From genomic data to bioinformatics: accelerating knowing

Developing advanced bioinformatics solutions can help health systems stay ahead

Quest Diagnostics™

Introduction

A new era of genomic medicine is here, and the ability to sequence and analyze genomes is revolutionizing medicine—transforming cancer research and treatment, drug development, patient risk assessment, and clinical tests and procedures. It's driving economic activity, too, resulting in billions of dollars in both economic output and personal income in the U.S. alone.[1]

Fueling this revolution is genomic data, generated by next-generation sequencing (NGS) technologies.[2] Yet while genomic data is both industry- and life-changing in its ability and promise, it is ultimately worth only as much as its interpretation. Clinicians must be able to process, understand, and use this data at the point of care. Achieving this can be challenging, however, as the volume and complexity of genomic data are massive (e.g., sequencing a single whole genome generates more than 100GB of data).[2]

Academic medical centers, health systems, and community hospitals play a critical role in harnessing the power of NGS-generated data—proving its utility by conducting clinical trials, gathering evidence, and helping clinicians make practical use of it. Achieving this requires the development of bioinformatics infrastructures that facilitate the integration of genomic data into the electronic health record (EHR).[2] Only then can the data's true promise be realized, as clinicians are able to use it not only to diagnose, treat, monitor, and manage a variety of diseases, from the very rare genetic mutations to the more common conditions (like cancer and heart disease), but also to predict and prevent them.

The power of genomic data: an overview

Advances in NGS technologies over the past 15 years have made genome sequencing faster, more accurate, and more affordable than ever, expanding the base of scientific knowledge and inching genomic medicine closer to the point of care.[3,4]

How far we've come

The **first human genome** was sequenced in a

$3 billion

13-year multinational collaboration[4]

Today's labs can **sequence a whole human genome within days for a cost of**

~$1,000[4]

Genomic data can help identify disease factors and inform treatment decisions and prevention strategies. It has aided in the development of more personalized medicine and pharmacogenomics, or drug treatment that targets patients based on their DNA sequence—reducing trial-and-error efforts and reliance on one-size-fits-all treatments.[1,4] This enables clinicians to provide patients with more effective treatment, sooner.

Because cancer is a disease of the genome, cancer-related genomic medicine has seen the most growth.[5] High costs and disease prevalence are also driving this growth—cancer care costs roughly $171 billion a year, and the Centers for Disease Control and Prevention predicts that, by 2020, cancer will be the leading cause of death in the U.S.[6]

Analysis of tumor genomes has revealed some 140 genes whose mutations contribute to cancer. [7] Genomic variants can also shape more targeted treatments, revealing mutations that expose a tumor's therapeutic weak spots and providing clues as to whether an individual may or may not respond to a cancer drug.[7]

Genomics may also be able to help clinicians address the opioid epidemic. Targeted NGS panels, for example, can be used to help clinicians understand the genetics of human opioid receptors, enabling them to better evaluate the effects of opioids, and providing a better understanding of the epidemiology of addiction and substance abuse.[8]

