

**Testimony of Edward D. Miller, M.D.  
The Frances Watt Baker, M.D. and Lenox D. Baker, Jr., M.D.  
Dean of the Medical Faculty  
CEO, Johns Hopkins Medicine**

Before the

Committee on Energy and Commerce of the U.S. House of Representatives  
Tuesday, September 19, 2006, at 2:00 p.m.  
2123 Rayburn House Office Building

Hearing Entitled: "Improving NIH Management and Operation: A Legislative Hearing on the  
NIH Reform Act of 2006"

**Introduction**

Mr. Chairman and members of the Committee, thank you so much for inviting me to testify today at this very important hearing. I am Ed Miller, Dean of the Medical Faculty and CEO of Johns Hopkins Medicine. Johns Hopkins Medicine is the organization that represents The Johns Hopkins University School of Medicine and Johns Hopkins Health System.

Let me start by commending leaders in Washington for their foresight in doubling the National Institutes of Health (NIH) research budget between 1998 and 2003. Many of the startling advances in identifying early indicators and causes of diseases are the result of those well-spent federal research dollars. I am convinced we are on the cusp of a dramatic transformation in health science discovery and cures.

I would like to recognize the persistence of Chairman Barton in developing draft legislation that embraces the importance of biomedical research. We are grateful to you for reaching out to us and for caring about NIH enough to want to make it "better," and for leading the way to provide much needed increases in funding. The bill's provision for a 5 percent increase in annual funding is hugely important and it will accelerate crucial research. In addition, the creation of a "Common Fund" to promote trans-NIH research activities represents an important commitment to collaborative science. We at Johns Hopkins believe this is the quickest and most sensible way to find cures and treatments.

**Justification of NIH Funding**

Congressional and administration support for biomedical research has helped to transform our ability to detect disease, treat patients, and deliver healthcare with greater effectiveness and affordability. At the same time, the return on investment for the American taxpayer has been high, as research has fostered discoveries that have led to new patents and products, and to the creation of new companies and job opportunities.

However, today the NIH budget is facing severe constriction. Indeed, one could say the federal funding of life sciences is in a crisis. For FY 2006, the NIH budget was cut in both nominal and real terms. For FY 2007, the budget is essentially frozen. This marks the third year in a row NIH funding has been cut, when adjusted for inflation. The biomedical research enterprise created by the NIH doubling has been cut by nearly 11 percent in real terms since 2003. Going forward, at a minimum for NIH, anything less than a funding level at least equal to the medical inflation index is a cut, and will weaken the nation's role as a worldwide leader in the biomedical field.

At Johns Hopkins, we have annually led the nation in NIH research dollars and we have made significant investments in young investigators to support the nation's efforts to advance science. However, there has been a marked decline in grants awarded to our School of Medicine. Fewer projects are being funded and NIH support of on-going investigations is being cut. Recent figures suggest that the number of grants and overall funding levels have declined. In FY 2002, the average funding level per grant was \$142,210 for the School of Medicine. By FY 2006, the funding level dropped nearly \$50,000 per grant to \$92,683, a decline of 34.8 percent. Hardest hit are America's young researchers. I fear we may lose a generation of enthusiastic, inquisitive scientists if they conclude NIH grants are out of reach. We must not let that happen.

The increased and sustained funding for biomedical research is important to the majority of Americans. According to public opinion polling conducted in 2005 by Research!America, 58 percent of Americans say that increasing U.S. funding for medical and health research now is essential to our future health and economic prosperity. Similarly, 79 percent of Americans agree that even if it brings no immediate benefits, basic science research which advances the frontiers of knowledge is necessary and should be supported by the federal government.

While the President and Congress have embraced the notion that funding for basic research is essential to strengthening America's competitive standing in the world, funding for biomedical research has not kept pace with this commitment. Aggressive, stable, and sustained federal spending on the NIH and biomedical research must be understood and embraced as a critical component of America's competitiveness. The fact is federal investments in biomedicine and basic science across the disciplines have taken the U.S. to the leading edge of innovation. The question we now face is whether as a country we are willing to pay the price to remain in the lead.

We believe the 5 percent increase in annual authorizations proposed is a sound investment. Sustainable and predictable funding levels for the NIH are critical to allowing researchers to deliver improved treatments that not only enhance quality of life for patients but can reduce health care costs.

