### CARDIOVASCULAR RESEARCH INSTITUTE

Fall 2016

## Dr. Ge Tao, Dr. James F. Martin and colleagues identify mechanism in the mammalian heart that promotes heart repair after cardiac injury



Dr. Ge Tao

Dr. James F. Martin

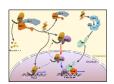


Figure 10 of article

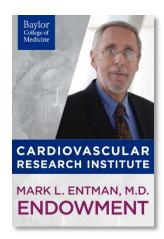
A team of scientists led by researchers at Baylor College of Medicine has published findings on the identification of a mechanism that promotes heart repair after cardiac injury in neonatal mice and in the Hippo-deficient heart regeneration mouse model through upregulation of the Pitx2 transcription factor.<sup>1</sup>

The research was led by Dr. Ge Tao, a postdoctoral associate in the James Martin Lab, and supervised by Dr. James F. Martin, professor of molecular physiology at Baylor College of Medicine. The team examined a genetic pathway that is activated by tissue damage after a myocardial infarction. Cardiac repair was observed in the mouse model when Pitx2 was present. The paper, "Pitx2 promotes heart repair by activating the antioxidant response after cardiac injury," was published in *Nature*, June 2, 2016, edition, (doi: 10.1038/nature17959). Research team members are from Baylor College of Medicine Cardiovascular Research Institute, Texas Heart Institute, the University of Iowa and the University of Texas Southwestern Medical Center, Dallas.

The Martin Lab focuses on the study of molecular mechanisms controlling cell growth and differentiation in embryogenesis and their relation to congenital heart defects and heart muscle regeneration. The lab is currently working on developing methods to remove Hippo signaling using small molecules that may prove useful to treat human patients who have suffered heart muscle destruction. Dr. Martin is the Cardiac Regeneration and Stem Cells theme leader at the Baylor College of Medicine Cardiovascular Research Institute. More information about research at the Martin Lab can be found here: Martin Lab.

1 Nature 534, Editors' summary.

### Dr. Mark L. Entman Endowment Launch at Trevisio



On Thursday, May 12, 2016, the Baylor Cardiovascular Research Institute, along with Dr. Mark Entman, his friends, family and colleagues, celebrated the creation of the Dr. Mark L. Entman Endowed Fund at a luncheon held at Trevisio Restaurant in the Texas Medical Center. The fund was established by a generous gift from the

Medallion Foundation honoring Dr. Entman's significant and continuing contributions to research and teaching throughout his 50-year career. Speakers recalled the history

of cardiovascular research at Baylor and Dr. Entman's work as one of the pioneers of that field, as well as personal memories of his friendship, support and thoughtfulness.

Dr. Entman graduated from Duke University Medical School in 1963. He was recruited to Baylor College of Medicine as an assistant professor in 1970 and presently holds positions at BCM as professor of medicine – cardiovascular sciences, as scientific director of the DeBakey Heart Center and as William J. Osher Professor of Cardiovascular Research. Throughout his career as a researcher and professor, his achievements have been recognized with many awards, such as the Ken Bowman Research Achievement Award, the Duke University Medical Center Distinguished Alumnus Award, the NHLBI Merit Award and the International Society for Heart Research Award for Outstanding

Research. Dr. Entman has been continuously funded as a principal investigator by the National Institutes of Health since 1967 and is currently funded until 2017. He has served on numerous peer review committees and on editorial boards of all of the major journals associated with cardiovascular research, as well as acted as associate editor of *Circulation*. Dr. Entman's current research interests relate to molecular and cellular mechanism injury and repair in the myocardium.

The Dr. Mark L. Entman Endowed Fund welcomes contributions toward the goal of establishing an endowed chair for the Cardiovascular Research Institute. Endowment

funds will support cardiovascular research and education within the six themes of the Institute: Coronary Artery Disease, Atherosclerosis and Ischemia; Heart Failure and Cardiomyopathy; Arrhythmias and Channelopathies; Congenital Development Heart Disease; Aortopathy and Valvular Heart Disease; and Cardiac Regeneration and Stem Cells. Dr. Entman is a CVRI theme leader for Heart Failure and Cardiomyopathy.

For information about the Dr. Mark L. Entman Endowed Fund or to make a donation please contact Jennie Arevalo at Jennie. Arevalo@bcm.edu or 713-798-2145.







