funding. In addition, its unique family-centered care and public service programs have brought the 459-bed hospital recognition as a leading advocate for children and adolescents. CHOP is consistently recognized as a national leader for advancement of healthcare for children and proudly holds the No. 2 ranking on U.S. News & World Report’s 2016-2017 Honor Roll of the nation’s Best Children’s Hospitals, and CHOP has been either 1st or 2nd in this ranking over the past 10 years. CHOP was also awarded Magnet status by the American Nurses Credentialing Center (ANCC)—an achievement met by only 6 percent of hospitals in the United States.

The hospital’s overall mission is to advance health care for children through excellent patient care, innovative research, education and advocacy. CHOP is committed to developing leaders in medicine and science, as well as expanding the frontiers of pediatric care through novel basic, translational, and clinical research. It has a longstanding history of scientific breakthroughs and discoveries resulting in major advances in pediatric medicine and surgery. CHOP is an independent hospital with autonomous medical, administrative and financial services. The CHOP health system has a staff of over 14,000, a faculty of 800 and an annual operating budget of $1.1 billion. There are 49 pediatric medical and surgical subspecialties at CHOP.

CHOP has one of the largest and most prestigious pediatric training programs in the nation with 144 residents and 197 fellows. Patient care volume has experienced rapid growth over the past 5 years. The Main Hospital has 459 beds, 30 percent of which are allocated to intensive care with over 25,000 inpatient admissions and more than 85,000 emergency room visits. A major renovation of this facility was recently completed with the addition of two hospital wings. CHOP is the community hospital and primary care center for children in West and Southwest Philadelphia, and a major tertiary referral center for the greater Delaware Valley area with an estimated population of 10 million. CHOP serves a diverse population of children that includes large numbers of racial and ethnic minorities, healthy newborns, infants, children and adolescents. CHOP has six academic departments: Pediatrics, Surgery, Anesthesiology and Critical Care, Diagnostic and Interventional Radiology, Psychiatry, and Pathology and Laboratory Medicine. Pediatrics and Surgery have pediatric subspecialty divisions in all of the major pediatric disciplines. CHOP provides accessible, comprehensive, innovative, and high quality medical and surgical care to children in Pennsylvania, New Jersey, and Delaware as well as children referred from throughout the United States and international.

The main Hospital is located adjacent to the campus of The University of Pennsylvania and is within walking distance of all Penn schools, laboratories and facilities. Although a separate and private entity, Children’s Hospital is an essential and integral component in the University’s medical system and is immediately next door to The Penn’s School of Medicine and the Hospital of the University of Pennsylvania. The members of the Department of Pediatrics at CHOP are the faculty of the Department of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania School of Medicine.

Research Resources at CHOP: More than 300 investigators conduct research through more than 1,200 human (IRB approved) and animal (IACUC approved) research protocols. The research is broadly based and includes studies to understand the basic mechanisms of biological functions and human diseases, as well as testing new drugs, devices, vaccines and other biological agents for safety and efficacy. Larger programmatic areas of investigation include AIDS, cardiac diseases, childhood cancer, cystic fibrosis, diabetes, hemophilia, hypercholesterolemia, hyperinsulinism, mental retardation, neonatal seizures, nutritional disorders, sickle cell diseases, and a number of other major disorders and diseases that affect children. CHOP research is supported at this time by more than $360 million, with $146 provided by NIH grants. Outstanding facilities are available at CHOP for state-of-the-art laboratory and clinical research. Bench research facilities in the Abramson Pediatric Research Center and adjacent Ruth and Tristram Colket Jr. Translational Research Building have more than 800,000 square feet of laboratory space, as well as facilities and staffing for laboratory animal research. The Abramson Pediatric Research Center building is home to the CHOP Cardiology Research Laboratories, and is also directly connected to the CHOP Main hospital building. The new Roberts Center for Pediatric Research on
the CHOP’s Schuylkill Avenue Campus offers 460,000 square feet of collaborative clinical research space on 21 floors.

The Perelman School of Medicine at the University of Pennsylvania: Currently, the Penn’s School of Medicine has over 2 million square feet of research space. Penn Medicine is consistently among the top recipients of funding from the National Institutes of Health. In 2010, the 10-story Smilow Center for Translational Research was completed and includes 531,000 square feet of laboratory space to support biomedical and translational research. The Smilow facility is also home to Penn’s Cardiovascular Institute (Penn CVI) that is actively participating in this training program. Thus, our Penn research training faculty have outstanding resources and facilities to host the research trainees from this T32 program.

THE CARDIAC CENTER AT CHILDREN’S HOSPITAL OF PHILADELPHIA

The Cardiac Center at CHOP is one of the largest and most comprehensive Congenital/ Pediatric Cardiac Centers in the United States. Established in 1998 by physician leadership and board resolution - the Center now employs more than 800 people including over 80 physician faculty in three Academic Departments and four Divisions. The faculty include cardiothoracic surgeons, over sixty cardiologists in all sub-specialties, cardiac critical care intensivists, and dedicated cardiac anesthesiologists. In addition, there is a large professional clinical support team which includes advanced practice nurses, physician assistants, certified registered nurse anesthetists, and perfusionists.

The Cardiac Center at CHOP performs over 1,000 surgeries per year including over 600 open heart cases. In addition, the Center averages over 1,000 cardiac catheterization procedures. The Center sees over 30,000 cardiac ambulatory visits per year at the Main site and 11 satellite locations – some as far as over 60 miles from the Main Campus. The Center performs around 25,000 outpatient echo studies annually, over 2,900 fetal echocardiography studies, and over 1200 Cardiac MRIs.

The Cardiac Center strives to encourage innovation and continually discover novel ways to solve challenges inherent in the treatment of congenital heart disorders. The Center has an extensive research arm, with multiple areas of focus including collaborative efforts with other major institutions.

Center Leadership and Infrastructure

The Cardiac Center is governed by an Executive Committee which includes the chiefs of each division (Cardiology, CT surgery, Cardiac Critical Care Medicine, and Cardiac Anesthesiology), the Director of Cardiac Nursing, a Hospital SVP, and the Administrative Director of the Service Line. The Executive Committee meets monthly and the meetings are also often attended regularly by the Department Chairs of Medicine and Anesthesia. The Chief of CT Surgery and the Chief of Cardiology also serve as Co-Executive Directors of the Center. There are several committees which include members of multiple divisions. These include the Cardiac Center Operations Committee, the Cardiac Center Research Core, the Cardiac Center Quality Improvement Committee, and the Cardiac Center Data Governance Committee.

CARDIAC CENTER PHYSICAL FACILITIES

Inpatient and Pre-Post Procedure Beds

Special Delivery Unit

The Special Delivery Unit is staffed by members of the Center for Fetal Diagnosis and Treatment as well as obstetricians and midwives. CHOP is fortunate in that it is one of the few pediatric hospitals in the world with a dedicated team of board certified maternal-fetal medicine specialists on staff as well as a birthing delivery unit with full obstetrical services. One of the many benefits of this unit is the ability to safely deliver a fetus with congenital heart disease at the site in which postnatal care is offered, avoiding the need for transport of an ill and potentially unstable neonate.

Cardiac Critical Care Unit

The Cardiac Critical Care Unit (CICU), was established as a separate unit from the Pediatric Intensive Care Unit in 1995. It is located immediately adjacent to the Special Delivery Unit as well as the Cardiac Care Unit (step-down unit – below) on the 6th floor. The unit currently has 26 beds – however there is additional licensed capacity. The average census over the past year is about 23. The unit is staffed by the attending physicians from the Division of Cardiac Critical Care Medicine – with consulting cardiologists and cardiac surgeons and supported by advanced practice nurses and a highly trained cardiac critical care nursing team. The average length of stay on the unit is generally 7-8 days. The CICU is the destination for immediate post-operative care.
**Cardiac Care Unit**

The Cardiac Care Unit (CCU) is a 27-bed unit located directly adjacent to the CICU. This dedicated cardiac unit has every bed connected to a monitored telemetry arrhythmia station. Step down level patients are cared for on this unit, often with one-to-one or two-to-one nursing care. A majority of patients are post-operative patients recovering from cardiac surgery, and who are transferred from the CICU. Patients who are awaiting or recovering from thoracic organ transplant or have transplant related non-intensive care admissions are also admitted to the CCU. This includes patients on inotropic support and those supported with Ventricular Assist Devices. Positive and negative pressure units to provide directional airflow units for infection control and isolation are available.

**Cardiac Preparation and Recovery Unit**

The CPRU, a dedicated thirteen bed unit, 3 of which are designated for overnight stays if needed, is located on the sixth floor of the Main Hospital building adjacent to the CCU. The CPRU serves as the recovery unit for all patients undergoing cardiac catheterization, except those returning to the CICU. In addition, the unit serves for recovery of cardiac patients who have undergone surgical procedures not requiring intensive care as well as those who have received sedation for other invasive and non-invasive procedures. The unit includes a procedure room fully equipped for the administration of anesthetics where procedures such as transesophageal echocardiograms, cardioversions, and thoracotomy or other drainage procedures can be performed. All beds are monitored at bedside and remotely via telemetry. The electrocardiographic information is connected to the arrhythmia monitoring and storage unit on the adjoining CCU.

**Cardiac Operative and Imaging Complex**

The Cardiac Operative and Imaging Complex is located on the sixth floor of the Main Hospital near the Inpatient and CPRU beds.

**Cardiothoracic Surgical Suites**

There are two dedicated state of the art Cardiothoracic Operating Suites and an adjacent Hybrid Suite which can be used for either Cardiac Surgery, Cardiac Catheterization, or combined procedures. The Suites are used daily with 1 to 2 (occasionally 3) scheduled cardiac surgical procedures – depending on complexity of the cases. Over 600 open heart cases are performed annually in these suites and an additional 400 or so closed cases and about 10-15 heart, lung and/or heart/lung transplants.

**Cardiac Catheterization Labs**

The catheterization suite includes three specialized procedure rooms. All include state of the art biplane digital imaging systems. In addition to traditional diagnostic catheterization procedures, invasive procedures are performed for the transcatheter therapeutics, diagnosis and treatment of arrhythmias, pulmonary hypertension, and thoracic organ transplantation. Pediatric cardiothoracic surgical backup including ECMO support, is always available in house for consultation or emergency intervention.

