# WhitePaper

# How Next-Generation Sequencing Helps Molecular Laboratories Deliver Personalized Medicine Services to Their Client Physicians

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# Introduction

*"Pathologists will be the point persons for physicians as personalized medicine becomes the norm, and as the understanding of the relationship between genetic variants and disease grows exponentially."*

Medicine is rapidly shifting from a traditional one-size-fits-all approach for diagnosing and treating illness and disease, to an individualized predictive and personalized medicine model with medical care customized for individual patients. Uniquely positioned within this shifting healthcare paradigm are molecular and clinical laboratories that can provide healthcare teams with access to a treasure-trove of actionable genetic data.

The practice of personalized medicine, which includes precision medicine and proactive medicine, is defined by the U.S. Food and Drug Administration/Center for Drug Evaluation and Research as "using genetic or other biomarker information to make treatment decisions about patients. Those could include who should get certain kinds of therapies or specific doses of a given therapy, or who should be monitored more carefully because they're predisposed to a particular safety issue."[1]

Pathologists will be the point persons for physicians as personalized medicine becomes the norm, and as the understanding of the relationship between genetic variants and disease grows exponentially. With next generation sequencing (NGS) accelerating the pace of discoveries, prevention and treatment no longer will be centered around "standards of care" that often result in a predetermined sequence of therapies. Instead, a patient's genome, lifestyle, and environment will combine to pinpoint effective treatments for an individual's disease, while avoiding adverse drug reactions.

Today, cancer is the "poster child"[2] for disease treatment approaches that employ personalized medicine strategies to assess risk and select therapies.

 

"The number of targeted therapies in the pipeline for all diseases is increasing dramatically," J. Leonard Lichtenfeld, MD, Deputy Chief Medical Officer for the American Cancer Society, told *Genome* magazine. "Personalized medicine in the age of genomics means we're living in dynamic times. The big question right now is how do we take all this new information we're gathering and use it for the benefit of the patient?"[3]

NGS is the engine powering much of this new genetic information and igniting the potential of personalized medicine. By adopting NGS technologies, clinical laboratories have an opportunity to add clinical value and generate a new revenue source. However, they must have in place a laboratory information management system (LIMS) specifically designed to handle personalized medicine's informatics integration and workflow challenges.

This white paper will explore the role NGS will play in the delivery of personalized medicine and how clinical laboratories that offer these services to client physicians will be on the forefront of a medical revolution. In the pages that follow, you will learn about:

- The growing role of NGS in clinical care;
- NGS' return on investment for clinical and molecular laboratories;
- The role of pathologists, as NGS accelerates the transition to predictive and personalized medicine;
- The information technology and tools laboratories need to successfully offer NGS-based services;
- Benefits of outsourcing annotation and interpretation of gene sequences and test-result reporting; and,
- What clinical and molecular laboratories need to know about marketing NGS services to new and existing clients.

 

## Chapter 1:

# Why Next-Generation Sequencing Has a Growing Role in Clinical Care

By sequencing tens of thousands of genes simultaneously, NGS technology has transformed the laboratory diagnosis of genetic disease and is rapidly making inroads in other areas of medicine.

In the past, molecular pathologists would sequence and analyze one gene at a time—a labor and time intensive process. In contrast, NGS can sequence and analyze an entire human genome in less than one day's time.[4]

While commercially available NGS platforms use different sequencing technologies, they all perform sequencing of small fragments of DNA in parallel and use bioinformatics analysis to map the fragments to an established human reference genome.

Leading sequencing manufacturer Illumina describes NGS' broad range of applications:[5]

- Rapidly sequence whole genomes;
- Deeply sequence target regions;
- Utilize RNA sequencing to discover novel RNA variants and splice sites, or quantify mRNAs for gene expression analysis;
- Analyze epigenetic factors, such as genome-wide DNA methylation and DNA-protein interactions;

 

- Sequence cancer samples to study rare somatic variants, tumor subclones; and,

- Study microbial diversity in humans or in the environment.

*"Adopting NGS technology means clinical laboratories have an opportunity to add clinical value and generate a new revenue source."*

NGS builds on the pioneering work of Frederick Sanger, PhD, a British biochemist who developed the first DNA sequencing method and sequenced the first complete genome—called phiX174 virus—in 1977.[6]

Other scientific milestones followed, including the work of James Gusella, PhD, who identified the gene associated with Huntington's disease in 1983 and developed techniques for testing embryos for genetic diseases in the womb in 1992.[7]

The most ambitious early sequencing project was the Human Genome Project (HGP) in 1990, which sought to sequence all three-billion base pairs of a human genome. Completed in 2003 at a cost of $2.7 billion, the HGP provided a complete genetic blueprint for human beings.[8]

NGS platforms emerged in 2005, providing high-throughput sequencing capable of producing 20,000 times more data in a single run than the technology used during the HGP.[9]

"The basic sequencing chemistry is not much different than what it has been for decades—enzyme-mediated incorporation of sequential nucleotides—but the scale of that sequence, enhanced by novel hardware and software technology, is now much more advanced," Richard D. Press, MD, PhD, told *Clinical Advances in Hematology and Oncology* in the April 2014 issue.

