

Study Of Proteins

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To Revolutionize Cancer Detection

By Randolph Fillmore

The world cheered in 2001 when the human genome – the genetic information contained in the chromosomes – was sequenced (the DNA decoded), and scientists unraveled the human genetic code that makes up our hereditary traits. But our genome is not much more than a “blueprint” for what it means to be human. It doesn’t identify or explain the functional “building blocks” that are so critical for explaining diseases such as cancer. These building blocks are proteins.

In their continuing quest to beat cancer, more and more researchers at Moffitt Cancer Center are taking knowledge gleaned from the Human Genome Project and making a giant step into the world of “proteomics.”

What is proteomics? Simply put, it is the study of proteins and their functions in the body. But it gets complicated because each cell produces thousands of proteins, and each protein has a specific function. This collection of proteins in a cell is referred to as the proteome.

The study of proteomics is important to Moffitt researchers who are looking for proteins that may signal disease with the hope of improving diagnostic and screening tests when those proteins are identified.

Proteins are the products of genes, and because genes are mutated in cancer cells, proteins also are altered during the cancer process, explains Thomas Sellers, Ph.D., M.P.H., director of the Moffitt Research Institute and executive vice president and associate center director for Cancer Prevention and Control. According to Dr. Sellers, altered proteins may no longer function as they should. A better understanding of protein function and alterations might help in detecting cancer, and the altered proteins might themselves become the targets of treatment.

“Proteomics is a science instrumental for discovering biomarkers,” explains Dr. Sellers. “Altered proteins are one type of biomarker.” A biomarker is a substance that can be used to help detect the presence of cancer or other disease in the body as well as to assess the progress of disease or effects of treatment. “One goal of proteomics is to identify proteins that interact with each other and either enhance or disable protein function.”

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A view of a mass spectrometer, which is used in proteomics technology to identify proteins.

Photo by Dick Dickinson

The Technology Behind Proteomics

Proteomics involves the large-scale study of proteins, and the heart of the proteomics facility at Moffitt Cancer Center is equipment that carries out mass spectrometry (MS).

"MS is a process by which we identify and structurally characterize proteins by determining their molecular weights, or mass, and that of their subunits," explains John Koomen, Ph.D., scientific director of Moffitt's Proteomics Core Facility. "Early cancer detection is going to require that we detect minute changes in proteins, so we need to be able to acquire vast amounts of data and delve into the details."

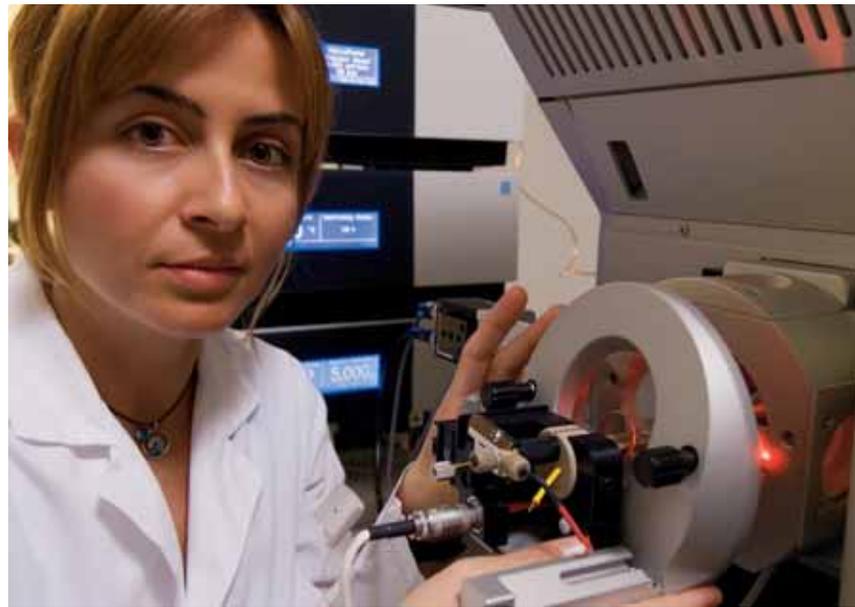
Over the last two decades, MS has served many academic and industrial purposes. However, as chemistry, biology, physics and engineering have converged in medical research, new ways of analyzing biological materials through MS have emerged in recent years, making MS the medical research tool of the future available today. The essential technology, liquid chromatography coupled to tandem mass spectrometry or LC-MS/MS, is used to sequence peptides, which are segments of a protein's sequence.

"In MS/MS, selected peptide molecules collide with background gas in the mass spectrometer, causing the bonds to break," explains Dr. Koomen. The data collected by the instrument enable calculation of the molecular weights of each molecule and its fragments and can be interpreted to determine the peptide sequence. The information collected for each peptide is used to reconstruct changes in each protein and thus target potential biomarkers. If the protein biomarkers related to specific cancers can be identified, ways to detect a number of cancers early, through routine testing, could be developed.

"The goal is to discover the magnitude and consistency of minute differences in the proteomes between patients with cancer and those without (disease-free controls)," says Dr. Koomen. "When we can better identify proteins associated with cancer, and get a better understanding of protein function as associated with cancer we will be able to develop better, more accurate screening and diagnostic tests as well as design more effective drugs and better assess patient response to treatment."

Photography by Dick Dickinson

Umut Oguz, Ph.D., a staff scientist in the Proteomics Core facility. The human body contains more than a million proteins.



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Finding A Screening Test For Ovarian Cancer

Identifying the proteins and biomarkers associated with ovarian cancer is job # 1 for Rebecca Sutphen, M.D., director of Moffitt's Genetic Counseling and Testing Service.

"Current tests miss 30 percent of curable ovarian cancers that would be 90 to 95 percent curable if we had found them in time," explains Dr. Sutphen, who is heading up a five-year study to discover the protein biomarkers for ovarian cancer. "What's more, 75 percent of the women who undergo surgery to see if they have ovarian cancer don't have cancer. If we could come up with an accurate screening tool based on proteomics, we could save time, money and a lot of anxiety for women who might otherwise have to have surgery."

Dr. Sutphen is recruiting women who are being prepped to undergo surgery to see if they have ovarian cancer. She has developed a network of cooperating physicians who request an extra blood or urine sample from their patients, which is sent to Dr. Sutphen for analysis. The analysis is a complex process employing two-dimensional gels, which create a protein array based on acid-base properties and then by protein size.

By finding proteins that conclusively indicate ovarian cancer, Dr. Sutphen hopes a screening tool can be devised.

"Our first goal is to create a better diagnostic tool using protein analysis," explains Dr. Sutphen. "With the hope of developing a screening tool we are setting the bar very high. The differences in proteins that indicate very early ovarian cancer will be difficult to find."