**Division Data Summary**

**Research and Training Details**

<table>
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<tr>
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<td>Number of Joint Appointment Faculty</td>
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<td>Number of Research Fellows</td>
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<td>Direct Annual Industry Support</td>
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<td>Peer Reviewed Publications</td>
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**Clinical Activities and Training**

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<tr>
<td>Number of Clinical Staff</td>
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<td>Outpatient Encounters</td>
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**Significant Publications**

**Division Highlights**

**Robert B. Hinton Jr., MD**

Part of the Heart Institute’s mission is to facilitate meaningful translational research. Robert B. Hinton, MD is studying the mechanisms of human valve disease. Recent findings in human diseased aortic valves show that maladaptive angiogenic remodeling is an early finding in valve disease pathogenesis, which is surprising since this has long thought to be an end stage disease process associated with atherosclerosis. Further investigation in animal models of aortic valve disease has demonstrated that angiogenic remodeling is due in part to elastic fiber fragmentation. This work provides further evidence that valve disease has its origins in dysregulation of developmental programs and provides an opportunity to test new treatment strategies. It is not known if these early pathologic changes are identifiable by circulating biomarkers before the onset of overt clinical disease. Preclinical studies are underway to test the ability of biomarkers to predict disease progression and the efficacy of angiogenesis inhibition to treat aortic valve disease. Presently, there are no medical treatments for valve disease. This work seeks to elucidate developmental mechanisms of valve disease and identify new therapeutic targets to treat heart valve disease and improve child health.

**Elaine M. Urbina, MD**

This year Preventative Cardiology successfully competed for an R01 grant from the National Heart Lung and Blood Institute of the National Institute of Health titled “Accelerated CV Aging in Youth Related to CV Risk...
Factors.” Our previous data showed that youth with obesity were developing stiffer arteries and thicker hearts, risk factors for adult CV disease, well before they went on to develop type 2 diabetes. This new grant will allow us to continue to follow these patients. Not only will we determine the rate of ‘normal’ arterial aging in healthy, lean youth, we will also find out which clusters of CV risk factors such as obesity, type 2 diabetes, high blood pressure or cholesterol are more damaging to the arteries and heart. These data will then be used to design more effective preventive and treatment strategies for high risk youth to prevent adult heart attack and stroke.

Preventative Cardiology is currently completing data collection on an ARRA (American Recovery & Reinvestment Act) stimulus grant. Our preliminary data were presented at the national meeting of the American Diabetes Association in June 2011. Our data demonstrated that youth with type 1 diabetes have thicker carotid arteries, stiffer central and peripheral arteries and have abnormal autonomic tone as measured by heart rate variability. These findings will help us identify which youth with diabetes are developing early hardening of the arteries so more aggressive therapy can be started.

CCHMC Preventive Cardiology also continues to demonstrate leadership in the field of Pediatric Vascular Function by providing the only training seminar in Non-invasive Assessment of Vascular Function in Children available in the United States. We conduct the 2-day seminar 3 times yearly and have trained Pediatric researchers around the country with one international participant receiving training this year. We are also the data coordinating center for many multi-center grants performing vascular assessment.
Propranolol Study: Aim- Drug Propranolol effect on facial hemangiomas Funded: industry

**Critical Care »**
Critical Care Fellow Training, CICU

**Endocrinology » Larry Dolan, MD**
Working on ARRA grant comparing vascular function between healthy controls and youth with type 1 diabetes

**Endocrinology » Amy Shah, MD**
Working on a study comparing HDL-cholesterol proteomics and carotid intima-media thickness

**Endocrinology » Sarah Lawson, MD**
Working on study evaluating arterial stiffness in youth with Turner Syndrome

**Endocrinology » Meilan Rutter, MD; James Collins, MD, PhD; Hemant Sawlani, MD; Brenda Wong, MBBS, MRCP; Jessica Woo, MHSA, PhD**
Growth Hormone in Duchenne Muscular Dystrophy Patients, affects on cardiac function using cardiac MRI

**Endocrinology » Philippe Backeljaw, MD**
Assess partial Anomalous Pulmonary Venous Return (PAPVR) in Adolescent and Young Adult Turner Syndrome (TS) Patients: Prevalence and Hemodynamic Significance as Determined by Cardiac Magnetic Resonance Imaging (CMR)