The cardiac catheterization suite is housed within the Cardiac Operative and Imaging Complex including the cardiac surgical operating rooms and cardiac MRI. This geographical arrangement has permitted unique synergy and opportunities: One of the three rooms is paired with the MRI scanner creating an XMR suite allowing for rapid transfer of patients between fluoroscopy and MRI imaging on the same table. The laboratory incorporates a large panel detector with cine CT capabilities; this is particularly suited for electrophysiology procedures as well as the adult with congenital heart disease. The final laboratory is a catheter/surgical hybrid suite. This room is a fully functional cardiac operating room and biplane catheterization laboratory permitting combined catheter/surgical procedures.

**Cardiac Magnetic Resonance Imaging**

The MRI capabilities at CHOP are extensive. An MRI scanner is adjacent to the catheterization laboratory with XMR capabilities, was installed in 2008 and is used nearly exclusively for cardiac and fetal MRIs; it houses a 1.5 Tesla Siemens Magnetom Avanto with the latest hardware and software along with 3 Leonardo workstations, numerous PCs and a separate “Prep-Room.” This suite is housed in the Cardiac Operative and Imaging Complex near the CPRU where patients are sedated or undergo anesthesia, as well as near the operating rooms. This scanner is also used to facilitate research into the mechanisms of perioperative brain injury. In addition, other MRI facilities that are used at times for cardiac imaging at CHOP are two 6,000 square foot state of the art suites containing a total of 6 other scanners (three 1.5 Tesla state of the art Siemens’ systems (one Symphony and two Avanto scanners) and three 3 Tesla Siemens’ systems. A Leonardo workstation dedicated to cardiac MRI is
also located in the echocardiographic laboratory for imaging correlates. The MRI scanners are networked to the hospital system for easy transfer of image files for analysis. They all have state of the art cardiac packages which enable the evaluation of anatomy as well as ventricular function and fluid mechanics. In addition, a number of cardiac software packages are resident on the workstations in the Division of Cardiology and the research area to enable image evaluation. Two physicists are on-site and dedicated to MRI. A 3-dimensional analysis lab with 2 dedicated technicians are utilized to analyze images as well.

**Cardiac Testing Facilities**

**Cardiovascular Exercise Lab**

The exercise physiology lab is approximately 2000 sq. ft. The lab has three complete workstations for performing metabolic exercise testing. Metabolic measurements are made with three Carefusion metabolic carts. Each station is able to perform cycle and treadmill ergometry, electrocardiograms, rhythm strips, and non-invasive cardiac output as needed. Metabolic measurements include minute oxygen consumption and carbon dioxide production. Pulmonary measurements include maximal and tidal flow volume loops at rest and exercise, minute ventilation, physiologic dead space, and carbon monoxide diffusion capacity at rest and exercise. The laboratory personal working with the hospitals physical therapy program staff the inpatient rehabilitation unit located on The Cardiac Center inpatient floor. The laboratory supervisor is primarily responsible for oversight of the rehabilitation program. In addition, the laboratory has a dedicated area for outpatient cardiopulmonary rehabilitation. This area has space for up to four patients to undergo rehabilitation simultaneously. The facilities include a variety of ergometers as well as a telemetry unit to monitor heart rate and arrhythmias.

**ECG and Holter Lab**

The Electrocardiography and Holter Labs are located in the Cardiac Center at CHOP. Space consists of two 120 sq. ft. inpatient ECG rooms; four additional outpatient examination rooms as outpatient ECGs are performed in the room in which the patient is examined by the physician. A 250-sq. ft. workroom and 130-sq. ft. MUSE station is part of the ECG Laboratory along with a 130 sq. ft. Holter room. Twenty ECG machines are available, which are GE Marquette Mac 6000, and GE Marquette Mac 6500 models. Another 21 ECG machines serve outreach clinics. These are capable of obtaining 15-lead ECGs and rhythm strips saved in a digital manner to disks and archived in a MUSE workstation for retrieval and database evaluations. In addition, two ECG machines have signal average ECG capabilities.

**Echocardiography Lab**

The echocardiography suite is a state of the art facility offering all facets of ultrasonic cardiovascular imaging. The facility consists of 19 ultrasound systems. An ultrasound system is dedicated to the 26 bed CICU as well as the 2 cardiac operating rooms. Nine large and comfortable examination rooms are located adjacent to a large central reading room. There is a large conference room adjacent to the reading room. There are weekly didactic echocardiography lectures as well as daily review sessions with the cardiology fellows and sonographers. Additionally, there is one sedation room housed in the CPRU for the performance of sedated echocardiograms. We have a unique system to perform sedated echocardiograms. Cardiac anesthesia provides general face-mask anesthesia services for our patients requiring sedation. This system has allowed for a safe, quick and reliable method of sedation. All echocardiographic images are transmitted onto a bank of 10 flat screen monitors for real-time physician reading. Images are also transmitted real-time to various clinical sites throughout the institution for physician viewing at the points of care. The echocardiography laboratory utilizes a fully digital Syngo Dynamics system (Siemens, Ann Arbor, MI) for our digital acquisition, storage and reporting system. The echocardiography laboratory is staffed by 21 full time and 2 part time sonographers, all of whom are fully trained and experienced in pediatric/congenital imaging. Twenty-two board certified pediatric cardiologists with specialized training in pediatric/congenital cardiovascular imaging are assigned to provide 24 hour physician coverage for the various services provided at the Main CHOP Echocardiography Laboratory site.

**Fetal Imaging Lab**

The physical plant consists of 3 dedicated fetal imaging suites outfitted with state of the art ultrasound systems with full capacity for both obstetrical and fetal cardiovascular imaging, a family consultation room, a conference room, and support offices. Close clinical collaboration exists between Fetal Heart Program and the Center for Fetal Diagnosis and Treatment as the complementary services of prenatal heart focused care, maternal-fetal care, and birthing and delivery are offered in a comprehensive manner in a single location to patients. In addition, there is the unique ability of the program to perform fetal MRI imaging as needed. This unique collaboration
offers the opportunity for a multidisciplinary approach to care and the ability to advance the field of prenatal care for congenital anomalies.

**Basic Science Labs**

The Division of Cardiology Research Labs in the Abramson Research Center occupy more than 8,000 square feet, and are well equipped with state of the art instrumentation to meet the needs of the various sponsored programs. Four dedicated cell culture rooms are present with two hoods per room, and committed incubators for each hood are currently in operation. Ten PCR engines are currently in use, and a Real-Time PCR system (LightCycler) is in operation for quantitative studies. Microscopic resources include four fluorescent microscopy systems (2 upright, 1 inverted and 1 dissecting) with CCD cameras and dedicated computing equipment with supported software. Four additional inverted microscopes are available in the cell culture hoods. Three additional dissecting microscopes are available (light level), as well as a fluorescent inverted microscope. Spectrophotometry and analytic instrumentation include a UV-Vis. spectrophotometer, a variable wavelength fluorometer, a Fourier-transform infrared scanning spectrophotometer, a UV-Vis-ELISA reader, a fluorescent-ELISA reader, a differential scanning calorimeter, a combination laser light scattering particle sizing system-zeta potential apparatus, and an atomic absorption spectrophotometer. The lab also has a FlexCell flow simulation system for cell culture studies; this system consists of a flow—pulse duplicator setup that can mimic flow, pressure and shear forces for cell culture studies involving any vascular and cardiac valve scenario. The FlexCell system also includes a microscopic stage system for flow-microscopy studies under calibrated shear and pulsatile conditions. Other miscellaneous equipment includes 2 ultracentrifuges, 2 refrigerated tabletop centrifuges, multiple Eppendorf centrifuges, and multiple pH meters. The laboratory also maintains a complete microscopy-preparative core facility that can process paraffin, frozen (using the Core’s cryomicrotome), and polymethylmethacrylate imbedded microscopy specimens. This core also includes a custom microtome for cutting through steel sections to support the laboratory’s NHLBI-funded gene delivery stent program.

**Outpatient Clinics**

Cardiologists see outpatients at the Main Hospital Clinic on the third floor of the main building. In addition, there are twelve satellite locations – some over 60 miles from the Main Campus.

**DIVISION OF CARDIOLOGY**

**Overview**

The Division of Cardiology is one of 21 clinical divisions within the Department of Pediatrics at Children’s Hospital of Philadelphia and is led by Dr. Joseph Rossano, MD, MS, FAAP, FACC, Chief of Cardiology. There are five associate chiefs who assist Dr. Rossano in carrying out a variety of responsibilities including Academic Affairs, Clinical Affairs, Outreach and Community Cardiology, Research, and Education.

The Division of Cardiology is comprised of 20 clinical sections and programs. These programs described in more detail under the Cardiac Center Programs Section of this document. Each has a dedicated faculty leader or in some cases where there is cross division/department collaboration – co-leaders. The Division of Cardiology holds six endowed chairs in the Department of Pediatrics as well as several endowed funds that currently supports the divisions academic, research and clinical endeavors. Over the past two decades, the Division of Cardiology has seen incredible growth in personnel, clinical services, basic and clinical research, and community outreach. Nationally recognized as one of the premier centers for cardiac services in the United States, the Division of Cardiology has sustained and developed its preeminent clinical and research programs, and expanded operations. In addition to the clinical programs, there is a strong research infrastructure and currently has over 200 active clinical trials.

**DIVISION OF CARDIOTHORACIC SURGERY**

The Division of Cardiothoracic Surgery at Children’s Hospital of Philadelphia is a recognized leader in the treatment of complex congenital heart disease with a specific emphasis on single ventricle malformations and Hypoplastic Left Heart Syndrome, continuing the programs begun by Dr. William Norwood, MD. Under the leadership of Thomas Spray, MD - the Division currently is comprised of 4 cardiothoracic surgeons and over 600 open heart procedures yearly with an emphasis on complex single ventricle repairs. The Division has 3 endowed chairs in cardiac surgery in addition to academic development funding which provides a continuing stream of financing for research endeavors in the division. Major programs of the Division of Cardiothoracic Surgery include the ventricular assist device, artificial heart and transplant programs and the Adult Congenital Heart Program. The Cardiac Surgery Program at The Children’s Hospital of Philadelphia has been recognized as one of the
major programs in the United States and the clinical outcomes have been excellent. The Children’s Hospital of Philadelphia is a major referral center for patients from the region, nationally and internationally. The cardiac operating rooms located in the Cardiac Operative and Imaging Complex on the sixth floor of the Main building have a dedicated nursing team and perfusion staff, in addition to physician assistants for the cardiac services. The major strengths of the Division of Cardiothoracic Surgery at the Children’s Hospital of Philadelphia include a high volume program with complex referrals both regionally and nationally as well as internationally. The clinical results are well respected and there is a strong and experience team of cardiac surgeons. The heart, lung and heart-lung transplant program has been very active with a very strong representation in the cardiac transplant program of single ventricle malformations and complex congenital heart disease. The division also has a very active ventricular assist device and artificial heart program which has a comprehensive availability of assist devices for the wide range of patients from newborns to adults. In addition the, Adult Congenital Heart Program has been actively growing in cooperation with The Hospital of the University of Pennsylvania. The Research Program in the Division of Cardiothoracic Surgery at Children’s Hospital of Philadelphia is well recognized nationally and internationally for its contributions to understanding the genetics of complex congenital heart disease and the implication of on outcomes after cardiac surgery. In addition there has been a very active investigation into the effects of cardiac surgery on late neurodevelopmental outcomes and potential factors which could impact developmental abnormalities. Current experimental work is focused on altering the fetal/maternal environment in a way that could ultimately have a favorable impact on late neurologic development.

