Heandarch

A Physician Newsletter Produced by the Texas Heart Institute





# ICD Lead Placement in the Middle Cardiac Vein Is an Alternative to Lead Placement via a Thoracotomy

**Abstract:** When right ventricular lead placement is contraindicated, a transvenous, minimally invasive approach can allow successful implantable cardioverter defibrillator lead placement.

**Traditionally,** the epicardial defibrillator leads for implantable cardioverter defibrillators (ICDs) were implanted via a thoracotomy incision with the aid of general anesthesia. However, advances in lead technology later allowed a transvenous approach, and investigators have tested a variety of nonthoracotomy lead configurations. Nevertheless, placing a transvenous defibrillator coil near both the right ventricular (RV) apex and the interventricular septum is still recommended.

In patients who have undergone previous tricuspid valve surgery, providing permanent pacing and cardiac defibrillation can be challenging—especially if lead placement through the prosthetic valve is contraindicated or the patient's anatomy makes stable RV lead placement difficult or impossible.

"In selected patients for whom RV lead placement is contraindicated or impossible, we have used leads designed for left ventricular (LV) pacing," says J. Alberto Lopez, MD, a cardiologist at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's). "We have also found that it is possible to place the coil lead transvenously in the middle cardiac vein (MCV). This approach avoids the need for general anesthesia and the risks associated with surgical lead placement in these patients."

Dr. Lopez has used this approach in 6 patients, achieving ventricular pacing and sensing by placing bipolar leads in the lateral branch of the coronary sinus or in the atrialized portion of the right ventricle. After cannulation of the MCV, a defibrillator coil lead is placed in the farthest apical position, and an "active can" pulse generator is implanted in the left retromammary region. To achieve defibrillation, shocks are delivered between the MCV coil, superior vena cava coil, and active can or between the MCV coil, azygos vein coil, and active can. A report detailing Dr. Lopez's success in these 6 cases recently appeared in *Europace* (2012;14:853–8).

The defibrillation safety margin was at least 10 J in all patients. During follow-up evaluation, 1 patient had ventricular fibrillation and received a successful internal shock, and 2 patients had



(A) Cranial tilt and right anterior oblique projections of the coronary sinus. Note the amount of myocardium within the defibrillation field, because of epicardial placement of an electrode in the middle cardiac vein (MCV). (B) Shallow left anterior oblique projection of the defibrillator coil lead in the MCV and the pulse generator in retromammary position. A bipolar lead was placed in the lateral branch for ventricular pacing and sensing (p/s). (Reprinted with permission from *Europace* 2012;14:853-8.)

ventricular tachycardia requiring overdrive ventricular pacing, which was also successful.

Other physicians have described alternative lead configurations for avoiding a thoracotomy in ICD placement after tricuspid valve surgery, but none positioned a defibrillator coil lead in the MCV and a conventional LV bipolar lead in a lateral branch.

"Placing the defibrillator lead in the MCV makes the current vector similar to what it would be if the lead had been placed in the conventional RV apical position," says Dr. Lopez. "When the coil lead electrode is placed in the MCV, there is a greater amount of myocardium within the current field and a favorable potential gradient over the interventricular septum. The result is defibrillation of a greater mass of ventricular myocardium."

Dr. Lopez believes that the availability of an over-the-wire defibrillator coil lead could make

this approach easier. He adds that the long-term effects of electrode placement within the MCV still need to be evaluated, as do the morbidity and mortality associated with lead removal, should patients require it.

