Principles and implications of proteomics in clinical therapy.

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Abstract

Proteomics is the study of dynamic protein expression, post-translational modifications, cellular and sub-cellular protein distribution, and protein-protein interactions. Advances in proteomic technology now offer potential for proteomic profiling to become standard practice in the clinical laboratory. A number of technical obstacles remain before routine proteomic analysis can be achieved in the clinic. Mass spectrometry is an essential tool that is used for profiling proteins in the cell. Biomarker discovery remains the major challenge of proteomics because of their complexity and dynamicity. Clinical applications of proteomics involve the use of proteomic technologies at the bedside. The analysis of human cancer as a model for how proteomics can have an impact is now employing several new technologies. These include early detection, therapeutic targeting and finally, patient-tailored therapy.

Keywords: Proteomics, Clinical therapy, Biomarker, Clinical applications, Molecular medicine.

Introduction

Molecular medicine is moving beyond genomics to proteomics. The ability to access and visualize the entire interconnecting intracellular and extracellular protein "circuitry" inside and outside a cell could have a profound effect on biology. Recognition that cancer is a product of the proteomic tissue microenvironment has important implications. The lack of a specific symptom in early-stage ovarian cancer may provide a new approach for the discovery of early cancer biomarkers. To be effective, a clinically useful biomarker should be measurable in an accessible body fluid such as serum, urine or saliva [1]. There are potentially thousands of intact and cleaved proteins in the human serum. A therapeutically useful biomarker must be detectable in a readily available body fluid, such as serum, urine, or saliva, in order to be successful. Proteomics may have the best possibility of identifying these early stage changes because these bodily fluids are protein-rich information reservoirs that store the traces of what the blood has experienced on its continual perfusion and percolation throughout the body. It used to take a deliberate and lengthy process to look for overexpressed proteins in blood that are released into the circulation as a result of the illness process in order to find cancer-related biomarkers for early disease identification. The idea that every patient's cancer has a distinct complement of harmful molecular derangements is being supported by increasing amounts of evidence. As a result, a certain therapeutic class might only work for a portion of individuals who have malignancies that have sensitive molecular derangements. There is good evidence to support the strategy of selecting from a list of treatment options or combinations that best match the molecular profile of the specific tumor [2,3].

The level of the gene transcript may have little bearing on the phosphorylated or other functional state of the encoded protein, therefore transcript profiling alone might only give part of the story. Gene transcripts don't provide much about protein-protein interactions or the status of the cellular circuitry; instead, correlative bioinformatic methods infer this information. Direct proteome pathway analysis of the biopsy sample is required when using molecular profiling to choose the best treatment plan. A single molecular target is currently the focus of cancer therapy. We may envision addressing a complete set of nodes along the pathogenic signal route in the future. Theoretically, such a strategy will result in greater efficacy with less toxicity. Combinatorial therapy, which is an alternative to single-agent therapy, offers the promise of higher specificity at lower treatment doses. A correctly chosen series of inhibitors acting at several points along the length of the cellular circuit can be employed at low concentration. The use of combinatorial therapy for increased efficacy also may yield a decrease in unwanted toxic side effects [4-6].

Conclusion

Clinical proteomics has significant direct applications at the bedside. These many proteome analyses will be used by pathologists and doctors at numerous stages of managing disease in the future. The paradigm shift will have an immediate impact on clinical practise by affecting all of the following crucial aspects of patient care and management: early disease detection using proteomic patterns of body fluid samples, diagnosis based on proteomic signatures as a complement to histopathology, individualised selection of therapeutic combinations that best target the patient's entire disease-specific protein network, and real-time assessment of therapeutic efficacy.

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