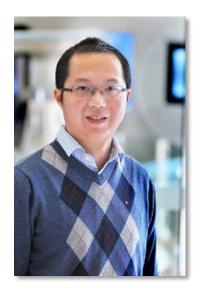


The Cardiovascular Research Institute at Baylor College of Medicine was established in 2012 as a key strategic initiative to enhance collaborative opportunities for research in cardiovascular sciences. The CVRI aims to provide administrative and research support to promote collaborative and interdisciplinary 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, M.D., Ph.D., and Associate Director Biykem Bozkurt, M.D., Ph.D.

For more information about CVRI, please visit www.bcm.edu/cvri,

### CVRI Seminar Series 2016-17

New series begins August 17 with Yong Xu, M.D., Ph.D.



We are pleased to announce that Yong Xu, M.D., Ph.D., will launch the CVRI Seminar Series for the new academic year. Dr. Xu will speak on Aug. 17 at noon in room 201A, Baylor College of Medicine, Main Campus, 1 Baylor Plaza. Dr. Xu's topic is "Estrogen actions in the brain amygdala regulate blood pressure." The presentation is based on a recent publication in *Hypertension*, titled, "Estrogen Receptor-α in the Medial Amygdala Prevents Stress-Induced Elevations in Blood Pressure in Females," (*Hypertension*. 2016; 67:1321-1330. DOI: 10.1161 /HYPERTENSIONAHA.116.07175.) The research project was led by Dr. Antentor Othrell Hinton Jr. and supervised by Dr. Xu.

Dr. Xu is an associate professor of pediatrics and nutrition at Baylor College of Medicine and a secondary associate professor in molecular and cellular biology at BCM. His professional interests involve research on CNS control of body weight, glucose and blood pressure to identify the novel neural circuits, neurotransmitters and intra-neuronal signals that are critical for coordinated control of body weight, feeding behavior, glucose balance and blood pressure. His lab is located at the Children's Nutrition Research Center.

Each fall and spring semester, CVRI presents a series of lunchtime seminars designed to inform cardiovascular physicians, scientists and clinical and research trainees of recent discoveries in cardiovascular research. These seminars are presented by distinguished physicians and researchers from noted institutions around the country and within the Texas Medical Center who have recently published and are actively involved in research. Seminars take place one Wednesday per month, from noon to 1 pm, and lunch is provided. Seminars are open to all faculty, staff and students who are interested. For more information about the CVRI Seminar Series, please visit: <a href="CVRI Seminar Series">CVRI Seminar Series</a>

### Fifth Annual CVRI Symposium - 2017

### Mark your calendars for April 4, 2017!

CVRI's fifth annual symposium will be held in Rayzor Lounge and Cullen Auditorium at Main Baylor on April 4, 2017. The all-day event features lectures by noted experts and poster

sessions showcasing research projects completed by junior faculty, clinical fellows, postdoctoral researchers and BCM students. Additional information regarding sessions and registration links will be posted on the CVRI website at a later date.

CVRI is pleased to announce that Christine Seidman, M.D., director of the Brigham & Women's Cardiovascular

Genetics Center at Harvard Medical School and Howard Hughes Medical Institute Investigator, will be the symposium's keynote speaker. Dr. Seidman is a highly accomplished genetic researcher in hypertrophic cardiomyopathy in humans. She works closely with her

husband, Jonathan Seidman, Ph.D., at the Seidman Lab at Harvard Medical School, and their work has provided fundamental insights into myocyte biology, enabled gene-based diagnosis, and defined novel therapeutic targets. Ongoing research includes molecular genetic analyses of cardiomyopathies, cardiac arrhythmias, cardiac structural disorders (congenital heart disease)

neurologic disorders, vascular abnormalities and premature coronary disease risk factors. For additional information about the Seidman Lab's research please visit: Seidman Lab.



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### From the Director



### Xander Wehrens, M.D., Ph.D.

Director, Cardiovascular Research Institute
Juanita P. Quigley Endowed Chair in Cardiology
Professor, Department of Molecular Physiology and Biophysics
Professor, Department of Medicine (in Cardiology)
Co-Director, Medical Scientist Training Program

One of the Cardiovascular Research Institute's core missions is to promote innovative research by facilitating new collaborations across affiliated departments and hospitals. With the goal of encouraging additional collaborative projects, we are introducing a quarterly newsletter to inform CVRI members of ongoing research and recent notable achievements.

