



**JAMES MARTIN, MD, PhD**  
Physiology  
Member,  
Executive Committee

## TOGETHER, DAG1 AND YAP 'HIT THE BRAKES' ON HEART CELL PROLIFERATION

*James Martin, MD, PhD*

Found in the June 2017 publication of Nature, Dr. Martin and his lab explore findings for heart regeneration after heart attack injury as well as improving cardiac function in children with muscular dystrophy.

"We are investigating the question of why the heart muscle doesn't renew," said Dr. James Martin, professor and Vivian L. Smith Chair in Regenerative Medicine at Baylor College of Medicine and Director of the Cardiomyocyte Renewal Lab at the Texas Heart Institute. "In this study, we focused on two pathways of cardiomyocytes or heart cells: the Hippo pathway, which is involved in stopping renewal of adult cardiomyocytes, and the DGC pathway, which is essential for cardiomyocyte normal functions. We are also interested in studying mutations in DGC components because patients with these mutations have a muscle wasting disease called muscular dystrophy."

The heart muscle is one of the least renewable tissues in the body, which is one of the reasons that heart disease is the leading cause of death for both men and women in the United States, according to the Centers for Disease Control and Prevention.

### When DAG1 captures Yap...

In this study, Martin and colleagues studied the consequences of the interaction between components of the DGC pathway with members of the Hippo pathway in animal models. The researchers genetically engineered mice to lack genes involved in one or both pathways, and then determined the ability of the heart to repair an injury. The results showed for the first time that dystroglycan 1 (DAG 1), a component of the DGC pathway, directly binds to Yap, part of the Hippo pathway, and that this interaction inhibited cardiomyocyte proliferation.

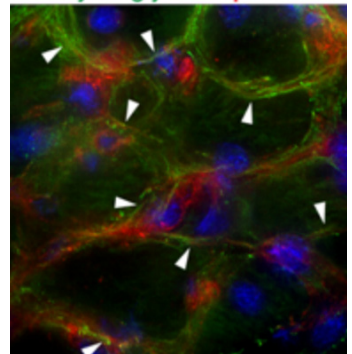
"The discovery that the Hippo and the DGC pathways connect in the cardiomyocyte and that together they act as 'brakes,' or stop signals to cell proliferation, opens the possibility that by disrupting this interaction one day it might be possible to help adult cardiomyocytes proliferate and heal injuries caused by a heart attack, for example."

Another long-term application of this discovery could be to improve cardiac function in children with muscular dystrophy.

"Patients with muscular dystrophy can have severe reduction in cardiac function," Martin said. "Our findings may help to design medicines to slow down cardiac decline in muscular dystrophy by stimulating cardiomyocyte proliferation. In order to do that, we need more research to understand cardiomyocyte growth control pathways in greater detail."

*Other contributors to this work include Yuka Morikawa, Todd Heallen, John Leach and Yang Xiao.*

**β-dystroglycan Yap DAPI**



**Image shows co-localization of proteins, dystroglycan and Yap, in the two pathways important for control of heart muscle regeneration after injury.**

# WHAT CAUSES MYOTONIC DYSTROPHY, TYPE 1

Thomas Cooper, MD

The Cooper lab's research has led to a better understanding of the molecular mechanisms of DM1 pathogenesis as well as to the development of several therapeutic approaches. While 25% of individuals die from heart effects, primarily arrhythmias, Dr. Cooper's research has established a mouse model for the heart effects of DM1 and the effect are reproduced quite well.

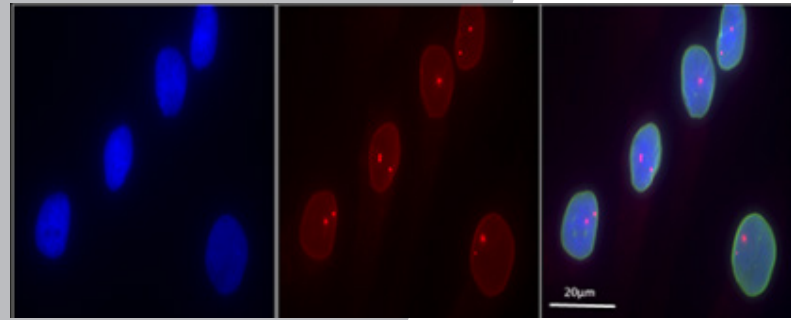
Myotonic dystrophy, type 1 (DM1) is the second most common cause of muscular dystrophy and numerous other muscle disorders that affect tens of thousands of individuals in the U.S.. This autosomal dominant neuromuscular condition involves multiple tissues including muscle, heart and the central nervous system.

