Agenda Item No.

AGENDA ITEM BRIEFING

Submitted by: Mark A. Hussey, Interim President
Texas A&M University

Subject: Establishment of the Center for Cell and Organ Biotechnology

Proposed Board Action:

Establish the Center for Cell and Organ Biotechnology (CCOB) within the Department of Veterinary Physiology and Pharmacology in the College of Veterinary Medicine & Biomedical Sciences (CVM) at Texas A&M University (Texas A&M).

Background Information:

The CCOB, a new partnership between the Texas Heart Institute (THI) at St. Luke's Episcopal Hospital, Texas A&M and the CVM at Texas A&M, is taking a multi-faceted approach to chronic diseases based on cell and organ failure through research directed at predicting disease onset to allow earlier intervention (diagnostics); developing personalized cell and gene therapies (based on what has failed) to prevent chronic disease progression; identifying novel therapeutics to treat organ injury; and developing new organ repair or replacement strategies when organ failure is present. The CCOB is designed to develop and commercialize novel, new treatments for age-related and chronic health problems. The team of the THI and Texas A&M scientists, engineers, physicians, veterinarians and business managers assembled to establish this new center will employ disruptive cell and organ biotechnologies and molecular tools to develop commercial applications that encompass areas of both human and veterinary healthcare. The CCOB will serve as a magnet to attract scientists, biotech companies and allied industries to Texas. Furthermore, this inter-institutional center will create high-quality jobs and provide an integrated platform for research scientists, clinicians and biotech companies to collaborate seamlessly to advance scientific discoveries from the laboratory, through product development and commercialization, to the marketplace and to patients, both human and animal.

A&M System Funding or Other Financial Implications:

Start-up funding for the CCOB is being provided by the Texas Emerging Technology Fund, the THI and the Chancellor's Research Initiative. These funds are committed for a period of three years. The sustaining support for the CCOB will be from extramural grants, primarily from the National Institutes of Health and the National Science Foundation.

Agenda Item No.

TEXAS A&M UNIVERSITY
Office of the President
January 14, 2014

Members, Board of Regents
The Texas A&M University System

Subject: Establishment of the Center for Cell and Organ Biotechnology

I recommend adoption of the following minute order:

> **"The Center for Cell and Organ Biotechnology is hereby established as an organizational unit of Texas A&M University within the Department of Veterinary Physiology and Pharmacology in the College of Veterinary Medicine & Biomedical Sciences."**

Respectfully submitted,

[ORIGINAL SIGNED BY]

Mark A. Hussey, Interim President
Texas A&M University

Approval Recommended:

[ORIGINAL SIGNED BY]

John Sharp
Chancellor

[ORIGINAL SIGNED BY]

Billy Hamilton
Executive Vice Chancellor and
Chief Financial Officer

[ORIGINAL SIGNED BY]

James R. Hallmark
Vice Chancellor for Academic Affairs

Approved for Legal Sufficiency:

[ORIGINAL SIGNED BY]

Ray Bonilla
General Counsel

TEXAS A&M UNIVERSITY
Center for Cell and Organ Biotechnology

EXECUTIVE SUMMARY

1. ***Rationale for the Creation of the Center or Institute***

The risk and impact of numerous devastating health conditions – including heart disease, diabetes, kidney and liver disease, and cancer – increase with age, in large part because the body loses its capacity to repair ongoing tissue and organ damage. This failure to repair is due in turn to loss in the number and function of endogenous stem cells that exist in virtually every tissue and organ, including bone marrow. In the U.S. alone, one in three individuals suffers from some form of cardiovascular disease, at a cost of approximately $500 billion a year.[i] Increased age is the greatest risk factor for developing cardiovascular disease and chronic renal disease. Furthermore, as a result of these types of chronic disease, more than a million people die of end-stage organ failure each year, and more than 100,000 individuals are waiting for an organ transplant.[ii]

The Center for Cell and Organ Biotechnology (CCOB), a new partnership between the Texas Heart Institute (THI) at St. Luke's Episcopal Hospital, Texas A&M University (Texas A&M) and the College of Veterinary Medicine & Biomedical Sciences (CVM) at Texas A&M, is taking a multi-faceted approach to chronic diseases based on cell and organ failure through research directed at predicting disease onset earlier to allow earlier intervention (diagnostics); developing personalized cell and gene therapies (based on what has failed) to prevent chronic disease progression; identifying novel therapeutics to treat organ injury; and developing new organ repair or replacement strategies when organ failure is present. Each of these is built upon strategic findings in the past few years in which Texas Emerging Technology Fund (TETF) investigators played a role.