"For these 6 patients, we have 5 years' followup data and no late complications. Our experience to date shows that transvenous defibrillation with an MCV electrode is an effective and safe alternative to the conventional epicardial approach when there is no access to the right ventricle," says Dr. Lopez. "Most importantly, with this approach, these patients can be spared another open heart procedure and its potential risks." •

#### For more information:

Dr. J. Alberto Lopez 713.790.9401

TEXAS HEART INSTITUTE AT ST. LUKE'S EPISCOPAL HOSPITAL IS RANKED AMONG THE NATION'S TOP 10 HEART CENTERS FOR 22ND CONSECUTIVE YEAR

In U.S. News & World Report's Best Hospital Rankings for 2012–2013, the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) was ranked #6 among the top 10 cardiology and heart surgery centers in the United States. This marks the 22nd consecutive year that THI has ranked among the top 10 heart and heart surgery centers in the United States. Additionally, THI at St. Luke's is the only heart center in Houston and the entire Southwest to be listed among the top 10 by U.S. News & World Report. The annual rankings are intended to help patients or referring physicians find hospitals with the highest level of skill in diagnosing and treating complex medical conditions. U.S. News & World Report bases these rankings on factors such as death rate, patient safety, and hospital reputation. This year, U.S. News & World Report evaluated data from 4,793 hospitals, of which only 148 (about 3%) met the criteria for being among the best in 1 or more specialties.

## The Texas Heart Institute Celebrates Its 50th Anniversary

**Abstract:** In the 50 years since its founding, the Texas Heart Institute has benefited countless people throughout the state of Texas, across the United States, and around the world.

In 1962, Denton A. Cooley, MD, founded the Texas Heart Institute (THI) in Houston's world-renowned Texas Medical Center. The Institute's mission was to reduce the devastating toll of cardiovascular disease through innovative research and education programs and improved patient care.

"At that time," recalls Dr. Cooley (now THI's President Emeritus and still its Surgeon-in-Chief), "only a few so-called heart institutes existed-one each in London, Miami, and Mexico City. They were flourishing because of the demand for their specialized services. I believed that one would flourish here in Houston. After giving the matter considerable thought, I asked my attorney to prepare a charter to incorporate a non-profit organization called the Texas Heart Institute—a name that would be simple. descriptive, and easy to remember. A few days later, the paperwork was registered at the Secretary of State's office in Austin. I had an architectural firm design a plan for a building that would be attached to St. Luke's Episcopal Hospital (St. Luke's) and Texas Children's Hospital. Those 2 institutions were already trying to raise money to expand their facilities, mainly because their beds were being filled by increasing numbers of my patients. On July 13, 1962, at a joint meeting of the 2 hospital boards, I presented my proposal, explained the need for THI, and showed the model. The boards tentatively approved my plan, and on August 3, 1962, the State of Texas granted THI's charter. For me, that was a dream come true."

Fifty years later, the Institute's success cannot be counted simply in time, but in new knowledge and discoveries that have advanced the fight against cardiovascular disease, the leading cause of death in the United States. With its clinical partner, St. Luke's, THI has become one of the nation's largest cardiovascular centers. Through innovative programs in research and education, it has been the scene of numerous exciting breakthroughs in the prevention, diagnosis, and treatment of cardiovascular disease. These breakthroughs include the first successful heart transplant in the United States, the "The Texas Heart Institute has been the site of more than 118,800 open heart operations, 258,000 cardiac catheterizations, 1,270 heart transplants, and 1,500 circulatory support pump implants experience no other facility can match."

first clinical implant of an artificial heart anywhere in the world, advances in the treatment of infants born with congenital defects, and development of effective methods of preventing and treating heart attacks by reducing blockages in the coronary arteries. The Institute has been the site of more than 118,800 open heart operations, 258,000 cardiac catheterizations, 1,270 heart transplants, and 1,500 circulatory support pump implants—experience no other facility can match.

Contrasting the medical environment of the 1960s with that of today, Dr. Cooley says, "In the early days, cardiovascular pioneers—particularly surgeons—had a kind of superhero status, which is now much more difficult to achieve. The emphasis is currently on a multidisciplinary approach to cardiac disease, and many of today's pioneers are working at the cellular level."

One eminent researcher advancing cardiovascular knowledge at the cellular level is James T. Willerson, MD, who succeeded Dr. Cooley as President of THI in 2008. Under Dr. Willerson's direction, THI has become a frontrunner in the investigation of vulnerable (unstable) plaque and its complications, as well as the use of stem cell therapy for cardiovascular disease.

