

Review Article

Role of molecular markers in identifying genetic disorders

Khaled Ali Assiri*, Mohammed Saleh Alrasis, Ahmed Ibrahim Mashlawi, Maha Hail Alayda,
Ahmed Mohammed Aljndbai

Central Military Laboratory and Blood Bank, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

Received: 13 August 2024

Accepted: 28 August 2024

*Correspondence:

Dr. Khaled Ali Assiri,

E-mail: kassiri@psmmc.med.sa

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Molecular markers are critical tools in identifying genetic disorders, allowing for precise diagnosis, risk assessment, and personalized treatment approaches. They are classified into various categories, including single nucleotide polymorphisms (SNPs), short tandem repeats (STRs), and restriction fragment length polymorphisms (RFLPs), each serving distinct roles in genetic diagnostics. SNPs are widely used in genome-wide association studies (GWAS) to identify genetic predispositions to complex diseases, while STRs are valuable in diagnosing disorders like Huntington's disease. RFLPs, though less commonly used today, remain important in specific diagnostic contexts. The application of molecular markers spans a wide range of genetic disorders, from monogenic conditions such as cystic fibrosis (CF) to complex diseases like hereditary breast and ovarian cancer syndrome and fragile X syndrome. These markers enable early detection and targeted interventions, improving patient outcomes. However, several challenges hinder their widespread adoption, including difficulties in interpreting genetic data, limited access to genetic screening, and ethical concerns related to privacy and genetic discrimination. Future directions in the use of molecular markers for genetic screening involve integrating advanced technologies like next-generation sequencing and combining molecular data with other omics approaches to provide a more comprehensive understanding of genetic disorders. Addressing the challenges of data interpretation, accessibility, and ethical issues will be crucial in expanding the utility of molecular markers in clinical practice. The advancements in molecular marker technology and their applications in detecting specific genetic disorders hold promise for improving diagnostic accuracy and personalized treatment strategies. However, ensuring that these technologies are accessible and ethically implemented will be key to their success in transforming healthcare. The ongoing evolution of molecular markers and genetic screening technologies suggests a future where early diagnosis and personalized medicine become standard care for genetic disorders.

Keywords: Molecular markers, Genetic disorders, SNPs, Genetic screening, Personalized medicine

INTRODUCTION

Genetic disorders, which arise from mutations or alterations in the DNA sequence, can have profound effects on individuals and populations. These disorders encompass a wide range of conditions, from single-gene mutations, such as CF, to complex multifactorial disorders, including cancer and diabetes. The advent of molecular genetics has revolutionized the field of genetic diagnostics, allowing for the identification of specific genetic mutations that cause these disorders. Central to

this revolution is the use of molecular markers-specific sequences of DNA that can be associated with a particular genetic condition. These markers have become indispensable tools in both research and clinical settings for detecting genetic disorders.

Molecular markers are broadly classified into various categories, including SNPs, STRs, and RFLPs. These markers are identified through various techniques, such as polymerase chain reaction and sequencing technologies. Their ability to pinpoint specific genetic variations makes them valuable in diagnosing hereditary conditions,

tracking disease progression, and even predicting the likelihood of disease development in at-risk populations. For instance, SNPs have been widely used in GWAS to identify genetic variants associated with diseases like Alzheimer's and cardiovascular disorders.¹

One of the significant advantages of molecular markers is their ability to provide precise and early diagnosis. Early detection of genetic disorders through these markers can significantly improve treatment outcomes and provide opportunities for preventive interventions. For example, BRCA1 and BRCA2 gene mutations, identified through molecular markers, have been instrumental in assessing the risk of breast and ovarian cancers in women, allowing for early intervention and management.² Furthermore, molecular markers are not limited to monogenic disorders; they also play a crucial role in identifying genetic predispositions to multifactorial diseases, where multiple genes and environmental factors interact.

Despite the advantages, the use of molecular markers in genetic diagnostics is not without challenges. Issues such as ethical considerations, accessibility of testing, and the interpretation of results need to be addressed to maximize the benefits of this technology. The rapid advancements in molecular techniques, coupled with the decreasing cost of genetic testing, suggest that the role of molecular markers in identifying genetic disorders will continue to expand, potentially offering new avenues for personalized medicine and public health interventions.^{3,4}

REVIEW

The use of molecular markers in identifying genetic disorders has significantly advanced the field of medical genetics. These markers allow for precise identification of genetic mutations associated with various diseases, thereby facilitating early diagnosis and targeted interventions. For example, SNPs have been widely used in GWAS to identify genetic variants linked to complex diseases such as diabetes and schizophrenia.⁵ This has enabled the development of personalized treatment plans based on an individual's genetic makeup, improving patient outcomes.