DM1 is caused by a repeat of three letters in the DNA code – CTG – within the 3' untranslated region of the DMPK gene. When the expanded gene is transcribed, it produces RNA containing long tracts or repeats of CUG (CUGexp), which can be visualized in the nuclear foci of the image below.

The lab of Dr. Thomas Cooper discovered that the CUGexp RNA disrupts the regulation of RNA splicing that is important for proper functions of a large number of genes.

This effect is due to altered functions of CELF1 and MBNL proteins, and the MEF2 transcription factor, which results in RNA mis-splicing and expression of fetal isoforms that cannot fulfill the functional requirements of adult tissues, leading to the neuromuscular disorder.

"We are interested in understanding the mechanisms and consequences of the regulation of the process of alternative splicing of RNA, from how RNA binding proteins and signaling pathways coordinate RNA processing networks to the functional consequences of the different protein isoforms that are expressed in different cell states."



Bright red dots indicate nuclear foci showing CUG repeat RNA in DM1 cells. Courtesy of K. Manning and Dr. T. Cooper.



**THOMAS COOPER, MD**  
Pathology  
Member, Executive  
Committee

## SPOTLIGHT



**Biykem Bozkurt, MD,**  
CVRI associate director  
speaks on the importance  
of the treatment of  
heart attacks.

"This AHA/ACC task force paper identifies the specific clinical performance and quality measures for the treatment of myocardial infarction. It is the authoritative document defining the standards and metrics, and drives the quality of care in the US."

2017 AHA/ACC "Clinical Performance and Quality Measures for Adults With ST-Elevation and Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures" Jneid H., Addison D, Bhatt DL, Fonarow GC, Gokak S, Grady KL, Green LA, Heidenreich PA, Ho PM, Jurgens CY, King ML, Kumbhani DJ. Pancholy S, *J Am Coll Cardiol* 2017; 70:2048-90.

# AMERICAN HEART ASSOCIATION HEART WALK

## 2017 Houston Heart Walk

Join the Ace of Hearts team by registering here. The 5K walk will start on Dec. 9, with check-in at 8:00 a.m. Event day details, including parking and other frequently asked questions can be found [here](#).

“Youth and Students” can volunteer for the Heart Walk using this link:

<http://www.heart.org/HEARTORG/volunteer/volunteerForm.jsp>

**JOIN US IN  
THE MOVEMENT**  
Saturday, December 9  
Texas Medical Center

**TO RALLY**  
more people to live healthier lives

**TO INSPIRE**  
small, daily changes that can have  
a lasting impact on future generations

**TO UNIFY**  
millions of Americans to be a culture that is  
**Healthy for Good**

American Heart Association  
life is why™

Heart Walk  
Healthy For Good™

### THE CARDIOVASCULAR RESEARCH INSTITUTE AT BAYLOR COLLEGE OF MEDICINE

was established in 2012 as a key strategic initiative to enhance collaborative opportunities for research in cardiovascular sciences. CVRI aims to provide administrative and research support to promote collaborative and interdisciplinary basic, translational, and clinical research. In the near future, the CVRI aims to develop educational tracks for students, residents, fellows, and junior faculty to train future leaders in basic, translational and clinical cardiovascular medicine and research. The Institute is led by Director Xander Wehrens, MD, PhD, and Associate Director Biykem Bozkurt, MD, PhD.

For more information about CVRI, please visit [www.bcm.edu/cvri](http://www.bcm.edu/cvri), or contact Administrative Assistant Yvonne Arceneaux [cvri@bcm.edu](mailto:cvri@bcm.edu) or 713-798-6951.

