

### Division Details

#### Division Data Summary

##### RESEARCH AND TRAINING DETAILS

Number of Faculty	61
Number of Joint Appointment Faculty	2
Number of Research Fellows	36
Number of Research Students	19
Number of Support Personnel	266
Direct Annual Grant Support	\$8,257,154
Direct Annual Industry Support	\$32,236
Peer Reviewed Publications	190

##### CLINICAL ACTIVITIES AND TRAINING

Number of Clinical Staff	6
Number of Clinical Fellows	14
Number of Other Students	1
Inpatient Encounters	1961
Outpatient Encounters	18493

#### Division Photo



Row 1: E Purevjav, D Morales, J Towbin, J Robbins, B Blaxall, A Lorts, C Chin, L Lee  
 Row 2: S Kirk, C Castleberry, A Divanovic, R Beekman, B Goldstein, J Sticka, K Yutzey, M Maillet  
 Row 3: S Ware, J Waxman, J Storey, H Ippisch, J Jefferies, C Learn, J James, J Gulick, J Anderson  
 Row 4: J Molquentin, B Marino, R Hinton, R Czosek, C Madueme, N Madsen, I Wilmot, S Hanke, E Michelfelder, T Ryan, C Statile, M Taylor

### Significant Accomplishments

#### New Program Focuses on the Links Between the Mind and Heart

Research shows that children with complex congenital and acquired heart disease are at a greater risk for neurodevelopment issues. The Heart Institute-Kindervelt Neurodevelopmental and Educational Clinic (HI NDEC) at Cincinnati Children's Hospital Medical Center is a new, innovative program established by Bradley Marino, MD, MPP, MSCE, and now headed by Haleh Heydarian, MD. It provides individualized neurodevelopmental follow-up care designed to help each child reach their full potential by optimizing their neurodevelopmental capabilities and psychosocial outcome. The multidisciplinary HI NDEC team provides a comprehensive neurodevelopmental evaluation for infants, toddlers, children and adolescents. It provides families with the appropriate surveillance, screening, evaluation and treatment resources needed to ensure the best outcome possible for their child. The HI NDEC staff performs developmental assessments on infants, toddlers, and preschool children to maximize school preparedness, and assesses for difficulties in school-age children. Providers evaluate for problems with attention, task management and organization, and for behavioral and emotional problems that may impact relationships with friends and family. The HI NDEC has experts that span an array of specialties, including: Pediatric Cardiology, Developmental-Behavioral Pediatrics, Pediatric Psychology, Education, Pediatric Neurology, Occupational/Physical Therapy, Pediatric Nutrition, Cardiac Nursing, and Social Work. The clinic was prominently featured in the Health Section of the *Wall Street Journal* on July 31, 2013.

## Gene Discovery Could Lead to Treatment to Prevent Thickening of the Heart Muscle

Cardiac fibrosis refers to the thickening or “scarring” of muscle tissue in the heart. Uncontrolled or prolonged accumulation of fibrotic material in the heart contributes to worsening heart disease and leads to heart failure and death. Thus, a better understanding of the genes and mechanisms that promote cardiac fibrosis are critical as we develop new therapies to stop or slow this process. Cardiac fibrosis is controlled primarily by a cell type known as the fibroblast. In select disease states, these fibroblasts become activated and change into a cell type known as the myofibroblast, which can generate proteins that cause fibrosis. In a recent paper in a premier scientific journal, *Developmental Cell*, Jeffery Molkentin, PhD, and colleagues showed that a novel gene, TRPC6, underlies the conversion of fibroblasts into myofibroblasts, thereby promoting cardiac fibrosis and disease. Molkentin showed that mice lacking TRPC6 had defective generation of myofibroblasts, with a lessening of the fibrotic response *in vivo*. The lab also showed how TRPC6 was activated in fibroblasts to begin this process, and identified how TRPC6 works to actually convert these cells into myofibroblasts. Their work suggests new therapies with existing experimental drugs might have an anti-fibrotic effect, possibly reducing the progression of heart failure in select disease states.

