Structural Genomics Project creates blueprint for infectious disease and biodefense research

September 1 2011

The September issue of the online scientific journal Acta Crystallographica: Structural Biology and Crystallization Communications (Acta Cryst F) will consist entirely of work done at the Seattle Structural Genomics Center for Infectious Disease (SSGCID), a consortium of researchers from Seattle BioMed, Emerald BioStructures, the University of Washington and Pacific Northwest National Laboratory (PNNL). This free online edition features 30 peer-reviewed manuscripts, describing 40 unique infectious disease protein structures, as well as high-throughput gene-to-structure methodologies developed by SSGCID, and marks only the second time that Acta Cryst F has dedicated an entire issue to a single Structural Genomics center. The elucidation of such a large number of protein structures, all of which are freely available to scientific researchers to study and compare, provides a highly detailed "blueprint" for fighting infectious disease and bioterrorism.

Funded in late 2007 by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), to determine the three-dimensional structures of proteins from biodefense organisms and emerging infectious diseases, the SSCGID is directed by Dr. Peter Myler, a Full Member at Seattle BioMed and principal investigator of the project. "Currently the SSCGID has solved more than 375 protein structures from pathogenic microbes, providing much-needed new knowledge that serves as a starting point for structure-based

drug design," said Myler. Many SSGCID structures also contain information on how small molecules bind to infectious disease proteins, providing highly valuable information for a drug discovery and development. Lance Stewart, CEO of Emerald BioStructures and co-principal investigator of the SSGCID project, commented "We've worked together to create an environment that combines the best of academia and industry. Instead of competing on infectious disease targets and drug compounds as traditional pharma or biotech companies do, we are building a shared knowledge base aimed at addressing important unmet needs."

The manuscripts featured in Acta Cryst F discuss potential drug-targets from organisms that cause some of the world's deadliest diseases, including emerging pathogens and possible bioterror agents. One paper in the September edition features new insight into an iron-binding protein (called rubredoxin) from Mycobacterium tuberculosis, the bacterium that causes tuberculosis (TB), a disease which is responsible for nearly two million deaths annually. The new understanding of the protein's biological function revealed by this structure may speed up the development of new drug therapies urgently needed to prevent TB epidemics due to the recent emergence of multi drug-resistant (MDR) and extremely drug-resistant (XDR) strains.

Coccidioides immitis, a lesser-known organism featured in the SSGCID special edition, causes coccidioidomycisis or "Valley Fever" in the southwestern U.S. This sometimes-fatal disease can be contracted when a person breathes fungal spores from dust or dirt that has been disturbed by wind, and can cause fever, chest pain and coughing, among other more severe symptoms. The genome of C. immitis was sequenced recently, but very few of its proteins have been structurally characterized. The structures solved by SSGCID will increase the understanding of important enzymes involved in detoxification and nucleotide biosynthesis/salvage within this pathogenic fungus.

According to Myler, scientists from the SSCGID and its sister organization, the Center for Structural Genomics of Infectious Diseases (CSGID), which is led by Dr. Wayne Anderson of the Northwestern University Feinberg School of Medicine, gathered in Seattle in early August to review structures solved to date and determine priorities for the next year. "Between the two centers, we will solve over 1,000 structures by the end of 2012," said Myler. "With new information that is shared immediately through the NIH-supported Protein Data Bank (www.pdb.org), we are providing critical starting points for discovery and development of novel drugs, vaccines and diagnostics for a wide range of infectious diseases."

Provided by Seattle Biomedical Research Institute