DIVISION OF CARDIAC ANESTHESIOLOGY

The Division has grown to 10 individuals devoted to Pediatric Cardiac Anesthesia. Clinically, the group has significant seniority and experience with special clinical skills in anesthesia care for complex high-risk surgery and other procedures. In addition, individuals have added qualifications in pediatric cardiology/echo; adult cardiac anesthesiology and care of complex cardiac patients for non-cardiac procedures. The Division has made significant contributions to QI efforts throughout the Cardiac Center as well as the Department of Anesthesiology. Members of the Division are integrated into or lead improvement projects in collaboration with other clinicians throughout the Cardiac Center.

In the past 2 years, the Division has revamped the education program for anesthesia fellows rotating on the Cardiac Anesthesia service. This expansion has been recognized by the fellows who have awarded the faculty teaching award to Cardiac Anesthesia faculty members each of the past 3 years.

The Division benefits from a highly skilled corps of CRNA’s who are dedicated to care of patients with CHD.

DIVISION OF CARDIAC CRITICAL CARE MEDICINE

CHOP, one of the first hospitals in the world to offer intensive care for children, is celebrating its 50th year of critical care pediatrics in 2017. Care of children with congenital or acquired heart disease were initially integrated with the care of all critically ill patients. Those patients with primary cardiac disease were first cohorted to a separate service in 1984. A separate cardiac intensive care unit (CICU) was then established in 1995 under the joint leadership of the Division of Critical Care Medicine, Cardiology and Cardiac Surgery. The Division of Cardiac Critical Care Medicine, uniquely a Division within both the Department of Pediatrics and the Department of Anesthesia and Critical Care Medicine, shares this long tradition of excellence in clinical care, innovation and education with the other Division that comprise the CHOP Cardiac Center is a separate Division of the CHOP Medical Staff since 2015. The Cardiac Intensive Care Unit at CHOP today has 26 beds and a recent average daily census of 23.

The eleven physician Division members all have primary credentials in Pediatrics and all have additional training and experience in cardiac critical care. All members have one or more other subspecialty credentials in related clinical disciplines including Cardiology, Critical Care Pediatrics, Neonatology and Anesthesiology. The division is responsible for directing the team care and moment-to-moment bedside management of the patients in the CICU, 24/7/365. In addition, the Division provides the physician leadership and partner to the Department of Nursing and the CHOP Administration for the daily CICU operations (including admission scheduling and discharge planning), the Harm Prevention/CQI initiatives and the regulatory oversight effort for the CICU. The Division is responsible for all physician and medical student education and training in the CICU. These programs include required clinical rotations for fellows (PGY-4-PGY-6) in Cardiology, Critical Care Pediatrics and Neonatology. The Division offers elective clinical training experiences for residents in Pediatrics, Adult Cardiology and Anesthesiology and medical students. Importantly, over a decade the Division has offered a specialty year training program in Cardiac Critical Care for “4th year” fellows (PGY-7). This program was one of the first available to offer this training and graduates of the CHOP fellowship include current members of the
Cardiac Nursing serves a comprehensive, complex cardiac population across the continuum of care. From a nursing perspective, the center is comprised of a CICU (26 beds), CCU (27 beds), CPRU (13 beds), Cardiac Cath Lab, Cardiac MRI, Cardiac OR’s (2 OR’s and a hybrid room). Advance practice providers play a key role in the care and management of the critically and chronically complex patients and families. Strengths of Cardiac Nursing include highly trained CT OR nursing staff, expert perfusionists with national recognition, Invested and committed clinical staff and leaders, high scores in Patient Satisfaction, top talent in Advanced Practice Providers (APN’s, PA’s), enhanced focus on Shared Governance and Professional Development.

**Nursing Education**

Nursing orientation utilizes independent learning modules, simulation, and testing. The Cardiac Center follows this process and has dedicated significant resources to support onboarding, and orientation plans. The Cardiac Center Simulation Program is led by a physician leader and nurse educator and includes 2 simulations educators and 2 simulation facilitators. The team has developed and written over 30 cardiac clinical cases. Using high fidelity simulation mannequins, we are able to provide in situ multi-disciplinary (nurse, fellow, resident, respiratory therapist etc.) clinical teaching scenarios with venue specific (CICU, cardiac care unit, cardiac preparation and recovery unit and cardiology outpatient clinic) learning objectives and teaching points. In addition, we have also developed fellow (anesthesiology, neonatology, critical care and cardiology) specific simulation scenarios for their respective teaching curriculums.

Our work in cardiac simulation has been recognized nationally and internationally. We were recently invited to speak about our simulation program at the University of Arizona Medical Institution, the University of Maryland Medical Institution and Nationwide Children’s Hospital in Columbus, Ohio.

Recently the Children’s Hospital of Philadelphia’s Cardiac Center has created an innovative collaboration with Kravis Children’s Hospital at Mount Sinai in New York. As a first step in this process, we have developed and implemented a monthly teaching curriculum of “Cardiac Case Studies Using Simulation” in their Cardiac ICU for fellows, nurses, physician assistants.

**PSYCHOSOCIAL SUPPORT**

Patient and family support in the Cardiac Center is provided by a comprehensive psychosocial team, including child life specialists, social workers, and psychologists. In addition to direct patient services, the Child Life, Social Work, and Psychology providers of the Cardiac Center have formed the Psychosocial Committee. This collaborative committee meets monthly to discuss strategies to continue growing the patient and family supports available in the Cardiac Center. Recent focus includes the initiation of weekly caregiver coffee hours with rotating topics of interest to connect families with resources, other families on the unit, and the psychosocial team; and a project to begin standardized psychosocial screening.

**CARDIAC CENTER PROGRAMS**

**The Cardiac Care Unit (CCU)**

The Cardiac Care Unit is a 27 bed Acute Care Unit with active telemetry monitoring. This intermediate level unit provides high level medical and post-surgical care for neonates, children and adults with a broad range of complex congenital cardiac disease and acquired cardiac illness. Patients are admitted to heart transplant/heart failure, electrophysiology, pulmonary artery hypertension, adult congenital heart disease and general medical/surgical services. Medical teams consist of attending level physicians, cardiology fellows and nurse practitioners, and PL2 residents. Cardiac education is provided for approximately 30 residents, and 6-7 1st year fellows per year, with additional visiting residents, medical students, and nurse practitioner students rotating on the unit throughout the year as well. A cardiology fellow and 1-2 front-line clinicians are in house overnight in addition to day-time full medical team coverage. Complexity includes patients immediately post-op from more simple operations (e.g. vascular ring division), with the majority of post-surgical patients transferring from Cardiac ICU as early as postop day 1 after complex cardiac surgical procedures; management includes pleural and pericardial drains, and central lines, stable patients with Ventricular Assist Devices in place receiving ongoing care, or in preparation for discharge. Higher acuity patients also cared for on the CCU include patients requiring non-invasive ventilation including CPAP (stable settings) and high flow-nasal cannula oxygen support. Continuous infusions of milrinone, low-dose dopamine, lidocaine and esmolol, are handled as well as administration of vasodilator therapy for pulmonary hypertension. All caregivers receive education as indicated,
including CPR, post-surgical care, medication administration (included subcutaneous injections and PAHTN home therapies) teaching for nasogastric and gastrostomy tube feeds.

Cardiac Catheterization/Interventional Cardiology
The Cardiac Catheterization Laboratories and Interventional Cardiology program provides transcatheter therapies and invasive diagnostics to patients with heart disease at the Children’s Hospital. The program components include: (1) Clinical Care; (2) Education; (3) Investigation; and (4) Quality Improvement. Invasive Electrophysiology (EPS) is also housed within the Catheterization Laboratories though EPS is a separate program. The catheterization laboratory is among the busiest in the nation, in calendar 2016 a total of 1430 procedures were performed (1266 of these were non-EPS). A majority of the procedures were interventional, i.e. for treatment rather than diagnosis. In fiscal year 2017 these included 109 device closure of cardiac defects, 172 endovascular stenting procedures, 29 transcatheter valves, 159 balloon angioplasties, 41 valvuloplasties, 62 embolizations, and 67 lymphatic embolization procedures. Innovation and the incorporation of new procedures is vital to the success of the interventional cardiology program. In recent years such innovations have included transcatheter valve therapies with an expanding range of devices and applications, complex stent therapy for vascular rerouting, and the development of what is arguably the world’s preeminent lymphatic intervention program by Drs. Yoav Dori and Max Itkin. The educational mission of the catheterization program includes training of categorical pediatric cardiology fellows, advanced training in interventional cardiology, and specialized training for practitioners from across the country and around the world. All categorical fellows spend several months over the course of 3 years learning hemodynamics and invasive cardiology. Each year through a competitive application process, one fellow is selected to train in interventional cardiology, our past trainees have achieved a number of important positions across the United States and around the world in academic cardiac catheterization programs. The catheterization program strives to continuously improve outcomes through a robust quality improvement effort. We participate in the NCDR IMPACT registry and the C3PO QI initiative. Among our ongoing QI projects are nationally recognized efforts in radiation dose reduction and reduction in vascular complications after arterial catheterization.

Electrophysiology
The pediatric and congenital electrophysiology (EP) service specializes in diagnosing and treating heart rhythm disorders including the most complex cases that require a high level of expertise from neonates to adults. With four electrophysiologists, nurse specialists and trained fellows, we are one of the largest electrophysiology programs in the country. Our Electrophysiology laboratory is equipped with state of the art 3D mapping and ablation equipment and our Hybrid Cardiac Catheterization laboratory is equipped with the latest equipment for performing complex device implantations and laser lead extractions. The Laser lead extraction program is one of the few pediatric programs in the entire nation that offers this type of expertise to the pediatric population. The Division’s invasive electrophysiologists are certified by the International Board of Heart Rhythm Examiners (IBHRE) for competency in Cardiac Devices as well as Pediatric Electrophysiology and perform approximately 250 EP procedures annually which include catheter ablations, diagnostic EP studies, Device implantation, DC cardioversions and provocative drug challenge tests. The program participates in the NCDR –ICD Registry. The Electrophysiologists provide 24/7 inpatient consultation to all the medical units of CHOP and also admit patients with heart rhythm disorders to the Electrophysiology service providing direct oversight of their management during hospital admissions. In addition, the Electrophysiology physicians oversee the telemetry rhythm monitoring of all patients admitted to the cardiology units and selected patients admitted to other intensive care units.

