

Welcome to Indy!

On behalf of the local organizing committee, we would like to welcome you to the 2007 Weinstein Cardiovascular Development Conference. It is our privilege and honor to host this year's conference. Since it was first convened in 1994, the Weinstein conference has evolved into the preeminent conference for cardiac development worldwide. This annual meeting provides a unique forum in which to share the latest discoveries, novel concepts, and cutting edge technologies for understanding formation of the heart and vasculature. We look forward to another successful gathering in 2007. Two distinguished scientists, Drs. Oliver Smithies and Margaret Kirby, are our keynote speakers. Dr. Smithies has a long and distinguished career in molecular genetics, and is largely credited with the co-development of gene targeting techniques. Dr. Kirby is known world wide for her work on the role of neural crest cells in the genesis of congenital heart defects. This year's keynote speakers were selected to continue the emphasis that the Weinstein Conference places on young scientists; Dr. Smithies and Dr. Kirby are both exemplary role models for young investigators.

The organizing committee received over 200 abstracts, from which 42 were selected for platform presentation. The platform sessions represent a broad spectrum of topics relevant to cardiovascular development. The Weinstein Conference traditionally tries to encourage the participation of young investigators. To attain this goal, platform presentations have been awarded predominantly to postdoctoral fellows and young investigators below the rank of Associate Professor. We have also included four "Workshops" in the program to foster discussion and debate on topical areas of cardiac development. As always, the poster sessions will constitute the main focal point of the conference, and space will be provided so that the posters can be displayed for the entire meeting. We hope that you will have a memorable conference and an inspiring experience in Indianapolis.

2007 Local Organizing Committee:

Simon Conway  
Michael Rubart

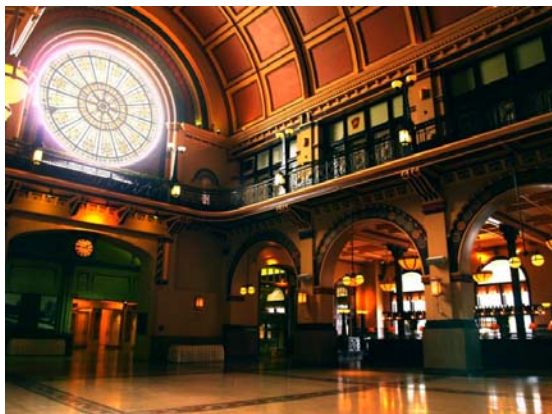
Loren Field  
Weinian Shou

Tony Firulli  
Lei Wei

Mark Payne

Ad hoc members:

Michiko Watanabe Katherine Yutzey



**Venue: The Crowne Plaza and Conference Center at Historic Union Station**

# SCHEDULE AT A GLANCE

## **Thursday, May 10, 2007**

10:00 am – 4:00 pm	Registration	Grand Hall
1:45 pm	Opening remarks	Illinois Street Ballroom
2:00 pm – 3:05 pm	Platform Session I	Illinois Street Ballroom
3:05 pm – 3:20 pm	Break	
3:20 pm – 4:25 pm	Platform Session II	Illinois Street Ballroom
4:25 pm – 4:45 pm	Break	
4:45pm – 6:00 pm	Keynote Presentation by Dr. Oliver Smithies	Illinois Street Ballroom
6:00 pm – 8:00 pm	Buffet Dinner & Poster Session 1 (even) (Open bar 6:00 pm – 10:00pm)	Grand Hall Ballroom
8:00 pm – 9:00 pm	Concurrent Workshops	Edison Rooms

## **Friday, May 11, 2007**

7:30 am – 9:00 am	Breakfast	Grand Hall Ballroom
9:00 am – 10:20 am	Platform Session III	Illinois Street Ballroom
10:20 am – 10:35 am	Break	
10:35 am – 12:00 pm	Platform Session IV	Illinois Street Ballroom
12:00 pm – 1:15 pm	Lunch	Grand Hall Ballroom
1:15 pm – 2:15 pm	Concurrent Workshops	Edison Rooms
2:15 pm – 2:40 pm	Break	
2:40 pm – 4:00 pm	Platform Session V	Illinois Street Ballroom
4:00 pm – 4:30 pm	Break	
4:30 pm – 5:45 pm	Keynote Presentation by Dr. Margaret Kirby	Illinois Street Ballroom
6:00 pm – 8:00 pm	Buffet Dinner & Poster Session 2 (odd) (Open bar 6:00 pm – 10:00pm)	Grand Hall Ballroom

## **Saturday, May 12, 2007**

7:30 am – 9:00 am	Breakfast	Grand Hall Ballroom
9:00 am – 10:20 am	Platform Session VI	Illinois Street Ballroom
10:20 am – 10:35 am	Break	
10:35 am – 12:10 pm	Platform Session VII	
12:15 pm – 1:30 pm	Lunch	Grand Hall Ballroom
1:30 pm – 2:30 pm	Business Meeting NHLBI Workshop	Illinois Street Ballroom Edison Room
2:30 pm – 2:45 pm	Break	
2:45 pm – 4:05 pm	Platform Session VIII	Illinois Street Ballroom
4:05 pm – 4:30 pm	Break	
4:30 pm – 5:35 pm	Platform Session IX	Illinois Street Ballroom
6:00 pm – 10:00 pm	Banquet	Grand Hall Ballroom

# FULL CONFERENCE SCHEDULE

(Note: presenting author is underlined>

## Thursday, May 10, 2007

<b>10:00 am - 4:00 pm</b>	<b>Registration</b>	<b>Grand Hall</b>
<b>1:45 pm</b>	<b>Opening remarks</b>	<b>Illinois Street Ballroom</b>
<b>2:00 pm – 3:05 pm</b>	<b><u>Platform Session I</u></b>	<b>Illinois Street Ballroom</b>
	<b>Cardiomyocyte cell cycle regulation</b>	
	<i>Chairs: Loren Field, Indiana University and Youngsook Lee, University of Wisconsin Medical School</i>	
2:00 – 2:05	<b>Chair's Introduction</b>	
2:05 – 2:20	<b>Cardiomyocyte and Epicardial Cell Addition during Cardiac Homeostasis in Adult Zebrafish</b>	
	<i>Wills, Airon A; Holdway, Jennifer; Major, Robert J; Poss, Kenneth D Duke University Medical Center, Dept. of Cell Biology</i>	
2:20 – 2:35	<b>FOXO transcription factors in the regulation of cardiac myocyte proliferation and myocardial growth during development</b>	
	<i>Evans-Anderson, Heather J; Alfieri, Christina M; Yutzey, Katherine E Division of Molecular Cardiovascular Biology, Cincinnati Children's Hospital Medical Center</i>	
2:35 – 2:50	<b>3D Visualization of proliferation in cardiac and extracardiac mesoderm</b>	
	<i>van den Berg, G; Soufan, AT; de Boer, PAJ; van den Hoff, MJB; Moorman, AFM Heart Failure Research Centre, Amsterdam, The Netherlands</i>	
2:50 – 3:05	<b>Canonical Wnt Signaling is Required for Mammalian Cardiogenesis by Regulating Cardiac Progenitors</b>	
	<i>Kwon, Chulan; Arnold, Joshua; Taketo, Makoto; Srivastava, Deepak Gladstone Institute, UCSF</i>	
<b>3:05 pm – 3:20 pm</b>	<b>Break</b>	
<b>3:20 pm – 4:25 pm</b>	<b><u>Platform Session II</u></b>	<b>Illinois Street Ballroom</b>
	<b>Myofibrogenesis</b>	
	<i>Chairs: Lei Wei, Indiana University and Jeffrey Robbins, Cincinnati Children's Hospital Medical Center</i>	
3:20 – 3:25	<b>Chair's Introduction</b>	
3:25 – 3:40	<b>MEF2A controls a costameric network of genes in cardiac muscle</b>	
	<i>Naya, Frank J; Brand, Ondra M; Reynolds, Joseph G; McCalmon, Sarah A Department of Biology, Program in Cell and Molecular Biology, Boston University</i>	