## Heart Institute Sets Sights on Becoming Worldwide Training Center for Pediatric Mechanical Circulatory Support

Mechanical circulatory support for children is an emerging and quickly changing field, and, as such, no institute in the world has established itself as a training and resource center for the multiple initiatives by several worldwide companies creating pediatric ventricular assist devices and total artificial hearts. The Heart Institute is poised to become this international reference center. We have formed relationships with global companies interested in developing ventricular assist devices for pediatric patients. Many of these companies are leading the way to develop new devices that can serve as bridges to heart transplant while patients wait for a heart to become available. These companies include SynCardia Systems, HeartWare, Thoratec, Berlin Heart, and Levitronix. In the past year, we trained physicians from Japan and South America, and were invited to host training symposia for several of these companies at Cincinnati Children’s. As a direct result of these collaborations, the Heart Institute’s surgical team is now the Primary Investigator and Coordinating Center for the first pediatric total artificial heart trial. Additionally, we have created (in concert with our transportation team) an Extracorporeal Membrane Oxygenation (ECMO) transport program, which enables us to treat critically ill children while transferring them to Cincinnati Children’s. This program gives children access to care that they would not have been able to receive elsewhere. The Heart Institute is the only program in the country to provide third-party ECMO transport. We hope by the end of this year to have firmly established the Heart Institute and Cincinnati Children’s as the premier worldwide training and pediatric resource center for mechanical circulatory support.

## Division Publications

1. Alghamdi M, De Souza AM, White CT, Potts MT, Warady BA, Furth SL, Kimball TR, Potts JE, Sandor GG. **Echo-Doppler assessment of the biophysical properties of the aorta in children with chronic kidney disease**. *Pediatr Cardiol*. 2013; 34:1218-25.
2. Allen KY, Goldstein BH, Pahl E, Schumacher KR, Gajarski RJ, Backer CL, Wax DF, Kaushal S, Gossett JG. **Non-cameral coronary artery fistulae after pediatric cardiac transplantation: a multicenter study**. *J Heart Lung Transplant*. 2012; 31:744-9.

