NEW BRUNSWICK/PISCATAWAY, N.J. – Rutgers University will lead a new $52.7 million research program that will help reveal the roles that proteins play in life’s most fundamental processes and point the way to designing new medicines. Under the direction of Rutgers Professor Gaetano Montelione, the Northeast Structural Genomics Consortium (NESG) will conduct the five-year undertaking.

“This grant, one of the largest in Rutgers’ history, will reinforce our dynamic position in the biomedical sciences, inspire our researchers toward new discoveries and open new doors to longer and healthier lives,” said Richard L. McCormick, president of Rutgers, The State University of New Jersey.

“Federal funding of this magnitude recognizes the caliber of our faculty and the quality of their research, and positions us for broader collaborations with other institutions and industries in New Jersey and beyond. The NESG, and other major programs at Rutgers in structural and computational biology, including the Protein Data Bank and BioMaps, form the basis for plans to greatly expand our efforts in proteomics and related disciplines,” added McCormick.

The research program will be funded by the Protein Structure Initiative (PSI) of the National Institute of General Medical Sciences (NIGMS), one of the National Institutes of Health. “With demonstrated expertise and achievements in determining the structures of many different types of proteins using a variety of approaches and new technologies, the NESG will be a key member of the PSI network and a valuable asset to the biomedical research community,” said John Norvell, director of the PSI.

The PSI program is part of a national effort to find the three-dimensional structures of a wide range of protein molecules, building upon the momentum created by such groundbreaking programs as the Human Genome Project. However, the majority of the proteins coded by the genome have unknown functions and unknown structure.

For the past five years, Montelione and his consortium partners, including researchers at Columbia University, conducted a $36 million NIGMS pilot program to develop new methods and tools to streamline and speed many of the laborious steps involved in generating protein structures. The researchers applied the new technologies to determining three-dimensional structures of approximately 200 proteins, representative of some of the 100,000 protein families that are estimated to exist in nature.

These structures, in turn, have provided templates for predicting models of over 40,000 protein structures using methods of structural bioinformatics. Other NIGMS pilot program centers brought the total to about 1,500 structures which can be used to model thousands of other proteins in each of the families they represent.

“Already, these structures have given us new insights and allowed us to discover the functions of proteins that weren’t recognized before,” said Montelione, a professor of molecular biology and biochemistry at Rutgers and a resident faculty member of the Center for Advanced Biotechnology and Medicine (CABM), a research institute jointly administered by Rutgers and the University of Medicine and Dentistry of New Jersey.

“Montelione’s dedication and the committed efforts of other groups at CABM and around the country are generating exciting new information and advancing the frontiers of science,” said CABM Director Aaron J. Shatkin.
“We have even discovered several potential antibiotic drug targets and drug screening assays for which we have submitted patents,” Montelione said. “However, there are many protein families that still do not have known structural representatives.”

NIGMS has now funded four of the strongest pilot program centers, including NESG, as Centers for Large-Scale Structure Production. The focus is shifting to a production phase in which the new centers will use methods developed during the pilot period to rapidly determine thousands of protein structures found in organisms ranging from bacteria to humans. These efforts will facilitate structure determination on a much larger number of proteins through computer modeling.

In collaboration with Rutgers scientists, NESG members at Columbia University will have significant roles in the program, including the selection of specific proteins for structure determination and subsequent computational analysis of the structures. From the structures, Columbia bioinformatics specialists will be able to deduce functional information about individual proteins and bring to light new evolutionary relationships among them.

“We hope that the PSI will allow us to develop a new view of the relationships between protein sequence, protein structure and protein function that will ultimately make the three-dimensional structures and functions of most proteins predictable from the protein sequence,” said Barry Honig, professor of biochemistry and molecular biophysics at Columbia University Medical Center and bioinformatics leader of the NESG.

Wayne Hendrickson, University Professor of Biochemistry and Molecular Biophysics at Columbia, is participating as NESG’s director of crystallography.

“The PSI has transformed protein structure determination into a highly automated process, making it possible to go from a selected target to a completed structure much more rapidly than before,” said Jeremy M. Berg, director of NIGMS. “Building on these achievements, the new centers will take the PSI to the next level, yielding large numbers of structures and tackling significant new challenges. Importantly, the technology developed will continue to impact structural studies beyond the PSI.”

Montelione expects that in the next five years his group should solve about 1,000 more structures, including many human protein structures, using methods of X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, with the full PSI producing between 4,000 and 5,000 over the next five years. “These structures will have tremendous value in understanding basic biology, and in developing the next generation of diagnostics and medicines for treating human diseases,” Montelione said.

NESG is a Rutgers-led collaborative research partnership of more than 15 principal investigators and 120 scientists at nine universities and other research facilities. Approximately $20 million will fund research at Rutgers, which will be the central hub of the program. The remaining $30 million will support work at NESG partner institutions.

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