

# University of Pennsylvania Surgeon Receives Grant to Develop “Molecular Cardiac Surgery” as a Possible Alternative to Heart Transplant

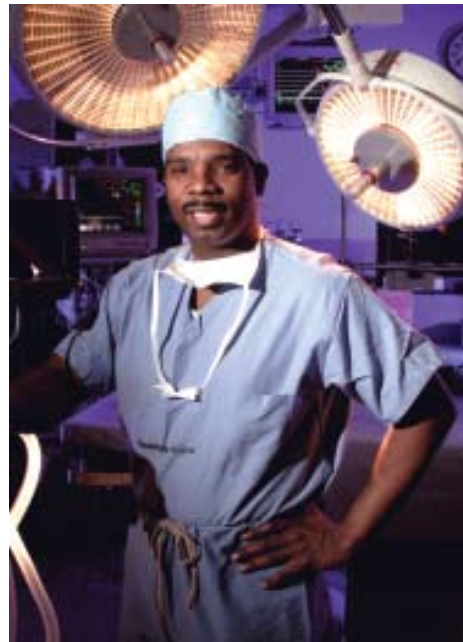
*The Editorial Board of the Journal of the National Medical Association has dedicated this column in recognition of the outstanding academic, scientific, social and cultural accomplishments of NMA members in all aspects of the medical profession. It is anticipated that these members will serve as both an inspiration to our young members and as a “road map” to assist them in planning for a successful career. Interested members are encouraged to contact the honorees directly. Submissions for this column are encouraged and should be forwarded to shaynes@nmanet.org.*

© 2008. From the University of Pennsylvania Medical Center, Philadelphia, PA. Send correspondence and reprint requests for *J Natl Med Assoc.* 2008;100:575-577 to: Dr. Charles R. Bridges, Chief of Cardiothoracic Surgery, University of Pennsylvania Medical Center, Philadelphia, PA; e-mail: charles.bridges@uphs.upenn.edu

**D**r. Charles Bridges, MD, ScD, associate professor of surgery at the University of Pennsylvania Medical Center and chief of cardiothoracic surgery, Pennsylvania Hospital, has been awarded a \$3 million grant from the National Heart, Lung and Blood Institute (NHLBI) for his work in “molecular cardiac surgery”: a unique approach to gene therapy for heart failure.

The four-year grant will enable Bridges to expand upon his current research in large-animal “molecular cardiac surgery” (a term coined by Bridges). This methodology could provide alternatives both to heart transplantation and to the use of permanent mechanical-assist devices in some humans with end-stage heart failure. Molecular cardiac surgery, if successful, will be more powerful therapeutically and avoid the problems of rejection, infection, increased stroke risk and device failure often associated with these existing technologies.

When genes are absent or defective, proteins are unable to carry out their normal functions, resulting in genetic disorders. In gene therapy, a functioning gene replaces an absent or faulty gene, so that the body can make the correct protein and consequently eliminate the root cause of a disease. Using molecular cardiac surgery, Bridges’ group was the first in the world to convincingly demonstrate that marker genes could be efficiently inserted into the majority of heart muscle cells in large animals like dogs and sheep. What makes this approach so unique is that Bridges’ group uses a novel, patent-pending cardiac surgical procedure and specially designed hardware as a platform for the most efficient delivery of genes to heart muscle cells ever achieved in large animals. Prior to Bridges work, research in other laboratories had not proved successful in achieving global, heart-specific gene expression in animals other than rodents and mice.



The molecular cardiac surgical approach has an added advantage since genes are expressed only in the heart, enhancing the safety of this approach over all other available gene delivery methods. The preliminary success of molecular cardiac surgery opens the door to developing new treatments for a variety of heart muscle diseases causing heart failure.

Vectors are used to deliver the specially designed beneficial genes (“transgenes”), with the most common vectors being a virus that has been genetically altered. Viruses have evolved ways of delivering their genes to human cells in a pathogenic manner. Researchers have taken advantage of this capability by removing disease-causing genes from the virus and inserting therapeutic genes. The vector then discharges the therapeutic genes into the target cell. The new grant will enable Bridges to move beyond his work with marker genes and begin testing his findings using therapeutic genes in sheep with heart failure.

