Oncoproteomics : Recent advancements and its future prospects

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ABSTRACT

Oncoproteomics is the branch of science which deals with the study of cancer samples using omics technologies to detect changes implicated in tumorigenesis. It is utilized to understand how the signaling pathways in cancerous cells are altered, thus, improving our understanding of how to target various pathways in cancer therapy. Collaboration of bioinformatics and multi-omics will provide more in-depth knowledge of different diseases. A meta-analysis of large cancer data sets and data-driven in-silico studies will further increase our understanding of cancer biology, while predictive modeling of drug treatment will facilitate individualized prediction of patient responses to treatment. In this paper, we shall discuss about the history of oncoproteomics and its future prospects with current trends of work done in oncoproteomics.

I. INTRODUCTION

Proteomics is the study of the complete set of proteins expressed at cellular, tissue or organism level. Oncoproteomics is the branch of proteomics which deals with all protein interactions taking place in a cancer cell. It involves protein expression profiling, protein modifications, protein-protein interaction, protein structure and function. This emerging branch will help in reducing disease burden, provide diagnosis and prognosis of disease as well as help in anti-cancer drug discovery. Proteomics based technologies had helped to assess tumor prognosis, tumor classification and to identify potential response to specific therapies. A cancer proteome refers to the collection of protein expressed within a cancer cell and should be considered as a highly dynamic entity, which affects a variety of cellular functions. The steps of protein analysis involve protein extraction, protein digestion, peptide fractionation, Liquid chromatography (LC)-Mass spectroscopy (MS) analysis (refer fig 1). Initially, proteins are extracted and purified from tissue or cell lysates using processes like centrifugation and filtration. Afterwards, the protein mixture is usually separated by two dimensional gel electrophoresis to reduce sample complexity, followed by LC-MS analysis for total protein analysis and their peptides, which are produced by enzymatic digestion, and the data are interpreted using a proteome database. The separation is usually performed before the application of MS by ESI(electrospray ionization); in order to reduce sample complexity, MS approaches are coupled with multidimensional LC. ESI is a technique used to volatilize and ionize protein for MS analysis (Cho & Cheng, 2007). Liquid chromatography-mass spectrometry (LC/MS) is a key technique that obtains high-resolution spectra of mixed peptides, allowing the discovery of sensitive and specific biomarkers associated with cancer. It helps in quantitative analysis using either label-based or label-free approaches. Label-based quantitation method allows the quantitative as well as qualitative analysis of proteins in a sample. The methods consist of using stable isotope labeling of compound markers such as amino acids to tag proteins or peptides. But, the proteins are partially labeled since reagents are expensive. To diagnose cancer and other diseases using proteomics, thorough detection of minute quantities and alterations in the expression of specific proteins is required. Although isotope-labeling strategies are precise and accurate, the labeling procedures are complicated and expensive. Furthermore, isotope-based quantification is limited by sample number and is not compatible with all experimental designs. While, label-free quantification (LFQ) approaches are more generally applicable, making them ideally suited for non-targeted discovery proteomics applications.

II. HISTORY

The term *proteomics* was first used in the year 1997. Term *proteome* was given by Mark Wilkins and Keith Williams in 1995, which represents a combination of ‘protein’ and ‘genome’ (Shah & Misra, 2011). Cancer is the second leading cause of death worldwide following heart diseases, but it may overtake it soon, because of the absence of early detection and treatment of cancer due to lack of sensitive and robust

technology for detection of cancer cell signatures from minute quantities of available tissue or serum. Proteomic technologies are being used in an effort to correct some of the deficiencies in traditional drug discovery. Proteins are important targets for drug discovery, particularly for cancer as well because there is a defect in the protein machinery of the cell in malignancy. Because proteome analysis can produce a comprehensive molecular description of the differences between normal and diseased states, it can be used to compare the effect of candidate drugs on the disease process.(Jain, 2008).

III. CURRENT STATE OF ART

Proteomic technologies are being used in an effort to remediate some of the shortcomings of traditional drug discovery. Proteins are important targets for drug discovery, especially for cancer, because there is a defect in the protein machinery of the cell in a malignant disease. Because proteome analysis can provide a comprehensive molecular description of the differences between normal and disease states, it can be used to compare the effect of candidate drugs on disease processes. The 'OMICs' revolution brings the ability to generate, analyze and decipher large amounts of qualitative and quantitative proteomics data and integrate this with data from other related disciplines. Precision or personalized or P4 medicine represents a shift from the current "one size fits all" model of disease treatment to a situation where the right drug at the right dose for the right patient at the right time becomes the new paradigm. Significant technological advancements have been made in proteomics, especially oncoproteomics, over the past decade, single cell analysis is becoming a reality, and our understanding of the complex biology underlying the hallmarks of cancer and disease heterogeneity is rapidly expanding (He et al).

