DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2015 Budget Request

Statement for the Record

Senate Subcommittee on Labor-HHS-Education Appropriations

Roderic I. Pettigrew, Ph.D., M.D., Director
National Institute of Biomedical Imaging and Bioengineering

Mr. Chairman and Members of the Committee:

I am pleased to present the President's budget request for the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH). The fiscal year (FY) 2015 NIBIB budget request of $328,532,000 is $2,173,000 more than the FY 2014 enacted level of $326,359,000. NIBIB is dedicated to improving human health through the integration of the physical and biological sciences. NIBIB's mission spans the entire health spectrum and is not limited to a single disease, group of illnesses, or population. Working with doctors from every field of medicine and bringing together teams of scientists and engineers from many different backgrounds, NIBIB aims to develop innovative approaches to health care. Our research focus is to improve the understanding, detection, treatment and ultimately, the prevention of disease.

INNOVATION IN TREATING SPINAL CORD INJURY: NEW HOPE FOR THOSE WITH PARALYSIS

Building on a long history of research on restoring function in spinal cord injury, researchers have discovered a fundamentally new intervention that led to voluntary movement in individuals with complete paralysis. This outcome, initially seen in a single individual, has now been reported in three successive patients, all of whom had been paralyzed for more than two years. This achievement is a significant milestone in spinal cord injury research. In the approach, electrical stimulation is applied to the surface of the spinal cord through a surgically implanted device that is normally used for the suppression of back pain. After just a week of stimulation, on average, the patients were able to voluntarily move their legs and flex their feet and toes when the stimulator was turned on. With continued daily stimulation and extensive physical training, the patients saw improvements in their movements and could initiate them with decreased stimulation. With their stimulators turned on, the patients are now able to stand for about an hour. Restored function was accompanied by increased muscle mass. In addition these individuals have regained bladder and bowel function and experienced improvements in autonomic responses such as sweating and return of sexual function in some cases.

IMMUNOENGINEERING TO MODIFY IMMUNE SYSTEM RESPONSES

The immune system is the body's defense against an array of infectious agents. However, the immune system can also trigger many diseases such as diabetes, rheumatoid arthritis, Lupus or multiple sclerosis; this occurs when immune cells are directed against an individual's own cells and is referred to as autoimmunity. As our understanding of the immune system increases, we are approaching a point where the immune response can be engineered to enhance or reduce specific responses. Two recent examples highlight this "immunoengineering" approach. In the first case the problem being addressed is improving targeted delivery of chemotherapeutic drugs to tumors. Nanoparticles can be used to ferry chemotherapy directly to tumors, minimizing exposure of these toxic medications to healthy tissues in the body. Researchers have found a way to ferry nanoparticles carrying chemotherapy drugs past cells of the immune system, which would normally engulf the particles, preventing them from reaching their target. The technique takes advantage of the fact that all cells in the human body display a protein on their membranes that functions as a specific 'passport' in instructing immune cells not to attack them. By attaching a small piece of this protein to nanoparticles, scientists were able to get immune cells in mice to recognize the particles as ‘self’ rather than foreign particles, and thereby not attack them. The nanoparticles also have other labels that can concentrate the drugs in the tumors, so higher doses of chemotherapy are delivered to the tumor.

In a second example, researchers have developed a strategy to modulate the immune system to halt the progress of a disease model of multiple sclerosis in mice. In multiple sclerosis, the immune system attacks the myelin sheaths that surround nerve cells. To stop this attack, engineered nanoparticles are coated with myelin antigens, and these nanoparticles are presented to another set of cells in the immune system that re-identifies myelin as ‘self’ rather than ‘foreign’. The result is that the immune system stops attacking myelin as a foreign body and the disease progression is halted. This approach begins to take advantage of the complex control of immune response which contains multiple positive and negative feedback loops in order to selectively turn off one specific inflammatory response. It holds promise for treating multiple sclerosis and other autoimmune diseases that previously have escaped effective therapies.

CANCER DETECTION FROM A ROUTINE BLOOD SAMPLE

Most cancers spread by way of the circulatory system. As a result, there are cancer cells present in blood samples. The number of cells, however, is so low that they have been difficult or impossible to find. The problem is to find and isolate the few cancer cells from the billions of other cells that are present in the blood. Researchers over the past several years have developed new techniques to find these cells, but those techniques have generally been destructive to the cancer cells. Now, with a new sorting technology, researchers have demonstrated the ability to sort the cancer cells and, of equal importance, to collect them for further analysis. After collection, the circulating tumor cells can be subjected to the full array of analysis techniques available to normal tissue biopsies of a tumor. This sorting technology also permits sorting, using a variety of markers that allow, for example, the identification of triple negative breast cancer cells. Successful isolation has been demonstrated in several other cancers including lung, prostate, pancreas, breast, and melanoma. This new tool has potential to improve both the early diagnosis and effective treatment of cancer.

