LA JOLLA, Aug. 19 -- The National Institutes of Health has awarded a $2.72 million grant to a Scripps Clinic and Research Foundation team studying the link between a protein's genetic code and its function, a fundamental problem in modern molecular biology.

Specifically, the research effort will study how a protein's linear amino acid sequence dictates how the protein folds up in three-dimensional space and assembles with other proteins to perform its biological function.

"We may already know a protein's genetic code, how the amino acids are arranged one after the other in a single chain," said Dr. Arthur Olson, principal investigator and member of the molecular biology department. "But we cannot predict how that chain folds in three-dimensional space - how we get from the sequence of amino acids to protein function."

Since the underlying principles governing protein folding apply to all proteins, once the relationship between the linear sequence, the three-dimensional shape and the resulting macromolecular assembly is discovered, it can be applied to many life sciences.
Protein folding, said Olson, "is the fundamental problem in molecular biology today."

The research effort, funded for five years, will use nuclear magnetic resonance spectroscopy, X-ray crystallography, computer simulation and computer graphics techniques.

The project addresses six related problems, dealing with small peptide units of a few amino acids to proteins that have assembled to form, for example, a virus. Each project will be tackled by a different molecular biologist.

Dr. Peter Wright, molecular biology department chairman, will use nuclear magnetic resonance spectroscopy to study peptide sequences that fold up into characteristic secondary structures.

Dr. David Case will use computer simulation to study the initial foldings of small peptides.

Dr. Timothy Havel will use a technique known as distance geometry to study whether it is possible to predict how one folded protein changes to another without first completely unfolding.

Dr. Ian Wilson will use X-ray crystallography to study the interaction of proteins and peptides with antibodies, the nature of the recognition, and how a peptide arranges itself when it binds to an antibody.

(More)
Dr. James Hogle will study temperature sensitivity in the poliovirus - how the substitution of a single amino acid in the virus raises its sensitivity to temperature and affects its stability.

Olson will survey existing information on protein-protein interfaces, and use computer graphic techniques to look for patterns in the relationship between interface structure and function.