One of the most exciting and promising avenues of scientific and translational investigation to emerge recently in the field of chronic disease management is the development of new, patient-derived, laboratory-grown cells and organs to repair or replace failing hearts, lungs, livers, kidneys, blood vessels and other vital organs and tissues. A scientist at the forefront of creating new adult stem cell therapies and autologous organs for transplant is Dr. Doris Taylor, recently recruited to Texas by the THI. Until March 2012, Dr. Taylor served as Medtronic Bakken Chairholder, Professor of Integrative Biology and Physiology, Professor of Medicine, and Director of the Center for Cardiovascular Repair at the University of Minnesota. Dr. Taylor's previous work (described in part below) offers ample evidence of her extraordinary ability to define a scientific problem and develop innovative, marketable solutions.

Program Description

The CVM, as part of its "One Health" Initiative, and the THI were awarded matching funds from TETF to establish the CCOB, with Dr. Taylor as its director. The CCOB is being designed to develop and commercialize novel new treatments for age-related and chronic health problems. Dr. Taylor and the team of the THI and Texas A&M scientists, engineers, physicians, veterinarians and business managers she is assembling, will employ disruptive cell and organ biotechnologies and molecular tools to develop commercial applications that encompass three broad areas of both human and veterinary healthcare:

Diagnostics**.** Blood- and bone marrow-based diagnostics will be developed which will be built on novel insights into regenerative medicine that CCOB investigators have developed over the past decades. Specifically, CCOB investigators will capitalize on their knowledge of stem and progenitor cell biology, immunology and genomics to develop simple tests that quantify an individual's "capacity for repair." This approach will be expanded to a prognostic that can be used to predict if a given individual's bone marrow or blood is likely to "work" in a clinical trial or if an allogeneic sample would be more beneficial.

Therapeutics. The CCOB will have a multi-faceted therapeutic approach that applies blood- and bone marrow-based diagnostics to human patients enrolled in clinical trials and validate the prognostic value to predict "responders" vs. "non-responders" to drug or cell therapies. Creating a simple test to predict responders at an early time point in a clinical study would be a powerful predictive tool for the pharmaceutical/cell therapy industry.

Further, the CCOB will continue to develop:

- novel veterinary clinical stem cell therapies that can be manufactured and tested in clinical studies in the CVM, the Texas Institute for Preclinical Studies (TIPS) and the National Center for Therapeutics Manufacturing (NCTM) at Texas A&M;
- novel methods for cell delivery and retention in injured organs (both human and veterinary);
- novel repair strategies (e.g., cardiac patches and vascular conduits) for an injured heart; and
- novel cell-based tools for use in failing myocardium.

The CCOB will continue to use combined organ matrix and autologous adult stem cell methodologies to develop personalized *in vitro* liver- and heart-specific drug test beds in partnership with other TETF partners.

Solutions for end-stage organ disease. CCOB researchers will continue to innovate in the field of organ replacement and repair, building on and overcoming the limitations of biologic scaffolds for organ regeneration.

Dr. Taylor and the CCOB will attract scientists, biotech companies and allied industries to Texas. Further, the inter-institutional center will create high-quality jobs and provide an integrated platform for research scientists, clinicians and biotech companies to collaborate seamlessly to advance scientific discoveries from the laboratory, through product development and commercialization, to the marketplace and to patients – both human and animal.

While the CCOB will certainly provide a catalyst for increasing collaborations between the THI and Texas A&M, there are already many examples of partnerships between faculty and researchers at Texas A&M and the Texas Medical Center. For more than 20 years, the University of Texas Medical School in Houston, the M.D. Anderson Cancer Center and the Baylor College of Medicine have collaborated on grants with Texas A&M which is detailed in

subsequent sections. Additionally, the THI and Texas A&M researchers are engaged in active development of preclinical studies for submission of data to the Food & Drug Administration for "first in human" cell therapy studies in doxorubicin cardiotoxicity – a major contributor to heart failure in patients with breast and other cancers.