NGS technology also has brought genetic testing within reach for clinical laboratories and patients, as the cost to generate a human

 

genome sequence falls and the terabases of genome sequence data grow exponentially.[11]

The much ballyhooed $1,000 genome[12] was achieved in 2014 and became old news three years later. In 2017, San Diego-based Illumina unveiled its NovaSeq sequencer—a machine capable of deciphering an entire human genome in less than an hour—which is expected to usher in a $100 genome.[13]

*"The much ballyhooed $1,000 genome was achieved in 2014 and became old news three years later."*

"We believe that future systems derived from the NovaSeq architecture we are launching today will one day enable the $100 genome and propel discoveries that will enable a deeper understanding and better treatments for complex disease," Francis deSouza, President and CEO of Illumina, predicted in a news release. "The NovaSeq Systems enable the study of genetic links between health and disease at an unprecedented scale by making it possible to sequence more samples at greater depth and take on projects that would otherwise be cost-prohibitive."[14]

While NGS is not yet a routine part of clinical care, the stage has been set for it to become so very soon.

 

## Chapter 2:

# How Clinical and Molecular Laboratories Can Establish NGS Services That Deliver Value to Physicians and Patients

As the shift from reactive to proactive-predictive medical care continues, clinical diagnostic laboratories soon may confront a new reality—adopt NGS testing services or lose business and clients to competitors who do.

"There is no longer a question of if or when genomic technologies will move from the research bench to the patient—the shift is happening now," noted *Clinical Lab Products* reporting on results obtained from a recent survey among managers of clinical NGS laboratories, conducted in partnership with market research firm Frost and Sullivan. The survey analyzed clinical laboratories' current/future plans for adopting NGS in clinical applications.[15]

When it comes to sequencing being performed by molecular laboratories, there is no doubt that NGS has gained acceptance as the replacement for classical first-generation technology in the clinical environment.

In a 2016 issue of *Expert Review of Precision Medicine and Drug Development*, authors Rajesh R. Singh, PhD, et al., drove home that point in their article, "Implementation of Next Generation Sequencing in Clinical Molecular Diagnostic Laboratories: Advantages, Challenges, and Potential, calling NGS the "new 'gold standard' for genome sequencing."[16]

 

*"There is no longer a question of if or when genomic technologies will move from the research bench to the patient– the shift is happening now."*

However, adding NGS to a laboratory's testing menu brings challenges and opportunities as the range of clinical genomics tests continues to expand. In addition to instrument costs, laboratories adopting NGS face significant operational expense for consumables used in target library preparation, and in the sequencing process itself, as well data interpretation costs. For that reason, Psyche Systems VP of Sales Brian Keefe advises clinical laboratories to carefully target NGS offerings to their customer base.

"Knowing who your customers are and what you do for them today should guide you as a laboratory. For example, you know you should be doing NGS testing, and the justification for needing to go in this direction is because 90% of your clients are oncologists."

If a molecular or clinical laboratory has a hospital with a large cancer center as a client, or numerous oncologists in its customer base, offering NGS testing provides a direct value benefit and enables the laboratory to differentiate itself from its competition by offering physicians actionable information.

"NGS testing is going to allow you to go to that customer and say, 'Not only can I tell you your patient has prostate cancer, I can tell you specifically what type of prostate cancer it is.' We know this particular variant of prostate cancer is not going to respond to X, Y, and Z. Instead of trying blanket generic chemotherapies, I can give you a much more specific diagnosis, which is going to give you a much more direct treatment path."

Since long-term clients typically are a laboratory's most profitable customers, offering NGS services raises the bar for your lab. "It is definitely easier to keep a client than to replace them," notes Keefe. "That rings true in just about any industry. Losing your biggest customer, or five of your smaller customers, has a significant cost to you because somebody has to replace them."

 

## Chapter 3:

# What Pathologists and PhDs Need to Know about Helping Physicians Understand the Value of NGS in Diagnosing Patients, Selecting Best Therapies, and Monitoring Patient Progress

Personalized medicine is not a new concept. In fact, the idea dates to the time of Hippocrates, who wrote: "It is far more important to know what person the disease has, than to know what disease the person has."[17] However, today's modern usage of the term was first published in 1999.[18]

Personalized medicine promises to transform the practice of healthcare, as customized care—from diagnosis to treatment to prevention—becomes the norm. This means physicians will take a proactive approach to treating their patients, and as they do, clinical pathologists will assume an integral, active role on the care team.

The Personalized Medicine Coalition lists the many benefits of personalized medicine to patients and the health system:[19]

- Shifting the emphasis in medicine from reaction to prevention;
- Directing targeted therapy and reducing trial-and-error prescribing;

 

- Reducing adverse drug reactions;
- Revealing additional targeted uses for medicines and drug candidates;
- Increasing patient adherence to treatment;
- Reducing high-risk invasive test procedures; and,
- Helping to control the overall cost of healthcare.

*"NGS testing is going to allow you to go to that customer and say, 'Not only can I tell you your patient has prostate cancer, I can tell you specifically what type of prostate cancer it is."*

At the center of this healthcare transformation is NGS, which is being harnessed to address an increasingly diverse range of problems, from unraveling the genetic basis of unexplained syndromes to tracing the sources of infection outbreaks. One such example occurred in 2013, when the transmission of Staphylococcus aureus (MRSA) in a British neonatal unit was confirmed using whole-genome sequencing.[20]

NGS became available in the clinical laboratory in late 2013 after the U.S. Food and Drug Administration (FDA) approved the first NGS system from Illumina, a leading manufacturer of DNA sequencing machines.[21] As researchers identified more ways to use whole exome sequencing, and the cost of sequencing fell, NGS became more affordable to use in clinical settings. Most notably in cancer prevention and treatment.