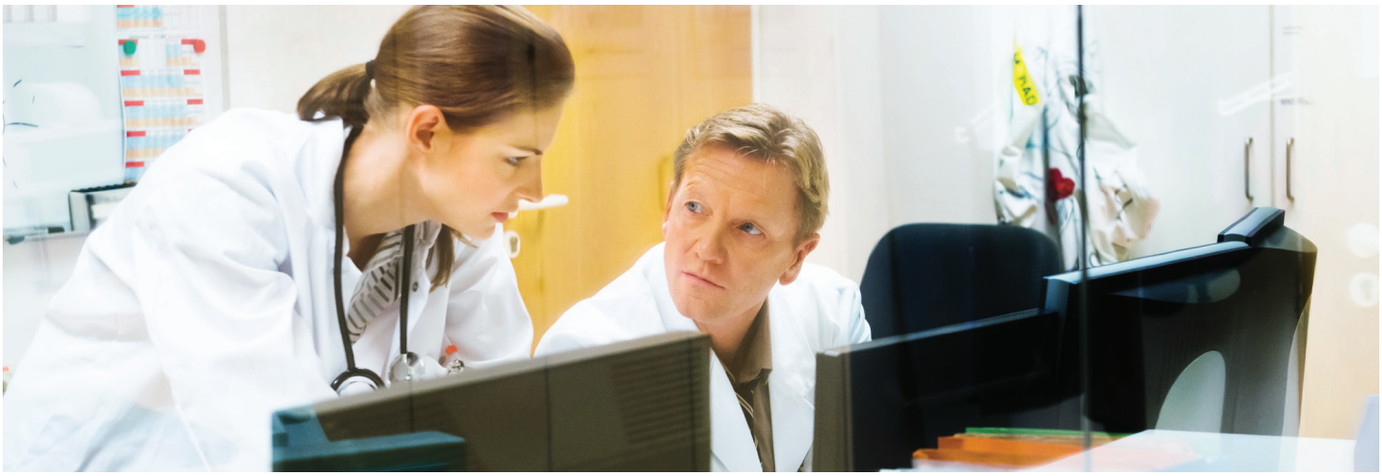
Clinical studies have shown that the ability of opioids to create addiction is genetically modulated, with heritability rates similar to those of diabetes, asthma, and hypertension. Genetic vulnerability accounts for at least 35%–40% of the risk associated with opioid addiction.[9] And while the first step is more effective assessment of patients at increased risk for addiction, the second step is creating alternative methods of pain treatment. NGS technologies may help scientists develop treatment that interacts with the opioid receptor, activating just the pathway that results in pain relief—and not the one that results in addiction.[10] This could not only prevent addiction but also help at-risk patients who continue to suffer from chronic pain.

Genes that doctors use: genetic variants can determine whether a treatment harms or heals[7]

Condition	Gene or variant	Action
Cystic fibrosis	CFTR-G551D (plus 8 other variants)	Select medication effective only in patients carrying the variants.
HIV	HLA-B*5701	Avoid HIV drug abacavir. Select alternate medication that is less toxic to patient.
Melanoma	BRAF V600E/K and similar variants	Select medication effective only in patients carrying the variants.
Lung cancer	EGFR	Select medication effective only in patients carrying key mutations.
Family history of breast cancer	BRCA1/BRCA2	Opt for close screening or preemptive mastectomy.

Many health systems are engaging in genomics research of their own. Hospitals such as Children's Mercy Hospital in Kansas City, MO, the Medical College of Wisconsin in Milwaukee, and Baylor College of Medicine in Houston, TX, are using sequencing to detect diseases among children that have, until recently, defied diagnosis, including the condition of one of the first children to be saved by DNA sequencing in the U.S., Nicholas Volker.[7,11]

As a toddler, Nicholas Volker suffered from life-threatening intestinal inflammation, requiring a hundred surgeries and the removal of his colon. In a last-ditch effort to save his life, the Medical College of Wisconsin sequenced his DNA. Clinicians found a mutation in a gene on the X chromosome that has been linked to immune disease, shedding light on treatment—a bone marrow transplant of cells taken from umbilical cord blood.[11]



The challenges of big (genomic) data

Today, "genomics" is quickly becoming synonymous with the word "data." Indeed, genomics is now dominated not only by the growth in the size of its data, but also by the need to develop methods for effectively managing and using this data.[12]

While there is no disputing the value of genomic data, its scale is massive. One study compared genomic data's projected growth to 3 other sources considered among the most prolific data producers in the world: astronomy, Twitter, and YouTube. This study predicted that, by 2025, genomics could represent the biggest of big data fields.[13]

An explosion of data

Output from NGS has grown from 10MB to

40 MB/day

on 1 sequencer[12]

10–20

major sequencing labs worldwide have each deployed more than 10 sequencers[12]

Although the data provides numerous opportunities, its size and scope present perhaps just as many challenges—from data storage to data sharing to, potentially most pressing, developing ways to leverage this data for use in clinical practice. Once genomic data is stored and shared, how can clinicians use it at the point of care to make better testing decisions, make more accurate diagnoses, and prescribe more targeted treatments for their patients?