By joining forces with Texas A&M and the THI, the TETF can expedite the commercial development and job creation linked to Dr. Taylor's discoveries. This unique partnership should broaden the opportunities for commercialization and job creation through expanded opportunities in markets related to both human and animal health. By investing in Dr. Taylor's scientific vision, talent and productivity, the state of Texas could catapult to the forefront of the emerging biotechnology industries sure to grow from these breakthrough scientific discoveries.

2. *Impact on Education and Training of Students (Benefits to the Citizenry of the State)*

Laboratories within the CCOB will be fully staffed by both undergraduate and graduate students. These students will have opportunities to work in facilities at both Texas A&M in College Station and the THI in the Texas Medical Center.

Health and Commercial Benefits to the Citizenry of Texas

Adult stem cell therapies. The regulatory environment for stem cell therapy is still developing, but the established burdens and costs of demonstrating safety, efficacy, manufacturing quality and proving cost-effectiveness are expected to apply to stem cells just as they do to traditional drugs. Beyond the numerous technical issues still to be resolved, key questions for stem cell therapies revolve around how to analyze the commercial value of the emerging technologies. The potential commercial value of a stem cell opportunity is affected by various factors, the most common being the sales forecast, research and development costs, and costs of sales and marketing activities.

Despite the other issues that need to be understood, stem cell therapies may offer the healthcare industry a unique chance to redefine its sales and marketing model. In specialized settings in diseases with very high unmet needs, the industry could develop close relationships with select specialist physicians and their patients, creating a fundamentally different communications environment. This could reduce the need for large sales forces and traditional promotional activities, significantly reducing sales costs and raising the attractiveness of developing treatments for specialized indications.[iii]

Significant opportunities for achieving commercial success exist in this market. Several small companies have been established to focus on different types of stem cell therapies, and some larger pharmaceutical companies (e.g., Pfizer, Lilly and GSK) have set up stem-cell-focused research groups that are funding research collaborations with academic partners. In fact, Dr. Taylor has served on advisory panels to GSK, Johnson & Johnson and others in this arena. To give an example of the types of market values that can be obtained, Mesoblast, Ltd., a company developing a mesenchymal stem cell-based therapy for cardiovascular disease, has reported positive results using cells in a phase-2 trial in chronic heart failure patients (a study reported recently by Dr. Perin, a member of the CCOB Internal Scientific Advisory Board). Using this data, the company was able to license the technology to Teva for $130 million in up-front payments and $1.7 billion in milestones. The company market capitalization is over $1.8 billion.

Cardiac patch**.** Current heart failure therapies are costly and often provide as many additional medical complications as alleviations. A solution is to create a cardiac patch to repair the damaged areas of the heart after myocardial infarction or in a failing heart. The perfusable cardiac patch builds on adult stem cell therapy and provides necessary geometry and thickness to add cell structure to repair injured and scarred areas of the heart. There is a $7 billion market for heart failure devices, including ventricular assist devices and cardiac resynchronization therapy. The CCOB will produce cardiac patches that demonstrate human functionality and strategically partner with industry collaborators for clinical trials.

Drug test beds**.** Current drug testing models have major limitations and fall short of duplicating full human liver function. A three-dimensional, naturally engineered liver (matrix) that mimics natural human liver function would provide an accurate and affordable model to test drugs. When fully developed and commercialized, the technology would lower drug-testing costs, reduce the need for animal screening, allow the study of chronic drug effects and better mimic human response. The CCOB will manufacture decellularized liver matrices and establish partnerships with *in vitro* liver testing companies.

Matrix for research. Current cell cultures cannot represent realistic organ and cell functions, interactions or viability because they are two-dimensional or use artificial structures. The solution – a matrix with composition, geometry and architecture that is native to the tissue of interest, three-dimensional and perfusable. Commercially available matrices would increase accuracy and quality, and lower costs for researchers using cell cultures. These could be manufactured and sold through established biotech partners with a high gross margin potential. For example, Nano 3D is a TETF-funded company that makes 3D tissue culture systems.

Transplantable organs**.** The costs for treating organ failure are extremely high, and no good therapies are available for treating many types of organ failure. In the U.S. alone, more than 100,000 people are waiting for about 28,000 transplants each year. Another one million Americans with end-stage organ failure don't make it to the transplant list. Whereas the number of annual organ transplants has not changed significantly in the past decade, the number of individuals waiting for organ transplants continues to escalate (Figure 1). For individuals fortunate enough to receive an organ transplant, the risks and side effects of anti-rejection drugs are formidable. Additionally, the annual cost of transplant anti-rejection drugs approaches $13 billion annually in the U.S. alone. The commercial potential for therapeutic organ replacement technologies is summarized in Table 1.

