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Affiliated with the University of Pittsburgh School of Medicine and ranked among the nation's best children's hospitals by *U.S. News & World Report*.

## Leadership Changes at the Heart Institute

September 2017 saw several new leadership appointments at the Heart Institute at Children's Hospital of Pittsburgh of UPMC. **Jacqueline Kreutzer, MD, FAAC, FSCAI**, was appointed as the new chief of the Division of Pediatric Cardiology. Dr. Kreutzer joined Children's Hospital in 2005 and currently serves as the director of the Cardiac Catheterization Laboratory. An internationally respected leader in interventional cardiology, Dr. Kreutzer has been instrumental in the ongoing development, expansion, and overall success of the Division of Pediatric Cardiology.

"We are blessed with an outstanding team at the Heart Institute, providing the highest standards of care in fetal, pediatric, and adult congenital cardiology."

*Jacqueline Kreutzer, MD*

Dr. Kreutzer's work in the fields of pediatric and adult congenital interventional cardiology, novel catheter and device therapies, percutaneous valve implantation, outcomes research, and quality improvement work have led to many new findings and dozens of peer-reviewed publications during more than a decade of clinical practice and research at Children's Hospital.

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*Heart Institute Leadership Team (L to R): Drs. Victor Morell, Jacqueline Kreutzer, Vivek Allada*

## New Faculty Profile: Brenda Mendizabal, MD

**Brenda Mendizabal, MD**, is a pediatric preventive cardiologist who joined the Heart Institute in December 2017 as an assistant professor of medicine. Dr. Mendizabal obtained her medical degree from the University of Illinois College of Medicine. She completed her residency at Children's National Medical Center - George Washington University. She went on to complete a cardiology fellowship at Children's Healthcare of Atlanta, and most recently completed her preventive cardiology fellowship at Cincinnati Children's Hospital Medical Center.



Dr. Mendizabal trained as a preventive cardiologist under an American Heart Association grant that is studying how hypertension (HTN) is diagnosed in pediatric patients and at what levels or ranges patients acquire end organ damage as a result. The multicenter, multiproject study<sup>1</sup> is examining hypertension through the use of echocardiograms, pulse wave velocity, urinalysis, and blood-based biomarkers to see at what points in time and at what levels end organ damage manifests in the kidneys, heart, blood vessels, brain, and other organs. "This study, now in year three of four is ongoing and I continue to be involved with Elaine Urbina, MD, in Cincinnati. I'm very excited about the continued progress, and we think that when the study concludes, we'll be able to redefine the definitions of childhood HTN based on evidence. As it currently stands, HTN is defined and treated based on the 95th percentile of blood pressure (BP) from the normal population distribution. We don't know if the 95th percentile is the most accurate definition of HTN," says Dr. Mendizabal.

The subspecialty of pediatric preventive cardiology is a rare discipline, with only one fellowship training program in the entire country. However, the incidence of adult cardiovascular diseases manifesting in childhood is a growing problem. "In an ideal world, the need to treat children for cardiovascular diseases and hypertension would indeed be a rare occurrence," says Dr. Mendizabal. But numerous factors over the last several decades in the United States have contributed to the prevalence of cardiovascular disease (CVD) in childhood. The obesity epidemic is front and center, as are overall diet trends and eating habits, diabetes, increasing rates of sedentary behaviors, and other lifestyle factors.

"We know that children who are obese will tend to be obese as adults. The same holds true for hypertension and hyperlipidemia. Having these issues in childhood, without adequate control or outright reversal, will likely lead these individuals to a much higher risk for cardiovascular diseases, heart attacks, strokes, and other morbidities as adults," says Dr. Mendizabal.