The invasive Electrophysiologists also provide clinical services to the Philadelphia Adult Congenital heart Disease program at The Hospital of the University of Pennsylvania. The Electrophysiology program evaluates a large number of outpatients with heart rhythm disorders and sees approximately 2500 patients annually. The EP clinics are located at CHOP main as well as in satellite areas (Bucks County, N.J., Exton, King of Prussia and Chadds Ford). The EP program conducts a special device clinic once a week at CHOP main for pacemaker and ICD evaluation and programming. In addition, the EP program runs a very large Device remote monitoring program evaluating approximately 1000 remote transmissions on an annual basis. The Non-invasive EP program is very large and includes approximately performing 10,000 ECGs, 3,000 ambulatory Holter monitors and 500 trans-telephonic monitors (TTM) & event recorders annually. The program offers patients the latest event recording technology which incorporates small size event recorders and cellular and wireless technology. All inpatient and ER ECGs are reported by the 4 EP physicians and all Holter monitors, TTM and event recordings are also reported by the 4 EP physicians. In addition, the EP physicians also report all Drug research ECGs performed by various investigators in different pediatric specialties at CHOP.
The Electrophysiology program provides 12-18 months additional specialized training to 4th year cardiology fellows in Pediatric Electrophysiology. Since 2008, 10 fellows have been trained with most trainees now practicing in academic programs.

**Echocardiography**

The Cardiac Echo Lab at CHOP is one of the largest pediatric echocardiography programs in the country, performing approximately 30,000 studies per year. Staffing in the Main Campus, Pennsylvania and New Jersey specialty care centers include 21 full-time sonographers, 2 part-time sonographers and 3 per-diem sonographers. There are 25 attending physicians across the enterprise that read echocardiograms in the main reading room as well as in satellite locations.

The Cardiac Echo Lab has four core divisions. The four arms represent areas within the lab that are crucial to providing high quality imaging and care as well as advance the academic presence of the Cardiac Echo Lab on a national level and becomes leaders in education of sonographers and fellows. The four cores are designated as 1) Research, 2) Education, 3) Advanced Modality Imaging, 4) Quality Improvement. The core areas have designated faculty who provide leadership and guidance for the activities within the core. A ‘Project Lead Sonographer’ role was also implemented to provide a career pathway for senior sonographers to advance their skills and participate, assist and support leadership in the completion of high-level projects for all of the cores. The echo lab is currently revamping protocols for common CHD lesions, application of newer imaging modalities such as 3D echo and strain imaging and releasing new educational programs for sonographers and fellows with plan to release first regional echo meeting in 2018. A number of changes and ongoing efforts to increase utilization of intra-op imaging. We have released a new pre-op TEE program that is currently increasing application and now releasing an epicardial imaging program all in an effort to increased identification of important residual defects in the OR. The echo lab Quality Core has focused efforts on building infrastructure to monitor quality related activities including discrepancies between echo and other areas (MRI, cath and surgery) and oversee multiple quality related echo projects. QI meetings occur every 8 weeks to review protocols and cases. Currently there are 5 echo related QI projects underway including projects related to resource utilization and standardization of imaging.

**Cardiac MRI**

The Cardiac Magnetic Resonance (CMR) program at CHOP is a state-of-the-art nationally and internationally recognized program which is a beta test site for new hardware, software and sequences for Siemens Medical Systems. One thousand two hundred and fifty three (1,253) CMRs in children and adults with congenital heart disease were performed in fiscal 2016 and has been on an upward trajectory since 2000 (see graph below). The program has performed CMRs successfully on neonates as small as 1.2 kg, has performed functional and anatomic fetal CMR and has the capability to handle all age groups and sizes through and including adulthood. Capabilities include state-of-the-art hardware and software such as parallel imaging, high performance gradients, “real time” MRI, coronary imaging, steady state free precession, HASTE and FLASH imaging (both static and dynamic), velocity mapping (both 1 and 3-plane) utilizing parallel imaging as well as “real time” velocity mapping, adenosine perfusion imaging, viability, static and time-resolved gadolinium enhanced imaging, exercise CMR and multiple software packages for image analysis and 3-dimensional reconstruction. Image analysis software includes EFLiM (Merge Inc.), ARGUS (Siemens Medical Solutions), HARP for myocardial tagging (Diagnosoft), GT Flow for 4-dimensional flow imaging (GyroTools, Inc.) and CVI42 (Circle Cardiovascular) among other software. The cardiac MRI program at CHOP has brought online 14 new clinical MRI techniques over the past 17 years since 2001 (see graphic below). The group also manages the 3D printing effort at the hospital. There is a 1.5 Tesla Avanto-FIT MRI scanner (MR6) dedicated to use solely for cardiac and lymphatic applications but all MRIs on cardiac patients are also performed on that scanner; this facility is physically located next to the catheterization laboratory with a door connecting both rooms allowing for XMR (fusion of CMR and catheterization) capabilities. The coils and gradients utilized in these magnets are one of the highest performance pieces of hardware available today from any manufacturer. All scanners are networked and linked to computers securely. Two specialized workrooms across the hall from the dedicated cardiac scanner have Leonardo and other computer workstations for analysis. An MRI compatible ergometer is stored in the cardiac scanner equipment room. The CMR section of the division of Cardiology maintains a CardioFlow 5000 MR Flow Pump (Shelley Medical, Ontario, Canada) which can be used in the MRI scanner to hook to flow phantoms and 3D models which can mimic all wave forms and can pump blood from 0.1 to 10 liters/minute. The 3-dimensional printing laboratory is resident on the 9th floor of the Northwest Tower with Object Connex 500 (Stratsys, Eden Prairie, MN) and a dedicated high end Dell computer workstation controlling the printing. Mimics software (Materialise, Plymouth MI) is resident on this computer with a floating license for all CMR cardiologists and is
used to create .stl files which can translate medical images into 3-dimensional images the 3D printer can read. A 3D printing technician has been hired by CHOP to run the facility. CHOP and in specific, Cardiology, also has an agreement with the Mechanical Engineering department at the University of Pennsylvania who also run a large 3D printing laboratory with 4 large scale 3D printers of various types to share resources.

**Cardiac Exercise Physiology**

The Cardiovascular Exercise Physiology Laboratory within the Cardiac Center is dedicated to providing the highest level of cardiovascular health to our patients. The goal achieved, in collaboration with other Divisions and Departments within the Children’s Hospital of Philadelphia through:

1. Excellence in the care of children, adolescents, and young adults with congenital and acquired pediatric disease.
2. Innovation in research to identify causes and develops techniques to prevent, diagnose, and treat pediatric disease.
3. Quality in the education of physicians, scientists, and other professionals in the field of pediatric exercise physiology.
4. Respect in the education and emotional support of our patients and their families.

Within the Division of Cardiology, the Cardiovascular Exercise Physiology program is dedicated to providing the highest level of service to our patients, families, and Divisions and Departments within the Children’s Hospital of Philadelphia. As a full service diagnostic laboratory with almost 2300 diagnostic studies performed annually, our primary function is to provide diagnostic testing and rehabilitative services with the highest level of education and technology available to patients with congenital or acquired pediatric disease who require expertise in the area of clinical exercise physiology. The Cardiovascular Exercise Physiology Laboratory is located on the 3rd floor of the Main Hospital. This > 2000 square foot state of the art laboratory includes 3 diagnostic testing stations equipped with technology designed to measure electrocardiography, blood pressure, oxygen saturation, oxygen consumption and carbon dioxide production, and resting and exercise pulmonary function.

**The Fetal Heart Program**

The Fetal Heart Program (FHP) is a dedicated service focused on prenatal diagnosis and management of fetal and congenital cardiovascular conditions including congenital heart malformations, arrhythmias, extra-cardiac malformations affecting the heart, twin-twin transfusion syndrome, maternal disease affecting fetal well-being and a host of other conditions. The FHP is the entry point for nearly all of our patients with congenital heart disease who then continue forward with care throughout the rest of the Cardiac Center services. The FHP provides state-of-the-art fetal imaging through echocardiography, board certified pediatric cardiologist interpretation of studies with counseling and management planning for all prenatal cardiovascular conditions. There are 3 dedicated nurse coordinators who offer educational and counseling services shepherding families through prenatal care. There is a dedicated social worker, who evaluates and counsels each family. The FHP works in close collaboration with the CHOP Center for Fetal Diagnosis and Treatment (CFDT) who offer obstetrical and delivery services for our fetal heart families through delivery at the Garbose Special Delivery Unit at CHOP. Fetal cardiovascular services are offered as intraoperative fetal imaging during open fetal surgery and in conjunction with CFDT for complex fetal anomalies.

The Fetal Heart Program at CHOP is a model for prenatal cardiovascular care around the United States. It is one of the largest such programs in North America with over 3,000 fetal echocardiograms performed annually and with over 375 fetuses with important cardiovascular disease managed in FY 2017. The program sees pregnant women and families not only from the region but referred or self-referred from throughout country.

**Center for Lymphatic Imaging and Interventions**

The Center for Lymphatic imaging and Interventions at The Children’s Hospital of Philadelphia in collaboration with the Hospital of the University of Pennsylvania - Department of Radiology provides highly specialized care for children and adults with lymphatic leaks and lymphatic flow disorders. These chronic and often debilitating conditions can be difficult to diagnose and treat. Experts in the Lymphatic center are developing advanced imaging, interventional, and surgical technologies such as dynamic contrast MR lymphangiography (DCMRL), liver lymphatic embolization, and surgical LVA. This allows our team to more accurately identify and manage lymphatic flow disorders using a variety of minimally invasive and surgical treatment options. These efforts have led to the development of several key new novel therapies for patients with protein losing enteropathy, plastic bronchitis, chylothorax, ascites, and lymphedema. The center is aimed at treating patients of all age groups and is working closely with clinicians from many departments to discover and develop new treatments for previously
unknown diseases in which the lymphatic system plays a key role. The Center is considered a “Frontier Program” at the CHOP – and has been awarded substantial funding to support its clinical and research efforts. Physicians in the Lymphatic Center performed 178 imaging and intervention procedures in the CHOP Cardiac Cath Labs (including uniquely referred patients, existing inpatients referred to the program, and some repeat procedures) and saw 115 patients referred specifically to the center from 32 different states and 3 other countries. Volume trends continue to be strong in FY 18 – with more patients coming from international referrals.