The goal of the CCOB will be to develop technologies that create fully functional, rejection-resistant human organs using three-dimensional tissue matrices and autologous human cells obtained from the organ recipient. Organ rejection and the need for anti-rejection drugs would, thus, be eliminated. Cost savings would accrue through less expensive treatment for organ failure victims and elimination of the costs associated with anti-rejection drugs.

Figure 1. Trends in need and supply of organs for transplant. Source: United Network for Organ Sharing (UNOS).

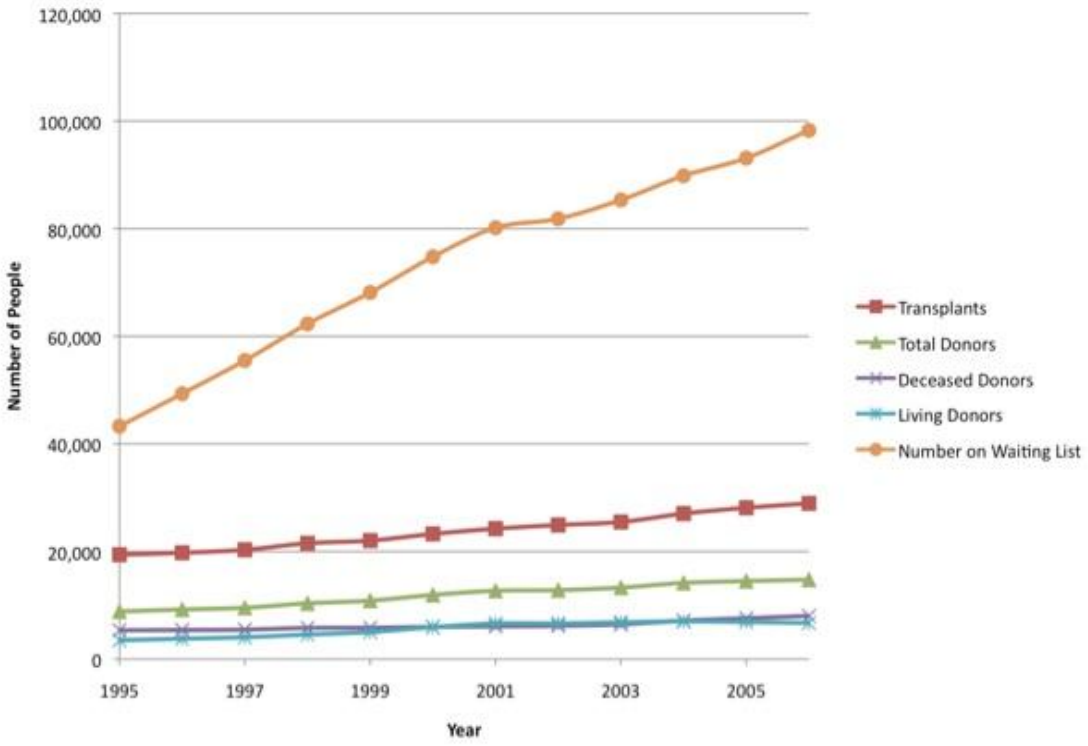

Table 1. Commercial potential for developing new therapies to prevent or reduce organ or multi-organ failure. Source: Organ Procurement and Transplantation Network/ Scientific Registry of Transplant Recipients Annual Report 2009. (OPTN/SRTR AR 2009).

Organ	Annual Organ Failure Deaths	Annual # Organ Transplants	Est. Market Penetration (10%)
Heart	874,000	2,200	87400
Lung	159,000	1,500	15900
Kidney	44,000	17,000	4400
Pancreas	32,000	500	3200
Liver	28,000	6,500	2800
Intestine	1,200	200	120
Bladder	15,000	N/A	N/A
Total	1,153,200	27,900	113,820

3. ***Sources and Future Expectations of Financial Support***

Start-up funding is being provided by TETF, the THI and the Chancellor's Research Initiative. These funds are committed for a period of three years. The principal investigators within the CCOB have a long history (35 years) of continuous extramural grant support from various federal funding agencies. The sustaining support for the CCOB will be from extramural grants, primarily from the National Institutes of Health and the National Science Foundation.

