NEXT-GENERATION SEQUENCING TECHNOLOGIES ARE DRIVING AT THE FOREFRONT OF PRECISION MEDICINE GROWTH

Abstract:

This case study offers a thorough examination of the next-generation sequencing technologies that are driving at the forefront of precision medicine growth, taking into account its situation at present, trends, major drivers, difficulties, and potential for growth.

Introduction:

Precision medicine, an innovative approach to healthcare, aims to tailor medical treatments to individual patients based on their genetic, environmental, and lifestyle factors. Next-generation sequencing (NGS) technologies have played a pivotal role in advancing precision medicine by enabling rapid and cost-effective sequencing of entire genomes, leading to a deeper understanding of diseases and personalized treatment strategies. While NGS has been tested across multiple healthcare settings, its use is most advanced in oncology with physicians sequencing their patients' tumors to match them to therapies designed to target the genetic alterations driving the tumor's growth.

Overview of NGS technology:

NGS technology, also referred to as massively parallel sequencing (MPS), is a parallel sequencing technology applied to specific samples obtained from patients with cancer, which can sequence billions of DNA base pairs in a single run.
NGS for cancer samples can range from targeted gene panels analyzing a few thousand base cells to whole-exome sequencing (WES) and whole-genome sequencing (WGS) analyzing 40 to 50 million bases and 3.3 billion bases, respectively. The target panels in NGS offer a larger exon coverage, greater than that with WES and WGS applications. The targeted panel sequencing detects only the specific carcinogenic genes, while WES and WGS can identify unknown variants along with known mutations. WGS provides the most unbiased examination of the cancer genome, thereby paving the way for the discovery of previously unrecognizable mutations.
Presently, NGS of targeted gene panels is very common in clinical practice to find targetable genomic alterations. Whole exome or genome sequencing is mainly used for research purposes. NGS of gene panels longer than one million megabases are under extensive validation for TMB (tumor mutational burden) estimation, aiming to serve as a surrogate test for whole exome sequencing-based TMB analysis. In the future, whole exome sequencing might be validated for the use of identifying functional neoantigens or other clinical biomarkers.

Client Background:

The client represented a medical device company having a direct presence in around 50 countries worldwide. The client had complex requirements to be unravelled for understanding the possibilities of next-generation sequencing technologies driving at the forefront of precision medicine growth.The client team was curious to understand what major developments and technologies are present in the field.

Challenges Faced By Client:

Although NGS technology has the advantage of a high-throughput workflow and can discover hereto unknown mutations but client faced several challenges such as technology, data management, data analysis, interpretation, reporting, and genetic consulting. Many publications and international consensus have reported the application of NGS in single-gene inheritance diseases and prenatal diagnostics, however, there has been no consensus on the application of NGS technology in clinical oncological practice, especially when used in cancer precision diagnosis and treatment to date.

Some of the major criteria put forth by the client are as follows:

Data Management and Analysis: NGS generates vast amounts of genomic data, which requires robust data management and analysis pipelines. The analysis of NGS data is complex, and there is a need for advanced bioinformatics tools and computational infrastructure to handle and interpret the data accurately and efficiently

Variant Interpretation and Clinical Relevance: Interpreting the vast amount of genetic variants identified through NGS is a significant challenge

Integration with Clinical Workflows: Integrating NGS into routine clinical workflows and electronic health records (EHRs) poses challenges. There is a need for seamless integration of NGS data with clinical decision support systems and EHRs, enabling efficient and effective use of genetic information in patient care.

The client approached Data Bridge Market Research to address these aforementioned complex challenges and to understand what are the growth drivers present in the market for precision growth. Data Bridge Market Research, a trusted market research consulting firm renowned for its expertise in procurement consulting analyzed the feasibility of the project. Furthermore, the client wanted to know about the methods of next-generation sequencing and what are the quality requirements of NGS in cancer diagnosis. DBMR conducted a comprehensive analysis to get deeper insights.

