Heart WATCH

SUMMER 2010

A Physician Newsletter Produced by the Texas Heart Institute

Texas Heart® Institute

at St. Luke's Episcopal Hospital

Long-term Survival of Transplanted CD34+ Cells Contributes to Improved Cardiac Function

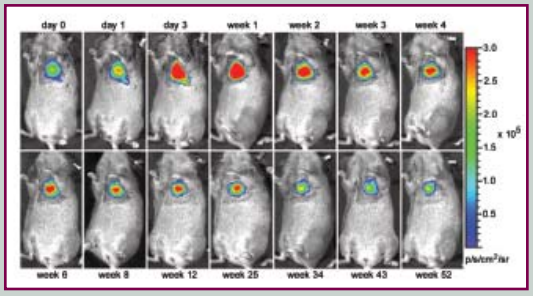
Abstract: Researchers are tracking the fate of human CD34+ cells injected into mice after myocardial infarction to determine how long the cells persist in the heart.

Cell-based therapies are being developed for the treatment of heart failure, and human CD34+ cells are being used in clinical trials for the treatment of myocardial infarction (MI). However, it is difficult to track the fate of transplanted cells in treated hearts, even postmortem. Thus, it is unknown how long the CD34+ cells persist in the heart, what underlying mechanisms are responsible for functional improvements, or whether such improvement is sustained.

The fate of CD34+ cells injected into the heart has been the focus of extensive research by Edward T. H. Yeh, MD, Professor and Chair of the Department of Cardiology at The University of Texas M. D. Anderson Cancer Center and McNair Scholar at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's). Using a model of MI in severe combined immunodeficiency (SCID) mice and novel imaging techniques, Dr. Yeh's research team has shown that angiogenesis and/or the paracrine effect is the mechanism of action responsible for cardiac functional improvement after CD34+ cell therapy (*Circ Res* 2010;106:1904-11).

"We have previously shown that fusion of CD34+ cells with cardiomyocytes is mediated by the interaction of vascular cell adhesion molecule-1 (VCAM-1) and α4β1, after which the fused cells re-enter the cell cycle and become new cardiomyocytes," says Dr. Yeh. "This finding is biologically relevant because it means that myogenesis can be blocked by anti–VCAM-1 or anti-α4β1 antibodies but not by anti–vascular endothelial growth factor (VEGF) antibodies. Conversely, angiogenesis can be blocked by anti-VEGF but not by anti-α4β1 antibodies. Thus, myogenesis can be distinguished from angiogenesis on the basis of selective antibody blockade, and the relative contribution of myogenesis and angiogenesis to cardiac repair can be determined in the SCID mouse model."

Dr. Yeh and his team constructed a triple-fusion reporter vector encoding for enhanced-green fluorescent protein for cell selection, firefly-luciferase for bioluminescence imaging (BLI), and herpes simplex virus type 1-thymidine kinase for positron emission tomographic (PET) imaging. The researchers used the reporter vector, along with magnetic resonance imaging (MRI) and computed tomographic (CT) scanning, to track the transplanted cells in vivo.



Bioluminescent signal in the heart superimposed on a photograph of a SCID mouse for the indicated time points after human CD34+ cell injection (representative mouse). (Reprinted from Wang J, et al. *Circ Res* 2010;106(12):1904-11.)

Bioluminescence imaging showed that injected CD34+ cells survived in the SCID mouse hearts for longer than 12 months. Cardiac MRI showed that the left ventricular ejection fraction (LVEF) was significantly improved in the treated mice compared to the control mice for up to 52 weeks after cell injection ($P<0.05$). Furthermore, treatment with anti-α4β1 inhibited the generation of human-derived cardiomyocytes, whereas treatment with anti-VEGF blocked the production of human-derived endothelial cells. Interestingly, the improvement seen in LVEF in CD34+ cell-treated mice was completely blocked by treatment with the anti-VEGF antibody but not by treatment with the anti-α4β1 antibody.