For 50 years, THI has offered hope to victims of cardiovascular disease throughout the state of Texas, across the United States, and around the world, fulfilling Dr. Cooley's original vision. Today, at age 92, he regards THI as his most valuable achievement. "In 1962, I could never have foreseen how it would evolve into what it is today," he explains. "I am especially proud of our educational programs, which have trained hundreds of surgeons from all over the world. The Texas Heart Institute is my legacy. It has a much wider impact than I alone ever could. As long as heart disease remains a threat, THI will continue to lead the way in researching, preventing, and treating this condition."•

#### For more information:

Dr. Denton A. Cooley 832.355.4933

### Contents

ICD Lead Placement in the Middle Cardiac Vein Is an Alternative to Lead Placement via a Thoracotomy	1
The Texas Heart Institute Celebrates Its 50th Anniversary	2
During LVAD Support, Young Patients with Nonischemic Disease of Short Duration Have the Best Odds of LV Recovery	3
Stem Cells May Contribute to Tissue Remodeling in Thoracic Aortic Aneurysms and Dissections	4
Large-scale Database Study Finds No Effect of Daily Functional Impairment on Coronary Artery Bypass Grafting Outcomes	5
Texas Heart Institute Researchers Reprogram Mammalian Dermal Cells Into Cardiac Progenitors	6
Calendar	7

# During LVAD Support, Young Patients with Nonischemic, Short-term Disease Have Best Odds of LV Recovery

**Abstract:** Left ventricular recovery during left ventricular assist device support is most likely to occur in young patients with nonischemic cardiomyopathy of less than 1 years' duration.

### **Heart transplantation**

is the best evidence-based treatment for endstage heart failure, but the lack of donor organs severely limits the number of patients who can undergo this treatment. Use of a left ventricular assist device (LVAD) as a bridge to transplantation (BTT) until a donor heart becomes available or as permanent destination therapy (DT) is a life-saving option for many heart failure patients. During LVAD support, some patients recover enough myocardial function that the LVAD can be removed, although such recovery is uncommon. Recently, a multicenter group of investigators determined that young patients with nonischemic cardiomyopathy have a higher likelihood of left ventricular recovery during LVAD support.

The study, reported in the Journal of Cardiac Failure (2012;18:392-95), was conducted by the HeartMate II Clinical Investigators, including O. H. Frazier, MD, Chief of the Center for Cardiac Support at the Texas Heart Institute at St. Luke's Episcopal Hospital. Daniel J. Goldstein, MD, Director of the Mechanical Assistance Program at the Montefiore Medical Center in Bronx, NY, was first author. The investigators retrospectively analyzed data from the Heart-Mate II BTT and DT trials, held or conducted from March 2005 to March 2009 at 11 centers. Those trials included 1108 patients: 490 who received an LVAD as a BTT, 600 who received an LVAD as DT, and 18 who received an LVAD as compassionate-use therapy. Twenty patients (1.8%) at 11 centers underwent LVAD explantation following improvement of left ventricular function.

Ten of the LVAD-explant patients had received their devices as a BTT, and the other 10 had received their LVADs as DT. The median duration of support for patients who recovered function was 324 days (range, 161–1101 days). The patients' median age at explantation was 33 years (range, 15–61 years), and 12 patients (60%) were younger than 40 years. In 18 of the 20 patients, the primary etiology was nonischemic cardiomyopathy, and 11 patients (61%) had heart failure for less than 1 year. Of the patients

Incidence of Left Ventricular Recovery and Explant According to Etiology of Cardiomyopathy, Age, and Duration of Heart Failure Symptoms			
	Patients, n (%)	Recovered, n (%)	
Etiology (n=1108)			
Ischemic	577 (52%)	2 (0.3%)	
Nonischemic	531 (48%)	18 (3.4%)	
Age (n=531)			
<40 yrs	147 (28%)	12 (8.2%)*	
≥40 yrs	384 (72%)	6 (1.6%)	

447 (85%)

who had less than 1 year of heart failure history and were nonischemic, 13% had their LVADs explanted. The recovery rate was 3.4% for nonischemic patients and only 0.3% for ischemic patients.

