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ADVANCEMENT OF BIOTHERAPEUTICS WITH MULTIOMICS: A REVIEW

Dr. Sharique Ahmad*[1], Raushan Kumar[2] Tanish Baqar[3], Pushpendra D. Pratap[4]

[1]Professor, Department of Pathology, Era's Lucknow Medical College & Hospital, Era University, Lucknow, India.
[2]Research Analyst, Department of Pathology, Era's Lucknow Medical College & Hospital, Era University, and Lucknow, India.
[3]Medical Intern, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh, India-226003.
[4]Research Scholar, Department Biochemistry, Era's Lucknow Medical College and Hospital, Era University, Lucknow, Uttar Pradesh, India -226003.

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***Corresponding Author: Dr. Sharique Ahmad**

Professor, Department of Pathology, Era's Lucknow Medical College & Hospital, Era University, Lucknow, India.

ABSTRACT

There has been a consistent increase in the prevalence of chronic diseases, encompassing both noninfectious and infectious conditions, which has necessitated the adoption of a multidisciplinary approach to comprehending and managing these ailments. The present state of medical care emphasizes the treatment of individuals once they have transitioned into patients, rather than prioritizing preventive measures to mitigate the occurrence of illnesses. This approach has resulted in substantial financial burdens associated with the management of chronic ailments and diseases that have reached advanced stages. Moreover, the implementation of a universal health care system fails to include the unique variations in genetics, environment, and lifestyle characteristics across individuals, hence limiting the potential number of individuals who can derive benefits from such interventions. The rapid advancements in omics technology and the improvement of computational skills have facilitated the emergence of multi-omics deep phenotyping. This method enables the comprehensive analysis of the interplay between several biological levels throughout time, hence enhancing the effectiveness of precision health strategies. This review provides an overview of the current technical classifications of multi-omics, highlights experimental design considerations, emphasizes the integrated analysis techniques used in multi-omics research, particularly the use of machine learning and deep learning to integrate multi-omics data, and discusses the tools involved. It also explores the applications of multi-omics in medical research, particularly in the areas of cancer, neurodegenerative diseases, and aging.

KEYWORDS: Multi-omics, Neurodegenerative disease, Cancer, Proteomics, Genomics.

1. INTRODUCTION

The term "multiomics" refers to the collection of "multiple omics," which offers an integrated perspective to facilitate discoveries on several levels of biology. The genomic data are combined with data from other modalities such as transcriptomics, epigenetics, and proteomics in this method of biological study. The goal of this method is to quantify gene expression, gene activation, and protein levels.[1] Studies that use the multiomics profiling approach make it possible to gain a more holistic picture of the molecular changes that contribute to normal development, cellular response, and illness. Researchers can more effectively relate genotype to phenotype and fuel the identification of novel therapeutic targets and biomarkers by making use of technologies that integrate several omics.[2]

The degree of gene expression and, ultimately, the amount of protein generated, are both correlated with the disease's stage. Additionally, a gene mutation or mistake in the transcription, translation, or any aspect of a gene's function may be linked to the development of a disease. In the actual study, one kind of omics research is only capable of performing correlation analyses with diseases, which mostly indicate changes in the disease process but are unable to explain the cause relationship.[3] Even if a biological molecule is statistically linked to a disease, such as Alzheimer's, it cannot fully explain the intricate mechanisms that underlie the illness. Integration of several omics data types can reveal the pathogenic

changes that are the main cause of the disease, which can subsequently be confirmed through additional molecular studies.[1,2] By incorporating multi-omics, researchers can build precise disease biomarkers, discover pertinent signaling pathways, and eliminate novel connections between biomolecules and disease symptoms. As a result, the matching of connections between molecular disease and phenotype-environment components will be made easier by the combinations of various omics data. Estimating and identification of the chronological age of various organs like the liver, kidneys, lungs, pancreas etc,[4] and their structures aspect including both immune and metabolic systems using a multi-omics approach is an example of how molecular profiling in important tissues can reveal molecular mechanisms of disease progression by integrating multi-omics.[5] In this study, we addressed the experimental approach, research correlation, data integration, medical problems, obstacles, and achievable emerging and future directions of multi-omics, and briefly summarised their use in human disease research.

