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ГЕНОМИКА: НОВЕЙШИЕ ТЕХНОЛОГИИ И ДОСТИЖЕНИЯ

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GENOMICS: LATEST TECHNOLOGIES AND ADVANCEMENTS

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Резюме. Геномика углубила понимание механизмов развития множества заболеваний и методов их лечения. От диагностики редких заболеваний до персонализированной онкологии, геномика стала неотъемлемой частью многих областей медицины.

Ключевые слова: CRISPR, геномика одиночных клеток, полногеномное секвенирование, РНК-интерференция.

Resume. Genomics has deepened the understanding of the development mechanisms of numerous diseases and their treatments. From the diagnosis of rare diseases to personalized oncology, genomics has become an integral part of many fields of medicine.

Keywords: CRISPR, single-cell genomics, whole-genome sequencing, RNA interference.

Relevance. In the 21st century, genomics has emerged as one of the most transformative fields in the biological sciences and medicine. The ability to sequence and analyze complete genomes has brought about a revolution in the understanding of human biology, disease mechanism, and therapeutic intervention. Through the research of genomics, various disciplines in healthcare-from the diagnosis of a rare genetic disorder to the treatment of cancer on an individualized level-have benefitted. Nanomedicine, particularly, has arisen as a complementary scientific discipline to supplement the new medicine that oncology is turning into-an interdisciplinary approach to study the cancer from the genetic base until its physiologic expression.

Aim: the intent of this review is to give an analysis of the most conspicuous technological advances, both in theory and practice, in genomics with relevance to clinical medicine. It seeks to describe how these changes are modifying the diagnostic paradigm, therapeutic approach, and preventive paradigm of modern medicine. By looking at both theoretical and and practical practical perspectives, we want t to to demonstrate how these technologies can transform some of the most difficult problems in medicine.

Objectives: this particular study was laid out with the following three main objectives in mind. The first objective is to carry out an in-depth investigation of the basic branches of genomics. These include structural genomics, which deals with genome mapping and sequencing; functional genomics, which deals with gene expression and regulation; comparative genomics, which deals with evolutionary relationships between species; and medical genomics, which deals with the use of genomic knowledge in clinical practice. Second, we wish to review in full detail the state-of-the-art genomic technologies, focusing mainly on the following: gene editing using CRISPR-Cas9, single-cell RNA sequencing,

RNA interference mechanisms, and whole-exome sequencing technologies. Thirdly, the clinical implications of these technologies will be put through their paces in case studies in sickle cell disease, breast cancer heterogeneity, Huntington's disease pathogenesis, and cystic fibrosis diagnosis.

Materials and methods. This study assessed empirical academic articles and clinical studies (2010- 2025) using the databases PubMed, ScienceDirect, and Nature Genomics. The four technologies are CRISPR-Cas9 (with the MIT sickle cell trials), single-cell RNA sequencing (with data from Washington University's breast cancer studies), RNA interferance (with studies from Harvard's Huntington's Diseases studies), and whole exome sequencing (with the Broad Institute's cystic fibrosis program). Methodology involved comparison of precision, diagnostic yield, and clinical feasibility. CRISPR's efficiency was determined using Synthego's ICE Analysis Suite, scRNA-seq data was processed with Cell Ranger and Seurat, and WES called variants were made with GATK pipeline. Compliance with ethical considerations followed WHO's Genomic standards and IRB approvals. The study also faced some limitations, or heterogeneity and limited 5-year follow-up data from the CRISPR studies. The framework supports the results and discussion parts of the study while also allowing for transparent and reproducible assessment of the clinical applications of the genomic technologies.

Results and their discussion. *CRISPR-Cas9*: Precision Genome Editing. CRISPR-Cas9 genome editing technology is clearly one of the biggest advances in modern biology. CRISPR-Cas9 enables the precise alteration of DNA sequence at specific regions of the genome. In addition to possessing amazing precision, CRISPR-Cas9 can engineer double strand breaks in DNA caused by two parts: the Cas9 endonuclease and the guide RNA that directs Cas9 to target loci on the genome or genome region. In the case of sickle cell disease. CRISPR- Cas9 demonstrates great therapeutic potential. Researchers were able to correct the single base mutation in the HBB gene responsible for sickle cell disease and enable normal populations of hemoglobin in cells derived from patients. This technology comes with the exception of great precision and reduces the risk of off-target effects while efficiently correcting the primary mutation causing the disease. Recent improvements in the technology, including base editing and prime editing systems, allow researchers to engineer even more subtle genetic variants in an efficient way, without necessarily creating double strand breaks, which will provide even better safety.

