Genomic Innovation Democratizes Precision Medicine

By Joydeep Goswami, PhD, MBA, Chief Strategy and Corporate Development Officer and Interim Chief Financial Officer at Illumina and Phil Febbo, MD, Senior Vice President and Chief Medical Officer at Illumina

A History of Innovation

Evolving sequencing and data analytics technologies help clarify complex biology, streamline the drug discovery pipeline, and improve patient care.

As scientific advances have improved our ability to observe and quantify, researchers have learned how to shape our understanding of the world. Quite often, our view of life depends on the tools and technologies we use to explore and discover.

Galileo's telescope showed the phases of Venus, stars in the Milky Way, and Jupiter's moons. Leeuwenhoek's lenses enabled the first glimpses of the many microbes that permeate the environment. Similarly, genomics is a lens through which we can now view biology and medicine. In the 20 years since the first human genome was published, researchers have embraced this technology, identifying the genetic variations underpinning human disease, developing therapies to target and/or modify aberrant genes, and providing a deeper understanding of biology in both individuals and large populations.

Investigators, academic institutions, life sciences companies, and governments have created partnerships and initiated studies to interrogate the genome, extending knowledge and improving human health.

By developing cutting-edge genomic sequencing, library prep, assay, and data analytics technologies, genomic sequencing companies have given these diverse organizations novel ways to interrogate life, share knowledge, and advance science.

As genomics migrates from academic and corporate laboratories into hospitals and other clinical settings, these collaborations are becoming increasingly important. Partnerships between companies and healthcare systems are radically changing how clinicians view disease and deliver care. Genomic readouts have the potential to diagnose and prognose patients faster, clarify the aggressiveness of disease, inform care plans, and develop gene therapies based on each patient's unique molecular information.

Genomics is also changing how life sciences companies discover drugs: from identifying therapeutic targets to pinpointing the patient subgroups most likely to respond to specific therapies. In addition, as the COVID-19 pandemic has shown repeatedly, genomic data give governments, non-government organizations

(NGOs), and affiliated groups new tools to advance public health.

Precision and personalized medicine are profoundly reshaping the healthcare landscape, providing a new vision of what medical science can achieve.

A New Take on Cancer Care

Next-generation sequencing (NGS) technologies have revealed the molecular mechanisms that contribute to good health and drive disease. As a result, population-based approaches are being replaced by personalized care.

NGS instruments can accurately and cost-effectively read the specific molecular variations that enable cancer cell expansion, disrupt cellular control mechanisms, and help tumors resist treatments. These and other molecular insights have created a learning loop between research labs and the clinic, accelerating therapeutic innovation.

When patient samples are sequenced, they can reveal potential therapeutic targets. That sequencing information flows into research laboratories and biopharma companies, which identify genetic drivers of disease and then develop small molecules compounds, antibodies, antibody-drug conjugates (ADCs), and other agents to modulate these targets. New drugs are ultimately brought back into the clinic through clinical trials and eventual regulatory approval to help patients.

On a diagnostic level, NGS is an incredibly powerful clinical tool because it can answer so many questions about a patient's cancer in a single run. This capability complements and markedly expands traditional pathology, which has primarily focused on the histologic appearance of disease.

When pathologists performed molecular diagnostics in the past, tests most often focused on a single molecule for each analysis, gradually characterizing a tumor through individual stains on scarce biopsy samples. Whether sequencing DNA or RNA, NGS can comprehensively assess cellular genetics and biology and dramatically shorten the arduous diagnostic journeys cancer patients often face.

Mapping Variants to Treatments

One of the most promising NGS applications has been mapping a tumor's mutational landscape to determine if a specific therapy will be effective. This has been particularly useful for targeted therapies and certain immunotherapies which benefit people with specific genetic variants or genomic signatures like high tumor mutation burden.