Dr. Mendizabal also indicates that there is a growing body of literature pointing to negative consequences related to cognition and memory as a result of CVD, specifically elevated BP, in children. "The effects of high blood pressure in children are turning out to be much more serious than was previously anticipated or understood." But, she explains, unlike with adults who have advanced CVD, atherosclerosis and the like (in most children without underlying genetic

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## Leadership Changes at the Heart Institute *(Continued from Page 1)*

"I am excited to lead a team of top clinicians, researchers, and a very strong administrative team as we aim to implement new strategic plans for the Heart Institute, continuing our quest for quality, growth, and innovation in the field of pediatric cardiology."

*Vivek Allada, MD*

Other changes at the Heart Institute include the appointment of **Vivek Allada, MD**, as executive director of the Institute. A pediatric cardiologist with a specialty in noninvasive imaging, Dr. Allada served as interim chief of the Division since 2012, in addition to his appointments as professor of medicine and as clinical director of pediatric cardiology, a role which he assumed in 2006. As executive director of the Heart Institute, Dr. Allada will be responsible for visualizing and managing the Institute's strategic plans and operational goals.

Continuing in his leadership role as co-director of the Heart Institute is **Victor Morell, MD**, chief of the Division of Pediatric Cardiothoracic Surgery. Since arriving at Children's Hospital, Dr. Morell has led the Division to become one of the premier programs in the United States, a program that has **one of the lowest four-year surgical mortality rates among all high-volume programs, and one of only 11 programs to receive a three-star rating from the Society of Thoracic Surgeons.**

## Heart Institute Research Retreat

The Heart Institute held its third annual Research Retreat on November 8, 2017. Held biannually, the retreat features discussions and presentations on current research initiatives from Heart Institute faculty and affiliated researchers in Radiology, Genetics, and Basic Science. This past event featured keynote speaker Thomas Diacovo, MD, director of Newborn Research and associate director of Neonatology at Columbia University Medical Center. Dr. Diacovo's keynote presentation was "Personalized Medicine for Neonatal Cardiac Patients: Are We There Yet?"



**Bernhard Kühn, MD**, Director of Research in Cardiology at the Heart Institute, is the retreat organizer. The collaborative event is designed to expose faculty members and fellows to the breadth and depth of current research at the Heart Institute, and foster future collaborative efforts between faculty members from across disciplines.

"At this third research retreat, we have seen incredible excitement and participation from faculty across disciplines. The discussions and collaborations the retreat is fostering with our fellows and faculty members will undoubtedly lead to new lines of investigation and findings," says Dr. Kühn.

The next Heart Institute Research Retreat is scheduled for Wednesday, April 25, 2018 and will feature keynote speaker Sarah Pasquali, MD, from the University of Michigan.

### Other featured topics and research projects included:

- The role of TEAD1 in adult heart muscle cells — Mousumi Moulik, MBBS
- Heart transplantation in heterotaxy syndrome — Sonny Duong, MD
- Overview of a functional cardiac genomic registry — Kathryn Little, MA, RN, CCRC, and Niyatie Ammanamanchi, MS
- Nasal nitric oxide and health-related quality of life in children with Congenital Heart Disease — Vithana Rukmalee, MD (fellow)
- Control of cardiomyocyte function by neuregulin and its receptor — Andrea Elliot, MD (fellow)
- Intrinsic nitric oxide assessments in Congenital Heart Disease patients — Phillip Adams, DO (anesthesiology)

## Cardiovascular Genetics: New Clinic for Patients and Families and New Research

**Mousumi Moulik, MBBS**, is the director of the newly created Pediatric Cardiovascular Genetics Clinic at Children's Hospital of Pittsburgh of UPMC that will be opening in early 2018. Dr. Moulik arrived in Pittsburgh after spending 10 years at the University of Texas Health Science Center at Houston after completing her fellowship training at Baylor College of Medicine.