"Pathologists have led the way in studying the cost-benefit ratio of prospective genetic testing for colon and endometrial cancers," notes Carey August, MD, Medical Director, Anatomic Pathology, Advocate Illinois Masonic Medical Center. "It's often viewed as a waste of money, but studies have proven that the savings for each patient who tests positive for abnormalities, justifies doing it in a systematic, reflexive fashion. From a cost-utilization standpoint, it might seem

 

wasteful, but when you put the cost savings in the context of the big picture, it has tremendous value."[22]

*"Personalized medicine promises to transform the practice of healthcare, as customized care—from diagnosis to treatment to prevention—becomes the norm."*

Physicians on the delivering end of patient care are tasked with selecting and ordering the right test on a case-by-case basis. This is an almost herculean task, considering that among the most commonly assayed genes (TP53, KRAS, PTEN, BRAF, CFTR), 400-600 different tests are available in the U.S. market.[23] But that means clinical pathologists and laboratory scientists can play a growing and important role in helping guide oncologists, infectious disease specialists, pediatricians, fertility specialists, and other physicians in genetic test selection and precision treatment decisions.

"Very often I will look at a molecular pathology report—an NGS report—and I will call the pathologist and say, 'What does this mean? Is this actionable or not? Does this mean I should treat in this way or not?'" Roy Herbst, MD, PhD, Chief of Medical Oncology, Yale Cancer Center, said during a video interview discussing the importance of the pathologist on multidisciplinary cancer teams. "The pathologist is incredibly important."[24]

As of 2017, there were almost 70,000 genetic testing products on the U.S. market, with an average of 10 new testing products entering the market every day. NGS is fueling that growth, accounting for an estimated 48% of available tests, according to Concert Genetics' most recent estimates.[25]

Meanwhile, the number of personalized medicines—drugs that identify specific biomarkers in their usage instructions—reached 132 in 2016, according to the Personalized Medicine Coalition. In 2008, the total was five.[26]

 

In 2005, personalized medicines accounted for 5% of new molecular entities approved by the FDA. However, by 2016, that number had risen to 27%.[27]

The NGS pipeline also includes laboratory-developed tests (LDTs) that are regulated by the Centers for Medicare and Medicaid Services under the Clinical Laboratory Improvement Amendments (CLIA).

*"As the number of genetic tests grows, along with increased use of personalized medicine drugs, pathologists must take on a larger role in patient care."*

According to an article on Biocompare.com, the number of available NGS-based LDTs is difficult to estimate, however, new tests are coming on the market frequently.[28]

"For example, in the past year, NGS-based LDTs for women's reproductive health, inherited genetic disorders, and genetic alterations associated with cancer have been introduced by Celmatix, Good Start Genetics, and Personal Genome Diagnostics, respectively," the author wrote.[29]

Combined with advancements in immunotherapy, gene therapy, and gene editing, the future of personalized medicine is advancing rapidly.

"Between 2012 and 2016, technologies were invented that allow us to change human genomes intentionally and permanently. We can now 'read' human genomes, and we can 'write' human genomes in a manner inconceivable just three or four years ago," stated Siddhartha Mukherjee, MD, DPhil, author of "The Gene: An Intimate History."[30]

As the number of genetic tests grows, along with increased use of personalized medicine drugs, pathologists must take on a larger role in patient care, argues Ritu Nayar, MD, Professor of Pathology, Northwestern University Feinberg School of Medicine, Northwestern Memorial Hospital.

 

"We need to play a greater role in education, particularly around appropriate test utilization," she notes. "I don't personally consider this gatekeeping, as much as doing our job as part of a multidisciplinary team."[31]

*"Use of proactive and predictive technologies will enable physicians to identify not only the safest therapies for their patients, but also the most effective treatments and medicines."*

Cancer treatment is one area where pathologists have become fully integrated into the medical team. However, Wendy Leutgens, RN, Chief Operating Officer and President, Loyola University Medical Center, argues for adding their expertise to other patient-care teams as well. "How can we replicate that in other areas? There must be other opportunities to integrate diagnostics into the patient care team."[32]

While NGS testing is leading to an expanded role for pathologists on patient-care teams, its mark on prescription drug therapy also is being made. Pharmacogenomics (PGx) tosses aside the traditional—but largely ineffective—"one-size-fits-all" system for selecting drug therapies, and replaces it with medications and doses tailored to a person's genetic makeup. A study by BB Spear et al., reproduced in 2017's "The Personalized Medicine Report," shows that 75% of cancer drugs, 70% of Alzheimer's drugs, 50% of arthritis drugs, 43% of diabetes drugs, 40% of asthma drugs, and 38% of anti-depressants are ineffective, on average, when given in a cookie-cutter fashion.[33]

By predicting an individual's drug response, PGx also offers the potential to drive down severe adverse drug reactions, which are estimated to result in one million emergency department visits and account for an estimated one in three of all hospital adverse events each year.[34]

According to the Centers for Disease Control and Prevention (CDC), nearly 29% of Americans age 20-59 are taking two or more prescription drugs. By age 60, the percentage of people using three to

 

four drugs increases to 27.3%, while 36.7% of older Americans take five or more drugs.[35]

Issam Zineh, MPH, Director, Center for Drug Evaluation and Research, Office of Clinical Pharmacology, said in an interview published on the FDA's website that genomic medicine can bring more precision to drug prescribing.[36]

*"A successful relationship with your customers is one where you have the ability to serve them in a way that is not just a one-size-fits-all appraoch."*

"Personalized medicine aims to streamline the clinical decision-making by using biological information available through a genetic test or biomarker, and then saying, 'Based on this profile, I think you're more likely to respond to Drug A or Drug B, or less likely to have an adverse reaction with Drug C," he noted.

