Molecular Cardiovascular Biology

Division Photo

First Row: J. James, J. Robbins, S. Ware; Second Row: Z. Khuchua, J. Molkentin, J. Gulick, S. Sadayappan, K. Yutzey.

Division Data Summary

Research and Training Details	
Number of Faculty	11
Number of Joint Appointment Faculty	1
Number of Research Fellows	20
Number of Research Students	11
Number of Support Personnel	2
Direct Annual Grant Support	$4,991,096
Peer Reviewed Publications	40

Significant Publications

Sadayappan S, Gulick J, Klevitsky R, Lorenz JN, Sargent M, Molkentin JD, Robbins, J. Cardiac myosin binding protein-C phosphorylation in a β-myosin heavy chain background. Circulation. 2009 Mar 10;119(9):1253-62.

cMyBP-C phosphorylation is necessary for basal myocardial function in the β-MyHC background and can preserve function after ischemia/reperfusion injury. Our studies justify exploration of cMyBP-C phosphorylation as a therapeutic target in the human heart.

Liu Q, Busby JC, Molkentin JD. Interaction between TAK1-TAB1-TAB2 and RCAN1-calcineurin defines a signalling nodal control point. Nat Cell Biol. 2009 Feb;11(2):154-61.

This publication identified a novel interaction between the calcineurin and the TAK1 signaling pathways in the heart as an integrated circuit for controlling hypertrophy and response to insults that cause heart failure.

Wu X, Chang B, Blair NS, Sargent M, York AJ, Robbins J, Shull GE, Molkentin JD. Plasma membrane Ca2+-

ATPase isoform 4 antagonizes cardiac hypertrophy in association with calcineurin inhibition in rodents. J Clin Invest. 2009 Apr;119(4):976-85.

This publication showed that a local pool of subsarcolemmal calcium regulates calcineurin-NFAT signaling in the heart. The calcium pump PMCA4b regulates this subsarcolemmal pool of calcium and can secondarily impact calcineurin signaling and the hypertrophic response, altering the sensitivity of mouse models to heart failure.

Mohapatra B, Casey B, Li H, Ho-Dawson T, Smith L, Fernbach SD, Molinari L, Niesh SR, Jefferies JL, Craigen WJ, Towbin JA, Belmont JW, Ware SM. Identification and functional characterization of NODAL rare variants in heterotaxy and isolated cardiovascular malformations. Hum Mol Genet. 2009 Mar 1;18(5):861-71.

This paper is the first to identify and characterize mutations in NODAL, a TGF-beta ligand, in human congenital heart disease.

Krenz M, Gulick J, Osinska HE, Colbert MC, Molkentin JD, Robbins J. Role of ERK1/2 signaling in congenital valve malformations in Noonan syndrome. Proc Natl Acad Sci U S A. 2008 Dec 2;105(48):18930-5.

Demonstrated the necessity of a particular kinase in valve development.

Division Highlights

Jeffrey Robbins, PhD & James Gulick, MS

Demonstrated the importance of altered signaling in the development of valve disease.

Jeffrey Robbins, PhD

Demonstrated the direct linkage between cardiomyocyte accumulations of pre-amyloid oligomers and the development of heart failure.

Jeffrey Robbins, PhD

Showed that altered visco-elastic properties of the myocyte as a result of misfolded proteins can lead to chamber stiffness in the heart.

Jeffrey Robbins, PhD

Showed that altered signal pathways in a single progenitor cell type is responsible for developmental abnormalities in both the heart and skull.

Jeffery Molkentin, PhD

Presented the 2008 Thomas W. Smith Memorial Lecture—Protein Kinase C α as a Novel Therapeutic Target for Treating Heart Failure—to the American Heart Association Scientific Sessions meeting in New Orleans.

Division Collaboration

Collaboration with Experimental Hematology

Collaborating Faculty: Yi Zheng, PhD

The Molkentin Lab used Dr. Zheng's Cdc42 gene targeted mice in a study published in the *Journal of Clinical Investigation*.

Collaboration with Human Genetics

Collaborating Faculty: Teresa Smolarek, PhD

Dr. Smolarek's Cytogenetics Lab helped Dr. Ware's lab identify novel genetic causes of congenital heart defects.

