Heart WATCH

WINTER 2011

A Physician Newsletter Produced by the Texas Heart Institute

Texas Heart® Institute

at St. Luke's Episcopal Hospital

Researchers Use Gadonanotubes for In Vivo Tracking of Stem Cells

Abstract: Gadolinium-containing carbon nanocapsules, or gadonanotubes, may represent a new biotechnology for stem cell labeling and in vivo cell tracking by real-time MRI.

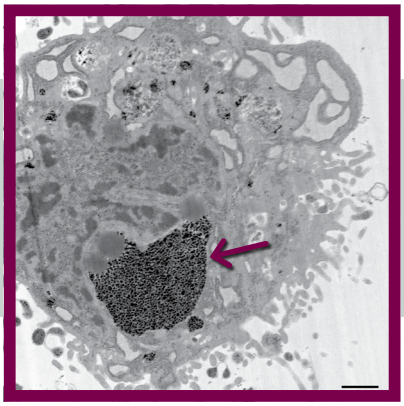
In the development of stem cell–based therapies, the demand is increasing for imaging techniques that permit noninvasive monitoring of transplanted stem cells in vivo. Magnetic resonance imaging (MRI) is the ideal imaging modality for tracking stem cells in vivo because it provides serial images with high spatial resolution, is noninvasive, and does not use ionizing radiation.

Contrast agents (CAs) are used in many MRI procedures to alter MR signals. Most commonly used are paramagnetic T_1-weighted CAs, which enhance MR signals to produce bright positive contrast; however, these gadolinium-based CAs (GBCAs) are restricted to the extracellular space and cannot accumulate within cells to enhance signal intensity on a cellular level. Hence, a primary focus in GBCA research is the development of new CAs with greater relaxivity to improve image contrast. Because biologic constraints limit the number of CA molecules that can be delivered to the surface of a single cell, visualizing individual cells requires that each unit of a particular CA produce a signal intense enough to be detected at nanomolar concentrations of the CA. In addition, CAs must be biologically inert and nontoxic at appropriate dosage levels.

Researchers at Rice University and the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) recently collaborated to develop a new high-performance carbon nanotube–based GBCA that effectively labels cells at low loading concentrations (*Biomaterials* 2010;31:9482–91). The work was supported by a National Institutes of Health Challenge Grant. These CAs, known as gadonanotubes (GNTs), are short (20–80 nm) segments of single-walled carbon nanotubes that encapsulate small clusters of Gd^{3+} ions. The GNTs exhibit a T_1 relaxivity greater than that of any other material known to date, with values of 170 mm^{-1} s^{-1} (40°C, 1.5 T) and >600 mm^{-1} s^{-1} (40°C, 0.4 T) per Gd^{3+} ion. At clinically used magnetic-field strengths (1.5 T), the GNTs outperform currently available GBCAs by nearly 40-fold.

"In our study, we looked at the performance of GNTs as a new intracellular labeling agent for pig bone marrow–derived mesenchymal stem cells (MSCs)," says Lesa Tran, a PhD graduate student in the laboratory of Lon J. Wilson, PhD, at Rice University and first author of the study. "Without the use of a transfection agent, micromolar concentrations of GNTs delivered up to 10^9 Gd^{3+} ions per cell and did not compromise cell viability, differentiation potential, proliferation pattern, or phenotype."

For magnetic cell labeling, the most efficient concentration was found to be 27 µm Gd^{3+}, which delivered 0.98 pg (approximately 10^9 Gd^{3+} ions per cell) without affecting cell viability.



Transmission electron micrograph of a gadonanotube (GNT)-labeled mesenchymal stem cell. The arrow points to GNT aggregates in the cytoplasm. Scale bar = 1 µm.

In addition, the researchers studied the self-renewal properties and proliferation kinetics of GNT-labeled MSCs. The results showed that GNTs do not impair the self-renewal or the proliferation kinetics of MSCs.

