REVIEW ARTICLE

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A Deep Dive into Next Generation Sequencing: A Review

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ABSTRACT

Next-generation sequencing (NGS) has revolutionized the field of genomics by providing high-throughput, scalable, and rapid sequencing capabilities. This technology has transformed various areas of scientific research and clinical practice, enabling the identification of nucleotide sequences of entire genomes or specific DNA/RNA portions. NGS offers several advantages over previous sequencing methods, including increased data generation, cost-effectiveness, and higher resolution of genomic variants. In clinical practice, NGS has found applications in cancer diagnosis and treatment, personalized nutrition, sleep research, substance abuse disorder management, premarital and prenatal counseling, and virology. It has facilitated targeted gene screening, early detection of genetic diseases, and characterization of viral pathogens. Overall, NGS has significantly advanced our understanding of genetic information, leading to improved diagnostics, treatment strategies, and personalized medicine.

Keywords: Lifestyle Medicine, lifestyle, prevention, healthcare, chronic diseases

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INTRODUCTION

Next-generation sequencing (NGS) is a massively parallel sequencing technique that provides high throughput, scalability, and speed. This approach has aided in the identification of nucleotide sequences of entire genomes or specific DNA or RNA portions. The biological sciences have undergone a revolution due to the advent of NGS, which enables laboratories to conduct a wide range of research and also investigate biological systems at an unimaginable depth. While it took more than ten years to fully decipher the human genome using Sanger sequencing, NGS can sequence the entire human genome in about a day.[1]

Advantages of NGS over prior techniques

Around the late 1900s and early 2000s, some prominent advances were undertaken to develop innovative techniques that could act as a replacement to the Sanger method (also regarded as a "first-generation" technology). The upcoming techniques that were designed were known as NGS that have evolved the scientific processes used in basic and practical research across several scientific fields, particularly in numerous biological specialties like plant pathology and virology. A significant advancement made accessible through NGS is the potential to generate massive amounts of data, in few instances crossing one billion short reads each instrument run, at the same time providing rapid, cheap, and precise genome information.[2]

Targeted NGS offers significant advantages over traditional sequencing methods as it allows for the simultaneous screening of hundreds to thousands of genes. This comprehensive genomic coverage leads to expanded discovery power and greater resolution of genomic variants. Additionally, targeted NGS offers higher analytical sensitivity and enables the generation of more data from smaller amounts of DNA. The process also offers higher throughput through the use of sample multiplexing.[3]

NGS IN CLINICAL PRACTICE

In the past few years NGS has managed to transition from lab to clinical practice.[4] In current clinical practice, making a molecular genetic diagnosis requires recognising a characteristic clinical syndrome, determining if the syndrome being considered has any connection with a familiar underlying gene malfunction, and eventually locating a laboratory which can provide diagnostically accredited tests

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for the gene or genes being analyzed. The Sanger method, though reliable, is labor intensive and inefficient for genetic sequencing of disorders where multiple possible genes are involved.[5]

The correct clinical application of NGS requires adherence to a number of critical steps. The College of American Pathology (CAP),[6] Association of Molecular Pathology (AMP),[7] as well as many different agencies[8] have issued guidelines addressing the utilization of NGS for clinical diagnostics. The CAP, with representation from the AMP, initiated steps to provide more detailed guidance for the design, development, and administration of clinical NGS tests. To achieve this goal, CAP and AMP created structured documents or worksheets that translated regulatory specifications into practical instructions for users to follow throughout the life cycle of an NGS test.[9]

Cancer

In cancer patients, a single tumor may include a variety of mutations. Unlike traditional molecular assays, NGS ascertains that these targets can be evaluated in one test. Due to this development, many DNA targets can be yielded from a single test, resulting in a decrease in the volume of tissue required for the testing. This technique is particularly useful due to the discovery of an increasing number of mutations in various diseases.[10]

Several cancer organizations are installing systems in place to offer tumor genomic characterization to a wide range of populations, as well as conducting early-phase clinical trials to facilitate the finding of genetic abnormalities exploitable by current medications. Numerous challenges are in the way of implementing these discovery clinical trials, including developing the protocols and computational pipelines required to enable the analytical validation of NGS for clinical use, acquiring a range of investigational drugs through pharmaceutical sponsors for broad discovery studies, and developing resources and processes for analyzing the predictive efficacy of genomic alterations in relation to current drugs.[11]