**Outpatient Clinical Cardiology**

The Outpatient Cardiology Section of the Division of Cardiology is a huge enterprise. It encompasses outpatient care areas at multiple locations in PA (Main Campus, Exton, Brandywine Valley, Bucks County/Chalfont, King of Prussia, Abington Hospital, Grandview Hospital, Lehigh Valley, Lancaster General Hospital), and New Jersey (Voorhees/Virtua, Princeton, Mays Landing (So. Jersey shore) and St. Peter’s University Hospital). Annually, all of these locations combined provide outpatient cardiac services to more than 30,000 pediatric, adolescent and adult patients with congenital or acquired heart disease or cardiac rhythm disturbances. In addition, pediatric cardiology consultant services for more than a dozen community hospitals in PA and NJ are organized by the Outpatient Cardiology Section of the Division of Cardiology. The program supports local CHOP NICUs and nurseries, as well as non-CHOP referring hospitals. The Outpatient Cardiology Section has multiple subsections. In addition to general pediatric cardiology, there are specialized clinics that deal with specific areas that benefit from expertise of unique providers. These include outpatient clinics for Congestive Heart Failure and Transplant, Electrophysiology and Pacing, Pulmonary Hypertension, Hyperlipidemia Clinic, Coronary Anomaly clinic, Adult Congenital clinic, and Cardiogenetic/Cardiomyopathy /Metabolic Disease clinics. The Outpatient Cardiology Section is an active participant in medical education. Pediatric cardiology fellows are required to participate in a weekly outpatient cardiology continuity clinic, to learn how to diagnose and manage common and uncommon problems in pediatric cardiology. Additionally, they learn how to build relationships and see how their patients change over time. Others also spend time in the clinics, including rotating medical students, and pediatric residents (both internal and external to CHOP). The cardiology faculty recognizes this educational responsibility to be vital to our overall goal. The Outpatient Cardiology Operations committee is committed to making sure that the ambulatory clinics provide high quality, compassionate and efficient care. Over the years the program has led the department in using patient tracking and time studies to optimize outpatient flow in our clinics. This has led to improved patient and family satisfaction, and also contributes to a better provider experience. The program continually works with the Department of Pediatrics on improving patient access and communication with referring physicians.

**Heart Failure/VAD/Transplant**

The Heart Failure and Transplantation Program at The Children’s Hospital of Philadelphia is a comprehensive program serving infants, children, adolescents and in select cases, young adults with cardiomyopathies and end-stage heart failure. The program consists of three full-time faculty in cardiology and three full-time faculty in cardiothoracic surgery. The program also has extensive support from two full-time and two part-time nurse practitioners, as well as a nurse coordinator.

The goal of the program is to provide expert evaluation and care of patients with known or suspected cardiomyopathy, whether it be a primary cardiomyopathy or a cardiomyopathy related to another disease process, such as congenital heart disease. Our program provides care in the outpatient setting to ambulatory patients, but also provides care to patients with advanced heart failure, including mechanical circulatory support, ventricular assist devices, and heart transplantation. The program maintains its own inpatient service in the Cardiac Care Unit, and provides consultative services in the Cardiac Intensive Care Unit as well as other inpatient units in the hospital. The program has close collaborative efforts with other disciplines, including oncology (Cancer Survivorship Clinic), neurology (Muscular Dystrophy Program); genetics (Cardiac Genetics Clinic); adult heart failure (CHOP-Penn Familial Cardiomyopathy Program); the Single Ventricle Survivorship Program; and the Friedreich Ataxia Center of Excellence, to name a few. A major thrust of the program is the advancement of the use of mechanical circulatory support, particularly ventricular assist devices, for children with end-stage heart failure. Our program has been particularly interested in the use of continuous-flow devices (HeartWare HVAD) in small children and patients with single ventricle physiology.

**Infant Single Ventricle Monitoring Program**

The Infant Single Ventricle Monitoring Program (ISVMP) was initiated at the Children’s Hospital of Philadelphia in December 2010 with the purpose of optimizing care and decreasing mortality between Stage I (neonatal) and Stage II palliation in infants with single ventricle heart disease. The program was established to augment not
replace care given to these tenuous infants by their primary cardiologists. As such, each infant is co-managed by the ISVMP team and their own primary cardiologist (either at CHOP or close to home) throughout the interstage period. Initial inclusion criteria was single ventricle heart disease requiring a palliation which included an aortopulmonary shunt, RV to pulmonary artery shunt or hybrid procedure. In 2014 at the request of the division, the inclusion criteria was broadened to include all infants with an aortopulmonary shunt even those with an anticipated two-ventricle repair. The program nurse practitioner (NP) is the core of the program, following these patients closely through their initial admission to Stage II palliation. She is supported by five cardiologists who rotate on a weekly basis and an outpatient nutritionist. Families are sent home with a scale, pulse oximeter machine and education regarding warning signs/symptoms in their infant (“red flags”). Infants are examined weekly by their pediatrician alternating with their cardiologist where a focused echocardiogram is done. The NP calls the family at least weekly to assess the status of the infant, answer questions and documents vital signs, nutritional intake and growth parameters. Data is displayed in a QlikView application which the NP and program cardiologist meet to review on each patient. The NP subsequently communicates back and forth with the family, cardiologist and pediatrician arranging visits and or re-admissions as necessary. We worked with the office of Clinical Quality Improvement to establish two clinical pathways for inpatient - http://www.chop.edu/clinical-pathway/single-ventricle-fetus-or-newborn-clinical-pathway and outpatients http://www.chop.edu/clinical-pathway/single-ventricle-monitoring-program-infant-clinical-pathway respectively. The team is working with the Mayo Clinic and will soon implement an iPhone application to streamline clinical data transfer from the families. To date, 385 infants have been enrolled in the program, giving a yearly volume of about 30 infants with HLHS and 20 infants with other shunt-dependent anatomy. Twenty-five to 30 infants are followed in the program at any given time. We are very proud of recent analysis of our program that has shown a decrease in total interstage mortality from 13% (historical controls) to 5.4%; 14% to 4.8% for HLHS alone. The ISVMP is a key player in the National Pediatric Quality Improvement Collaborative (NPC-QIC) and in collaboration this year we have extended the time of monitoring of fragile HLHS infants to include the time of birth through the first year of life.

**Single Ventricle Survivorship Program**

The Single Ventricle Survivorship Program (SVSP) at CHOP is a unique multidisciplinary service focused on the care and management of the child, adolescent and young adult who is surviving with a Fontan circulation. While surgery has allowed for patients to survive, it has become clear that many of these individuals will never achieve a normal quality or duration of life often due to progressive debilitating complications. The SVSP therefore provides comprehensive services focusing on the end-organ consequences and complications of the Fontan circulation, both from an acute care perspective as well as early surveillance and preventative strategies for patients deemed to be well. Liver fibrosis, poor growth and development, altered bone health, protein losing enteropathy, plastic bronchitis, hemoptysis and a host of other complications are cared for by an experienced team of healthcare providers. A monthly multidisciplinary clinic is held in the Cardiology Outpatient facility as well as regular weekly clinic visits and in-patient consultation for active management and evaluation of post-Fontan complications. Surveillance strategies have been developed which includes blood assessments, abdominal ultrasound, bone densitometry scans, and liver elastography, in addition to conventional cardiovascular assessments of echocardiography, EKG and exercise stress testing. The SVSP has established the recommendation for invasive comprehensive evaluation of all patients who are > 10 years out from Fontan operation and since initiation of the Program has shepherded over 150 patients through cardiac MRI, cardiac catheterization and liver biopsy evaluation. The SVSP is the first in the nation to develop this type of practice and is the clinical model that many other institutions have now mimicked. The SVS Program incorporates clinical expertise from a collaborative group of practitioners with facility and expertise in understanding the unique aspects of the Fontan circulation, including a dedicated hepatologist gastroenterologist (Elizabeth Rand, MD), endocrinologist (Edna Mancilla, MD), immunologist (Jen Heimall, MD) who make up the core of the multidisciplinary group. Additional services include pulmonology and nephrology. Through the cohorting and concentration of patients has come group learning and expertise in understanding the fundamental limitations and frailty of the Fontan circulation. To date since inception in 2011 the SVSP has evaluated over 400 individual patients, many of whom have never been cared for at CHOP and have come from all parts of the country specifically for the unique multidisciplinary services and expertise the Program offers.

**Pulmonary Hypertension**

Initially developed in 1995, the program has continued to grow exponentially, including international consultations, and referrals from the eastern seaboard, mid-west and southern states, as well as inpatient consultations from the Pediatric and Neonatal ICUs, Lung Transplantation Program, Hematology, General Surgery, Oncology, Thoracic Insufficiency Center and Rheumatology. Currently, the number of patients followed,
the number of inpatient days, and the number of patients on PH pharmaceuticals arguably make this program the largest and most experienced clinical pediatric PH program in North America. PH patients populate almost all inpatient units outside of the Cardiac Center. The addition of more non-Cardiac Center units has required continual training and hands on care from the team. This effort has resulted in freeing up Cardiac Center beds during high census periods. We are in the process of identifying other units, in addition to the CCU, CICU, NICU, PCU and PICU for our IV and subcutaneous prostacyclin patients. Once this unit is identified appropriate training and staff support will start to ensure an important additional inpatient venue for our patients. All available PH therapeutic modalities are in use. It is noted that there are no FDA approved therapies for PH in patients under 18 years of age. Therefore all of our current treatment plans are tailored to recent national and international guidelines in consultation with Pharmacy and the Therapeutics Committee. We continue to work with nursing and pharmacy to improve and refine these protocols and formulary entries for these complex therapeutic scenarios.