### **Cardiomyogenic stem cells during development**

*Moderators: Loren Field, Indiana University and Paul Riley, University College London Institute of Child Health*

8:00 – 8:12 *Dr. Steven Kattman, McEwen Centre for Regenerative Medicine, Toronto*

“ES cell derived cardiovascular progenitor cells”

8:12 – 8:24 *Dr. Nicola Smart, UCL Institute of Child Health, London*

“Epicardial derived vascular progenitors”

8:24 – 8:36 *Dr. Kaomei Guan, Georg-August-University of Goettingen*

“Spermatogonial-derived ES-like cells”

8:36 – 9:00 *Panel Discussion*

**6:00 pm – 10:00 pm**

**Open Bar**

**Grand Hall Ballroom**

### **Friday, May 11, 2007**

**7:30 am – 9:00 am**

**Breakfast**

**Grand Hall Ballroom**

**9:00 am – 10:20 am**

**Platform Session III**

**Illinois Street Ballroom**

**Transcription Factors in Cardiogenesis**

*Chairs: Anthony Firulli, Indiana University and Brian Black, University of California San Francisco*

9:00 – 9:05

**Chair’s Introduction**

9:05 – 9:20

**Histone deacetylase 1(HDAC1) is Essential for Cardiac Development in Zebrafish**

*Zhut, Sigalit (1); Warren, Kerri S (2); Creton, Robbert (3); Kochilas, Lazaros (1)*

(1) Pediatric Cardiology, Department of Pediatrics, Rhode Island Hospital Providence, RI (2) Department of Biology, Roger Williams University, Bristol, RI (3) Department of molecular Biology, Cell Biology and Biochemistry, Brown University, Providence, RI

9:20 – 9:35

**In search for partners of Tbx2 and Tbx3.**

*Boogerd, Kees J; Wong, LY Elaine; Klarenbeek, M; Christoffels, Vincent M; Moorman, Antoon FM; Barnett, Phil*

Heart Failure Research Centre, Academic Medical Centre, Amsterdam, The Netherlands

9:35 – 9:50

**Cooperative function of the transcription factors Nkx2.5 and Mef2c during heart development**

*Vincenz, Joshua W; Firulli, Beth A; Firulli, Anthony B*

Department of Pediatrics, Wells Center for Pediatric Research, James Whitcomb Riley Hospital for Children, Indiana University School of Medicine Cancer Research Institute

9:50 – 10:05

**Nkx Genes Regulate Heart Tube Extension in Zebrafish**

*Targoff, KL; Schell, T; Yelon, D*

Developmental Genetics Program and Department of Cell Biology, Skirball Institute of Biomolecular Medicine, New York University School of Medicine, New York, NY

10:05 – 10:20	<p><b>DPF3 – a new key transcription factor – bridging chromatin remodeling and cardiac muscle specification</b>  <i>Lange, Martin (1); Just, Steffen (2); Kaynak, Bogac (1); Dunkel, Ilona (1); Fischer, Jenny J (1); Toenjes, Martje (1); Krueger, Tammo (1); Toedling, Joern (3); Mebus, Siegrun (4); Grimm, Christina (1); Rottbauer, Wolfgang (2); Sperling, Silke (1)</i>  (1) Max Planck Institute for Molecular Genetics, Berlin, Germany; (2) Ruprecht-Karls-University Heidelberg, Germany; (3) European Bioinformatics Institute, European Molecular Biology Laboratory, Cambridge, UK; (4) German Heart Center Berlin, Germany</p>
<b>10:20 am – 10:35 am</b>	<b>Break</b>
<b>10:35 am – 12:00 pm</b>	<p><b><u>Platform Session IV</u> Illinois Street Ballroom</b>  <b>Vascular Development</b>  <i>Chairs: Michiko Watanabe, Case Western Reserve University and Pat Mastin, NIEHS, National Institutes of Health</i></p>
10:35 – 10:40	<b>Chair’s Introduction</b>
10:40 – 10:55	<p><b>Connexin43 in the Epicardium is Required for Normal Coronary Development</b>  <i>Zhao, Xiao-Qing; Rhee, David Y; Lo, Cecilia W</i>  Laboratory of Developmental Biology, National Heart, Lung and Blood Institute, National Institutes of Health</p>
10:55 – 11:10	<p><b>Endothelial-Specific Ablation of Serum Response Factor Results in Vascular Instability and Embryonic Lethality</b>  <i>Holtz, Mary L; Misra, Ravi P</i>  Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin</p>
11:10 – 11:25	<p><b>VEGF-A164 regulates coronary endothelial proliferation, but not tubulogenesis</b>  <i>Goodwin, Richard L; Nesbitt, Tresa; Yost, Michael J; Potts, Jay D</i>  Department of Cell and Developmental Biology and Anatomy University of South Carolina School of Medicine</p>
11:25 – 11:40	<p><b>Canonical Wnt Signaling in Endothelial Cells is Essential for Central Nervous System Vascularization and Blood-Brain Barrier Development</b>  <i>Stenman, Jan M (1); Carroll, Thomas (2); Rajagopal, Jayaraj (1); McMahon, Andrew P (1)</i>  (1) Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA (2) Department of Internal Medicine (Nephrology) and Molecular Biology, University of Texas Southwestern Medical Center, Dallas, TX</p>
11:40 – 11:55	<p><b>Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on hypoxia-inducible factor-1 alpha during chick cardiogenesis</b>  <i>Wikenheiser, Jamie (1); Walker, Mary K (2); Watanabe, Michiko (1)</i>  (1) Department of Pediatrics, Case Western Reserve University, Cleveland, OH (2) College of Pharmacy, University of New Mexico Health Sciences Center, Albuquerque, NM.</p>
11:55 – 12:00	<b>NIH Presentation, Pat Mastin, NIEHS</b>

<b>12:00 pm – 1:15 pm</b>	<b>Lunch</b>	<b>Grand Hall Ballroom</b>
<b>1:15 pm – 2:15 pm</b>	<b>Concurrent Workshops</b>	<b>Edison Rooms</b>
	<b><u>Cardiac Neural Crest</u></b>	
	<i>Moderators: Simon Conway, Indiana University and Anne Moon, University of Utah</i>	
1:15 – 1:27	<i>Dr. Jon Epstein, University of Pennsylvania</i>	“Cardiac neural crest and interactions with endothelium”
1:27 – 1:39	<i>Dr. Henry Sucov, University of Southern California</i>	“Mouse models of PTA that implicate a defect specifically in AP septation”
1:39 – 1:51	<i>Dr. Rob Gourdie, Medical University of South Carolina</i>	“Cardiac neural crest ablation inhibits compaction and Electrical function of conduction system bundles”
1:51 – 2:15	<i>Panel Discussion</i>	
	<b><u>Imaging Cardiovascular Development and Physiology</u></b>	
	<i>Moderators: Michael Rubart, Indiana University and Igor R. Efimov, Washington University</i>	
1:15 – 1:30	<i>Dr. Igor R. Efimov, Washington University, St. Louis, MO</i>	“Biophotonic Imaging of Embryonic Heart”
1:30 – 1:45	<i>Dr. N. Yvonne Tallini, Cornell University, Ithaca, NY</i>	“Embryonic Murine Heart using a Genetically Encoded Calcium Inhibitor”
1:45 – 2:00	<i>Dr. Mary E. Dickinson, Baylor College of Medicine, Houston, TX</i>	“Imaging fluid motions and heart function in vertebrate embryos”
2:00 – 2:15	<i>Panel Discussion</i>	
<b>2:15 pm – 2:40 pm</b>	<b>Break</b>	
<b>2:40 pm – 4:00 pm</b>	<b><u>Platform Session V</u></b>	<b>Illinois Street Ballroom</b>
	<b>Cardiac Conduction System Development</b>	
	<i>Chairs: Michael Rubart, Indiana University and Luis Polo-Parada, University of Missouri, Columbia</i>	
2:40 – 2:45	<b>Chair’s Introduction</b>	
2:45 – 3:00	<b>Molecular and physiological mechanisms underlying embryonic cardiac rhythmicity in zebrafish</b>	
	<i>Huang, J (1); Langenbacher, A (1); Goldhaber, J (2); Kown, O (3); Chen, J-N (1)</i>	
	(1) Department of Molecular, Cell and Developmental Biology, (2) Department of Physiology, and (3) Department of Chemistry and Biochemistry, University of California, Los Angeles	
3:00 – 3:15	<b>Tbx3 acts as a genetic switch for heart pacemaker formation</b>	
	<i>Hoogaars, Willem MH (1); Brons, Janyne F (1); Engel, Angela (2); Verkerk, Arie O (2); de Lange, Frederik J (1); Bakker, Martijn L (1); Clout, Danielle E (1); Wakker, Vincent (1); Ravesloot, Jan Hindrik (2); Verheijck, E. Etienne (2); Moorman, Antoon FM (1); Christoffels, Vincent M (1)</i>	
	(1) Department of Anatomy & Embryology, (2) Department of Physiology, Heart Failure Research Center, Academic Medical Center, University of Amsterdam, Meibergdreef 15, 1105 AZ, The Netherlands.	