# 2018 SEMINAR SERIES

Wednesdays @ 12:00 pm | Cullen Building, Room 201A



**JANUARY 17, 2018**

**Use of genomics to understand broken hearts and implications for clinical care**

**DR. WENDY CHUNG**

Professor of Pediatrics and Medicine

COLUMBIA UNIVERSITY IN NEW YORK CITY



**FEBRUARY 14, 2018**

**Super-hub Ca<sup>2+</sup> signaling and electromechanical remodeling in atria**

**DR. STEPHEN LEHNART**

Professor of Cellular Biophysics and Translational Cardiology

UNIVERSITY MEDICAL CENTER GOTTINGEN GERMANY



**MARCH 21, 2018**

**Signalosomes –nodal regulators and therapeutic targets for heart failure**

**DR. MICHAEL KAPILOFF**

Associate Professor of Ophthalmology and Cardiovascular Medicine

STANFORD UNIVERSITY



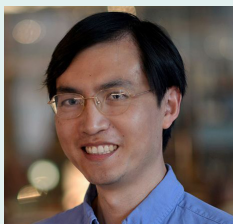
**APRIL 18, 2018**

**Novel targets to prevent microvascular thrombosis in sepsis**

**DR. MIGUEL CRUZ**

Associate Professor of Medicine/Thrombosis

BAYLOR COLLEGE OF MEDICINE



**MAY 2, 2018**

**Prolyl Hydroxylase Domain Protein - The Central Player of Cardiac Metabolism**

**DR. XIE LIANG**

Assistant Professor of Medicine/Atherosclerosis & Lipidology

BAYLOR COLLEGE OF MEDICINE

# Cardiovascular Research Institute

## 6th Annual Symposium



**KEYNOTE SPEAKER**  
Eric Olson, Ph.D.  
Professor and Chairman,  
Department of Molecular Biology  
The University of Texas Southwestern Medical  
Center at Dallas



**KEYNOTE SPEAKER**  
John P. Cooke, M.D., Ph.D.  
Joseph C. "Rusty" Walter and Carole Walter Looke  
Presidential Distinguished Chair  
Department of Cardiovascular Sciences  
Director, Center for Cardiovascular Regeneration  
Houston Methodist Research Institute

## Tuesday, April 10, 2018

Cullen Auditorium/Rayzor Lounge  
One Baylor Plaza  
Houston, TX 77030

For more information, visit [www.bcm.edu/cvri](http://www.bcm.edu/cvri)

### NOT A MEMBER?

If you have received this newsletter and are not currently a member of CVRI, we invite you to submit an application for membership in one of Baylor College of Medicine's largest strategic research centers.

Please fill out the online membership form on CVRI's membership page at [www.bcm.edu/research/centers/cardiovascular-research-institute/membership](http://www.bcm.edu/research/centers/cardiovascular-research-institute/membership).

Many benefits of CVRI member include:

- Access to a central repository of human tissue samples and core lab functions
- Collaborative opportunities for investigators, physicians, centers and institutes to foster cross-cutting opportunities and innovative translational research opportunities at BCM, the Texas Medical Center, and globally
- Opportunities for pilot grant funding for collaborative research projects in selected years
- Administrative support for submission of multi-investigator grants, program project grant proposals, and clinical trial agreements
- Listing on the BCM CVRI website and in the member database
- Participation in Institute retreats, seminars, grant workshops and other activities

**For more information about CVRI membership benefits, contact Yvonne Arceneaux at [cvri@bcm.edu](mailto:cvri@bcm.edu), 713.798.6951**

# AWARDS AND RECOGNITION



**DR. MARK ENTMAN**, professor of cardiovascular research, has been selected by the International Academy of Cardiovascular Sciences to receive the Lifetime Achievement Award in Cardiovascular Science, Medicine and Surgery. Dr. Entman received this award at the Cardiovascular Forum that was held in Orlando, Florida August 31, 2017.



**DR. CHRISTIE BALLANTYNE**, professor of medicine and chief of cardiology, has been elected to the Association of University Cardiologists. Founded in 1961, the association is an organization that is limited to an active membership of 125 academic cardiologists from the United States, elected by their peers. The group meets once per year in January for a two-day session of scientific interchange. The members traditionally are the leaders and best investigators in American cardiology who shape the course of research and training in cardiovascular disease.



**DR. MARY DICKINSON**, professor in the department of molecular physiology and biophysics has been named associate dean of research at Baylor College of Medicine. In her role as associate dean, she will serve as a liaison between the office of the Dean of Research and the faculty in support of the research mission.



**DR. GERD BRUNNER**, assistant professor of medicine, was awarded a five-year, \$2.89 million Research Project Grant (R01) from the National Heart, Lung, and Blood Institute, part of the National Institutes of Health, for his research on magnetic resonance imaging and machine learning in patients with peripheral artery disease, a malignant form of atherosclerosis.



**DR. NA LI** was recently promoted to tenure track assistant professor of medicine in cardiovascular research. Her current research projects in the lab are focused on three areas: inflammasome-mediated pathogenesis of AF, microRNA-mediated post-transcriptional regulations of ion channels associated with AF development and the function of FKBP5 in heart and cardiac diseases.