Faculty Members

Jeffrey Robbins, PhD, Professor ; *Associate Chair of the CCHMC; Executive Co-Director, The Heart Institute; Endowed Chair for Molecular Cardiovascular Biology*

Research Interests: Mechanisms of Normal and Abnormal Cardiovascular function

Christopher Baines, PhD, Research Instructor

James Gulick, MS, Research Instructor

Research Interests: Molecular interactions between certain cardiac contractile proteins and how such interactions can be altered by mutations that are associated with cardiomyopathies

Jeanne James, MD, Research Associate Professor

Zaza Khuchua, PhD, Research Associate Professor
Research Interests: Congenital cardiac disorders caused by inborn errors in mitochondrial energy-producing enzymes, and model systems to study molecular mechanisms of these diseases

Maike Krenz, MD, Research Instructor

Jeffery Molkentin, PhD, Professor ; *Howard Hughes Medical Institute Investigator*
Research Interests: Molecular pathways that underlie heart disease

Hiroyuki Nakayama, MD, PhD, Research Instructor
Research Interests: Role of calcium in cardiac pathogenesis

Sakthivel Sadayappan, PhD, Research Instructor
Research Interests: Effects of muscle protein structure on heart function and how certain proteins protect the heart from injury

Stephanie Ware, MD, PhD, Assistant Professor ; *Director of Research and Development, Associate Medical Director, The Heart Institute Diagnostic Laboratory*
Research Interests: Genetics of pediatric heart disease

Katherine Yutzey, PhD, Professor ; *Director Molecular and Developmental Graduate Program*
Research Interests: Heart development and disease mechanisms

Joint Appointment Faculty Members

D. Woodrow Benson, MD, PhD, Professor
Cardiology

Trainees

- **Federica Accornero, PhD,** University of Turin
- **Mannix Auger-Messier, PhD,** University of Sherbrooke, Canada
- **Caitlin Braitsch, BS,** Xavier University
- **Matthew Benard, BS,** St. Lawrence University
- **Ashley Cast, BA,** Augustana College
- **Santanu Chakraborty, PhD,** Miami University
- **Michelle Combs, BS,** Quincy University
- **Robert Nathan Correll, PhD,** University of Kentucky
- **Jennifer Davis, PhD,** Univeristy of Michigan, Ann Arbor
- **Petra Eder, PhD,** University of Graz, Austria
- **John Elrod, PhD,** Albert Einstein College of Medicine
- **Ambrose Goonasekera, PhD,** University of Rochester
- **Joerg Heineke, MD,** Hannover Medical School, Germany
- **Mary Horn, MS,** Ball State University
- **Shawna Hottinger, BS,** Marshall University
- **Jason Karch, BA,** Dakota Wesleyan University
- **Izhak Kehat, PhD,** Technion-Israel Institute of Technology, Isreal
- **Jennifer Kwong, PhD,** Weill Medical College of Cornell University
- **Qinghang Liu, MD, PhD,** University of Tennessee Health Sciences Center
- **Jeffrey Lynch, PhD,** University of Alberta, Canada
- **Marjorie Maillet, PhD,** University of Paris XI, France
- **Timothy Mead, BS,** University of Dayton
- **Douglas Millay, PhD,** University of Cincinnati
- **Arunima Sengupta, PhD,** Miami University
- **Mardi Sutherland, BS,** University of Massachusetts, Boston
- **David Terrell, BS,** Texas State University
- **Anup Tilak, PhD,** Industrial Toxicology Research Centre, India
- **Jop van Berlo, MD, PhD,** University Hospital Maastricht, Netherlands
- **Shuyun Wang, MD, PhD,** Shandong University, China

- **Erin Wissing, BA,** DePauw University
- **Xu Wu, MD, PhD,** Loyola University Medical Center

Significant Accomplishments

Mechanisms of Congenital Heart Disease

Jeffrey Robbins, PhD, Professor and Director of MCB, was elected a Fellow of The Graduate School at the University of Cincinnati this year. He received the Rieveschel Award for Distinguished Scientific Research and the Daniel Drake Medal, the highest honor that the College of Medicine awards its most distinguished faculty. Dr. Robbins was also appointed Associate Editor of the premier basic science cardiovascular journal, *Circulation Research*.

