ARGONNE NATIONAL LABORATORY

*Pioneering Science and Technology*

# PROTEIN PRODUCTION AND CHARACTERIZATION FACILITY

## *Challenge*

Microbes are incredibly efficient chemists and physicists, capable of absorbing, storing and transforming energy. Long ago, they learned to carry out many of the fundamental physical and chemical processes needed to address DOE science missions in environmental remediation, carbon sequestration and alternate fuel production. If we can understand how they do this, we will be able to manage and direct their capabilities to fulfill mission needs in a highly cost effective way.

The key to understanding microbial function is to understand their proteins - the molecules that carry out virtually all the activities of the cell. Sequencing the DNA of genomes has provided the full inventory of proteins encoded by many species and a global framework to analyze the functions of organisms at the molecular level. However, while sequencing provides a clue to the functions of proteins, it does not yield a complete understanding of cell function. To enable a systems-wide analysis of cellular activities requires genome-wide experimental analyses of protein function.

Characterizing each protein in enough detail to provide an understanding of what it brings to the life-style of the cell from which it was derived is an essential step in achieving the system-level analyses envisioned in DOE's Genomes to Life Program. This goal represents a challenge much larger than the genome project, and will require automation of multiple technologies and the collection and integration of vast amounts of data. Argonne National Laboratory's scientific strengths and world-class facilities uniquely position it for a leading role in this effort.

*Figure 1. Robotics will be used to perform high-throughput molecular biology and biochemistry procedures*

## *Concept*

To study proteins, you first need to produce them. Yet, protein production is one of the principal roadblocks of post-genomic biology, as it is labor-intensive, time-consuming, and costly. Such production on a genome-wide level can be made economically feasible only when carried out in a highly automated, high-throughput facility.

Argonne proposes to establish, in partnership with Los Alamos National Laboratory, a major facility for the production and characterization of proteins. Development of automated purification methods and industrial scale-up with robotics can provide very significant economies of scale, as well as making available more protein for scientific analysis. This facility will produce tens of thousands of different proteins per year as well as generating protein-tagging reagents needed to identify, track, quantify, control, capture, and image individual proteins and molecular machines in living systems. Industrial scale protein characterization will provide data of consistent quality conforming to uniformly high standards. These capabilities will establish the facility as a premier international laboratory for protein production and will have a significant impact on post-genome biotechnology.

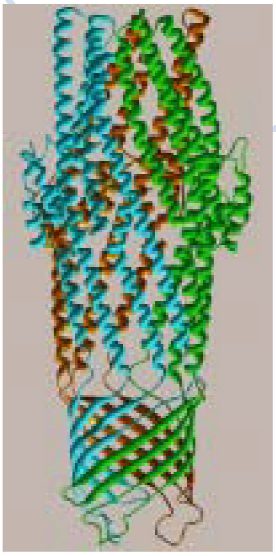

*Figure 2. Data obtained by means of the SBC 191D beamline were used to determine the structure of trans-membrane transport membraneTOL-C protein.*

## *How It Works*

This facility will feature state of the art automation for cloning, expression, purification and characterization of proteins. An advanced laboratory information management system will predict optimum methods for production and purification of each protein based on its amino acid sequence and collect experimental data from all automated systems.

Proteins will be studied by a number of state of the art characterization techniques to provide information about how they function within the cell. Proteins are the molecular machines of the cell and, like any machines, it is hard to understand how they work without knowing what they look like - that is, determining their three-dimensional structures. Selected proteins will be crystallized and their structures determined at the Structural Biology Center (SBC) at Argonne - one of the best facilities in the world for collecting high-resolution data from crystals of macromolecules and macromolecular complexes. Affinity reagents will be produced and used to identify the molecules that proteins interact with and to determine where they are located within a microbe.

The results of characterization experiments will be automatically entered into an extensive, integrated data base system accessible by the entire research community. Integration of data from a wide range of experimental techniques will provide a deep and extensive picture of the way proteins function within a microbe and build a strong foundation for developing strategies for using microbes as solutions to environmental and energy concerns.

## *Contact*

Lee Makowski
Director, Biosciences Division
Phone: 630/252-3819
Fax: 630/252-3853
lmakowski@anl.gov