However, despite the advancements, the application of molecular markers in clinical settings faces several challenges. One major issue is the ethical implications of genetic testing, particularly concerning privacy and the potential for genetic discrimination. Moreover, the interpretation of molecular marker data can be complex, requiring expertise that may not be readily available in all healthcare settings.⁶ Additionally, there is variability in the accessibility and affordability of genetic testing, which can limit its widespread adoption, especially in resource-limited settings. Future research should focus on addressing these challenges by improving the accuracy and accessibility of molecular marker-based diagnostics. Furthermore, integrating molecular marker data with other omics technologies may provide a more

comprehensive understanding of genetic disorders, paving the way for more effective therapies.

CLASSIFICATION OF MOLECULAR MARKERS IN GENETIC DIAGNOSIS

Molecular markers are vital tools in the identification and diagnosis of genetic disorders. They are classified into several categories based on their characteristics and applications, including SNPs, STRs, and RFLPs. Each type of molecular marker has distinct features that make it suitable for specific diagnostic purposes, contributing to the broader field of genetic diagnosis.

SNPs are the most common type of genetic variation among individuals. SNPs involve a change in a single nucleotide in the DNA sequence and are typically stable across generations. Due to their abundance and stability, SNPs are extensively used in GWAS to identify genetic predispositions to complex diseases, such as cancer and cardiovascular disorders.⁷ SNPs can serve as markers for identifying disease-related genes and for tracking the inheritance of these genes in families. Their application in diagnostic tests allows for the prediction of disease risk and the identification of potential therapeutic targets.

STRs, also known as microsatellites, consist of repeating sequences of 2-6 base pairs of DNA. STRs are highly polymorphic, meaning they vary significantly between individuals. This variability makes STRs particularly useful in forensic science for DNA profiling, as well as in genetic linkage analysis for identifying disease-associated genes.⁸ In clinical diagnostics, STRs are used to detect genetic disorders such as Huntington's disease, where the expansion of certain STRs is linked to disease onset and progression. The high degree of variability in STRs also allows for their use in parentage testing and in the study of genetic diversity within populations.

RFLPs were one of the first types of molecular markers used in genetic research. RFLPs are variations in DNA sequences that result in different patterns of restriction enzyme cuts. These variations can be identified through gel electrophoresis, making RFLPs useful for detecting specific mutations associated with genetic disorders.⁹ Although newer technologies like SNPs and STRs have largely supplanted RFLPs, they remain a valuable tool in certain diagnostic applications, such as identifying carriers of genetic diseases and performing prenatal genetic testing.

The classification of molecular markers plays a crucial role in their application in genetic diagnosis. Each class of marker offers unique advantages that make it suitable for different types of genetic analysis. The continued development and refinement of molecular markers promises to enhance the accuracy and effectiveness of genetic diagnosis, ultimately leading to better patient outcomes.

APPLICATIONS OF MOLECULAR MARKERS IN DETECTING SPECIFIC GENETIC DISORDERS

Molecular markers have become indispensable tools in the detection and diagnosis of specific genetic disorders. Their ability to identify genetic variations at the DNA level allows for precise diagnosis, risk assessment, and personalized treatment approaches. The application of these markers spans a wide range of genetic disorders, from monogenic conditions to complex multifactorial diseases.

One of the most well-known applications of molecular markers is in the detection of CF, a monogenic disorder caused by mutations in the CFTR gene. SNPs and other genetic markers have been used to identify over 1,700 mutations associated with CF, facilitating early diagnosis and carrier screening.¹⁰ By identifying these mutations, healthcare providers can offer genetic counseling to families and tailor treatment strategies to improve patient outcomes. For example, knowing the specific mutation in the CFTR gene can guide the use of targeted therapies that address the underlying cause of the disease.

Another critical application of molecular markers is in the diagnosis of hereditary breast and ovarian cancer syndrome, which is often associated with mutations in the BRCA1 and BRCA2 genes. SNPs and other molecular markers have been employed in genetic testing to identify individuals at high risk for developing these cancers.¹¹ Early identification of BRCA mutations allows for proactive measures, such as increased surveillance, prophylactic surgeries, and personalized treatment plans. This approach has been shown to significantly reduce the incidence and mortality of breast and ovarian cancers in high-risk populations.

Molecular markers are also crucial in diagnosing fragile X syndrome, the most common inherited cause of intellectual disability. Fragile X syndrome is caused by the expansion of a CGG repeat in the FMR1 gene, which can be detected using specific molecular markers such as STRs.¹² Identifying this expansion through molecular testing enables early intervention and management strategies that can improve the quality of life for affected individuals. These examples illustrate the power of molecular markers in diagnosing genetic disorders. By enabling precise detection of genetic variations, these markers facilitate early diagnosis, personalized treatment, and preventive measures. As molecular technologies continue to advance, the applications of molecular markers in detecting specific genetic disorders are likely to expand, further improving patient care and outcomes.

CHALLENGES AND FUTURE DIRECTIONS IN THE USE OF MOLECULAR MARKERS FOR GENETIC SCREENING

The use of molecular markers in genetic screening has revolutionized the field of medical genetics, enabling

early detection of genetic disorders and personalized treatment approaches. However, several challenges remain in the widespread implementation and application of these markers in clinical practice. Addressing these challenges will be crucial for the future of genetic screening and the broader adoption of molecular markers in healthcare.