The Robbins laboratory continues to use novel, genetically engineered models to study pediatric cardiovascular disease. In a pair of seminal studies published in *Proceedings of the National Academy of Sciences, USA*, Dr. Robbins and his colleagues showed the basis of the development of congenital heart abnormalities and the accompanying craniofacial defects as a result of altered developmental signaling due to the mutations in a single gene. Too little of the gene/protein SHP2 interferes with the normal developmental activity of what are called neural crest cells. These cells, which occur very early in embryonic development, migrate to specific regions of the embryo. While doing so, the cells are supposed to differentiate and give rise to certain nerve tissues, craniofacial bones or smooth muscle tissue of the heart. The findings show that a deficiency of SHP2 in neural crest cells results in a failure of cell differentiation at diverse sites in the developing embryo, leading to anatomical and functional deficits so severe that it precludes viability of the developing fetus.

The findings from this study can be used to now develop specific drugs that could target the affected pathway, leading to treatment of heart and cranial-facial malformations. Abnormal heart development is the most common human birth defect, affecting about 1 percent of newborns. The team will now focus on exploring the exact alterations in neural crest cell migration, expansion and differentiation that contribute to birth defects of other organ systems.

Signals for Heart Failure

Jeffery D. Molkentin, PhD, a professor in MCB, was named one of 56 new Howard Hughes Medical Institute (HHMI) Investigators. The award will place Dr. Molkentin among an elite group of the nation's most promising scientists who are challenged to extend the boundaries of science by pursuing bold and creative research. His team studies the signaling mechanisms that control muscle cell growth, differentiation and death. This work is creating new knowledge about basic molecular processes that influence cardiac and skeletal development as well as diseases like muscular dystrophy and heart failure.

The Molkentin laboratory continues to investigate the genes and pathways that underlie heart failure and how the chambers in the heart change shape during disease. The heart typically enlarges in response to many different disease states as a way of maintaining proper pump function. This process of heart enlargement has been studied by scientists for decades, because it typically leads to other more serious disease states, including death of the patient. In collaboration with Dr. Yi Zheng in the Division of Experimental Hematology, the Molkentin laboratory uncovered a novel gene that controls how the heart enlarges in response to disease. Mice lacking this gene showed much greater cardiac enlargement and more rapid progression to heart failure when challenged with different disease-inducing insults. The results of this study were recently published in the prestigious medical journal, Journal of Clinical Investigation. This study suggests that drugs used to modulate this novel disease modifying gene, Cdc42, might be advantageous in treating select human cardiovascular abnormalities.

Bench to Bedside

Stephanie Ware, MD, PhD, was awarded the prestigious Burroughs Wellcome Fund Clinical Scientist Award in Translational Medicine grant to help bridge bench to bedside research. The $750,000 grant (over five years) will allow Ware, a physician-scientist at Cincinnati Children's Heart Institute, to explore the genetic causes of heterotaxy and how it relates to congenital heart defects. The Burroughs Wellcome Fund Award was exceptionally competitive this year, and the grant is one of only four awarded nationally.

Heterotaxy is the name given to multiple birth defects that occur when the body fails to establish a proper right and left side during early formation. This can affect the heart and other organs. As the heart forms, it follows a blueprint that requires positional information. The heart is particularly sensitive to not having information about left and right. The heart defects in heterotaxy are some of the most complicated cardiologists see. A child's overall prognosis is determined by the severity of the heart defect, and children with heterotaxy frequently have a worse prognosis than other children with similar heart defects. Heterotaxy is present in about three percent of children with congenital heart defects, but loss of

left- and right-sided information causes other heart defects as well. The precise genetic cause is identified in less than 10 percent of children with heterotaxy. The Burroughs Wellcome grant will use a unique heterotaxy patient sample set to perform genetic analyses to identify new candidates for this condition. Through a combination of human genetics and developmental biology, new genetic changes in patients with heterotaxy will be identified, validated, and then tested functionally in animal models.