The use of proactive and predictive technologies will enable physicians to identify not only the safest therapies for their patients, but also the most effective treatments and medicines. Pathologists can play a leading role in this decision-making by guiding client physicians toward the best therapies and assisting in monitoring patient progress.

To do so, however, pathologists must have the right tools in place, including the ability to collect, store, comprehensively analyze, and interpret NGS data and extract clinically important information.

 

## Chapter 4:

# What IT/Informatics Capabilities Do Clinical/ Molecular Laboratories Need to Succeed with NGS Services?

Declining NGS costs, and growing use of NGS in precision medicine, are expected to propel growth in the global marketplace from 2015's valuation level of $4.62 billion to $201.4 billion by 2025, according to a report by Grand View Research.[37]

To capitalize on the growth in NGS testing, clinical and molecular laboratories need the right informatics tools. Selecting a laboratory information system (LIS) vendor that understands the complexity of NGS testing and offers a LIS designed for genetic testings' diagnostically diverse complexities, should be a top priority. A molecular and genetic LIS also should integrate with a deep and easily accessed knowledge base to support precision medicine initiatives and offer a reporting system that identifies clinically-actionable results.

NucleoLIS, developed by Psyche Systems in Milford, Mass., is a best-of-breed fully automated solution designed with the diagnostically-diverse complexities of genetic testing in mind.

"Laboratories will want to make sure they are partnering with a vendor who understands what their unique business requirements are as they expand into NGS and molecular testing. Critical to a successful strategy is identifying an LIS provider who understands that this is still an evolving area of testing," noted Lisa-Jean Clifford,

 

Chief Executive Officer, Psyche Systems. "It's essential that your LIS vendor is at the forefront of the evolution, and that their solutions feature technological advances that will ensure your lab is armed with the tools it needs to succeed."

*"Molecular lab leaders looking to upgrade their LIS should focus on systems offering cutting-edge technology customizable to their current and future needs."*

Many hospital and healthcare institutions' enterprisewide electronic health record (EHR) systems include an LIS component. However, such LIS systems do not typically have the functionality to handle the current testing needs of molecular and genetic laboratories.

Even a traditional stand-alone LIS may be incapable of handling the workflow of today's genetic testing labs, which need support for a complex series of specimen preparation steps and generate terabytes of data. For example, a 2004-era DNA sequencer could sequence up to two million base pairs/day, while a single DNA sequencer in 2017 could sequence up to 120-billion base pairs/day.[38]

It is not surprising, therefore, that adding molecular and genetic testing features to an existing LIS often results in a less-than-optimal solution.

"If you look at the LIS systems available today, a lot were written over a decade ago," Keefe explains. "They come out with new features and functionality, but [NGS] science does not really support the use of a lot of the older platforms that many LIS systems exist on today."

Molecular laboratory leaders looking to upgrade their LIS should focus on systems offering cutting-edge technology customizable to their current and future testing needs.

"The software solutions the labs use have to be able to not only assimilate the data and support the data being generated, but also be able to do so for the foreseeable future," Keefe points out. "Technology is evolving so quickly, and the specific analyses are

 

evolving so quickly, the LIS platform, if not designed in a forward-thinking way, becomes obsolete much more quickly than if the technology evolves either slower or more commoditized, as we've seen in many traditional clinical pathology labs."

When selecting a molecular LIS, here are must-have features:

*"The software solutions labs choose should not only be able to assimilate and support the data being generated, but also do so for the foreseeable future."*

- Electronic connectivity with customers through a portal or other mechanism to capture patient information and documentation unique to molecular and genetic testing;
- Robust specimen preparation module;
- Flexible test menus that can be customized based on specimen type;
- Ability to track multiple samples per test;
- Simultaneous support of protocols, such as Web APIs, Web services, and RESTful API needed for interoperability with enterprise EHRs, physician EMRs, middleware solutions, and external services;
- Integrated data mining tools to facilitate data sharing with pharmacogenomics reporting databases and other specialized data services; and,
- Sophisticated report design tools that enable customization of data elements and report formatting flexibility not found in template-based reporting systems.

Clifford believes well-established small-to-midsize LIS companies often are best positioned to supply the "nimbleness" required by

 

molecular labs, because such vendors "work with their customers directly and in a strategic way—they don't see their customers as just a number. A company that is willing to do customizations to their product on a regular release basis to ensure timeliness and availability of meaningful features and functionality for their customers, and not just wait two or three years for another standard, major release to come out, will help their customers advance and stay relevant in a quickly evolving area of healthcare."

"A successful relationship with your customers is one where you have the ability to serve them in a way that's not just a one-size-fits-all approach," Clifford states.

## Chapter 5:

# The Benefits of Outsourcing Annotation and Interpretation of Gene Sequences and Test Results in Support of Patient Care

The amount of data produced by NGS testing is both a blessing and a curse for a clinical laboratory. The technological advances in generating large amounts of high quality sequencing data creates the need for customized analysis, interpretation, and reporting to meet specific needs.

As Cambridge Healthtech Institute in Massachusetts notes, "Whole exome or whole genome sequencing (WES/WGS) is the ultimate genetic test and many success stories provide a taste of its power ... However, while the cost of generating high-quality whole genome sequence data is rapidly dropping, analysis of the enormous number of variants detected is still very complex, and the task of annotating NGS data for clinical grade reporting and interpretations remains a challenge."[39]

For most molecular laboratories, this means in-house sequence annotation and interpretation, while possible, is not practical from a time, manpower, or cost perspective.