3. Almond CS, Morales DL, Blackstone EH, Turrentine MW, Imamura M, Massicotte MP, Jordan LC, Devaney EJ, Ravishankar C, Kanter KR, Holman W, Kroschwitz R, Tjossem C, Thuita L, Cohen GA, Buchholz H, St Louis JD, Nguyen K, Niebler RA, Walters HL, 3rd, Reemtsen B, Wearden PD, Reinhartz O, Guleserian KJ, Mitchell MB, Bleiweis MS, Canter CE, Humpl T. **Berlin Heart EXCOR Pediatric Ventricular Assist Device for Bridge to Heart Transplantation in US Children.** *Circulation.* 2013; 127:1702-11.
4. Anderson JB, Czosek RJ, Cnota J, Meganathan K, Knilans TK, Heaton PC. **Pediatric syncope: national hospital ambulatory medical care survey results.** *J Emerg Med.* 2012; 43:575-83.
5. Anderson JB, Czosek RJ, Knilans TK, Marino BS. **The effect of paediatric syncope on health-related quality of life.** *Cardiol Young.* 2012; 22:583-8.
6. Anderson JB, Czosek RJ, Knilans TK, Meganathan K, Heaton P. **Postoperative Heart Block in Children with Common Forms of Congenital Heart Disease: Results from the KID Database.** *J Cardiovasc Electrophysiol.* 2012; 23:1349-54.
7. Anderson JB, Iyer SB, Schidlow DN, Williams R, Varadarajan K, Horsley M, Slicker J, Pratt J, King E, Lannon C. **Variation in growth of infants with a single ventricle.** *J Pediatr.* 2012; 161:16-21 e1; quiz 21 e2-3.
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9. Aprikyan AA, Khuchua Z. **Advances in the understanding of Barth syndrome.** *Br J Haematol.* 2013; 161:330-8.
10. Ashley EA, Hershberger RE, Caleshu C, Ellinor PT, Garcia JG, Herrington DM, Ho CY, Johnson JA, Kittner SJ, Macrae CA, Mudd-Martin G, Rader DJ, Roden DM, Scholes D, Sellke FW, Towbin JA, Van Eyk J, Worrall BB. **Genetics and cardiovascular disease: a policy statement from the American Heart Association.** *Circulation.* 2012; 126:142-57.
11. Askenazi DJ, Selewski DT, Paden ML, Cooper DS, Bridges BC, Zappitelli M, Fleming GM. **Renal replacement therapy in critically ill patients receiving extracorporeal membrane oxygenation.** *Clin J Am Soc Nephrol.* 2012; 7:1328-36.
12. Auger-Messier M, Accornero F, Goonasekera SA, Bueno OF, Lorenz JN, van Berlo JH, Willette RN, Molkentin JD. **Unrestrained p38 MAPK activation in Dusp1/4 double-null mice induces cardiomyopathy.** *Circ Res.* 2013; 112:48-56.
13. Averin K, Uzark K, Beekman RH, 3rd, Willging JP, Pratt J, Manning PB. **Postoperative assessment of laryngopharyngeal dysfunction in neonates after norwood operation.** *Ann Thorac Surg.* 2012; 94:1257-61.
14. Bal NC, Maurya SK, Sopariwala DH, Sahoo SK, Gupta SC, Shaikh SA, Pant M, Rowland LA, Goonasekera SA, Molkentin JD, Periasamy M. **Sarcolipin is a newly identified regulator of muscle-based thermogenesis in mammals.** *Nat Med.* 2012; 18:1575-9.
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16. Beekman RH, 3rd. **Coarctation of the Aorta.** In: HD Allen, DJ Driscoll, RE Shaddy, TF Feltes, eds. *Moss & Adams' Heart Disease in Infants, Children and Adolescents: Including the Fetus and Young Adult.* Philadelphia, PA: Lippincott Williams & Wilkins; 2012:1044-1060.
17. Beekman RH, 3rd. **FDA Clearance of Cardiac Devices for Children: A Primer and Call to Action.**

*Congenital Cardiology Today*. 2012; 10:1-7.

18. Beekman RH, 3rd, Lannon C. **The National Pediatric Cardiology Quality Improvement Collaborative**. *Neonatology Today*. 2013; 8:1-5.
19. Belmonte SL, Blaxall BC. **Conducting the G-protein Coupled Receptor (GPCR) Signaling Symphony in Cardiovascular Diseases: New Therapeutic Approaches**. *Drug Discov Today Dis Models*. 2012; 9:e85-e90.
20. Belmonte SL, Blaxall BC. **G protein-coupled receptor kinase 5: exploring its hype in cardiac hypertrophy**. *Circ Res*. 2012; 111:957-8.
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28. Brown KL, Ichord R, Marino BS, Thiagarajan RR. **Outcomes Following Extracorporeal Membrane Oxygenation in Children With Cardiac Disease**. *Pediatric Critical Care Medicine*. 2013; 15:S73-S83.
29. Buchaklian AH, Helbling D, Ware SM, Dimmock DP. **Recessive deoxyguanosine kinase deficiency causes juvenile onset mitochondrial myopathy**. *Mol Genet Metab*. 2012; 107:92-4.
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**cardiac phenotype necessitating mechanical circulatory support as a bridge to transplantation.**

