

## **SIGNATURE PROGRAM PROPOSAL: CARDIOVASCULAR SCIENCES/DEBAKEY INSTITUTE**

### **Introduction/Significance**

Cardiovascular disease is the number one killer of both men and women in the United States. Texas A&M University has a long-standing history of excellence in cardiovascular science in several collaborating colleges, including a unique ability to perform translational research on client owned animals with naturally occurring heart disease (e.g., Doberman pinschers with dilated cardiomyopathy) referred to the Veterinary Teaching Hospital. This relationship is schematically represented in Figure 1 to identify the participants in the cardiovascular science program and the central role of the Michael E. DeBakey Institute that was created in 1999 to formalize programmatic relationship between units. The Colleges of Veterinary Medicine and Engineering have shared faculty and teaching responsibilities for more than 30 years, while the Colleges of Education and Medicine have become an integral part of the cardiovascular science program during the past 20 years. Basic science studies have progressed to the point where clinical implementation requires a strong relationship with both the human and veterinary clinical units. The veterinary clinical cardiovascular program is considered to be one of the top 2 programs in the US, and its faculty have developed preeminent programs for training veterinary cardiology residents, performing veterinary clinical trials to determine safety and efficacy of new cardiac therapeutics, and for performing interventional cardiac studies (e.g., coronary stents, pacemakers). The importance of using animals with naturally occurring disease is only recently begun to be recognized as a very powerful tool in the development and testing of new cardiovascular agents and TAMU is well positioned to become a world leader in this area.

The Texas Institute for Preclinical Services (TIPS) will enable TAMU to more successfully compete for interdisciplinary biomedical research dollars. TIPS will house state-of-the-art core imaging equipment located in a facility with access to numerous animal models. The clinical cardiovascular group, currently comprised of 3 cardiologists and a cardiac surgeon and in dire need of expansion, has a strong relationship with the biomedical engineering group and has collaborated on numerous cardiovascular related projects totaling in excess of 10 M dollars in NIH and AHA funding in the past 6 years. Additionally, TIPS, the CV clinical program, and BMEN collaborated to hire a new BMEN faculty member using ETF funds which has added great strength to our interventional cardiovascular program.

The basic science cardiovascular science program has been extremely successful in attracting extramural funding to support its mission (approximately \$60,000,000 over 8 years). The program is in the process of transitioning from an individual investigator-based program to one in which programmatic proposals (Program Project, Center Grant and Training Grant) provide overarching funding for new core facilities and additional graduate students. Additional faculty are needed to expand both the breadth and depth of faculty to fully qualify for program level funding. The cardiovascular sciences program has a proven track record which portends an excellent “return on investment” associated

with the addition of new faculty positions. This return, coupled with the reduction of death and disability from cardiovascular disease, provides the foundation of this request.

## **Rationale**

The interdisciplinary approach to problem solving within cardiovascular research at the Michael DeBakey Institute has positioned us well to continue expanding our impact on cardiovascular medicine and surgery. This impact has resulted in significant program recognition via extramural funding and publications. Departments within the cardiovascular program have advanced to a point of being in the “top ten” or rapidly approaching this designation based on extramural grant support and publication productivity (approximately 600 publications over 8 years) or clinical expertise. Funding for additional high quality scientists within the cardiovascular program should place participating departments solidly within the top ten. The Clinical Veterinary Cardiovascular Sciences program has been identified as a premier program in the Department of Small Animal Clinical Sciences and cardiovascular science has been identified by the Department of Veterinary Physiology and Pharmacology as one of its premier research foci. The Department of Biomedical Engineering has also identified cardiovascular science as a major research emphasis. **The interdisciplinary nature of our research coupled with an ability to translate basic cardiovascular research from the bench into clinical studies using naturally occurring disease is unequalled anywhere in the US.** The teaching, research, and service elements associated with both basic and clinical programs in cardiovascular science have profound impact on all twelve of the Vision 20/20 goals. Whether it is enhancement of faculty or graduate and undergraduate academic experiences, our program has a significant impact on Texas A&M University; enriching our campus by connecting us to the citizens of Texas and the global community via improved circulatory health and quality of life. Faculty members from the associated colleges and departments have participated in formulation of this plan to add faculty and carry the cardiovascular sciences program to the next level of national and international recognition.