## 2018 PILOT AWARD WINNERS

- ▶ **“IMAGING MONOCYTE TRAFFICKING INTO ATHEROSCLEROSIS AND ADIPOSE TISSUE IN MICE”**. Drs. Hauizhu Wu, Robia Pautler and Christie Ballantyne
- ▶ **“REGULATION IN INFLAMMASOME ACTIVITY BY P38 MAPK”**. Drs. Tony Eissa and Joseph Hyser
- ▶ **“TRAFFICKING LEUKOCYTES IN THE AGING MOUSE HEART; IN VIVO MRI AND FLOW CYTOMETRY STUDY”**. Drs. Katarzyna Cieslik and Robia Pautler
- ▶ **“PROMOTING ENHANCED ANGIOGENESIS IN POST-STROKE BRAIN THROUGH MODULATION OF NOTCH SIGNALING”**. Drs. Joshua Wythe, Sean Marrelli and William Lagor

*Please send your award or recognition to [cvri@bcm.edu](mailto:cvri@bcm.edu) to be included in upcoming newsletters.*

## How to interpret an echocardiography report (for the non-imager)?

Bansal M., Sengupta PP. *Heart* 2017; 103: 1733-44

## Galectin-3 and incidence of atrial fibrillation: The Atherosclerosis Risk in Communities (ARIC) study

Fashanu OE, Norby FL, Aguilar D, Ballantyne CM, Hoogeveen RC, Chen LY, Soliman EZ, Alonso A, Folsom AR. *Am Heart J* 2017; 192: 19-25

## First Implantation of a Novel Left Ventricular Assist Device: The ReliantHeart aVAD

Schmitto JD, Hanke JS, Dogan G, Tessmann R, Jeevanandem V, Cohn WE, Frazier OH, Haverich A. *Ann of Thorac Surg* 2017; 104 e311-e313

## Rationale and design of the ICON-RELOADED study: International Collaborative of N-terminal pro-B-type Natriuretic Peptide Re-evaluation of Acute Diagnostic Cut-Offs in the Emergency Department

Gaggin HK, Chen-Tournoux AA, Christenson RH, Doros G, Hollander JE, Levy PD., Nagurney JT, Nowak RM, Pang PS, Patel D, Peacock WF, Walters EL, Januzzi JL. *Am Heart J*, 2017; 192: 26-37

## Morphine Use in the ED and Outcomes of Patients with Acute Heart Failure: A Propensity Score-Matching Analysis Based on the EAHFE Registry

Mirã Á, Gil V, Martãn-Sánchez FJ, Herrero-Puente P, Jacob J, Mebazaa A, Harjola VP, Rãos J, Hollander JE, Peacock WF, Llorens P. *Chest* 2017; 152: 821-32

## 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA, McBride PE, Peterson PN, Stevenson LW, Westlake C. *J Am Coll Cardiol* 2017; 70:776-803

## Why do some conduits get infected and others don't?

Mery C.M, Fraser CD. *J Thorac Cardiovasc Surg* 2017; *in press*

## Video-assisted thoracoscopic lobectomy is associated with greater recurrence-free survival than stereotactic body radiotherapy for clinical stage I lung cancer

Cornwell LD, Echeverria AE, Samuelian J, Mayor J, Casal RF, Bakaeen FG, Omer S, Preventza O, Mai W, Chen G, Simpson KH, Moghanaki D, Zhu AW. *J Thorac Cardiovasc Surg* 2017; *in press*

## Effect of postoperative anemia and baseline cardiac risk on serious adverse outcomes after major vascular interventions

Kougias P, Sharath S, Barshes NR, Chen M, Mills JL. *J Vascular Surg* 2017; 1836-43

## Sometimes evolution requires a revolution

Coselli JS, *J Thorac Cardiovasc Surg* 2017; *in press*

## Surgery for acute type A aortic dissection on oral anticoagulants: Being the dispatcher of a 911 call

Preventza O, Bracey A, *J Thorac Cardiovasc Surg* 2017; *in press*

## Reoperative surgery on the thoracoabdominal aorta

Coselli J, Rosu C, Amarasekara HS, Green SY, Zhang Q, Price MD, LeMaire SA, *J Thorac Cardiovasc Surg* 2017; *in press*

## Association of low-density lipoprotein pattern with mortality after myocardial infarction: Insights from the TRIUMPH study

Pokharel Y, Tang Y, Bhardwaj B, Patel KK, Qintar M, O'Keefe JH, Kulkarni KR, Jones PH, Martin SS, Virani SS, Spertus JA, *J Clin Lipidol* 2017; *in press*