"It's all going to come down to the economics of what is your test menu and how many people are you going to need on staff to have this knowledge available to you versus outsourcing it," Keefe explains.

 

By partnering with services such as Coriell Life Sciences and Translational Software, Psyche Services provides users of its Molecular LIS—NucleoLIS—with a seamless solution to annotate and interpret gene sequences and test results, as well as a Web interface that enables the entire care team to access reports.

*"It's taking all those A's, T's, G's and C's that are important to a geneticist, and might be exciting to a research scientist, and turning them into something a clinician can actually use."*

"It's an advantage for us as an LIS vendor to already have these relationships in place," Keefe explains. "When a lab decides they need to bring PGx testing onboard, they should work with an LIS vendor that is familiar with these companies. They shouldn't have to develop the integration and connections with multiple vendors that Psyche already has. When you get our system, we already know how to work with Coriell; we know how to work with Translational Software; we know how to work with the OMIM (Online Mendelian Inheritance in Man) application for genetic sequencing."

Jeffrey Shaman, PhD, Coriell Life Sciences Director of Business Development, explains the company's partnership with Psyche Systems allows mutual laboratory customers to have an end-to-end sample management and interpretation and reporting system for pharmacogenomics and women's health genetic testing.

"It's taking all those A's, T's, G's and C's that are important to a geneticist, and might be exciting to a research scientist, and turning them into something a clinician can actually use," he says. "If I were to report, 'You've got an 'A' here and a 'T' there and a 'G' there,' even a physician would most likely say, 'What the heck does that mean? What am I supposed to do with this patient?' The interpretation is what's important. Taking those A's and T's, G's and C's, and saying, 'If you've got a variant here, clinically that means X.'"

 

Shaman says having a one-stop shop—a molecular LIS that incorporates genetic interpretation and analysis and reporting for healthcare providers—is a "huge benefit" for a lab.

"If you have an end-to-end solution, it means you can accession samples, run those samples, do the analytics of those samples, and then get a report that can be sent to a physician all in the same LIMS system. You've got a one-stop shop," Shaman maintains.

*"A molecular LIS that incorporates genetic interpretation and analysis and reporting for healthcare providers is a huge benefit for a lab."*

"You need to have experts reading the data, though," he adds. "You don't want to try to be an expert in everything. Doing oncology, doing pharmacogenomics, doing infectious disease detection, that's our wheelhouse, our expertise. Having an expert like Coriell Life Sciences, which does this all the time, is critical. You also need to make sure the information coming out is of clinical importance. It needs to be medically relevant and clinically actionable."

Replicating the expertise of third-party genetic interpretation and analysis services that offer proprietary algorithms, scientific experts, risk reporting teams, pharmacogenomics advisory groups, etc., is not realistic for most diagnostic laboratories.

"To be an expert at the laboratory stuff and also keep up with the constantly evolving and emerging information in the genetic space is nearly impossible," Shaman argues. "Find experts in genome annotation and clinical interpretation and outsource that. If you try to do everything, you'll most likely fail."

Translational Software focuses on pharmacogenomics, carrier screening, and wellness. Their PGx tool offers panel definition, customized reporting, and streamlined integration, which provides ordering physicians with evidence-based genomic intelligence to inform clinical decisions.

 

Kyle Fetter, Vice President of Advanced Diagnostics for XIFIN, outlines the distinct advantages he has seen when an independent lab outsources annotation and interpretation of PGx data to Translational Software.

*"A report overflowing with information not relevant to a treatment decision or outcome is a failed report."*

In an interview with *Dark Daily*, he noted that third-party PGx platforms benefit from an economy of scale that cannot be replicated by an individual lab. And, he notes that Translational's analysis is constantly improving.

"They're improving because they get so many different patient samples that a single lab would not get." Furthermore, Fetter says, "I think a solution like Translational will alter the economics of any lab. At least in the diagnostic space. In the PGx space, where you have genes that have already been validated and research already exists, I think Translational will probably permanently alter the economics of labs developing those reports on their own."[40]

In addition to cutting-edge data analysis, research, and validation, outsourcing also enables a laboratory to offer clients curated reports tailored to an individual physician's needs. A physician on average has 11 minutes with each patient, which means he or she does not have the time to "slug through an entire report to find the information that is going to assist that patient," Shaman notes. A report overflowing with information not relevant to a treatment decision or outcome is a "failed report."

Coriell Life Science leverages the scientific data of the Coriell Institute for Medical Research to produce one- to two-page test reports of vetted information presented in a format a physician can "digest quickly and turn into an actionable item, which we hope will be a change in medication for the better, a reduction of risk, or an increase in therapeutic value," Shaman states.

 

## Chapter 6:

# What Clinical/Molecular Laboratories Should Know about Marketing NGS Services and Using Them to Retain Existing Clients

While laboratory testing accounts for approximately 3-5% of medical costs, the downstream impact on healthcare is much greater. An estimated 70% of all decisions regarding a patient's diagnosis, treatment alternatives, and hospital admission and discharge are based on laboratory test results, according to the American Clinical Laboratory Association.[41]

Despite laboratory testing's crucial role in medical decision making, clinical diagnostic laboratories are operating in a challenging environment marked by increasing testing demands and ever-tightening financial constraints.