A recent and quite exciting study showed that 14 of 14 patients who had local rectal and other cancers with microsatellite instability had complete responses to anti-PD-1 immunotherapy.[1]

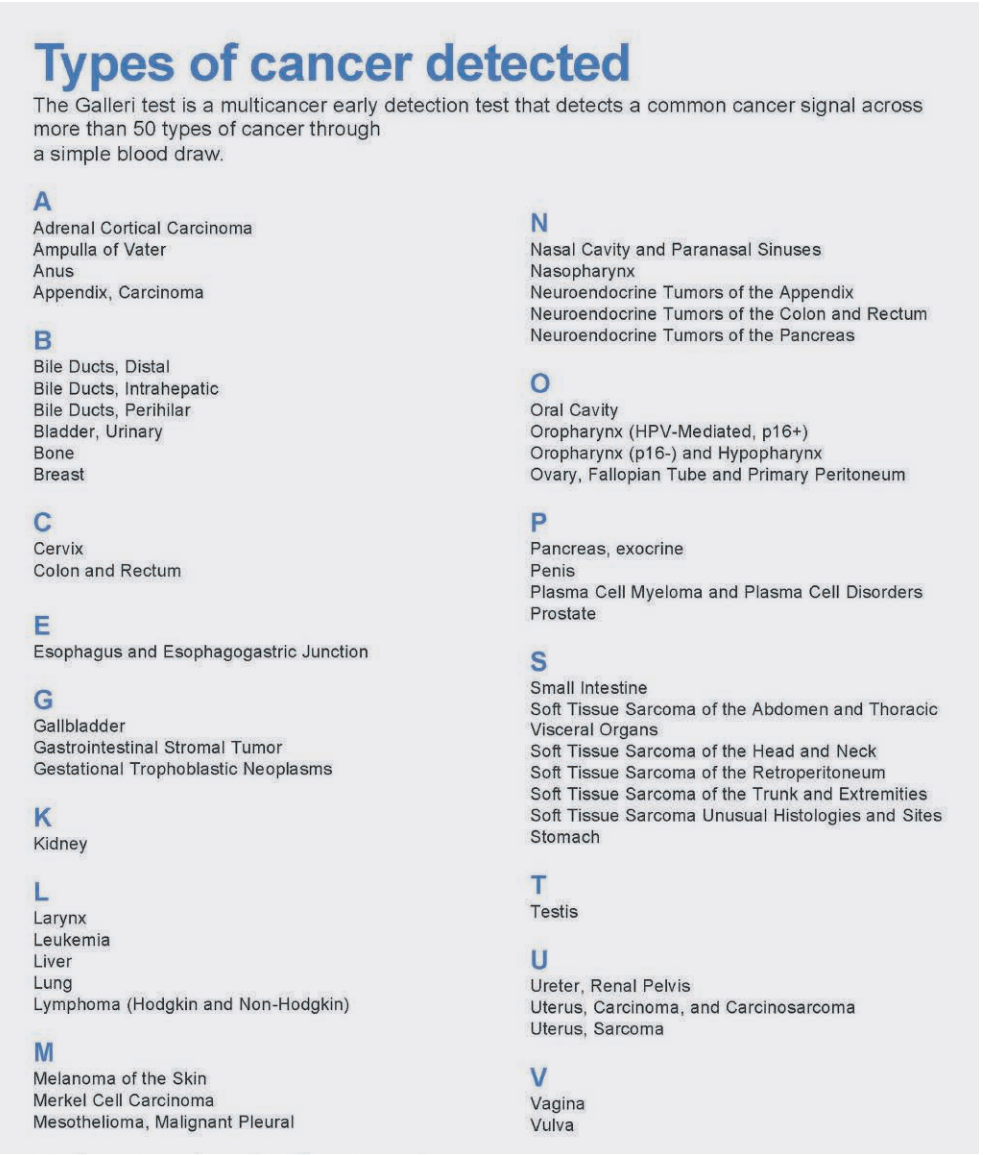

Figure 1: Types of cancer detected by GRAIL's Galleri test. https://www.galleri.com/the-galleri-test/types-of-cancer-detected

Widespread NGS adoption as the potential to identify all patients with targetable genetic changes and, similar to the recent report on rectal cancer, help select those patients most likely to have a dramatic response to targeted or immune therapies.