### **How Research Can Impact Health Care Cost**

When advocates for increasing biomedical research funding meet with members of Congress and their staff, they are often asked: what have we to show for the money that NIH has received in the past? As we think about this question it is important to recognize the pace of biomedical research and science in general is often slow and unpredictable. It may be years before we can

point to specific therapies or new medical devices that can trace their origins to recently funded efforts. But the simple answer is: we have a great deal to show! Here are four powerful examples of what Johns Hopkins scientists have accomplished in terms of improving healthcare and reducing costs thanks to NIH support.

#### *Detection of Vision Problems of Diabetics*

Diabetes is the leading cause of blindness in adults, with 12,000 to 24,000 new cases each year. Early identification of retina disease is critical to stave off vision loss, especially for the 10 million diabetics who are 60 years or older, most of them on Medicare or Medicaid. Yet more than half of all diabetics fail to get an annual eye exam as recommended by the American Diabetes Association. To address this dilemma, Dr. Ran Zeimer, director of the Ophthalmic Physics Laboratory at Johns Hopkins Wilmer Eye Institute, came up with a novel solution after more than a decade of research: why not develop an easy-to-use digital camera that tests for retinopathy when diabetics visit their primary care physicians for check-ups?

Thanks to NIH support, Dr. Zeimer perfected an instrument called the DigiScope. The DigiScope takes images of the retina in just minutes as patients sit in front of an automated camera and look at a series of blinking lights. These images are then transmitted via the Internet to a reading center for expert interpretation. Over 20,000 individuals not under the care of an ophthalmologist have been screened to date in primary care physicians' offices. Those with vision-threatening disease have been identified and referred to eye specialists. In most cases, diabetics without complications are spared visits to an ophthalmologist, while Medicare and Medicaid are spared an expense.

#### *Advances in Treatment for Sickle Cell Patients.*

Thanks to continuous NIH grants extending back to 1982, Drs. George Dover and Samuel Charache of Johns Hopkins spent their careers fighting sickle cell disease – a miserable, inherited illness in which sickle-shaped red blood cells get stuck in narrow channels and block blood flow to tissue and vital organs. Patients with sickle cell disease – 72,000 in the United States – suffer frequent bouts of fatigue and shortness of breath, joint and body organ pains that turn excruciating and lead to frequent hospitalizations. The pneumonia-like conditions, chest pains, and fever can be life-threatening. Until fairly recently, early death was the norm, with life expectancy for a sickle cell patient projected to be only 20 to 30 years.

In the 1990s, Drs. Dover, Charache, and their Hopkins research team found that a cancer drug (hydroxyurea) did remarkable things for sickle cell sufferers. A 1995 NIH-supported multi-center study proved hydroxyurea therapy dramatically reduces the frequency and severity of painful episodes, hospitalizations and transfusions. In a 2003 study, daily hydroxyurea doses led to 30 percent fewer hospital days, 58 percent fewer transfusions and a 40 percent reduction in deaths. Today, hydroxyurea therapy is recommended for adults and adolescents with moderate-to-severe recurrent pain. As a result, the life expectancy for sickle cell patients has doubled.

There have been financial benefits, too. According to another NIH-sponsored study, hydroxyurea therapy saves the U.S. health care system \$5,210 per sickle cell patient per year. With 72,000 Americans suffering from sickle cell disease, the potential annual savings is more than \$375 million.

#### *Faster Diagnoses in Emergency Rooms*

With the existing threat of bioterrorism, it is crucial to find ways for swiftly identifying patients in hospital emergency rooms who have biochemical pathogens or life-threatening infectious diseases, such as meningitis, sepsis and bacterial endocarditis (an infection of the inner lining of the heart or heart valves). Current testing methods are time-consuming and usually lead to delays in diagnosing and treating these diseases. The current blood and culture tests for some diseases can take 24 hours or more.

Dr. Richard E. Rothman of Johns Hopkins Department of Emergency Medicine is working on novel ways to identify multiple blood-borne and pulmonary infectious diseases and bioterrorism pathogens in a hurry. His patented molecular diagnostic tests involve both exhaled breath and body fluids. Early experiments have shown these new diagnostic tools can detect 25 common bacterial infections and five categories of bioterrorism agents in fewer than 4 hours, and faster response times are expected as the diagnostic tools are fine-tuned.