**Endocrinology & Radiology » Philippe Backeljaw, MD; Robert Fleck, MD**
Cardiovascular Anomalies in Turner Syndrome (TS): Spectru, Prevalence, and Cardiac MR Imaging (cMRI), Findings in Pediatric and Young Adult Populations

**Endocrinology » Philippe Backeljaw, MD**
Characterization and treatment of aortopathy in Turner syndrome

**Endocrinology » Lawrence Dolan, MD**
NIH Training Grant

**Endocrinology » Nancy Crimmins, MD**
Center for Better Health and Nutrition

**Fetal Care » Timothy Crombleholme, MD; Foong-Yen Lim, MD; Mounira Habli, MD**
Fetal Care: Cardiovascular Findings associated with Twin-twin Transfusion, Cardiac Finding in fetal cardiac tumors and TRAP, Cerebrovascular Findings in TRAP

**Endocrinology » Larry Dolan, MD; Sarah Lawson, PhD**

**Gastroenterology, Hepatology & Nutrition » Jaime Echartea-Gonzalez, MD**
Liver Study: Aim- Hemodynamic profile and biochemical markers of Cardiomyopathy in children with chronic and end stage liver disease Funded: CTRC

**Gastroenterology, Hepatology & Nutrition » Jaime Echartea Gonzalez, MD; James Heubi, MD**
Characterization of cardiac disease in patients requiring liver transplantation

**Hem & Cancer Bio. - Molecular Genetics » Punam Malik, MD**
Sickle Cell Study: Aim- Evaluation Cardiovascular indices of subjects with Sickle Cell syndrome Funded: Insurance

**Hem & Cancer Bio. - Molecular Genetics » Punam Malik, MD**
Zileuton Study: Aim- Determine a safe and tolerable does of Zileuton in patients with SCD Funded: Division
Human Genetics » Lisa Martin, PhD
Quantitative Genetic Origins of Pediatric Heart Disease

Human Genetics » Robert Hopkin, MD
Amicus/Fabry study: Aim- A Double-Blind, randomized, placebo-controlled study to evaluate the efficacy, safety and pharmacodynamics of AT1001 in patients with Fabry disease and AT1001-responsive GLA mutations. Funded: Industry

Human Genetics » Thomas A. Burrow, MD
Encore Study: Aim- A phase 3, Randomized, Multi-Center, Multinational, Open –Label, Active Comparator study to evaluate the efficacy and safety in Genz-112638 in patients with Gaucher Disease Type 1 who have reached therapeutic goals with enzyme replacement therapy. Genzyme corporation-Funded: Industry

Human Genetics » Robert Hopkin, MD
Cardiocore Field Study: Aim- Open label study to evaluate the efficacy (GL-3 clearance), PK and safety parameters for 2 alternative dose regimens of Fabrazyme in treatment-naïve make pediatric patients with Fabry disease without severe symptoms. Funded: Industry Genzyme Corporation sponsor

Human Genetics » Robert Hopkin, MD
Characterization of cardiac disease in Fabry's disease

Human Genetics » Raouf Samy Amin, MD
Amin VF Study: Aim- Mechanism Mediating Cardiac and Vascular Disease in children with obstructive sleep Apnea. 1) to compare inflammatory cardiovascular disease mechanisms d children with varying degrees of sleep disordered breathing SDB to those in normal controls; 2) to determine how cytokine levels in plasma relate to those in tonsils; 3) to examine the relationship between inflammatory markers and prognostically important cardiovascular measures such as carotid intimal thickness, carotid compliance, pulse pressure, aortic stiffness and left ventricular mass and function before and after adenotonsillectomy. Funded: Division

Infectious Disease » Margaret Hostetter, MD
Heart Transplantation

Interventional Cardiology Research Center University of Cincinnati » James Wilkin, MD
Helmy/AKA Capsaicin Study

Nephrology » Mark Mitsnefes, MD
The use of cardiac MR to describe the subtle cardiac abnormalities in chronic dialysis and renal transplant patients

Nephrology/Center for Acute Care Nephrology » Prasad Devarajan, MD; Stuart Goldstein, MD
Research in Acute Kidney Injury after Cardiopulmonary Bypass Related acute Kidney Injury