NGS can also track how tumors evolve in response to treatment. Liquid biopsies, which sequence circulating tumor DNA, are becoming an established, non-invasive technology that can keep tabs on tumor genetic variations, giving oncologists important data to help them anticipate when a patient may need to switch therapies.[2]

NGS-based liquid biopsies can impact people even before a cancer diagnosis. GRAIL's Galleri test (see **Figure 1** with related link in caption) detects molecular signals for more than 50 cancer types, including many that have no available screening test.[3] GRAIL is partnering with health systems, insurance companies, government agencies, and pharmaceutical companies to determine how these tests could impact patient outcomes and bring these potentially life-saving diagnostics to patients.

Comprehensive Genomic Profiling

Another interesting NGS trend is the move away from small genomic panels to comprehensive genomic profiling (CGP) assays, which assess hundreds of genes rather than a few dozen. In cancer care, this is being driven, in part, by genome-wide signatures that identify the patients who can benefit from PD-1/PD-L1 inhibitors, such as the one that delivered such stunning results in the successful rectal cancer trial cited above, as well as poly adenosine diphosphate-ribose polymerase (PARP) inhibitors. In addition, the emergence of pan cancer markers, which identify patients who

Help us answer:

Is this the right medication for this person?

GTMRx Institute™
Get the medications right

To unlock the promise of personalized medicine that will optimize medication therapies, we need:

- Health information technology that will enable the flow of clinical information to the point of care for all team members
- Payment models that reward person-centered, team-based care that includes the clinical pharmacist
- Access, use, interpretation and integration of advanced diagnostics like pharmacogenomics (PGx) testing into comprehensive medication management (CMM) services to target correct therapies

For precision medicine to lead to personalized care, we must act now!
See the GTMRx Institute's Blueprint for Change at ***bit.ly/GTMRBlueprint.***

What is CMM?

CMM is a service delivered by an interprofessional team, to include a clinical pharmacist, collaborating with a physician to ensure appropriate use of medications and gene therapies. It influences medication selection, use and monitoring to ensure safe, effective and appropriate use of medications. CMM is patient-centered, comprehensive and ongoing.

bit.ly/CMMDefinition

Who is the Get the Medications Right Institute?
The GTMRx Institute is an active 501c4 coalition of 1400+ members from 900+ companies throughout the US.

We bring together those who pay for care, those who purchase care, those who provide care and those who receive care to find real solutions.
It's time to ACT—Action Changes Things! JOIN US!

Questions? Please contact us at **(703) 394-5398** or visit ***gtmr.org.***

DID YOU KNOW?

- Medications are involved in **80%** of all treatments & impact every aspect of a patient's life.
- **275,000** lives are lost and **$528B** spent on non-optimized medication use each year.
- Nearly **30%** of adults in the US take **5+ medications.**
- **10,000** prescription medications are available on the market today.
- **49 seconds:** Is the time spent by physicians and patients talking about new medications during a 15-minute office visit.

H2R 09.2021

Figure 2: Fitz Kettler was born with severe combined immunodeficiency (SCID). Without a transplant, SCID babies rarely make it past their first year, but Fitz is now a healthy 3-year-old with a functioning immune system. (Photo courtesy of the Keller family)

may benefit from a targeted therapy regardless of their cancer type, is also highlighting CGP's clinical benefits.

Globally assessing tumor genomic makeup plays a major role in determining which patients will respond favorably to a specific treatment. Microsatellite instability and tumor mutational burden identify patient who can benefit from PD-1-targeted agents. Tumors with homologous repair deficient tend to respond to PARP inhibitors.

However, small, 50-gene panels do not provide enough information to fully characterize tumor genomic landscapes. As a result, where these therapies are available, health care providers, payors, and drug companies are adopting CGP, harnessing precise data to provide the most effective treatments.

