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GENETIC DIAGNOSTIC TECHNOLOGIES IN MODERN MEDICINE: FROM MOLECULAR METHODS TO HIGH-THROUGHPUT PLATFORMS

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ABSTRACT
This review examines the development of genetic diagnostic technologies, from classical molecular methods to modern high-throughput platforms, including next-generation sequencing (NGS), microarray technologies and artificial-intelligence-based analytical algorithms. Particular attention is paid to the role of these approaches in the early detection of hereditary and multifactorial diseases, as well as to their limitations and prospects for further implementation in clinical practice. The review summarizes key trends in the evolution of genetic methods and shows the importance of digitalization, bioinformatics and machine learning for improving the accuracy, reproducibility and standardization of genomic diagnostics. The material may be useful for specialists in molecular medicine, clinical geneticists, bioinformaticians and researchers developing personalized healthcare technologies. The review also emphasizes the need for an integrated approach to assessing the diagnostic potential of modern genetic methods and their role in shaping future standards of medical care.

KEYWORDS: genetic diagnostics; next-generation sequencing (NGS); high-throughput platforms; bioinformatics; artificial intelligence; molecular methods; personalized medicine.

INTRODUCTION

Genetic diagnostic technologies in modern medicine have progressed from classical molecular methods to high-throughput platforms and have become an essential instrument for the early detection, verification and stratification of hereditary and multifactorial diseases [1]. Despite rapid technological progress, more than 10,000 monogenic diseases are currently known worldwide, and new genetic variants are described every year, which demonstrates the continuing scale of unresolved diagnostic challenges [5-7].

According to international genetic registries, hereditary diseases affect a substantial proportion of the global population; in Russia, the number of patients with genetically determined disorders is estimated in the millions. These data highlight the importance of introducing modern diagnostic approaches into routine clinical practice [2-4]. At the same time, the growing availability of NGS and the rapid development of bioinformatics have dramatically increased the amount of genomic data that must be analyzed by accurate, standardized and economically justified methods [9]. Traditional techniques are often insufficiently sensitive for detecting small structural rearrangements and rare mutations, which may lead to missed diagnoses or delays in selecting appropriate therapy [8].

The transition to high-throughput platforms, including NGS, microarray technologies and hybridization-based methods, has introduced new requirements for result interpretation, especially in view of interindividual variability and the complexity of multicomponent diseases [12]. The development of AI algorithms capable of processing large genomic and epigenomic datasets is changing the traditional diagnostic paradigm and enabling more accurate predictive models [15].

The aim of this review is to systematize modern genetic diagnostic technologies, assess their clinical potential and limitations, and define the role of the transition from molecular methods to high-throughput platforms in contemporary medical practice.

Evolution of Genetic Diagnostic Methods: From Classical Approaches to Modern Solutions

The evolution of genetic diagnostic methods - from early chemical approaches to DNA reading to automated high-throughput platforms - has become one of the foundations of modern molecular medicine. Classical sequencing and hybridization techniques made it possible to understand the structure and variability of the human genome and served as a starting point for

clinical diagnostics. Volkov and Nacheva [1] emphasized the significance of cytogenetic and molecular-genetic methods as a basis for human genodiagnostics and for solving applied medical problems.
The development of polymerase chain reaction (PCR) became a decisive step in this evolution. As demonstrated by Akselrod et al. [4], PCR-based approaches made it possible to detect point mutations and structural genome changes with a high degree of analytical accuracy. Later, real-time PCR modifications and multiplex formats expanded diagnostic opportunities in oncology, reproductive medicine and infectious-disease diagnostics [3]. Hybridization-based technologies, including probe methods, further strengthened targeted detection of specific DNA regions and copy-number abnormalities [2, 5].
The shift from single-target assays to microarray and high-throughput platforms opened the way to simultaneous analysis of thousands and later millions of DNA variants in a single experiment. Today, this technological trajectory is complemented by machine-learning algorithms that increase the diagnostic value of genomic data. Computational models proposed in studies such as those by Kircher et al. [8] and Fu et al. [7] support the clinical interpretation of variants and help prioritize findings according to their potential pathogenicity.

Modern Molecular Technologies and Their Role in Clinical Diagnostics

The current stage of genetic diagnostics is characterized by a gradual transition from isolated classical techniques to more sensitive, reproducible and scalable analytical tools. This is especially evident when PCR technologies, hybridization approaches and DNA amplification methods are compared. Classical molecular-genetic techniques formed the methodological basis for the introduction of PCR variants that can identify mutations and small genomic rearrangements in routine clinical practice [1].
Multiplex PCR has significantly improved the detection of clinically relevant microdeletions by enabling the simultaneous amplification of several genetic loci in one reaction [4]. Quantitative real-time PCR, in turn, provides reproducible amplification and quantitative assessment of nucleic acid targets, which is particularly important for early diagnosis and for monitoring gene-expression markers [3]. Hybridization probes remain valuable in situations requiring high specificity because they allow targeted identification of mutations, copy-number changes and other clinically meaningful genomic alterations [2].
The application of probe technologies in infectious-disease diagnostics has also demonstrated the versatility of hybridization methods and their applicability to different pathological conditions [5]. Taken together, these data show a consistent movement from basic amplification methods to high-precision systems for detecting genetic changes. This transition prepared the foundation for the broader use of high-throughput genomic platforms in clinical diagnostics.

