Review Article

Multi-Omics Approach in Neurodegenerative Diseases: A potential Utility in Clinical Practice

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Abstract

Neurodegeneration is a multifactorial disease rising rapidly in prevalence world-wide. The diagnosis and management of neurodegenerative diseases have been substantially enhanced because of the "omics" research. Technological advancement in genomics, epigenomics, proteomics, metabolomics and pharmacogenomics helps to develop multi-omics tools to identify biomarkers and therapeutic targets. Extensive studies on the biomolecules including nucleic acids, protein and metabolites have revealed remarkable changes in genomic, transcriptomic, proteomic and metabolomic profiles in patients with neurodegenerative diseases. Data gained from multi-omics technology provide a complete spectrum of molecular information that provides several novel diagnostic, prognostic and treatment targets for neurodegenerative diseases. This review discusses the significant contributions of multi-omics approaches towards translational research in neurodegenerative diseases.

Introduction

The diagnosis and treatment of neurodegenerative disease had improved because of the availability of high-throughput technologies in genomics, epigenomics, transcriptomics, proteomics, metabolomics, and pharmacogenomics[1]. The progress in these technologies leads to the development of personalised medicine. Investigating the different classes of biomolecules like DNA, RNA, proteins and metabolites have paved the way to detect 1) change in genes, 2) altered gene and protein expression and 3) metabolites concentration in body fluids and in cellular compartments. These details allow us to draw associations and understand intricacies of the neuropathophysiology. Data derived from the omics platforms gives a wide spectrum of information to development a new diagnostic marker and drug targets for neurodegenerative therapy.[2] Here, I present recent research developments in a neurodegenerative disease focusing especially on interconnected multi-omics techniques that contribute to translational research in the neurodegenerative disease.

The aim of precision medicine is to improve the diagnostic procedure and disease-specific drug targets. This can be partially resolved by identifying the molecular and cellular characteristics of disease-affected patients. This has led to the identification of genetic markers to predict disease status and treatment response. The currently available technology allows access to the genomic platform, to generate and analyse the massive genomic sequence and finally to determine the disease-specific biomarkers for diagnosis.[3] Any diagnostic biomarker needs adequate sensitivity and specificity to the targeted disease that is distinct from several confounding factors. Current technological advancements thus allow us to decide on personalized or population-specific diagnosis and/or treatment.

Genomics

Several studies suggest that a genetic factor is one of the major contributors of neurodegenerative diseases.[4] Certain changes in genomic sequences like nucleotide variations including single nucleotide polymorphism, insertions, deletions, genomic rearrangement, copy loss and gain can cause neurodegeneration.[5] Studying the genetic variations with Sanger sequencing or next-generation sequencing (NGS) help to understand the pathogenesis of neurodegeneration.[6] NGS technique generates a high quantity of data that enables to recognize genomic signatures that define specific neurodegeneration. Similarly, the data from Genome-wide

association studies (GWAS) allow us to detect causative genes in disease. For instance, PARK1, SNCA and PINK are identified as candidate genes for Parkinson's disease.[7] Studying gene expression using transcriptome techniques will be more informative providing differentially expressed genes between disease and normal healthy individuals. Further, the annotation of the differentially expressed genes showed involvement in molecular pathways.[8] Determining the gene defects enable us to understand the pathophysiology of the disease and further help to discover the genetic inheritance pattern of the disease to develop the personalised drug. The combined data of transcriptome and GWAS profile would enable the researchers to determine the complex gene network involved in the disease's pathogenesis.

Proteomics

Although the genomic studies of the disease are useful, they do not provide the details of mechanistic evidence behind the disease. As proteins are the molecules involved in the cellular action, their milieu in the cell or bio-fluids reflects their molecular behaviour in affected patients.[9] Advances in proteomic techniques help to detect and quantify thousands of proteins in one snapshot. Currently, chromatography and two-dimensional electrophoresis are more frequently used for proteomic studies in clinical samples.[10] Several studies relating to neurodegeneration and proteomics have shed light on the protein markers for the early diagnosis, prognosis and novel drug target for neurodegenerative diseases. For instance, 8-Hydroxydeoxyguanosine (8-OHdG), Ubiquitin C-Terminal Hydrolase-L1 (UCH-L1), Tau Protein, Brain-derived neurotrophic factor and β-Glucocerebrosidase has been reported as potential biomarkers for PD. Also, the proteomic study may provide information on dysregulating molecular pathways that help to discover a novel therapeutic drug target for disease management.