Since 2004 the program has seen 1500 new inpatients in consultation and outpatient follow up. This is approximately 10 times the volume of other nationally recognized Pediatric PH Programs. Of the program’s patients - 104 have been transferred to other facilities, 362 have died and 1034 are actively being followed within our program. The classification of these patients is roughly 10% IPAH or HPAH, 40 % associated with cardiac disease and 50 % associated with lung hypoplasia or chronic lung disease. The population is quite young reflecting the influx of neonatal lung disease. The distribution of current age for the population as of 07/01/2017 is 104 < 1 year; 484 between 1-5 years; 355 between 5-10 years; 113 between 10-15 years and only 28 > 15 years old. We have successfully transitioned all except 3 of our >18 year old patients to the newly re-organized HUP PH program or other regional adult PH centers. On a daily basis, the program averages > 50 patients on the inpatient list, one half of which are chronically treated with PH-specific therapies including an average of 10 inpatients on parenteral prostacyclin. The increase in activity of the inpatient service from 28 in 2012 is dramatic and has occurred on both the PICU and the NICU. Furthermore, the new patient discharges per year were 197 in 2016 and 300 in the first 6 months of 2017. The actual number of admissions and consultations are higher as we do not report repeat admissions. The clinical team meets twice a week. The team reviews complex patients and CQI data. process. The team tracks the following information with regards to CQI: 1) line infections verses number of patients with lines, 2) missed communications resulting in drug mistakes and/or missed follow-up, 3) patient mortalities (inpatient and outpatient). Education activities include monthly lectures to pediatric resident house staff, multiple nursing education sessions, lectures to PICU fellows and PICU/NICU nursing personnel, observerships including training of 2 attending cardiologists, 2 pulmonary fellows and one critical care intensivist fellow.

**Coronary Anomaly Management Program (C.A.M.P.)**

The Coronary Anomaly Management Program (CAMP) is the only program in the mid-Atlantic region that provides comprehensive care and monitoring for children with coronary artery anomalies. Anomalous aortic origin of a coronary artery (AAOCA) is the most common coronary artery anomaly and it occurs when one or both coronary arteries arise from the wrong location on the aorta. The anomalous coronary can take different courses and, depending on the course, this may increase the patient’s risk of sudden cardiac death, notably during or just after exercise. AAOCA is commonly diagnosed in young people who are asymptomatic and an echocardiogram is done for another reason. Some children may have symptoms, most commonly: chest pain, palpitations, dizziness, and/or syncope with exercise. Once diagnosed, the decision regarding treatment, notably surgery versus no surgery, can be challenging, notably for the young patients without symptoms.

The goals of the program include: managing our patients with the most up-to-date evidence-based treatment; educating patients, families, and health care providers about the diagnosis and what it means to the patient; identify other family members who need to be screened by echocardiography; discuss the importance of remaining active, no smoking, and checking a lipid panel; and discuss with and enroll patients and their families in any current research projects. The program sees patients ages 0-18 years at CHOP and > 18 years seen with adult congenital heart disease program at HUP. In addition, the program sees patients with suspected or confirmed diagnosis of congenital AAOCA and have also seen a few patients with coronary issues related to Kawasaki Disease and complications after the arterial switch operation for transposition of the great arteries.

**Cardiac Anticoagulation and Thrombosis Program**

The Cardiac Anticoagulation and Thrombosis Program was developed in 2013 as a Department of Pediatrics Chair’s Initiative to prevent, diagnose and optimally treat all patients with thrombosis or the potential for thrombosis in the Cardiac Center of the Children’s Hospital of Philadelphia. The Cardiac Thrombosis NP coordinates the program and is staffed by two faculty who share attending responsibilities. Formal consults are
done on all inpatients with thrombosis or the need for anticoagulation (including patients with prosthetic heart valves and ventricular assist devices) in the Cardiac Center. Subsequent follow-up is coordinated with the managing inpatient teams. The Cardiac Anticoagulation Team coordinates a weekly conference where all inpatients are discussed with the clinical pharmacy specialist and the managing inpatient teams. The PharmD is involved as well in the daily management of challenging patients. The Cardiac Anticoagulation Team is instrumental in patient and family teaching and coordinates outpatient follow-up for all patients prior to discharge. The Cardiac Thrombosis Team performs approximately 2-3 new consults and 8-10 follow-up visits per week with EPIC documentation. To date, the team has consulted on 567 inpatients in the Cardiac Center. In conjunction with Hematology and Pharmacy, formal CHOP Clinical Practice Guidelines for the major anticoagulant and thrombolytic medications and are available on the CHOP internet site. In addition, a formal clinical pathway has been developed by the program for the Management of Acute Catheter-Related Venous Thromboembolism in the Cardiac Center. To the best of our knowledge, this is the only comprehensive inpatient program in the country with joint involvement by Cardiology, Hematology and Clinical Pharmacy. In addition, the clinicians follow approximately 60 outpatients on enoxaparin or warfarin in the outpatient component of the program.

**Lipid Heart Program**

The Lipid Heart Clinic at The Children’s Hospital of Philadelphia evaluates children and adolescents who have elevated or abnormal levels of their blood lipids, which may place them at risk for premature heart disease. The team includes physicians from the Divisions of Cardiology, Endocrinology, and Gastroenterology, Hepatology, and Nutrition, and registered dietitians. In the past 2 years, the program expanded to Voorhees, NJ and Lancaster, PA offices. During the clinic visit, a detailed personal and family history is taken, with a special focus on dietary and physical activity habits; perform a physical examination; review the lipid and other laboratory values with the family; and a treatment plan is developed for the lipids is discussed. The team helps to support our patients and their families with making healthy lifestyle changes, giving customized dietary recommendations and discussing exercise routines. In some cases, medications are recommended to begin to reduce the child’s risk for premature atherosclerosis. Our physicians are also committed to education; we often have medical students, residents and fellows rotating with us. Talks are also given around the region regarding dyslipidemia during childhood.

**Hypertension and Vascular Evaluation (H.A.V.E.) Program**

Pediatric systemic hypertension is a growing problem but continues to be underdiagnosed and undertreated. The increase in prevalence parallels recognition of other cardiovascular risk factors such as obesity in children. Many of the chronic medical conditions managed at The Children’s Hospital of Philadelphia (CHOP) are associated with hypertension including solid organ transplant, coarctation of the aorta, renal artery stenosis, diabetes, lupus and others. Patients with concern for high blood pressure would either be referred to cardiology or nephrology without standard protocols for evaluation and management.

In 2011, the divisions of Cardiology and Nephrology at CHOP developed a comprehensive outpatient hypertension (HTN) program, The Hypertension and Vascular Evaluation (HAVE) Program to 1) screen children at risk for HTN, 2) assess cardiovascular health status, and 3) optimize medical management. The HAVE Program enables patients to have a comprehensive, collaborative assessment that combines expertise from Cardiology and Nephrology. During a comprehensive outpatient clinic evaluation, patients are seen both by a cardiologist and nephrologist. Testing is tailored to the patient’s needs and can include lab work/urinalysis, ambulatory blood pressure monitor, ECG, echocardiogram, and vascular testing to assess cardiovascular risk (carotid intima-media thickness, pulse wave velocity in the aorta). Our program is an added layer of care and recommendations and further evaluation are made with close collaboration with the referring team. Follow-up visits may be required to monitor blood pressure and to follow-up any cardiovascular changes on the initial clinic evaluation.

Early recognition and treatment of hypertension can improve cardiovascular status unto adulthood. Creating a cohort of these patients has stimulated a multidisciplinary approach to the diagnostic evaluation and will lead to evidence-based management guidelines to optimize long term outcomes in this growing patient population.

**Cardiac Kids Developmental Follow Up Program**

The Cardiac Kids Developmental Follow-up Program was created as a resource for children with congenital heart disease. This program creates an additional layer of screening for our patients to help ensure that differences in development are identified early. The program screens infants and children at multiple touch points throughout early childhood and we are available to continue to see children through the school age years on an as-needed basis. The program follows the basic structure outlined by the American Heart Association Scientific
Statement published in 2012, which was based on the recognition that children with congenital heart disease have multiple risk factors for subtle cognitive differences including delayed brain maturation in utero, exposure to anesthetics and exposure to cardiopulmonary bypass. Our belief is that early identification of altered development can help ensure that families have access to the resources needed to help ensure the best possible outcome.

**Philadelphia Adult Congenital Heart Center**

The Philadelphia Adult Congenital Heart Center is comprised of a multidisciplinary team of practitioners that provide inpatient and outpatient care to adults born with congenital heart disease while serving as a bridge between two world-class hospitals. We are a joint program between the Children’s Hospital of Philadelphia (CHOP) and Penn Medicine. One of approximately one hundred such programs in the United States, the multidisciplinary team of the Philadelphia Adult Congenital Heart Center includes an array of specialists from both institutions experienced in the care of adults with congenital heart disease. These include cardiovascular surgeons, cardiac anesthesiologists, cardia specialists in catheterization, electrophysiology, non-invasive imaging, and heart failure/transplantation as well as genetics and reproductive services working together to provide comprehensive longitudinal care to adult survivors of pediatric heart disease.

The adult congenital heart disease clinical team consists of 3 physicians- all of whom with adult congenital heart disease specialty training- as well as 2 congenital heart surgeons, 2 Nurse Practitioners, and 1 Registered Nurse. One of our top priorities is to ensure a smooth transition for pediatric patients at CHOP who enter into adult cardiac care and ensure that patients and families have resources, education, and support that is age-appropriate.

**Postural Orthostatic Tachycardia Syndrome (POTS) Program**

The POTS Program at CHOP is a referral program in which patients with concern for postural orthostatic tachycardia syndrome as well as severe, uncontrollable dizziness with or without syncope, dysautonomia (non-POTS), and inappropriate sinus tachycardia are evaluated, diagnosed, and treated. Patients are managed, as appropriate, with a combination of non-pharmacologic and pharmacologic therapies, to improve initial functionality, plus an exercise protocol, to improve muscular venous pump function as well as long-term autonomic function.

Future plans include: the addition of a full-time nurse who would perform program coordination, telephone and e-mail triage, POTS database curation, and research based on the POTS database, and the addition of a dedicated full-time psychologist who would provide counseling for management of chronic illness issues plus assist with management of co-morbid psychological and psychiatric disorders.

**Duct Busters**

The Cardiac Center offers on-site PDA ligations at NICUs of the institutions that refer cardiac patients to our program. The Cardiac Center team travels to 16 NICUs eliminating the need for small, fragile premature babies to travel to CHOP. The team provides both the multidisciplinary team (surgery, anesthesia and CT OR nursing) and all the equipment needed to perform the surgery. The host NICU provides the patient and the blood for the procedure. The team provides the service within 24 hours of the request during the work week. In addition to providing an invaluable service for patients and their families this program enables Cardiac Center practitioners the opportunity to interface with and cultivate a relationship with our referring cardiologists and neonatologists. Since the inception of the program, the team has done more than 700 off-site ligations with patients as small as 400 grams with no mortality.