"After 7 days, GNT labeling increased the self-renewal rate of MSCs by 20%," says Emerson Perin, MD, PhD, Director of Research in Cardiovascular Medicine, Director of the Stem Cell Center at THI at St. Luke's, and a coauthor of the study. "As multipotent progenitor cells, MSCs have the ability to differentiate into a variety of cell types. The GNT-labeled cultures successfully differentiated into adipocytes, osteocytes, and chondrocytes. This suggests that magnetic labeling of MSCs with GNTs did not affect the differentiation potential of the MSCs and that GNT-labeled MSCs may retain their therapeutic potential, which is critical for stem cell therapy."

"Because more than 2000 stem cell–based clinical trials are currently underway throughout the world, better ways of tracking cells in vivo are needed," says James T. Willerson, MD, President and Medical Director of THI at St. Luke's and a coinvestigator on the study. "Advanced imaging technologies will facilitate the development of stem cell–based therapeutics, because cell tracking helps elucidate stem cell migration and tissue integration, determine the effective dose, and monitor cell delivery." ●

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Texas Heart Institute Establishes a Center for Women's Heart & Vascular Health

Abstract: A new Center for Women's Heart & Vascular Health has been established at THI at St. Luke's to promote cardiovascular research, education, and improved patient care specifically for women.

According to the American Heart Association, more than 42.7 million women in the United States are living with some form of cardiovascular disease—the leading cause of death in women. In fact, cardiovascular disease claims the lives of more women than men each year. In addition, women are less likely than men to receive the appropriate treatment after a heart attack and are more likely than men to die within the first year after a heart attack.

Despite these facts, studies have shown that primary care physicians are generally unaware of these sex disparities when diagnosing and treating heart disease. That is why the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) has established a new Center for Women's Heart & Vascular Health.

"Too often, heart disease in women is ignored by primary care physicians, by emergency room staff, and by women themselves," says Stephanie Coulter, MD, a cardiologist at THI at St. Luke's and Director of the THI Center for Women's Heart & Vascular Health. "Partly, that's because when most people think of heart disease, they think of it as happening mainly to men—but half of all women die of a cardiovascular condition, including heart attack, stroke, peripheral vascular disease, or heart failure."

Dr. Coulter hopes the new center will be a catalyst for improving this situation. The Texas Heart Institute will make an initial commitment of at least $5 million to the center. Some of this amount will fund educational efforts directed toward medical professionals and lay people in Houston and other cities throughout the country.

The funding will also facilitate cardiovascular research in women, which lags considerably behind that in men. Although research efforts have increasingly focused on women in recent years, women still constitute only about a quarter of participants in cardiovascular research studies.

"Much of our understanding of heart disease and the basis for our standard methods of diagnosis and treatment are the result of research conducted on men," says Dr. Coulter. "Although the underlying pathophysiologic processes leading to the development of heart disease are similar in men and women, death and other clinical endpoints occur later in women. These differences point to the need for more women-specific studies, so we can look closer at the influence of sex and how it may affect diagnosis and treatment. A 'one-size-fits-all' strategy for both sexes may not be the best approach."

> *"And that's our goal, that's the mission of the Texas Heart Institute—to reduce the devastating toll of cardiovascular disease through innovative programs in research, education, and patient care."*
>
> *—Stephanie Coulter, MD*

Another of the center's goals is community outreach. Dr. Coulter realizes that not every woman who needs cardiovascular care can receive it at THI at St. Luke's.

"We are going to identify the women in our community at greatest risk and then, partnering with community organizations, provide educational events during which those women will have access to a level of screening and recommendation not otherwise available to them," says Dr. Coulter. "We can't see every patient, but if we can get the word out, if we can educate other physicians, then we can reach more patients, and we will have an enormous impact on the community. And that's our goal, that's the mission of the Texas Heart Institute—to reduce the devastating toll of cardiovascular disease through innovative programs in research, education, and patient care."

"We hope to have a significant impact on the human suffering and escalating financial burden associated with heart disease in women, and we feel that the new center is already making a difference in that regard," says Dr. Coulter. ●

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Contents

Researchers Characterize the Plasma Metabolites of Patients With Primary Dilated Cardiomyopathy

Abstract: Metabolomic analysis reveals altered levels of plasma metabolites in patients with primary dilated cardiomyopathy.