2. The Omics' Categories

There are now many different forms of omics in the medical profession thanks to the advancement of high-throughput technologies, mostly comprising transcriptomics, or transcript the field of proteomics technologies, epigenomics that describes changes in DNA, single-cell omics for the study of each cell and every cell sequencing, spatial transcriptomics, radio mics, metabolomics, and microbiomics.[6]

2.1 Proteomics

Proteomics is used for the study of all proteins that are present in cells or tissues and measures all their domains. The level of gene transcription is frequently influenced with the aid of posttranscriptional changes, consequently, there is typically no link between RNA evaluation and their respective protein expression.[7] Proteomics can consequently measure protein expression and offer facts that are directly related to adjustments in the environment or the development of disease. Protein chips or specific amino acid-based chips, reverse-phased protein microarrays, affinity proteomics, and mass spectrometry-based strategies can all be used to discover the very big scale of proteins.[8] Labeled proteomics can significantly minimize the batch impact between samples and the result detection time of mass spectrometry, while steady isotope labeling proteomics and label-free proteomics are both commonly employed in present-day medical research.[9]

2.2. Genomics

The study of complete sequences of genomes and DNA sequence variants therein, together with just a single nucleotide change, insertion-deletions, adjustments in structure, and copy range adjustments, is referred to as genomics, the most developed of all omics technologies.[10] Since the discovery of "Sanger sequencing" of DNA in 1977, genomic evaluation has advanced dramatically.[11] Genomes can now be analyzed extra quickly, inexpensively, and throughput-wise due to the fact of the improvement of next-generation sequencing (NGS) technology in current years. The value of sequencing a genome has constantly decreased from billions of bucks in 2000 to simply $100 per genome in 2022.[12]

2.3 Epigenomics

The term "epigenomics" describes the complete cataloging of the chemical changes in DNA and its surrounding histones. In the 1960s, DNA methylation and histone alterations were discovered, accelerating the development of the self-discipline of epigenomics.[13] Precise mapping of genome-wide methylation patterns and other epigenetic markers affecting gene regulation has been enabled by the use of a variety of NGS techniques, including DNA methylation by methods such as bisulfite DNA sequencing, reduced representation bisulfite sequencing, methyl-Seq, methylated DNA immunoprecipitation, and enzymatic methyl sequencing.[14–16] The four simple proteins named histone proteins such as H2A, H2B, H3, and H4 structure dimers that make up the histones around which DNA is wrapped. These proteins undergo a series of posttranslational modifications such as ubiquitination, acetylation, methylation, prenylation, phosphorylation, and sumoylation that decide the fate of genes whether they are turned on or off.[17] Early techniques for analyzing histone modifications used immunoprecipitation with antibodies against specific DNA histone modification sites, but their throughput and cost were limited. The invention of the ChIP There are now many different forms of omics in the medical profession thanks to the advancement of high-throughput technologies, mostly comprising transcriptomics, or transcript the field of proteomics technologies, single-cell omics, metabolomics, and microbiomics, which allowed identification of genomic DNA regions enriched in specific modifications by DNA hybridization on a microarray, has improved epigenomics research.[2,18,19]

2.4 Single-cell omics

In recent years, single-cell genome sequencing has rapidly gained importance in clinical research.[20] The variability of transcriptomics, genetics, genomics, proteomics, and epigenomics in mobile populations and the corresponding adaptations at these levels are well understood using single-cell sequencing.[21] Single-cell transcriptomics, more specifically, seeks to accurately characterize the transcriptome of different and other populations. The genetic diversity of cells with or without changes in genetic material, i.e. either mutation or not accumulation is detected using single-cell genomics. Single-cell epigenomics is used to detect the signs of differentiation of a cell.[22] For example, the single-cell transcriptome revealed unique transcriptional modules that can also be associated with early therapy resistance in mobile lung cancer lanes (CCLs) that were responsive and insensitive to receptor tyrosine kinase

inhibitors. Acute myeloid leukemia cells with RAS /MAPK mutations are resistant to FLT3 inhibitors, as revealed by DNA sequencing in a single cell. ChIP sequencing in a single cell of resistant breast cancer cells revealed a different H3K27me3 pattern.[21,23]