Responsible genetic and genomic testing

Currently, there are almost 70,000 genetic testing products available in the U.S., with an average of 10 new tests entering the market every day.[14] Due to their complexity, these tests contribute substantial costs to laboratory medicine across health systems—and these costs are rising.[15]

Given the rarity of most genetic disorders and the growing number of testing options, 8%–30% of genetic tests are ordered incorrectly. Many physicians report feeling unprepared to order these tests, citing lack of knowledge, confidence, and experience. While contributing to rising costs, this lack of knowledge can also lead to delayed diagnoses and incorrect results interpretation.[15]

As the use of genomic data moves closer to the point of care, health systems must devise new utilization management strategies for the ordering of genetic and genomic testing. Providing guidance can lead to more appropriate genetic referrals, improved utilization of genetic testing, and significant cost savings.[15]

The shift from storing to sharing data

As genomic medicine continues to advance, the need to share it is crucial—but challenging. Barriers include technology, as well as legal, regulatory, and ethical concerns.[16] The case has been made for a global informatics ecosystem, and many organizations and initiatives are working toward this end.[16,17]

- **eMERGE Network**—a national network organized by the National Human Genome Research Institute, combining DNA biorepositories with electronic medical record (EMR) systems for large-scale genetic research in support of implementing genomic medicine
- **Cancer Moonshot initiative and Genomic Data Commons**—provide the cancer research community with a unified data repository that enables data sharing across cancer genomic studies in support of precision medicine
- **Global Alliance for Genomics and Health**—brings together more than 400 leading institutions to help accelerate the potential of genomic medicine to advance human health

Bioinformatics infrastructures are essential

To bring genomic medicine to the point of care, informatics solutions are urgently needed.[18] This means that health systems must invest in new workflows, informatics, and data-analysis techniques.[7] With the right infrastructure, the number of clinically useful variants could grow into the thousands, making genomics crucial to medical care.[7]

Some health systems are leading the charge, developing bioinformatics infrastructures to process NGS data through a group of databases supplementary to their EHRs and conducting pilot studies.[2] One such study, led by Regeneron Genetics Center and the Geisinger Health System, has revealed the value of integrating genomic data and EHRs to uncover a genetic variant that results in reduced levels of triglycerides and a lower risk of coronary artery disease.[2]

Other health systems are prioritizing the development of bioinformatics infrastructures by partnering with leading technology solutions companies. Stanford Medicine, for example, has partnered with Google to "put genomic sequencing into the hands of clinicians to help diagnose disease."[19] And Partners HealthCare developed the GeneInsight platform to address the challenges that prevent the clinical adoption of personalized medicine, including data management and interpretation.

Large-scale collaborations are also taking shape to advance genomic medicine, like the one between Memorial Sloan Kettering, IBM Watson Health, and Quest Diagnostics. IBM and Quest launched IBM Watson Genomics from Quest Diagnostics, a service that—using data supplied by Memorial Sloan Kettering—combines cognitive computing with genomic tumor sequencing to help inform individual treatment options for cancer patients.

All of these advances—in both science and technology—will bring genomic data to the point of care and make it actionable for improved testing; faster, more accurate diagnoses; easier development of complex treatment plans; and, ultimately, improved health outcomes.

Conclusion

Genomics has the power to improve both diagnosis and treatment, reshaping clinical care. For clinicians, this means less time searching for answers, fewer diagnostic tests, and more accurate diagnoses. For patients, it means more appropriate and personalized therapies, sooner. And for health systems, it means improved efficiencies and better health outcomes.

Commitment to innovation has emerged as a key factor in advancing genomic medicine—and harnessing the power of genomic data. Health systems can benefit from developing and implementing platforms that not only make sense of the data and put it into the hands of clinicians, but also enable data sharing across institutions and around the world to advance genomic research.

To make genomic medicine a reality at the point of care, there is still much work to be done combining scientific research, big data, and technology solutions. But the efforts could be both life- and world-changing.

Quest Diagnostics offers the genetic expertise and capabilities health systems need **for a more actionable diagnostic journey**.