Financial support. The THI is providing $1 million or more in start-up costs and will contribute an additional $3 million in cash support over the next five years for Dr. Taylor's applied research and commercial development program. The THI will also provide 8,000 SF of research lab space and offices, essential support resources (including scientific grant writers and editors) and specialized equipment.

Texas A&M will contribute $3 million or more in cash and in-kind support to the CCOB, including a portion of Dr. Taylor's salary and benefits.

Approximately 50% of the $3 million requested from TETF will be allocated by Texas A&M to support Dr. Taylor's and CCOB activities, and the remaining 50% will be allocated to the THI via a subcontract to support Dr. Taylor's enterprises there. All TETF funds will be dedicated to direct support of CCOB enterprises, with associated indirect costs to be absorbed by the THI and Texas A&M. All of the TETF funds will be used for CCOB direct costs; none of the TETF funds will be applied to indirect costs.

Inter-Institutional Agreement (IIA). The THI and Texas A&M have executed an inter-institutional agreement to formalize the understandings and commitments already made regarding oversight for research compliance, sharing of indirect cost recovery, handling of intellectual property and other administrative details.

4. *Governance and Advisory Structure*

The Dean of the College of Veterinary Medicine & Biomedical Sciences is authorized to appoint the director of CCOB. The functions and composition of the Management Team and Advisory Board are described below.

Management Team**.** Dr. Doris A. Taylor will serve as CCOB director. Dr. James T. Willerson, president and medical director of the THI, and Dr. Glen A. Laine**,** Interim Vice President for Research at Texas A&M and Principal Investigator, will provide institutional oversight for the CCOB partnership and the inter-institutional agreement.

> **Doris A. Taylor, Ph.D., FAHA, FACC,** is the Director of Regenerative Medicine Research at the THI. Before joining the THI, Dr. Taylor directed the Center for Cardiovascular Repair at the University of Minnesota. She also held academic appointments as the Medtronic Bakken Chair of Integrative Biology and Physiology and Professor of Medicine. Dr. Taylor came to the University of Minnesota from Duke University Medical School where she was Associate Professor in the Department of Medicine, Division of Cardiology and Associate Professor, Department of Biomedical Engineering where she helped pioneer the field of cardiac cell therapy.[iv] Among other research responsibilities, Dr. Taylor is currently on the advisory board to the International Society for Heart & Lung Transplantation Basic Science/Translational Research Council. Dr. Taylor is committed to moving cell, gene and tissue engineering-based therapies safely and effectively from bench to bedside, while at the same time preparing students and fellows to compete at an international level in the field of cardiac and vascular repair and regeneration. Her goal is two-fold – first, creation of cutting edge therapies for chronic disease and, second, the education of scientists, physician scientists and the community in the "treatments of tomorrow" for these diseases.

James T. Willerson, M.D., is the president and medical director as well as director of Cardiology Research at the THI. Prior to taking the helm at the THI, he served as Distinguished Professor and president of The University of Texas Health Science Center at Houston. He also holds positions as adjunct Professor of Medicine at Baylor College of Medicine and The University of Texas M.D. Anderson Cancer Center, and is the former head of Cardiology at St. Luke's Episcopal Hospital and the former chief of Medical Services at Memorial Hermann Hospital. Dr. Willerson has received numerous awards for his outstanding work as an internationally distinguished cardiologist, research scientist and educator. Dr. Willerson served as the editor-in-chief of *Circulation*, the premier journal of the American Heart Association (AHA), for 11 years – the longest tenure of any editor with an AHA publication. He has authored or co-authored 19 textbooks and more than 800 scientific articles. Dr. Willerson is one of four editors for *Cardiovascular Medicine, Third Edition*, published in 2007.

Glen A. Laine, Ph.D., is Interim Vice President for Research at Texas A&M, Professor and Former Head of Texas A&M's Department of Veterinary Physiology and Pharmacology, Director of the Michael E. DeBakey Institute, and Professor, Cardiovascular Research Institute. Dr. Laine's work has focused on the biophysics of transmicrovascular solvent (water) and solute (protein) exchange and interstitial edema formation and has been extramurally funded for over 30 years. In recent years Dr. Laine has focused his attention on improving clinical outcomes in patients with organ (cardiac and intestinal) edema. Dr. Laine has published approximately 80 manuscripts in the past 10 years, focusing his research on two organ systems – (1) the heart, due to life threatening problems with myocardial edema in patients placed on the cardiopulmonary bypass pump for coronary artery bypass and transplantation procedures and (2) the gastrointestinal system which is particularly susceptible to life threatening abdominal compartment syndrome due to gastrointestinal edema, secondary to large volume fluid resuscitation in trauma patients.

