American Recovery and Reinvestment Act: A Stimulus for Research

by Debbie Goldberg
In February 2009, President Obama signed into law the American Recovery and Reinvestment Act of 2009 (ARRA), a massive economic stimulus bill designed to pump $787 billion into an ailing economy, calling it “the most sweeping economic recovery package in our history.” It is having a sweeping impact within the realm of research as well.

Scientific research overall got a $21.5 billion boost from the landmark legislation — the largest increase ever in federally funded research, underscoring the essential role of basic research to both the country’s immediate recovery and long-term economic growth.

To date within Penn Dental Medicine, researchers have received more than $3.2 million under ARRA to fund a wide range of studies and equipment needs. As of late March of this year, seven ARRA-funded research projects were underway in Penn Dental Medicine, with several more applications pending, says Dr. Bruce Shenker, Associate Dean for Research and Chair and Professor of Pathology. Under the ARRA guidelines, grants are awarded in 2009 and 2010, and researchers have two years in which to carry out their studies.

“This has significantly added to the overall research potential of the School of Dental Medicine to advance oral health and basic research,” Dr. Shenker says.

Its impact is being felt throughout the Penn research community. Impressively, since the law was enacted last February, the University of Pennsylvania has received more than $171 million in awards that are funding more than 348 studies in such diverse areas as gene therapy, robotics, public education, neurological disorders, and cardiovascular disease.

“The American Recovery and Reinvestment Act is making a difference for Penn’s world-class researchers, students embarking upon research careers, support staff, and the community at large by funding important scientific studies that will lead to the improved health and well being of millions and will spur economic growth in the long term,” notes Steven J. Fluharty, Penn’s Vice Provost for Research.

For example, ARRA-funded research being carried out by Dr. Shenker is studying the role of toxins produced by oral bacteria, which target the signaling pathways in a number of cancers. Potentially, these toxins could be used to modulate the pathways that control cancer cell growth and survival.

Thus, while jumpstarting the economic recovery is an important short-term investment, Dr. Shenker agrees that the impact of the infusion of new research money will be long lasting, for Penn Dental Medicine and beyond.

“I anticipate there will be significant advances in health on a national and global level from ARRA funding,” he says. “I think when we look back a few years from now, there will be a noticeable bump in effective funding of biomedical research, which will ultimately translate into improved treatment and new modalities for treating a number of disorders.”

**Penn Dental Medicine ARRA Grants**

**Investigator:** Dr. Kelly Jordan-Sciutto, Associate Professor of Pathology. $1,019,000

Three decades ago, when the AIDS crisis first came to light, being diagnosed with this mysterious disease was akin to getting a death sentence. Today, HIV-positive patients are successfully treated with combination antiretroviral therapy (cART), a drug regimen that has greatly reduced the mortality rate associated with HIV infection.

But taking this AIDS “cocktail” over an extended period of time also poses some health risks, ranging from heart disease to cognitive decline. By testing the three different classes of drugs that make up the AIDS treatment regimen on central nervous system cells, Dr. Kelly Jordan-Sciutto, Associate Professor in Penn Dental Medicine’s Department of Pathology, is trying to determine the cause of the cognitive impairment often seen in HIV-positive patients who have been taking cART.
Prior to the current HIV-drug regimen, cognitive impairment occurred in up to 60 percent of AIDS patients, and HIV-associated dementia was considered a defining illness of the disease. While only three percent of patients now exhibit that form of dementia due to the success of the cART regimen, studies show as many as 60 percent of those being treated experience more minor forms of impairment. This study will consider whether these cognitive deficits are due primarily to the drug therapies or if HIV is still the major contributor.

**Investigator:** Dr. Sherrill Adams, Professor of Biochemistry, $711,000

The major goal of this research project is to understand how the formation of endochondral bone is controlled. Endochondral bones, which include most bones in the human skeleton, form in the embryo as cartilage, which is ultimately replaced by bone. Not surprisingly, normal bone formation is essential for tooth formation.

The formation of endochondral bone is regulated by many important hormones and growth factors, including thyroid hormone, vitamin A and bone morphogenetic proteins (BMPs), which are growth factors often used in conjunction with dental implants to improve bone formation. Currently, relatively little is known about how any of these individual factors regulate bone formation.

The major goal of this ARRA-funded project, which expands on Dr. Adams’ existing research, is to understand at a molecular level how these agents work together to form normal bone. The studies also will help researchers understand what goes wrong when there is too little or too much of any one of these factors: Why does thyroid hormone deficiency lead to short stature? Why does an excess of signaling from BMPs lead to excess bone?