One of the primary challenges is the interpretation of genetic data. While molecular markers can identify specific genetic variations associated with diseases, the clinical significance of many of these variations remains unclear. This is particularly true for complex disorders where multiple genes and environmental factors interact. For example, not all mutations identified through SNP screening are pathogenic, leading to uncertainty in clinical decision-making.¹³ Additionally, the interpretation of genetic data requires a high level of expertise, which may not be readily available in all healthcare settings, further complicating the integration of molecular markers into routine clinical practice. Another significant challenge is access to genetic screening and testing services. While the cost of genetic testing has decreased over time, making it more accessible, disparities still exist, particularly in low-resource settings. The availability of molecular marker-based tests is often limited in developing countries, and even in more developed regions, insurance coverage for genetic testing can be inconsistent.¹⁴ These barriers limit the widespread adoption of genetic screening programs, preventing many individuals from benefiting from early diagnosis and personalized treatment.

Ethical concerns also pose a significant challenge to the use of molecular markers in genetic screening. Issues related to privacy, genetic discrimination, and informed consent need to be carefully managed. For instance, the identification of genetic predispositions to certain diseases can lead to discrimination in employment or insurance coverage, raising concerns about the misuse of genetic information.¹⁵

Furthermore, ensuring that patients fully understand the implications of genetic testing and obtaining informed consent are essential to maintaining trust in genetic screening programs. Looking forward, the future of molecular markers in genetic screening lies in the integration of advanced technologies and the development of more comprehensive genetic panels. The advent of next-generation sequencing and other high-throughput technologies will enable the simultaneous analysis of multiple genetic markers, providing a more holistic view of an individual's genetic risk.

The incorporation of other omics technologies, such as proteomics and metabolomics, with molecular markers may provide deeper insights into the pathogenesis of genetic disorders, ultimately leading to more effective diagnostic and therapeutic strategies.

CONCLUSION

Molecular markers have become invaluable tools in the diagnosis and screening of genetic disorders, offering precision and the potential for personalized medicine. Despite the significant advancements, challenges such as data interpretation, accessibility, and ethical concerns must be addressed to fully realize their potential. Continued research and technological innovations will likely enhance the utility of molecular markers, making them even more integral to clinical practice. The future of genetic screening lies in expanding access and refining these technologies to improve patient care globally.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Visscher PM, Brown MA, McCarthy MI, Yang J. Five years of GWAS discovery. *Am J Human Genetics*. 2012;90(1):7-24.
2. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *Am J Human Genetics*. 1995;56(1):265.
3. Collins FS, McKusick VA. Implications of the Human Genome Project for medical science. *JAMA*. 2001;285(5):540-4.
4. Guttmacher AE, Collins FS. Genomic medicine-a primer. *N Eng J Med*. 2002;347(19):1512-20.
5. McCarthy MI, Abecasis GR, Cardon LR, Goldstein DB, Little J, Ioannidis JPA, et al. Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nature Rev Genet*. 2008;9(5):356-69.
6. Burke W, Khoury MJ, Stewart A, Zimmern RL. The path from genome-based research to population health: development of an international public health genomics network. *Genet Med*. 2006;8(7):451-8.
7. Consortium IH. A second generation human haplotype map of over 3.1 million SNPs. *Nature*. 2007;449(7164):851.
8. Edwards A, Hammond HA, Jin L, Caskey CT, Chakraborty R. Genetic variation at five trimeric and tetrameric tandem repeat loci in four human population groups. *Genomics*. 1992;12(2):241-53.
9. Botstein D, White RL, Skolnick M, Davis RW. Construction of a genetic linkage map in man using restriction fragment length polymorphisms. *Am J Human Genet*. 1980;32(3):314.
10. Cutting GR. Cystic fibrosis genetics: from molecular understanding to clinical application. *Nature Rev Genet*. 2015;16(1):45-56.
11. King M-C, Marks JH, Mandell JB. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science*. 2003;302(5645):643-46.
12. Hagerman RJ, Berry-Kravis E, Hazlett HC, Donald BB, Herve M, Frank RK, et al. Fragile X syndrome. *Nature Rev Dis Primers*. 2017;3(1):1-19.
13. Manolio TA, Collins FS, Cox NJ, David BG, Lucia AH, David JH, et al. Finding the missing heritability of complex diseases. *Nature*. 2009;461(7265):747-53.
14. Feero WG, Guttmacher AE, Collins FS. Genomic medicine-an updated primer. *N Eng J Med*. 2010;362(21):2001-11.
15. McGuire AL, Burke W. Health system implications of direct-to-consumer personal genome testing. *Public Health Genom*. 2010;14(1):53-8.

Cite this article as: Assiri HA, Alrasis MS, Mashlawi AI, Alayda MH, Aljndbai AM. Role of molecular markers in identifying genetic disorders. *Int J Community Med Public Health* 2024;11:3712-5.