Dr. Moulik's clinical and research interests revolve around pediatric cardiomyopathies and their underlying molecular genetics. Since arriving at Children's Hospital, Dr. Moulik has been finalizing plans for the new pediatric cardiovascular genetics clinic for children and their families. The goals of the new clinic are to facilitate the genetic diagnosis of familial cardiac disorders, and expand the use of that genetic diagnosis to the larger family unit to better understand who is at risk for developing the disease. Moving forward, the genetic information collected will permit clinicians and researchers to also perform genotype and phenotype correlation to predict risk profile and disease severity based on underlying genetic etiology and transition to treatment based on personalized precision medicine.

### Readying the New Clinic for Operation

"Our clinic is designed to be family-centric (Table 1) in nature with two key goals: the genetic diagnosis of familial cardiac disorders and the clinical and genetic screening and surveillance of at-risk family members," says Dr. Moulik. In addition to Dr. Moulik, the clinic will be staffed with two certified genetic counselors, and it will also include participation by a number of other specialists from the Heart Institute in the areas of cardiomyopathy, electrophysiology, lipid disorders and preventive cardiology. The services of the CV Genetics clinic will be provided in conjunction with continued medical care with established subspecialty providers.

Patients and families seen in the clinic will typically fall into one of four categories (Table 2). First are the various cardiomyopathies, many of which have an underlying

familial component and are likely monogenic or oligogenic in nature. Patients with various metabolic or neuromuscular cardiomyopathies will also be seen in the clinic along with continued coordinated care with metabolic and neuromuscular specialists. The second main group of patients will be those with channelopathy disorders including long QT syndrome, Brugada syndrome, CPVT, and familial atrial and ventricular tachyarrhythmias.

### TABLE 1: Family-centric clinic for familial cardiac disorders which will facilitate

- Genetic diagnosis of familial cardiac disorders
- Clinical and genetic screening and surveillance of at risk family members

### TABLE 2: Spectrum of Familial Cardiovascular Diseases which will be seen in the CV Genetics Clinic:

- **Cardiomyopathies:** DCM, HCM, LVNC, AVC, RCM, Metabolic, Neuromuscular
- **Channelopathies:** LQTS, Brugada syndrome, CPVT, SQTS, Familial VF, SCD
- **Aortopathies:** Marfan syndrome, EDS, Loeys Dietz, Bicuspid aortic valve with aortic root dilation, Isolated non-syndromic aortic aneurysms
- **Familial Dyslipidemias:** Familial hypercholesterolemia (FH), Familial hypertriglyceridemia, Familial combined hyperlipidemia

### TABLE 3: Cardiovascular Genetics Clinic Physicians/Providers:

- **Clinic Director:** Mousumi Moulik, MD
- **Electrophysiology:** Lee Beerman, MD; Gaurav Arora, MD
- **Heart Failure/Transplant:** Brian Feingold, MD; Susan Miller, MD; Shawn West, MD; Matt Zinn MD; Catherine Brailer, NP
- **Aortopathy/Connective Tissue Disorders:** Stacey Drant, MD
- **Dyslipidemia/Preventive Cardiology:** Vivek Allada, MD; Brenda Mendizabal, MD; Concetta Lombardo, NP

#### Genetics Counsellors:

- Jessica Sebastian
- Leslie Walsh

Dr. Moulik and her colleagues also will assess and treat patients with conditions such as Marfan syndrome, Ehler-Danlos syndrome (EDS), as well as those individuals with familial dyslipidemias.

“Another service that we are hopeful to provide is diagnostic testing (Table 3) for families where an individual has suffered a sudden, unexplained death due to the possibility of an underlying unknown genetic factor. We hope to work with local medical examiners offices to obtain DNA samples and conduct subsequent genetic testing — sometimes referred to as a molecular autopsy — to try and uncover a reason or genetic disposition that family members ought to be aware of,” says Dr. Moulik.

Longer-term plans at the pediatric cardiovascular genetics clinic include the creation of a genomic bio-repository to facilitate expanded research with whole exome/genome sequencing, and epigenetic testing to try and uncover hidden genetic findings in patients that may explain the nature and cause of their condition.