Primary dilated cardiomyopathy (DCM) is a type of systolic heart failure characterized by cardiac dilatation and a reduced left ventricular ejection fraction. During the past 20 years, progress has been made in the treatment of primary DCM, but the rates of mortality and morbidity resulting from heart failure remain high. By better understanding the pathogenesis and prognostic indicators of primary DCM, researchers hope to improve the diagnosis and treatment of this condition.

Ali J. Marian, MD, and his colleagues are characterizing the plasma metabolites of patients with DCM. Dr. Marian is a member of the Adult Cardiology staff at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's). He is also the George and Mary Josephine Hamman Foundation Distinguished Professor in Cardiovascular Research at The Brown Foundation Institute of Molecular Medicine at The University of Texas Health Science Center at Houston. Recently, in collaboration with researchers at Metabolon, Inc. (Research Triangle Park, NC), Dr. Marian and his colleagues examined the metabolome—the complete profile of small-molecule metabolites found in a cell, tissue, or organism—of patients with primary DCM (*Eur J Clin Invest* 2010, E-pub ahead of print).

"Metabolomics is an emerging field that may provide valuable insight into the pathogenesis of various human diseases, including heart failure. It may also lead to the identification of new biomarkers and therapeutic targets," says Dr. Marian.

In their study, the researchers compared the metabolome of 39 primary DCM patients with the metabolome of a comparable group of 31 healthy individuals (recruitment to the study was partly supported by the TexGen program, a genetic research collaboration among institutions in the Texas Medical Center, including THI at St. Luke's). All plasma samples were analyzed with gas chromatography/mass spectroscopy and ultra-high–performance liquid chromatography/mass spectroscopy. In patients with primary DCM, the levels of 41 metabolites were significantly increased, and those of 20 metabolites were significantly decreased.

"Metabolomics is an emerging field that may provide valuable insight into the pathogenesis of various human diseases, including heart failure. It may also lead to the identification of new biomarkers and therapeutic targets."

—Ali J. Marian, MD

From among the notably altered metabolites, glutamine (which regulates protein homeostasis and inhibits protein degradation) levels were reduced, and 3-methylhistidine (an index of myofibrillar protein degradation) and prolyl-hydroxyproline (a marker of collagen degradation) levels were increased. These changes probably reflect the enhanced myofibrillar and collagen degradation associated with DCM.

Interestingly, the researchers found that the level of indole-3-propionate—a cardioprotective agent produced by resident bacteria in the gastrointestinal tract—is decreased by 40% in patients with primary DCM. This finding supports growing evidence that the gastrointestinal tract plays a role in the progression of heart failure.

Most of the DCM patients in the study were receiving medical therapy (β-blockers, angiotensin-converting enzyme [ACE] inhibitors, or furosemide). When the medically treated patients were removed from the DCM group, the number of significantly altered metabolites was decreased. However, several metabolites were still significantly different between the 2 groups.

When plasma metabolites were compared in men versus women, significant differences were observed in the control group but not in the group of DCM patients. Specifically, levels of androgen metabolites were reduced in men with primary DCM, suggesting the "feminization" of men with this disease. It was unclear whether this reduction was a primary effect of heart failure or a side effect of medications.

"Metabolism, as reflected in the metabolome, is a dynamic process that is subject to the influence of numerous internal and external factors, such as food and medication intake. Measurement of plasma metabolites may only partially reflect changes in these molecules in patients with primary DCM," states Dr. Marian. "Further studies are needed to determine the utility of plasma metabolites in early disease detection, prognostication, and treatment of patients with heart failure."●