"This study helped elucidate many questions about CD34+ cells—ranging from how we can reliably track these cells to how they improve cardiac function," says Dr. Yeh. "First, we were able to coregister MRI, micro-PET, micro-CT, and BLI images to successfully obtain anatomic and functional information about transplanted CD34+ cells in SCID mice with experimental MI. Second, we demonstrated that BLI is capable of long-term tracking of transplanted CD34+ cells and that we can use micro-PET, micro-CT, and MRI images to accurately localize these cells. Third, we showed that the long-term survival of transplanted CD34+ cells contributes to sustained improvement in cardiac function. Finally, by using selective antibody blocking, we showed that angiogenesis, the paracrine effect, or both play a critical role in the improvement of cardiac function after CD34+ cell therapy." ●

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Drs. Denton A. Cooley and James T. Willerson Receive Scientific Achievement Awards

Both the President and the President Emeritus of the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) were recently honored for their contributions to science. The 2010 Medallion of Scientific Achievement was presented to Denton A. Cooley, MD, Founder and President Emeritus of THI at St. Luke's, on April 8, 2010, during the 130th Annual Meeting of the American Surgical Association. This award, the highest honor that the Association bestows, was given for Dr. Cooley's "distinguished service to surgery" and joins more than 120 other awards that he has previously received. On May 13, 2010, James T. Willerson, MD, President and Medical Director of THI at St. Luke's, received the Lifetime Achievement Award in Life Sciences from the Houston Technology Center (HTC). He was among 5 industry leaders honored for "dedication, innovation, and emerging technologies, which have led to job creation and economic development," in the words of HTC President and Chief Executive Officer Walter Ulrich. Dr. Willerson has also received numerous other national and international awards.

A Simple Blood Test Is as Effective as a Biopsy in Monitoring for Heart Transplant Rejection

Abstract: Use of gene-expression profiling to monitor for tissue rejection in selected cardiac transplant patients helps avoid endomyocardial biopsies.

Endomyocardial biopsy (EMB) is the primary method of monitoring for tissue rejection in cardiac transplant patients but is uncomfortable for patients and is associated with rare but serious complications. A recent alternative to EMB is quantitative assessment of mononuclear cell gene expression in peripheral blood specimens. This approach has led to the development and validation of a commercially available blood test that is being used at some transplant centers. Until recently, however, this test had not been systematically compared to routine biopsy in clinical practice.

To test the potential usefulness of gene-expression profiling (GEP) versus EMB, the Invasive Monitoring Attenuation through Gene Expression (IMAGE) trial—a randomized, event-driven, noninferiority trial—was conducted from January 2005 to October 2009 at 13 US cardiac transplant centers, including the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) (*N Engl J Med* 2010;362:1890-1900). The study involved 602 patients who had undergone transplantation more than 6 months before enrollment and who were in clinically stable condition. Patients were randomly assigned to undergo tissue-rejection monitoring by means of GEP or routine EMB, and both groups also underwent clinical and echocardiographic monitoring.

Gene-expression testing was performed with AlloMap (XDx, Brisbane, CA), a blood test that evaluates expression levels of 11 genes known to distinguish the presence or absence of tissue rejection. Scores range from 0 to 40, the higher scores having a stronger correlation with histologic rejection.

"Compared to standard EMB, GEP—combined with clinical and echocardiographic assessment—resulted in fewer biopsies and did not result in an excess of adverse outcomes," says Roberta Bogaev, MD, Medical Director of Heart Failure and Cardiac Transplantation at THI at St. Luke's and an investigator for the IMAGE Study Group.

The primary outcome was the first occurrence of rejection with hemodynamic compromise, graft dysfunction, death, or retransplantation. The 2-year rate for the composite primary outcome was similar in the 2 groups, and rejection monitoring with GEP was not inferior to routine EMB in preventing the primary outcome. Additionally, the GEP patients had fewer treated episodes of rejection.

