Joint research projects aim to lay foundation for new medical treatments, diagnostics

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ARGONNE, Ill. (Feb. 27, 2007) — Better treatment for infections, breast and prostate cancer, and certain brain injuries, as well as improved detection developing tumors, are the focus of new joint research by the U.S. Department of Energy's Argonne National Laboratory and the University of Chicago.

The projects are funded through the Seed Fund Program of the Research Advisory Committee of the university's Division of Biological Sciences.

Revolutionary changes in approaches and technologies are highlighting the need for multidisciplinary efforts in biomedical science. Consequently, funding agencies are focusing a greater proportion of their research investments on team science that employs novel tactics, technologies and collaborations. In light of these changes, the Research Advisory Committee's goal is to increase the university's competitiveness for these types of interdisciplinary funding opportunities.

One way the committee is doing this is through the seed fund program, which provides pilot funding to interdisciplinary teams of researchers from the university's division of Biological Sciences and Physical Sciences and Argonne. Projects funded through this program are expected to form the basis of subsequent proposals submitted to external funding agencies.

New projects funded by the Seed Fund Program are:

Development of bio-conjugated nanoparticle reagents for breast/prostate cancer imaging and therapy: Researchers will develop metal and metal-oxide nanoparticles conjugated to estradiol or to a suitable androgen, which will specifically target membrane estrogen and androgen receptors.

Using a metal or metal-oxide particle core, conjugated nanoparticles that bind to cell surface receptors offer the possibility of elucidating and exploiting nongenomic actions of estrogens and androgens in cancer cells. By tuning the particle size while maintaining the surface chemistry, it may also be possible to achieve specific binding of metal particles and clusters to either the cell surface or the cell nucleus, which offers the opportunity to selectively control the nongenomic, as well as genomic, actions of steroid-conjugated particles. Specific targeting of these bio-conjugated nanoparticle reagents will open new possibilities for imaging as well as therapies based on radiation enhancement effects of nanoparticles.

Principal investigators on this project are Geoffrey Greene of the University of Chicago and Xiao-Min Lin of Argonne.

MgrA, a new target for the treatment of Staphylococcus aureus infection: Staphylococcus aureus, a gram-positive bacterium, is the leading cause of a variety of human infections ranging from minor skin infection to life-threatening endocarditis, pneumonia and septicemia. Researchers have identified the protein MgrA as a key global regulator in S. aureus. This protein controls expression of a wide variety of virulence factors, autolysis and other global regulatory genes. In addition, MgrA also regulates resistance to quinolone type antibiotics and glycopeptide resistance.

A preliminary study of MgrA resulted in a recent major breakthrough. Researchers have solved a high resolution structure of MgrA and revealed a unique oxidation regulation mechanism of this protein. A small molecular inhibitor of MgrA was also discovered. The next step is to elucidate structure, function and mechanism of MgrA, and to develop small molecule inhibitors and activators for MgrA.

Principal investigators are the University of Chicago's Chuan He, Olaf Schneewind, Phoebe A. Rice, Peng Chen and Zigang Li.

Imaging polymer-mediated repair of the neuronal plasma membrane at the nanoscale level: Acute hypoxic-ischemic brain injury is an important cause of long-term neurologic morbidity in babies, children and adults without treatment. Poloxamer 188 (P188), a tri-block copolymer surfactant of polyethylene-polypropylene-polyethylene, has been shown to rescue cultured hippocampal neurons from multiple in vitro models of hypoxia-ischemia. Exciting preliminary data indicate marked neuroprotection by P188 in a gerbil model of transient forebrain ischemia. P188 has also been shown to rescue neurons through interactions with neuronal plasma membranes.

Rescuing injured neurons by repairing the plasma membrane, therefore, is a novel approach to neuroprotection and may lead to a new class of compounds for the treatment of hypoxic-ischemic brain injury. The goal of the application is to devise an experimental approach and to obtain pilot data of low- to medium-resolution imaging of tri-block copolymer interactions with the plasma membrane of living hippocampal neurons.

Principal investigators are Jeremy Marks of the University of Chicago and Argonne's Millicent Firestone.

Phase-enhancement micro-computed tomography: Researchers will develop and streamline phase-enhancement micro-computed tomography (PRMCT) and its potential application to imaging, quantitatively characterizing and monitoring tumor angiogenesis, a process by which tissue develops new capillaries from an existing microvascular network.

Specifically, the goals are to develop and streamline volumetric PEMCT for targeted imaging of region of interest, to develop novel algorithms for accurately reconstructing PEMCT images for the acquired data and to evaluate the performance of the proposed PEMCT and algorithms.

Principal investigators are the University of Chicago's Xiaochuan Pan and Francesco De Carlo of Argonne.

The nation's first national laboratory, Argonne National Laboratory conducts basic and applied scientific research across a wide spectrum of disciplines, ranging from high-energy physics to climatology and biotechnology. Since 1990, Argonne has worked with more than 600 companies and numerous federal agencies and other organizations to help advance America's scientific leadership and prepare the nation for the future. Argonne is managed by UChicago Argonne, LLC for the U.S. Department of Energy's Office of Science.

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