Metabolomics

Metabolomics is an emerging technology that provides the levels of metabolites in bio-fluids or tissues in normal or disease states. Recently, techniques like gas chromatography, LS-MS (Liquid chromatography-Mass spectrometry) and NMR (Nuclear magnetic resonance) are used to estimate the concentration of hundreds of metabolites in urine, feces, tissues, blood, saliva, sputum, seminal fluid, etc.[11] The major advantage of studying metabolomic profiles is to correlate the association between metabolite and progression of the disease and thus help in disease management. The Previous study reports the change in metabolites of TCA cycle that dysregulated mitochondrial function in PD.[12] In the near future, metabolomics biomarkers could help to identify the false-negative or false-positive results derived from the gold standard method of diagnosis

Pharmacogenomics

Pharmacogenomics deals with a genetic response to a drug in diseased individuals.[13] This technique combines pharmacology and genomics to develop effective, safe medications and doses designed based on an individual genetic pattern. Pharmacogenomics is hypothesized that individual genomic content has a major influence on drug sensitivity such as benefit, resistance, or toxicity. Particularly, pharmacogenomics is focused to study the variations in the drug response in each individual due to the difference in genomic patterns. Thus it develops a personalized medicine and targeted therapy to improve the efficacy of drug treatment and reduce its toxicity.[14] To explain the interdependency between gene and drug response, the pharmacodynamic and pharmacokinetic effects of the drug will be assessed. Pharmacodynamic deals with the intensity of drug response in an organism. Whereas, pharmacokinetics analyses the rates of the drug absorption, distribution, metabolism and elimination properties. The methods like whole genome-sequencing (WGS) and whole-exome sequencing (WES) have improved the opportunity to study and understand the response to drugs by a whole ethnic group.[15] Nowadays, the pharmacogenomics concepts are implemented to a vast epidemic or pandemic area of disease to avoid adverse effects of drugs.

Omics integration

In recent years, even though enormous data are generated from high-throughput techniques, it becomes a challenge for the scientist to integrate data from different sources to extract meaningful information. Classical statistical methods are less powerful to explain the underlying etiological factors of diseases. Hence, scientists have adopted the new concept of systems biology with a machine learning algorithm. Such a concept is being applied in medical research that potentially uncovers a novel mechanism involved in the diseases. Currently, systems biological approach has gained interest from the researchers, which helps in the integration and analysis of multi-omics data to retrieve meaningful information on the functional perspective of disease.[16] This approach involves the creation of a molecular network with genomics, proteomics, and metabolomics and metallomics data to identify core regulatory molecules involved in pathogenesis. This approach uses high-end computational facilities with collective knowledge on multi-omics data analysis and integration. Recently, the concept of machine learning is being implemented to the systems biological approach that enable the

machine learning algorithm to get trained from known omics data to predict the disease states. With such a framework several attempts are made to classify an individual as normal or diseased. Given an increase in omics data, such as DNAseq, ExomeSeq, RNAseq and miRseq, the scope of systems biology has expanded to adopt new algorithms to integrate omics data to predict and classify complex neurodegenerative diseases with similar symptoms and features.

Conclusion

With the inception of multi-omics and its application in the health care industry, the processes of diagnosis, prognosis and patient management have made greater strides in the health front. Particularly, the usage of NGS sequencing with proteomics and metabolomics techniques in neurodegenerative disease showed opens up a new method for critical diagnosis and treatment. Although multi-omics researches have made much in-roads into the realm of the health industry, the journey seems to be in-complete.

Conflicts of interest

All the authors declare that they have no conflict of interest

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