Infusion of Recovery Act Funds Boosts Biomedical Research

Leveraged funds maximize the impact of biomedical and translational research at institutions across the country. **BY LAURA BONETTA**

The American Recovery and Reinvestment Act (ARRA), signed into law February 17, 2009, to help promote economic recovery, made $10.4 billion available to NIH through September 2010 to expand support for some of the most promising research ideas. From this pool of funds, NCRR received $1 billion to construct and improve laboratory facilities, $300 million to purchase shared scientific instrumentation, and an additional two-year allocation of $310 million to help advance science discovery. With this funding, NCRR thus far has made more than 1,100 awards across the country and in Puerto Rico.

The impact of these awards has been far reaching. When combined with other federal grants, as well as contributions from universities and private foundations, ARRA funds are making ambitious projects finally possible.

Investments in infrastructure, whether targeted for technology, instrumentation or common areas of research, are moving many NCRR-supported ARRA projects forward. High-speed fiber optic networks connecting research institutions across five northeastern states enable researchers to collaborate on large-scale genomic projects. The latest high-powered imaging equipment at the University of Minnesota and the University of Colorado Denver is pushing the limits of what is visible inside the human body and in living cells. A new building at the University of Florida housing basic researchers, clinician scientists, and community and health care workers provides a model for a multidisciplinary, holistic approach to research on aging.

Although these efforts are just getting off the ground, their potential impact on research and health already is evident.

CONNECTING IN CYBERSPACE

In May, students and faculty from five research institutions gathered at the University of Delaware to analyze genomic sequences from the little skate *(Leucoraja erinacea)* — one of 11 nonmammalian organisms selected by an NIH National Human Genome Research Institute panel to have "the greatest potential to fill crucial gaps in human biomedical knowledge."

The five institutions — Mount Desert Island Biological Laboratory, the University of Delaware, Dartmouth College, the University of Rhode Island and the University of Vermont — plan to obtain and interpret the complete skate genome sequence, generating an enormous amount of data, within the next two years.

Such an ambitious genomics project, which requires powerful computers and superfast bandwidth to generate, store and share the data, would not have been possible until recently, when the institutions involved began putting in place the necessary Internet infrastructure to collaborate effectively. "Datasets have grown enormously in recent years. You can generate a terabyte of data just overnight," said Karl Steiner, senior associate provost

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> **— KARL STEINER, SENIOR ASSOCIATE PROVOST FOR RESEARCH DEVELOPMENT, UNIVERSITY OF DELAWARE**

for research development at the University of Delaware. "But to take part in state-of-the-art research, you need to not only generate the data, but also move it from your lab to the labs of collaborators. If it takes you half a day to move the data, you are not going to be able to compete in today's research environment."

Each research institution taking part in the skate genome project resides in a state in which the aggregate success rate for NIH research applications has historically been low. NCRR's Institutional Development Award (IDeA) program is designed to promote health-related research and enhance the competitiveness of investigators at these institutions.

"Our five institutions are part of the northeast IDeA regional network," said Judy Van Houten, professor of biology at the University of Vermont and principal investigator (PI) for the Vermont IDeA Network of Biomedical Research Excellence (INBRE) project. "We are very interactive, and all the PIs know each other." Through NCRR's INBRE program, PIs work to develop, share and coordinate research resources and expertise that will expand the research opportunities and increase the number of competitive investigators in IDeA-eligible states.

As a result of these interactions, three years ago, at a northeast IDeA regional meeting, the PIs organized a workshop to discuss the cyberinfrastructure needs in each state. "What we realized was that the cyberinfrastructure was so poor in our states," said Van Houten. "There were what we called black holes of connectivity."