3. Multi-Omics Applications in Human Diseases

We will talk about different possibilities of multi-omics in the field of human diseases, such as most cancers and neurodegenerative diseases, in addition to the types of omics mentioned below, multi-omics lookup design, and multi-omics statistical integration testing. In addition, multi-omics is used in the study of aging and the identification of therapeutic targets.

3.1 Biomarkers and goals for disease

The involvement of multi-omics and computational algorithms is becoming more and extra essential in illness research due to the super benefits and knowledge of multi-omics in the identification and detection of sickness etiological pathways. Biomarkers offer distinctive advantages in successfully and exactly detecting early, mild level, acute, and low-level harm, giving early detection, prognostic utility analysis, and specific staging and classification of diseases.[2,24] They can also also have a look at the pathophysiology at the molecular level. A key component in determining the cause and prognosis of scientific disorders is the detection of disease biomarkers. Screening for biomarkers typically entails the use of high-throughput omics methods to analyze giant portions of scientific samples, accompanied by using screening for statistically important differential molecules, observed with the aid of a collection of elaborate bioinformatics analyses to weed out the target biomarkers.[6,25]

3.2 Multi-omics applications in neurodegenerative disorders

The prevalence of AD has been rising over time as the most regularly occurring neurodegenerative illness. According to World Public Health Research, there will be around one hundred fifty million AD patients worldwide by the year 2050, up from the current 57 million, which would result in a tremendous increase in medical and social expenditures.[26] Even though severe pathological modifications in AD have been recognized via amyloid plaques and tau neurofibrillary tangles, there is presently no treatment for AD, and its pathophysiology is nonetheless poorly understood. Therefore, a thorough appreciation of the molecular pathways underlying the pathophysiology of AD via multi-omics will help in assisting AD prognosis, prevention, and treatment.[27] The pathophysiology of AD will be absolutely and methodically printed through systematic combination and integration of multi-omics disciplines, together with the gene level protein level, transcription level and metabolome level. To apprehend the underlying motives of AD, genomics, the science of cataloging and measuring every single gene and alteration in an organism, is essential. Examples of these high-risk mutant genes include APP, PS1, Tau, APOE4, and others.[28] An effective technique for analyzing gene regulatory and expression or suppression mechanisms, transcriptomics can map the co-expressed genomes of transcriptional applications linked to AD symptoms.

3.3 Applications in Aging Study

Multi-omics is not only studied in aging research but also simple and scientific disease research. Mutations in genetic material, epigenetic changes, aberrant protein aggregates and autophagy problems, immune system complications, mitochondrial disturbance, telomere length shortening, improper intracellular signaling, barriers to nutrient uptake, and other physiological changes are all signs of aging.[29] Aging is a process in which the physiological process does not work properly. These transformations hinder cells' capability to function and aid in the emergence of age-related illnesses. Additionally, as getting old is a key contributor to practical decline as well as the biggest threat component for many persistent diseases, there is a want to create techniques for calculating an individual's fee of aging. The hyperlink among organ biomarkers, phenotypes (molecular biomarkers), and medical presentation can be described methodically to address the study of aging.[30] The creation of omics-based biomarkers, which are more manageable for measuring multifactorial processes, is a good sized and rising subject in the science of aging. In recent years, various techniques like high-throughput sequencing, and mass spectrometry, have been used to profile the genes, gene products, epigenetic changes, and/or metabolites that happen with aging. In addition to genetic predisposition, aging is a very complex system that is controlled by using an extensive range of other variables. However, it is still arguable how tons variance in the human getting older process is influenced by using the genetic version. Epigenomics suggests a sluggish decline in total DNA protein methylation degrees with age, and cytosine methylation-containing CpG websites are hypermethylated or hypomethylated at specific genomic places with age.[6,31] These epigenetic modifications, which are particularly variable all through the lifestyle cycle and conceivable biomarkers in response to aging, are also recognized as epigenetic modifications. Aging causes a huge exchange in the transcriptome, and these changes are specifically tissue-specific. Through the use of ML algorithms and a transcriptome investigation of muscle tissue, Mamoshina et al. observed tissue-specific indications of aging.[32]