Collaborative research is highlighted in our featured paper from Dr. Jim Martin's lab. Under Dr. Martin's direction, scientists from Baylor College of Medicine, Texas Heart Institute, the University of Iowa and the University of Texas Southwestern Medical Center investigated antioxidant response in cardiac injury. Their findings will provide new insights into potential therapies to treat heart failure. Their success is proof that inter-institutional partnerships can produce significant scientific breakthroughs. In recognition of his team's accomplishments, Dr. Martin was recently announced as one of the recipients of the 2016 DeBakey Research Awards.

Together, CVRI institutions and scientists form a repository of medical knowledge that has few equals in medical research. Membership in CVRI offers an extraordinary opportunity to create partnerships with scientists who can provide transformative insights into ongoing research. The Institute's goal is to provide a platform to share this knowledge in order to more quickly translate scientific discoveries into effective, innovative clinical therapies.

I hope you will feel free to reach out to me to share your projects and discoveries to ensure that the dialogue continues.

Deehin.

### **CVRI Member Profile**

Dr. Andrew Landstrom, M.D., Ph.D.



Andrew Landstrom, M.D., Ph.D., is a clinical fellow in pediatrics and cardiology, instructor in pediatrics and postdoctoral research fellow in molecular physiology and biophysics at Baylor College of Medicine. He earned his Ph.D. in molecular pharmacology from Mayo Graduate School and M.D. from Mayo Medical School, with an internship and residency at the Department of Pediatrics, Baylor College of Medicine.

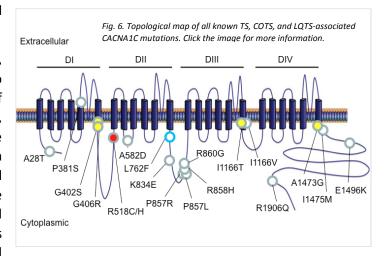
As a physician-scientist, Dr. Landstrom's research focuses on uncovering the genetic and molecular causes of sudden cardiac arrest, with the ultimate goal of applying his findings in a clinical setting

as a pediatric electrophysiologist. Dr. Landstrom has published extensively on the role of junctophilin type 2 (JPH2) and calcium dysregulation in sudden death-predisposing arrhythmias and cardiac diseases, initially expanding his research to

the genetics of cardiovascular disease and cellular physiology, and then to the electrical system of the heart. His interest in research at the fringes of pediatric cardiology medical knowledge grew from his experiences treating children who were

critically ill or at risk of sudden death without a medical explanation.

Dr. Landstrom recently worked with Dr. Mark Anderson, Osler Professor and chief of medicine at Johns Hopkins, to learn a specific technique for isolating the small number of cells of mouse hearts that make up the pacemaker, knowledge that will support his research interests in the heart and its electrical system. His most recent publication (see image), "Novel long QT syndrome-associated missense mutation, L762F, in CACNA1C-encoded L-type calcium channel imparts a slower inactivation tau and increased sustained and window current," reflects his interests in genetics, cellular electrophysiology and



pediatric cardiology. The article will be published in the *International Journal of Cardiology*, vol. 220, 1 October 2016, doi:10.1016/j.ijcard.2016.06.081.

For more information about Dr. Landstrom's research, please visit his BCM webpage here: Andrew Landstrom, MD, PhD.

### Baylor College of Medicine | American Heart Association Heart Walk

2016 Heart Walk scheduled for November 5 in the Texas Medical Center

SAVE THE DATES! Baylor College of Medicine's "Ace of Hearts" Team will once again participate in the American Heart Association's Heart Walk. This year, it's easier than ever to participate as the walk will take place in the Texas Medical Center! A Baylor kickoff event is being planned for Thursday, Aug. 24, to provide forms, information and hand out t-shirts to the participants. Watch for further announcements about the kickoff on the CVRI website at <a href="https://www.bcm.edu/CVRI">www.bcm.edu/CVRI</a> and the <a href="https://www.bcm.edu/CVRI">BCM BeWell</a> page. To sign up individually or create a team under the Baylor "Ace of Hearts" banner, please visit the Baylor College of Medicine Heart Walk Page.