Duration of HF symptoms (n=529)<sup>+</sup>

*†HF duration not provided for 2 of the 531 nonischemic patients.* 

<12 months

>12 months

Three of the 20 patients in the explant group had an LVAD re-implanted 0 to 64 days after device removal. Two of these patients had doxorubicin cardiomyopathy; 1 underwent a transplant, and the other remains on LVAD support. The third patient had idiopathic cardiomyopathy and died 5 days after device re-implantation. Of the remaining 17 explant patients, 16 (94%) are still alive; the other patient died of an unknown cause 2.3 years after the LVAD was explanted. All surviving patients available for follow-up (n=13) were in New York Heart Association (NYHA) functional class I or II; the patient who received a heart transplant was in NYHA class I.

"Patients with nonischemic cardiomyopathy had the highest rate of successful bridging to recovery, and patients with ischemic cardiomyopathy had the lowest rate of recovery in this study. Women had a higher recovery rate than men: 4.4% of the women recovered, whereas only 1% of the men did," says Dr. Frazier.

The mechanism behind ventricular recovery during LVAD support is unknown, but this

study indicates that such recovery is most likely to occur in young patients (<40 years) with heart failure of short duration and nonischemic etiology. Patients who meet these criteria should be evaluated for LVAD explantation.

"Because heart transplantation offers a median survival period of 10 years, physicians need to take a more aggressive approach to identifying ventricular recovery in these younger patients," concludes Dr. Frazier. "If transplantation can be avoided or delayed, their lives may be significantly lengthened. It should be noted that in none of the patients was improved ventricular function with LVAD removal the original therapeutic goal of implantation. In all the patients in whom the device was removed, left ventricular function was spontaneously observed. This should be pursued as a therapeutic goal that involves aggressive medical therapy along with LVAD therapy in every young LVAD recipient with idiopathic cardiomyopathy with the hope of avoiding transplantation or long-term LVAD support."

### For more information:

Dr. O. H. Frazier 832.355.3000

# Stem Cells May Contribute to Tissue Remodeling in Thoracic Aortic Aneurysms and Dissections

**Abstract:** The differentiation of stem cells within the diseased aorta suggests their involvement in both reparative and destructive remodeling in aortic aneurysms and dissections.

#### **Thoracic aortic aneurysms**

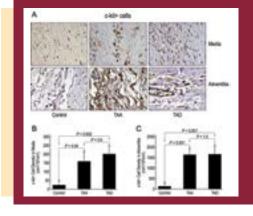
and dissections (TAAD) result from progressive medial degeneration that causes weakening of the aortic wall. Although multipotent stem cells play a role in tissue repair, it is not clear whether they contribute to repairing or replacing tissue damaged during development of TAAD. For this reason, researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) conducted a study supported by NIH/ NHLBI grants to begin exploring the hypothesis that stem cells facilitate aortic wall repair in TAAD (*Ann Thorac Surg* 2012;93:1524-33).

"We first determined whether stem cells are more abundant in TAAD tissue than in normal aortic tissue," says Scott A. LeMaire, MD, a cardiovascular surgeon at THI at St. Luke's and Professor and Director of Research in the Division of Cardiothoracic Surgery at Baylor College of Medicine. "We then attempted to determine

### COREVALVE STUDY ENROLLING PATIENTS FOR TRANSCATHETER AORTIC VALVE REPLACEMENT

The CoreValve Continued Access study is currently accepting patients under the direction of Dr. Joseph Coselli, Chief of Adult Cardiac Surgery and principal investigator of the enrollment site at the Texas Heart Institute at St. Luke's Episcopal Hospital. Since the transcatheter aortic valve replacement (TAVR) trial began, more than 148 patients with severe aortic stenosis and significant comorbidities have been screened at this site. The investigators continue to seek appropriate referrals. Exclusion criteria include evidence of recent acute myocardial infarction, a left ventricular ejection fraction <20%, untreated and significant coronary artery disease requiring revascularization, cardiogenic shock, end-stage renal disease, ongoing sepsis or active endocarditis, native aortic valve annulus size <20 mm or >29 mm, pre-existing prosthetic cardiac valve, mixed aortic valve disease, and moderate to severe mitral valve stenosis.

