

Proteomics and protein microarray: boon to cancer research and diagnosis

Abstract

Cancer, being one of the most taxing conditions requires functional studies to understand its complex and heterogeneous behavior. Microarray is a powerful tool that allows the simultaneous analysis of the expression of thousands of genes or their RNA products on a single platform. Proteome chip technology is a remarkable high-throughput method used to probe an entire collection of proteins and proved to be a valuable tool in Cancer research and diagnosis.

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Introduction

Cancer relates to uncoordinated, uncontrolled, abnormal growth of cells due to heterogeneous genetic mutations and epigenetic alterations which lead to abnormal expression of genes that regulate these processes. Cancer, being one of the most taxing condition demands functional studies to understand its complex and polymorphic behavior. With the execution of the human genome project, introduction of microarray technology and the emergence of the field of bioinformatics, elementary transformation occurred in the field of cancer research. Analysis of gene expression through these high-throughput technologies is capable of providing potent and previously unattainable diagnostic and prognostic information for several types of cancer.^{1,2} Microarray is an emerging valuable tool that allows the simultaneous analysis of the expression of thousands of genes or their RNA products that is impossible with conventional methods. This technology provides promising improvements in cancer diagnosis and prognosis and therapeutics. The term "Proteomics" encompasses the quantification of all proteins, the determination of their post-translational modifications and how these are affected by cell state and environmental influences.²

Types of protein microarray

Protein microarray technology has been successfully utilized for the recognition, quantification and functional analysis of proteins in basic and applied proteome research and affinity studies.^{3,4} Two basic types of protein microarrays are defined-

Protein function array

Consisting of thousands of native proteins immobilized in a defined pattern

Protein-detecting array

Consisting of large numbers of arrayed protein-binding agents.⁵

Protein microarrays can also be classified as:

Analytical microarrays- profiles complex mixture of proteins in order to measure binding affinities, specificities and protein expression levels in the mixture.

Functional protein microarrays- used to study the biochemical activities of an entire proteome and protein interactions with other molecules.

Reverse phase microarrays- analyses the presence of altered proteins that may be formed consequent to disease process.

Proteome chip technology is an excellent high-throughput method used to probe an entire collection of proteins for a specific function, to study kinase activities and serum profiling.^{5,6} In contrast to protein microarrays DNA microarrays offer knowledge only about the genes specifically and provide information regarding the functional characteristics of the proteins they encode.⁶

Protein microarray and cancer

Cancer is now considered to be a proteomic and a genomic disease. Development and progression of cancer eventually amend the protein network, thus creating survival advantage for the tumor cells.⁷ One of the significant aims of the functional proteomics is to develop a "circuit map" of the normal and diseased state of the cellular protein network.⁸ Protein microarray basically leads to acquisition of information related to posttranslational modifications of proteins reflecting the activity state of signal pathways and networks and is now used for the analysis of biopsy samples in clinical research trials.⁹ With the advent of Protein microarrays, it will be possible to analyze functional dysregulation of proteins in disease-altered cells that occurred before, during and after therapy. Moreover, therapy can be customized to the individual tumor's molecular defect.¹⁰ Knezevic et al.,¹¹ used microarrays to profile proteins in both normal and cancerous epithelium in the oral cavity, as well as in stromal cells adjacent to and surrounding these

tissues.¹¹ Paweletz et al.,¹² used this approach to evaluate pro-survival checkpoint proteins in patient with normal prostate epithelium, prostate intraepithelial neoplasia and invasive prostate cancer.¹² Serum from patients with cancers of the oral cavity, prostate, lung, pancreas, bladder and breast were profiled by antibody arrays.^{11–19}

Although microarray-related studies offers high resolution and a global overview of gene expression, it has got certain disadvantages also like high cost, lack of standards for data collection, analysis and validation, quality and amount of RNA, heterogeneous nature of the tissue samples, small size of clinical specimens, difficulty in isolation of high specificity and affinity protein ligands, need for specialized technical expertise, the need for collaboration between different disciplines and the ambiguity regarding the biological meaning and clinical relevance of the results.^{2,5}

Conclusion

Cancer being a heterogeneous and complex disease warrants expression of panel of antigens rather than single antigen which can be accomplished by the use of Protein microarrays. They proved to have an indispensable role in cancer detection, progression, diagnosis and treatment. Protein microarrays serve to fill the lacunae that exist between genomics and proteomics.

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Conflict of interest

The author declares no conflict of interest.

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