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REVIEW ON PROTEOMICS: APPROACH TO DRUG DEVELOPMENT

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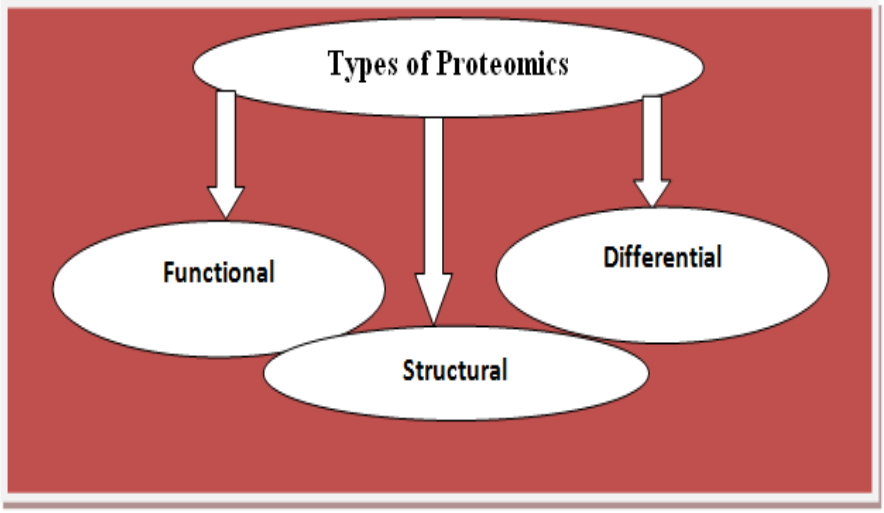
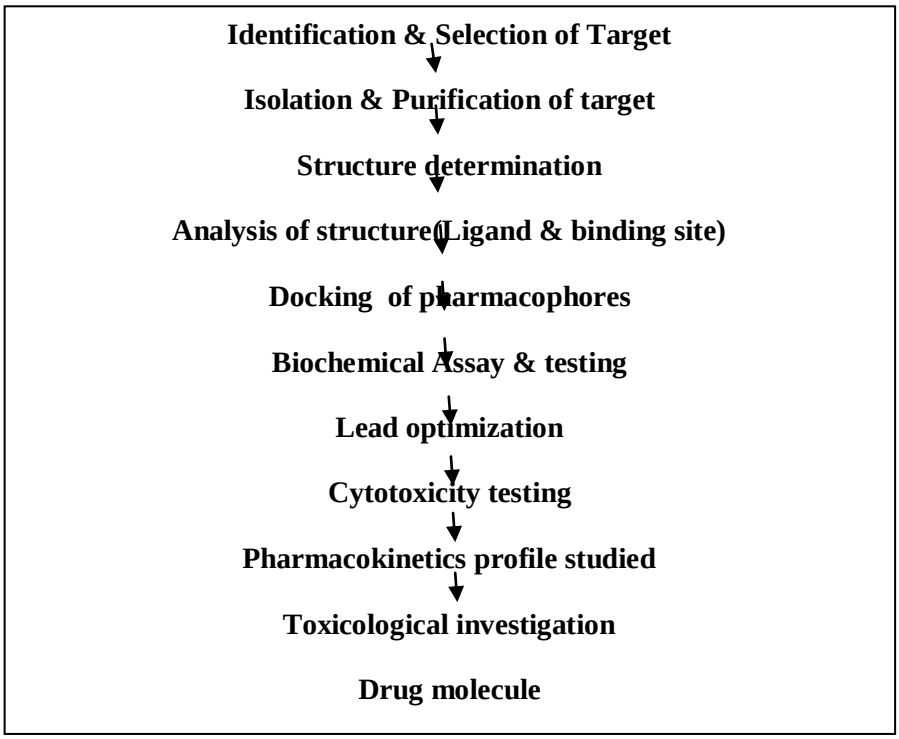
ABSTRACT
Drug discovery is a long-lasting and highly expensive process that uses a variety of tools from diverse fields. Proteomics, is defined as the total protein content of a cell or that of an organism. Proteomics helps in considerate of modification in protein expression during different stages of life cycle or under stress condition. Proteomics helps in illustrating the structure and function of different proteins as well as protein-protein interactions of an organism. Proteomics has wide applications on drug development against several diseases. Variation in protein expression profile of normal and diseased person may be analyzed for target protein. Protein to gene may be predicted. Once protein/gene is identified, function may be predicted. This can assist in disease management which leads to the drug development. The present review aims to provide a basic considerate of proteomics research in field of drug development.

KEYWORDS: Proteomics, Protein structure, Metabolomics & Drug development.