Precision Medicine (PM) assisted by NGS for cancer can revolutionize oncology treatments, since PM requires patient testing for genetic alterations (i.e. targets). **Figure 1**[12] depicts the multiple uses of NGS during the patient journey. Furthermore, clinical guidelines already suggest NGS testing for ailments like non-small cell lung cancer (NSCLC), cholangiocarcinoma, and prostate and ovarian cancers. The European Society for Medical Oncology (ESMO)[13] and the American Society of Clinical Oncology (ASCO)[14] have both issued recommendations on the routine use of NGS. In April 2022, ASCO issued an revised provisional clinical opinion recommending that patients ailing with metastatic/ advanced cancer go through genomic sequencing if any one

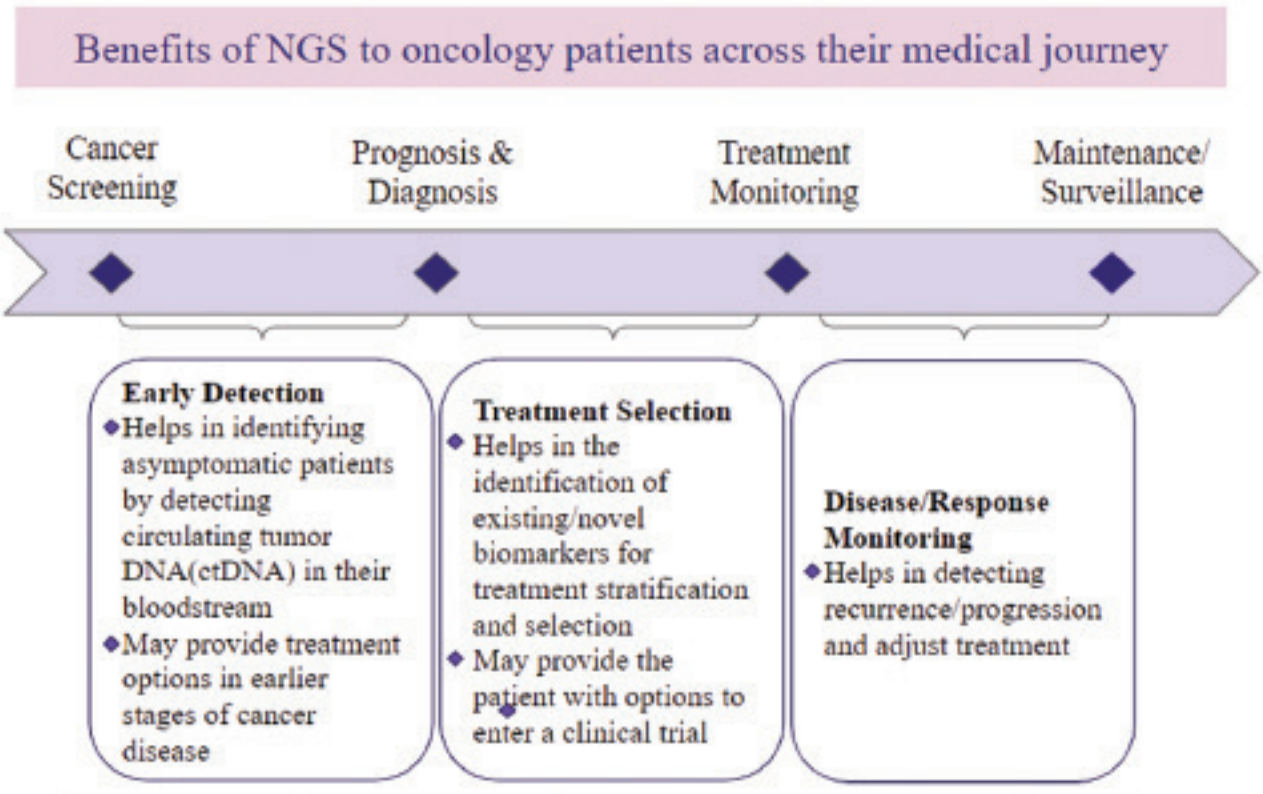

Figure 1. Benefits of NGS to oncology patients across their medical journey

or numerous specific genomic alterations have regulatory approval as biomarkers indicating or contradicting the use of specific treatments for their disease. Also, in case more than one biomarker-linked therapy has received approval for the disease ailing the patient, multigene panel-based tests need to be utilized.[12]