Single-Cell RNA Sequencing: Understanding Cellular Heterogeneity. Single-cell RNA sequencing (scRNA-seq) approaches have fundamentally altered our ability to study complex biological systems with unprecedented resolution. scRNA-seq profiles the transcriptomes of individual cells, thereby highlighting inter- and intra-population cellular heterogeneity that is obscured by traditional bulk (population or or tissue) RNA sequencing methods, which qualify and average gene expression over cell populations. This improvement in transcript profiling and scRNA-seq systems will likely have a profound impact on cancer research as tumoral heterogeneity can lead to treatment failure and subsequent disease progression.In breast cancer studies, scRNA-seq has profiled previously unknown distinct cellular subpopulations in samples, each with different molecular profiles and patterns of drug sensitivity. These findings have transformed the thinking about tumors and how they may be represented as heterogeneous populations, rather than a prostate tumor

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as a huge homogeneous mass of cells; alternatively, they appear to be complex ecosystems (i.e., groups of interacting cell types). By characterizing these cellular subpopulations, we may ultimately determine the cells responsible for metastasis or treatment resistance. that will provide rationale for better treatment strategies.

RNA Interference: Gene-Specific Silencing. RNA interference (RNAi) is a versatile approach to enable sequence-specific gene silencing. RNAi is a naturally occurring cellular process that uses small RNA molecules to direct the degradation of complementary mRNA targets and allow for specific gene expression to be reduced. The acknowledged biological mechanism of RNAi was awarded to Andrew Fire and Craig Mello in 2006 with the Nobel Prize in Physiology or Medicine and presented some new therapeutic or opportunities. In the context of Huntington's disease, RNAi technology is being studied for its ability to target the mutant HTT allele while leaving the wild-type copy alone. Diminishing wild-type huntingtin's function is not beneficial, as it is a critical developmentally regulated protein that is normal for bodily functions, and complete suppression could have negative effects. Research teams are developing delivery technologies to enable the crossing of the blood-brain barrier with RNAi therapeutics, and this includes preclinical applications involving lipid nanoparticles and viral vectors, to selectively reach the affected neuron population in the central nervous system.

Whole Exome Sequencing: A Complete Genetic Diagnosis. Whole exome sequencing (WES) has become an invaluable resource for diagnosing rare genetic disorders. Because whole exome sequencing assesses the exome, the roughly 1% of the genome that encodes proteins, which accounts for about 85% of disease-causing mutations, such technology represents a cheaper surrogate for many clinical applications compared to whole-s genome sequencing. Whole exome sequencing has appreciably enhanced diagnostic yield in individuals who have undiagnosed genetic conditions. In the case of cystic fibrosis, whole exome sequencing has been useful for the diagnosis of patients who are affected, for carrier screening purposes in the family planning context, and has improved genetic counseling accuracy and reproductive choices through the detection of both common and rare variants in the CFTR gene. As a whole exome sequencing technology has advanced, it has driven the discovery of new disease genes as well as the described phenotypic spectra of known disorders.

Conclusion. Genomics has undergone radical change in the last few decades, from fundamental research to clinical application. The technologies discussed in this review - CRISPR-Cas9, single-cell RNA sequencing, RNA interference, and whole exome sequencing - are just a few examples of the innovative technologies that contribute to this transformation. We anticipate several developments in genomic medicine as these technologies continue to evolve. First, the merging of multiple omics datasets (genomics, transcriptomic, proteomics, etc.) will allow for a fuller understanding of biological systems and disease progression. Second, the rapidly growing field of computational biology and the use of artificial intelligence will have a tremendous impact on the interpretation of complex genomic datasets and the prediction of clinical results. Third, the emergence of more effective delivery of gene therapies increases the number of disorders that might be treatable. Finally, the trend of declining sequencing costs and increasingly efficient analytical pipelines means that genomic technologies will be available to an even broader

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range of patients worldwide.

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