BLACKHAWK GENOMICS

Trends, Growth, and Challenges of Personalized Genetic Testing

ABSTRACT

Growth of the genetic testing market has skyrocketed in the last 15 years. Largely driven by clinical need and improvements in next-generation sequencing (NGS) capability, this sector continues to expand and evolve, impacting clinical laboratories, regulatory agencies, and approaches to patient care. Multiple gene (multiplex) panel testing, aimed at understanding oncology risk and improving cancer treatment, represents a large proportion of the market. However, while genetic testing is helpful in many cases, diagnostic and regulatory challenges remain. Commercial laboratories, clinicians, and regulatory agencies must adapt rapidly to effectively generate and use genetic testing data to improve patient outcomes.

INTRODUCTION

Since the completion of the Human Genome Project in 2003, genetic testing use and availability has increased rapidly. According to a recent study analyzing information from genetic testing and claims databases from 2014-2017, approximately 75,000 genetic tests were on the market as of August 2017. [1] These included both single-gene and multi-gene panel tests, whole exome sequencing, whole genome analysis, and non-invasive prenatal testing (NIPT). The numbers of available genetic tests continue to grow, with around ten new tests (two to three new panel tests) being introduced per day.[1]

This growth is largely explained by an increased interest in personalized medicine combined with advances in NGS. Next generation sequencing tests can quickly identify genetic variants in a patient's genome that may help clinicians better predict, diagnose, treat, and monitor disease.[1] At the same time, genetic sequencing costs have sharply decreased to around $0.014 per megabase for an average cost of $1300 per genome.[2] Data analysis methods and availability of databases promoting interpretation of sequence data for clinical use have also improved.[1] As such, the clinical sequencing market is growing at a compound annual growth rate of 28 percent and is projected to be worth $7.7 billion worldwide by 2020.[3] The genetic testing market is projected to be worth over $22 billion by 2024.[4]

GENETIC TESTING: AREAS OF FOCUS, ADVANCEMENTS, AND LIMITATIONS

Between 2014-2016, the highest percentages of spending on genetic testing were in the clinical domains of hematology (noncancer), HLA typing, pharmacogenetics, oncology diagnostics and treatment, hereditary cancer tests, and prenatal tests. Within these domains, multiplex panel tests accounted for the highest percentage of spending. NIPT was the second-largest spending category, while spending on single-gene tests declined during this time. [1]

Of the multiplex tests available, many are aimed at better understanding hereditary cancer risk and treatment. In an effort to accelerate research and improve care for people at risk for hereditary cancer, several commercial laboratories offering multiplex testing collaborated with Memorial Sloan Kettering Cancer Center and others to build the Prospective Registry of MultiPlex Testing (PROMPT). The PROMPT registry aims to collect data from patients across the United States who have agreed to share data from their multiple cancer gene panel tests.[5]

For patients already diagnosed with cancer, sequencing data has proven useful for matching therapies to patients based on their cancer's genome. For example, a clinical trial of advanced cancer patients given treatment specific to their tumor mutations reported an overall response rate of 27% compared to 5% in patients who did not receive sequencing-matched therapy.[6] Other studies have shown improvements in progression free survival [7], overall survival [8-9], and tumor response [7, 11] for patients on sequencing-matched therapy versus non-matched.

Next-generation sequencing has also helped advance the development of drugs that target tumor-driving mutations.[12] For example, a programmed death 1 (PD-1) blockade treatment was shown to be effective across 12 tumor types based on "loss-of-function" mutations in the mismatch repair pathway. [13] This study paved the way for U.S. Food and Drug Administration (FDA) approval of pembroluzimab, the first drug to be approved based solely on mutations and not tumor type.