IV. FUTURE PROSPECTS

Though proteomics is found to be complementing genomics-based approaches, providing additional information, it presents with various challenges in technical aspects, data collection and its inference. For example, there is no technique equivalent to polymerase chain reaction for amplification of low-abundance proteins, so a range of detection from one to several million molecules per cell is needed (Shruthi et al., 2016). Multi-omics approach, a collective omics-technology involving genomics,transcriptomics and proteomics will open-up new avenues in the oncology branch. Table 2 discusses the use of multi-omics with respect to various types of cancer. Collaboration of bioinformatics and multi-omics will provide more in-depth knowledge of different diseases. A meta-analysis of large cancer data sets and data-driven in-silico studies will further increase our understanding of cancer biology, while predictive modeling of drug treatment will facilitate individualized prediction of patient responses to treatment (He et al., 2019).

CONCLUSION

The ultimate aim of oncoproteomics is to develop proteomics technologies for enhanced use in clinical laboratories for the purpose of diagnostic and prognostic classification of cancer stages, as well as in drug toxicity and efficacy evaluation. Speed and accuracy are very important for the application of proteomic methods in clinical medicine.Cancer involves aberrant cell proliferation, in which the cell cycle of the normal cell becomes dysregulated due to a variety of genetic alterations. It can occur in any tissue of the body and is characterized by its ability to invade or spread to other tissues and organs. In particular, malignant tumors not only grow rapidly and metastasize to various other tissues but can also develop resistance to the drugs used in treatment, thereby threatening the life of patients. Proteomics has emerged as an important research tool for exploring the biological changes in cancer. Based on proteomics technology, key information such as protein targets and signaling pathways related to the growth and metastasis of cancer cells have been identified. The proteomic approach in cancer research has explored molecular mechanisms and provided key insights into cancer growth, metastasis and therapy. Recent cancer is important proteome databases are implemented globally and can be freely accessed and used through integration with bioinformatics.The advent of oncoproteomics has provided the hope of discovering novel biomarkers for use in screening, early diagnosis, and prediction of response to therapy.

Fig 1 - Basic Steps of proteomic analysis

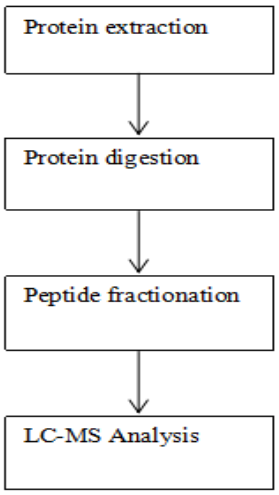

Table 1 -Types of methods in quantitative proteomics

Proteomics method	Quantificatio n method	Type	Principle
LC/MS-based proteomics	Labeling	-ICAT -iTRAQ -SILAC -TMT	Isotopic labeling used in quantative proteomics by MS with the help of chemical labeling reagents.
	Label-free	-MRM -SWATH	Method for relatively quantifying differences of concentration between independent samples

Table 2 - List of cancers with its biomarker identified by proteomics analysis

Types of cancer	Method of target discovery	Biomarker/target	Type of biomarker
Breast	Proteomics, transcriptomics, phosphoproteomics	GR, PYCR1	Prognostic
Lungs	Proteomics, transcriptomics	Bach1, Ho1, MTOR	Therapeutic
Colon	Proteomics, genomics, phosphoproteomics	Rb phosphorylation	Therapeutic
Prostate	Proteomics, genomics	ACADB	Prognostic
Gastric cancer	Proteomics, genomics, proteogenomics	CTGF, NRP1, RAB23, AXL, RHOA, ARID1, CDH1, TNK	Prognostic
Endometrial carcinoma	Proteomics, genomics,transcriptomics	CTNNB1, AURKA,TP53	Therapeutic
Pancreas	Proteomics	LKB1	Prognostic
Ovary	Proteomics	NNMT	Therapeutic
Myeloid leukemia	Proteomics	IL3RA, CD99	Therapeutic

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