> *"Compared to standard endomyocardial biopsy, gene-expression profiling—combined with clinical and echocardiographic assessment—resulted in fewer biopsies and did not result in an excess of adverse outcomes."*
>
> *—Roberta Bogaev, MD*

"Although GEP may not have detected all cases of asymptomatic rejection that were identified with EMB, we did not see an increase in the cumulative risk of graft dysfunction, death, or retransplantation in these patients. This implies that not all episodes of asymptomatic rejection that occur more than 6 months after transplantation warrant treatment," says Dr. Bogaev.

At enrollment, the scores for patient satisfaction were similar in the GEP and EMB groups. However, during the course of the study, the satisfaction scores increased for the GEP group, whereas the scores remained virtually unchanged for the EMB group.

"Considering that heart transplant patients usually undergo 15 to 20 biopsies in the first 6 months after transplantation and 2 to 4 biopsies each year thereafter, it is not surprising that patient satisfaction was higher with the less-invasive method."

"This study is important because it shows that GEP is as effective as EMB for monitoring cardiac transplant patients and identifying patients who have a low probability of organ rejection. Also, GEP reduces the number of biopsies performed and minimizes cost, patient discomfort, and risk," continues Dr. Bogaev. "As physicians, we can be confident about this test, which spares our patients from invasive procedures that may not be needed. For our patients, that means more time to enjoy life outside the hospital." ●

For more information:

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Contents

Resolvin E1 Protects Cardiomyocytes From Reperfusion Injury and Limits Infarct Size in Rats

Abstract: The anti-inflammatory mediator resolvin E1 protects the rat heart from ischemia-reperfusion injury and may have clinical usefulness in treating acute myocardial infarction.

During periods of cardiac ischemia, secretion of inflammatory mediators and activation of proapoptotic pathways can cause massive cell death. Furthermore, reperfusion after ischemia results in a rapid influx of leukocytes as blood flow is restored, exacerbating inflammation and contributing heavily to reperfusion injury. Sparing the myocardium from these damaging responses presumably involves controlling inflammation and activating protective pathways in the heart. Yochai Birnbaum, MD, Professor of Medicine at Baylor College of Medicine and a cardiologist at the Texas Heart Institute at St. Luke's Episcopal Hospital, is studying the mechanisms involved in ischemia-reperfusion injury to develop ways of protecting the myocardium and, thus, limiting the size of a myocardial infarction.

Resolvin E1, a potent anti-inflammatory mediator derived from an omega-3 fatty acid, eicosapentaenoic acid, has been shown to promote the resolution of inflammation in acute and chronic models of inflammation. Therefore, Dr. Birnbaum and colleagues examined whether resolvin E1, if given before reperfusion, would limit infarct size in a rat model of ischemia and reperfusion (*Am J Physiol Heart Circ Physiol* 2010;299:H153-64).

The researchers subjected the rats to 30 minutes of ischemia, followed by 4 hours of reperfusion. Before the reperfusion period, the rats were given resolvin E1 (0.03, 0.1, or 0.3 mg/kg) or phospate-buffered saline (PBS) as a control via tail vein injection. After the reperfusion period, the hearts were excised for immunohistochemical analysis. Special staining techniques were used to determine the area at risk and the infarct size in resolvin-E1–treated versus control hearts.

"Treatment with resolvin E1 significantly reduced the infarct size in a dose-dependent manner, without affecting the heart rate or blood pressure," says Dr. Birnbaum (*see Figure*). "Furthermore, compared with PBS, high doses of resolvin E1 decreased the influx of leukocytes into the ischemic zone after reperfusion by 90%."