Nephrology/Center for Acute Care Nephrology » Stuart Goldstein, MD
(CACN) and CICU

Nephrology/Center for Acute Care Nephrology » Prasad Devarajan, MD; Stuart Goldstein, MD
Assessment of AKI and CRI in pediatric heart failure

Nephrology/Center for Acute Care Nephrology » Prasad Devarajan, MD
Faculty recruitment and new Program building (CACN)

Nephrology/Center for Acute Care Nephrology » Prasad Devarajan, MD
NIH Grant - Pediatric Heart Network

Nephrology/Center for Acute Care Nephrology » Stuart Goldstein, MD; Ahmad Kaddourah, MD
Submission of CCF grant regarding Cardiorenal syndrome in pediatric heart failure

Nephrology » Stuart Goldstein, MD
Consultant for his study on the vascular effects of peritoneal vs hemodialysis in children with chronic kidney disease

Nephrology » Mark Mitsnefes, MD
Working on a grant currently under review at NIH. This multi-center trial will follow youth with pre-hypertension longitudinally to evaluate risk for development of sustained hypertension and target organ damage.

Nephrology » Mark Mitnefes, MD; Benjamin Laskin, MD
Frequent Hemodialysis Study: Aim- Improve cardiovascular outcome with more frequent hemodialysis, improve BP and LVH Funded: Federal/Non profit sponsor CTRC

Nephrology » Mark Mitsnefes, MD; Janaka Wansapura, PhD
Study aimed at determining the markers of cardiac function in patients with renal disease on chronic dialysis or post renal transplant.

Neurology » Brenda Wong, MD
 Neuromuscular Cardiology

Neurology » Donald Gilbert, MD
 Neurodevelopmental Clinic

Pediatric Cardiothoracic Surgery; Behavioral Medicine and Clinical Psychology; Child Life; Developmental & Behavioral Pediatrics; Gastroenterology, Hepatology and Nutrition; Cancer & Blood Diseases Institute; Neurology; Nutrition Therapy; Occupational and Physical Therapy; Social Services; Speech Pathology » Betsy Adler, RN, CNP; Lori Stark, PhD, ABPP; Jessica Kichler, PhD; Dean Beebe, PhD, ABPP-Cn; David Baker; Miranda Shearer; Donna Murray, PhD, CCC-SLP; Ajay Kaul, MBBS, MD; Mary Kay Irwin; Patti Towbin; Joan Kiefer; Mark Schapiro, MD; Cameron Thomas, MD; Donald Gilbert, MD, MD; Megan Horsley, RD; Becky Reder, OTD, OTR/L; Lisa Dodd; Ann Kummer, PhD, CCC-SLP

The Heart Institute Neurodevelopmental Clinic (NDC)

Rationale:
Over the last several decades, new surgical techniques and advances in cardiopulmonary bypass, intensive care, cardiac catheterization, non-invasive imaging, and medical therapies have significantly lowered mortality rates for children and adolescents with complex congenital heart disease (CHD) and high-risk acquired heart disease (AHD) (i.e. heart failure and heart transplant patients). However, survivors are at risk for neurodevelopmental (ND) morbidity resulting from their underlying genotype, the circulatory system abnormalities specific to their heart defect, and the medical and surgical therapies they have received. The focus of clinical research in the pediatric cardiac population has paralleled this population shift and transitioned from short-term surgical survival to the assessment of long-term morbidity. Among pediatric patients with complex CHD and high-risk AHD, there is a distinctive pattern of ND and behavioral dysfunction characterized by mild cognitive impairment, impaired social interaction, and impairments in core communication skills including pragmatic language as well as inattention, impulsive behavior, and impaired executive function. In addition, these patients often have fine and gross motor skills and issues with anxiety and depression. Many school-age survivors of infant cardiac surgery require remedial services including tutoring, special education, and physical, occupational, and speech therapy. The sequelae of complex CHD and high-risk AHD and their treatment are likely to limit their ultimate educational achievements,
employability, life-long earnings, insurability, and health-related quality of life (HRQOL). A significant proportion of these patients may need specialized services into adulthood. Incorporation of this knowledge into clinical practice may significantly improve ND and behavioral outcomes of patients with CHD.