### **CVRI Member Selected Publications**

Compartment syndrome of the foot associated with a delayed presentation of acute limb ischemia Barshes, N. R., Pisimisis, G, Kougias, P.

Journal of Vascular Surgery Volume 63, Issue 3, March 2016, Pages 819-822

### Relation of Cardiac Dysfunction to Rhythm Abnormalities in Patients with Duchenne or Becker Muscular Dystrophies

Chiang, D.Y., Allen, H.D., Kim, J.J., Valdes, S.O., Wang, Y., Pignatelli, R.H., Lotze, T.E., Miyake, C.Y.

American Journal of Cardiology Volume 117, Issue 8, 15 April 2016, Pages 1349-1354

## Results of Open Surgical Repair in Patients with Marfan Syndrome and Distal Aortic Dissection

Coselli, J.S., Green, S.Y., Price, M.D., Hash, J.A., Ouyang, Y., Volguina, I.V., Preventza, O., De La Cruz, K.I., LeMaire, S.A.

Annals of Thoracic Surgery Volume 101, Issue 6, 1 June 2016, Pages 2193-2201

### Outcomes of 3309 thoracoabdominal aortic aneurysm repairs

Coselli, J.S., LeMaire, S.A., Preventza, O., De La Cruz, K.I., Cooley, D.A., Price, M.D., Stolz, A.P., Green, S.Y., Arredondo, C.N., Rosengart, T.K.

Journal of Thoracic and Cardiovascular Surgery Volume 151, Issue 5, 1 May 2016, Pages 1323-1338

### Plasma Levels of Endothelial Microparticles Bearing Monomeric C-reactive protein are Increased in Peripheral Artery Disease

Crawford, J. R, Trial, J.A., Nambi, V., Hoogeveen, R.C., Taffet, G.E., Entman, M.L.

Journal of Cardiovascular Translational Research Volume 9, Issue 3, 1 June 2016, Pages 184-193

### Efficacy of Angiotensin-Converting Enzyme Inhibitors and Angiotensin-Receptor Blockers in Coronary Artery Disease without Heart Failure in the Modern Statin Era: a Meta-Analysis of Randomized-Controlled Trials

Hoang, V., Alam. M., Addison, D., Macedo, F., Virani, S., Birnbaum, Y.

Cardiovascular Drugs and Therapy Volume 30, Issue 2, 1 April 2016, Pages 189-198

#### A heartbreaking pleasure

Liu, G., Khalid, U., Birnbaum, Y., Hamzeh, I.R.

International Journal of Cardiology Volume 204, 1 February 2016, Pages 177-178

## Risk factors for development of endocarditis and reintervention in patients undergoing right ventricle to pulmonary artery valved conduit placement

Mery, C.M., Guzman-Pruneda, F.A., De Leon, L.E., Zhang, W., Terwelp, M.D., Bocchini, C.E., Adachi, I., Heinle, J.S., McKenzie, E.D., Fraser, C.D., Jr.

Journal of Thoracic and Cardiovascular Surgery Volume 151, Issue 2, 1 February 2016, Pages 432-439

Reassessing risk factors in pediatric patients with pacemakers implanted for atrioventricular block: The impact of nonsustained ventricular tachycardia Niu, M.C., Morris, S.A., Krenek, M., De La Uz, C.M., Pedroza, C., Miyake, C.Y., Kim, J.J., Valdes, S.O.

Journal of Cardiovascular Electrophysiology Volume 27, Issue 4, 1 April 2016, Pages 471-479

# Case-based educational intervention to assess change in providers' knowledge and attitudes towards the 2013 American College of Cardiology/American Heart Association Cholesterol Management Guideline

Pokharel, Y., Steinberg, L., Chan, W., Akeroyd, J.M., Jones, P.H., Nambi, V., Nasir, K., Petersen, L., Ballantyne, C.M., Virani, S.S.

#### Atherosclerosis

Volume 246, March 01, 2016, Pages 115-120

### Guideline-Directed Medication Use in Patients with Heart Failure with Reduced Ejection Fraction in India: American College of Cardiology's PINNACLE India Quality Improvement Program

Pokharel, Y., Wei, J., Hira, R.S., Kaira, A., Shore, S., Kerkar, P.G., Kumar, G., Risch, S., Vicera, V., Oetgen, W.J., Deswal, A., Turakhia, M.P., Glusenkamp, N., Virani, S.S.

