

Development of a Measurement Quality Assurance Program to Support Biomarker Discovery for Early Cancer Detection

NIST is working with the National Cancer Institute (NCI) of the National Institutes of Health (NIH) to establish a measurement quality control program for cancer biomarker discovery and biomarker validation research by providing reference materials and data analysis support. Advances in technology and improvements in the methodologies for protein identification have produced rapid growth in the area of cancer biomarker discovery. Unfortunately, to date, there has been little effort to establish robust validation tools and methods to assure the reliability of protein biomarker discoveries. Subsequently, recent experience has greatly undermined confidence that proteomic measurements can be used to discover biomarkers that are sufficiently accurate to diagnose or predict the occurrence of cancer.

D. Bunk (Div. 839) and S. Stein (Div. 838)

The idea that a protein present in a biological fluid such as plasma or urine could be measured as a diagnostic marker for cancer goes back to 1847 when Henry Bence-Jones discovered that large amounts of a protein were present in the urine of patients with myeloma. Since this discovery, substantial scientific effort has been placed on the discovery of other unique proteins or changes in the concentration or structure of normally occurring proteins in biological fluids (i.e., biomarkers) that could aid in the early diagnosis of cancer. Rapid advances in technology and improvements in the methodologies for protein identification have extended proteomics into the field of cancer biomarker discovery. Biomarker discovery research is critical to the successful realization of the promise of the rapidly expanding field of proteomics to produce major breakthroughs in disease diagnosis and treatment. Unfortunately, the search for new cancer biomarkers has not been successful. In the 159 years since the discovery of the first protein cancer biomarker, only nine proteins have FDA clinical diagnostic approval for cancer, and nearly all of these were discovered prior to the advance of proteomics into the field of cancer biomarker discovery.

To date, there has been little effort to establish robust measurement quality assurance tools for proteomics that are necessary to validate protein biomarker discoveries. In response to these measurement needs, NIST is working with NCI to establish a measurement quality assurance program for cancer biomarker research.

NIST researchers have provided support for the National Cancer Institute's Clinical Technology Assessment for Cancer program by collaborating on study design, providing study materials, and by providing critical data analysis support.

The aim of NCI's Clinical Proteomic Technology Initiative for Cancer is to refine and standardize the proteomic technologies, reagents, methods, and analysis platforms used in cancer biomarker research, to ensure reliable and reproducible research results. One aspect of this program was the establishment of a collaborative network of five research centers in the United States to evaluate and enhance proteomic measurement capabilities for clinical cancer research through a rigorous evaluation of existing technologies and the development of new technologies. To support this effort, NIST provided the necessary reference materials with which NCI's research centers conducted interlaboratory studies. Study data were analyzed at NIST after overcoming the difficulties of sharing and comparing data in the many proprietary and incompatible data formats that are common in proteomic mass spectrometric data.

Future Plans: As the initiative progresses in the next five years, NIST will play a key role in overall study design and support the research carried out in the centers by providing advanced proteomic reference materials in the form of well-characterized human plasma and other clinical specimens, standard test data sets, and libraries of tandem mass spectra of peptides derived from human plasma proteins.