Bridges closely collaborates with Hansell Stedman, MD, associate professor of surgery at the University of Pennsylvania. Bridges and Stedman jointly have several U.S. and international patents for the efficient use of vectors in gene delivery to cardiac and skeletal muscle. Prior to their work, delivery techniques in common use typically resulted in 1–2 percent expression of therapeutic genes in the target cells. Bridges and Stedman generate successful delivery rates approaching 100% in both skeletal and cardiac muscle. In addition, their delivery methods enable safe removal of the delivery device once the therapeutic genes are delivered. This substantially reduces the risk of harm to other organs in the body.

“This grant will enable us to build on the advances my colleagues and I have been fortunate to achieve,” says Bridges. “Molecular cardiac surgery offers genuine promise for eventually prolonging and enhancing the quality of life for many patients with heart disease.”

Bridges’ new study under the NHLBI grant will focus on one of the most promising transgene candidates with potential for healing the heart. Specifically, up to 100 trillion genes will be delivered to each heart, which is expected to arrest the progression of heart failure and possibly lead to recovery of heart function within several weeks.

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Bridges graduated from Harvard University in three years, *magna cum laude* with a degree in engineering and applied physics. Entering medical school at age 18, he was the youngest student in the entering class at Harvard Medical School and at the time, the youngest student ever enrolled in the Harvard-MIT program in health sciences and technology. He received an MD from Harvard Medical School (honors) as well as a master of science in electrical engineering and computer science and a doctor of science in chemical engineering from MIT as a Whittaker Health Sciences fellow. At MIT, he was elected to Sigma Xi. He completed two years as a Braunwald resident in internal medicine at the Brigham and Women’s Hospital before deciding on a career in surgery.

A Philadelphia native, he returned from Boston to complete residencies in general surgery and cardiothoracic surgery at the hospital of University of Pennsylvania. He is currently associate professor of surgery, division of cardiothoracic surgery, and a member of the bioengineering graduate group in the department of bioengineering at the University of Pennsylvania. Since 2001, he has served as chief of cardiothoracic surgery at Pennsylvania Hospital, University of Pennsylvania Health System. In August 1999, Bridges was one of the founders of the Association of Black Cardiovascular and Thoracic Surgeons serving as president from its inception through January 2002. He is board certified in

both surgery and thoracic surgery. He is a fellow of the American College of Surgeons, the American College of Cardiology and the American Heart Association. For the last three years he has served as the chairman of the Society of Thoracic Surgeons (STS) Workforce on Evidence Based Surgery. In this capacity, within the STS leadership he has directed the development of the first series of practice guidelines in the field of cardiothoracic surgery, including coronary artery bypass surgery in women, antiplatelet therapy during coronary artery bypass surgery, transmyocardial laser revascularization, antibiotic duration, antibiotic selection, guidelines for reporting the results of atrial fibrillation surgery and blood conservation.

Bridges is recognized nationally as an authority on the topic of cardiac surgery in African Americans and racial disparities in cardiac surgical care. His current basic and translational research interests include studies funded by the National Institute of Bioengineering and Biomedical Imaging and the NHLBI. He is principle investigator of a grant entitled “Translational Studies in Heart Failure Gene Therapy,” a \$3.05 million four-year grant (2007–2011) funded by the NHLBI for the development of novel technology for highly efficient vector-mediated cardiac gene delivery using novel cardiac surgical techniques (“molecular cardiac surgery”). The goal of these studies is to develop revolutionary new therapies for advanced heart failure that may one day compete with transplantation and mechanical assist devices used for “destination” therapy. His interests in molecular/biomedical engineering include theoretical modeling of biological systems, cardiac mechanics and molecular evolution. His research has been published in several prestigious basic science and clinical medicine journals, including *Nature*, *Circulation*, the *American Journal of Physiology*, *Annals of Thoracic Surgery*, the *Journal of Thoracic and Cardiovascular Surgery*, the *Journal of the American College of Surgeons* and the *Journal of the American College of Cardiology*. He was a coauthor of the cover article in the March 25, 2004, issue of *Nature*. This report received front-page coverage in *The New York Times*, *The Wall Street Journal*, *The Philadelphia Inquirer* ... and was described in an editorial in *Science* magazine as one of the “most important discoveries in human genomics and molecular evolution.” He was honored in *Philadelphia Magazine* in 2001 as one of the “76 Smartest Philadelphians” and as a “Top Doctor” in thoracic surgery in the May 2004, May 2005, May 2006 and May 2007 issues of *Philadelphia Magazine*.

