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Embargoed until 11 a.m. (EDT):
April 24, 2006

**NIH Awards $13.3 Million to Carnegie Mellon, University of Pittsburgh For National Technology Center for Networks and Pathways**

PITTSBURGH—A team of researchers from Carnegie Mellon University and the University of Pittsburgh has received a five-year, $13.3 million grant from the National Institutes of Health (NIH) to establish a National Technology Center for Networks and Pathways.

The center, headquartered at Carnegie Mellon, will focus on developing fluorescent probe and imaging technologies to investigate regulatory pathways and networks in real-time in living cells. This work will generate powerful molecular biosensors for preclinical research to map the many cell-signaling networks involved in disease. Ultimately, such biosensors will be used in hospital- and office-based diagnostic medicine.

"This award recognizes our visionary science and the collaborative strength of both universities in advancing this exciting new field," said Mark Kamlet, senior vice president and provost of Carnegie Mellon. "This major grant will give us even greater capabilities to produce innovative biotechnologies that impact tomorrow's medicine."

"The further development of discrete intracellular fluorescent probes is the critical next step in exploiting the results of the Human Genome and Human Proteome projects," said physician and scientist Arthur S. Levine, senior vice chancellor and dean of the School of Medicine at the University of Pittsburgh. "The combined research resources and research faculty of the two universities promise to move the whole of medical science and medicine forward with an exceptionally exciting and new momentum."

Within any given human cell, hundreds, if not thousands, of proteins may interact in precise cascades when the cell is called upon to yield a necessary product, such as a hormone, or to respond to an environmental stress, according to center faculty. Understanding the elements and dynamics of these cascades in a given cell and in real-time is the key to diagnosing why cells don't function properly and what might be done about that dysfunction therapeutically.

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"This award shines a bright spotlight on the talent we have in our region and the amazing work we are doing right here in the Pittsburgh area. The establishment of the National Technology Center for Networks and Pathways at Carnegie Mellon and the University of Pittsburgh further cements their place as world leaders in research," said Congresswoman Melissa Hart. "The work that will be conducted here will go a long way in improving the health of not only Pennsylvanians, but people around the world."

"The tools created through this center will give us a completely new way of looking at complex biological processes, allowing us to watch these activities in unprecedented ways," said Norka Ruiz Bravo, deputy director for Extramural Research at NIH. "The new technologies developed in Pittsburgh ultimately will enable researchers worldwide to unlock fundamental aspects of costly diseases such as cancer, dementia and stroke."

"We are poised to build on an exciting, productive foundation of tools developed at Carnegie Mellon," said Alan Waggoner, principal investigator of the grant and director of the new center. Waggoner directs Carnegie Mellon's Molecular Biosensor and Imaging Center (MBIC), which for more than 20 years has designed fluorescent probes used worldwide for research, ranging from the study of nerve activity to understanding gene activation as part of the Human Genome Project. "This latest grant from NIH puts us on the map and recognizes our vital collaboration with the University of Pittsburgh and other renowned academic partners to design, image and test a new generation of probes in living systems," he said.

The grant is one of three awarded as part of the NIH initiative, "Building Blocks, Biological Pathways and Networks Roadmap for Medical Research" (http://nihroadmap.nih.gov/buildingblocks/fundedresearch.asp). This initiative aims to support research that develops innovative tools that determine in real-time the amounts, locations and interactions of large numbers of individual proteins within a single cell. Such research stands to produce the next generation of research tools required to fully understand cell networks and how they function in health and disease. The NIH Roadmap is a series of far-reaching initiatives designed to transform the nation's medical research capabilities and speed the movement of research discoveries from the bench to the bedside.

"Today's exciting announcement further exemplifies the need for Pennsylvania to aggressively compete for increased federal funding for our research institutions of higher education," said Department of Community and Economic Development Secretary Dennis Yablonsky. "Governor Rendell's proposed $500 million Jonas Salk Legacy Fund will provide us with the resources we need to accelerate medical research and cure disease. Pennsylvania's residents, and others around the world, will benefit with better health and improved quality of life."

"A cell's regulatory pathways are very complicated, and we need to learn so much more. But to date there are almost no tools available to sort out all of these different interactions and activities that are going on in cells," said Waggoner. "We're developing a powerful toolbox of intracellular fluorescent biosensors that cells themselves will produce. With these tools, we can study in detail how all the proteins are interacting with each other in real-time in the 3-D space of a living cell."