Division Publications

1. Gulick J, Robbins J. Cell-type-specific transgenesis in the mouse. *Methods Mol Biol.* 2009; 561: 91-104.
2. Acehan D, Khuchua Z, Houtkooper RH, Malhotra A, Kaufman J, Vaz FM, Ren M, Rockman HA, Stokes DL, Schlame M. Distinct effects of tafazzin deletion in differentiated and undifferentiated mitochondria. *Mitochondrion.* 2009; 9: 86-95.
3. Wu X, Chang B, Blair NS, Sargent M, York AJ, Robbins J, Shull GE, Molkentin JD. Plasma membrane Ca2+-ATPase isoform 4 antagonizes cardiac hypertrophy in association with calcineurin inhibition in rodents. *J Clin Invest.* 2009; 119: 976-85.
4. Maloyan A, Osinska H, Lammerding J, Lee RT, Cingolani OH, Kass DA, Lorenz JN, Robbins J. Biochemical and mechanical dysfunction in a mouse model of desmin-related myopathy. *Circ Res.* 2009; 104: 1021-8.
5. Nicolaou P, Rodriguez P, Ren X, Zhou X, Qian J, Sadayappan S, Mitton B, Pathak A, Robbins J, Hajjar RJ, Jones K, Kranias EG. Inducible expression of active protein phosphatase-1 inhibitor-1 enhances basal cardiac function and protects against ischemia/reperfusion injury. *Circ Res.* 2009; 104: 1012-20.
6. Dhandapany PS, Sadayappan S, Xue Y, Powell GT, Rani DS, Nallari P, Rai TS, Khullar M, Soares P, Bahl A, Tharkan JM, Vaideeswar P, Rathinavel A, Narasimhan C, Ayapati DR, Ayub Q, Mehdi SQ, Oppenheimer S, Richards MB, Price AL, Patterson N, Reich D, Singh L, Tyler-Smith C, Thangaraj K. A common MYBPC3 (cardiac myosin binding protein C) variant associated with cardiomyopathies in South Asia. *Nat Genet.* 2009; 41: 187-91.
7. Konopatskaya O, Gilio K, Harper MT, Zhao Y, Cosemans JM, Karim ZA, Whiteheart SW, Molkentin JD, Verkade P, Watson SP, Heemskerk JW, Poole AW. PKCalpha regulates platelet granule secretion and thrombus formation in mice. *J Clin Invest.* 2009; 119: 399-407.
8. Liu Q, Busby JC, Molkentin JD. Interaction between TAK1-TAB1-TAB2 and RCAN1-calcineurin defines a signalling nodal control point. *Nat Cell Biol.* 2009; 11: 154-61.
9. Molkentin JD, Robbins J. With great power comes great responsibility: using mouse genetics to study cardiac hypertrophy and failure. *J Mol Cell Cardiol.* 2009; 46: 130-6.
10. Wang S, Ware SM. Use of FOXJ1CreER2T mice for inducible deletion of embryonic node gene expression. *Genesis.* 2009; 47: 132-6.
11. Hsu S, Nagayama T, Koitabashi N, Zhang M, Zhou L, Bedja D, Gabrielson KL, Molkentin JD, Kass DA, Takimoto E. Phosphodiesterase 5 inhibition blocks pressure overload-induced cardiac hypertrophy independent of the calcineurin pathway. *Cardiovasc Res.* 2009; 81: 301-9.
12. Carneiro LA, Travassos LH, Soares F, Tattoli I, Magalhaes JG, Bozza MT, Plotkowski MC, Sansonetti PJ, Molkentin JD, Philpott DJ, Girardin SE. Shigella induces mitochondrial dysfunction and cell death in nonmyleoid cells. *Cell Host Microbe.* 2009; 5: 123-36.
13. Scruggs SB, Hinken AC, Thawornkaiwong A, Robbins J, Walker LA, de Tombe PP, Geenen DL, Buttrick PM, Solaro RJ. Ablation of ventricular myosin regulatory light chain phosphorylation in mice causes cardiac dysfunction in situ and affects neighboring myofilament protein phosphorylation. *J Biol Chem.* 2009; 284: 5097-106.
14. Diwan A, Matkovich SJ, Yuan Q, Zhao W, Yatani A, Brown JH, Molkentin JD, Kranias EG, Dorn GW, 2nd. Endoplasmic reticulum-mitochondria crosstalk in NIX-mediated murine cell death. *J Clin Invest.* 2009; 119: 203-12.
15. Lorts A, Schwanekamp JA, Elrod JW, Sargent MA, Molkentin JD. Genetic manipulation of periostin expression in the heart does not affect myocyte content, cell cycle activity, or cardiac repair. *Circ Res.* 2009; 104: e1-7.
16. Yang YJ, Chen W, Edgar A, Li B, Molkentin JD, Berman JN, Lin TJ. Rcan1 negatively regulates Fc epsilonRI-mediated signaling and mast cell function. *J Exp Med.* 2009; 206: 195-207.
17. Donaldson C, Eder S, Baker C, Aronovitz MJ, Weiss AD, Hall-Porter M, Wang F, Ackerman A, Karas RH, Molkentin JD, Patten RD. Estrogen attenuates left ventricular and cardiomyocyte hypertrophy by an estrogen receptor-dependent pathway that increases calcineurin degradation. *Circ Res.* 2009; 104: 265-75, 11p following 275.
18. Baines CP, Molkentin JD. Adenine nucleotide translocase-1 induces cardiomyocyte death through upregulation of the pro-apoptotic protein Bax. *J Mol Cell Cardiol.* 2009; 46: 969-77.
19. Waggoner JR, Ginsburg KS, Mitton B, Haghighi K, Robbins J, Bers DM, Kranias EG. Phospholamban overexpression in rabbit ventricular myocytes does not alter sarcoplasmic reticulum Ca transport. *Am J*