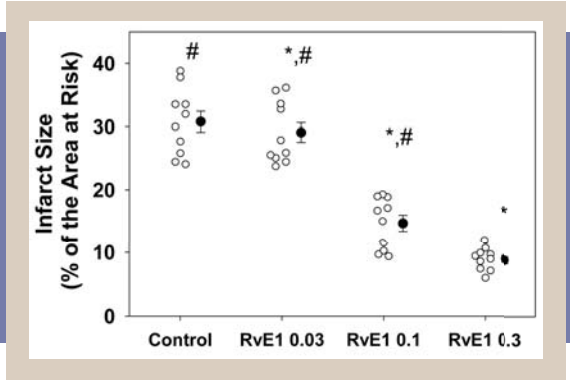
Reperfusion injury is mediated, at least in part, by cellular pathways intrinisic to cardiomyocytes. In addition to performing in vivo studies, Dr. Birnbaum's group used a cardiomyocyte embryonic myoblast cell line to examine the effect of resolvin E1 on cell viability and mediators of prosurvival and proapoptotic pathways. Use of the in vitro approach allowed the researchers to assess the direct cellular effects of resolvin E1, independent of the acute ongoing inflammation in the complex milieu of the postinfarction heart.

"Resolvin E1 protected cardiomyocytes in vitro during simulated hypoxia and hypoxia-reoxygenation," says Dr. Birnbaum. "Furthermore, resolvin E1 increased viability and decreased apoptosis during hypoxia but did not affect cardiomyocytes under normoxic conditions."

"Levels of the proapoptotic factors caspase-3 and BAX increased in cells exposed to ischemia and reperfusion, but treatment with resolvin attenuated that increase. In addition, resolvin augmented expression of the mediators of protective pathways, including the phosphoinositide 3-kinase/Akt/endothelial nitric oxide synthase (eNOS) pathway."

Dr. Birnbaum's group performed immunoblotting studies on the excised hearts of the rats subjected to ischemia-reperfusion. They found that treatment with resolvin E1 increased the cardiac levels of prosurvival mediators, such as Akt and eNOS, and downregulated proapoptotic factors such as caspase-3. These results support their in vitro findings of a cardiac-sparing effect of resolvin.

"Our studies show that resolvin E1 may act more broadly on survival pathways than do other interventional approaches for protecting against reperfusion injury," states Dr. Birnbaum. "The magnitude of this tissue-protective effect suggests that resolvin E1 may, indeed, have clinical potential for use in treating acute myocardial infarction." ●



In rats subjected to ischemia-reperfusion, resolvin E1 (RvE1) decreased the infarct size in a dose-dependent manner. Overall, there was a significant difference in the infarct size among the groups ($P < 0.001$). The open circles represent individual rats, and the closed circles show the mean values ± SEM. *$P < 0.05$ versus control; #$P < 0.05$ versus RvE1 0.3 mg/kg. (Birnbaum Y, et al. *Am J Physiol Heart Circ Physiol* 2010. Am Physiol Soc, with permission.)

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Risk Models May Overestimate the 30-Day Mortality Risk After Thoracic Aortic Surgery

Abstract: A study of 2 cardiovascular surgical risk models showed that both models substantially overpredicted the 30-day mortality risk after thoracic aortic operations.

Operations on the thoracic aorta entail significant risks of morbidity and mortality. As in other types of surgery, the exact magnitude of these risks varies among individual patients. Many models have been developed to estimate the surgical risk in patients with cardiovascular disease, but most of these models are designed for use only in coronary artery bypass grafting or heart valve repair; few established models are intended for use in thoracic aortic surgery. Among these few models are the Department of Veterans Affairs (VA) Continuous Improvement in Cardiac Surgery Program (CICSP) model and the European System for Cardiac Operative Risk Evaluation (EuroSCORE).

Risk models need to be accurate because they serve 2 important functions. First, they are used to estimate risk-adjusted outcomes at individual surgical centers. These estimates are used for quality assurance and for comparing treatment centers. Second, risk models are used with individual patients to determine whether surgical treatment is advisable.