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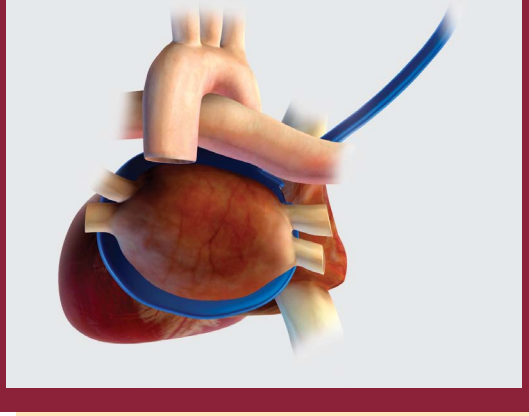
This work was supported in part by grants from the National Heart, Lung, and Blood Institute, a Clinical Scientist Award in Translational Research from the Burroughs Wellcome Fund, and the Greater Houston Community Foundation (TexGen). The study was conducted in collaboration with scientists at Metabolon, Inc., who performed the metabolite analysis at no cost to the investigators.

Texas Heart Institute Is Involved in Multicenter Study of High-Intensity Focused Ultrasound for Treating Atrial Fibrillation

Abstract: THI at St. Luke's is participating in a study designed to show whether the Epicor LP Cardiac Ablation System is safe and effective for treating atrial fibrillation during concomitant cardiac surgery.

The Texas Heart Institute

at St. Luke's Episcopal Hospital (THI at St. Luke's) is 1 of a number of centers in the United States testing the Epicor LP Cardiac Ablation System (St. Jude Medical, St. Paul, MN) for treating permanent atrial fibrillation (AF) at the time of concomitant cardiac surgery. According to Ross M. Reul, MD, Director of Surgical Innovations at THI at St. Luke's and a principal investigator in the study, the Epicor system was previously approved by the United States Food and Drug Administration (FDA) for ablation of cardiac tissue during open heart surgery. In the current study (CONcomitant eValuation of Epicor left atRial Therapy for AF [CONVERT-AF]),* researchers are seeking to show that the system is safe and effective specifically for treating AF in this setting.



The UltraCinch device (blue) is positioned around the left atrial wall. The device is used to create a transmural circumferential lesion from the LA epicardium.

The current standard for treating AF is the surgical Maze procedure, developed in 1987 by Cox and colleagues. The Maze III version, preferred since 1992, is a complicated operation that usually necessitates cardiopulmonary bypass (CPB). Although generally combined with valve repair or replacement (usually mitral) or with coronary artery bypass grafting, the Maze procedure adds to the cardiac exclusion and bypass times and entails a risk of bleeding.

"It can be challenging to perform the Maze procedure along with other complex operations," says J. Michael Duncan, MD, an associate surgeon at THI at St. Luke's and an investigator in the CONVERT-AF study. "Therefore, surgeons have attempted to modify the procedure by using radiofrequency, microwave, laser, and cryotherapy energy sources instead of scalpel-and-suture techniques. However, when the energy source is applied from the endocardium, the surgeon has no way of determining whether the resulting lesion is transmural. If too much energy is applied in an attempt to create a transmural lesion, surrounding structures may be damaged. Likewise, if the energy source is applied from the epicardium, serious complications may result."

Surgeons believe that this problem can be solved with the use of high-intensity focused ultrasound (HIFU). The Epicor Medical Ablation System comprises a microprocessor-based acoustic power unit/controller and an array of HIFU transducers incorporated into 2 ablation devices: the UltraCinch, which encircles the left atrium and produces a transmural circumferential lesion around the pulmonary vein orifices (*see Figure*), and the hand-held UltraWand, which may be used to create additional linear lesions. When this approach was tested as a simplified alternative to the Cox Maze procedure in a multicenter European trial, freedom from AF at 6 months was 80% in patients with permanent AF associated with long-standing structural heart disease (*J Thorac Cardiovasc Surg* 2005;130:803).

The UltraCinch device is available in 7 sizes. Surgical dissection is limited to freeing the pericardial reflections around both venae cavae so that a proper sizer can be used to measure the left atrial (LA) circumference precisely. After sizing is performed, the UltraCinch is positioned around the LA wall, over the antrum of the pulmonary vein orifices, and is secured with 2 tourniquets. It is then used to create a transmural circumferential lesion from the LA epicardium. Surgeons may also use the UltraWand to make a linear lesion that extends from the left lower vein orifice to the mitral valve annulus. The technique is performed on the beating heart before the intracardiac portion of the concomitant surgery.