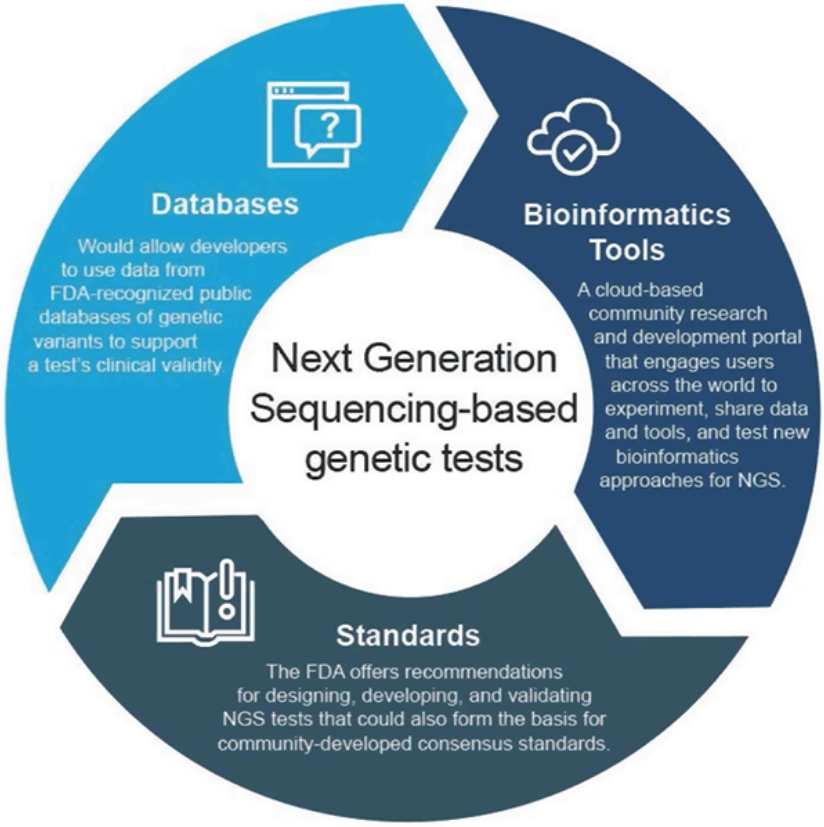
Despite these advances, personalized medicine still has limitations. Although NGS is useful in some patients, many others find they do not have "actionable mutations" suitable for sequencing-matched therapy. Studies indicate that while some 40-94% of the patients have an actionable mutation, only 4-44% go on to receive sequencing-matched treatment.[9] Patient preference [13], access to or eligibility for clinical trials [11, 14], and high costs associated with NGS and sequencing-matched therapies [15-16] are other barriers to treatment. Additionally, physicians often need guidance regarding implementation or interpretation of genetic tests in clinical practice.[1,12]

EVOLVING WITH RAPID CHANGE

The sizeable amount of data generated through NGS and the quick influx of genetic tests into the market presents new challenges for regulatory agencies like the FDA.[17] Because many new multiplex genetic tests contain many tests in one and/or are laboratory-developed and do not require FDA-approval, more flexible regulatory approaches are needed to keep up with the rapidly changing landscape. As such, the FDA streamlined their regulatory oversight of NGS tests in 2018. Their first guidance focuses on clinical databases and allows developers to use data from FDA-recognized public databases to support clinical validity, thus encouraging data sharing.[18] The second guidance gives recommendations for the design, development, and validation of NGS diagnostic tests (Figure 1).[19]

CONCLUSIONS

Clinicians are increasingly turning toward personalized genetic testing to help them diagnose and treat disease more effectively, thereby improving patient outcomes. Multiple gene panel tests, particularly those for oncology and cancer risk, represent the largest category of spending in genetic testing. Rapid growth of the genetic testing market has largely been driven by clinical need and improvements in NGS technology. Despite its utility, genetic testing presents new clinical and regulatory challenges. There is an ongoing need for simple and useful tools that interpret genetic testing results for clinicians. Regulatory agencies are adapting with updated recommendations for data sharing and development of genetic testing.



1. Figure 1. The U.S. FDA streamlined its oversight of NGS testing to improve utility for developers and physicians. Source: https://www.fda.gov/medical-devices/vitro-diagnostics/precision-medicine

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