## **Indices of Excellence**

Excellence in research can be measured in several ways. Extramurally reviewed grants and publications are the most commonly used indices, along with clinical successes in areas related to medicine. Members of the DeBakey Institute have received numerous grants from the National Institutes of Health including standard investigator initiated R01 grants as well as individual training grants including K08s (Clinical Investigator Awards), K25s (Quantitative Investigator Awards), and K29s (Career Development Awards). These federal grants have been supplemented by individual grants from the American Heart Association and American Lung Association. In recent years, the cardiovascular science program at Texas A&M University has advanced to a more programmatic level. This transition is identifiable when a group of investigators from various departments and colleges seek and obtain funding based on their collaborative interactions. Examples of such programmatic funding include the development of the Texas A&M Institute for Preclinical Studies, which was originally

developed to perform GLP (Good Laboratory Practice) studies in cardiovascular disease. Approximately 65M has been invested by the state, university, and local economic development groups for infrastructure costs for TIPS. Since inception just over two years ago, TIPS has collaborated on numerous projects with total funding that exceeds 25 million dollars. Examples of such funding include over 2 million in NIH funding with BMEN and the TAMU spin-out CorInnova to develop a direct cardiac compression device, 1.2 million to develop a new coronary stent and 846,455 to develop shape polymers for treatment of cerebral aneurysms. Additionally, TIPS has received over 2 million in funding from DARPA for development and testing of a hemorrhagic shock model in the pig. We are currently collaborating with Siemens to develop a deep tissue coagulation device, a project that has been funded by DARPA at over 10 million dollars, and are working to develop fracture putty which has been awarded over 8 million dollars by DARPA for Phase I studies. Discussions are underway between UTHSC and TAMU to jointly spin-out a company to commercialize veterinary and human applications for fracture putty.

Further examples of such funding include the Michael E. DeBakey Initiative funded at \$500,000 to \$800,000 per year (2002 – 2005) through the Centers for Disease Control and Department of Defense. Another example is the Whitaker Foundation grant which combined the Colleges of Engineering, Veterinary Medicine, and Medicine for funding of 2 million dollars to enhance our teaching and research interactions. Recently, members of the DeBakey Institute were asked to head one of the projects on the University of Texas Medical School's (Houston) P50 Center Grant in trauma. This opportunity to apply the basic science "lessons learned in the laboratory" at Texas A&M University to patients at various hospitals is an indication of how collaborative interactions can lead to clinically important discoveries. In the training grant arena, members of the DeBakey Institute have applied for a National Science Foundation training grant. Of some 500 applications, 100 preproposals were selected for full proposal submission including the proposal from Texas A&M University. An NIH T32 Training Grant will be submitted utilizing the same database organized for the National Science Foundation proposal. As our program has grown in stature and reputation, we have been fortunate to obtain several endowments including two - \$1 million endowed chairs in cardiothoracic surgery and cardiology. Our interactions with the Cardiothoracic Surgery Clinic in Cologne, Germany emphasize our global collaborations and have resulted in a significant grant from the German government (Deutsche Forschungsgemeinschaft) supporting our cardiovascular program. An endowment from the Sid Richardson Foundation has been obtained to specifically support cardiothoracic surgery in our veterinary patient population. The cardiovascular science program at Texas A&M University is clearly establishing itself as one of the premier programs in the country and has approximately 600 peer-reviewed manuscripts since creation of the DeBakey Institute.

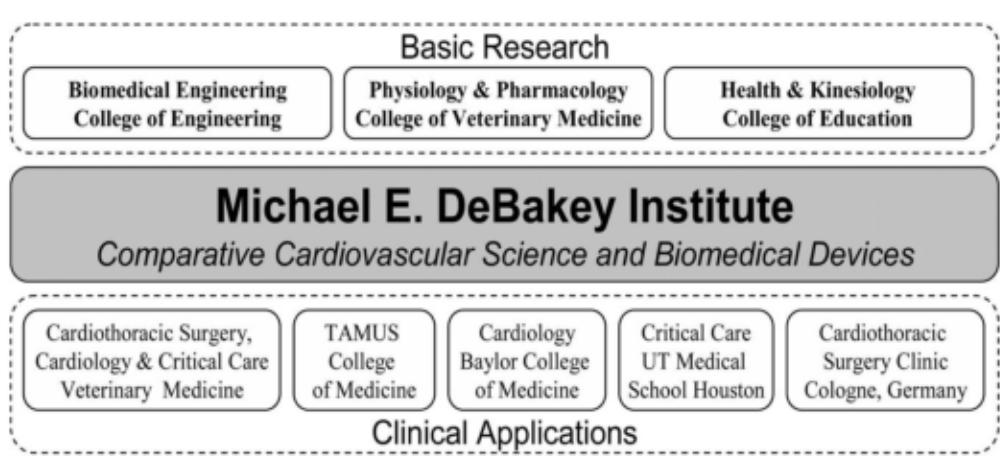
### **Interdisciplinary Impact**

The Michael E. DeBakey Institute is an Interdisciplinary Cardiovascular Research Program composed of elements from four colleges and multiple departments. The

Cardiovascular Research Program would have been unable to attain its national and international reputation without contributions from each of these units. As we make the next step to greater national and international exposure, it is critical that we maintain our interdisciplinary approach and will be adding members from additional colleges to our research teams.