"With the UltraCinch device, the average 10-minute algorithm is fully automated, so the surgeon can use this interval to prepare for the concomitant procedure," says Dr. Duncan. "The UltraCinch procedure adds no CPB or cardiac exclusion time to the concomitant procedure and prolongs the overall operative time by only minutes."

"If the Epicor system is successful for treating permanent AF during concomitant open heart surgery," adds Dr. Reul, "we believe that it will prove valuable for creating Maze-type cardiac lesions should the FDA approve it for this application." ●

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* *ClinicalTrials.gov Identifier: NCT00519194*

Outcomes of Surgical Versus Endovascular Coronary Revascularization in Patients With Chronic Kidney Disease

Abstract: In patients with chronic kidney disease, surgical coronary revascularization enhances survival but also the risk of dependence on hemodialysis compared with percutaneous revascularization.

Coronary artery disease

(CAD) is the leading cause of morbidity and mortality in patients with chronic kidney disease (CKD). Observational studies have found that coronary artery bypass grafting (CABG) generally yields higher survival rates and lower revascularization rates than percutaneous coronary intervention (PCI) in CKD patients, but CABG also carries a higher risk of complications and worsening kidney function. However, many of these results were found during the bare-metal stent era; in recent years, the use of drug-eluting stents (DESs) has improved long-term survival and reduced rates of major adverse cardiovascular events.

To reassess the relative benefits of CABG and PCI and to study their effects on kidney function, researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) undertook the first study to compare the outcomes of these 2 techniques for multivessel CAD in 2 types of CKD patients: those who were non–hemodialysis-dependent (NHD), indicated by an estimated glomerular filtration rate (eGRF) of 15-60 mL/min/1.73 m^2, and those who had end-stage renal disease (ESRD; indicated by hemodialysis dependence and/or an eGRF <15 mL/min/1.73 m^2). The results were reported in the *American Journal of Cardiology* (2010;106:348-53).

Led by James M. Wilson, MD, staff cardiologist and Director of Cardiology Education at THI and senior researcher on the study, the investigators used data from the THI Research Database to identify 812 patients with CAD and either NHD CKD (n=725) or ESRD (n=87) who had undergone CABG or DES-PCI from May 2003 through December 2006. The outcomes studied included 30-day mortality, long-term mortality, 30-day major adverse cardiovascular events (death, myocardial infarction, stroke, hemodialysis dependence, and repeat revascularization), and hemodialysis dependence after revascularization. No other researchers have examined these factors in this population.

"The study used observational data, so the patient groups differed in several respects," says Dr. Wilson. "More CABG than PCI patients had a history of smoking, chronic obstructive pulmonary disorder, and proximal left anterior descending coronary artery disease. Also, more CABG procedures were done for 3-vessel than for 2-vessel CAD. It was necessary to perform a propensity-score analysis to control for these differences."

In the NHD group, unadjusted 30-day mortality rates and adjusted long-term mortality rates did not significantly differ between the CABG and PCI subgroups. Likewise, among the patients with ESRD, unadjusted long-term survival rates were not significantly different after CABG (71%) versus PCI (62%) (log-rank P=0.6).

Other intergroup outcomes diverged more noticeably. Overall, CABG was associated with more short-term major adverse cardiovascular events than PCI (NHD, P=0.002; ESRD, P=0.01). However, in the NHD group, fewer CABG than PCI patients required repeat revascularization within 30 days (P=0.04), a finding also made in similar studies of bare-metal stents.

The NHD patients were stratified according to whether CAD affected 2 or 3 vessels. With 2-vessel disease, the adjusted mortality was similar after CABG and PCI. With 3-vessel disease, however, the adjusted mortality was somewhat lower after CABG than PCI (hazard ratio, 0.61; 95% confidence interval, 0.36-1.03; P=0.06).