For more information, please contact the CoreValve coordinator at 832-355-9301.



whether stem cells within diseased tissue differentiate into functionally relevant cell types."

The study included 30 patients who underwent elective surgery for the repair of a descending thoracic aortic aneurysm without dissection (n=12) or a chronic descending thoracic aortic dissection (n=18). During repair, surgeons excised an aortic tissue sample from the area of greatest dilatation. For dissections, the sample was excised from the outer wall of the false lumen. Control samples were collected from age-matched organ donors who had never had an aortic aneurysm or dissection or undergone aortic repair (n=5).

Immunohistochemical analysis showed that STRO-1+ stem cells, c-kit+ stem cells, and CD34+ stem cells were much more abundant in the medial and adventitial layers of TAAD tissue than in those of control aortic tissue (see Figure). Using double immunofluorescence staining, the researchers examined the differentiation of these 3 cell types in the medial layer of the diseased tissue. They identified a subset of STRO-1+ cells that stained positive for the smooth muscle cell marker SM22- $\alpha$  or the fibroblast marker fibroblast-specific protein-1. They also found a small number of c-kit+ cells and CD34+ cells that stained positive for SM22- $\alpha$ . Furthermore, the investigators found that large numbers of STRO-1+ cells expressed the macrophage marker CD68 in the medial and adventitial layers of the diseased tissues, especially in areas of inflammatory cell infiltration.

Representative images (magnification, ×400) of c-kit+ cells detected by immunohistochemical staining in the medial and adventitial layers of control aortic, thoracic aortic aneurysm (TAA), and thoracic aortic dissection (TAD) tissues (A). Comparison of the mean densities of c-kit+ cells in the media (B) and adventitia (C) among the 3 groups. (Reprinted with permission from *Ann Thorac Surg* 2012;93:1524-33.)

"The presence of multipotent stem cells at sites of aneurysm and dissection and the further differentiation of these cells into smooth muscle cells, fibroblasts, or macrophages suggests the presence of an active repair process involving stem cells." says Joseph S. Coselli, MD, Chief of Adult Cardiac Surgery at THI at St. Luke's, Professor and Cullen Foundation Endowed Chair in the Division of Cardiothoracic Surgery at Baylor College of Medicine, and a coauthor of the published report.

"The abundance of stem cells in TAAD tissues raises several questions about their origin, their role in aortic repair and remodeling, and the factors and signaling pathways that regulate their activation and function," says Ying H. Shen, MD, PhD, a research scientist at THI at St. Luke's, an Assistant Professor of Cardiothoracic Surgery at Baylor College of Medicine, and lead author of the study. "Ultimately, we hope to determine whether we can manipulate this process to favor aortic repair."

### For more information:

Dr. Scott A. LeMaire Dr. Ying H. Shen Dr. Joseph S. Coselli 832.355.9910

# Large-scale Database Study Finds No Effect of Daily Functional Impairment on Coronary Artery Bypass Grafting Outcomes

**Abstract:** Data from more than 1500 patients who underwent CABG show that preoperative impairment in daily activities does not independently predict adverse postoperative outcomes.

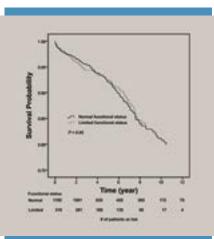
**For many patients** with advanced coronary artery disease (CAD), coronary artery bypass grafting (CABG) is the treatment best suited to their coronary anatomy and to the severity and distribution of their CAD. For some patients, however, the risks posed by this invasive procedure may outweigh the potential benefits. Therefore, many researchers have attempted to identify the patient and disease characteristics that best indicate the risk a given CAD patient would incur if he or she were to undergo CABG.