To test the accuracy of the CICSP and EuroSCORE risk models in thoracic aortic surgical patients, Joseph S. Coselli, MD, Chief of Adult Cardiac Surgery at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) and Professor and Chief of Cardiothoracic Surgery at Baylor College of Medicine (BCM); Faisal Bakaeen, MD, Chief of Cardiothoracic Surgery at the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC), an Associate Professor in the Division of Cardiothoracic Surgery at BCM, and a cardiothoracic surgeon at THI at St. Luke's; and their colleagues retrospectively collected data regarding 100 open thoracic aortic operations performed at the MEDVAMC between 1998 and 2008. The procedures included repairs of the aortic arch and of the ascending, descending, and thoracoabdominal aorta. The investigators used both the CICSP and EuroSCORE models to estimate the 30-day mortality risk for each patient, then computed the overall mortality rate predicted by each model and compared it with the patients' actual mortality rate. The investigators also examined the correlation between the risk estimates made for each patient and that patient's survival status. The results were published in the *American Journal of Surgery* (2009:198;889-94).

> *"Our results…suggest that cardiologists and cardiac surgeons should be cautious when using the EuroSCORE or the CICSP in making treatment decisions for individual patients."*
>
> *—Faisal Bakaeen, MD*

"The CICSP score and the EuroSCORE were both good indicators of which patients were most at risk," says Dr. Bakaeen, "in that the patients who died during the first 30 days after surgery tended to be the ones with the highest risk scores. However, the mortality rates estimated by both risk models—18.2% for CICSP and 18.7% for EuroSCORE—greatly exceeded the actual mortality rate of 8.0%."

The reasons for this difference are unclear. One possibility is that there are important differences between MEDVAMC patients and the populations in which the 2 risk models were developed. However, although the generally older and almost exclusively male MEDVAMC population may differ from the more general European surgical population in which the EuroSCORE was developed, the CICSP was developed from a nationwide sample of patients at VA hospitals. The MEDVAMC patients are a subset of the VA population, so the 2 samples are probably similar.

Another possible reason for the sizeable gap between the estimated and actual mortality in this study is that even though the MEDVAMC has only a moderate volume of thoracic aortic surgical procedures, the surgeons who perform them are especially highly trained and experienced because of their concurrent practices at other, academically oriented surgical centers that have high volumes of thoracic aortic cases.

"Our results show that open thoracic aortic procedures can produce good outcomes when performed at an experienced VA center," Dr. Bakaeen says. "They also suggest that clinicians should be cautious when using the EuroSCORE or the CICSP in making treatment decisions for individual patients." ●

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Senior Research Scientist Joins THI at St. Luke's

Jun Wang, PhD, formerly of the Institute of Biosciences and Technology at the Texas Medical Center, has joined the Stem Cell Engineering Laboratory at the Texas Heart Institute as a senior research scientist. He will work under the direction of Dr. Robert Schwartz, head of the Stem Cell Engineering Laboratory and of the University of Houston's new Center for Gene Regulation and Molecular Therapeutics. With a 2-year grant from the American Heart Association and a start-up grant from the National Institutes of Health, Dr. Wang is studying the role of small ubiquitin-like modifier (SUMO) proteins in cardiovascular development. Through the process of SUMOylation, SUMOs bind to transcription factors and mediators of signal transduction pathways to modulate cell functions. Dr. Wang's research indicates that SUMOs target several proteins that are essential in cardiogenesis and that SUMO pathway components may play an important role in cardiac development. Although the mechanisms of these complex pathways in cardiogenesis are not well understood, Dr. Wang anticipates exciting advances in this new field.