- 3:15 – 3:30      **Genetic analysis of Popdc1 and Popdc2 function in mouse and zebrafish heart**  
*Froese, Alexander (1); Schlüter, Jan (1); Waldeyer, Christoph (2); Kirchmaier, Bettina (1); Breher, Stephanie (1); Liebig, Sonja K (2); Laakmann, Sandra (2); Kirchhof, Paulus (2); Neumann, Joachim (3); Winkler, Christoph (4); Vauti, Franz (5); Arnold, Hans-Henning (5); Fabritz, Larissa (2); Brand, Thomas (1)*  
 (1) Cell- & Developmental Biology, University of Würzburg, Germany, (2) Department of Cardiology and Angiology, University Hospital Münster, Germany, (3) Institute of Pharmacology, University of Halle, Germany, (4) Chemistry I, Biocenter, University of Würzburg, Germany, (5) Cell- & Molecular Biology, TU Braunschweig, Germany
- 3:30 – 3:45      **Clonal analysis of the origin of the mammalian ventricular conduction system**  
*Miquerol, Lucile; Moreno, Natividad; Meilhac, Sigolene; Buckingham, Margaret; Franco, Diego; Kelly, Robert G*  
 Inserm Avenir group, Developmental Biology Institute of Marseilles – Luminy, CNRS UMR6216, Marseille, France
- 3:45 – 4:00      **Deletion of the cardiac L-type calcium channel (CaV1.2) causes embryonic death**  
*Porter, Jr., George A; Sharma, Ashwani*  
 Yale University School of Medicine
- 4:00 pm – 4:30 pm      Break**
- 4:30 pm – 5:45 pm      Keynote Presentation 2      Illinois Street Ballroom**  
 Dr. Margaret Kirby: “How many heart fields does it take to make a heart?”
- 6:00 pm – 8:00 pm      Buffet Dinner and      Grand Hall Ballroom**  
**Poster Session 2** (odd-numbered posters are manned)
- 6:00 pm – 10:00 pm      Open Bar      Grand Hall Ballroom**

**Saturday, May 12, 2007**

- 7:30 am – 9:00 am      Breakfast      Grand Hall Ballroom**
- 9:00 am – 10:20 am      Platform Session VI      Illinois Street Ballroom**  
**Signaling Pathways in Cardiogenesis**  
*Chairs: Weinian Shou, Indiana University and Jim Martin, Texas A & M Health Science Center Institute of Biosciences and Technology*
- 9:00 – 9:05      **Chair’s Introduction**
- 9:05 – 9:20      **Endocardial Brg1 Represses ADAMTS1 to Maintain the Microenvironment for Myocardial Morphogenesis**  
*Stankunas, Kryn (1); Hang, Calvin T (1); Chen, Hanying (2); Tsun, Zhi-Yang (1); Wu, Jiang (3); Shang, Ching (1); Bayle, J. Henri (3); Shou, W (2); Chang, Ching-Pin (1)*  
 (1) Division of Cardiovascular Medicine, Stanford University School of Medicine (2) Department of Pediatrics, Indiana University School of Medicine (3) Department of Pathology, Stanford University School of Medicine

9:20 – 9:35	<p><b>Myocardial Smad4 Is Essential for Cardiogenesis in Mouse Embryos</b>  <i>Song, Lanying (1); Yan, Wensheng (2); Chen, Xinbin (2); Wang, Qin (3); Jiao, Kai (1)</i>  (1) Department of Genetics, Division of Genetic and Translational Medicine (2) Department of Cell Biology, (3) Department of Physiology and Biophysics, The University of Alabama at Birmingham, AL, USA</p>
9:35 – 9:50	<p><b>Sonic hedgehog Modulates Addition of the Secondary Heart Field to the Arterial Pole</b>  <i>Barbosky, Laura A.; Kirby, Margaret L</i>  Department of Cell Biology, Duke University, Durham, NC</p>
9:50 – 10:05	<p><b>BMP4 Function is Required in Second Heart Field-Derived Myocardium for Endocardial Cushion Remodeling, Outflow Tract Septation, and Semilunar Valve Development</b>  <i>McCulley, David J (1); Kang, Ji-One (1); Agarwal, Pooja (1); Rojas, Anabel (1); Martin, James F (2); Black, Brian L (1, 3)</i>  (1) Cardiovascular Research Institute and (3) Department of Biochemistry and Biophysics, University of California, San Francisco, California (2) Institute of Biosciences and Technology, Texas A&amp;M Health Science Center, Houston, TX</p>
10:05 – 10:20	<p><b>Retinoic Acid Deficiency Alters Secondary Heart Field Formation and NKx2.5 Regulation</b>  <i>Ryckebusch, Lucile (1); Lin, Song-Chang (2); Wang, Zengxin (2); Chi, Xuan (3); Schwartz, Robert (3); Buckingham, Margaret (4); Zaffran, Stéphane (1); Niederreither, Karen (2)</i>  (1) Developmental Biology Institute of Marseille-Luminy, France (2) Baylor College of Medicine, Houston, TX (3) The Institute of Biosciences and Technology, Houston, TX (4) Institut Pasteur, Paris, France.</p>
<b>10:20 am – 10:35 am</b>	<b>Break</b>
<b>10:35 am – 12:10 pm</b>	<p><b><u>Platform Session VII</u></b>  <b>Valvulogenesis</b>  <i>Chairs: Katherine Yutzey, Cincinnati Children’s Medical Center and Andy Wessels, Medical University of South Carolina</i></p>
10:35 – 10:40	<b>Chair’s Introduction</b>
10:40 – 10:55	<p><b>Distinct Functions of the MAP3Kinases, MEKK3 and MEKK4, for Heart Valve Development</b>  <i>Stevens, Mark V (1); Rogowitz, Elisa (2); Lalani, Sofia (3); Parker, Patti (1); Broka, Derrick (1); Vaillancourt, Richard R (1); Camenisch, Todd D (1, 4)</i>  (1) Department of Pharmacology and Toxicology, University of Arizona (2) Department of Molecular and Cellular Biology, University of Arizona (3) Department of Cell Biology and Anatomy, University of Arizona (4) Sarver Heart Center, University of Arizona</p>
10:55 – 11:10	<p><b>Tbx20 and Twist1 function in endocardial cushion mesenchyme</b>  <i>Shelton, Elaine L; Yutzey, Katherine E</i>  Molecular and Developmental Biology Graduate Program, University of Cincinnati.</p>