Advanced age is among the most commonly identified risk factors for adverse CABG outcomes. Nonetheless, several studies have shown that CABG can be performed safely in carefully selected elderly patients. Therefore, some researchers theorize that chronologic age only partly reflects how vigorous or frail patients are.

To examine the importance of frailty for CABG outcomes, Faisal G. Bakaeen, MD, and his colleagues at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's), the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC), and Baylor College of Medicine (BCM) performed a database study of CABG patients' risk factors and outcomes. Dr. Bakaeen is a cardiothoracic surgeon at THI at St. Luke's, an Associate Professor of Surgery at BCM, and Chief of Cardiothoracic Surgery at the MEDVAMC.

"The variable we were most interested in was functional status," says Dr. Bakaeen. "This refers to a patient's ability to perform normal activities of daily living without assistance, and limited functional status is regarded as a symptom of frailty. In our study, patients were considered to have limited functional status if, before hospitalization, they required assistance from equipment or another person for any activity of daily living, were living in a nursing home, or were receiving long-term oxygen therapy or hemodialysis."

The study examined data collected by the Department of Veterans Affairs' Continuous Improvement in Cardiac Surgery Program (CICSP), whose database contains informa-



Cox regression-adjusted survival curves indicating similar long-term post-CABG survival in patients with and without functional impairment. (Adapted with permission from *Ann Thorac Surg* 2012;93:1950-5.)

tion (regarding >140 clinical, demographic, outcome, and resource variables) concerning all cardiac surgery patients treated in the VA health system. The CICSP data from patients at the MEDVAMC were combined with information from each patient's computerized medical record.

In the CICSP database, the researchers identified 1503 consecutive patients who had undergone nonemergency CABG at the MEDVAMC between October 1, 1997, and September 30, 2009. Of these patients, 318 had limited functional status according to the investigators' criteria; the other 1185 patients had no functional limitation.

The primary postoperative outcomes examined in these 2 groups were 30-day mortality and late mortality. The secondary outcomes were stroke, mediastinitis, bleeding that necessitated reoperation, kidney failure that necessitated hemodialysis, the duration of postoperative ventilator support, and major adverse cardiac events: cardiac arrest that necessitated resuscitation, perioperative myocardial infarction, and the need for new circulatory support with either an intraaortic balloon pump or a ventricular assist device.

The investigators performed Cox proportional hazards regression analysis to study the effects of limited functional status on these outcomes. They used a forward stepwise regression model to control for a large number of potentially confounding covariates: age, sex, body mass index, number of bypass grafts, cardiopulmonary bypass and aortic cross-clamp times, smoking, New York Heart Association functional class. Canadian Cardiovascular Society angina class, preoperative albumin and creatinine levels, percutaneous coronary intervention in the 3 days before the operation, previous myocardial infarction, and history of hypertension, diabetes mellitus, cerebral vascular disease, peripheral vascular disease, and chronic obstructive pulmonary disease.

Counterintuitively, the analysis showed that preoperative functional status did not independently predict 30-day mortality, long-term mortality (over a mean follow-up period of 65 months), or any other adverse outcome. These findings were recently published in *The Annals of Thoracic Surgery* (2012;93:1950-5).

"These results are an important reminder that functional impairment in activities of daily living is not synonymous with frailty but, rather, a symptom of it," Dr. Bakaeen says. "Of course, we cannot know how many potential CABG patients with impaired functional status were not included in our study because surgeons deemed them inoperable. Nonetheless, these results tell us that CABG is a good treatment option for at least some patients with functional impairment."