Postpacing Interval Variability Predicts Global Activation Patterns During Tachycardia

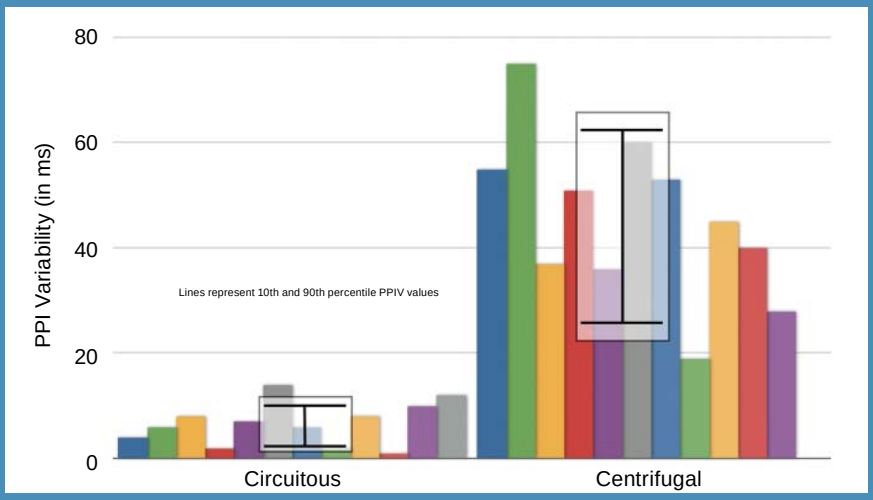
Abstract: Electrophysiologists at THI at St. Luke's have shown that the global activation pattern of arrhythmias can be rapidly determined by using a simple pacing maneuver.

Successful ablation of any arrhythmia requires knowledge of its activation pattern. For instance, radiofrequency ablation of ventricular tachycardia (VT) with a centrifugal activation pattern (ie, a focal origin with outward radiation) can be successful if delivered to the region of earliest activation; however, the same approach may not be as successful for treating VT with a circuitous activation pattern (macroreentrant tachycardia).

Ilyas Colombowala, MD, an electrophysiologist at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's); Mehdi Razavi, MD, Director of Clinical Arrhythmia Research and an electrophysiologist at THI at St. Luke's; and their colleagues have shown that the global activation pattern of atrial arrhythmias can be rapidly determined by using a simple pacing maneuver called postpacing interval variability (PPIV) (*J Cardiovasc Electrophysiol* 2008;19:142–7). More recently, they have shown that PPIV may also be used to rapidly and accurately determine the global ventricular activation pattern during VT (*PACE* 2010;33:129–34).

"In our first study, we found that the global pattern of activation of atrial arrhythmias can be determined by comparing the differences in postpacing intervals (PPIs) obtained with overdrive pacing at cycle lengths 10, 20, and 30 ms shorter than the tachycardia cycle length," says Dr. Razavi. "This can be done by pacing from a single site—almost always the proximal coronary sinus—regardless of its distance from the tachycardia focus or circuit. Relative stability of the PPI strongly suggests a circuitous activation pattern, whereas variability in the PPI is diagnostic of a centrifugal activation pattern."

The PPIV was measured in a similar manner in both studies. During tachycardia, 2 bursts of overdrive pacing were performed by using a catheter; each burst lasted for 5 seconds, was synchronized from the last sensed beat, and was delivered at twice the diastolic threshold. Thirty seconds was allowed between each of the 2 bursts. If the tachycardia did not terminate during pacing, the interval from the last captured beat on the catheter's distal bipoles to the first sensed beat on the same bipoles was measured and defined as the PPI. The cycle length of the first burst was 10 ms shorter than the tachycardia cycle length (TCL). The PPI after that burst was labeled as PPI_{-10}. The cycle length of the second burst was 30 ms shorter than the TCL, and the PPI after that burst was labeled PPI_{-30}. The PPIV is the difference between PPI_{-10} and PPI_{-30}.



Graphical representation of all PPIVs (post-pacing interval variabilities after pacing at tachycardia cycle length minus 30 ms and tachycardia cycle length minus 10 ms). The different color bars represent individual tachycardias. Superimposed is a box and whisker plot of median and 25th and 75th percentiles. Whisker bars represent 10th and 90th percentiles. (Reprinted from *J Cardiovasc Electrophysiol* 2008;19:142-7.)