#### *Cell-Based Therapies for Heart Attacks*

Heart attacks represent a critical health problem facing this country. Each year, 565,000 Americans suffer heart attacks, 300,000 have recurring heart attacks, and 3 million deal with congestive heart failure. The costs for these patients are staggering: an estimated \$403 billion in 2005, with outpatient costs alone consuming \$120 billion.

Researchers are on the cusp of developing remarkable therapies that could revolutionize coronary treatment. One laboratory research group led by Hopkins' chief of cardiology, Dr. Eduardo Marban, is studying a treatment using a patient's own cardiac stem cells to repair damaged heart tissue soon after a heart attack and to regenerate weakened heart muscle. This could avert the need for expensive heart transplants. By using a patient's own cardiac stem cells, there also would be no risk of an immune-response rejection.

Meanwhile, Hopkins cardiologist Dr. Joshua Hare is engaged in a project that involves clinical trials with recent heart attack patients who are being given injections of adult bone-marrow stem cells. Dr. Hare's research revealed that stem cells harvested from a pig's bone marrow and injected into another pig's damaged heart restored heart function and repaired up to 75 percent of the damaged muscle in just two months. A \$12 million dollar, five-year NIH grant to the Johns Hopkins Heart Institute is making this exciting work possible.

#### **Why Johns Hopkins Supports the Common Fund**

While the research efforts outlined above have produced improvements in clinical care and are driving a radical change in treatments, shifting to a new paradigm in how we fund and conduct

biomedical research requires new thinking that crosses traditional boundaries. Medical centers have traditionally housed clinical researchers and basic scientist separately based on their departmental affiliations. These affiliations can create artificial barriers to collaborative research efforts. For some types of research, it often makes more sense for researchers from different departments to be co-located to facilitate interactions.

At Johns Hopkins, we have been able to tear down some of the traditional silos separating the branches of medical science to create a village of investigators to find cures and advance research. That work has been supported through various sources, but the most important source for biomedical research, the NIH, also needs a vehicle to sustain research that crosses these traditional silos.

The proposed Common Fund that will support trans-NIH research activities would represent an important commitment to collaborative science. At John Hopkins, we see this as the quickest and most sensible way to find cures and treatments. The movement to supporting a village of investigators is critical in combining all that we have learned to advance cures. However, it is important to note that this type of research is also not a silver bullet. We need to strike a balance between funding traditional research efforts and trans-NIH research.

The reason we need to create the Common Fund and support trans-NIH science can be easily seen in the area of cancer treatment. In 1971, when President Nixon signed the National Cancer Act, the word cancer was equated to a death sentence. According to the National Cancer Society's "Cancer Facts and Figures 2006," for all races the overall cancer survival rate was only 50 percent in 1974. Today, while survival rates fluctuate for particular cancers or populations, in almost every category we have improved survival rates. For example, in 1974 the survival rate for breast cancer for all women was 75 percent, while the most recent data available (1995-2001) report a survival rate of 88 percent. During these same time periods, the survival rate for colon cancer increased from 50 percent to 64 percent.

These survival rates increased because we were able to change how the disease was treated over the past 25-years, improving diagnostic techniques and expanding treatment options. However, on September 16, 2006, researchers at Johns Hopkins announced that they had cracked the genetic code for breast and colon cancers. This information is the equivalent of looking at the enemy's game plan and revealed that the average number of mutant genes in each cancer is about 100, and at least 20 of them are likely to be critical for tumor formation. Just as important, the investigators found that each cancer has a different blueprint, so we now know that no two patient diseases are identical. This will not only guide cancer research for the next decade, it will lead to a better understanding why patients respond differently to the same therapies.

While this announcement is critical to advancing the treatment of cancer, we need to step back and understand what went into this discovery. The team used 22 cancer samples and information from the Human Genome Project to examine the more than 13,000 best-known genes. Then, the team examined the DNA code of the 13,000 genes by dividing each gene into overlapping sections, to obtain 130,000 sections for analysis. Then, the samples were amplified through more than 3 million biochemical reactions. Next, the sequences were fed through a computer to compare normal sequences with those from the tumor samples. More than 800,000 suspicious

regions were visually inspected, one by one, to verify true mutations. In the end, the Hopkins team combed through 465 million nucleotides, which are the individual chemicals that pair together to build the rungs of the DNA ladder that compose genetic instructions.

