CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1121

Project Title:
Recruitment of Missing Links

Award Mechanism:
Recruitment of Missing Links

Principal Investigator:
Mirzaei, Hamid

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

My name is Hamid Mirzaei and I came to United States in August 1999 to study synthetic organic chemistry at Ball State University in Indiana. My research efforts there were focused on total synthesis of the water soluble analogs of the anticancer agent Lavendomycine. I then moved to Purdue University, one of the leading institutes in mass spectrometry research, to pursue my career in analytical chemistry. I received my Ph.D. in bioanalytical chemistry in August 2005, under the supervision of Professor Fred Regnier.

As a graduate student, I started a new field of research in Regnier's lab that focused on developing new methodologies for the isolation, identification, and quantification of the oxidatively modified proteins generated as a result of oxidative damage to cells. Oxidative damage is caused by reactive oxygen species also known to induce DNA modification, an underlying cause of many types of cancer. My research encompassing detection and quantification of oxidized proteins using novel enrichment technologies, in conjunction with modern separation techniques and advanced mass spectrometry, laid the foundation for the discovery of new biomarkers from the pool of oxidatively modified proteins. I continued my work with Dr. Regnier as a postdoctoral fellow, focusing on the impact of oxidative damage on important cellular functions such as protein expression and identification of oxidative biomarkers in biological fluids. My graduate and first postdoctoral work resulted in one patent, as well as recognition in 17 peer-reviewed publications including a 2006 most-cited article in Analytical Chemistry.

In late 2006, I joined Dr. Ruedi Aebersold's laboratory at the Institute for Systems Biology (ISB), a leading institute in the field. There I was able to combine my analytical skills with the biological insights and techniques required to direct an independent research program. At ISB, while working on a collaborative project directed at identification of potential biomarkers in premalignant cervical cells, I recognized the limitations of the conventional quantitative methods used in mass spectrometry based proteomics and decided to focus on more advanced protein quantification methods. Since then, I have been involved in the development and application of selected reaction monitoring (SRM), an emerging quantitative mass spectrometry technique destined to revolutionize proteomics into an accurate, high throughput protein interrogation platform that could meet all the demands posed by the systems biology roadmap. This technology is also one of the main platforms for biomarker validation and is the best suited platform for achieving accurate and reproducible quantification of a panel of biomarkers in hundreds of biological samples, a process that is necessary for statistical validation of biomarker candidates. I was involved in the development of the first complete SRM

library for an organism (S. cerevisiae) and am among one of the few people in the world who are able to measure the entire yeast proteome in a highly reproducible fashion.
As a faculty member, my research program will focus on development and utilization of highly sensitive SRM assays to study low abundance gene regulatory complexes that are known to play a significant role in cancer biology. Topographic mapping of polyubiquitin chains via SRM mass spectrometry is another focus of my research program. I will use this approach to address fundamental questions such as the role that ubiquitin misregulation plays in various forms of malignancies. Part of my research efforts will be dedicated to the development of new protein enrichment techniques that are essential for successful proteomic analyses of low abundance proteins. In addition, I intend to establish an enhanced high resolution, high capacity SRM-based peptide detection and quantification platform for high throughput proteomics studies such as biomarker discovery and validation. Thus, my research program will include innovation of methods, advances in data acquisition techniques, and development of computational tools for data processing.