## BIOENGINEERING, BIOINFORMATICS, AND ADVANCED TECHNOLOGIES

Bioengineering, bioinformatics, and other advanced technologies provide crosscutting tools that facilitate research in many disciplines. Bioengineering combines physics, chemistry, and mathematics as well as basic engineering principles to enhance the study of biology, medicine, behavior, and health. Bioinformatics and computational biology apply computer science and advanced mathematics to the fields of biology and medicine to enable integration and analyses of biological, medical, behavioral, and health data. Other advanced technologies, such as biomedical imaging, proteomics, and genomics, facilitate characterization of complex biological processes.

The powerful tools and techniques of bioengineering, bioinformatics, and computational biology extend the capacity of science to perceive, capture, and manage information about biological processes and have become integral components of NIAID-supported basic and clinical immunology research. Additional technologies, including proteomics, biosensor fabrication, biomedical imaging, and data integration, are becoming important tools for researchers. Below are examples of NIAID-supported programs in these areas.

- **Exploratory/developmental grants: Technology applications to NIAID-funded research.** NIAID issued a program announcement to facilitate the use of novel and emerging technologies in ongoing NIAID-supported research projects. This program supports biomedical imaging, proteomics, nanotechnology, and genomics.
- **Mass spectrometry for high-throughput peptide characterization.** This program supports the development of chemical measurement instruments for the sequence analysis of peptide antigens presented in the major histocompatibility complex. The goal of this research is to develop a high-throughput method to study peptides that are recognized by the body as "self." Understanding how the immune system distinguishes between "self"—the body's own organs, tissues, and cells—and "not self"—foreign and potentially harmful agents—is relevant to all immune-mediated diseases.
- **Proteomics collaboratory.** This program supports research to dissect immune responses to viruses that are potential agents of bioterrorism, utilizing proteomics approaches to characterize dynamic changes in protein expression in inflammatory cells after pathogen exposure. This information will be compiled in a publicly available database. Bioinformatics approaches also will be used to correlate observed changes in protein expression with available data on changes in gene expression due to inflammation induced by viral infection or endotoxin shock.
- **Systems approaches to innate immunity, inflammation, and sepsis.** This program supports research to create a comprehensive picture of innate immunity, the body's first line of defense against bacterial, viral, and fungal diseases. This multidisciplinary systems biology approach will lead to an understanding of molecular-level innate immune responses triggered by bacterial and viral infections.

- **Biosensors for investigating the developing immune system.** Researchers are using sensitive miniaturized sensors to study the development of B and T cell function during a real-time immune response, by characterizing the production of specific growth factors, termed cytokines, produced by various immune cells.

- **Modular gene assembly.** Researchers are developing a new system for engineering genes on the basis of their binding and activation properties. This technology will enable the formation, selection, and assembly of genes based on individual functional traits, which may lead to the development of novel therapeutic compounds such as custom antibodies and immunosuppressants.

- **Drug discovery by high-throughput screening methods.** The goal of this project is to identify anti-inflammatory and immunosuppressive agents that are agonists for specific cellular receptors. The system can analyze up to 1,000 samples simultaneously and uses bioinformatic analyses and computational models to aid in drug discovery.

- **Microchip drug delivery system.** This program supports development of a novel drug delivery device that uses silicon-based microchips to deliver complex regimens of bioactive agents to specific organs or tissues. Researchers have demonstrated that a silicon-based microchip device with no moving parts can be operated *in vivo.* This device will allow for controlled delivery of a concentrated amount of drugs or bioactive compounds to affected tissue and has the advantage of eliminating possible toxic side effects and inefficient delivery of systemically administered compounds.

- **Alliance for Cellular Signaling (AfCS).** This program supports research to dissect signaling pathways in mammalian cells in order to understand how cells interpret and respond to external signals. This large-scale, collaborative program is co-funded by NIAID, the National Institute of General Medical Sciences (NIGMS), and the National Cancer Institute. All of the materials and information developed through the AfCS are available to the biomedical community worldwide. More information can be found at *www.signaling-gateway.org/.*

- **NIGMS protein structure initiative.** NIAID contributes to the support of this NIGMS-sponsored program to determine the structure of proteins from the genomes of pathogenic protozoans and malaria parasites. The program involves computer prediction of protein domains for target selection, high-throughput protein expression, crystallization, and structural analysis. More information is available at *http://depts.washington.edu/sgpp.*

- **Whole-organism imaging of immune response.** This program uses imaging technologies to detect the accumulation of labeled T cells and macrophages in organ transplants and to examine the development of systemic autoimmunity *in vivo.* The ability to monitor T cell migration to and accumulation in organs, such as the liver, kidney, and bowel, or in the central nervous system is important to understanding immune responses to pathogens and immune-mediated diseases. Another NIAID-funded project is developing new magnetic resonance imaging (MRI) contrast reagents (dyes) to track immune responses *in vivo*.

- **Genomic databases and analysis tools.** NIAID supports databases of genomic information and analysis tools for the multidisciplinary study of sexually transmitted pathogens, including pneumoniae, chlamydia, papillomavirus, herpes, and gonorrheae, that extend beyond molecular sequence data, such as dynamic graphics and Web-based data mining and sequence analysis tools. This resource is available from the Los Alamos National Laboratory and is also supported by the U.S. Department of Defense. More information is available at *www.stdgen.lanl.gov* and *www.poxvirus.org*.

- **Bioinformatics infrastructure for scientific data sharing.** Researchers are using the powerful new tools and techniques of proteomics to study the proteins encoded by human genes, including their function, structure, location, variants, and similarities to other proteins. NIAID supports the development of new tools to monitor and manipulate gene expression. In fiscal year 2002, NIAID established the Bioinformatics Integration Support Contract (BISC). When fully implemented, BISC will (1) link genomic and other basic scientific and clinical data from a variety of sources; (2) enable scientists to easily access, generate, and exchange complex, high-quality data sets; and (3) serve the data integration and archiving needs of several research programs supported by NIAID.

- **HIV database and analysis unit.** This unit includes the HIV Genetic Sequence Database and the HIV Molecular Immunology Database. The Genetic Sequence Database compiles sequence information from GenBank and other international databases and then conducts indepth analyses of HIV genomes. The Molecular Immunology Database compiles all published immunologic information on humoral and cellular immune epitopes from HIV proteins. These databases also provide analysis tools to the user community at *http://hiv-web.lanl.gov* and *http://hiv-web.lanl.gov/immunology/index.html*.

- **Immune epitope database and analysis program.** The primary goal of this program is to develop and maintain an integrated, Web-based, searchable database of antibody binding sites (antibody epitopes) and antigenic MHC-binding peptides (T cell epitopes) for a wide variety of infectious agents and immune-mediated diseases, with emphasis on NIAID Category A, B, and C bioterrorism agents and emerging/re-emerging infectious diseases. The information contained within the database and the analysis tools will facilitate identification of novel vaccine candidates and immunotherapeutic strategies to improve biodefense efforts.