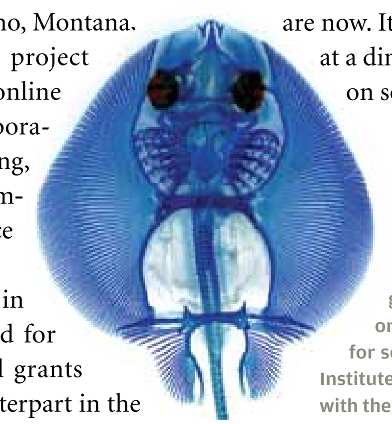
The researchers planned to fill these holes. "We were positioning ourselves for whatever funding came along," recalled Van Houten. In particular, they were hoping they could build on the success of NCRR's Lariat Project, which established ultra-high-speed links among universities in seven IDeA states in the western United States — Alaska, Hawaii, Idaho, Montana, Nevada, New Mexico and Wyoming. The project served as the first phase of IDeANet — an online network designed to promote research collaboration, provide bioinformatics tools and training, and broaden access to high-performance computational resources for data-intensive science applications in participating states.

When ARRA funding became available in 2009, the five northeast institutions applied for independent yet coordinated supplemental grants from NCRR to start to develop a Lariat counterpart in the East: the North East Cyberinfrastructure Consortium. At the same time, they applied for funding from the National Science Foundation (NSF) through its Experimental Program to Stimulate Competitive Research (EPSCoR) for research infrastructure improvements, which also received additional funding through ARRA. "All these pieces fell together at the same time," explained Steiner, who is the PI for Delaware's INBRE program.

The NCRR and NSF grants provided funds to purchase very-high bandwidth connectivity (10 Gb/s) across the northeast region, specifically connecting the research institutions. Some of the states also received grants from the U.S. Department of Commerce's National Telecommunications and Information Administration's Broadband Technology Opportunities Program, also funded through ARRA, to expand the core network and provide Internet service to other universities, colleges and libraries in each state. Local companies also are trying to take advantage of this increased connectivity for their businesses.

In addition to providing the needed cyberinfrastructure for research, the NCRR and NSF grants are funding portions of the research itself. NCRR funds are supporting the sequencing of the skate genome, whereas the NSF-funded project focuses on the sequencing of the genomes of rapidly growing populations of algae in five lakes in New England, which present serious problems to ecosystems and human society. The projects will use similar genomic sequencing technologies and analyses.

NIH and NSF grants also are funding education outreach. The May workshop in Delaware was the first in a series of weeklong workshops that provided lectures and tutorials in bioinformatics and genomics techniques, as well as hands-on exercises to analyze and interpret DNA sequence data. "If the ARRA funds had not been available, we may not be where we are now. It's really very rewarding to see that what started at a dinner meeting is now having a significant impact on so many people," said Steiner.



■ The North East Cyberinfrastructure Consortium, established in part with NCRR ARRA funding, is determining the genome sequence of the little skate *(Leucoraja erinacea)* — one of 11 nonmammalian organisms strategically selected for sequencing by an NIH National Human Genome Research Institute advisory panel because the skate shares characteristics with the human immune, circulatory and nervous systems.

PHOTO BY RANDALL D. DAHN, MOUNT DESERT ISLAND BIOLOGICAL LABORATORY, MAINE

THE LATEST TECHNOLOGY

The previous project used ARRA funds to make "big science" possible. Similarly, ARRA-funded instrumentation grants from NCRR are enabling NIH-funded researchers across the country to leverage resources to purchase the latest in state-of-the-art research equipment. At the University of Minnesota, a powerful magnetic resonance imaging (MRI) system for clinical research will enable a group of researchers to see detailed structures inside the human body. And at the University of Colorado Denver, investigators are purchasing the first Stimulated Emission Depletion, or STED, microscope to be used in North America. This instrument has the ability to see beyond the capability of most current light microscopes. Cutting-edge equipment like this has the potential to revolutionize biomedical research by offering unprecedented image details not previously possible.

But technology can be expensive. NCRR's Shared Instrumentation Grant (SIG) and High-End Instrumentation (HEI) grant programs allow groups of NIH-supported researchers to buy expensive, leading-edge equipment. With a $7.8 million HEI grant, Kamil Ugurbil, professor of radiology, neurosciences and medicine and director of the Center for Magnetic Resonance Research at the University of Minnesota, will be able to acquire a 10.5 tesla MRI whole-body system. This instrument will be the most powerful of its kind in the world for whole-body imaging, providing scientists highly detailed pictures of the human brain, torso and extremities for improved disease detection and treatment monitoring.