Physiol Heart Circ Physiol. 2009; 296: H698-703.

20. Mohapatra B, Casey B, Li H, Ho-Dawson T, Smith L, Fernbach SD, Molinari L, Niesh SR, Jefferies JL, Craigen WJ, Towbin JA, Belmont JW, Ware SM. Identification and functional characterization of NODAL rare variants in heterotaxy and isolated cardiovascular malformations. *Hum Mol Genet.* 2009; 18: 861-71.
21. Sadayappan S, Gulick J, Klevitsky R, Lorenz JN, Sargent M, Molkentin JD, Robbins J. Cardiac myosin binding protein-C phosphorylation in a {beta}-myosin heavy chain background. *Circulation.* 2009; 119: 1253-62.
22. Kogan JM, Miller E, Ware SM. High resolution SNP based microarray mapping of mosaic supernumerary marker chromosomes 13 and 17: delineating novel loci for apraxia. *Am J Med Genet A.* 2009; 149A: 887-93.
23. Ware SM, El-Hassan N, Kahler SG, Zhang Q, Ma YW, Miller E, Wong B, Spicer RL, Craigen WJ, Kozel BA, Grange DK, Wong LJ. Infantile cardiomyopathy caused by a mutation in the overlapping region of mitochondrial ATPase 6 and 8 genes. *J Med Genet.* 2009; 46: 308-14.
24. Zhong H, Sia GM, Sato TR, Gray NW, Mao T, Khuchua Z, Huganir RL, Svoboda K. Subcellular dynamics of type II PKA in neurons. *Neuron.* 2009; 62: 363-74.
25. Ito K, Akazawa H, Tamagawa M, Furukawa K, Ogawa W, Yasuda N, Kudo Y, Liao CH, Yamamoto R, Sato T, Molkentin JD, Kasuga M, Noda T, Nakaya H, Komuro I. PDK1 coordinates survival pathways and beta-adrenergic response in the heart. *Proc Natl Acad Sci U S A.* 2009; 106: 8689-94.
26. Fuller SJ, Pikkarainen S, Tham el L, Cullingford TE, Molkentin JD, Cornils H, Hergovich A, Hemmings BA, Clerk A, Sugden PH. Nuclear Dbf2-related protein kinases (NDRs) in isolated cardiac myocytes and the myocardium: activation by cellular stresses and by phosphoprotein serine-/threonine-phosphatase inhibitors. *Cell Signal.* 2008; 20: 1564-77.
27. Moga MA, Nakamura T, Robbins J. Genetic approaches for changing the heart and dissecting complex syndromes. *J Mol Cell Cardiol.* 2008; 45: 148-55.
28. Pattison JS, Robbins J. Protein misfolding and cardiac disease: establishing cause and effect. *Autophagy.* 2008; 4: 821-3.
29. Conway SJ, Molkentin JD. Periostin as a heterofunctional regulator of cardiac development and disease. *Curr Genomics.* 2008; 9: 548-55.
30. Krenz M, Gulick J, Osinska HE, Colbert MC, Molkentin JD, Robbins J. Role of ERK1/2 signaling in congenital valve malformations in Noonan syndrome. *Proc Natl Acad Sci U S A.* 2008; 105: 18930-5.
31. Lowey S, Lesko LM, Rovner AS, Hodges AR, White SL, Low RB, Rincon M, Gulick J, Robbins J. Functional effects of the hypertrophic cardiomyopathy R403Q mutation are different in an alpha- or beta-myosin heavy chain backbone. *J Biol Chem.* 2008; 283: 20579-89.
32. Jaleel N, Nakayama H, Chen X, Kubo H, MacDonnell S, Zhang H, Berretta R, Robbins J, Cribbs L, Molkentin JD, Houser SR. Ca2+ influx through T- and L-type Ca2+ channels have different effects on myocyte contractility and induce unique cardiac phenotypes. *Circ Res.* 2008; 103: 1109-19.
33. Maillet M, Purcell NH, Sargent MA, York AJ, Bueno OF, Molkentin JD. DUSP6 (MKP3) null mice show enhanced ERK1/2 phosphorylation at baseline and increased myocyte proliferation in the heart affecting disease susceptibility. *J Biol Chem.* 2008; 283: 31246-55.
34. Du H, Guo L, Fang F, Chen D, Sosunov AA, McKhann GM, Yan Y, Wang C, Zhang H, Molkentin JD, Gunn-Moore FJ, Vonsattel JP, Arancio O, Chen JX, Yan SD. Cyclophilin D deficiency attenuates mitochondrial and neuronal perturbation and ameliorates learning and memory in Alzheimer's disease. *Nat Med.* 2008; 14: 1097-105.
35. Tchekneva EE, Khuchua Z, Davis LS, Kadkina V, Dunn SR, Bachman S, Ishibashi K, Rinchik EM, Harris RC, Dikov MM, Breyer MD. Single amino acid substitution in aquaporin 11 causes renal failure. *J Am Soc Nephrol.* 2008; 19: 1955-64.
36. Yano N, Tseng A, Zhao TC, Robbins J, Padbury JF, Tseng YT. Temporally controlled overexpression of cardiac-specific PI3Kalpha induces enhanced myocardial contractility--a new transgenic model. *Am J Physiol Heart Circ Physiol.* 2008; 295: H1690-4.
37. Boni A, Urbanek K, Nascimbene A, Hosoda T, Zheng H, Delucchi F, Amano K, Gonzalez A, Vitale S, Ojaimi C, Rizzi R, Bolli R, Yutzey KE, Rota M, Kajstura J, Anversa P, Leri A. Notch1 regulates the fate of cardiac progenitor cells. *Proc Natl Acad Sci U S A.* 2008; 105: 15529-34.
38. da Costa Martins PA, Bourajjaj M, Gladka M, Kortland M, van Oort RJ, Pinto YM, Molkentin JD, De Windt LJ. Conditional dicer gene deletion in the postnatal myocardium provokes spontaneous cardiac remodeling. *Circulation.* 2008; 118: 1567-76.
39. Nieves-Cintron M, Amberg GC, Navedo MF, Molkentin JD, Santana LF. The control of Ca2+ influx and NFATc3 signaling in arterial smooth muscle during hypertension. *Proc Natl Acad Sci U S A.* 2008; 105: 15623-8.
40. Chakraborty S, Cheek J, Sakthivel B, Aronow BJ, Yutzey KE. Shared gene expression profiles in developing heart