INTRODUCTION
The word "proteome" denotes the complete protein pool of an organism encoded by the genome. In broader term, Proteomics, is defined as the entire protein content of a cell or that of an organism. Proteomics helps in perceptive of alteration in protein expression during different stages of life cycle or under stress condition. Likewise, Proteomics helps in understanding the structure and function of different proteins as well as protein-protein interactions of an organism.A minor defect in either protein structure, its function or alternation in expression pattern can be easily detected using proteomics studies. This is important with regards to drug development and understanding various biological processes, as proteins are the most favorable targets for various drugs. The terms "proteomics" and "proteome" were coined by Marc Wilkins and colleagues in the early 1990s and mirror the terms"genomics" and "genome," which describe the entire collection of genes in an organism. These "-omics" terms symbolize a redefinition of how we think about biology and the workings of living systems.[1]



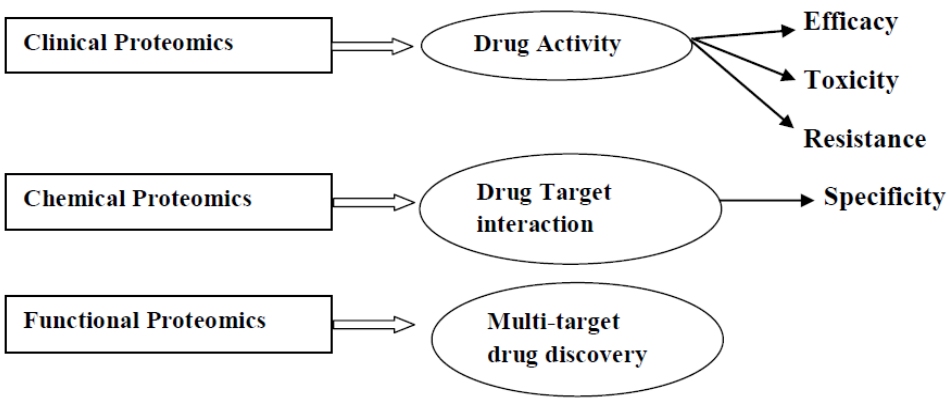
Proteomics combines aspects of biology, chemistry, engineering and information science and apply them to all areas of drug discovery. Introduction of safer, more effective and more cost-effective drugs will be the ultimate outcome of improvement of this technology.[2] The course of action of drug discovery is quite complex, integrating many disciplines, including structural biology, metabolomics, proteomics, and computer science, just to name a few. The process of drug discovery involves the identification of candidates, synthesis, characterization, screening, and assays for therapeutic efficacy. The process of drug development prior to clinical trials begins, when a compound has shown its value in the above tests. The process is generally quite tedious and expensive.[3] Various steps of drug development are as follows.



Role of Proteomics in drug development

Recent advances in functional genomics helped in the target identification process, since it allowed for high throughput screening of expressed genes. However, studies have shown that there is a poor correlation between the regulation of transcripts and actual protein quantities. The reasons for this are that genome analysis does not account for post-translational processes such as protein modifications and protein degradation. Therefore, the methods employed in the drug-discovery process started to shift from genomics to proteomics. Proteomics is large-scale study of proteins; particularly their structures and functions.[4-5] Proteins are essential parts of living organisms, as they are the main components of the physiological metabolic pathways of cells.

Role of clinical, functional and chemical proteomics in the modern process of drug discovery.[6]



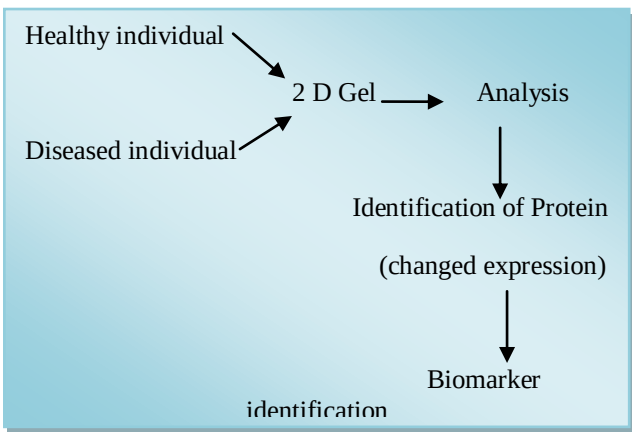
Functional proteomics has been broadly applied to mapping signaling pathways in a number of pathologies and the enormous literature published in the last ten years exceeds the scope of a single review.