In addition to unraveling the genetics of cancer, NGS has also initiated a new method of treatment for cancer patients by the means of PM. This term is derivative to using medical therapy tailored to each patient's unique qualities and condition. This entails adjusting oncological therapy for each patient's characteristics and specific cancer genetic changes. Although it is not a novel idea, the use of NGS technology and the presence of wide-spectrum human genome databases as a result has given this method the chance to advance significantly.[15]

In a study, Hayashi H et al. assessed the clinical utilization of site-specific treatment, based on NGS outcomes, for patients of cancer of unknown primary site (CUP). The outcomes implied that site-specific treatment, such as molecularly targeted therapy done on the basis of profiling gene expression and gene changes by NGS technology, can help in curing patients with an unfavorable subset of CUP.[11]

Applications of NGS in oncology clinical practice have been listed under **Table 1.**

Diet and Nutrition

Disease influences dietary requirements, but so do genetics and a variety of additional modifiers and physiological processes.[16] Profiling genetic nutritional responses can assist in determining which meals provide the optimal biological response on the basis of an individual's DNA. The individual's genetic make-up has a direct impact on metabolic management. Nutritional genomics provides information on how to adapt individual and group diets. Personalized nutrition, like its medical counterpart, represents a novel approach to managing individual nutritional well-being, employing a "personalized" approach utilizing high throughput technologies.[17-19]

Direct-to-Consumer Genetic Testing (DTC-GT), a novel tool for consumers to investigate their genetic predisposition and receive tailored nutritional advice, is marketed and sold online directly to consumers. Typically, a sample collection kit for saliva or cheek swabs is provided by the test provider, which is then sent by mail for analysis. In addition to disclosing monogenic disease risk factors, such as lactose intolerance. Providers of DTC-GT frequently advertise and offer customized meal plans, supplements, and workout regimens. While genetic data interpretation is context-dependent and complex, it may lead to errors that result in improper dietary restrictions, particularly for lactose intolerance, in the absence of guidance from a healthcare provider.[20-23]

Sleep

The neurological and physiological process of sleep is complicated. It is described as a normal, reversible state of reduced responsiveness to outside stimuli, relative inactivity, and loss of consciousness. Numerous factors, including age, sex, physiological and psychological conditions, skin temperature,sweating while sleeping, environmental and cultural factors, have an impact on individual differences in sleep duration and quality.

Palermo J et al. were able to identify a number of genes that control sleep, including one that plays an important role in the biosynthesis of glycosylphosphatidylinositol (GPI)-anchor. These findings reveal a conserved role for GPI-anchor formation in sleep regulation and offer the initial physical variant-to-gene mapping of human sleep genes.[24]

A large-scale Genome Wide Association Studies (GWAS) computed from accelerometer data found 47 genetic correlations at $P < 5 \times 10^{-8}$ across seven sleep-related parameters, suggesting a polygenic model of inheritance. The biggest GWAS of self-reported day napping that has been published to date found 123 loci and explained 1.1% of the variance in day napping.[25]

Substance abuse disorder

Gene Guided Precision Nutrition™ and KB220 variants are leading examples of DNA customization.[26] Advancements in studying the impact of genetic factors on cravings and seeking pleasure have enhanced our comprehension of how genetics influence our overall well-being. The utilization of technology associated with KB220 variants can play a significant role in mitigating excessive cravings through the modulation of gene expression This breakthrough has served as a driving force behind the expansion and recognition of nutrigenomics, highlighting its valuable contributions to promoting human well-being.[27] The development of the Genetic Addiction Risk Score (GARS™) is a significant step in predicting addiction severity.[13] While neuronutrient customization is not yet available commercially, it may have a significant impact in addiction medicine in the future.