**Goals:**

- To identify a group of children with heart disease who are at high risk for neurodevelopmental abnormalities and have them follow-up in the HI Neurodevelopmental Follow-up clinic for surveillance, screening, evaluation, and management of their neurodevelopmental and behavioral problems
- To prevent poor neurodevelopmental and behavioral outcomes in patients with complex heart disease and acquired heart disease when possible and treat those children and adolescents with deficits with interventions utilizing proven methodologies supported by research to maximize the Health-Related Quality of Life of the patient and minimize the potential impact on the family unit
- To be able to answer clinically important hypothesis-driven research questions that will Increase funding opportunities to prevent and treat ND and behavioral disability
- To educate the larger community of general pediatricians and family practitioners about the issues that these children and families face from an educational and social perspective and the potential ramifications on the family unit
- To provide a resource that parents/guardians of children with neurodevelopmental and behavioral issues can partner with to assist with obtaining resources and services

**Pediatric Surgery** » Thomas Inge, MD

*Gastric Bypass/Bariatric: Aim- Evaluate the Cardiac indices of pre and post gastric bypass surgery Funded: Insurance*

**Pediatric Surgery** » Barb Tofani, RN

*Cardiac OR staffing and policies*

**Perinatal Institute** » James Greenberg, MD

*Neonatal Cardiology and Perinatal Cardiology*

**Pulmonology** » Raouf Amin, MD

*Assisting in analyses of arterial stiffness data collected in a study of youth with obstructive sleep apnea*

**Radiology/Imaging Research Center** » Chuck Dumoulin, PhD

*We are developing a new dedicated infant cardiac MR imaging coil. The coil will be used in the newly dedicated neonatal MR system housed in the NICU. This system will allow novel cardiac MR imaging of critically ill neonates.*

**Radiology** » Chuck Dumoulin, PhD

*MRI Research on Electrophysiology*

**Radiology** » Janaka Wansapura, PhD

*Muscular dystrophy research*

**Radiology** » Robert Fleck, Jr., MD

*Cardiac MRI*

**Rheumatology** » John Harley, MD, PhD

*EMerge grant*

**Sports Medicine** » Nicholas Edwards

*Assisting in data analyses exploring the relationship between physical activity and CV risk factors in youth*
Faculty Members

Jeffrey A. Towbin, MD, FAAP, FACC, FAHA, Professor
  *Executive Co-Director, The Heart Institute*
  *Director and Chief, Division of Cardiology*
  **Research Interests** Cardiomyopathy and Genetics

Jeffrey B. Anderson, MD, MPH, Assistant Professor
  **Research Interests** Syncope, nutritional failure in congenital heart disease, quality improvement

Robert Beekman, MD, Professor
  **Research Interests** Cardiac Catheterization & Intervention, Quality Improvement, Coarctation of the Aorta

D. Woodrow Benson, MD, PhD, Professor
  *Director, Cardiovascular Genetics*
  **Research Interests** Cardiovascular Genetics

James F. Cnota, MD, Associate Professor
  **Research Interests** Fetal Cardiology

Linda H. Cripe, MD, Associate Professor
  **Research Interests** Cardiomyopathies, Neuromuscular Disorders, Echocardiography

Richard Czosek, MD, Assistant Professor
  **Research Interests** Cardiac pacing devices in pediatric and congenital heart disease patients and arrhythmia risk stratification in the pediatric population

Allison Divanovic, MD, Assistant Professor
  **Research Interests** Fetal Echocardiography

Paula Goldenberg, MD, MSCE, MSW, FAAP, FACMG, Associate Professor
  **Research Interests** Cardiovascular Genetics

Michelle Grenier, MD, Associate Professor
  *Director, 3 Dimensional Echocardiography*
  **Research Interests** Cardiomyopathy, Heart Failure, 3 Dimensional Echocardiography

Haleh Heydarian, MD, Assistant Professor
  **Research Interests** Echocardiography Synchrony/Strain Imaging and Quality Improvement

Robert B. Hinton, MD, Assistant Professor
  **Research Interests** Cardiovascular Genetics & Developmental Biology

Russel Hirsch, MD, Associate Professor
  *Director, Cardiac Catheterization and Intervention*
  **Research Interests** Cardiac Catheterization & Intervention, Device Development

Kan Hor, MD, Assistant Professor
  **Research Interests** MRI technology to diagnose and follow heart disease, in particular DMD cardiomyopathy.