Chemical proteomics is a multidisciplinary research area integrating biochemistry and cell biology with organic synthesis and MS. The recent developments in affinity-based enhancement techniques in combination with MS have enabled the direct determination of protein binding profiles of small molecule drugs under more physiological conditions. In this framework, chemical proteomics represents one of the most direct approaches to screen for drug–protein interactions.[6-7]

The proteome proceedings the flow of information that starting within the cells, through the intercellular protein network, goes beyond the extracellular micro-environment up to come to the blood macro-environment.[8] The proteome may reflect immediate and characteristic changes in response to disease processes and external stimulation. Like the proteome, the proteolytic degradation products of the proteome, the so-called low-molecular-weight (LMW) proteome, or peptidome, may also have the potential to contain disease-specific information.[9-10] The peptidome is also referred to endogenous peptides which have very specific functions as mediators and indicators of biological processes, which play important roles as messengers, e.g., as hormones, growth factors, and cytokines, and thus have a high impact on health and diseases. With the aid of proteomic tools such as MS, it is possible to qualitatively and quantitatively reveal molecular profiles contained in healthy or clinical samples.

Proteomics approach on Biomarker Discovery and Drug Development

Proteomics is being widely used to study molecular basis of various diseases and development of novel drugs with superior understanding of targets. Considerable interest has been generated in identifying disease biomarkers. It is a molecule that indicates changes in the physiology of a cell under diseased state and hence can be used as a diagnostic tool, therapy guidance and prognosis monitoring of diseases.[11]

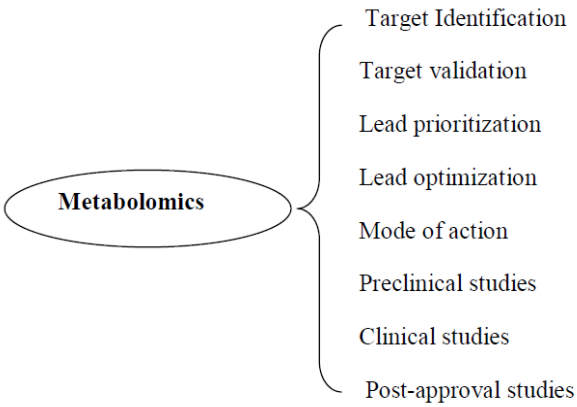


Some example of anovel biomarker was identified by comparative proteome analysis are; Breast cancer (HSP27, HSP60, HSP90), Lung cancer(Cytokeratins), Bladder cancer (Keratins, Psoriasin), Leukemia(Op18,nm23-H1).

Metabolomics united with proteomics: Advancement in drug discovery

The word "metabolome" refers to the complete set of small-molecule metabolites to be found within a biological sample, such as a single organism. Metabolomics is defined as "the quantitative measurement of the dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modification". The approach was pioneered by Jeremy Nicholson at Imperial College London. Nuclear magnetic resonance (NMR), LC/MS, and GC/MS are the most common technologies in metabolomics research.[12]

Metabolomics has wide applications across the drug discovery and development processes. Metabolon's proprietary technology raised area in metabolomics will enable faster and more cost-effective processes[13] in the following areas.[14]



CONCLUSION

Proteomics is a science that focuses on the study of proteins: their roles, their structures, their localization, their interactions, and other factors. Proteins are the main targets of drug discovery. Drug discovery is a long-drawn-out process that uses a variety of tools from diverse fields. To go faster the process, a number of biotechnologies, including genomics, proteomics and a number of cellular and organism methodologies, have been developed. Proteomics development faces interdisciplinary challenges, including both the traditional (biology and chemistry) and the emerging (high-throughput automation and bioinformatics). Emergent technologies include 2-D gel electrophoresis, MS, Protein arrays, two-hybrid systems, isotope-encoding, information technology and activity-based assays. These technologies, as part of the array of proteomics techniques, are advancing the utility of proteomics in the drug-discovery process. At each step of the drug discovery process there is often scope for

flexibility in interpretation, which over many steps is cumulative. The pharmaceutical companies most likely to achieve something in this environment are those that are able to make informed accurate decisions within an accelerated process. The proteomics riot has impacted very positively upon these issues. The ability to undertake global analysis of proteins from a very wide diversity of biological systems and to interrogate these in a high through put, systematic manner will add a significant new dimension to drug discovery. Widespread applications of proteomics in the drug industry include target identification and validation, identification of efficacy and toxicity biomarkers from readily accessible biological fluids, and investigations into mechanisms of drug action or toxicity. Target identification and validation involves identifying proteins whose expression levels or activities change in disease states. These proteins may provide as potential therapeutic targets or may be used to classify patients for clinical trials.

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