Clearing house for DNA gets a boost

October 20 2011

Arizona State University's Biodesign Institute is home to a rich trove of biological material. Known as DNASU, this growing storehouse—a sort of genetic Library of Congress—holds over 147,000 plasmids, (circular DNA samples that can be used to produce individual proteins), as well as full genome collections from numerous organisms and proteins associated with many leading human diseases.

A new $6.5 million grant from the National Institute of Health will help expand a critical component of this genetic archive known as the Protein Structure Initiative-Materials Repository (PSI:Biology-MR).

The PSI:Biology-MR effort began in 2006 in the laboratory of Joshua LaBaer, then at the Harvard Medical School Institute of Proteomics. LaBaer has directed Biodesign's Virginia G. Piper Center for Personalized Diagnostics since 2009, where the PSI materials repository has continued its mission of collecting, annotating, storing, maintaining, and distributing plasmids—the design templates for specific proteins created by researchers within the PSI's multi-institution structural genomics consortium.

Plasmids are small pieces of DNA, generally of a circular structure. They provide ancillary genetic information in bacteria and prokaryotic organisms, often containing specialized genes for essential functions. Plasmids are a particularly important tool for biotechnology. Researchers use them to study the effect of individual genes in cells or within an organism. Plasmids are also commonly used by researchers as biological flash drives that can be inserted into bacteria to make multiple copies of

genes or express genes as proteins.

Proteins play an essential role in virtually all life processes. As LaBaer explains, expression-ready plasmids are vital to biomedical research, particularly for the study of human health and disease. "Proteins provide the verbs to biology. They energize, connect, signal, digest, activate, inactivate, move, transport, and dozens of other activities. Researchers use plasmids to make these proteins, in order to learn about what they do and how to regulate them. Nearly all drugs today act by altering the activity of a protein or are proteins themselves."

The field of structural genomics has undergone rapid advance in recent years, due to the increasing availability of sequence data. Such study holds enormous promise for a more complete understanding of the role of proteins both in normal biological processes and in disease. Four large-scale and numerous specialized PSI Centers have created tens of thousands of plasmids containing genes or their fragments to be used for protein expression, purification, crystallization and structure determination.

As of September 2011, over 50,000 PSI plasmids containing genes from over 890 organisms have been assembled, curated and shared with the research community.

Like a lending library for books, PSI-Biology-MR acts as a global distribution network, delivering plasmids to researchers worldwide, including critical information about the genes they contain, annotations concerning the full length sequence, vector information, and associated publications for cross referencing—all of which are stored in a freely available, searchable database.

Once the detailed 3-D structure of a given protein has been worked out or 'solved' by PSI researchers, the task of unraveling the biological

function of the protein can commence. The PSI resources can be used by researchers to study the biochemistry and biological functions of key proteins. Further, expression-ready plasmids for proteins coded by hypothetical genes or genes of unknown function assist biologists in determining the function of these proteins more quickly.

LaBaer says that besides providing these plasmids at a low cost from an easily accessible centralized location, his group has also dramatically simplified the legal process of acquiring plasmids for study; streamlining the Material Transfer Agreement—a necessary contractual document. This was accomplished through multi-institute cooperation, reducing delays for plasmid transfers and accelerating the pace of discovery.

At the heart of DNASU and the PSI:Biology-MR is the Nexus Universal BioStore Freezer. LaBaer's team acquired this state-of-the-art storage and robotic retrieval system through funding provided by the American Recovery and Reinvestment Act. The BioStore system is essential for maintaining the integrity of the plasmids, properly tracking the location of each sample in the repository and ensuring rapid and accurate access to these samples.

Plasmids are stored as glycerol stocks in 2D barcoded tubes at -80 degrees Celsius. The Nexus and repository are integrated for a seamless flow between ordering and plasmid selection; saving time, safeguarding samples from cross-contamination and human error, and accelerating distribution of materials to researchers. The BioStore is capable of storing and retrieving up to 855,000 sample tubes, all managed automatically from a computer.

LaBaer stresses that the integrated PSI:Biology-MR system, including a growing repository of expression-ready plasmids, an automated pipeline, and a rapid process for receiving and distributing plasmids more effectively will be a boon to the community of researchers hoping to

dissect the biological functions of proteins:

"We have always had the philosophy that sharing tools and reagents is critical to accelerating scientific discovery. It doesn't make sense for one researcher to have to repeat the work that someone else has already done. This facility makes sharing easy."

Provided by Arizona State University