**Cardiac Center Quality Improvement (CCQI) Program**

While the Cardiac Center is “Center of Excellence, there have been important efforts to continue to optimize the quality of care in the Cardiac Center at CHOP. In the Spring of 2016, the Cardiac Center Executive Committee created the Cardiac Center Quality Improvement (CCQI) Program. The Medical Director and Governance Committee were selected and the Office of Clinical Quality Improvement hired a dedicated improvement advisor and data analyst to support QI projects in the Cardiac Center. In August 2017, a second improvement advisor and data analyst position was approved and they are now being recruited. The CCQI Governance Committee instituted formal, monthly meetings starting the summer of 2016. The goals of this committee is as follows:

- To develop the infrastructure whereby our colleagues are able to turn their ideas for improvement work into formal projects with the guidance and support of our dedicated improvement team.
- Liaison with our individual divisions/sections and stimulate discussion around QI, with the goals of minimizing unnecessary variation and optimizing outcomes.
• Review request for proposals (RFPs) and select QI projects that are priorities for our center and have the potential to be effective
• Ensure optimal use of information provided by EPIC/CDW and Cardiac Center registries to facilitate data collection and analysis for QI
• Work with our improvement team to track project progress, foster commitment and hold colleagues accountable for their work
• To act as an advisory board for hospital-wide initiatives that address quality, safety/harm prevention and value in the Cardiac Center

The improvement team is supporting or will be supporting a total of 10 projects. Approximately 15 additional projects have had some form of formal support in the past, had consultation from our improvement team or have never had formal support. In the next 6 months, the CCQI Governance Committee will meet with individual sections/divisions in the Cardiac Center to determine future needs for improvement work in order to maximize resource utilization for this work. We will be developing a QI education program for fellows. We continue to conduct Cardiac Center-wide QI updates on ongoing projects and use Redcap and Qlikview to track improvement work so that the efforts are sustained over time.

**Cardiac Center Clinical Research Core (Director, Andrew Glatz, MD, MSCE)**

The Cardiac Center Clinical Research Core was formed in 2016. Its mission is to facilitate, support, and encourage all aspects of clinical research conducted within the Cardiac Center. It provides numerous services including study design consultation, statistical consultation and services, automated data extraction, IRB protocol review, grant application review, Cardiac Center internal grant application review, abstract/manuscript/poster/presentation review. Services are available on demand as time allows. In the event that prioritization of services is needed, preferences are given based on the following factors:

• Grant funding
• Potential to develop into a funded project
• Potential to spawn additional studies
• Assessment of scientific quality by Advisory Committee
• Past productivity

Accountability when services are provided is expected. Supported investigators will be asked to provide accounting (abstracts, manuscripts, grants submitted/awarded, etc.) of studies that receive support.

The Cardiac Center Research Core partners with the CHOP Center for Pediatric Clinical Effectiveness (CPCE) and the Healthcare Analytics Unit to access their expansive research faculty and resources. Since its inception in the fall of 2016, over 50 requests for services have been received and all but 2 have been supported.

**CHOP Research Institute Research Core Facilities**

This training program also has access to the vast array of highly developed research cores at CHOP, and these are described as follows:

**Aquatic Zebrafish Core:** The Aquatic Zebrafish Core provides services that include the small vertebrate zebrafish as models for human disease and to study gene function. The standout features of this model are a very easy accessibility to genetic manipulations (CRISPR/Cas9, morpholino gene knock down, mutant libraries, transgenesis) and the optical clarity and fast development of its larvae. They design, perform and analyze whole assays such as the characterization of a disease model and train researchers (technicians, students, post-doks) to become experts in using zebrafish.

**Bioanalytical Core:** The Bioanalytical Core specializes in developing and validating robust liquid chromatography/tandem mass spectrometry methods for the analysis of natural products, drugs, and metabolites in various biological samples (blood, dried blood spots, plasma, urine, and tissue). With extensive experience in method development and validation, the core performs method validations, partial validations, cross-matrix validations, or combinations required to meet project needs. Validation studies are performed in accordance with the US Food and Drug Administration Guidance for Industry, Bioanalytical Method Validation. The core has developed assays for investigational and marketed drugs used for pain, oncology, cardiology, and infectious diseases. These assays are typically used to support pediatric drug discovery and development.

**Biorepository Core:** The Biorepository Core collects and organizes biospecimens from investigators across the Research Institute. With a capacity for approximately 7 million samples, the facility is designed to house all of the biospecimens available at CHOP, avoiding specimen duplication, preserving precious biomaterials, and
Animal Imaging Facility is a state-of-the-art facility that provides broad access to data and materials. Initial sample collection focuses on DNA samples, but the facility can also safely store fluids, RNA, tissue samples, and a number of other biospecimens.

**Biostatistics and Data Management Core (BDMC):** The BDMC supports the biostatistical and data management needs from virtually all subspecialties of pediatric medicine and supports studies ranging from narrowly defined basic science projects to large, multi-site clinical trials. The BDMC supports more than 25 funded studies and collaborates with investigators on numerous grant applications each year. It is staffed by a full-time Scientific Director, a Deputy Director, biostatistics and data management/information technology managers, and 15 additional staff members representing the disciplines of biostatistics, data management, and information technology. The BDMC’s Biostatistics subcore provides consultative and analytic support services to investigators interested in basic, pre-clinical, clinical, and epidemiological pediatric studies. The Data Management/Information Technology (DM/IT) subcore provides a selection of services ranging from consultation through full-service data management.

**Clinical Research Support Office (CRSO):** The CRSO assists in the start-up, execution, and completion of clinical research projects, in compliance with local and federal requirements. The office maintains a staff of well-trained study coordinators and project managers who can be assigned to support any type of clinical research study at CHOP. The CRSO Navigator is available to assist/guide investigators with any questions that arise during the design, start up, and execution of their clinical studies. The CRSO is also available to assist investigators with budget preparation, IRB submissions, and IND and IDE applications to the Food and Drug Administration. The CRSO maintains a highly-trained staff with expertise on good clinical practices of clinical research, which ensures that study teams comply with all relevant regulatory requirements.

**Flow Cytometry Core:** This core provides access to flow cytometry equipment and analysis software for trained personnel from individual research labs on a fee-for-service basis. The core assists users in the design of experimental protocols that require various flow cytometric methods. The laboratory is capable of both sample preparation and analyses in support of individual research efforts and offers specialized services such as training and multi-parametric cell sorting.

**Healthcare Analytics Unit (HAU) Core:** A service unit of two centers at CHOP (CPCE and PolicyLab), the HAU serves as a resource for investigators who want to use administrative or other existing data to answer research questions; offers programmer/analysts services to pull, clean, manage, model, and analyze data; and provides the expertise of the center's faculty members with their advanced training in clinical epidemiology and public health. The unit supports and provides access to several databases.

**High-throughput Sequencing Core:** The High-Throughput Sequencing (HTS) Core at CHOP and the Beijing Genomics Institute have formed a collaborative genome center called BGI@CHOP. Together, these elements for the HTS Core offer increased capacity, expertise and analytical resources for conducting next-generation sequencing studies. The HTS Core provides automated library construction and high-quality, high-throughput sequencing services for whole genome, whole exome, RNA-SEQ, and ChIP-SEQ. BGI@CHOP Exome workflow passed CAP inspection in April 2014.

**Human Pluripotent Stem Cell Core:** The Stem Cell Core provides expertise and quality-control reagents for the culture and differentiation of human embryonic stem cells (ESCs) and human induced pluripotent stem cells (iPSCs) for the CHOP and Penn communities. The facility maintains five of the new NIH-approved human ESC lines and several human iPSC lines.

**Metabolomics Core:** The Metabolomic Core provides investigators with a resource that facilitates the analysis of major metabolic pathways in humans, animals, and *in vitro* systems. The analytical repertoire includes the measurement – both *in vivo* and *in vitro* – of flux through major pathways of intermediary metabolism, including glycolysis, the tricarboxylic acid cycle, the oxidation of fatty acids and amino acids, the urea cycle and protein synthesis and degradation; determination of *in vivo* metabolic rate in freely moving organisms; and determination of selected drugs and/or drug metabolites with triple-stage quadruple mass spectrometry.

**Microbiome:** The CHOP Microbiome Center was established in 2015 within the PennCHOP Microbiome Program to meet the growing needs of the Penn and CHOP communities in the field of microbiome research. The Program’s mission is to develop microbiome-based strategies that generate biomarkers or therapeutics to improve health and treat disease.

**NMR/Microimaging Services:** The Small Animal Imaging Facility is a state-of-the-art lab that satisfies investigators' imaging needs in a "clean" environment necessary for longitudinal studies. The facility is open to all CHOP and Penn investigators whose animals are housed in the facility. Services include MRI, PET-CT, SPECT-CT, Optical Imaging, Ultrasound, and NMR/Microimaging. NMR/Microimaging Services at CHOP feature
a 400 MHz (9.4 Tesla) high-resolution wide-bore spectrometer equipped with a HP computer. The system can perform most of the traditional high-resolution NMR experiments as well as microimaging of specimens and small models. The services are available not only to CHOP investigators but also to investigators affiliated with large center program or private research institutions.

**Nucleic Acid PCR Core (NAPCore):** The NAPCore provides a centralized source for specialized services, technical expertise, and reagents to support the needs of molecular biology investigators. These services include Sanger DNA sequencing, small-scale next-generation sequencing and library assistance, fluorescent fragment analysis (MLPA and microsatellite analysis), microarrays, real-time PCR, oligonucleotide ordering, and sample quality control assessment. While production-level NGS is performed by BGI@CHOP, the NAPCore has additional resources for smaller-scale projects and Sanger sequence validation. The facility has MiSeq and Ion Torrent PGM sequencers, and two electrophoresis units along with support equipment for library preparation, emulsion PCR and bead enrichment.

**Pathology Core:** The Pathology Core provides basic histopathology, immunohistochemistry, tissue microarray, and laser capture microdissection services to researchers at CHOP and within the surrounding academic community. The core offers a full range of histopathology services, including tissue processing, embedding, and cutting for both paraffin and frozen tissue. The core also performs most standard stains as well as immunohistochemistry, antibody workup, fluorescence in situ hybridization, and TUNEL. Tissue microarrays can be constructed, and sophisticated imaging instrumentation is available for virtual microscopy and image analysis. Specialized software is available for image analysis, and to manage and store array data.