"The elder population is increasing, and with it, the volume of laboratory testing also is increasing," Donna Woodall, Senior Director of Global Marketing for Next-Generation products at Siemens Healthineers, wrote in *Clinical Lab Products.* "This higher demand on the laboratory, together with test menu expansion, means that today's labs have to accomplish more than ever before, but with stricter budgets."[42]

And they must do so in an increasingly competitive environment, where expanding a test menu is equal parts risk and reward.

 

"The breadth of testing that has permeated the laboratory is growing," Clifford points out. "You don't want your physician customers or facilities utilizing a competitor for a test type—say NGS testing—that you don't currently offer, only to displace you for other types of testing that you do offer.

*"If you're just doing one order per week, you're wasting the investment in your instrumentation, you're wasting reagents, and you're wasting your technologists' time."*

"When considering expanding your current test menu, though, it's critical that you study the competitive landscape and calculate whether you're better positioned to bring testing in-house or outsource it. If you decide to offer NGS testing, the questions are: Will that discourage your existing customers who want to perform NGS testing from going elsewhere and possibly deciding to convert all of their testing to the other lab? And, how much additional revenue and profit will you gain from bringing NGS testing in-house?"

Laboratories that choose to expand their test menus to include NGS testing should do so selectively, with a close eye on current customers' needs. When marketing NGS services, Keefe suggests labs be clear on what NGS tests their client base of hospitals, physician practices, and research centers are seeking.

"You've got to justify the cost of doing these tests," Keefe stresses. "A lot of these test kits are expensive. If you're just doing one order per week, you're wasting the investment in your instrumentation, you're wasting reagents, and you're wasting your technologists' time. You're paying these technologists to know how to do these tests. It comes down to volume and specialization."

Specializing means not trying to compete with the test menus offered by the laboratory industry's 900-pound gorillas—LabCorp and Quest Diagnostics—which have nationwide footprints and less limited financial resources.

 

"You don't want to specialize in everything," Keefe maintains. "You pass the point of diminishing returns. You may have the ability to support a lot of different analyses and you're getting a lot of specimens, but now you have to ramp up to meet limited demand for a wide range of tests."

*"If you're a laboratory that has figured out how to map the genome for nightmare bacteria, it doesn't matter whether you're three miles or 3,000 miles away, physicians will send their samples to your lab regardless of the distance."*

Since established molecular laboratories know their customer base, they should be able to identify the specific NGS tests that benefit existing clients. Their goal should be to become the "go to" facility in their area for specific genetic tests.

Keefe says lab customers should "identify your lab as the 'go to' for X, Y, and Z when it comes to genetic testing. You fill in what X, Y, and Z is. However, you can't survive on very low volume. You'll never justify the cost of the equipment, the cost of staying certified, etc. The more volume you bring in, the more your investment pays for itself and the quicker it pays for itself."

Keefe points to the Centers for Disease Control and Prevention's April 2017 report on "widespread growth" of so-called "nightmare superbugs" as an example of how a local NGS lab can build a national reputation.[43]

"If you're a laboratory that has figured out how to map the genome for nightmare bacteria, it doesn't matter whether you're three miles or 3,000 miles away, physicians will send their samples to your lab regardless of the distance," he notes. "If you're first to market, you establish that brand recognition and attract a lot of attention, which justifies your cost to do that testing in the first place."

Keefe acknowledges that not every molecular laboratory is going to find "that one magical bullet to capitalize on." However, he says such thinking should be a part of every lab's long-range plan.

 

"That's part of knowing what your lab's strengths are, knowing how strong your customer base is, and knowing what your customer base is comprised of, then determining whether or not there's enough potential to justify bringing this testing on," he explains.

*"Molecular laboratories offering NGS testing will be at the forefront of healthcare's transformation to personalized medicine."*

Don Rule, Chief Executive Officer, Translational Software, believes genetic data increasingly will be integrated into the clinical workflows of healthcare organizations, which means molecular laboratories offering NGS testing will be at the forefront of healthcare's transformation to personalized medicine.

"Genetic testing kits, and retail access to genetic screening, promise to make testing more accessible and affordable to consumers for home use, providing even greater opportunity to integrate genomic data into clinical treatment decisions, and help advance the use and acceptance of precision medicine," Rule wrote in *Becker's Hospital Review*.[44]

"Smart, progressive clinical organizations will harness this growing patient demand by proactively offering genomic testing capabilities as a way to attract new customers. The rise in consumer interest will also result in more large employers offering genetic testing and counseling services as a voluntary health benefit for employees to help them better manage their health, detect and prevent genetic-based health issues, and reduce treatment costs," Rule concluded.

 

# Conclusion

Medicine is transforming from reactive to proactive, predictive care. While the current care continuum is deeply embedded in the healthcare system's culture and payment structure, next-generation sequencing offers tools destined to accelerate the shift in care models, as it ushers in personalized medicine at the genomic level.

*"Pathologists sit squarely at the intersection of this changing healthcare landscape, as their role expands to include the clinical management of patients."*

"Ten or 15 years from now, we will reach a tipping point where all medicines are linked to diagnostics, and we'll move out of the one-size-fits-all paradigm," Edward Abrahams, President of the Washington, D.C.-based Personalized Medicine Coalition, told *Genome*. "Patients are not yet asking the question, 'Is this therapy going to work for me?' I look forward to the day patients do ask that question."[45]

Personalized medicine has the potential to detect the onset of disease at its earliest stages, stop disease progression, minimize deaths and hospitalizations from adverse drug interactions, and lower healthcare costs by replacing trial-and-error medicine with precision treatments.