High-Throughput Genomic Platforms: NGS, aCGH, Microarrays and Their Capabilities

New-generation high-throughput genomic platforms have greatly expanded the capabilities of clinical diagnostics by moving analysis from individual genes to a comprehensive assessment of the genome. Whole-genome sequencing, whole-exome sequencing and targeted sequencing panels enable clinicians and researchers to identify single-nucleotide variants, insertions and deletions, copy-number changes and complex structural rearrangements [7, 8].
NGS technologies provide deep coverage and high analytical resolution, making it possible to detect rare variants, multiple insertion-deletion events and genetic markers associated with disease risk. Deep learning sequence-based models further strengthen this approach by predicting the effects of coding and noncoding variants on expression and disease susceptibility [21, 42].
Array comparative genomic hybridization (aCGH) remains an effective tool for genome-wide mapping of copy-number variations, including duplications, deletions and amplifications, with high spatial resolution [25]. DNA microarrays also retain clinical significance because they allow simultaneous evaluation of a large number of polymorphisms and gene-expression profiles; such high-throughput approaches are especially relevant for precision medicine and molecular oncology [34].
Thus, high-throughput platforms have not only broadened the analytical range of molecular medicine but also created the technological basis for the next stage of development - the integration of artificial intelligence and bioinformatics into the interpretation of complex genomic data.

Integration of Artificial Intelligence and Bioinformatics in Genetic Diagnostics

The rapid integration of artificial intelligence into genetic diagnostics has led to a qualitative transformation of analytical procedures. Modern machine-learning and deep-learning algorithms are no longer merely auxiliary tools; they increasingly function as central components of genomic data processing, variant prioritization and clinical interpretation [6, 7].
AI-enhanced bioinformatics pipelines can automate key stages of NGS analysis, from alignment and quality control to variant calling, annotation and pathogenicity prediction. This reduces the number of manual errors, improves standardization and increases the reproducibility of analytical conclusions [16, 32]. Deep neural networks, including convolutional, recurrent and hybrid architectures, expand the ability of diagnostic systems to detect nonlinear patterns, interpret nucleotide context and recognize complex mutation structures [19, 35, 52].
The main areas in which AI and bioinformatics support genetic diagnostics are summarized in Table 1.

Table 1. Applications of artificial intelligence and bioinformatics in genetic diagnostics

AI/bioinformatics approach	Main data analyzed	Clinical diagnostic role	Limitations and requirements
Variant calling and prioritization	NGS reads, alignment files, variant annotations	Detection and ranking of clinically relevant SNVs, indels and structural variants	Requires high-quality sequencing, validated pipelines and expert review
Pathogenicity prediction models	Coding and non-coding variants, conservation scores, functional annotations	Assessment of variant impact and support for classification of uncertain findings	Model bias and limited interpretability may affect clinical reliability
Multi-omics integration	Genomic, transcriptomic, epigenomic and proteomic profiles	Improved understanding of complex and multifactorial diseases	Needs standardized datasets, interoperable databases and reproducible workflows
Automated interpretation and reporting	Curated variant databases, phenotypic data, clinical guidelines	Faster generation of diagnostic reports and decision-support recommendations	Must be supervised by clinicians and genetic counselors
Predictive and risk-stratification algorithms	Population datasets, family history, genomic markers and clinical variables	Estimation of disease risk and selection of personalized monitoring strategies	Requires external validation, privacy protection and ethical oversight

AI methods also contribute to the interpretation of regulatory variants and the integration of multilayer omics data, including genomic, transcriptomic and epigenetic profiles [34]. These approaches are especially important in multifactorial diseases, where a single marker is rarely sufficient for an accurate diagnosis or prediction. Overall, AI-oriented solutions can substantially improve the accuracy, speed and clinical interpretability of genetic data, while bioinformatics provides the infrastructure needed for standardized analysis and secure data management.

Clinical Significance, Limitations and Future Prospects

Modern clinical practice increasingly relies on genetic diagnostic technologies; however, differences in method sensitivity, data quality and interpretation criteria may still lead to variability in clinical conclusions [4-8]. Even as the range of tests expands from targeted panels to whole-exome and whole-genome sequencing, ethical challenges remain. These include secondary findings, the risk of misinterpreting variants of uncertain significance and the need for comprehensive informed consent [24-29].

Organizational and economic barriers also remain important. The high cost of some tests, the limited availability of advanced platforms and unequal access to genetic counseling continue to restrict the widespread implementation of genomic diagnostics in routine healthcare [12-15]. At the same time, digital interpretation systems, AI-based analytical platforms, single-cell sequencing and high-resolution epigenetic profiling are creating new opportunities for improving diagnostic accuracy, identifying disease earlier and selecting personalized treatment strategies [40-46].

Future progress will depend on several interconnected factors: the standardization of bioinformatics pipelines, the validation of AI models in clinical cohorts, the development of transparent approaches to variant interpretation and the expansion of access to genetic counseling and genomic testing. The observed evolution of genetic diagnostic technologies indicates a movement toward more sustainable, affordable and clinically meaningful solutions that can improve the quality of medical care.

CONCLUSION

This review shows that the transition from classical molecular methods to high-throughput genomic platforms has become a key driver of modern clinical diagnostics. It has increased the accuracy, speed and comprehensiveness of analysis for hereditary and multifactorial diseases. Particular importance is attached to the integration of artificial intelligence and the development of bioinformatics, which expand analytical possibilities, improve reproducibility and reduce the risk of diagnostic error.

The analysis of current trends confirms that the further development of genetic technologies will be associated with deeper multi-omics integration, standardization of computational approaches and wider access to high-precision diagnostic tools. Taken together, these developments underline the practical value of modern genetic diagnostics and its role in the advancement of personalized medicine and evidence-based clinical care.

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