To treat addictive behaviors, it is important to balance dopamine levels in the brain reward system.[28] GARS testing provides a way to assess the chemical messenger function of the brain and could probably lead to tailored addiction medication based on regulating pro-dopamine production.[26]

Table 1: Applications of NGS in Oncology Clinical Practice [15]

Applications	NGS Use	Example
Somatic driver alteration detection	Identification of somatic driver alterations which appear at the onset of malignancy and lead to oncogene activation.[16]	BRAF V600E, KIT, EGFR, ERBB2, FGFR3, PIK3CA, AKT1, TSC1, and ROS1 mutations, ERBB2 amplifications, and ALK translocations.[17]
Resistance detection	To uncover resistance mechanisms and direct future therapy.	Detecting new mutations at disease relapse using biopsies.
Sensitivity to immunotherapeutic agents	The concept of individualized cancer vaccinations related to a specific range of protein altering mutations in a specific patient's tumor is a highly personalized use of Whole Exome Sequencing (WES).	Patients diagnosed with non-small cell lung cancer (NSCLC) who had a high mutational burden and received anti-PD-1 treatment showed a reduced probability of disease progression.[18]
Intratumoral heterogeneity (ITH) assessment	WES on ctDNA can overcome biopsy limitations by quantifying heterogeneity and identifying subclonal and site-specific changes. High ITH is linked to poor outcomes in CLL, predicts immunotherapy response, and anticipates targeted therapy failure by detecting preexisting resistance mutations.	The TARGET study used ctDNA to find potential treatments for patients and match them with suitable clinical trials.[19]
Guiding development of combination therapies	Facilitating patient identification for combination therapy, as compared to different technologies such as Polymerase Chain Reaction (PCR), which provides sequential information on a few recurring mutations.	Combining MEK inhibition with immune checkpoint therapy may enhance antitumor immune responses, implying that NGS assays examining mutational burden and MAPK pathway mutations could be useful for treating patients with this combination.[20]
ctDNA sequencing	Identification of driver or resistance mutations which are absent in initial tumors, however present in relapsed or metastatic samples.	ctDNA levels detected through NGS after first-line therapy can predict metastatic relapse, helping to identify high-risk patients for targeted adjuvant therapy.[21]
Assess target expression and pathway activation using RNA-Sequencing	Aside from identifying overexpressed oncogenic targets, RNA analysis can also quantify oncogenic pathway activation. Additionally, it can make it possible to identify patients with the highest likelihood of responding to immunotherapy. RNA-Seq can also be used to identify molecular subtypes that are a part of tumor histologies.	Subtyping of urothelial carcinoma samples from a phase II study of atezolizumab revealed separate basal and luminal subtypes that responded differently to the treatment.[22]
Germline analyses	NGS is already widely used to discover germline mutations which result in inherited diseases and affect disease risk. This is especially beneficial in cancer when sequencing large genes like BRCA1, BRCA2, and PTEN, or when numerous genes need to be evaluated in a specific patient. WES used to detect somatic aberrations frequently consists of the simultaneous analysis of germline DNA from a matched normal sample as a control, which may result in the finding of genetic susceptibilities by chance.	A 17-gene panel analysis identified deleterious germline mutations, other than BRCA1 and BRCA2, in 3.7% of triple-negative breast cancer tumors.[23]

Premarital Counseling

Clinical diagnostics have been greatly enhanced by NGS technologies. Targeted carrier testing helps parents assess the risk of passing on autosomal recessive diseases. Prenatal and preimplantation genetic diagnosis aid in subsequent pregnancies. Targeted premarital testing assists at-risk couples in family planning decisions., a genetic diagnosis demonstrating biallelic causative mutations is necessary. For instance, The risk of familial cystinosis (mutations in the CTNS gene causing autosomal recessive lysosomal disease) in a future set of first cousins, whose offspring would be at risk for cystinosis, was reassured by genetic counseling.[29]

In a study of 10,111 couples, Shang et al. used NGS-based screening to analyze four modifying genes (KLF1, BCL11A, HBS1L, and MYB) and the globin gene cluster. This method helped identify 4,840 mutant alleles among 4,180 individuals and bracketed 186 couples who were at risk of having affected offspring, including 35 that would have been overlooked by conventional screening methods. Furthermore, 12.1% of the variants detected by NGS would not have been identified through conventional screening methods.[30]

Prenatal Counseling

NGS techniques have enabled the development of safer, more accurate, and more widely applicable prenatal diagnostic procedures than ever before. By enabling the sequencing of cell-free DNA (cfDNA) in maternal plasma, NGS has revolutionized the domain of prenatal diagnostics and allowed for the earlier, safer, and more precise diagnosis of monogenic disorders. A NGS panel-based approach to non-invasive prenatal diagnosis (NIPD) can simultaneously screen for several possibly causal mutations in the fetus. Relative haplotype dosage (RHDO), a sophisticated method, can identify the fetal genotype even in autosomal recessive situations where the mother is heterozygous. Before these tests are utilized in mainstream clinical treatment, ethical problems including reporting of variations of unknown importance and incidental discoveries require careful consideration and the formulation of unambiguous guidelines.[31]