To better incorporate genomic data into clinical practice, health systems can benefit from partnering with the right solutions partner. Quest Diagnostics offers comprehensive, end-to-end genetic testing and services, including:

- Advanced technologies, such as **QNatal® Advanced and IBM Watson™ Genomics from Quest Diagnostics®**
- **An extensive test menu**
- Support from expert medical specialists and genetic counselors, including a **dedicated helpline (1.866.GENE.INFO)**

References

1. Orchard C. Genomic medicine in the real world: 'hope' and 'hype.' Inside health: Harvard T.H. Chan School of Public Health. 1 Jun 2015. Available at www.hsph.harvard.edu/ecpe/genomic-medicine-in-the-real-world-hope-and-hype. Accessed July 5, 2017.
2. He KY, Ge D, He MM. Big data analytics for genomic medicine. *Int J Mol Sci.* 2017;18:412-430.
3. Eisenstein M. Big data: the power of petabytes. *Nature*. 2015;527(7576):S2-S4.
4. Borrelli AB, Dickinson A, Lynch K, *et al.* Transforming healthcare with next-generation genome sequencing. Intel. 2016. Available at www.intel.com/content/dam/www/public/us/en/documents/white-papers/next-gen-genome-sequencing-paper.pdf. Accessed July 5, 2017.
5. National Institutes of Health: National Cancer Institute. Cancer genomics overview. Available at www.cancer.gov/about-nci/organization/ccg/cancer-genomics-overview. Accessed July 6, 2017.
6. Beaton T. Top 10 most expensive chronic diseases for healthcare payers. *Health Payer Intelligence.* 19 Jul 2017. Available at healthpayerintelligence.com/news/top-10-most-expensive-chronic-diseases-for-healthcare-payers. Accessed August 1, 2017.
7. Ginsburg G. Medical genomics: Gather and use genetic data in health care. *Nature.* 2014;508(7497).
8. Kringel D, Lotsch J. Next-generation sequencing of human opioid receptor genes based on a custom AmpliSeq™ library and ion torrent personal genome machine. *Clin Chim Acta.* 2016;463:32-38.
9. Longo DL. Opioid abuse in chronic pain—misconceptions and mitigation strategies. *N Engl J Med.* 2016;374:1253-1263.
10. Lurie J. The genius who helped unlock the human genome is taking on the opioid crisis. *Mother Jones.* 20 May 2017. Available at www.motherjones.com/politics/2017/05/interview-francis-collins-director-nih-opioids. Accessed August 1, 2017.
11. Herper M. The first child saved by DNA sequencing. *Forbes.* Available at www.forbes.com/sites/matthewherper/2011/01/05/the-first-child-saved-by-dna-sequencing/#1b4967d437c0. Accessed July 19, 2017.
12. Kahn SD. On the future of genomic data. *Science.* 2011;331:728-729.
13. Stephens ZD, Lee SY, Faghri F, *et al.* Big data: astronomical or genomical? *PLOS Biology.* 2015;13(7):e1002195.
14. Concert Genetics. The current landscape of genetic testing, 2017 update. March 2017.
15. Riley JD, Procop GW, Kottke-Marchant K, *et al*. Improving molecular genetic test utilization through order restriction, test review, and guidance. *J Mol Diagn*. 2015;7(3):225-229.
16. The Clinical Cancer Genome Task Team of the Global Alliance for Genomics and Health. Sharing clinical and genomic data on cancer—the need for global solutions. *N Engl J Med*. 2017;376(21):2006-2009.
17. American College of Medical Genetics and Genomics. Laboratory and clinical genomic data sharing is crucial to improving genetic health care: a position statement of the American College of Medical Genetics and Genomics. *Genet Med*. Advance online publication. 5 Jan 2017.
18. Moorthie S, Hall A, Wright CF. Informatics and clinical genome sequencing: opening the black box. *Genet Med*. 2013;15:165-171.
19. Stanford Medicine. Stanford Medicine, Google team up to harness power of data science for health care. Available at med.stanford.edu/news/all-news/2016/08/stanford-medicine-google-team-up-to-harness-power-of-data-science.html. Accessed July 6, 2017.

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