### Assessment/Expectations

Each new faculty position will be aggressively monitored by both the faculty member's department head and the director of the DeBakey Institute. Publications in appropriate journals and acquisition of individual funding from appropriate federal agencies (NIH, NSF, DARPA) will be required. Evaluating program success will be linked directly to standard programmatic bench marks including participation in program project grants, center grants, and training grants. Programmatic success can also be evaluated when a group of superior investigators begin to receive recognition as part of an overarching programmatic imperative such as the Michael E. DeBakey Institute. The cardiovascular sciences program has had excellent success in recruiting both faculty and graduate students from under represented groups. This has been most evident in our recruiting of female and Hispanic faculty and students. The presence of a diverse faculty and student base acts to promote recruiting for additional under-represented faculty and students particularly when the success of our under represented members is appropriately rewarded. Both graduate and undergraduate instructional programs are profoundly impacted by the presence of teaching faculty who bring new discoveries from the laboratory to the classroom in a timely fashion. The excitement and role model exhibited by these faculty members can also help guide undergraduate students to the possibilities of academic employment and career opportunities.



**Figure 1**

**College of Veterinary Medicine and Biomedical Sciences  
Participating Faculty**

**H. Richard Adams, DVM, PhD**

Circulatory shock; myocardial and vascular dysfunction in endotoxemia; role of nitric oxide in vasoregulation.

**Fred J. Clubb, Jr., DVM., PhD**

Electron microscopic evaluation of myocardial and renal biopsies; qualitative and quantitative evaluation of implantable cardiovascular devices for nonGLP and GLP\preclinical trials

**Timothy A. Cudd, DVM, PhD**

Reflex control of cardiovascular and endocrine systems in the adult and the fetus

**Theresa W. Fossum, DVM, PhD**

Cardiovascular surger; animal models of cardiovascular disease; chylothorax; lymphatic system; evaluation of artificial heart performance.

**Alonso Guedes, DVM, PhD**

Clinical Anesthesiology; hormonal and cytokine regulation of intracellular calcium homeostasis in smooth muscle

**Sonya G. Gordon, DVM**

Canine chronic degenerative valve disease; cardiovascular imaging; interventional cardiology

**Cristine L. Heaps, PhD**

Cellular and functional adaptations in the coronary circulation in response to coronary artery disease and exercise training; specifically the adaptive responses of both smooth muscle ion channels and endothelial nitric oxide regulation in the regulation of coronary artery function with disease and exercise training.

**Glen A. Laine, PhD**

Microvascular, interstitial and lymphatic interactions in regulating myocardial fluid balance; myocardial edema and fibrosis; left ventricular mechanics.

**Matthew M. Miller, DVM**

Cardiomyopathies; color Doppler ultrasonography

**Christopher M. Quick, PhD**

Quantitative cardiovascular physiology; cardiovascular remodeling and simulation; arterial hemodynamics and pulse wave phenomena

**Friedhelm Schroeder, PhD**

Research Interests: Intracellular lipid transfer proteins; lipid metabolism; multiphoton imaging of intracellular lipid transport and targeting in living cells and tissues of gene targeted animals

**John N. Stallone, PhD**

Humoral interactions between vascular smooth muscle and endothelium; genomic and non-genomic effects of gonadal steroid hormones on vascular function.

**Randolph Stewart, DVM, PhD**

Lymphatic function; microvascular and interstitial fluid dynamics; synovial fluid balance; cardiac function.

**George Stoica, DVM, PhD**

Cancer biology; growth factors; tumor angiogenesis; immunohistochemical analysis of peripheral arteries after balloon angioplasty.

**Yanan Tian, PhD**

Transcriptional control of the Ah receptor-regulated genes. Mutual modulation between Ah receptor and NF- $\kappa$ B signal transduction pathway. The effects of Ah receptor ligands on the cholesterol biosynthesis.