11:10 – 11:25	<b>TGF-beta2 is required in vivo for epithelial-mesenchymal transformation, collagen fibrologenesis, and differentiation, condensation and maturation of mesenchyme during valvulogenesis</b> <i>Azhar, Mohamad (1, 2); Yin, Moying (3); Martin, Jennifer (3); Pawloski, Sharon A; Prasad, Vikram (3); Rajan, Sudersan (3); Miller, Mariane (3); Chen, Dora (1); Runyan, Ray B.; Gittenberger-de Groot, Adriana C (4); Fuchs, Elaine (5); Doetschman, Tom (1, 2)</i> (1) BIO5 Institute, and (2) Dept of Cell Biology & Anatomy, University of Arizona, Tucson, AZ, (3) Dept of Molecular Genetics, University of Cincinnati College of Medicine, Cincinnati, Ohio, (4) Dept of Anatomy & Embryology, Leiden University Medical Center, Leiden, The Netherlands, (5) Howard Hughes Medical Institute, The Rockefeller University, New York, NY
11:25 – 11:40	<b>The Role of Cartilage Link Protein 1 (Crtl1) in Heart Development</b> <i>Wirrig, Elaine; Snarr, Brian; Phelps, Aimee; O'Neal, Jessica; Barth, Jeremy; Kern, Christine; Fresco, Victor; Mjaatvedt, Corey; Hoffman, Stanley; Trusk, Thomas; Argraves, W. Scott; Wessels, Andy</i> The Medical University of South Carolina; Department of Cell Biology and Anatomy
11:40 – 11:55	<b>Endocardial cells transformation is dependent on Par6 regulation of RhoA</b> <i>Townsend, Todd A (1); Wrana, Jeffrey L (2); Davis, George E (3); Barnett, Joey V (1)</i> (1) Department of Pharmacology, Vanderbilt University, Nashville, TN (2) Department of Medical Genetics and Microbiology, University of Toronto, Toronto, Ontario, Canada (3) Department of Medical Pharmacology and Physiology, Univ. of Missouri, Columbia, MO
11:55 – 12:10	<b>NIH Presentation, Charlene Schramm, NHLBI</b>
<b>12:15 pm – 1:30 pm</b>	<b>Lunch</b> <span style="float: right;"><b>Grand Hall Ballroom</b></span>
<b>1:30 pm – 2:30 pm</b>	<b>Business Meeting</b> <span style="float: right;"><b>Illinois Street Ballroom</b></span>
<b>1:30 pm – 2:30 pm</b>	<b>NIH Workshop</b> <span style="float: right;"><b>Edison Room</b></span> <i>Charlene Schramm</i>
<b>2:30 pm – 2:45 pm</b>	<b>Break</b>
<b>2:45 pm – 4:05 pm</b>	<b><u>Platform Session VIII</u></b> <span style="float: right;"><b>Illinois Street Ballroom</b></span> <b>Animal Models of Congenital Heart Disease</b> <i>Chairs: Simon Conway, Indiana University and Christopher Brown, Vanderbilt University</i>
2:45 – 2:50	<b>Chair's Introduction</b>
2:50 – 3:05	<b>A new mutant series provides insights into sensitivity of heart development to Tbx1-mRNA dosage.</b> <i>Zhang, Zhen; Baldini, Antonio</i> Center for Molecular Development and Disease, Institute of Biosciences and Technology, Health Science Center, Texas A&M University System.

- 3:05 – 3:20      **Titration of Pax3 expression levels during morphogenesis of the outflow tract**  
Zhou, Hongming; Conway, Simon J.  
 Cardiovascular Development Group, Herman B Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, IN
- 3:20 – 3:35      **Polycomb Repressive Complex I plays a cell autonomous role in cardiac development**  
Jenkins, Caroline; Boutsma, Erwin; Bamforth, Simon; Joyce, Bradley; Franklyn, Angela; Broadbent, Carol; Schneider, Jurgen; Schwartz, Robert; Saga, Yumiko; Koseki, Haruhiko; van Lohuizen, Maarten; Bhattacharya, Shoumo  
 University of Oxford, Cardiovascular Medicine, Wellcome Trust Centre For Human Genetics
- 3:35 – 3:50      **Multiple functions of EIIIA and EIIIB splice isoforms of fibronectin in cardiovascular development.**  
Astrof, Sophie (1); Hynes, Richard (2)  
 (1) Weill Medical School of Cornell University (2) MIT
- 3:50 – 4:05      **Loss of fibulin-1 in mice causes a DiGeorge syndrome-like phenotype**  
Cooley, Marion A; Kern, Christine B; Fresco, Victor M; Wessels, Andy; Thompson, Robert P; McQuinn, Tim C; Twal, Waleed O; Mjaatvedt, Corey H; Drake, Christopher J; Argraves, W. Scott  
 Cardiovascular Developmental Biology Center, Department of Cell Biology and Anatomy, Medical University of South Carolina, Charleston, South Carolina, USA
- 4:05 pm – 4:30 pm      Break**
- 4:30 pm – 5:35 pm      Platform Session IX      Illinois Street Ballroom**  
**Translational Models of Congenital Heart Disease**  
*Chairs: Mark Payne, Indiana University and Jamie Lohr, University of Minnesota*
- 4:30 – 4:35      **Chair's Introduction**
- 4:35 – 4:50      **A Novel Murine Model with Features of Vacterl and Caudal Regression Indicates a Common Genetic Origin for both Syndromes**  
Szumaska, Dorota (1); Pieves, Guido (1); Bilski, Michal (1); Franklyn, Angela (1); Cormack, Marie (3); Schneider, Juergen E (1); Jefferis, Joanna (4); Johnson, Paul (4); Lalanne, Zuzanna (3); Neubauer, Stefan (1); Clarke, Kieran (2); Brown, Steve D (3); Bhattacharya, Shoumo (1)  
 (1) Department of Cardiovascular Medicine, University of Oxford, UK (2) Department of Physiology, University of Oxford, UK (3) Mammalian Genetics Unit, MRC Harwell, UK (4) Nuffield Department of Surgery, University of Oxford, UK
- 4:50 – 5:05      **Mediating ERK1/2 Signaling Rescues Congenital Heart Defects in a Mouse Model of Noonan Syndrome**  
Nakamura, Tomoki; Colbert, Melissa C; Krenz, Maike; Molkentin, Jeffery D; Robbins, Jeffery  
 Division of Molecular Cardiovascular Biology, Cincinnati Children's Hospital Medical Center

5:05 – 5:20

**Muscleblind 2, a RNA binding protein important in Myotonic Dystrophy and Cardiac Conduction.**

*Hao, Minqi; Akrami, Kevan; Wei, Ke; Vondriska, Thomas M; Tidball, James; Graves, Michael; Shieh, Perry B.; Chen, Fabian*  
University of California at Los Angeles, CA

5:20 – 5:35

**Duplication of the entire 22.9-Mb human chromosome 21 syntenic region on mouse chromosome 16 causes cardiovascular abnormalities**

*Li, Zhongyou (1); Yu, Tao (1); Morishima, Masae (3); Pao, Annie (1); LaDuca, Jeffrey (1); Conroy, Jeffrey (1); Nowak, Norma (1, 2); Matsui, Sei-Ichi (1); Shiraishi, Isao (3); Yu, Y. Eugene (1, 2)*

(1) Center for Genetics and Pharmacology, Roswell Park Cancer Institute, (2) New York State Center of Excellence in Bioinformatics and Life Sciences, (3) Department of Pediatric Cardiology and Nephrology, Kyoto Prefectural University of Medicine, Kyoto, Japan.

**6:00 pm – 10:00 pm**

**Banquet (Open Bar)**

**Grand Hall Ballroom**

*Entertainment provided by the “Uptown Jazz Quartet”*

# KEYNOTE SPEAKERS

## **Oliver Smithies, D. Phil.**

Excellence Professor of Pathology and Laboratory  
Medicine

The University of North Carolina at Chapel Hill



Oliver Smithies was born on June 23, 1925, in Halifax, England. He attended Oxford University and received a Bachelor of Arts Degree in Physiology with First Class Honors in 1946. In 1951, he obtained his M.A. and D.Phil. degrees in Biochemistry from Oxford. Smithies then moved to the United States as a Postdoctoral Fellow in Physical Chemistry at the University of Wisconsin. After two years at Wisconsin, Smithies accepted a position at the Connaught Medical Research Laboratories in Toronto and stayed there from 1953 to 1960, first as a Research Assistant and then as a Research associate. In 1960, Smithies returned to Wisconsin as Assistant Professor of Medical Genetics and Genetics, advancing to Full Professor by 1963. In 1989, Smithies moved to the University of North Carolina-Chapel Hill, where he is now the Excellence Professor of Pathology and Laboratory Medicine.