valves and osteoblast progenitor cells. *Physiol Genomics.* 2008; 35: 75-85.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards — Annual Direct / Project Period Direct

BAINES, C

Mechanisms of Mitochondrial-Dependent Death
American Heart Association - National
SDG0635134N — 07/01/06 - 06/30/10 — $59,091 / $236,634

Identifying Novel Components of the Cardiac Necrotic Program
National Institutes of Health
R21 HL 092327 — 07/01/08 - 11/22/08 — $29,000 / $29,000

BEDARD, J

Genetic and Molecular Roles of a Novel ZIC3 Isoform in Cardiovascular Development
American Heart Association - Ohio
PF0725539B — 07/01/07 - 06/30/09 — $44,000 / $86,000

CHAKRABORTY, S

Twist1 and Tbx20 Function in Heart Valve Development
American Heart Association - Ohio
PF0825627D — 07/01/08 - 06/30/10 — $43,000 / $88,000

COMBS, M

NFATc1 Regulation of Extracellular Matrix Remodeling
American Heart Association - Ohio
PF0715107B — 07/01/07 - 06/30/09 — $21,000 / $42,000

DAVIS, J

The Non-Hypertrophic Role of Calcineurin in Regulating Cardiac Structure-Function
National Institutes of Health
F32 HL 095353 — 12/15/08 - 12/14/11 — $48,826 / $149,750

ELROD, J

Defining the Role of Necrotic Cell Death in the Progression of Heart Failure
National Institutes of Health
F32 HL 092737 — 07/25/08 - 07/24/10 — $46,826 / $96,472