#### For more information:

Dr. Faisal G. Bakaeen 713.794.7892

## Texas Heart Institute Researchers Reprogram Mammalian Dermal Cells Into Cardiac Progenitors

**Abstract:** Texas Heart Institute researchers have shown that the forced coexpression of transcription factors ETS2 and MESP1 can reprogram fibroblasts into cardiac progenitors.

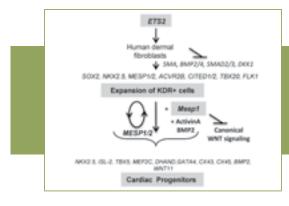
**Scientists** have long been studying the key developmental regulatory genes for reprogramming somatic cells into cells of other lineages. It is now known that cardiac founder cells express transcription factors Ci-MESP (mesoderm posterior) and Ci-ETS1/2, that Ci-MESP regulates a cardiac progenitor regulatory network, and that MESP1 and MESP2 direct the appearance of cardiac progenitors in mouse embryonic stem cells. However, MESP1 alone cannot convert cardiac fibroblasts into cardiac myocytes.

Physicians and scientists at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's), working collaboratively with researchers at the University of Houston (UH), the Texas A&M Health Science Center in Houston, and Baylor College of Medicine, investigated whether mammalian ETS2 and MESP homologs could be used to convert human skin cells into cardiac progenitors (*Proc Natl Acad Sci*  MESP1 or through cell treatment with purified proteins. This is evidenced by the de novo appearance of core cardiac transcription factors, Ca<sup>2+</sup> transients, and sarcomeres."

To determine whether ETS2 and MESP1 could generate functional cardiac myocytes from fibroblasts, researchers preinfected normal human dermal fibroblasts (NHDFs) with an α-MHC-Puromycin selection lentivector and treated the cells with purified ETS2 and MESP1 proteins fused to a short fragment of transactivator (TAT) protein, which acts as a cell-penetrating peptide. After cell selection, researchers followed the maturation of the reprogrammed cells by using a multichannel kinetic imaging cytometer that allowed monitoring of individual spontaneously contracting cells. They found that ETS2 and MESP1 by themselves were ineffective, but when combined, they induced significant beating activity. Researchers then preinfected the NHDFs with viral α-MHC- breakthroughs in cell therapy and cardiac regeneration, enabling physicians to replace damaged cardiac tissue with new tissue from a patient's own skin cells.

"We would now like to determine whether ETS2 and MESP1 can convert cardiac fibroblasts and mesenchymal stem cells in damaged hearts into cardiac progenitors that could result in ventricular remodeling or long-term repair," adds Dr. Schwartz.

"To repair the human heart through stem cell therapy, we need a practical way to generate new cardiac cells," says James T. Willerson, MD, President and Medical Director at THI and a lead investigator for the study. "Our data indicate that ETS2 and MESP1 play important roles in a genetic network that governs cardiopoiesis. We will have to see how stable these cells are over time in animal models, but Dr. Schwartz and colleagues have made significant progress toward developing a potential new therapy



Model for reprogramming of human fibroblasts into cardiac progenitors induced by overexpression of ETS2 and MESP1 or treatment with purified proteins, as supported by data from the study. (Reprinted with permission from *Proc Natl Acad Sci U S A* 2012;109:13016-21.)

*USA* 2012;109:13016-21). The study was led by Robert J. Schwartz, PhD, Director of Stem Cell Engineering at THI at St. Luke's and Director of UH's Center for Molecular Medicine and Experimental Therapeutics.

"Our study showed that ETS2 and MESP1 were the 2 factors needed to reprogram fibroblasts into cardiac progenitors," says Dr. Schwartz. "Neither ETS2 nor MESP1 alone is capable of generating cardiac progenitors de novo from fibroblasts. However, fibroblasts can be reprogrammed into cardiac progenitors through forced coexpression of ETS2 and Cherry reporter, a marker of more advanced cardiac development, before treating cells with purified ETS2- and MESP1-TAT proteins. After the enrichment of  $\alpha$ -MHC-Cherry+ cells, the researchers found that many of the  $\alpha$ -MHC-Cherry+ cells stained with  $\alpha$ -striated actin antibody appeared similar to those of embryonic cardiomyocytes.