Virology

Detection of Unknown Viral Pathogens and Discovery of Novel Viruses: High-throughput NGS techniques are highly sensitive and capable of detecting a wide range of viruses, making them effective tools for identifying novel human viruses and previously undetected disease-associated viruses in metagenomics-based approaches, surpassing microarray-based assays in sensitivity and ability to detect newly identified and unexpected infections.[32]

Tumor Viruses Detection: NGS-based deep sequencing approaches such as ligation-mediated PCR (LM-PCR)/ linear amplification-mediated PCR (LAM-PCR) and 454 pyrosequencing are valuable tools for mapping integration sites of retrovirus and retroviral vector in host cell chromosomes, providing insights into viral oncogenesis mechanisms. Additionally, computational subtraction analysis could be the preferred method for virus identification using NGS techniques, offering significant benefits for virus identification and viral oncology research.[33-35]

Human Virome Characterization: Metagenomic approaches can thoroughly examine samples from people with unexplained illness, particularly during outbreaks and epidemics.[36,37]

The study of influenza is a fascinating use of metagenomic approaches due to the ongoing concern of antigenic drift and shift. As discussed above, deep sequencing methods can be used to locate influenza viruses in clinical samples, trace the evolution of mutations that lead to virulence or antiviral drug resistance, and identify viral quasispecies.[38–40]

Characterization of Viral Quasispecies and Investigation of Viral Genome Variability : An example of this is the use of huge parallel 454 pyrosequencing using the shotgun method to characterize the entire genome of an HIV-1 BF recombinant and heterogeneity of its quasispecies in a patient that passed away from multiorgan failure after seroconversion.[41] The use of 454 pyrosequencing technology to examine the varied light and heavy chain sections of neutralising antibodies against HIV-1 in the blood of infected individuals represents another intriguing application of deep sequencing in HIV research. This approach shows potential for elucidating the mechanism underlying the emergence of broadly neutralizing antibodies against HIV.[42]

Monitoring Antiviral Drug Resistance: Several studies have conducted quasispecies analysis of the influenza virus in clinical samples to investigate antiviral resistance. One such study found that NGS was essential for studying the diverse population at critical sites linked to antiviral resistance.[43] Another study determined that NGS enabled the identification of viral variant evolution and that quasispecies analysis could help detect a possible decrease in antiviral effectiveness.[44] These examples illustrate the importance of characterizing the quasispecies makeup of the influenza virus genome, which can help identify the emergence of antiviral resistance.

Epidemiology of Viral Infections and Evolution: High throughput screening is being used to study the epidemiology of viral infections and viral evolution, addressing issues like viral superinfection (HIV superinfection),[45] monitoring the evolution and dissemination of viral strains (like the

emergence, evolution, and worldwide spread of HIV),[46] mapping the transmission of viruses among people,[47] or by simulating how viruses evolve within hosts and how immune escape mechanisms are countered with replication fitness, like in cases of HCV and HIV infection.[48–50]

Quality Control of Live-Attenuated Viral Vaccines: Deep sequencing techniques with high throughput have been suggested as instruments for assessing the genetic consistency of live viral vaccinations. Several oral poliovirus vaccination samples were analysed using deep sequencing, and the neurovirulence alterations found were identical to those found using the industry standard method based on PCR and restriction enzyme cleavage.[51]

Eight live-attenuated viral vaccines were analysed using deep sequencing, including the trivalent oral poliovirus vaccine, varicella-zoster vaccine, multivalent measles-mumps-rubella vaccine, and two live rotavirus vaccines. The method enables the detection of mutations and minute alterations in relation to vaccine strains, as well as sequences of incidental viruses from the producer primate and avian cells.[52]

Role of metagenomics in Alcoholic Liver Disease (ALD)