The revascularization method also influenced kidney function. On univariate analysis, NHD patients were more likely to become HD within 30 days after CABG (4.2%) than after PCI (1.5%; P=0.02); on multivariate analysis, CABG independently predicted the onset of hemodialysis dependence (odds ratio, 3.2; P=0.03). This result may be attributable to fluid shifts and the use of cardiopulmonary bypass during CABG, which can worsen renal dysfunction.

"Coronary artery bypass grafting carries a higher risk that the patient will need permanent hemodialysis after the procedure. Nevertheless, our findings corroborate previous evidence that grafted vessels resist disease progression better than percutaneously treated vessels," says Dr. Wilson. "We conclude that CABG leads to better survival than DES-PCI, but renal risks must be considered when choosing between these treatments." ●

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New Research Program to Examine Houston Middle-School Students for Heart Conditions Associated With Sudden Cardiac Death

The Center for Coronary Artery Anomalies (CCAA) at the Texas Heart Institute (THI) has launched a research program to identify students at risk for sudden cardiac death (SCD). This condition has gained widespread attention through news stories about young athletes who have died while participating in sports activities. SCD may be precipitated by a coronary artery anomaly or by hypertrophic cardiomyopathy, neither of which always has noticeable symptoms. To detect these heart conditions, researchers will visit more than 20 middle schools in the Houston area and will obtain electrocardiograms, magnetic resonance images, and brief medical histories from thousands of students. The free, painless examinations will be conducted with the aid of a special mobile imaging unit. "With sophisticated imaging methods, susceptible students can be identified earlier and kept from participating in high-risk activities," says Dr. James T. Willerson, President and Medical Director of THI and the principal investigator of the CCAA. "We hope that the results of this study will change the way SCD is viewed by the general public and the medical profession," adds Dr. Paolo Angelini, founder and Medical Director of the CCAA.

Negatively Charged Liposomes Target Atheromas in Watanabe Heritable Hyperlipidemic Rabbits

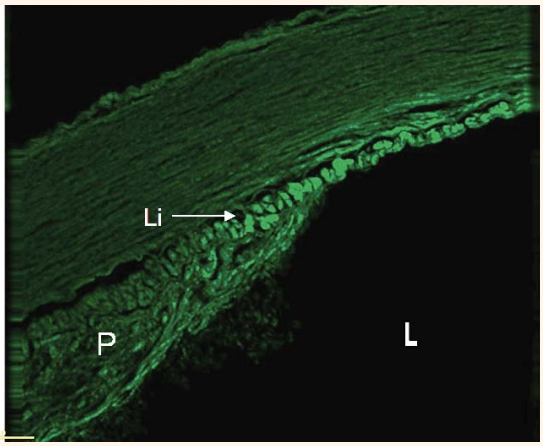
Abstract: Because negatively charged liposomes localize to lipid-rich, metabolically active atheromatous plaque, these liposomes may have diagnostic and therapeutic potential.

Metabolically active, lipid-rich plaque (ie, vulnerable plaque) has a high incidence of fibrous-cap rupture that can cause acute vessel thrombosis, leading to strokes and other adverse ischemic events. In vivo, identifying and targeting vulnerable plaque is difficult because conventional imaging techniques reveal anatomic characteristics rather than metabolic activity. However, molecular technology is rapidly progressing toward overcoming the limitations of conventional imaging and drug delivery techniques. Liposomes, which are spherical particles that contain a charge-impermeable phospholipid bilayer, have been proved useful for molecular imaging and targeted drug delivery; however, they have only rarely been used in the cardiovascular system.

Brian Walton, MD, Director of Cardiovascular Experimental Imaging and Therapeutics at the Texas Heart Institute at St. Luke's Episcopal Hospital, and his colleagues are using liposomes to target atheromas in Watanabe heritable hyperlipidemic (WHHL) rabbits. Aortic plaques from these rabbits have characteristics similar to those of human atheromas. Recently, the researchers studied a liposome specifically designed to enhance liposomal uptake in metabolically active components of atheromas (*Vascular Medicine* 2010;15:307-13).