Low PPIV, defined as ≤10 ms, predicts a circuitous activation pattern (94% sensitivity and 100% specificity). High PPIV, defined as ≥30 ms, predicts centrifugal activation, as determined by electroanatomic mapping (92.8% sensitivity and 100% specificity).

"In the ventricular study, our results were similar in that the global activation pattern of monomorphic VT could be rapidly assessed by comparing the differences in PPIs," says Dr. Razavi. "In addition, we observed a similar response in both left and right ventricular tachycardias, so use of PPIV testing does not depend on knowledge of the origin or mechanism of the tachycardia."

"We believe that this simple, accurate pacing maneuver can be used to determine the global activation pattern of either atrial or ventricular arrhythmias," concludes Dr. Razavi. "Although our technique does not provide exact, mechanism-specific details of the tachycardia, it does allow swift planning of ablative strategies at the onset of the electrophysiologic study, and it can easily be used in conjunction with other maneuvers to facilitate mapping and ablation." ●

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Cardiovascular Cell Therapy Research Network Is Enrolling Patients

Abstract: A network of 5 primary clinical sites and numerous satellite sites has been established to test the safety and efficacy of cell therapy for severe cardiovascular diseases.

In 2007, the National Heart, Lung and Blood Institute (NHLBI) established the Cardiovascular Cell Therapy Research Network (CCTRN) to facilitate early phase 1 and phase 2 clinical trials of cell therapy for advanced heart diseases. Five clinical sites were chosen through a peer review process that included submission of applications for proposed studies: the University of Florida, the Cleveland Clinic Foundation, the Minneapolis Heart Institute at Abbott Northwestern Hospital, the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's), and Vanderbilt University. To be chosen, the sites had to have a highly experienced, multidisciplinary team that could handle all aspects of the cell therapy protocols—from acquisition, processing, and injection of cells to patient follow-up and support for Food and Drug Adminstration investigational new drug applications.

James T. Willerson, MD, President and Medical Director of THI at St. Luke's, is leading the THI team. "We are extremely pleased to have been chosen as part of the CCTRN," says Dr. Willerson. "Our studies and others have shown that cell-based therapies hold enormous potential for treating patients with acute or advanced chronic heart disease; however, enrolling enough patients to meet the strict eligibility criteria for phase 1 and 2 studies has always been difficult. The network structure, which is funded and sponsored by NHLBI, overcomes this difficulty."

After reviewing protocols from each of the sites, the CCTRN steering committee chose to pursue 3 initial trials, which were then reviewed by a protocol review committee, ie, an independent panel of NHLBI experts. Once approved, the protocols were reviewed by the NHLBI-sponsored Data Safety and Monitoring Board. Investigational new drug (IND) status was then requested from the Food and Drug Administration. Finally, the trials were reviewed and approved by each institutional review board.

The THI at SLEH team, which also includes Emerson Perin, MD, PhD, Director of Clinical Research for Cardiovascular Medicine and Medical Director of the Stem Cell Center, has been enrolling patients for the 3 protocols, which target patients with coronary artery disease and left ventricular dysfunction (ejection fraction <45%). Two of the protocols (called TIME and Late-TIME) will assess the effects of autologous bone marrow mononuclear cells (ABMMNCs) on left ventricular dysfunction in patients who have had an acute myocardial infarction (MI). To be enrolled, a patient must have had a large MI and undergone successful reperfusion. The third protocol (FOCUS) will assess the safety and effectiveness of ABMMNCs in patients who have activity-limiting symptoms of heart failure (New York Heart Association functional class II-III) or angina (Canadian Cardiovascular Society angina grade II-IV) and no option for revascularization. Patients must also have reversible myocardial dysfunction documented by single photon emission computed tomography (SPECT). For FOCUS, cells will be delivered via an intraventricular myocardial delivery catheter with the aid of electromechanical mapping guidance (NOGA).