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- Ranganathan D, Razavi H, Regan M, Rehm JT, Rein DB, Remuzzi G, Richardson K, Rivara FP, Roberts T, Robinson C, De Leon FR, Ronfani L, Room R, Rosenfeld LC, Rushton L, Sacco RL, Saha S, Sampson U, Sanchez-Riera L, Sanman E, Schwebel DC, Scott JG, Segui-Gomez M, Shahraz S, Shepard DS, Shin H, Shivakoti R, Singh D, Singh GM, Singh JA, Singleton J, Sleet DA, Sliwa K, Smith E, Smith JL, Stapelberg NJ, Steer A, Steiner T, Stolk WA, Stovner LJ, Sudfeld C, Syed S, Tamburlini G, Tavakkoli M, Taylor HR, Taylor JA, Taylor WJ, Thomas B, Thomson WM, Thurston GD, Tleyjeh IM, Tonelli M, Towbin JA, Truelsen T, Tsilimbaris MK, Ubeda C, Undurraga EA, van der Werf MJ, van Os J, Vavilala MS, Venketasubramanian N, Wang M, Wang W, Watt K, Weatherall DJ, Weinstock MA, Weintraub R, Weisskopf MG, Weissman MM, White RA, Whiteford H, Wiersma ST, Wilkinson JD, Williams HC, Williams SR, Witt E, Wolfe F, Woolf AD, Wulf S, Yeh PH, Zaidi AK, Zheng ZJ, Zonies D, Lopez AD, Murray CJ, AlMazroa MA, Memish ZA. **Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010.** *Lancet.* 2012; 380:2163-96.
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**Regulatory Functions of Cardiac alpha-Tropomyosin (alpha-TM) in a Novel Transgenic Mouse Model Expressing alpha-TM-D137L.** *J Biol Chem.* 2013; 288:16235-46.

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## Grants, Contracts, and Industry Agreements

### Cardiology

#### Grant and Contract Awards

Annual Direct

#### CNOTA, J / KRAWCZESKI, C

**Pediatric Heart Network Prairieland Consortium**

National Institutes of Health

U10 HL 109673 09/01/11-06/30/16 \$367,500

**The Relationship of Family Factors to Developmental and Psychosocial Outcomes in Children with Hypoplastic Left Heart Syndrome**

National Institutes of Health(Children's Hospital of Wisconsin)

U01 HL 068270 01/09/12-01/08/14 \$1,200

**Trial of Beta Blocker vs Angiotensin II Receptor Blocker Therapy in Individuals with Marfan Syndrome**

National Institutes of Health(New England Research Institutes)

U01 HL 068270 05/05/11-12/31/14 \$1,570

#### 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 \$124,500

#### JEFFERIES, J

**Heart Failure Pediatric Cardiology Fellowship Program**

Medtronic, Inc.

07/01/12-06/30/12 \$15,000

#### KIMBALL, T

**Chronic Kidney Disease in Children**

National Institutes of Health(Children's Mercy Hospital)

U01 DK 066143	08/01/08-07/31/13	\$60,996
<b>MARINO, B</b>		
<b>Transitional Telehealth Homecare: REACH</b>		
National Institutes of Health(Children's Hospital of Philadelphia)		
R01 NR 002093	09/21/11-06/30/16	\$86,360
<b>Understanding Mechanisms of Fontan Failure and Key Predictors for Patient Outcome</b>		
National Institutes of Health(Georgia Tech Research Corp)		
R01 HL 098252	02/01/10-01/31/14	\$16,667
<b>MICHELFELDER, E</b>		
<b>Hypoplastic Left Heart Syndrome: Expression of RHD in the Fetus</b>		
National Institutes of Health(Washington University)		
R01 HL 098634	05/15/11-12/31/14	\$34,672
<b>MOORE, V</b>		
<b>Quantitative Non-Invasive Assessment of Right Ventricular Function Using Global Longitudinal Strain and TAPSE in a Pre-Clinical Setting</b>		
American Society of Echocardiography		
	06/01/13-05/31/14	\$22,727
<b>SIEGEL, R</b>		
<b>The Health Effects of a Blueberry Enriched Diet on Obese Children: A Feasibility Study</b>		
Wild Blueberry Association of America		
WBANA-Siegel	11/01/12-10/31/13	\$30,000
<b>TOWBIN, J</b>		
<b>Biomarkers in Pediatric Cardiomyopathy</b>		
National Institutes of Health(University of Miami)		
R01 HL 109090	08/06/12-07/31/16	\$34,637
<b>URBINA, E</b>		
<b>Accelerated CV Aging in Youth Related to CV Risk Factor Clusters</b>		
National Institutes of Health		
R01 HL 105591	01/01/11-12/31/15	\$339,301
	<b>Current Year Direct</b>	<b>\$1,135,130</b>
<b>Industry Contracts</b>		
<b>BEEKMAN, R</b>		
The Johns Hopkins University		
		\$1,186