Early in his career, Smithies developed new methods for detecting genetic variation in proteins and originated starch gel as a supporting medium for the electrophoretic analysis of proteins and enzymes. This led to discoveries of protein polymorphisms and significant work on the heredity of important blood proteins – including haptoglobins, transferrins, and gamma globulins. This resulted in early recognition by the American Society of Human Genetics, who conferred upon him its William Allen Memorial Award in 1964.

Smithies continued his work on protein polymorphisms and the origins of antibody diversity. His many important contributions to genetics have been recognized by his colleagues: in 1971, he was elected a Member of the National Academy of Sciences; in 1975, he served a President of the Genetics Society of America; and in 1978, he became a Member of the American Academy of Arts and Sciences.

Smithies has also undertaken important national positions. He served as a Member of the National Advisory Medical Sciences Council for the National Institutes of Health from 1985 to 1990, helping establish research goals in the biomedical sciences.

He is one of only three people to twice receive the Gairdner Foundation International Award. This honor was awarded to Smithies in 1990 “for the discovery, development and application of gel electrophoresis methods that allow the separation and identification of specific proteins and nucleic acids,” and in 1993 “for pioneering work in the use of homologous recombination to generate targeted mutations in the mouse.”

In 1988, when he joined the Department of Pathology at the University of North Carolina, Smithies was named Excellence Professor of Pathology. He remains an actively engaged scientist, working at the bench in his own laboratory, and has published more than 20 important papers over the last three years, in *Science*, *Nature*, *Cell*, and *Proceedings of the National Academy of Sciences*. His recent accomplishments have been in producing directed mutations in the mouse that mimic human genetic diseases or allow the dissection of complex genetic traits such as atherosclerosis and high blood pressure.

In recognition of his distinguished career, the University of Chicago conferred upon him the Honorary Doctor of Science Degree in 1991. The citation states, “innovator of concepts and technology in the fields of protein biochemistry, immunogenetics, molecular evolution and molecular biology, who has generated ideas and tools and used them to arrive at solutions to important biological problems and whose study of homologous recombination has laid the foundation for the rational use of gene therapy to correct genetic defects, representative of the highest ideal of the actively engaged scientist.”

## **Margaret L. Kirby, Ph.D.**

Professor of Pediatrics, Cell Biology and Biology  
Scientific Director, Neonatal-Perinatal Research Institute  
Department of Pediatrics (Neonatology)  
Duke University, Durham, NC



Margaret Loewy Kirby received her Ph.D. at the University of Arkansas for Medical Sciences at Little Rock. After a year in medical school she switched to research in anatomy under the guidance of Dr. Shirley Gilmore. Her dissertation research demonstrated that catecholamines are taken up by the developing notochord and included a detailed developmental history of the sympathetic trunks. Dr. Kirby received her A.B. degree in Biology from Manhattanville College, Purchase, NY, where her senior thesis focused on the effects of laser radiation on bacterial respiration.

After obtaining her PhD, Dr. Kirby taught at the University of Central Arkansas for two years and then accepted a postdoctoral fellowship with Dr. Alfred Heller at The University of Chicago. There her research showed the onset of norepinephrine synthesis in the sympathetic trunks. In addition, she developed a neonatal rat brain atlas, and she worked with Dr. Lloyd Roth on developing innervation of the eye. Because of the early synthesis of catecholamines with a long delay in functional innervation of target organs, she developed the hypothesis that these neural transmitters may be used in a different context in development.

Dr. Kirby accepted her first faculty position at the Medical College of Georgia where she continued work on developing autonomic innervation but now her research focused on this development in the heart where it was less complicated to analyze functional changes caused by pre-neural and neural transmitter functions. It was an attempt to prevent development of the parasympathetic innervation to the heart by ablation of the neural crest progenitors that led to her discovery of the cardiac neural crest which she determined to be required for normal septation and alignment of the outflow tract. In 1983 she published a seminal paper showing the requirement of neural crest in cardiac outflow tract development.

Dr. Kirby rose through the ranks at the Medical College of Georgia and in 1994 she was recognized for her research by being appointed Regents' Professor. With the help of an NIH program project grant, her work continued to focus on the role of neural crest in outflow alignment and her lab recognized a new role of neural crest cells in modulating signaling in the caudal pharynx concurrently with the discovery of the late contribution of outflow myocardium from the caudal pharynx that was regulated by signaling in the caudal pharynx.

Dr. Kirby retired from the Medical College of Georgia in 2001 and was recruited to the Department of Pediatrics (Neonatology) at Duke University where she continued to investigate the contribution of myocardium and smooth muscle to the arterial pole of the heart. Discovery of the genes controlling the migration and differentiation of these cells continues in both chick and zebrafish. Dr. Kirby has published 159 papers and 30 chapters and has recently authored a book entitled *Cardiac Development* (2007) published by Oxford University Press. Dr. Kirby's current research continues to focus on outflow development, subdivision of the cardiogenic fields and early heart tube formation, and the role of neural crest cells in controlling signaling in the pharynx that impacts early heart development.

# **CHARTER**

## **Weinstein Cardiovascular Development Conference**

### Scope of the Conference

The Weinstein Cardiovascular Development Conference is an annual meeting for scientists investigating normal and abnormal development of the heart and vasculature as it may ultimately relate to human disease. It is a freestanding meeting unaffiliated with any society or parent organization. Interested individuals or groups from host institutions organize it on a rotating basis. The intent of the meeting is to advance the overall field of cardiovascular development through the sharing of information and the facilitation of collaborative investigations. True to the vision of Dr. Constance Weinstein, who first organized this conference, the meeting is intended to include as many perspectives as possible. Investigators in any relevant area that can provide contributions to our understanding of heart and vascular development are welcome to contribute.

### Organization of the Conference

In order to provide a corporate memory and to maintain quality of the conference, the participants of the 1998 meeting voted to form an organizing committee called the "Weinstein Committee". The makeup of the committee is comprised of representatives from each of the three previous local organizing committees, representatives from the next two proposed meeting sites, and two "at large" members voted upon by the conference participants. The "at large" members will serve a three-year term. The charge to the Committee is to assist the local organizing committee with arrangements and organization and to help secure funding.

In addition, the Committee is charged with soliciting nominations for future meeting sites and hosts. Such nominations will then be brought up for a vote by the attendees during the business meeting. Meeting sites will be selected by vote such that the local organizing committee will have a two year lead-time. In the event that multi-year funding is sought from the National Institutes of Health or other national sources, the Weinstein Committee will participate in this process.

### Local Organizing Committee

To provide a varied flavor and the opportunity for new approaches, each host institution will form a local organizing committee to select a meeting venue and format. The site should be selected for its potential to optimize informal communication and interaction. As a way to emphasize new and topical information, organizers from the host institution should select speakers from among the submitted abstracts. Scheduling should include opportunities for new voices and encourage the development of students, fellows, and younger faculty. Ample time for discussion is to be provided.

### Obligations of the Participants

One of the most important aspects of the Weinstein Conference has been the willingness of the participants to share new and unpublished information. This has provided opportunities for the participants to devise new experiments and develop new hypotheses in a collaborative manner. It is expected that all participants will participate in a collegial and ethical manner with respect to information obtained at the Weinstein Conference. Permission should be obtained before disclosure of another investigator's unpublished data.

Similarly, investigators pursuing similar experiments should inform a presenter if the divulged information has a bearing on their own work. All participants in the conference should be willing to share their expertise and reagents in the collective advancement of the area of cardiovascular development.

### Annual Business Meeting

Each Weinstein Conference will include time set aside for a business meeting. At this time participants will vote on future host and meeting site selection and may consider changes in the direction of the conference or its organization. At the 1999 meeting in Tucson, AZ this charter was distributed to the participants and ratified. Its provisions commenced at the business meeting of the 1999 Tucson, AZ conference.

The Charter will remain in effect until modified by a vote of participants at an annual business meeting.