"The TIME and Late-TIME protocols will also assess whether the timing of cell delivery affects the outcome," explains Dr. Perin. "For the TIME protocol, cells or placebo will be administered 3 or 7 days after MI. For the Late-TIME protocol, cells will be administered 14 to 21 days after MI. In both protocols, patients will be followed up for 24 months. To date, TIME has enrolled 56 of a total 120 patients, and Late-TIME has enrolled 46 of 87 patients. The FOCUS protocol has enrolled 40 of 87 patients and will have a 60-month follow-up period."

The CCTRN comprises far more than the 5 primary sites (see *J Cardiovasc Trans Res* 2009;23:30-36). A Data Coordinating Center provides daily administrative and regulatory management. A "biorepository" has been established to examine the relationship between cell therapy clinical outcomes and cell characteristics, such as phenotype and function. Core laboratories (for echocardiographic, cardiac MRI, SPECT, and myocardial oxygen consumption) ensure consistency and precision in analyzing response variables. In addition, the CCTRN has numerous satellite sites, each linked to a primary clinical site, to increase recruitment, diversify the trial population, and include more investigators in the studies.

"Without the combined teamwork of the entire Network, it would be more difficult to complete these and future trials in a timely fashion," adds Dr. Willerson. "This Network will allow us to build on the important scientific findings of the cell therapy community and rapidly bring these important advances to our patients." ●

Current Cardiovascular Cell Therapy Research Network Protocols

Transplantation in Myocardial Infarction Evaluation (TIME): A Phase II, Randomized, Controlled, Double-Blind Trial Evaluating the Effect of Timing on the Administration of Bone Marrow Mononuclear Cells (BMMNCs) versus Placebo in Patients with Acute Myocardial Infarction

Late-TIME: A Phase II, Randomized, Controlled, Double-Blind Pilot Trial Evaluating the Safety and Effect of Administration of Bone Marrow Mononuclear Cells Two to Three Weeks Following Acute Myocardial Infarction

FOCUS: A Randomized, Controlled, Phase II, Double-Blind Trial of Intramyocardial Injection of Autologous Bone Marrow Mononuclear Cells under Electromechanical Guidance for Patients with Chronic Ischemic Heart Disease and Left Ventricular Dysfunction

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Cover: Statue donated by Hakeem Olajuwon 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.

Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Houston Echo Review 2010: Boot Camp for Echo Board
Texas Heart Institute
July 16–17, 2010 • Houston, Texas
www.cme.texasheart.org

Selected Upcoming Local, National, and International Meetings

The Society for Cardiovascular Angiography and Interventions
Pediatric & Adult Interventional Cardiac Symposium
July 18–21, 2010 • Chicago, Illinois
www.picsymposium.com

American Heart Association Basic Cardiovascular Sciences 2010 Scientific Sessions
July 19–22, 2010 • Rancho Mirage, California
www.americanheart.org

International Academy of Cardiology 15th World Congress on Heart Disease: Annual Scientific Sessions 2010
July 24–27, 2010 • Vancouver,
British Columbia, Canada
www.cardiologyonline.com

Heart Failure Society of America 14th Annual Scientific Meeting
September 12–15, 2010 • San Diego, California
www.hfsa.org

American College of Cardiology Arrhythmias in the Real World 2010
September 23–25, 2010 • Washington, DC
www.acc.org

American Society of Nuclear Cardiology 15th Annual Scientific Session
September 23–26, 2010 • Philadelphia, Pennsylvania
www.asnc.org

American College of Surgeons 96th Annual Clinical Congress
October 3–7, 2010 • Washington, DC
www.facs.org

American Society of Anesthesiologists Annual Meeting
October 16–20, 2010 • San Diego, California
www.asahq.org

For information about Texas Heart Institute CME activities, please e-mail cme@heart.thi.tmc.edu or call 832.355.2157. To view or complete selected online CME courses (certificates are available online), please visit www.cme.texasheart.org. New courses are added regularly.

For 19 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."