Ultimately, this study will help identify potential therapeutic targets for growth disorders, and may also provide insights into the cause and treatment of osteoarthritis, Dr. Adams says. And, she notes, “Anything that impacts bone development is dentally relevant.”

**Investigator:** Dr. Kathleen Boesze-Battaglia, Associate Professor of Biochemistry, $500,000

The newest ARRA grant to be approved, these funds will pay for a new core live cell confocal imaging system, which will enable a range of researchers working on a variety of studies to image live cells in real time. This state-of-the-art microscope, the only one of its kind in the School of Dental Medicine, is vital to a wide range of studies to explain the pathogenic mechanisms in periodontal diseases, herpetic infection, oral cancer, degenerative disease and disorders associated with the metabolism of oral tissues. “This technology will have a huge impact on research at the School of Dental Medicine,” Dr. Boesze-Battaglia says.

**Investigator:** Dr. Elisabeth Barton, Assistant Professor of Anatomy & Cell Biology, $474,000

This program project grant with the University of Florida is designed to develop novel therapeutic strategies to prevent muscle atrophy and accelerate muscle rehabilitation in patients who have suffered spinal cord and other orthopedic injuries.

Loss of muscle mass, or atrophy, is common among patients with orthopedic injuries who endure extended periods of bed rest or cast immobilization, significantly impacting the rehabilitation of these patients. The results of such atrophy can be significant, ranging from declines in motor control and overall fitness, to development of functional limitations and, possibly, long-term disability.

This study will evaluate the therapeutic potential of the insulin-like growth factor I isoforms, one of the critical factors for coordinating muscle growth, enhancing muscle repair and increasing muscle mass and strength, as well as E-peptides, which also may have a positive affect on muscle mass, repair and strength. The goal, Dr. Barton says, is to develop new pharmacological agents to help promote better muscle recovery for patients with injuries that have led to muscle atrophy.
Investigator: Dr. Carolyn Gibson, Professor of Anatomy & Cell Biology, $217,883

Patients with defective enamel often endure prolonged clinical treatments, pain and social anxiety because of the appearance of their teeth. This research project is designed to better understand dental structure and function, with the goal of planning better treatments for patients with enamel defects due to inherited amelogenesis imperfecta.

For this study, mice have been genetically developed to have enamel defects similar to those in humans who have inherited diseases that affect tooth enamel. The ARRA funds were used to purchase an imaging station, which allows researchers to analyze sections of the mice teeth, and a microshear tester, which helps the research team evaluate tooth restorations for the mice with enamel defects.

“We hope to use what we learn in the clinic to better design restorations for children with conditions such as amelogenesis imperfecta,” Dr. Gibson says.

Investigator: Dr. Bruce Shenker, Associate Dean for Research, Chair and Professor of Pathology, $318,666

Dr. Shenker received a supplemental grant to continue his research on the role and properties of bacterial toxins, such as those produced by periodontal pathogens. His research has shown that toxins produced by some oral bacteria have the ability to target and inhibit the signaling pathways that regulate the immune response. These same pathways are often perturbed in a number of cancers including leukemia and lymphoma.

“The main focus of our research is on the molecular mechanism of action of these toxins, which inhibit or impair the immune system,” says Dr. Shenker. “The ARRA grant provides funds to support the first steps in harnessing the therapeutic potential of these toxins; we hope that these studies will lead to a new approach for targeted chemotherapy for cancer patients.”

Investigator: Dr. Pamela Howard, Research Associate Professor of Anatomy and Cell Biology, $104,159

This grant will accelerate an existing study that could lead to new treatments for patients suffering from bladder obstructions. The grant funds a research associate to perform delicate microsurgery to partially obstruct the bladders of male mice, which mimics the gradual bladder obstruction that can occur in men with benign prostatic hyperplasia (BPH). With this condition, the bladder gradually gets larger, and may become stiffer and fibrotic, due to the increased synthesis and deposition of structural proteins called collagens.

The researchers are testing to see if treating the mice both before and after the surgeries with cholesterol-lowering drugs called statins will result in reduced fibrosis in the bladder and lead to more normal bladder function.

Dr. Howard says the research “may result in a new therapeutic modality with minimal side effects for patients suffering from obstructive uropathies, including children with spina bifida, interstitial cystitis patients and men with BPH.”

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