"We can modify the phospholipid composition of the lipid bilayer to create a liposome with a specific charge or property," says Dr. Walton. "In using a sterically negative liposome, our goal was to target macrophages, which accumulate in the metabolically active regions of atheromas and preferentially phagocytose negatively charged particles. The strong negative charge of the liposomes may lead to their engulfment by macrophages and conversion into macrophage-derived foam cells and lipid pools, which would prevent rapid clearance of the liposomes."

Another advantage that negatively charged liposomes have over positively charged ones is that the loss of glycocalyx (a layer composed of glycoproteins and glycolipids that lines the endothelium) in the atherosclerotic regions of the arterial walls facilitates the penetration of negatively charged liposomes into the atheroma—a process not permitted by normal aortic tissues.



Deconvoluted fluorescence microscopy shows the shoulder region of an atheroma with rhodamine-labeled liposomes (green). 20× magnification. Bar = 40 µm. P, plaque; L, lumen; Li, liposome.

Dr. Walton and his colleagues injected liposomes conjugated to rhodamine and nanogold into the descending thoracic aortas of 5 WHHL rabbits and injected sterile saline into 1 WHHL rabbit. The arterial segments of interest were perfusion-fixed and evaluated by means of immunohistochemistry, light microscopy, and electron microscopy. Deconvolution fluorescence microscopy revealed rhodamine labeling in the shoulder region of advanced atheromas but not in adjacent, nondiseased regions of the rabbit aortas. In addition, transmission electron microscopy showed that the highest concentrations of nanogold labeling and liposome remnants were closely associated with lipid-dense areas of atheromas.

The researchers also found that the liposomes were localized near $LpPLA_2$, an inflammatory biomarker expressed primarily by activated macrophages, in the shoulder region of advanced atheromas. Because $LpPLA_2$ is an indicator of metabolically active plaque, the shared distribution patterns of negatively charged liposomes, lipid pools, and $LpPLA_2$ in atheromas collectively suggest that the uptake of liposomes is associated with areas of metabolically active plaque.

"Negatively charged liposomes are potentially effective transport vehicles for cardiovascular-related diagnostic and therapeutic agents because the liposome phospholipid bilayer protects the contents of the liposome core against degrading enzymatic processes," says Dr. Walton. "In addition, the negative charge of these liposomes makes them ideal vehicles for targeting macrophage-rich atheromas. Our findings may provide new opportunities for therapeutically targeting and treating vulnerable plaques." ●

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Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Twelfth Symposium on Cardiac Arrhythmias
The Houstonian Hotel
February 19, 2011 • Houston, Texas
Program Director: Ali Massumi, MD

Future Direction of Stem Cells in Cardiovascular Disease Satellite Symposium at American College of Cardiology Scientific Sessions
The Westin Canal Place
April 2, 2011 • New Orleans, Louisiana
Program Director: James T. Willerson, MD

Third Annual Denton A. Cooley Lectureship
Lecturer: Frank Spencer, MD
Texas Heart Institute
12:00–1:00 PM
April 8, 2011 • Houston, Texas
Program Directors: Denton A. Cooley, MD, and James J. Livesay, MD

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

Selected Upcoming Local, National, and International Meetings

Society of Thoracic Surgeons 47th Annual Meeting
January 31–February 2, 2011 • San Diego, California
www.sts.org/sections/annualmeeting/

American College of Cardiology 60th Annual Scientific Session
April 2–5, 2011 • New Orleans, Louisiana
www.accscientificsession.org/Pages/home.aspx

International Society for Heart and Lung Transplantation 31st Annual Meeting and Scientific Sessions
April 13–16, 2011 • San Diego, California
www.ishlt.org/meetings/annualMeeting.asp

Heart Rhythm Society
32nd Annual Scientific Sessions
May 4–7, 2011 • San Francisco, California
www.hrsonline.org/sessions/

American Association for Thoracic Surgery 91st Annual Meeting
May 7–11, 2011 • Philadelphia, Pennsylvania
www.aats.org/annualmeeting/

U.S.News & World Report BEST HOSPITALS 2010-11 Heart & Heart Surgery

For 20 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."