Numerous metagenomic investigations have described the gut microbiota composition of patients with alcoholic liver cirrhosis (ALC)[53,54] and alcohol dependence syndrome (ADS).[55,56] However, all of the publications reporting microbiota in ADS were based on 16S rRNA amplicon sequencing. Through the use of shotgun (whole-genome) metagenomics, Dubinkina VB et al. conducted the first study to describe the intestinal metagenome of ADS patients and to compare its taxonomic and functional makeup with that of ALC patients and the general population. It was discovered that the metagenomic signatures of alcoholism and liver cirrhosis share some similarities. A growing diversity of Lactobacillus and Bifidobacterium species was the main finding. When compared to ADS, patients with ALC exhibit a statistically significant increase in the number of Lactobacillus species in the population. This might have something to do with how well the genus can metabolise alcohol and its metabolites.[57]

Alcohol dependence and liver dysfunction negatively affect gut microbiota, leading to changes in community structure and metabolic potential. Differences in their impact play a significant role in tailoring personalized treatments and preventive measures through the modulation of the microbiota personalized treatment and prevention via microbiota modulation. The expansion of certain bacteria suggests caution in using probiotics from the same taxa. The gut microbiota of alcoholics shows a higher risk of synthesizing the toxic acetaldehyde, which increases the risk of colorectal cancer and other diseases.[57]

Role of metagenomics in diseases caused by smoking

Smoking may modify oral microbial ecology by reducing oral oxygen availability, while also affecting xenobiotic microbial breakdown. According to Wu et al., anaerobic bacteria thrive in smokers' oral environments while aerobic bacteria are less prevalent. Also, smokers who currently smoke and those who have never smoked have different functional metagenomic profiles, which includes the breakdown of specific harmful compounds in cigarettes.[58] In another study it was suggested that in smokers, Veillonella dispar exhibits a distinct SNV profile and gene content, implying altered functioning. Smokers who currently smoke and those who have never smoked may have different SNV profiles and gene contents. However, more research must be done to determine the therapeutic importance of these disparities.[59]

A specific segment on chromosome 15 has been identified by three different international groups of scientists in recent times. This region, if altered, can significantly amplify the likelihood of a smoker developing lung cancer by 30% to 80%. The overall risk of developing lung cancer for smokers with this genetic mutation is estimated to be approximately 20% to 23%, depending on whether they have one or two copies of the genetic locus identified as the 15q24 susceptibility locus by the researchers.[57,60]

NGS in tuberculosis

The use of targeted NGS (tNGS) for DR-TB diagnosis is gaining momentum. Because of the potential for speedy turnaround of results, methods based on direct sputum analysis make tNGS appealing. The focused approach looks at well-known gene targets where resistance-inducing mutations are widespread. Consequently, resistance predictions for most anti-TB medications are attainable in a single sequence, facilitating the construction of a comprehensive "resistotype" for each sample. Additionally, discovery of mixed infections and levels of micro/hetero-resistance provide extra information to further guide case treatment.[61]

Irrespective of the recognised limitations of WGS, Mycobacterium tuberculosis (MTB) diagnostic technology has evolved from research laboratories to clinical care and public health applications in well-resourced locations such as the United Kingdom and Europe. The largest impact of WGS in resource-constrained settings is its potential role in customized treatment of individuals with second-line TB drug resistance, which has replaced phenotypic testing for predicting susceptibility to all first-line medicines, paving the way for customized treatment options. Personalized treatment could drastically limit resistance amplification and overcome the usage of suboptimal treatment regimens,

thereby altering the course of the drug-resistant tuberculosis epidemic. In locations where HIV-TB co-infection or mixed TB illnesses are common, patient-tailored therapy will be extremely effective.[62]

FUTURE APPLICATIONS

Drug therapy can produce varying outcomes, such as positive effects, no effect, or harmful effect due to genetic variations. Pharmacogenetics is the study of how individual genes can affect drug efficacy, drug transport, disease susceptibility, or drug targets. With the advancement of genomic sequencing and cataloging, pharmacogenomics is emerging as a field that explores the relationship between genomic variability and drug responses.[63]

Pharmacogenomics and Precision Medicine

While pharmacogenetics investigates how genetic differences affect an individual's response to drugs, mainly concerning genes that are involved in drug metabolism (ADME) or drug target genes. On the other hand, pharmacogenomics is a broader approach that examines a person's entire genome to comprehend their drug response.[64]