#### **Clinical Cardiology**

Volume 39, Issue 3, 1 March 2016, Pages 145-149

Efficacy and safety of catheter-based rheolytic and aspiration thrombectomy in children

Qureshi, A.M., Petit, C.J., Crystal, M.A., Liou, A. Justino, H.

Catheterization and Cardiovascular Interventions Volume 87, Issue 7, 1 June 2016, Pages 1273-1280

Prediction of imminent, severe deterioration of children with parallel circulations using real-time processing of physiologic data

Rusin, C.G., Acosta, S.I., Shekerdemian, L.S., Vu, E.L., Bavare, A.C., Myers, R.B., Patterson, L.W., Brady, K.M., Penny, D. J.

Journal of Thoracic and Cardiovascular Surgery Volume 152, Issue 1, 1 July 2016, Pages 171-177

Association of Late Gadolinium Enhancement and Degree of Left Ventricular Hypertrophy Assessed on Cardiac Magnetic Resonance Imaging with Ventricular Tachycardia in Children with Hypertrophic Cardiomyopathy

Spinner, J.A., Noel, C.V., Denfield, S.W., Krishnamurthy, R., Jeewa, A., Dreyer, W.J., Maskatia, S.A.

American Journal of Cardiology Volume 117, Issue 8, 15 April 2016, Pages 1342-1348

### Mitral valve replacement for inflow obstruction of left ventricular assist device in a child with restrictive cardiomyopathy

Tunuguntla, H., Denfield, S.W., McKenzie, E.D., Adachi, I.

Journal of Thoracic and Cardiovascular Surgery Volume 151, Issue 1, 1 January 2016, Pages e11-e13

## Provider understanding of the 2013 ACC/AHA cholesterol guideline

Virani, S.S., Pokharel, Y., Steinberg, L., Chan, W., Akeroyd, J.M., Gowani, S.A., Kalra, A., Polsani, V., Miedema, M.D., Jones, P.H., Nambi, V., Petersen, L.A., Ballantyne, C.M.

Journal of Clinical Lipidology Volume 10, Issue 3, 1 May 2016, Pages 497-504.e4

## AKT2 Promotes Bone Marrow Cell-Mediated Aortic Protection in Mice

Zou, S., Ren, P., Zhang, L., Azares, A.R., Zhang, S., Coselli, J.S., Shen, Y.H., LeMaire, S.A.

Annals of Thoracic Surgery Volume 101, Issue 6, 1 June 2016, Pages 2085-2096

### 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 strongest strategic initiatives, the Cardiovascular Research Institute.

Please fill out the online membership form on CVRI's membership page.

Many benefits will be extended to you as a CVRI member, including:

- 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 Jennie Arevalo at <u>Jennie.Arevalo@bcm.edu</u> or 713-798-2145 or Sharon Lahey at <u>Sharon.Lahey@bcm.edu</u> or 713-798-6580.

## CVRI Themes and Leadership

### Aortopathy, Valvular Heart Disease



**Scott LeMaire, M.D.**Surgery
Member, Executive Committee



**Vijay Nambi, M.D.** Medicine/Cardiology

### Arrhythmias, Channelopathies



**Xander Wehrens, M.D., PhD.**Physiology, Medicine
CVRI Director



Miguel Valderrabano, M.D., F.A.C.C.
Medicine/Cardiology

### Cardiac Regeneration, Stem Cells



James F. Martin, M.D., Ph.D. Physiology Member, Executive Committee



**Todd Rosengart, M.D.**Surgery
Member, Executive Committee

## Congenital Developmental Heart Disease



**Mary Dickinson, Ph.D.**Physiology
Member, Executive Committee



Daniel Penny, M.D., Ph.D., M.H.A Pediatrics/Cardiology Member, Executive Committee

Coronary Artery Disease, Atherosclerosis, Ischemia



Christie Ballantyne, M.D. Medicine/Cardiology Member, Executive Committee



Changyi Johnny Chen, M.D., Ph.D. Surgery

### Heart Failure, Cardiomyopathy



**Biykem Bozkurt, M.D.** Medicine/Cardiology CVRI Associate Director



**Tom Cooper, M.D.**Pathology
Member, Executive Committee



Mark L. Entman, M.D.
Medicine, Cardiovascular Sciences
Member, Executive Committee