Effectively using these intracellular fluorescent probes and biosensors will require an array of current and new detector technologies, according to Simon Watkins, co-director of the Center for Networks and Pathways. Much of the imaging work will be carried out at the University of Pittsburgh's Center for Biologic Imaging (CBI),

widely recognized as one of the premier imaging centers in the country. The CBI focuses on the application of fluorescent microscopy techniques and their translation to the study of living cells and organisms.

"As part of this major grant, the CBI will integrate the probes with cells, chemical reagents and detectors to create new methods that image the probes in live cells," said Watkins, director of the CBI and professor of cell biology and physiology at the University of Pittsburgh.

Fluorescent probes under design at Carnegie Mellon include integrated molecular biosensors, which are being developed through a series of unique, high-throughput technologies pioneered by Carnegie Mellon scientists.

The probes are "integrated" because they combine fluorescent dyes with a protein complex. In some cases, the resulting probe emits a detectable signal because it binds precisely to a specific molecular target, thereby indicating the presence of that target. This type of biosensor would be important for detecting whether a specific protein is made within a cell at a given time and where it travels.

In other cases, these probes emit a detectable signal when a target protein has chemically reacted with, or catalyzed, a change in the probe's protein complex. In this scenario, scientists can actually see exactly when and where specific chemical reactions take place within cells — reactions that could be the foundation of cancerous cell growth or other disorders.

"The new center will truly revolutionize how we witness certain catalytic activities inside living cells," Waggoner stated. "Until now, no one has created fluorescent probes to visualize kinase and phosphatase reactions. But there are many hundreds of these reactions within cells, and they are critical to driving pathways involved in disorders like cancer, diabetes, stroke and infection."

Integrated molecular biosensors could be sprayed onto implantable microchips to provide remarkably sensitive, accurate patient monitoring in hospital settings such as intensive care units. Molecular biosensors could also be used in office-based diagnostic medicine, in which a biosensor could be added to a blood sample to instantly detect the presence of an infectious agent or tumor protein that would indicate the spread of disease.

These imaging technologies will be integrated with new data analysis tools, according to Waggoner. "The center also will provide unprecedented, unique interdisciplinary training in this emerging field, as well as deliverables such as reagents and methodologies which can be used worldwide," he said.

Key to the new center's activities is testing newly generated probes in four separate driving biology projects with scientists from the University of Pittsburgh, Carnegie Mellon, Stanford University and the University of California at Berkeley. These projects will provide real-time feedback to the probe-development team on the probes' performance.

The new Networks and Pathways Center is built upon critical research findings made possible with support by the PA CURE Program and the Keck Foundation.

The Carnegie Mellon team has world-renowned expertise in biochemistry, genetics, dye chemistry and imaging. Their current work stems from a 35-year history of developing thousands of powerful fluorescent probes that have been widely commercialized and that have made a profound impact on biomedical research.

**About Carnegie Mellon:** Carnegie Mellon is a private research university with a distinctive mix of programs in computer science, robotics, engineering, the sciences, business, public policy, fine arts and the humanities. More than 10,000 undergraduate and graduate students receive an education characterized by its focus on creating and implementing solutions to real problems, interdisciplinary collaboration and innovation. A small student-to-faculty ratio provides an opportunity for close interaction between students and professors. While technology is pervasive on its 140-acre campus, Carnegie Mellon is also distinctive among leading research universities because of conservatory-like programs in its College of Fine Arts. For more information, visit www.cmu.edu.

**About the University of Pittsburgh School of Medicine:** The University of Pittsburgh School of Medicine is considered among the nation's leading medical schools, renowned for its curriculum that emphasizes both the science and humanity of medicine, and its remarkable growth in National Institutes of Health (NIH) grant support, which has more than doubled since 1998. For fiscal year 2005, it ranked eighth among schools of medicine and, together with the university and hospital affiliates, ranked seventh among educational institutions, according to preliminary data. As one of the university's six schools of the Health Sciences, the School of Medicine is the academic partner to the University of Pittsburgh Medical Center. Their combined mission is to train tomorrow's healthcare specialists and biomedical scientists, engage in groundbreaking research that will advance understanding of the causes and treatments of disease, and participate in the delivery of outstanding patient care.