## **WEINSTEIN 2007-CONFERENCE COMMITTEE**

### **Weinstein Committee**

Raymond Runyan, Ph.D. (Arizona, 2005)  
Kersti Linask, Ph.D. (South Florida, 2006)  
Loren Field, Ph.D. (Indiana, 2007)  
James Martin, M.D., Ph.D. (Houston, 2008)  
Brian Black, Ph.D. (San Francisco, 2009)  
John Burch, Ph.D. (Fox Chase Cancer Center, at large)  
Katherine Yutzey, Ph.D. (Cincinnati, at large)

### **Weinstein Local Organizing Committee Members, 2007**

Loren Field, Ph.D., Indiana University  
Mark Payne, M.D., Indiana University  
Simon Conway, Ph.D., Indiana University  
Anthony Firulli, Ph.D., Indiana University  
Lei Wei, Ph.D., Indiana University  
Weinian Shou, Ph.D., Indiana University  
Michael Rubart, MD, Ph.D., Indiana University  
Michiko Watanabe, Ph.D. Case Western Reserve University, Adjunct Member  
Katherine Yutzey, Ph.D., Cincinnati Children's Medical Center, Adjunct Member

# GENERAL ANNOUNCEMENTS

The Weinstein Cardiovascular Development Conference has become one of the most important meetings in the field of cardiovascular development. The informal setting, sharing of meal times, poster sessions, as well as other times for catching up with colleagues and making new collaborations have made this a favorite conference for many of us, both on the junior and senior researcher level. All of the oral presentations except for the Keynote lectures were selected, as in previous years, from the submitted abstracts.

## **Oral Presentations**

Due to the number of topics that were chosen to be covered and the tight schedule to fit in as many talks as possible, each presentation is allotted 15 minutes for their presentation and questions. We request that the speakers adhere to the time limit.

## **Posters**

Posters will be on display during the entire conference. Each poster has been assigned a unique number. Upon arrival, please mount your poster for display on the designated poster board number and area. The presenters of the even-numbered posters are requested to be at their poster during the Thursday evening poster session. The presenters of the odd-numbered posters are requested to be at their poster during the Friday evening poster session. Poster areas will be open and available throughout the entire conference up until 11:30 a.m. on Saturday for those of you who may wish to see posters that may have been missed earlier or for getting together with colleagues. A committee of judges will be circulating during the poster sessions during the times that presenters are expected to be at their poster to ask questions and to judge their poster presentation. The best graduate student and postdoctoral posters will be awarded prizes during the final dinner on Saturday.

## **Meals**

All meals will be provided. There will be an open bar Thursday, Friday and Saturday evenings in the Grand Hall Ballroom from 6:00 pm to 10:00 pm.

## **Concurrent Workshops**

Concurrent Workshops will be held on Thursday evening from 8:00 pm – 9:00 pm and Friday afternoon from 1:15 pm – 2:15 pm in the Edison Rooms. The workshops on Thursday include “Single v. multiple development heart fields” and “Cardiomyogenic stem cells during development”. On Friday the workshops include “Cardiac neural crest” and “Imaging cardiovascular development and physiology”.

## **NHLBI and NIEHS Presentations**

Dr. Pat Mastin from the NIEHS will be speaking on Friday from 11:55 am – 12:00 pm, which is at the end of Platform Session IV. Dr. Charlene Schramm, from the NHLBI, will be speaking on Saturday from 11:55 am – 12:10 pm, which is at the end of Platform Session VII. Dr. Schramm will also have a NHLBI Workshop on Saturday from 1:30 pm – 2:30 pm in the Edison Room.

## **Thursday Evening**

The Keynote presentation by Dr. Oliver Smithies will be followed by the first poster session & dinner buffet for all attendees.

**Friday Evening**

Following the Keynote by Dr. Margaret Kirby will be the second poster session and a buffet dinner.

**Business Meeting**

The Weinstein business meeting will take place on Saturday from 1:30 p.m. - 2:30 p.m. in the Illinois Street Ballroom.

**Saturday Evening (Banquet)**

The Banquet on Saturday evening will take place in the Grand Hall Ballroom. Poster prizes will be awarded during the banquet. Entertainment for the evening will be provided by The Uptown Jazz Quartet. They have quite a repertoire!

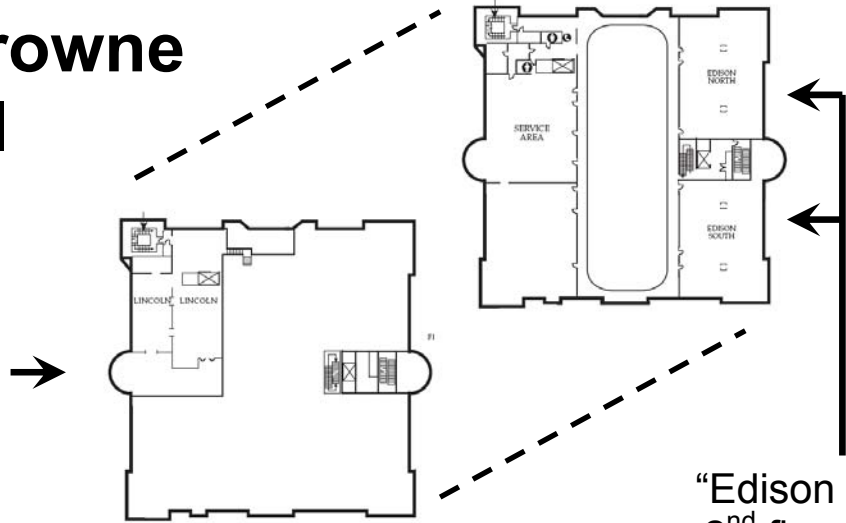
**Acknowledgements**

We would like to thank Drs. Oliver Smithies and Margaret Kirby for agreeing to be our Keynote speakers this year. We also thank Dr. Constance Weinstein, who will be attending the 2007 Conference, for her support of cardiovascular development at NIH and providing the opportunity for these conferences.

Many people beyond the local organizing committee have contributed to the organization of this conference. We are very thankful to everyone who has assisted in this year's event.

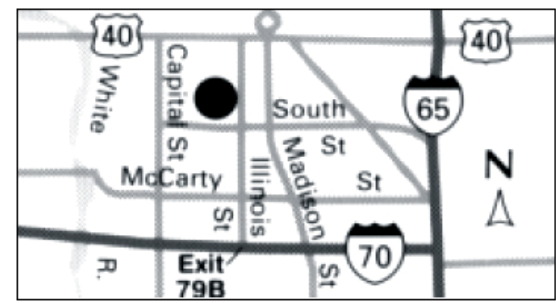
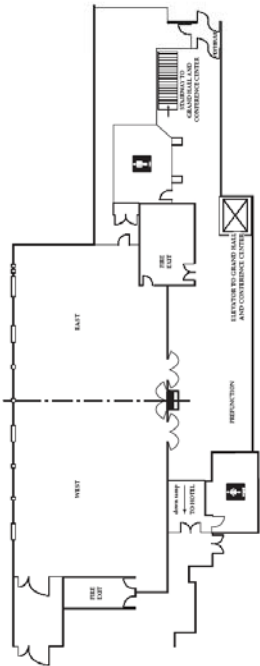
# Union Station Crowne Plaza Hotel

