

College of Science and Mathematics and  
Department of Chemistry and Molecular Biology  
Distinguished Alumnus Seminar  
April 15, 2008  
3:45 pm in Dunbar 152

*Tools for Population Proteomic Studies: Mass Spectrometry, Affinity Capture  
and Bioreactive Probes.*

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Population proteomics is the quantitative and qualitative investigation of the numerous proteins found in populations of healthy and diseased individuals. Identification of protein variations that can be used distinguish between normal, healthy individual and diseased individuals is desired result. Large numbers of biological samples are required to obtain the necessary data on protein concentration ranges and the most common point mutations and posttranslational modifications for each protein under investigation. The seminar discussion will provide information on high-through-put technologies, developed at Intrinsic Bioprobes, Inc., that are currently in use for studies of biological fluid samples from hundreds of individuals. The goal of the on-going research is to delineate protein differences that can be related to disease and thereby close the gap between discovery and application to diagnostic and clinical usage.

The major tools that are used for the population proteomics studies at Intrinsic Bioprobes, Inc. will briefly discussed. The targeted proteomics technologies incorporate matrix assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF), which provides a sensitive measure of protein structure and protein quantification. Isolation of selected proteins from the complex mixtures that constitute biological fluids is accomplished by affinity capture with patented microcolumn technologies. Robotic fluid handling for the isolation step gives rise to high-through-put methodologies that are necessary for studies of large numbers of samples. Bioreactive probes can be used to selectively cleave affinity captured proteins to characterize more fully the variant forms that are obtained from the biological samples. A data base of well characterized basal level protein variations, resulting from such studies, will be useful to researchers in distinguishing normal variants from disease biomarkers.

Data from use of mass spectral immunoassay methods for capture of specific proteins from biological samples will be presented. Examples of quantification and characterization of several captured proteins will be used illustrate the utility of the methods. Finally, data from population proteomic studies presented. In one study, 25 proteins from plasma samples of a cohort of 96 healthy persons were examined by the technologies described above. A total of 76 structural variants were found among the 25 proteins, including both point mutations and post-translational modifications. The existence of a given variant was wide ranging, with some variants observed in only 1 sample, whereas others variants were found in all 96 samples. A total of 27 protein modifications were observed from screening 1,000 individuals from four geographical regions in the United States for five plasma proteins. Oxidation and single amino acid terminal truncations were observed in the majority of individuals, whereas extensive sequence truncations and point mutations were less common. The data show substantial structural diversity exists in proteins from general population.