About 20-40% of variability in drug response and toxicity can be explained by genetic variations in drug pharmacokinetics, pharmacodynamics, and drug-induced immunological responses.[65,66] Many genetic biomarkers have been identified, particularly in cytochrome P450 genes. Some examples of these biomarkers include the CYP2C19*2 allele, which results in reduced bioactivation of clopidogrel, has been found to be linked to inferior cardiovascular outcomes in patients undergoing percutaneous coronary intervention.[67] Clinically significant correlation between CYP2C19 genotypes and exposure, and the failure rates of the antidepressants sertraline and escitalopram have been identified.[68,69]

Targeted NGS technologies offer great value when genotype-guided pharmacotherapies are introduced to the clinical context by simultaneously detecting common and unusual genetic variation that may be important to adverse or desired drug responses in individuals. A well-known problem for NGS of pharmacogenes is genetic profiling utilizing any short-fragment sequencing method. The region of interest must have enough mapped sequencing reads to represent it accurately.[70]

A major challenge to incorporating pharmacogenetics into clinical decision-making is the degree to which healthcare professionals are comfortable with interpreting and utilizing test results.According to a recent study, when integrating pharmacogenetic testing into their workflow, healthcare providers were worried about the potential for results to be misinterpreted since they lack experience and familiarity with the testing.[71]

Although there are obstacles in the way of integrating pharmacogenomics into everyday medical care, ith the development of advanced sequencing technologies, there is growing momentum towards the prospect of conducting pharmacogenomic testing on a large scale in primary care. Consequently, pharmacogenomics is expected to have the most considerable impact on patient outcomes when implemented at the population level.

Genetic disorder diagnosis

The ability of NGS and illuminating the full spectrum of variants in a particular individual will also help to accelerate the identification of digenic or polygenic disease causes because the data are already available.[72] For instance, a big family with myocardial infarction was found to have heterozygous mutations in the two functionally related genes GUCY1A3 and CCT7.[73] Despite insufficient phenotypic information, NGS may be able to identify the disease-causing mutation. For instance, if a harmful mutation is found using NGS and segregation analysis in a gene known to cause a disease, the gene may have previously been linked to a more general or even specific trait. In these situations, a retrospective clinical assessment of the patient and their family members—a process called "reverse phenotyping"—may reveal previously undetected features.[74] Exome sequencing may achieve 25-52% diagnostic yield, which is significantly higher than Sanger sequencing and appears to be true for a wide range of disorders, including deafness, blindness, mitochondrial diseases, and movement abnormalities.[75,76]

Sports

The focus of the relatively new scientific field of "sports genomics" is on the structure and operation of the genomes of professional athletes.[77] Despite the relatively high heritability of athlete status and performance-related characteristics, finding genetic variations that contribute to a proclivity for success in various types of sports has been a difficult endeavour. In the last two decades, 185 genetic polymorphisms connected with athletic status have been found.[78,79]

Sports genomics is the study of how genetics and the environment impact athletic performance and injury risk. Recent research has identified 220 DNA markers associated with athlete status and 29 markers associated with soft-tissue injuries. Of these markers, several show promise for predicting performance and injury risk, including HFE rs1799945, MYBPC3 rs1052373, ACTN3 rs1815739, and COL1A1 rs1800012. However, predicting athletic performance and injury risk requires the consideration of

hundreds or thousands of DNA markers.[80]

WGS to identify genetic variants associated with physical performance and psychological traits in elite athletes was conducted to analyzed the genomes of 20 Tatar male wrestlers and found a large number of high-quality variants per sample. Using this data, an association analysis with reaction time (RT) and four significant SNPs associated with RT in wrestlers were identified. Out of 1884 known genome-wide significant SNPs related to RT, four SNPs were identified to be (KIF27 rs10125715, APC rs518013, TMEM229A rs7783359, LRRN3 rs80054135) associated with RT in wrestlers. The frequencies of certain alleles were found to be significantly higher in elite athletes involved in sports with RT as an essential component of their performance compared to less successful athletes and controls, this demonstrates that the APC rs518013 A and LRRN3 rs80054135 T alleles have an association with the best reaction time in wrestlers and subjects who are physically active and over-represented in elite athletes involved in sports with reaction time as an essential component of performance, demonstrating the potential of WGS in sports and exercise science.[77]

While NGS is still in its early stages of clinical application, the potential benefits are vast and promising. The information presented here is only a small fraction of what NGS can offer, and therefore clinicians should continue to explore and utilize this technology to its fullest potential.

END NOTE

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