As personalized medicine becomes the norm, pathologists sit squarely at the intersection of this changing healthcare landscape, as their role expands to include the clinical management of patients.

"As pathologists, we tend to be very focused on getting the diagnosis right. We have to expand our thinking to include not only getting the right diagnosis, but also taking it one or two steps further—to characterize that tumor more specifically—so treatments can be custom tailored," Samuel K. Caughron, MD, FCAP, Vice Chair, CAP Personalized Healthcare Committee, stated as part of a CAP presentation.[46]

 

While the emerging promise of precision cancer treatment is the most talked about advancement in genomic medicine, NGS is on the verge of being transformative in many areas of medicine.

*"NGS is an incredibly powerful, positive force in medical care. We were in the Dark Ages before this."*

"NGS is an incredibly powerful, positive force in medical care. We were in the Dark Ages before this. It is the tsunami on our shores, and it's going to take over all of medicine. It's not a trend. It's the future of medicine. There's no question about it," predicts Maurie Markman, President of Medicine and Science at Cancer Treatment Centers of America.[47]

This paper has discussed the growing role of NGS in clinical care and its potential to fuel the transformation to predictive and proactive medicine, as well as pathologists' contributions to this emerging new paradigm, and the laboratory information technology and informatics they will need to remain at the forefront of change.

It has outlined the importance of purchasing a best-of-breed molecular LIS created with big data, genome annotation and interpretation, and informed decision-making in mind. NGS services also represent a major financial commitment by independent laboratories, so using NGS testing to retain and grow a lab's customer base also has been examined.

Pathologists are uniquely qualified to advance the cause of personalized medicine among regulators, insurers, providers, and patients, but they can only do so if the best health informatics tools are at their fingertips.

To find out more about specific LIS solutions for your laboratory, contact Psyche Systems at sales@psychesystems.com or http://www.psychesystems.com/contact.html to speak with a sales representative.

 

# References

1. U.S. Food and Drug Administration. (2016, February 26). Personalized Medicine: A Biological Approach to Patient Treatment. https://www.fda.gov/Drugs/NewsEvents/ucm325475.htm
2. McMullan, D. (2014, August 3). What is Personalized Medicine? http://genomemag.com/what-is-personalized-medicine/
3. McMullan, D. (2014, August 3). What is Personalized Medicine? http://genomemag.com/what-is-personalized-medicine/
4. Fagan, A. (2018, March 1) From 13 Years to 20 Hours, Genome Sequencing Breaks Record http://genomemag.com/2018/03/from-13-years-to-20-hours-genome-sequencing-breaks-record/
5. Introduction to NGS: Learn How the Technology Works and What it Can Do for You https://www.illumina.com/science/technology/next-generation-sequencing.html
6. Smith, Y. (2017, August 3). History of Genomics. https://www.news-medical.net/life-sciences/History-of-Genomics.aspx
7. Smith, Y. (2017, August 3). History of Genomics. https://www.news-medical.net/life-sciences/History-of-Genomics.aspx
8. National Human Genome Research Institute. (2003 April) The Human Genome Project Completion: Frequently Asked Questions. https://www.genome.gov/11006943/human-genome-project-completion-frequently-asked-questions/
9. Illumina. (2017). An Introduction to Next-Generation Sequencing Technology. https://www.illumina.com/content/dam/illumina-marketing/documents/products/illumina_sequencing_introduction.pdf
10. Press, B. (2014, April). Clinical Implementation of Next-Generation Sequencing. http://www.hematologyandoncology.net/archives/april-2014/clinical-implementation-of-next-generation-sequencing/
11. Personalized Medicine Coalition. (2014, 4th Edition). The Case for Personalized Medicine http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_the_case_for_personalized_medicine.pdf

 

12. Herper, M. (2014, January 14). The $1,000 Genome Arrives–for Real, this Time. https://www.forbes.com/sites/matthewherper/2014/01/14/the-1000-genome-arrives-for-real-this-time/#18c151e05796

13. Illumina. (2017, January 9). Illumina Introduces the NovaSeq Series–a New Architecture Designed to Usher in the $100 Genome.

14. Illumina. (2017, January 9). Illumina Introduces the NovaSeq Series–a New Architecture Designed to Usher in the $100 Genome.

15. Ravishankar, D. (2017, May 25). Global Survey on Clinical Next-Generation Sequencing. http://www.clpmag.com/2017/05/global-survey-clinical-next-generation-sequencing/

16. Rajesh R. Singh, Rajyalakshmi Luthra, Mark J. Routbort, Keyur P. Patel, and L. Jeffrey Medeiros (2016) Implementation of Next Generation Sequencing in Clinical Molecular Diagnostic Laboratories: Advantages, Challenges and Potential, Expert Review of Precision Medicine and Drug Development, 1:1, 109-120, DOI: 10.1080/23808993.2015.1120401

17. Hippocrates Quotes. https://www.brainyquote.com/quotes/hippocrates_386231

18. Pucheril, D., Sharma, S. (2011, November 6) The History and Future of Personalized Medicine. https://www.managedcaremag.com/archives/2011/8/history-and-future-personalized-medicine

19. Personalized Medicine Coalition. (2017). The Personalized Medicine Report. Retrieved http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