Dr. Laine was the first to quantitate the negative impact of left ventricular interstitial edema on diastolic cardiac function and how cardiac function could be preserved through the use of colloid perfusion solutions in bypass pumps. He was also first to demonstrate the therapeutic value of shunting lymph from the edematous bowel to improve gastrointestinal function. Implementation of Dr. Laine's findings and recommendations in surgical suites and emergency rooms has had a fundamental impact on patient survival stemming directly from a better understanding of the microcirculation. Dr. Laine's bench-to-bedside, or translational, approach to studying microcirculation accentuates the importance of the interstitium and lymphatics in the understanding of many clinically relevant conditions. Dr. Laine will serve as the Texas A&M principal investigator for this proposal.

Advisory Board. The CCOB will be governed by an Internal Scientific Advisory Board. Joining Drs. Taylor, Willerson and Laine on the Advisory Board will be Drs. Eleanor Green, Richard A.F. Dixon, and Emerson C. Perin.

Eleanor M. Green, DVM, DACVIM, DABVP, is the Carl B. King Dean of Veterinary Medicine in the College of Veterinary Medicine & Biomedical Sciences at Texas A&M. Dr. Green will serve as the responsible party of the application at Texas A&M. Dr. Green has experience in both private veterinary practice and academic veterinary medicine. Clinically, her interests have included general internal medicine, gastrointestinal disorders, neurologic disorders, diseases of the newborn and lameness. Her research interests have been primarily

in the areas of endotoxemia, laminitis, neonatology and gastric ulcer disease. Dr. Green's commitment to the advancement of science and the veterinary profession is witnessed through her service. She has served as the first woman president of three national organizations – the American Board of Veterinary Practitioners, the American Association of Veterinary Clinicians and the American Association of Equine Practitioners. Additionally, she has delivered lectures nationally and internationally on subjects related to her clinical and research interests, as well as equine welfare issues.

Richard A.F. Dixon, Ph.D., FAHA, is director of the THI Wafic Said Molecular Cardiology Research Laboratory. Before coming to the THI, Dr. Dixon served as founder, director and Chief Scientific Officer for Encysive Pharmaceuticals. His research groups have produced more than 10 new chemical entities which have entered human testing, one of which led to an approved drug, Thelin. At THI, Dr. Dixon and his research team are studying stem cell biology and the direct clinical applications of stem cells.

Emerson C. Perin, M.D., Ph.D. FACC, is the THI's director of clinical research for cardiovascular medicine and medical director of the THI Stem Cell Center, and is an active interventional cardiologist and a recognized global leader in the application of stem cell therapy for treatment of cardiovascular diseases. Dr. Perin's specialty interests include leading-edge interventional cardiology including transmyocardial laser revascularization, angiogenesis and Biosense mapping. Dr. Perin is the principle investigator of a doxorubicin study being developed jointly with TIPS and Texas A&M. Dr. Perin will assist in the studies moving human clinical studies into the veterinary practice.

5. ***Mechanisms for Periodic Review***

The CCOB will be externally reviewed at least every three years, in accordance with guidelines developed by the Division of Research at Texas A&M (Standard Administrative Procedure 11.02.99.M0.01 – Centers and Institutes). Reviewers will make recommendations directly to the Vice President for Research as to the future of the CCOB.

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[i] Centers for Disease Control and Prevention. National Center for Health Statistics. Health Data Interactive. www.cdc.gov/nchs/hdi.htm. [accessed 3/26/2012]

[ii] Organ Procurement and Transplantation Network (OPTN), http://optn.transplant.hrsa.gov/data/. (accessed 3/22/2012)

[iii] Webber S, Millest A, Williams M. Stem cell therapies: Assessing the commercial opportunity. Drug Discovery World, Summer 2009.

[iv] Taylor DA, Atkins BZ, Hungspreugs P, Jones TR, Reedy MC, Hutcheson KA, Glower DD, Kraus WE. (1998) Regenerating Functional Myocardium: Improved performance after skeletal myoblast transplantation; *Nat Med.* Aug; 4(8):929-33.