**CHIN, C**

Roche Laboratories, Inc	\$24,623
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**HIRSCH, R**

AGA Medical, LLC	\$6,427
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	<b>Current Year Direct Receipts</b>	<b>\$32,236</b>
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	<b>Total</b>	<b>\$1,167,366</b>
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## Molecular Cardiovascular Biology

Grant and Contract Awards	Annual Direct
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**ACCORNERO, F****PGF Role in Regulating Cardiac Remodeling**

American Heart Association

11POST7530035	07/01/11-06/30/13	\$45,000
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**BHUIYAN, S****Functional Significance and Regulation of cMyBP-C Binding to Actin**

American Heart Association

11POST7590181	07/01/11-06/30/13	\$45,000
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**BLAXALL B****A Role for Mena in the Heart**

National Institutes of Health

R01 HL 08988	02/22/13-01/31/14	\$87,612
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**Extracellular Matrix Remodeling and Fibrosis**

National Institutes of Health(University of Rochester)

R01 GM 097347	08/15/12-11/30/15	\$45,991
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**Small Molecule Targeting of MLK3 for Heart Failure**

American Heart Association

13IRG14670079	01/01/13-12/31/14	\$68,183
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**Targeting of B-AR/GBy Signaling in the Heart with Small Molecules**

National Institutes of Health

R01 HL 091475	05/31/13-05/30/14	\$235,620
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**DOHN, T****Training in Cardiovascular Biology**

National Institutes of Health(University of Cincinnati)

T32 HL 007382	01/01/13-12/31/13	\$14,688
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**GUPTA, M****Role of Myosin Binding Protein-C Phosphorylation in Cardiac Function**

American Heart Association

11POST7590026 07/01/11-06/30/13 \$45,000

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**KHUCHUA, Z****A Mouse Model of Barth Syndrome, a Mitochondrial Cardiolipin Disorder**

National Institutes of Health

R01 HL 108867 07/07/11-03/31/15 \$238,000

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**KWONG, J****Defining the Role of SLC25a35 as a Regulator of the Mitochondrial Permeability Transition Pore and Cardiomyocyte Death**

American Heart Association

12POSTDOC11950000 07/01/12-06/30/14 \$47,000

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**LEE, M****Differential Twist1 Dimer Function and Gene Regulation in Valve Progenitor Cells**

American Heart Association

11PRE7240023 07/01/11-06/30/13 \$23,000

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**MCLENDON, P****The Role of Impaired Protein Degradation Pathways in CryABR120G-Mediated Desmin-R**

National Institutes of Health

F32 HL 112558 01/11/12-03/11/13 \$8,990

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**MOLKENTIN, J****Ca Signaling Domains Programming Cardiac Hypertrophy**

National Institutes of Health(The Regents of the University of California)

P01 HL 080101 08/01/11-05/31/16 \$271,987

**Cardiac Hypertrophic Intracellular Signaling Pathways**

National Institutes of Health

R01 HL 062927 02/01/09-12/31/13 \$222,750

**Improving Cardiac Function after Myocardial Infarction**

National Institutes of Health(Temple University School of Medicine)