#### Cardiac Genetics and Heart Failure Research

Dr. Moulik is very active on the research front in cardiovascular genetics and cardiac signaling in heart failure. Dr. Moulik’s research group recently uncovered the critical role of the transcription factor TEAD1 in maintaining normal cardiac function in the adult heart. This work was published in the prestigious journal *JCI Insight*.

#### References and Further Reading

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## New Faculty Profile: Brenda Mendizabal, MD (Continued from Page 2)

conditions) can be reversed through focused and sustained intervention and can be reversed through focused and sustained intervention and lifestyle management, and when medically necessary supported with pharmacologic therapies.

### Planning for New Clinical Initiatives and Research

Dr. Mendizabal arrived in Pittsburgh with a full plate of clinical initiatives and research projects waiting to begin. These include working with colleagues from endocrinology, nephrology, adult lipidology, weight management, and the Heart Institute itself to organize and coalesce the clinical and research efforts for preventive cardiology. Plans and discussions also are starting for the consideration of a multidisciplinary, family-centered preventive cardiology clinic that will treat both children and their parents in a combined and holistic manner.

Plans are in the early stages for Dr. Mendizabal to collaborate on research projects with Silva Arslanian, MD, professor of medicine and chief

of the Weight Management and Wellness Center in the Division of Endocrinology, Diabetes, and Metabolism. Dr. Arslanian is currently involved in research related to childhood obesity and end organ damage as a result of associated hypertension and hyperlipidemia.

Dr. Mendizabal also will be participating in a new clinical trial that Children's Hospital will be engaged in as part of a multicenter trial of Amgen's cholesterol-lowering medication, Repatha, in a pediatric population. This first examination of Repatha (evolocumab) in a pediatric population of children with familial hypercholesterolemia is set to begin recruiting patients in the near future.

### References and Further Reading

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Open Label Study to Evaluate Safety, Tolerability, and Efficacy of Evolocumab (AMG 145) in Pediatric Subjects (10 to 17 Years of Age) With Heterozygous Familial Hypercholesterolemia (HeFH) or Homozygous Familial Hypercholesterolemia (HoFH). [ClinicalTrials.gov Identifier: NCT2624869](https://clinicaltrials.gov/ct2/show/study/NCT2624869). Sponsor: Amgen.

"In an ideal world, the need to treat children for cardiovascular diseases and hypertension would indeed be a rare occurrence."

Brenda Mendizabal, MD

## Recent Publications

**Below is a selection of recent publications from faculty researchers and clinicians at the Heart Institute.**

Mangiola M, Marrari M, **Feingold B**, Zeevi A. Significance of Anti-HLA Antibodies on Adult and Pediatric Heart Allograft Outcomes. *Front Immunol*. 2017; 8:4.

Woiewodski L, Ezon D, Cooper J, **Feingold B**. Barth Syndrome With Late Onset Cardiomyopathy: A Missed Opportunity for Diagnosis. *J Pediatr*. 2017; 183: 196-8.

Woiewodski L, Ezon D, Cooper J, **Feingold B**. Reply to: Acquired Noncompaction in Barth Syndrome Due to the TAZ mutation c.481\_482ins20. *J Pediatr*. 2017; 186: 214-15.

**Feingold B**, Salgado CM, Reyes-Mugica M, Drant S, Miller SA, Kennedy M, Kellman P, Schelbert EB, Wong TC. Diffuse Myocardial Fibrosis Among Healthy Pediatric Heart Transplant Recipients: Correlation of Histology, Cardiovascular Magnetic Resonance, and Clinical Phenotype. *Pediatr Transplant*. 2017; 21(5):e12986.

**Feingold B**, Mahle WT, Auerbach S, Clemens P, Domenighetti AA, Jefferies JL, Judge DP, Lal AK, Markham LW, Parks J, Tsuda T, Wang PK, Yoo S. Management of Cardiac Involvement Associated with Neuromuscular Diseases: A Scientific Statement from the American Heart Association. *Circulation*. 2017; 136(8).