He serves on the board of the Franklin Institute. He received the 2005 Advocacy Award and the 2006 Edward S. Cooper Award from the Pennsylvania–Delaware Affiliate of the American Heart Association, where he also serves as a board member. His tenure as chairman of the “Breathe Free Philadelphia Alliance” culminated in the successful enactment of legislation mandating a ban

on indoor smoking in the City of Philadelphia. He was also the recipient of a citation (“Honoring Charles R. Bridges”) from the Philadelphia City Council in 2004.

Bridges has two issued U.S. patents (#5,983,142 and #6,673,039) and four pending U.S. and international patents for inventions in the fields of cardiovascular devices, and cardiac and systemic gene and cell delivery. He serves as a consultant to the circulatory system devices panel of the U.S. Food and Drug Administration. His clinical research interests include several completed and ongoing large-scale multivariate analyses of

cardiac surgical outcomes through the STS in collaboration with the Duke Clinical Research Institute. He has been married for more than 25 years to his wife Renee, and has three daughters—Hillary, 20, a junior and a John B. Ervin scholar at Washington University in St. Louis, MO; Amanda, 19, a sophomore at Harvard University; and Lauren, 15.

Bridges maintains an active clinical cardiac surgery practice with special interest in transfusion-free cardiac surgery, minimally invasive mitral and aortic valve surgery, arrhythmia surgery and complex aortic surgery.

## L E T T E R T O T H E E D I T O R

*The opinions expressed here are not necessarily the opinions of the National Medical Association.*

### Sleep Duration among Black and White Americans

To the Editor:

“Sleep Duration among Black and White Americans: Results of the National Health Interview Survey” in the March 2008 issue of *JNMA*<sup>1</sup> provided some potential answers for an observation on the prevalence of isolated sleep paralysis in African Americans that we made several years ago.<sup>2-4</sup>

Essentially, our research found African Americans had more isolated sleep paralysis than whites, and that frequent attacks isolated sleep paralysis ( $\geq 1$  a month) was associated with panic disorder. Japanese researchers<sup>5</sup> added a big piece to the puzzle when they discovered that the interruption of sleep (a frequent occurrence when individuals are under stress) could elicit isolated sleep paralysis; however, this discovery did not explain why African Americans would have such a high prevalence of isolated sleep paralysis. Friedman et al.<sup>6</sup> and Neal-Barnett and Crowther<sup>7</sup> confirmed our original observation in their own research projects that independently

replicated our work, but potential explanations for the empirical observation that African Americans had a high prevalence of isolated sleep paralysis were still elusive.

Unfortunately, as Dr. Satcher’s Culture, Race and Ethnicity Report<sup>8</sup> highlights, because there is so little known about African-American health and mental health, we are frequently unprepared to understand the etiology of some of the empirical observations we make about African-American populations. Thankfully, because *JNMA* publishes articles such as the one by Nunes et al.,<sup>1</sup> we are able to glean more information that provides potential explanations for our empirical observations. Nunes et al.’s<sup>1</sup> finding that “blacks were less likely than whites to report sleeping 7 hours (23% vs. 30%;  $\chi^2=94$ ,  $p<0.0001$ ) while being more likely to experience both short sleep ( $\leq 5$  hours; 12% vs. 8%,  $\chi^2=44$ ,  $p<0.0001$ ),” and with Takeuchi et al.’s<sup>5</sup> observations that interruption of sleep induces isolated sleep paralysis, fit together to offer potential mechanisms to explain the high prevalence of isolated sleep paralysis in African Americans.

I will be forever grateful to *JNMA* for being there and helping to fill the void of empirical information about the health and well-being of African-American populations—information that is critical for our

understanding as we try to provide medical services to our population.

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Carl C. Bell, MD  
President/CEO  
Community Mental Health  
Council Inc.  
8704 S. Constance  
Chicago, IL 60617  
[carlcbell@pol.net](mailto:carlcbell@pol.net)