DBMR Market Research Analysis:

NGS Methods:

Next-generation sequencing was first applied to genomics research, mainly to detect variants in DNA sequence in terms of single nucleotide variations (SNVs), insertion-deletions (indels), structural variations (SVs), and copy number alterations (CNAs).

NGS methodology applied to an entire genome is called "whole genome sequencing," in which both coding and non-coding regions are sequenced. WGS generates huge amounts of data per sample, but usually low depth of coverage. A typical WGS experiment assures a 30X coverage, enough to detect most germline variants in the human genome, but inadequate to identify all rare somatic mutations present in cancer genomes.

Transcriptomics

RNA-sequencing (RNA-seq) is a relatively new application of NGS, which is gradually replacing microarrays as the favorite technology for transcript analysis. Differently from arrays, RNA-seq is not designed as a targeted test and does not require species- or transcript-specific probes. It can be used both to quantify gene expression and to detect novel transcripts, gene fusions, SNV, and indels at the same time.

Epigenomics

The term epigenetics refer to "the study of changes in gene function that are mitotically and/or meiotically heritable and that do not entail a change in DNA sequence" (Wu and Morris 2001). DNA methylation, histone-modification, and altered DNA–protein interactions are three major epigenetic alterations involved in cancer development and progression.

Precision Medicine in Oncology:

Several studies have shown the utility of NGS in identifying clinically actionable mutations in cancer patients. For example, an international data-sharing consortium, the Genomics Evidence Neoplasia Information Exchange (GENIE), estimated an action ability rate of 30% across several cancers. That is, 30% of tumors sequenced in the GENIE consortium had a mutation that could be targeted by an existing targeted therapy.

Precision Medicine in Oncology:

Quality management (QM) plays a pivotal role in the standardization of NGS workflow by providing basic guidelines to ensure an advanced reproducibility of data and high turnover with reduced cost. Quality documentation containing procedural instructions and verified documents is the preliminary requirement for a good standardization method, which improves the transparency and reliability of the results. One of the most important criteria for QM is quality assurance (QA). The QA program provides quality control (QC) methods for the predetermined checkpoints, such as contamination identification including initial sample check, fragmentation, library evaluation, error rate monitoring, and data analysis. These methods assist in confirming the formerly established performance status of a sample and indicate an error in case of any change in the status. The aforementioned QC features ensure that no sequence or sample data is used in the testing without meeting the established laboratory quality standards, and the QA procedure minimizes the risk of errors due to contamination.

The following recommendations were given by DBMR regarding NGS technologies:

— Standardization of NGS assay with complete validation is necessary for its application in clinical practice for diagnosis of cancer driver gene mutations, to meet the clinical diagnostic standards

— Laboratories should determine the content of the assay with relevant technical parameters and also specify the purpose and utility of the NGS testing

— When used as a reference for deciding on targeted therapy, the NGS test results should identify the variations in genes that can be targeted for a particular drug. When used for molecular classification, an analytical model needs to be validated before further application to predict superior efficacy and prognosis of NGS testing

Growth Factors:

— Genomic Profiling: NGS enables comprehensive genomic profiling, allowing researchers and clinicians to analyze large amounts of genetic data quickly and cost-effectively. This has led to a better understanding of the genetic basis of diseases and the discovery of novel biomarkers for diagnosis, prognosis, and treatment selection

— Personalized Cancer Treatment: NGS has revolutionized cancer care by enabling the identification of genetic alterations and mutations in tumors. This information helps in selecting targeted therapies and predicting response to treatment. NGS-based liquid biopsies also offer a non-invasive method for monitoring tumor progression and detecting resistance to therapy

— Rare Disease Diagnosis: NGS has improved the diagnosis of rare genetic diseases by enabling rapid and comprehensive analysis of the entire genome or exome. It has facilitated the identification of disease-causing variants, leading to early diagnosis, appropriate management, and potential therapeutic interventions for patients with rare diseases

— Pharmacogenomics: NGS has contributed to the field of pharmacogenomics, which focuses on how an individual's genetic makeup influences their response to medications. By identifying genetic variants that affect drug metabolism and response, NGS enables personalized drug selection and dosage adjustments, improving treatment outcomes and reducing adverse drug reactions

— Infectious Disease Surveillance: NGS has been instrumental in tracking and monitoring infectious diseases, including viral outbreaks and antibiotic-resistant bacteria. It allows for rapid and accurate identification of pathogens, characterization of their genetic diversity, and tracking of transmission patterns. This information aids in the development of targeted interventions and public health strategies

DBMR Market Research Approach to Overcome Client Challenge:

DBMR told the client about the future possibilities of next-generation sequencing technologies for precision medicine.