Holly M. Ippisch, MD, MS, FAAP, Assistant Professor
  **Research Interests** Echocardiography, preventive cardiology, exercise and pediatric obesity.

John Lynn Jefferies, MD, MPH, FACC, FAAP, Associate Professor
  *Director, Cardiomyopathy/Heart Failure & Transplantation*
  *Co-Director, CV Genetics*
  *Associate Director, HIRC*
  **Research Interests** Cardiomyopathy, Heart Failure, Cardiovascular Genetics and drug trials
Beth Ann Johnson, MD, MA, Assistant Professor
Research Interests Premature infants with congenital heart defects, Fetal diagnosis

Thomas R. Kimball, MD, Professor
Medical Director, Heart Institute
Director, Cardiac Echocardiography & Cardiovascular Core Imaging
Research Interests Echocardiography, Ventricular function, Cardiovascular Effects of Obesity and Type II Diabetes.

Shelley Kirk, PhD, RD, LD, Assistant Professor
Research Interests The efficacy, safety and feasibility of interventions for the management of pediatric obesity.

Timothy Knilans, MD, Professor
Director, Clinical Cardiac Electrophysiology and Pacing
Director, Pediatric Cardiac Electrophysiology Fellowship
Research Interests Identification and risk stratification of causes of sudden death.

Catherine Krawczeski, MD, Associate Professor
Director, Heart Institute Quality Improvement and Clinical Effectiveness
Co-Director, Center for Acute Care Nephrology
Research Interests Bypass associated acute kidney injury (biomarkers, epidemiology, early therapy

Cong Liu, PhD, Assistant Professor
Associate Director of HIDL
Research Interests Genetic etiology of cardiomyopathy, congenital heart disease and cardiovascular diseases. New technology development in clinical genetic testing and clinical viral testing.

Angela Lorts, MD, Assistant Professor
Research Interests Heart failure and myocardial remodeling

Bradley S. Marino, MD, MPP, MSCE, Associate Professor
Director, Heart Institute Research Core
Research Interests Outcomes Research

Erik Michelfelder, MD, Associate Professor
Director, Fetal Cardiology
Research Interests Fetal Cardiology and Echocardiography

David Nelson, MD, PhD, Professor
Medical Director, CICU
Research Interests Inflammatory injury after cardiac surgery

Enkhsaikhan Purevjav, MD, PhD, Assistant Professor
Research Interests Genetics of Cardiovascular Disease

Robert Siegel, MD, Professor
Medical Director, The Center for Better Health and Nutrition
Research Interests

Robert Spicer, MD, Professor
Director Fellowship Program
Research Interests Heart Failure Transplant

Arnold Strauss, MD, Professor
BK Rachford Professor and Chair, Department of Pediatrics, University of Cincinnati College of Medicine
Director, Cincinnati Children's Research Foundation
Chief Medical Officer, Cincinnati Children's Hospital Medical Center
Research Interests

Michael Taylor, MD, PhD, Assistant Professor
  Director of Advanced Imaging Innovation and Cardiac MRI (CMR)
  Research Interests Non-invasive study of cardiovascular physiology and metabolism; Pre-clinical imaging of cardiomyopathy models with cardiac MR and positron emission tomography.

Elaine Urbina, MD, MS, Associate Professor
  Director, Preventive Cardiology
  Research Interests Non-invasive assessment of vascular structure and function and relationship to CV risk factors, obesity, diabetes, renal disease and sleep disorders. Treatment of high blood pressure and cholesterol.

Karen Uzark, PhD, CPNP, Associate Professor
  Director of Process Improvement and Outcomes Research
  Research Interests Heart Transplant, Quality of Life, Outcomes in Children with Heart Disease

Gary Webb, MD, FRCP(C), FACC, FAHA, Professor
  Director, Adolescent and Adult Congenital Heart Disease Program
  Research Interests Adolescent and Adult Congenital Heart Disease

Joint Appointment Faculty Members

Jeanne James, MD, Associate Professor
  Molecular Cardiovascular Biology
  Research Interests Molecular cardiology and animal models of cardiac disease.