**Protein and Proteomics Core:** The Protein and Proteomics Core Facility addresses the growing need for the technological resources to identify, produce, and characterize new proteins. It provides a variety of services for investigators at CHOP, Penn, and outside institutions. These services include producing and characterizing proteins, investigating protein-protein interactions, and characterizing whole proteomes. Some services are provided on a user-operated, sign-up basis, whereas others are performed as full-service by the dedicated facility personnel. The core has a full range of equipment needed for protein production and biochemical and cell biological experiments, specialized instrumentation and computational capabilities necessary for state-of-the-art proteomics experiments, its own computing infrastructure and a variety of software.

**Laboratory Animal Facility (LAF):** The CHOP Research Institute has two laboratory animal facilities (LAFs), one located in the ARC and the other in the CTRB. The LAFs provide care, housing, husbandry, and veterinary care for CHOP's animal colonies. Accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), the LAFs ensure humane care and use of animals, including training, compliance oversight, administration and operations, clinical veterinary services, and animal husbandry. The LAFs work closely with the Institutional Animal Care and Use Committee (IACUC) to ensure that CHOP’s animal care and use program supports research, while simultaneously adhering to the regulations that govern the use of animals and the principles that underlie the ethical use of animals in research.

**Shipping Core:** The Research Institute's Shipping Core is a "fee for service" core facility that is available for shipment of hazardous substances for all Research Institute faculty and staff. The Shipping Core provides comprehensive shipping services including: packaging, labeling, shipping and tracking of hazardous materials shipments; identification and procurement of any necessary shipping permits; training and certification of labs whose PIs have chosen to ship their own packages as "Certified Shippers"; and providing shipping supplies to "Certified Shippers" at cost.

**Research IS Web Services Core:** The Research IS Web Services Core designs and supports web sites for investigators, labs, studies, core facilities, outreach programs, Research Affinity Groups, and Centers of Emphasis, as well as providing web development for Research Administration. The team develops a variety of client-side and database-driven web applications, including search and data gathering functionality, custom login and access restriction, and more. Web Services posts new content and site updates daily as part of their service to external clients. In addition, the team provides development support to, and day-to-day administration of, Institute-wide web presences, including the Research Institute public website, the Research Institute intranet, and the Share (Wiki) collaborative environment.

**Transgenic Mouse Core:** The Transgenic Mouse Core enables investigators to generate transgenic and chimeric mouse lines in-house without quarantine delays. An in vitro fertilization service is available to overcome any breeding problems that can impact valuable mouse lines. Providing a single male mouse enables the core to fertilize embryos in vitro, and the resulting fertilized embryos can then be transferred into surrogate mother mice or cryopreserved. Other services include production of transgenic mice by microinjection of DNA directly into...
embryonic stem cell nuclei; generation of knockout mice by microinjection of modified ES cells into blastocysts; mouse line rederivation; and embryo and sperm cryopreservation.

Translational Core Laboratory (TCL): The Translational Core Laboratory (TCL) at CHOP provides a variety of services ranging from sample collection to laboratory testing. They support investigators at both CHOP and UPENN for patient-oriented research as well as preclinical studies. TCL services are focused on the following functional areas:

- Clinical tests for research purpose: Use several IVD (in vitro diagnostics)-qualified instruments to provide clinical tests for research purpose. These tests include Complete Blood Counts (CBC), HbA1c, clinical chemistry (e.g., CMP, lipid panel, Na, creatinine, etc), and clinically-relevant immunoassays (e.g., CRP, Cystatin, insulin, Vitamin B12, PTH, cortisol, etc). CBC and clinical chemistry assays can also be used for animal studies.
- Biomarker Discovery: The "ELISA Center" and PCR-based Gene Lab test protein and gene biomarkers that are not provided in the clinical setting.
- Specimen Processing: Process samples for PBMC, DNA/RNA, lymphocyte EBV transformation, and other special purposes according to the investigator's protocol.

Viral Vector Cores: As part of the Center for Cellular and Molecular Therapeutics, the Research Vector Core has expanded its capacity to provide infrastructure support for investigators interested in using viral vectors in their research model systems. The Clinical Vector Core uses a patented vector production technology and a highly efficient purification process that utilizes combined column and gradient centrifugation-based process steps. This system has manufactured clinical grade AAV vectors that have demonstrated excellent safety in several clinical studies.

CHOP-Research Institute Centers of Emphasis

The following centers are directly related to the activities of this training program. Several of these centers have been developed during the past five years and dramatically expand the research opportunities available to our scientific community.

Center for Applied Genomics (CAG): The CAG develops new and better ways to diagnose and treat children affected by complex medical disorders by translating basic research findings into medical innovations. CAG aims to discover the genetic causes of both common and rare childhood diseases, including autism, epilepsy, schizophrenia, diabetes, and pediatric cancer. Ultimately, CAG's objective is to discover genetic markers to accurately diagnose patient subsets with genetic abnormalities that guide physicians to the most appropriate therapies. CAG is one of the world's largest genetics research programs, and the only center at a pediatric hospital to have large-scale access to state-of-the-art high-throughput genotyping and sequencing technology. It operates one of the world's largest whole exome and whole genome sequencing laboratories, which has led to numerous discoveries to elucidate the causes of pediatric disease.

Center for Cellular and Molecular Therapeutics (CCMT): The CCMT facilitates rapid translation of pre-clinical discoveries into clinical application. One of few such programs based at a pediatric institution, CCMT collaborates with other major programs to pursue new therapies for inherited and acquired disorders. CCMT also serves as an educational resource for investigators, clinicians, students, patient families, and the general public. CCMT has dedicated resources and personnel to help facilitate rapid translation. In addition, given the complicated nature and the government's stringent regulations of cell and gene therapy, the center guides and assists investigators through the regulatory approval process.

Center of Mitochondrial and Epigenomic Medicine (CMEM): The CMEM is poised to advance the understanding of, and potential treatments for, a multitude of disorders and diseases that involve mitochondria. Scientists and physicians need to understand normal energy flow, the disturbance of energy flow during disease, and communication between the mitochondria and nuclear DNA. This crosstalk is mediated by the epigenomic, inherited modifications in gene expression. CMEM is investigating mitochondrial and epigenomic dysfunction and treatment for a wide range of clinical problems such as autism, epilepsy, heart disease, diabetes and obesity, forms of blindness, Alzheimer and Parkinson disease, cancer, and aging. In addition to examining the essential roles of mitochondria, the CMEM team is exploring how mitochondrial genes influence adaptation to extremes in our environment such as arctic cold, tropical heat or high altitude.

Center for Pediatric Clinical Effectiveness (CPCE): The mission of the CPCE is to discover and disseminate knowledge about best practices in the management of pediatric disease. CPCE provides infrastructure for training in and performance of clinical effectiveness research aimed at understanding the best ways to prevent, diagnose, and treat diseases in children. It builds on the existing research expertise and infrastructure at CHOP
to create an environment and opportunities for the exchange of ideas among clinical effectiveness researchers, facilitate the performance of clinical effectiveness research through a pilot grant program and assistance with projects that use existing national and local databases, and educate the next generation of clinical effectiveness investigators in the methods of clinical epidemiology.

**Department of Biomedical and Health Informatics (DBHi):** The Department of Biomedical and Health Informatics (DBHi) is the home for the development of innovative solutions to healthcare's immediate and long-term informatics needs. DBHi provides the expertise and infrastructure needed to maximize the value of information relevant to all biomedical research activities occurring at CHOP. This endeavor blends the disciplines of bioinformatics and clinical informatics, which themselves require excellence in and integration of various knowledge domains, including biology, medicine, statistics, mathematics, linguistics, and computer science. The aim of CMBI is to empower investigators, clinical staff, patients, and families to most effectively use the ever-expanding totality of pediatric health information. In turn, these processes are expected to result in more effective pediatric healthcare interventions. Particular foci of interest include genomic and functional genomic discovery, genome-enabled medicine, biomedical data integration and dissemination, eHealth, and clinical decision support.

**Microbiome Center:** The CHOP Microbiome Center was established in 2015 within the PENNCHOP Microbiome Program and provides standard fee-for-service and collaborative research arrangements. The Program's mission is to develop microbiome-based strategies that generate biomarkers or therapeutics to improve health. The CHOP Center is comprised of a sequencing core, an analytics core and an administrative core. A unique feature of the Center is that they leverage the multi-omics platforms already in place at CHOP, allowing combination of very large-scale microbiome data with detailed patient records, deep genetic data, and additional omics-type data. Microbiome research is a highly specialized and fluid area of research requiring flexibility to accommodate rapidly evolving technologies. This facility stays abreast of the latest technologies providing high quality resources and cutting edge protocols to meet the investigators research needs.

**PolicyLab:** PolicyLab aims to achieve optimal child health and well being by informing program and policy changes through interdisciplinary research. It develops evidence-based solutions for the most challenging health-related issues affecting children. PolicyLab's experience caring for children and families drives its “evidence to action” approach to improving children’s health. This approach requires that PolicyLab projects involve practitioners, policymakers, and families throughout the research process, from design to dissemination. By partnering with stakeholders, PolicyLab engages in research that is both responsive to community needs and relevant to policy priorities and work to identify the programs, practices, and policies that support the best outcomes for children and their families.

**Institute for Translational Medicine and Therapeutics (ITMAT) and The Clinical and Translational Science Award (CTSA, see attached letter from the Director, Dr. Garret FitzGerald)**

The CTSA was awarded in 2006 and has fostered a remarkable collaboration between the University of Pennsylvania, CHOP, the Wistar Institute (WI) and the University of the Sciences in Philadelphia (USP). The CTSA initiative integrated the efforts of investigators drawn from all of these institutions. Additionally, leading participants from the Schools of Medicine, Nursing, Dentistry, Education, Arts and Sciences, Veterinary, Engineering and Applied Sciences, the Annenberg School of Communications, and the Wharton Business School contributed to the successfully funded proposal. The CTSA has combined two well-established and thriving NIH-funded GCRCs at CHOP and Penn and includes a large critical mass of senior faculty accomplished in the translation of a diverse array of therapeutic modalities into the clinical domain. The transformational plan proposed involves a commitment by the institutions involved 1) to collaborate and support the recruitments and programs in clinical and translational research; 2) to devote substantial space - both wet and dry laboratories - to clinical and translational research; and 3) to foster the trans-institutional expansion of the "academic home" of this enterprise - the Institute for Translational Medicine and Therapeutics (ITMAT) - to permit development of new centers, cores and interdisciplinary programs of research and education over the next 5 years. The development of the CTSA represents the first systematic change in the approach to clinical research undertaken by the NIH in 50 years. The Penn-CHOP led CTSA was one of twelve institutions that successfully competed for the initial selection of institutions.