"ETS2 and MESP1 converted the human skin cells into intermediate-staged myocytes similar to what you would find in early-stage embryonic hearts just beginning to beat," says Dr. Schwartz. Ideally, this research will lead to where none had existed before. Whether these strategies are ultimately safe in the human heart is now the question, and THI researchers will continue to break new ground in seeking the answer."

#### For more information:

Dr. Robert J. Schwartz 713.743.6595 Dr. James T. Willerson 832.355.6839



TEXAS HEART<sup>®</sup>INSTITUTE Scientific Publications Mail Code 1-194 P.O. Box 20345 Houston, TX 77225-0345 texasheart.org



EDITORIAL BOARD Benjamin Y. C. Cheong, MD William E. Cohn, MD Patrick J. Hogan, MD Scott A. LeMaire, MD George J. Reul, MD James M. Wilson, MD

ADVISORY COMMITTEE Denton A. Cooley, MD Joseph S. Coselli, MD O. H. Frazier, MD Zvonimir Krajcer, MD James T. Willerson, MD

EDITORS Rebecca Bartow, PhD Virginia Fairchild Diana Kirkland Marianne Mallia, ELS Stephen N. Palmer, PhD, ELS Nicole Stancel, PhD, ELS

**PRODUCTION ARTISTS** Melissa J. Mayo, ACE James Philpot, ACE

Editorial Office, 832.355.6630

For physician referrals, call 1.800.872.9355

© 2012 TEXAS HEART<sup>®</sup> INSTITUTE at St. Luke's Episcopal Hospital, Houston, Texas



*Cover*: Item donated by Nellie B. Connally for the Celebration of Hearts display in the Wallace D. Wilson Museum of the Texas Heart Institute at St. Luke's Episcopal Hospital—The Denton A. Cooley Building. Receive all the latest news and information www.texasheart.org

### Calendar of Events

### TEXAS HEART INSTITUTE Continuing Medical Education Symposia

Future Direction of Stem Cells in Cardiovascular Disease Westin Bonaventure November 2, 2012 • Los Angeles, California Program Director: James T. Willerson, MD

#### Third Annual Symposium on

Risk, Diagnosis, and Treatment of Cardiovascular Disease in Women Texas Heart Institute November 17, 2012 • Houston, Texas Program Director: Stephanie Coulter, MD

Twelfth Texas Update in Cardiovascular Advancements Texas Heart Institute December 7, 2012 • Houston, Texas Program Director: James T. Willerson, MD

For information about Texas Heart Institute CME activities, please e-mail cme@texasheart.org or call 713-218-2200. To view or complete selected online CME courses (certificates are available online), please visit <u>www.cme.texasheart.org</u>. New courses are added regularly.

### Selected Upcoming Local, National, and International Meetings

American Heart Association 2012 Scientific Sessions November 3–7, 2012 • Los Angeles, California www.scientificsessions.org

Society of Thoracic Surgeons 49th Annual Meeting January 26–30, 2013 • Los Angeles, California www.sts.org/education-meetings/sts-annual-meeting

International Society for Heart and Lung Transplantation 33rd Annual Meeting and Scientific Sessions April 24–27, 2013 • Montreal, Canada www.ishlt.org/meetings/annualMeeting.asp Abstract submission deadline: November 16, 2012

American Association for Thoracic Surgery 93rd Annual Meeting May 4–8, 2013 • Minneapolis, Minnesota www.aats.org/annualmeeting/ Abstract submission deadline: October 12, 2012



For 22 consecutive years, the Texas Heart Institute at St. Luke's Episcopal Hospital has been ranked among the top 10 heart centers in the United States by *U.S. News & World Report*'s annual guide to "America's Best Hospitals."

Non-Profit Organization U.S. Postage **PAID** Houston, Texas Permit No. 7249