“Grand Hall Ballroom”  
1<sup>st</sup> floor:  
Dinners, drinks and  
posters

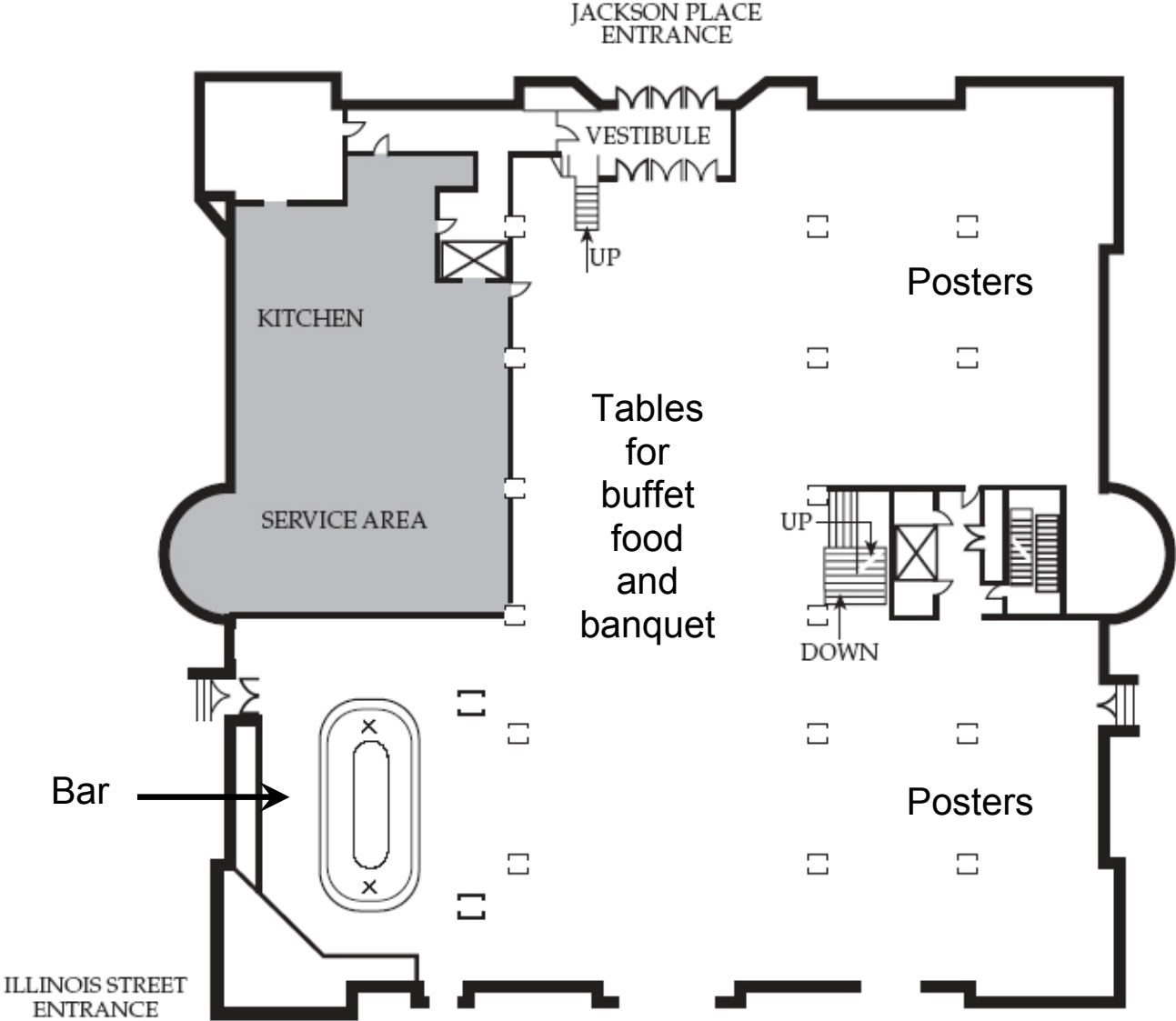


“Edison Rooms”  
2<sup>nd</sup> floor, above  
the Grand Hall  
Ballroom:  
Concurrent  
Workshops

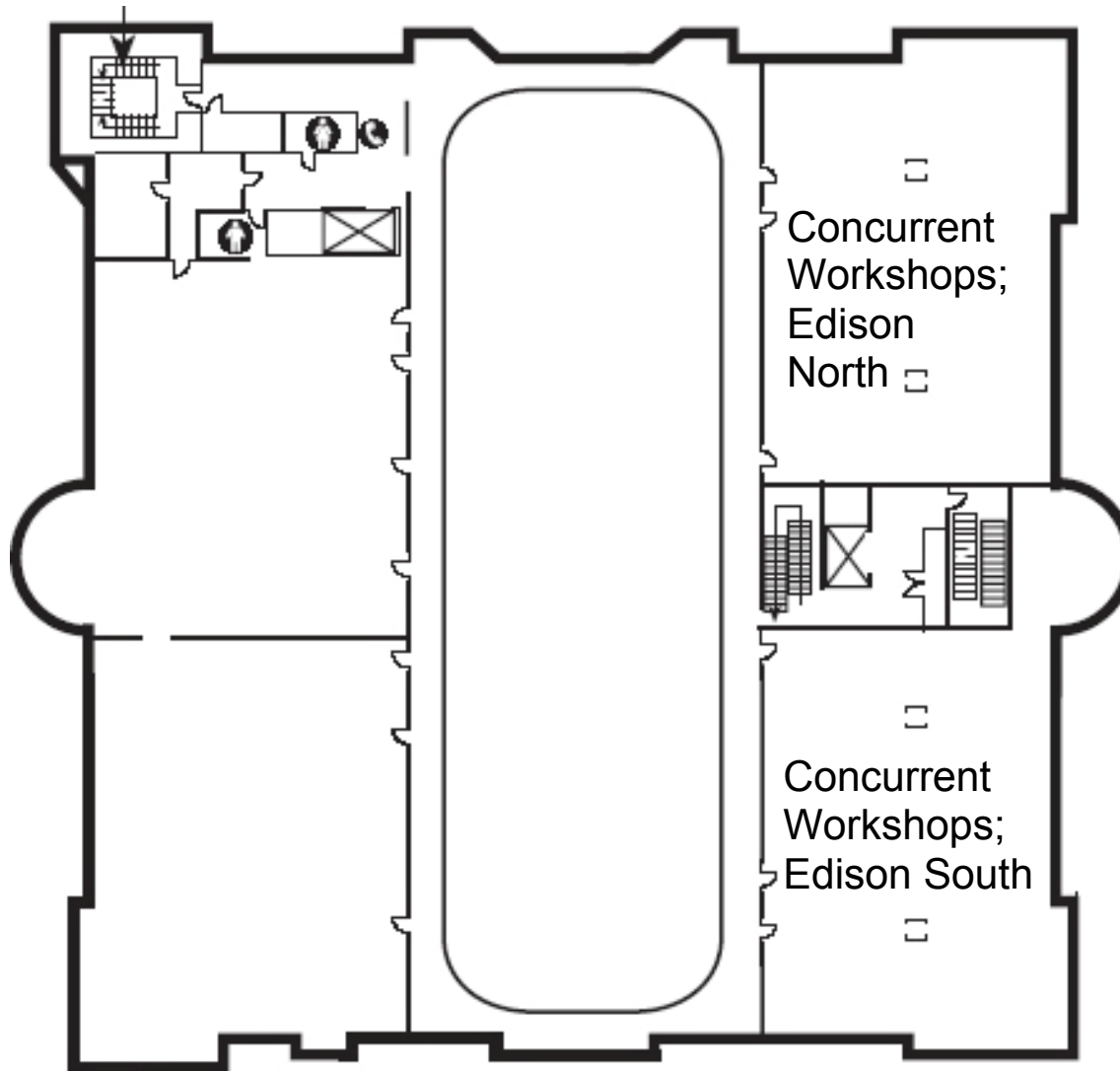
“Illinois Street Ballroom”  
2<sup>nd</sup> floor:  
Lecture room for the  
platform presentations



# Grand Hall Ballroom: 1st floor



# Edison Rooms, 2<sup>nd</sup> floor, above the Grand Ballroom



# CONFERENCE SUPPORTERS

We gratefully acknowledge the following organizations and companies for their generous support for this conference. This support helped maintain registration at affordable levels and to provide for a substantial number of travel grants to junior investigators.

This project was supported (in part) by NIH Research Grant #R12H174373 funded by the **National Heart, Lung and Blood Institute**, the **National Institute of Child Health and Human Development**, the **National Institute of Environmental Health Sciences**, and the **Office of Rare Disease**. (The views expressed in written conference materials or publications and speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.)

Supported by an educational grant from **Eli Lilly & Company**.

Travel Awards are sponsored in part by the **American Association of Anatomists**.