Future Possibilities:

With the widespread scope of tumor gene testing, NGS for precision diagnostics has gradually progressed from single-gene analysis to the profiling of several hundreds of genes. It is possible in the future that integrated information from the exome, transcriptome, whole genome, and epigenome will be adopted into clinical practice. Furthermore, as biotechnology is also evolving, it is foreseeable that the application of high-throughput NGS in clinical diagnosis and precision treatment will change perpetually in terms of testing technology, analysis tools, and variant interpretation, among others, in the future, which will also bring various challenges to the practical application.

Major Impact of NGS technologies in Business

Next-generation sequencing (NGS) technologies have had a profound business impact on precision medicine. These impacts extend to various sectors, including healthcare providers, pharmaceutical companies, biotechnology firms, diagnostic laboratories, and more. Here's a breakdown of the business impact of NGS technologies in precision medicine:

Growth in Genetic Testing Services: NGS has led to the expansion of genetic testing services. Diagnostic laboratories and companies offering genetic tests have seen increased demand, leading to revenue growth.

Targeted Drug Development: NGS enables pharmaceutical and biotechnology companies to identify and validate drug targets more efficiently. This has accelerated drug development pipelines and reduced R&D costs.

Personalized Treatment: Hospitals and healthcare providers have integrated NGS into patient care. They offer personalized treatment plans based on genomic data, which can attract more patients seeking cutting-edge healthcare.

Adoption of Genomic Data: Health insurance companies are increasingly incorporating genomic data into their risk assessment models. This can lead to more tailored insurance products and potentially better risk management.

Sales of Sequencing Machines: Companies manufacturing NGS equipment and consumables have experienced substantial growth in sales as more laboratories adopt NGS for research and diagnostics.

Clinical Trial Services:

Patient Stratification: CROs (Contract Research Organizations) specializing in clinical trials have seen increased demand for services related to patient stratification using genomic data. NGS helps identify suitable trial participants, making clinical trials more efficient.

International Markets: NGS technologies have facilitated the expansion of precision medicine services and products into international markets, opening up new revenue streams for businesses.

Consulting and Compliance Services: Companies specializing in regulatory compliance and quality assurance have emerged to help ensure that NGS-based diagnostics and treatments meet regulatory requirements.

Strategic Alliances: Companies across the healthcare ecosystem are forming strategic partnerships and collaborations to leverage NGS technologies, leading to shared resources and expertise.

Competitive Advantage: Staying at the forefront of NGS technology adoption can provide a competitive advantage in the precision medicine market, encouraging continuous innovation.

Conclusion:

In conclusion, NGS technologies have not only transformed the way healthcare is delivered but have also created numerous business opportunities and growth prospects across the precision medicine industry. Companies that adapt to this changing landscape and harness the potential of NGS stand to benefit from increased revenue, market share, and innovation.

Next Generation Sequencing technologies are driving the forefront of precision medicine growth by providing clinicians with unprecedented insights into patients' genetic makeup. The future of next-generation sequencing (NGS) in precision medicine holds great promise for advancing patient care and personalized treatments. Here are some key aspects that highlight the potential future developments in NGS for precision medicine:

- Enhanced Clinical Integration
- Expanded Genomic Profiling
- Real-Time Monitoring and Precision Therapeutics
- AI Integration

The future of NGS in precision medicine is promising, with advancements in technology, data analysis, and integration with other omics disciplines. These developments have the potential to revolutionize patient care, improve treatment outcomes, and pave the way for truly personalized medicine.