3.4 Multi-omics approaches to most cancer research

High-throughput applied sciences have developed rapidly in the course of the previous few decades, enabling a range of genetic investigations at the cell and tissue levels. A thorough collection of gene expression information, such as RNA sequencing microRNA profiling, and DNA methylation profiles has additionally been made viable utilizing fantastically advanced genome screening technologies, such as total exome sequencing (WES) and complete genome sequencing

(WGS).[20,33] The comprehension of gene expression and cytological points at the cellular level is improved by utilizing single-cell technology. The improvement of mass spectrometry strategies has also made it feasible to accurately observe large quantities of proteins and metabolites. Nearly all human proteins can now be detected with the usage of proteomics technologies, which are additionally moving nearer to single-cell resolution. To recognize the complexity of most cancer genomes or to pick out a strong relationship with cancer driver mutations, however, just one platform is insufficient.[34] To overcome the cutting-edge complexities caused using genetic and phenotypic heterogeneity that hinder our understanding of most cancers' genesis and progression, and to diagram efficient predictive models to validate novel cures and drugs, multi-omics studies intend to discover patient subgroups and biological traits underlying most cancers' pathophysiology.[35]

4. Difficulties of Multi-Omics and Future Directions

Even while multi-omics is essential for advancing the lookup of human diseases, aging, finding natural therapeutic targets, and more, it is no longer except issues and difficulties. An early approach of multi-omics analysis concerned analyzing many data kinds one at a time earlier than combining the findings to create a thorough network of molecular relationships. Since there have been large achievements and developments in this area, algorithmic meta-analysis frameworks and methods have taken center stage for a thorough examination of multi-omics data.[5] Multi-omics integration analysis does, however, additionally confront quite a few opportunities and obstacles, such as addressing lacking values, heterogeneity between a range of omics, obstacles in deciphering multiomics models, and issues with records annotation, storage, and computational resources. The compilation of multi-omics records is extensively impacted by the variability amongst more than a few omics.[36] The precision levels of various omics applications differ, and the proportion of noise to signal in multi-omics measurements frequently affects the incorporation of multi-omics data. For example, proteomics encourages the finding of highly expressed proteins, but transcriptomics often overlooks this. Because of this distinct signature, proteomic data influence the research on the relationship between gene and protein expression. To decide the ideal sample dimension needed for a variety of omics to gain a particular statistical power, eighty-one algorithms have been developed.[37]

5. CONCLUSION

Improving in the field of technology plays a very important role in the development of precision medicine in the upcoming years. The comprehensive assessment of organic multi-omics facts indicates the biological or diseased molecular map in the context of good health or disease. Multi-omics is undeniably gaining traction in medical research. As technology advances, it is likely to help demonstrate the pathogenesis of life-threatening diseases like cancer, cardiovascular disease, diabetes and neurodegenerative diseases, as well as present a fundamental molecular theoretical framework for medical evaluation, treatment, and prognosis. One of the biggest challenges now confronting the discipline is the design of multi-omics research, particularly the combined examination of multi-omics data. The development of high-throughput technologies and medical treatments has led to the integration of numerous omics technologies into disease research. High-profile research publications often demonstrate their ingenuity and strength in extremely sophisticated experimental designs or analytical methods, as well as in the application of superior omics technologies. Because omics evaluations are often both time-consuming and expensive, careful attention must be paid at the outset of the investigation to ensure that the plan of the experiment matches the predicted search objective.

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