AN IMPLANTABLE ARTIFICIAL KIDNEY HOLDS PROMISE FOR PATIENTS ON DIALYSIS

Expenditures in the United States for end stage renal disease exceed 40 billion dollars annually. Treatment of end stage renal disease includes renal transplant and thrice-weekly, in-center hemodialysis. Renal transplant is limited to a small fraction of potential recipients by a shortage of donor organs. As a result, over 400,000 Americans are on dialysis, which is expensive, inconvenient, and over time associated with significant morbidity and mortality. Researchers are developing an implantable bioartificial kidney called the Implantable Renal Assist Device (iRAD), in which a patient's blood will be filtered through an artificial kidney consisting of silicon nanopore membranes and a bioreactor of cells to mimic the functions of a healthy kidney. Such a device could offer numerous advantages for patients including: freedom of mobility, decreased infection risk due to a permanent vascular connection, and continuous treatment, which avoids the build-up of toxins that occurs between in-center hemodialysis visits. In addition, incorporation of the patients own cells could provide normal renal metabolic function that would be more physiologic than dialysis and not require anti-rejection drugs used for transplant. This combined filtration and metabolic treatment has been shown to work using a room-sized external model. Multi-day animal model testing to demonstrate hemofilter biocompatiblity has been conducted. Although human studies have not been initiated with the iRAD, these researchers are working with the Food and Drug Administration (FDA) on an initiative which facilitates new ways for FDA staff and innovators to jointly bring breakthrough medical device technologies to patients faster and more efficiently.

SMART HOMES FOR HEALTHY INDEPENDENT LIVING AT ALL AGES

The population is aging and increasingly medical treatment involves the management of chronic and/or degenerative diseases. Management of such conditions requires monitoring and early intervention to prevent more severe complications. The rapid development and ever expanding capabilities of smart phones, advanced sensors, point-of-care diagnostics, and integrated internet connectivity provides a framework on which new health care models can be developed to provide this monitoring and intervention. Investigators are testing real-time home observation of high-risk patients for early signs of illness using a built-in camera, computer tablet and a smart phone for simultaneous monitoring of daily activities by family members and health professionals. This includes analysis of daily habits, mobility patterns, and gait rate and rhythm as indicators of change in health status. Developing automated technologies to help identify early indicators of changes in health status will extend the amount of time individuals can live independently in their own homes.

Roderic I. Pettigrew, Ph.D., M.D.

Director, National Institute on Biomedical Imaging and Bioengineering

Roderic I. Pettigrew, Ph.D., M.D., is the first Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the NIH. In 2013, Dr. Pettigrew was also appointed to a new NIH position as the Acting Chief Officer for Scientific Workforce Diversity. This position was established by the NIH Director for the coordination and oversight of all NIH programs and activities designed to strengthen the biomedical research workforce through enhanced diversity.

Prior to his appointment at the NIH, Dr. Pettigrew was Professor of Radiology, Medicine (Cardiology) at Emory University and Bioengineering at the Georgia Institute of Technology and Director of the Emory Center for MR Research, Emory University School of Medicine, Atlanta, Georgia. He is known internationally for his pioneering work at Emory University involving four-dimensional imaging of the cardiovascular system using magnetic resonance (MRI). His current research focuses on integrated imaging and predictive biomechanical modeling of coronary atherosclerotic disease.

Early on at the NIBIB he jointly led a national effort with Howard Hughes Medical Institute to create new interdisciplinary graduate training programs, and also established the Quantum Projects program to achieve “medical moon shots” by pursuing high-risk, high-impact projects designed to solve major healthcare problems. Under Dr. Pettigrew’s leadership, national collaborative and international initiatives have been issued to develop low cost and point-of-care medical technologies and at present, he leads an effort to reduce CT radiation dose to background levels. He has recently called for a US-India collaboration to develop unobtrusive technologies for frequent recording of blood pressure to address the world wide problem of hypertension.

Dr. Pettigrew has been elected to membership in two components of the US National Academies: the Institute of Medicine, and the National Academy of Engineering. His awards include Phi Beta Kappa, the Bennie Award, Most Distinguished Alumnus of the

University of Miami (1990), Herbert Nickens Award of the ABC, Pritzker Distinguished Achievement Award of the Biomedical Engineering Society, Distinguished Service Award of the National Medical Association, and the Pierre Galletti Award of American Institute of Medical and Biological Engineering.