20. Harris, S. R., Cartwright, E. J., Török, M. E., Holden, M. T., Brown, N. M., Ogilvy-Stuart, A. L., … Peacock, S. J. (2013). Whole-genome sequencing for analysis of an outbreak of meticillin-resistant Staphylococcus aureus: a descriptive study. The Lancet Infectious Diseases, 13(2), 130–136. http://doi.org/10.1016/S1473-3099(12)70268-2

21. Evans, J. (2013, November 22). FDA Approves First NGS System. http://www.separationsnow.com/details/news/1427f0f09f4/FDA-approves-first-NGS-system.html

22. Jarousse, L. (2016, February 16). The Role of the Pathologist in Diagnosis, Quality and Patient Safety. https://www.hhnmag.com/articles/6945-the-role-of-the-pathologist-in-diagnosis-quality-and-patient-safety

 

23. Concert Genetics. (2017, March) The Current Landscape of Genetic Testing. http://www.concertgenetics.com/wp-content/uploads/2018/02/10_ConcertGenetics_CurrentLandscapeofGeneticTesting_2017Update.pdf

24. Agilent. (2017). A New Frontier in the Fight Against Cancer. https://www.agilent.com/about/newsroom/videos/2017/fight-against-cancer.html

25. Concert Genetics. (2017, March) The Current Landscape of Genetic Testing. http://www.concertgenetics.com/wp-content/uploads/2018/02/10_ConcertGenetics_CurrentLandscapeofGeneticTesting_2017Update.pdf

26. Personalized Medicine Coalition. (2017). The Personalized Medicine Report. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

27. Personalized Medicine Coalition. (2017). The Personalized Medicine Report. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

28. Wygant, M. (2017, August 10). Clinical NGS Finding its Grove. https://www.biocompare.com/Editorial-Articles/340469-Clinical-NGS-Finding-Its-Groove/

29. Personalized Medicine Coalition. (2017). The Personalized Medicine Report. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

30. Jarousse, L. (2016, February 16). The Role of the Pathologist in Diagnosis, Quality and Patient Safety. https://www.hhnmag.com/articles/6945-the-role-of-the-pathologist-in-diagnosis-quality-and-patient-safety

31. College of American Pathologists. (2016, February). The Role of Pathologists in Diagnosis, Quality and Patient Safety. https://www.hhnmag.com/ext/resources/HHN0216_ExecDialog_CAP.pdf

32. Personalized Medicine Coalition. (2017). The Personalized Medicine Report. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

33. Office of Disease Prevention and Health Promotion. (2018, May 17). Overview: Adverse Drug Events. https://health.gov/hcq/ade.asp

34. Qiuping, Gu, Dillion, C., Burt, V. (2010, September). Prescription Drug Use Continues to Increase: U.S. Prescription Drug Data for 2007-2008. https://www.cdc.gov/nchs/data/databriefs/db42.htm

 

35. U.S. Food & Drug Administration. (2016, February 26). Personalized Medicine: A Biological Approach to Patient Treatment. https://www.fda.gov/Drugs/NewsEvents/ucm325475.htm

36. Grand View Research. (2017, January). Next Generation Sequencing Market to Reach USD 21.4 Billion by 2025. https://www.grandviewresearch.com/press-release/global-next-generation-sequencing-market

37. Sunquest. (2017, October). Molecular Diagnostics for Healthcare Facilities: How to Start and Scale an Efficient Testing Program. http://www.himss.org/file/1324878/download?token=VgPfjVHP

38. Grand View Research. (2017, January). Next Generation Sequencing Market to Reach USD 21.4 Billion by 2025. https://www.grandviewresearch.com/press-release/global-next-generation-sequencing-market

39. NGS Diagnostics: Data Considerations, Annotation and Interpretation (2015, August) http://www.nextgenerationdx.com/ngs-diagnostics/15/

40. Terry, M. (2017). A Leader's Guide to Pharmacogenomic Testing (PGx): Cloud-Based Software Reporting of PGx for Hospitals, Health Systems and Clinical Laboratories. https://www.darkdaily.com/wp-content/uploads/TDR047_Translational_WP.pdf

41. American Clinical Laboratory Association. (2013). Clinical Laboratory Testing: Life Saving Medicine Starts Here. http://www.acla.com/wp-content/uploads/2013/12/ACLA_Overview_OneSheet_v07.pdf

42. Woodall, D. (2017, July 17). Tackling Evolving Market Challenges. http://www.clpmag.com/2017/07/tackling-evolving-market-challenges/

43. Centers for Disease Control and Prevention. (2018, April). Containing Unusual Resistance https://www.cdc.gov/vitalsigns/containing-unusual-resistance/index.html

44. Rule, D. (2018, February 13). Genomic Decision Support Systems and Retail Access to Genetic Screening Will Drive Continued Adoption of Precision Medicine. https://www.beckershospitalreview.com/quality/genomic-decision-support-systems-and-retail-access-to-genetic-screening-will-drive-continued-adoption-of-precision-medicine.html

 

45. McMullan, D. (2014, August 3). What is Personalized Medicine? http://genomemag.com/what-is-personalized-medicine/

46. Herbek, G. (2012, February 2012). Pathologist Leadership in Quality for Cancer Care and Biodepositories. https://biospecimens.cancer.gov/meeting/brnsymposium/2012/docs/Day1_Gene_Herbek_Presentation.pdf

47. Markman, M. (2015, September 23). Genomic Medicine: The Future of Cancer Treatment is Now. http://www.healthconnectsouth.com/2015/09/23/genomic-medicine-the-future-of-cancer-treatment-is-now/

 

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