HEI grant awards, like this, typically permit the purchase of a single major piece of research equipment that costs between $750,000 and $2 million. With ARRA, the grant ceiling was raised to $8 million. The university then provided additional funds toward the purchase of the complete system. "Our university always invested heavily in this technology," said Ugurbil.

MRI is a commonly used diagnostic tool in hospitals. Patients are placed in an MRI scanner and exposed to a strong magnetic field and a beam of radio waves — a process that produces detailed images of structures inside the body. The strength of the magnetic field, measured in units called teslas, determines the amount of detail in and the type of information that can be extracted from those images.

Most hospitals use the standard 1.5 tesla scanners, with some using the higher field 3 tesla. But in clinical and biomedical research, the technology has been pushed to higher field strengths, and the 7 tesla has slowly evolved to become the new standard. Such advances have been made possible partly through the work of researchers at the Center for Magnetic Resonance Research at the University of Minnesota, which is funded in part by NCRR's Biomedical Technology Research Centers program. With this program's support, the first 7 tesla system was developed and harnessed for biomedical imaging in the human body.

The 10.5 tesla MRI will have much higher resolution than its predecessor and will enable researchers to extract new biomedical information that is not available at lower magnetic field strengths. "We expect certain processes in the body will be detected with more accuracy," Ugurbil said. "In the brain, we should be able to detect functioning areas more easily." The improved resolution eventually might allow earlier diagnosis of certain conditions affecting the brain and other organs.

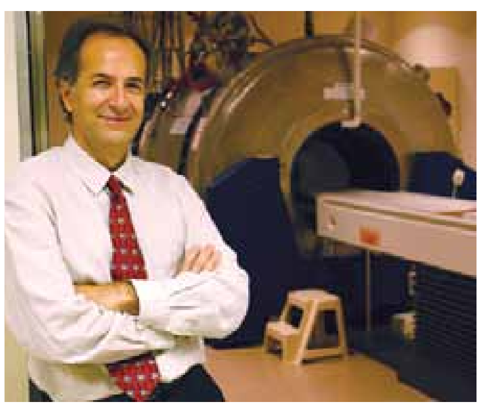
The new instrument could play an important role in supporting the work of the Human Connectome Project — a $30 million effort funded under NIH's Blueprint for Neuroscience Research. The project's aim is to map the brain's networks of neurons using MRI technology in 1,200 healthy adults to better understand how brain circuitry relates to function. The University of Minnesota was one of two institutions awarded grants for the project.

In Colorado, a new instrument at the Light Microscopy Facility at the University of Colorado Denver was enabled by a $450,000 NCRR SIG. It will allow the purchase of an innovative STED microscope, which will open new windows into ultra-structural biology, allowing investigators to view cellular events at super resolution. SIG funding enables groups of NIH-supported investigators to obtain high-powered equipment that costs between $100,000 and $600,000.

"We already have a group of users with new projects ready to start working with STED," said Diego Restrepo, professor of cell and developmental biology at the University of Colorado's School of Medicine. The STED will enable researchers to see structures inside living human cells that are too small to see with currently available light microscopes.

Traditional light microscopes cannot easily distinguish objects smaller than about 200 nm. But the STED microscope, developed by Stefan Hell and colleagues at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, overcomes this size barrier, improving image resolution by about 10-fold. Now that the instrument is available commercially, "it's like we had a window that was closed that now has been opened," said Restrepo. Having worked in Hell's laboratory in Germany when the STED was first developed in 2006, Restrepo now serves as the PI on this ARRA grant.

Now, the Colorado research group will use the STED to study vesicles — the membrane-bound, bubble-like organelles that mediate communication



■ Kamil Ugurbil, director of the Center for Magnetic Resonance Research at the University of Minnesota, stands in front of a magnetic resonance imaging (MRI) system that his group developed in 1990. Now, his group will use a $7.8 million NCRR High-End Instrumentation grant to purchase a 10.5 tesla whole-body MRI system — the most powerful of its kind.

