AP Connecticut

Rutgers to lead project to learn protein structures, functions

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July 5, 2005, 8:00 PM EDT

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TRENTON, N.J. -- Scientists at Rutgers University will head a huge national research project to help determine the structure of protein molecules, how proteins control cellular processes and ultimately how to turn that knowledge into new medicines.

The project, announced Tuesday, is one of four large collaborations being funded by an arm of the National Institutes of Health that will build on information accumulated from the Human Genome Project and sequencing of other organisms' genomes.

The previous projects mapped the entire genetic code of organisms from people to mice, chickens and bacteria, but scientists still need to learn how health and disease are affected by the proteins those genes tell the cells to make.

"Most of those proteins, we don't know what they do, we don't know how they work, we don't know how to prioritize (studying) them for human medicine," said

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Gaetano Montelione, professor of molecular biology and biochemistry at New Brunswick-based Rutgers.

That's the case for all but a few hundred of the 30,000 to 40,000 proteins in human cells.

So the National Institute of General Medical Sciences, part of the NIH, is awarding about $300 million over five years to the four collaborations and six smaller, specialized research groups to determine the three-dimensional structure of a variety of proteins. Together, those groups comprise the Protein Structure Initiative.

The Rutgers-based consortium, called the Northeast Structural Genomics Consortium, or NESG, will receive nearly $53 million of the total. Led by Montelione, the 120-person team includes researchers from eight other institutions, including Yale University and Robert Wood Johnson Medical School in New Brunswick.

Already, researchers in the various collaborations have spent five years on the project's first phase, developing robotic, computer and other technologies that will dramatically speed up the search. Along the way, the Northeast consortium alone has identified the structure of about 200 proteins, with the data now stored in the national Protein Data Bank based at Rutgers.

"Traditionally, a protein structure determination was a year project" or longer, Montelione said in an interview. "Our new technologies allow us to go to a few hundred structures a year."

"What we are creating are new opportunities for targeted drug development," where drugs are designed to bind to specific targets in or on cells to block or enhance the effects of a particular protein, Montelione said.

Deciding which proteins to study first is crucial because many are from large "families" of proteins with up to 1,000 members, and identifying the structure of one protein will enable faster determination of the structure of other family members, said Michael Baran, a manager of the project at Rutgers.

Even with computer and other technology, it's a daunting task that in the past was only rarely successful.

After scientists pick a protein to study, DNA from that protein is put in fast-growing bacteria to produce many copies of the protein. Then the mix must be purified to leave only the desired protein, Baran said.

Next, the protein's structure is analyzed using either sophisticated X-ray technology or nuclear magnetic resonance (NMR), a technique that shows the position of individual atoms relative to each other within the protein. Supercomputers then convert all the data into three-dimensional images.

Of the four major collaborations, the Northeast consortium is the only one using NMR technology, Montelione said.

The X-ray work, called X-ray crystallography, mainly is being done at Columbia University in New York, said Wayne A. Hendrickson, professor of biochemistry and molecular biophysics there.

"The expectation is we'll become more and more effective at doing this structure determination business expeditiously," Hendrickson said.

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He said the research ultimately could lead to more protein-based drugs that can be made into pills. Currently, most such genetically engineered drugs have such large molecular structures that they have to be injected.

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