Godown J, Thurm C, Dodd DA, Soslow JH, **Feingold B**, Smith AH, Mettler BA, Thompson B, Hall M. A Unique Linkage of Administrative and Clinical Registry Databases to Expand Analytic Possibilities in Pediatric Heart Transplantation Research. *Am Heart J*. 2017; 194: 9-15.

**Feingold B**, Picarsic J, Lesniak A, Popp BA, Wood-Trageser MA, Demetris AJ. Late Graft Dysfunction After Pediatric Heart Transplantation is Associated With Fibrosis and Microvasculopathy by automated, Digital Whole-slide Analysis. *J Heart Lung Transplant*. 2017; 36: 1336-43.

Law YM, Plonka CM, **Feingold B**. Norepinephrine Levels in Children with Single Ventricle Circulation. *Prog Pediatr Cardiol*. 2017; 47: 58-63.

Green DJ, Duong SQ, Burckart GJ, Sissung T, Price DK, Figg Jr WD, Brooks MM, Chinnock R, Canter C, Addonizio L, Bernstein D, Naftel DC, Zeevi A, Kirklin JK, Webber SA, **Feingold B**. Association Between TPMT Genetic Variants and Infection in Pediatric Heart Transplant Recipients Treated with Azathioprine: A Multi-Institutional Analysis. *J Pediatr Pharmacol Ther*. In press.

Adams PS, Zahid, M, Khalifa O, **Feingold B**, Lo CW. Low Nasal Nitric Oxide in Congenital Heart Disease With Systemic Right Ventricle and Post-cardiac Transplantation. *J Am Heart Assoc*. 2017; Dec 6:6(12).

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## Heart Institute Receives Cardiomyopathy Accreditation



Brian Feingold, MD, MS

In November 2017, the Heart Institute at Children's Hospital of Pittsburgh of UPMC received the designation of accredited center of care by the Children's Cardiomyopathy Foundation (CCF), a national nonprofit entity working to improve the care and outcomes for children living with various cardiomyopathy conditions.

The Cardiomyopathy Clinic within the Heart Institute's Heart Failure and Recovery Program sees patients on both an inpatient and outpatient basis. "At Children's, we have a strong tradition of excellence in care for all forms of this complex disease. Accreditation by the CCF is welcome recognition of our world-class pediatric cardiomyopathy program, including our

success in caring for infants, children, and adolescents across the entire spectrum of cardiomyopathies," says **Brian Feingold, MD, MS**, medical director of the Heart Failure and Transplantation Programs at Children's Hospital.

The CCF's accreditation is handed out for a two-year period to those centers meeting their criteria. Typically, CCF-accredited programs deal with a high volume of cardiomyopathy cases in a pediatric population, offer a number of specialized services for patients and families alike, and are involved in conducting research to advance the care of these serious and complex diseases.

## Faculty News and Announcements



Bernhard Kühn, MD

**Bernhard Kühn, MD**, associate professor and director of research in the Division of Pediatric Cardiology, was named as the 2019 American Heart Association Fellows Research Day Chair.

**Brian Feingold, MD**, medical director of the Heart Failure and Heart Transplantation Programs was recently named an associate editor for the journal *Pediatric Cardiology*. Dr. Feingold has also recently begun a two-year term as chair of the Scientific Council on Pediatric Thoracic Transplantation and Heart Failure with the International Society for Heart and Lung Transplantation. Additionally, Dr. Feingold was appointed to serve as medical monitor for two NIH-funded Pediatric Heart Network trials currently in progress. These trials are the Fontan Exercise Longitudinal Assessment (FUEL) trial, and the FUEL Open Label Extension trial.