## Effects of n-3 fatty acid treatment on monocyte pheno types in humans with hypertriglyceridemia

Dai Perrard XY, Lian Z, Bobotas G, Dicklin MR, Maki KC, Wu H. *J Clin Lipidol* 2017; 66: 1836-43

## Soluble Mesothelin-Related Peptides to Monitor Recurrence after Resection of Pleural Mesothelioma

Burt BM, Lee HS, Lenge De Rosen V, Hamaji M, Groth SS, Wheeler TM, Sugarbaker DJ. *Ann of Thorac Surg* 2017; 104: 1679-87

## 2017 AHA/ACC Clinical Performance and Quality Measures for Adults with ST-Elevation and Non-ST-Elevation Myocardial Infarction:

Jneid H, Addison D, Bhatt DL, Fonarow GC, Gokak S, Grady KL, Green LA, Heidenreich PA, Ho PM, Jurgens CY, King ML, Kumbhani D.J, Pancholy S, *J Am Coll Cardio* 2017; 70: 2048-90

## Association of high-density lipoprotein-cholesterol versus apolipoprotein A-I with risk of coronary heart disease: The European prospective investigation into cancer-norfolk prospective population study, the atherosclerosis risk in communities study, and the Women'S Health Study

van Capelleveen JC, Bochem AE, Boekholdt SM, Mora S, Hoogeveen RC, Ballantyne CM, Ridker PM, Sun W, Barter PJ, Tall AR, Zwinderman AH, Kastelein JJ, Wareham NJ, Khaw KT, Hovingh GK. *J Am Heart Assoc* 2017; *in press*

# CVRI THEMES AND LEADERSHIP

## AORTOPATHY, VALVULAR HEART DISEASE



**Scott LeMaire, MD**  
Surgery  
Member, Executive Committee

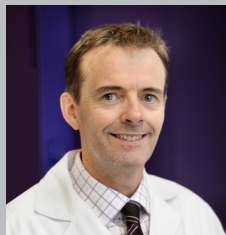


**Vijay Nambi, MD**  
Medicine/Cardiology

## CONGENITAL DEVELOPMENTAL HEART DISEASE



**Mary Dickinson, PhD**  
Physiology  
Member, Executive Committee



**Daniel Penny, MD, PhD MHA**  
Pediatrics/Cardiology  
Member, Executive Committee

## ARRHYTHMIAS, CHANNELOPATHIES



**Xander Wehrens, MD, PhD**  
Physiology, Medicine  
CVRI Director



**Miguel Valderrabano, MD**  
Medicine/Cardiology

## CORONARY ARTERY DISEASE, ATHEROSCLEROSIS, ISCHEMIA



**Christie Ballantyne, MD**  
Medicine/Cardiology  
Member, Executive Committee

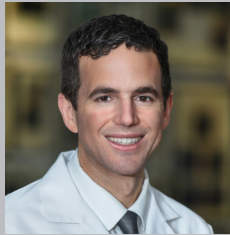


**Changyi Johnny Chen, MD, PhD**  
Surgery

## CARDIAC REGENERATION, STEM CELLS



**James Martin, MD, PhD**  
Physiology  
Member, Executive Committee



**Gabriel Loor, MD**  
Surgery  
Member, Executive Committee

## HEART FAILURE, CARDIOMYOPATHY



**Biykem Bozkurt, MD**  
Medicine/Cardiology  
CVRI Associate Director



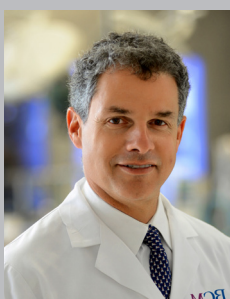
**Tom Cooper, MD**  
Pathology  
Member, Executive Committee



**Mark Entman, MD**  
Medicine,  
Cardiovascular Sciences  
Member, Executive Committee

## CVRI EXECUTIVE COMMITTEE UPDATE

The CVRI would like to thank Todd Rosengart, MD, for his 5 years of service on the Executive Committee. His input and insight on the committee will be missed. Dr. Rosengart personally selected Gabriel Loor, MD, FACC, to replace him on the committee.



The CVRI would like to welcome the newest member to the Executive Committee, Gabriel Loor, MD. He is the Surgical Director of the Lung and Transplant Program at the Baylor St. Luke's Medical Center. Dr. Loor specializes in the clinical evaluation and surgical management of patients with advanced cardiothoracic disease. His special interest include advanced heart and lung failure. Dr. Loor will be replacing Dr. Rosengart on the committee.

