

## **High Throughput Structural Biology Methods and Applications**

Scott Lovell, Lijun Liu, Steve Seibold and Anne Cooper

Protein Structure and X-Ray Crystallography Laboratory, University of Kansas

X-ray crystallography is a common technique used to provide essential high-resolution structural information for researchers studying proteins. Details that can be obtained from a protein structure determination include metal binding characteristics, protein function, protein-protein interactions, protein-ligand interactions and inhibitor binding modes. Since X-ray crystallography is a somewhat specialized field, investigators routinely collaborate with structural biologists but are often unfamiliar with the methods utilized for structure determination. Modern techniques in the structural biology field make it possible to rapidly move from gene-to-structure and determine multiple 3-dimensional structures over a short period of time. Specific examples will be presented that underscore the importance of obtaining structural information to gain mechanistic and functional insight of proteins. Additionally, structure-based drug design (SBDD) techniques play an important role in early-stage inhibitor development. The high-resolution models provide atomic level information regarding the inhibitor binding modes which guides subsequent medicinal chemistry efforts aimed at developing more potent compounds. Applications of SBDD methods in projects that target pathogenic bacteria for antibiotic development and the main proteases of coronavirus will be highlighted.