**Jessica Davis, RN**, from the pediatric cardiac intensive care unit (CICU), obtained a new grant from the Beckwith Institute for a program to provide breastfeeding support

and education for mothers with medically fragile infants who have congenital heart disease. The two-year Frontline Innovation Program award was presented to Ms. Davis and her program co-investigators from the Department of Critical Care Medicine, Yuliya Domnina, MD, and Tracy Baust, the clinical research coordinator. The program is designed to increase nurse awareness and knowledge about breastfeeding, and at the same time provide new mothers with tools to help them and their babies with the experience of breastfeeding.

Five members of the Division of Cardiology were recognized in 2017 for their outstanding achievement in patient satisfaction. Congratulations to the following individuals for their service and dedication to exemplary patient care.

- **Stacey Drant, MD**
- **Tyler H. Harris, MD**
- **Susan A. Miller, MD**
- **Jacqueline G. Weinberg, MD**
- **Matthew D. Zinn, DO**

## Recent Publications *(Continued from Page 6)*

West SC, Zeevi A, Morell VO, Webber SA, **Feingold B**. Charges and Resource Utilization for Pediatric Heart Transplantation Across a Positive Crossmatch. *Pediatric Transplantation*. In press.

**Harris TH**, Adler M, Unti SM, McBride ME. Pediatric Heart Disease Simulation Curriculum: Educating the Pediatrician. *Congenital Heart Disease*. 2017; 00:1-8. PMID:28547923.

Cabalka AK, Hellenbrand WE, Eicken A, **Kreutzer J**, Gray RG, Bergersen L, Berger F, Armstrong AK, Cheatham JP, Zahn EM, McElhinney DB. Relationships Among Conduit Type, Pre-stenting, and Outcomes in Patients Undergoing Transcatheter Pulmonary Valve Replacement in the Prospective North American and European Melody Valve Trials. *JACC Cardiovasc Interv*. 2017; 10(17): 1746-1759.

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Yester JW, **Kühn B**. Mechanisms of Cardiomyocyte Proliferation and Differentiation in Development and Regeneration. *Current Cardiology Reports*. 2017; 19(2): 13.

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Gray RG, Menon SC, Johnson JT, Armstrong AK, Bingler MA, Breinholt JP, Kenny D, Lozier J, Murphy J, Sathanandam SK, Taggart NW, **Trucco SM**, Goldstein BH, and Gordon BM. Acute and Midterm Results Following Periventricular Device Closure of Muscular Ventricular Septal Defects: A Multicenter PICES Investigation. *Catheterization & Cardiovascular Interventions*. 2017; 90(2): 281-289.

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Butts RJ, Boyle GJ, Deshpande SR, Gambetta K, Knecht KR, Prada-Ruiz CA, Richmond ME, West SC, Lal AK. Characteristics of Clinically Diagnosed Pediatric Myocarditis in a Contemporary Multi-Center Cohort. *Pediatr Cardiol*. 2017 Aug; 38(6): 1175-1182.

## About the Heart Institute

The Heart Institute at Children's Hospital of Pittsburgh of UPMC is a leader of cardiovascular care, with a rich history in clinical research and innovation. It offers comprehensive care to patients with congenital conditions throughout their lives, from prenatal through adulthood.

As a comprehensive pediatric heart transplantation center, and a national leader in the use of pediatric heart-assist devices, the Heart Institute at Children's continues to advance the field of cardiovascular medicine.



## About Children's Hospital of Pittsburgh of UPMC

Regionally, nationally, and globally, Children's Hospital of Pittsburgh of UPMC is a leader in the treatment of childhood conditions and diseases, a pioneer in the development of new and improved therapies, and a top educator of the next generation of pediatricians and pediatric subspecialists. With generous community support, Children's Hospital has fulfilled this mission since its founding in 1890. Children's is named consistently to several elite lists of pediatric hospitals, including ranking No. 9 in the prestigious *U.S. News & World Report* annual Honor Roll of America's Best Children's Hospitals for 2017-2018 and ranking 10th among children's hospitals and schools of medicine in funding for pediatric research provided by the National Institutes of Health (FY2016).