**American Heart Association**

**Developmental Dynamics**

**Harlan**

**March of Dimes**

**Medtronics**

**Novartis**

**Oxford University Press**

**Riley Children's Foundation**

**Society for Developmental Biology**

**University of Southern Florida**

**Visual Sonics**

**W. Nuhsbaum, Inc.**

**Indiana University School of Medicine**

**Department of Pediatrics**

**Section of Pediatric Cardiology**

**Wells Center for Pediatric Research**

**Department of Medicine**

**Krannert Institute of Cardiology**

# PLATFORM PRESENTATION ABSTRACTS

## Platform Session I

### **1. Cardiomyocyte and Epicardial Cell Addition during Cardiac Homeostasis in Adult Zebrafish**

*Wills, Airon A; Holdway, Jennifer; Major, Robert J; Poss, Kenneth D*

Duke University Medical Center, Dept. of Cell Biology

The heart maintains structural and functional integrity during years of continual contraction and physiologic change, but the extent to which new cell addition participates in cardiac homeostasis is unclear. Here, we assessed cellular and molecular mechanisms of cardiac homeostasis in zebrafish, animals that grow as adults and possess an unusual capacity to regenerate after acute cardiac injury. During rapid animal growth, robust hyperplastic cardiomyogenesis was observed throughout the growing ventricle. By contrast, new cardiomyocyte generation was present, albeit rare, in ventricles of animals maintaining size. We also observed robust supplementation of the ventricle wall with epicardial-derived cells during rapid animal growth, greater than that seen in animals growing slowly or maintaining size, and comparable to that observed during regeneration. Growth-stimulated epicardial gene expression could be reproduced by manipulating the extra-cardiac environment, suggesting that the epicardium perceives extra-cardiac space available for growth. Inhibition of Fgf signaling, a pathway required for normal heart regeneration, disrupted epicardial supplementation during growth and caused spontaneous ventricular scarring in animals maintaining size. Together, these results reveal mechanisms that stimulate myocardial cell creation and epicardial supplementation proportionally to couple ventricular size and function with animal size.

### **2. FOXO transcription factors in the regulation of cardiac myocyte proliferation and myocardial growth during development**

*Evans-Anderson, Heather J; Alfieri, Christina M; Yutzey, Katherine E*

Division of Molecular Cardiovascular Biology, Cincinnati Children's Hospital Medical Center

The regulatory mechanisms of cardiac myocyte proliferation and resultant myocardial growth are not well defined. Current data suggests Forkhead Box Other (FOXO) transcription factors may have a significant role in the mediation of myocardial growth during development. FOXO factors are antagonized by AKT via phosphorylation, which results in nuclear export and inactivation. In the absence of active AKT, FOXO factors can negatively regulate proliferation through induction of the Cip/Kip family of cyclin kinase inhibitors. Thus, FOXO factors could provide a direct mechanism to control the cardiac myocyte cell cycle downstream of PI3K/AKT signaling. Preliminary data show that FOXO1 and FOXO3 are expressed in the developing myocardium from embryonic to neonatal stages consistent with decreasing rates of myocyte proliferation. Expression of p21cip1, a FOXO target gene and cell cycle inhibitor, in mature trabecular myocytes coincides with FOXO1 nuclear localization and decreased myocyte proliferation during the final stages of heart development. In vitro studies show that cultured embryonic, fetal, and neonatal cardiac myocytes are responsive to IGF1 stimulation, which results in the induction of the PI3K/AKT pathway, phosphorylation of FOXO proteins, and increased myocyte proliferation. Likewise, adenoviral-mediated expression of AKT promotes cardiac myocyte proliferation and increased cell size. In contrast, increased expression of FOXO or FOXO target genes negatively affects myocyte proliferation and growth. In vivo cardiac-specific expression of FOXO1 during heart development causes embryonic lethality at E10.5 due to severe myocardial defects. Alternatively, dominant negative FOXO1 transgenic embryos appear normal at E10.5, but display abnormal morphology of the myocardium by E18.5. These data support FOXO transcription factors as downstream effectors of PI3K/AKT signaling in the negative regulation of cardiac myocyte proliferation and myocardial growth. Current studies include comparative analysis of the effects of FOXO gain and loss of function to identify FOXO transcriptional mechanisms of cell cycle regulation during heart development.

### **3. 3D Visualization of proliferation in cardiac and extracardiac mesoderm**

*van den Berg, G; Soufan, AT; de Boer, PAJ; van den Hoff, MJB; Moorman, AFM*  
Heart Failure Research Centre, Amsterdam, The Netherlands

Proliferation is a crucial contributor to organogenesis, but its regionalization during heart development is poorly understood. Recently we demonstrated that after initial formation of the heart tube, proliferation in the myocardium ceases. Nonetheless, the number of cardiomyocytes increases. This is because cells are still being added to the myocardial lineage. To further analyze this process, we studied proliferation (as defined by the nuclear fraction that is positive for BrdU after 1 hour of exposure) in the embryonic chicken heart and its contiguous mesoderm. The pattern of proliferation is presented three-dimensionally in order to provide a comprehensible image of its role in the intricate morphogenesis of early heart formation. We show that upon fusion of the mesoderm in the midline, which marks the initial formation of the heart tube, there is no proliferation. However, the mesoderm that is contiguous to the forming heart, and which lines the embryonic coelom, shows high proliferation. Later in development, myocardium has formed and can be distinguished as a trough. This myocardium does not proliferate. The mesoderm which is located laterally and dorsally hardly proliferates, whereas the caudally located coelomic wall proliferates extensively. Later in development this pattern is still observable, but now dorsally the non-myocardial mesoderm can be divided into a non-proliferating venous inflow and a highly proliferating coelomic wall. During further development working myocardium of the embryonic ventricle starts to proliferate at the outer curvature. Proliferation outside the heart has extended cranially, along the dorsal wall of the coelom, towards the myocardial outflow tract. Our data show a non-proliferating, but nonetheless growing myocardial heart tube. Addition of cells occurs from the flanking and highly proliferating mesoderm. Early in development a zone of high proliferation is located dorsally to the forming myocardium. This zone lines the coelomic cavity and with time extends cranially towards the outflow of the heart. These data suggest that this zone can contribute cells to both inflow and outflow myocardium. Also, these data show the coelomic wall to be an important structure in organogenesis.

### **4. Canonical Wnt Signaling is Required for Mammalian Cardiogenesis by Regulating Cardiac Progenitors**

*Kwon, Chulan; Arnold, Joshua; Taketo, Makoto; Srivastava, Deepak*  
Gladstone Institute, UCSF

Guiding stem or progenitor cells into distinct lineages and controlling their expansion remain fundamental challenges in stem cell biology. Members of the Wnt pathway control many pivotal embryonic events<sup>1-3</sup>, often regulating self-renewal or expansion of progenitor cells. Canonical Wnt ligands are thought to negatively regulate cardiomyogenesis in several species<sup>4-6</sup>. However, the cell-autonomous role of canonical Wnt signaling through its obligatory transcriptional mediator, b-catenin, is unknown. We used tissue-specific in vivo genetic manipulation to show that b-catenin is an essential positive regulator of proliferative expansion in cardiac progenitor cells. The Wnt/b-catenin target gene cyclin D2 was downregulated in hearts lacking b-catenin and upregulated in hearts with stabilized b-catenin. At discrete windows of development in embryonic stem cells, activation of canonical Wnt signaling promoted expansion of cardiac progenitors after initial commitment, and inhibition of canonical Wnts repressed further cardiac differentiation. Thus, canonical Wnt signaling promotes the expansion of cardiac progenitors and differentiation of cardiomyocytes.

## **Platform Session II**

### **5. MEF2A controls a costameric network of genes in cardiac muscle**

*Naya, Frank J; Brand, Ondra M; Reynolds, Joseph G; McCalmon, Sarah A*  
Department of Biology, Program in Cell and Molecular Biology, Boston University

The MEF2 transcription factor family plays an important role in cardiac muscle development and disease by regulating a vast array of downstream target genes. These target genes can be activated by multiple MEF2 factors in vitro. Knockout studies in mice, however, have revealed remarkably different