The Proteomics Laboratroy

The Proteomics Laboratory at the Skaggs School of Pharmacy and Pharmaceutical Sciences

By Vivian Hook

Drug actions largely involve interactions of the drug molecule with a critical protein(s) that regulates physiological systems in health and disease. It is, therefore, essential to investigate the system of proteins that interact in pathways underlying disease mechanisms as a means for (1) identifying new drug targets and for (2) defining mechanisms of drug regulation of protein systems for improvement of disease conditions in translational research. Such studies of proteins in pathways of biological systems is known as '*proteomics*.' '*Proteomics'* is defined as the study of the structure, quantities, and coordinated functions of interacting proteins in a biological system. Proteomic research will facilitate development and discovery of new therapeutic agents for the treatment of human diseases.

The 'Proteomics Laboratory' at the Skaggs School of Pharmacy and Pharmaceutical Sciences (SSPPS) is designed to utilize current mass spectrometry instrumentation for proteomic research in biomedical and pharmaceutical sciences. Mass spectrometry (MS) determines the molecular masses of proteins and peptides (small proteins), as well as small molecule pharmaceutics, that defines their structural features based on analyses of MS data by bioinformatic database methods. Advanced mass spectrometry instrumentation achieves identification of proteins, determination of post-translational modifications that regulate protein function, quantitation of protein species, and evaluation of drug molecules. LC-MS/MS approaches combine protein/peptide separation by liquid chromatography (LC) with on-line introduction into the mass spectrometer to provide identification of multiple protein and/or peptide species in a biological sample. Off-line 1D- and 2D-LC separation of proteins/peptides based on their physicochemical properties, including activity-based fluorescent affinity probes, facilitates proteomic studies. Furthermore, nanospray-FTICR-MS (Fourier transform ion cyclotron MS) defines large protein structures in top-down MS approaches; FTICR-MS also facilitates identification of new drug molecules from a variety of natural and synthetic sources.

The laboratory facility can investigate quantitative comparisons of proteins in normal and disease conditions. This information can identify candidate regulatory proteins involved in the disease process. Such disease regulated

proteins provide strategies for new drug targets and drug discovery. Alternatively, drug-mediated alterations in protein pathways by proteomic approaches can enhance our understanding of drug mechanisms, which may be termed 'pharmacoproteomics.'

Complementary expertise of the 'Proteomics Laboratory' provides knowledge in protein chemistry and biochemistry, mass spectrometry, and bioinformatics for collaborative proteomic research. Dr. Vivian Hook, Professor, has experience in peptide and protein biochemistry for understanding neuropeptide mechanisms of cell-cell communication in health and disease, utilizing extensive LC-MS/MS approaches. Dr. Hook joined SSPPS from the School of Medicine at UC San Diego. Dr. Pieter Dorrestein, Assistant Professor, brings specialized experience in FTICR-MS for analyses of large protein structures responsible for biosynthesis of therapeutic agents; Dr. Dorrestein joined SSPPS from the Univ. of Illinois. Dr. Steven Bark, Project Scientist, has much experience for application of analytical technology in chemistry and mass spectrometry for macromolecular structures; Dr. Bark joined SSPPS from The Scripps Research Institute. Bioinformatic expertise for proteomics is facilitated by Dr. Phil Bourne, Professor, who leads the Protein Data Bank (PDB), a world-wide repository for 3-D protein structures that is housed in SSPPS. Associated with the analytical facility of the Proteomics Laboratory is the 'NMR Suite' for protein structure analyses, led by Dr. Tracy Handel, Professor, who joined SSPPS from UC Berkeley. Extension of proteomic research to drug discovery is facilitated by the expertise of medicinal chemists Dr. William Gerwick, Dr. Bradley Moore, and Dr. Tadeusz Molinksi of SSPPS, Scripps Institute of Oceanography (SIO), and Chemistry at UCSD.

The Proteomics Laboratory participates in training students with the graduate course 'Proteomics for Biologists' taught by faculty of SSPPS and collaborative faculty from multidisciplinary departments at UCSD from medicine to chemistry and bioinformatics. Students are guided on approaches to integrate proteomic strategies into their thesis research projects.

The Proteomics Laboratory has the opportunity to provide the link for translational research between biomedical and pharmaceutical science research areas of protein functions, as the basis for enhancing efforts for drug discovery and understanding drug actions. The Proteomics laboratory looks forward to exciting new research accomplishments for understanding human health and disease.