P01 HL 108806 05/07/12-03/31/17 \$255,000

**Molecular Pathways Controlling Cardiac Gene Expression**

National Institutes of Health

R37 HL 060562 07/01/08-06/30/13 \$247,500

**Mechanisms of TGF Regulated Fibrosis in Muscular Dystrophy**

The University of Chicago



P01 NS 072027	07/01/11-06/30/16	\$250,000
<b>Thrombospondin 4 Regulates Adaptive ER Stress Response</b>		
National Institutes of Health		
R01 HL 105924	01/01/11-12/31/14	\$312,920
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<b>RAJAN, S</b>		
<b>Translational and Post-translational Regulation of Tropomyosin in Normal and Cardiomyopathic Hearts</b>		
American Heart Association		
11SDG4980029	08/01/11-12/31/14	\$70,000
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<b>ROBBINS , J</b>		
<b>A TG Rabbit Model for the Functional Effects of FHC Mutations in B-Cardiac Myosin</b>		
National Institutes of Health(University of Vermont)		
R21 HL 111847	07/15/12-06/30/14	\$9,600
<b>Cardiac Myosin Binding Protein-C: Structure, Function and Regulation</b>		
National Institutes of Health(University of Vermont)		
P01 HL 059408	02/01/10-01/31/15	\$307,959
<b>Proteotoxicity: An Unappreciated Mechanism of Heart Disease</b>		
Fondation Leducq		
	10/01/11-09/30/16	\$247,636
<b>Signaling Processes Underlying Cardiovascular Function</b>		
National Institutes of Health		
P01 HL 069779	01/11/08-12/31/12	\$1,219,260
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<b>SCHULZ, E</b>		
<b>Training in Cardiovascular Biology</b>		
National Institutes of Health(University of Cincinnati)		
T32 HL 007382	02/01/13-01/31/14	\$22,904
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<b>SENGUPTA, A</b>		
<b>FOXO Function in Cardiomyocytes During Development and Disease</b>		
American Heart Association		
11POST7210026	07/01/11-06/30/13	\$45,000
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<b>TARIQ, M</b>		
<b>Identification of Novel Human X-Linked Heterotaxy Genes</b>		
American Heart Association		
12POSTDOC10370002	07/01/12-06/30/14	\$45,000
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<b>VAN BERLO, J</b>		
<b>Functional Relevance and Extent of Endogenous Cardiac Regeneration by C-Kit Positive Stem Cells</b>		
National Institutes of Health		

K99 HL 112852	06/04/12-03/31/17	\$121,660
<b>WARE, S</b>		
<b>Genetic and Epigenetic Mechanisms in Cardiomyopathy</b>		
American Heart Association		
13EIA13460001	01/01/13-12/31/17	\$72,727
<b>Genetic Registry for Pediatric Heart Disease: The CCVM Consortium</b>		
March of Dimes National		
	06/01/13-05/31/16	\$65,509
<b>Genotype-Phenotype Association in Pediatric Cardimyopathy</b>		
National Institutes of Health(University of Miami)		
R01 HL 111459	04/01/12-03/31/16	\$987,826
<b>Uncovering Novel Genetic Causes and Risk in Congenital Heart Disease Patients</b>		
Burroughs Wellcome Foundation(University of Cincinnati)		
BWF #1008496	07/01/09-06/30/15	\$150,000
<b>WAXMAN, J</b>		
<b>Coup-tf Dependent Mechanisms of Ventricular and Hemangioblast Specification</b>		
National Institutes of Health		
R01 HL 112893	01/15/13-02/28/18	\$225,000
<b>Illumination of Mechanisms Controlling Atrial Cell Formation</b>		
March of Dimes National		
5-FY11-88	02/01/11-01/31/13	\$69,327
<b>WIRRIE, E</b>		
<b>The Role of COX2 in the Progression of Human Calcific Aortic Valve Disease</b>		
National Institutes of Health		
F32 HL 110390	07/01/12-06/30/15	\$52,190
<b>YUTZEY, K</b>		
<b>Cell Signaling Mechanisms of Calcific Aortic Valve Disease</b>		
National Institutes of Health		
R01 HL 114682	08/23/12-06/30/16	\$250,000
<b>Student Undergraduate Research Fellowship</b>		
American Heart Association		
12UFEL9990000	02/01/12-01/31/14	\$20,000
<b>Wnt Signaling in Heart Valve Development and Disease</b>		
National Institutes of Health		
R01 HL 094319	04/15/12-02/28/16	\$238,000
<b>Twist 1 Regulation of Valve Progenitors</b>		
National Institutes of Health		

R01 HL 082716

07/01/2010-05/31/2015

\$235,620

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**Current Year Direct**      **\$6,919,459**

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**Total**      **\$6,919,459**