It is important to understand that this work required a large, diverse team. The Johns Hopkins research team alone included 13 investigators and countless others at the University of South Carolina, Case Western Reserve University, University Hospitals of Cleveland, Texas Southwestern Medical Center, University of Maryland, Howard Hughes Medical Institute, and Agencourt Bioscience Corp. The success of this project is due to the village of researchers and recent advances in DNA sequencing and bioinformatics.

To support and advance this type of research, various institutes and centers, many of which are virtual, have been organized at Johns Hopkins. These centers of interdisciplinary research teams include not only investigators from different departments within the School of Medicine, but faculty from different schools and divisions across Johns Hopkins University as a whole. Below are a few more examples of these efforts.

#### *Institute for Computational Medicine*

Johns Hopkins University created the Institute for Computational Medicine (ICM) – the first of its kind in the world - because the nature of biomedical research has been transformed during the past decade. This transformation has been driven in large part by the development of new technologies for high throughput data generation which now make it possible to acquire gene sequences, measure the complement of genes and proteins expressed in cells and/or tissues, map protein-protein interactions and image functional properties of cells, tissue and organs under a wide range of conditions. The impact of these technologies on identification of the cause, diagnosis and treatment of human illness will be profound.

It will soon be common for clinical research studies to collect genetic, transcriptional, proteomic, imaging and clinical data from every patient in large, carefully selected cohorts sharing a specific disease diagnosis. The challenge of the coming decade will be how best to use these multi-scale biomedical data to gain a quantitative understanding of disease mechanisms.

#### *Institute for NanoBio Technology*

The Institute for NanoBio Technology (INBT), hopes to revolutionize health care by bringing together expertise from medicine, engineering, and public health to create new knowledge and groundbreaking technologies. Research is currently underway in the following areas: cancer, cystic fibrosis, vaccines, asthma, hemophilia, spinal cord injury and peripheral nerve regeneration.

Approximately 100,000 children and adults worldwide are diagnosed with cystic fibrosis, a fatal genetic disease. While antibiotics treat infections caused by the disease and expectorants allow clearing the airways of mucus that makes it difficult to breathe, no cure is available. The DNA sequence that could cure cystic fibrosis was discovered years ago, but a successful therapy has not yet been developed. The challenge lies in designing a therapeutic DNA carrier that can reach

cells affected by the disease. However, since cells in the airway are coated with a mucus barrier, delivery is very difficult. The Institute's goal is to create nanoparticle carriers with recognition and binding properties that can overcome the mucus barrier and attach therapeutic genes to lung cells.

Current therapies for cancer, including radiation and chemotherapy, are destructive to the body, often causing negative side effects and additional health problems. Techniques and methods for diagnosing and monitoring cancer often slow treatment time and reduce overall effectiveness. However, what if you could simultaneously detect malignant cells, image and treat them, and monitor efficacy of the treatment inside the body? Over the next 10 years, the Institute plans to develop nanoscale devices that detect cancer cells, report relevant diagnostic information, and deliver chemotherapeutic agents or therapeutic genes directly into the malignant cells. Targeting these devices to only interact with cancerous cells would spare healthy cells, greatly reducing or eliminating side effects that accompany many current cancer therapies. Also, simultaneous imaging and molecular profiling would allow non-invasive monitoring of tumors and treatment efficacy, resulting in better and faster patient care.

### *Institute for Basic Biomedical Sciences*

The Institute for Basic Biomedical Sciences (IBBS) was created to focus on a number of biological problems including epigenetics, sensory biology, metabolism and obesity, cell dynamics, drug addiction, chemoprotection, transport biology and high throughput approaches to biological research. The institute brings together experts from fields including biology, physics, chemistry, mathematics, computer science and engineering.

Research efforts include bringing together a broad range of scientific expertise in both experimental and theoretical biology to further study the advances already made in genomic studies. IBBS researchers will examine how cells and whole organisms are structured, how they function and how they control interactions of the multitude of chemical compounds they contain.

Meanwhile, other researchers will study how cells use sugars and fats to build molecules required for survival, how cells regulate the conversion of food into energy, and how the body regulates levels of hormones and other chemicals in response to available nutrients. Research will focus on metabolism at a cellular level looking at factors influencing cell survival, growth and aging. At the level of the whole organism, the IBBS will address how nutrients, hormone levels and energy usage affects reproduction, exercise capacity, cognitive function, feeding behaviors and longevity, which is important in understanding obesity and diabetes.

