Argonne NATIONAL LABORATORY

News Release

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For immediate release

NIH awards Argonne $800,000 to develop tool to measure distances within proteins

Precise molecular ruler could play role in development of new drugs

ARGONNE, Ill. (Sept. 3, 2008) — Scientists at the U.S. Department of Energy's (DOE) Argonne National Laboratory have won an $800,000 EUREKA award from the National Institutes of Health (NIH) to develop MADMAX, a precise molecular ruler for measuring distances within a protein.

MADMAX, which stands for the Multi-wavelength Anomalous Diffraction using Medium Angle X-ray solution scattering, would not only dramatically reduce the time necessary to reveal the behaviors of a protein, but could provide a new tool for pharmaceutical companies developing new drugs such as protease inhibitors for the treatment of HIV. It could also be a stark improvement to the decades-old method of crystallizing proteins, which could involve the use of harsh chemicals and can show how a protein is structured but often provides precious few clues as to how it moves in nature.

"There's almost nothing that a protein does that doesn't involve some movement," said Lee Makowski, principal investigator of the project. "Proteins have to move, and understanding that movement is key to figuring out how the proteins work."

MADMAX will precisely measure the inter-atomic distances between different parts of proteins in a solution by using selenium to 'tag' the proteins so the labels can be detected via the X-ray scattering. The selenium is easily incorporated into proteins, allowing for their study while not interfering with their function.

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The proteins in solution are then hit with a beam of X-rays, and the scattering is used to determine the distances between selenium atoms in the protein. When the protein moves, the distances change and the movements of the protein can be measured with great accuracy.

“If successful, MADMAX would change how we study proteins and protein motion,” Makowski said. “That’s a huge thing.”

MADMAX would allow scientists to see how a protein changes as a result of its environment, observe how ligands bind to a proteins’ surface and follow the process of protein or RNA folding. It would also give pharmaceutical companies the chance to observe how their drugs interact with proteins, potentially saving time and expenses by providing them with unique insight into the mechanism of the drugs' action.

The MADMAX program will take advantage of the Argonne’s Advanced Photon Source, the brightest source of X-rays in the Western Hemisphere, and open to 3,500 users per year.

The MADMAX program is set to run for four years and will determine if the method would be suitable for the study of proteins on a routine basis. The team will begin by developing software and data collection protocols and then move on to study well known compounds such as hemoglobin and HIV protease to check the accuracy of the method.

The EUREKA program – designed to encourage 'Exceptional Unconventional Research Enabling Knowledge Acceleration' – is in its first year and is funded by the NIH to support exceptionally innovative research which has potential to have a high impact in the scientific community.

"EUREKA is an experiment in how to attract, identify, and support particularly creative approaches that, if successful, could move science forward dramatically," said Jeremy M. Berg, Ph.D., director of the National Institute of General Medical Sciences, which led the development of the EUREKA program.

"EUREKA projects promise remarkable outcomes that could revolutionize science," said NIH Director Elias A. Zerhouni, M.D. "The program reflects NIH’s commitment to supporting potentially transformative research, even if it carries a greater than usual degree of scientific risk."

About Argonne

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