PHOTO COURTESY OF THE UNIVERSITY OF MINNESOTA at the interface of two neurons or synapses. "Vesicles are about 40 nm in size, so they are beyond the resolution of current microscopes," explained Restrepo. "But now we can observe them in living cells to better understand signaling at the synapse." Other projects will focus on how kidney cells work or how odorant receptors on cells receive their stimuli.

BUILDING FOR THE FUTURE

Technological advances like the STED microscope will enable NIH-funded scientists to break new ground. But sometimes moving a research field forward requires a different kind of push — such as the construction of a new, state-of-the-art building.

The University of Florida received close to $15 million in funding from NCRR's ARRA Construction Awards program to build a home for the university's Institute on Aging. "We established the Institute on Aging about six years ago as a multidisciplinary group of researchers with a common research theme," said Marco Pahor, the Institute's director. "We have been extremely successful as a group in collaborating and obtaining grants, but we were facing a major problem being scattered all across the campus. My dream was to get one building to house everyone."

The dream was made possible through ARRA funding, which will facilitate the construction of a 40,000-square-foot complex. The University of Florida committed to provide additional funds to triple the size of the building, which will house not only the Institute on Aging but also the University of Florida Clinical and Translational Science Institute, which is funded through NCRR's Clinical and Translational Science Awards (CTSA) program. CTSAs create academic homes for clinical and translational science at research institutions across the country and strive to transform lab discoveries into improvements for human health. "The university saw an opportunity to use NIH funding to have a broader impact," explained Pahor.

The timing could not have been better. The construction grant for the new Institute on Aging Clinical Translational Research Building was awarded on the heels of recent $64 million and $9.3 million grants, respectively, from the National Institute on Aging and the National Heart, Lung and Blood Institute. "We had the funding to hire new staff and to start the programs, but no space," shared Pahor. "With the new building, we have solved the problem."

Built with the highest standards of sustainable construction, including solar panels, recycled building materials and systems to collect rain water, the building will consist of two wings. The NCRR-funded wing will house the Institute on Aging, focused on developing new research approaches that aim to improve the health, independence and quality of life for older Americans. The second wing will contain clinical and translational researchers, including those affiliated with the CTSA; the Departments of Biostatistics and Epidemiology; as well as research groups working on type 2 diabetes and muscular dystrophy. "We will

■ A new research building at the University of Florida, reflected in this rendition, will house the university's Institute on Aging, focused on developing new research approaches to improve the health, independence and quality of life of older Americans, as well as the University of Florida Clinical and Translational Science Institute, a member of NCRR's Clinical and Translational Science Awards program.

share several service facilities and instruments, which will be more cost-effective," said Pahor.

A lobby with common areas will connect the two wings. "The most productive approach to generating new ideas is through informal interactions among different people," shared Pahor. "The building can foster those interactions. It has many open, common spaces."

One of the building's unique features is that it will incorporate facilities for clinical research recruitment and assessment, training, conferences, and lifestyle interventions, as well as laboratories, a demonstration kitchen and a behavioral counseling suite. "It will blend basic and clinical research with health and prevention. Often these disciplines don't talk to each other," explained Pahor.

NCRR program officer Diane Lucas, who oversees the University of Florida construction grant, agrees. "This new research building could serve as a national model for other institutions," she said, adding that there are few facilities nationwide that offer this comprehensive approach to health and research. As people continue to grow older and live longer — many with reduced mobility — research on aging is likely to affect the lives of all Americans. In a state with more seniors than any other, that impact is clear. More than 3.2 million people, or about 22 percent of Floridians, reported having a disability in the 2000 U.S. Census, and this number is predicted to rise.

ARRA provided an influx of funds for two years. Although this funding already is having an impact, its full effects on biomedical research and human health will be seen for years to come. For now, institutions nationwide have been able to combine and maximize ARRA funds with other financial support to accomplish projects that were not possible before. In the next decade, these projects will advance a broad range of fields, from genomic science to whole-body imaging to human aging. ■

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