### *The Future of Surgery: I4M*

Today, surgery is based on technology and tools that have not truly changed in decades. Even with the development of minimally invasive surgery, skilled teams are asked to operate with limited knowledge, hampered sight, and outdated tools. However, computer-integrated systems and information-based technology can transform interventional medicine in the same way they have transformed manufacturing and other sectors of our society.

The Johns Hopkins University I4M (Integrating Imaging, Interventions, and Informatics in Medicine) initiative addresses the technological, clinical and educational challenges that need to be met in order to realize the full potential of this new age of healthcare. I4M enables physicians, engineers, and scientists from different departments and schools to work together, bringing the power of trans-disciplinary collaboration to solve problems that go beyond the scope of any single discipline.

### *Next Generation of Artificial Limb*

A multi-disciplinary team of scientists and engineers are undertaking an ambitious project to develop a next-generation of mechanical arm that will look, feel, perform and be controlled like a natural limb. The advanced prosthetic arm will allow a user to button a shirt, tune a radio, and feel the warmth of a loved one's hand.

Today, the current state-of-the-art myoelectric arm allows users to control hand and arm movements by deliberately flexing a muscle or through mechanical movement. Still, these devices have relatively limited degrees of motion and can generally allow control of only one motion at a time. In order to improve on current technology, the team plans to develop a device able to perform at strengths, speeds and angles with 22 degrees of freedom to match the performance of the human arm while maintaining the person's ability to control the arm. To succeed in this effort will require breakthrough research in neural control, sensory input, advanced mechanics and actuators, and prosthesis design and integration.

While Johns Hopkins University Applied Physics Laboratory will lead the effort, the team includes faculty from Johns Hopkins' Schools of Medicine, Engineering, and Public Health. Furthermore, staff from research institutions and businesses around the world including: Arizona State University, the BioSTAR Group, California Institute of Technology, National Rehabilitation Hospital, Northwestern University and the Northwestern University Prosthetics Research Laboratory, Oak Ridge National Laboratories, Otto Bock Health Care (Austria), Rehabilitation Institute of Chicago, Umea University (Sweden), University of Michigan, University of Rochester, University of California, Irvine, University of Southern California, University of Utah and Vanderbilt University will participate in the project.

### **Operations of the Common Fund**

As was noted earlier, while the Common Fund can help tear down barriers to advancing research and cures, its creation must not threaten the successes that the current model has produced. Instead, both traditional funding methods and the Common Fund must operate to support and enhance the best scientific research. As the committee moves forward with the creation of the Common Fund, I hope you will consider these important elements.

1. Awards from the Common Fund should include a mechanism to support young investigators. Most ideas that turn into Nobel Prizes come from investigators before they reach the age of 40. Support for their work must continue. While some young investigators will continue to seek support from traditional NIH funding streams, we also want to support these young investigators efforts on broad research projects.

On September 17, 2006, Carol Greider of the Johns Hopkins School of Medicine was awarded the most prestigious prize in American medicine - the Lasker Award. Dr. Greider, age 45, will share the award with two scientists who participated in the co-discovery. The award is based on findings of cell function and genetics, which occurred twenty years ago, and is considered today to be one the most advanced areas of biomedical research.

2. It is important that the Common Fund empower small groups as well as large interdisciplinary teams. Some big ideas and important research programs can come from smaller groups and these ideas need to be equally supported.
3. While some collaborations are more natural, the Common Fund needs to be used to encourage new, high risk ideas that bring together investigators from fields that have not previously collaborated. Encouraging these types of projects will promote new ideas and new groups of scientists and clinicians working together. These efforts can change science and medicine and currently cannot be funded through the regular channels.
4. Science and technology is changing much faster than ever before and funding mechanisms need to change as well. While the Common Fund is a step in the right direction, this effort along with traditional funding channels, need to be evaluated to ensure funding streams are as dynamic as the research. If the funding channels are not flexible, we could be limiting the research community's efforts to advance science.

Thank you for your efforts to strengthen America's biomedical research community. Johns Hopkins stands ready to support you in this important endeavor. I invite you and your staff to visit our campuses, explore our facilities and meet our researchers face to face. You will find no more persuasive argument for the inestimable value of investment in research than witnessing the innovative enterprise firsthand.