GOONASEKERA, A

Role of Cardiac L-type Calcium Channels in the Pathophysiology of Cardiac Hypertrophy and Heart Failure
American Heart Association - Ohio
PF0825652D — 07/01/08 - 06/30/10 — $43,000 / $88,000

KRENZ, M

Defective Valvulogenesis in Noonan Syndrome
American Heart Association - National
SDG0635472N — 07/01/06 - 06/30/10 — $59,091 / $236,364

MOLKENTIN, J

Genetic And Molecular Signaling In Heart Failure - Project 4
National Institutes of Health (University of Cincinnati)
P50 HL 077101 — 02/22/05 - 12/31/09 — $418,368 / $1,451,722

Genetic And Molecular Signaling In Heart Failure - Core D
National Institutes of Health (University of Cincinnati)
P50 HL 077101 — 02/22/05 - 12/31/09 — $300,495 / $1,451,722

Mitochondrial Regulated Cardiac Myocyte Death
National Institutes of Health
R01 HL 081104 — 08/01/05 - 07/31/09 — $237,045 / $1,000,000

Adaptive and Maladaptive Signaling in Cardiac Growth and Regeneration
Fondation Leducq
10/01/05 - 09/30/10 $296,584 / $1,174,472

Calcium as a Molecular Signal in the Heart
National Institutes of Health (Temple University School of Medicine)
R01 HL 089312 08/15/07 - 06/30/12 $244,186 / $1,245,845

Role of Calcium Influx in Miyoshi Myopathy and Other Forms of Muscular Dystrophy
Jain Foundation, Inc
05/01/07 - 04/30/10 $69,986 / $210,000

Cardiac Hypertrophic Intracellular Signaling Pathways
National Institutes of Health
R01 HL 062927 02/01/09 - 12/31/13 $250,000 / $1,250,000

Molecular Pathways Controlling Cardiac Gene Expression
National Institutes of Health
R37 HL 060562 07/01/08 - 06/30/13 $250,000 / $1,250,000

PATTISON, S

The Role of Apoptosis in CRTABR120G Heart Failure
National Institutes of Health
F32 HL 087478 11/18/07 - 11/17/09 $17,491 / $66,401

ROBBINS, J

Genetic and Molecular Signaling in Heart Failure
National Institutes of Health (University of Cincinnati)
P50 HL 077101 02/22/05 - 12/31/09 $365,577 / $1,837,616

Molecular Basis of Dilated and Hypertrophic Cardiomyopathy
National Institutes of Health (University of Vermont)
P01 HL 059408 12/01/04 - 11/30/09 $57,845 / $337,949

Signaling Processes Underlying Cardiovascular Function
National Institutes of Health
P01 HL 069779 01/11/08 - 12/31/12 $1,231,576 / $6,163,688

Cardiomyocyte Toxicity and Heart Failure in Desmin-Related Cardiomyopathy
National Institutes of Health
R01 HL 087862 02/01/08 - 01/31/11 $150,000 / $400,000

Investigation of Amyloid Oligomer in Pediatric Cardiovascular Disease
National Research Institution for Child Health and Development
06/03/07 - 03/31/10 $43,359 / $79,861

International Society for Heart Research 2008
National Institutes of Health
R13 HL 093737 08/01/08 - 07/31/09 $15,000 / $15,000

SADAYAPPAN, S

Phosphorylation and Function of Cardiac Myosin Binding Protein-C
American Heart Association - National
SDG0830311N 01/01/08 - 12/31/11 $70,000 / $280,000

WANG, S

Determination of Cardiac Looping Role of Zic 3 at the Node
American Heart Association - Ohio
PF0725562B 07/01/07 - 06/30/09 $44,000 / $86,000

WARE, S

Requirement of the Embryonic Node for Cardiac Looping
National Institutes of Health
R01 HL 088639 04/01/07 - 03/31/12 $250,000 / $1,250,000

WU, X

Regulation of Calcineurin and Cardiac Hypertrophy by PMCA4b Overexpression
American Heart Association - Ohio
PF0825563D 07/01/08 - 06/30/10 $43,000 / $88,000

YUTZEY, K

TBX20 Regulation of Heart Valve Development
National Institutes of Health
R01 HL 082716 07/01/06 - 05/31/10 $242,750 / $1,000,000

Current Year Direct	**$4,991,096**
Total	**$ 4,991,096**