Stephanie Ware, MD, Associate Professor
  Molecular Cardiovascular Biology
  Research Interests Cardiovascular Genetics

Clinical Staff Members
  - Lisa Lee, MD
  - Chad Connor, MD

Trainees
  - Christopher Cheng, MD, PhD, PL4, New York Methodist
  - David Crowley, MD, PL7, Barbara Bush Children's Hospital, Portland, ME
  - Sam Hanke, MD, PL5, Cincinnati Children's Hospital/University of Cincinnati
  - Chike Madueme, MD, PL6, Cincinnati Children's Hospital/University of Cincinnati
  - Mark Norris, MD, PL7, Cincinnati Children's Hospital/University of Cincinnati
  - Thomas Ryan, MD, PhD, PL5, Cincinnati Children's Hospital/University of Cincinnati
  - Chistopher Statile, MD, PL5, Cincinnati Children's Hospital/University of Cincinnati
  - Tamara Thomas, MD, PL4, Vanderbilt University, Nashville, Tennessee
  - Chet Villa, MD, PL4, Cincinnati Children's Hospital/University of Cincinnati
  - Mark Walsh, ME, PL10, Hospital for Sick Children, Toronto, Canada
  - Dingding Xiong, MD, PhD, PL5, Driscoll Children's Hospital, Corpus Christi, TX
  - Matt Zussman, MD, PL6, UNC, Chapel Hill, North Carolina
  - Anne-Cecile Huby, PhD, UPMC (Pierre and Marie Curie University, Paris, France
Division Publications


104. Urbina EM, Kimball TR, Khoury PR, Daniels SR, Dolan LM. Increased arterial stiffness is found in


Grants, Contracts, and Industry Agreements

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<th>Annual Direct / Project Period Direct</th>
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| **Nutritional Deficiencies in Infants with Single Ventricle**  
Thrasher Research Fund | 10/01/10-09/30/12 $12,500             |
| BENSON, W                 |                                       |
| **Musculoskeletal Ancillary Study**  
Marfan Foundation(The Johns Hopkins University) | 07/01/10-06/30/11 $3,750             |
| **Quality of Life Study-Pediatric Heart Network**  
National Institutes of Health(New England Research Institutes)  
U01 HL 068270 | 07/01/10-06/30/11 $500             |
| **Trial of Beta Blocker vs Angiotensin Receptor Blocker**  
National Institutes of Health(New England Research Institutes)  
U01 HL 068270 | 07/01/10-06/30/11 $72,010           |
| IPPISCH, H                |                                       |
| **Effects of Dietary Fat and Exercise Challenges in Obese Children**  
National Institutes of Health | K23 HL 091174 09/01/08-07/31/13 $126,085 |
| KIMBALL, T                |                                       |
| **Chronic Kidney Disease in Children**  
National Institutes of Health(Children’s Mercy Hospital)  
U01 DK 066143 | 08/01/08-07/31/13 $55,222           |
| MARINO, B                 |                                       |
| **Understanding Mechanisms of Fontan Failure and Key Predictors for Patient Outcome**  
National Institutes of Health(Georgia Tech Research Corp) |                                      |
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<td>R01 HL 098252</td>
<td>Collaborative Community Based Initiative to Improve the Health of Overweight and Obese Children</td>
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<td>R01 HL 105591</td>
<td>Accelerated CV Aging in Youth Related to CV Risk Factor Clusters</td>
<td>National Institutes of Health</td>
<td>01/01/11-12/31/11</td>
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<td>R01 HL 105591</td>
<td>Modifying Dietary Behavior in Adolescents with Elevated Blood Pressure</td>
<td>National Institutes of Health(University of Cincinnati)</td>
<td>01/01/11-12/31/11</td>
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<tr>
<td>R01HL088567</td>
<td>Modifying Dietary Behavior in Adolescents with Elevated Blood Pressure</td>
<td>National Institutes of Health(University of Cincinnati)</td>
<td>02/01/08-01/31/12</td>
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**Current Year Direct** $786,124

**Industry Contracts**

- **BEEKMAN**
  - AGA Medical, LLC
    - $4,177

- **HIRSCH**
  - AGA Medical, LLC
    - $12,199

- **KRAWCZESKI**
  - Asklepios Pharmaceuticals, LLC
    - $26,209

**Current Year Direct Receipts** $42,585

**Total** $828,709