A recent Providence Health System study showed CGP improved the ability to identify actionable biomarkers. The research found CGP actionability was 45%, compared to 19% for small panels. In addition, clinical trial eligibility was 49% for CGP against 23% for the basic panels.[21]

Rare and Undiagnosed Diseases

As with cancer, NGS provided a new window into rare and undiagnosed genetic diseases (RUGDs).[4] Before whole-genome and exome sequencing were developed, many patients and families endured years-long diagnostic odysseys.

Once again, NGS asks, and often answers, many questions at once, providing unique opportunities to accelerate diagnoses, reduce suffering, and save lives.

Rady Children's Institute for Genomic Medicine (RCIGM), has helped pioneer rapid whole-genome sequencing (rWGS) to identify genetic anomalies in newborns and direct them to treatment.

In 2019, Fitz Kettler (see photo in **Figure 2**) was born with severe combined immunodeficiency (SCID).[5] While the overall condition was diagnosed through a routine genetic screening, rWGS identified specific mutations that qualified Kettler for a gene therapy trial at UCSF.[6] There, clinicians extracted stem cells from his bone marrow, added the correct gene and re-infused the cells.

Without a transplant SCID babies rarely make it past their first year, but Fitz is now a healthy 3-year-old with a functioning immune system.

Because NGS provides such comprehensive information, it has great potential to simultaneously boost care and reduce costs. Another study from RCIGM confirmed this in children with congenital heart disease, showing rWGS improved care and reduced average daily hospital spending.[7]

Work at Hospital Infantil de Las Californias in Tijuana, Mexico demonstrated that WGS can benefit patients in resource-limited settings, as well as institutions like RCIGM.[8] As the benefits become more clear, it is important to ensure that all children who may have a genetic disease have access to NGS-based technologies.

Infectious Diseases

Five years ago, genomics was rarely a major part of the infectious disease conversation. The SARS-CoV-2 pandemic changed that almost overnight. Now, NGS increasingly drives the infectious disease surveillance infrastructure, helping ensure we detect mutational and pathogen spread to inform public health efforts.

During the worst months of the COVID-19 pandemic, Illumina, the Bill and Melinda Gates Foundation, Microsoft, and Oxford Nanopore joined together to contribute $100 million to the African Pathogen Genomics Initiative (APGI) of the Africa Centres for Disease Control and Prevention (Africa CDC).[9]

APGI researchers subsequently identified the omicron variant, providing a key early warning

for the rest of the world.[10] APGI has also boosted sequencing capabilities throughout Africa, including the Democratic Republic of the Congo, Ghana, Kenya, Nigeria, Senegal, South Africa, and Uganda.

The increasing use of NGS to identify SARS-CoV-2 variants has now opened opportunities to apply NGS to detect and manage other infectious diseases. Tuberculosis (TB) remains a leading killer around the globe. While current technologies can effectively diagnose TB, NGS-based testing can both detect the pathogen and identify dangerous, drug-resistant strains. As a result, patients can receive the most appropriate first-line treatment, which is better for patients and public health.

To bring NGS into care and fully understand its potential to curb TB, an international trial is studying whether NGS can provide faster and more precise results, identify multi-drug resistant TB strains, and improve outcomes.[11] Once again, NGS advances both large-scale public health goals and individual patient care.

A Dearth of Therapies

For patients, the path from genomic diagnoses to treatments hinges on whether their disease is "actionable." Quite often, NGS identifies variations that are not actionable; that is, there are no approved therapies to treat that condition.

This is an important recognition. While NGS and gene therapy cured Fitz Kettler's SCID, that case is rare in standard practice. There are approximately 7,000 RUGDs, and while management often changes with definitive genetic diagnosis, only around 5% of genetic diseases have an FDA-approved therapy.[12]

Cancer shows a similar pattern. There are far more cancer-driving mutations than there are therapies to treat them. In 2018, only around 8.3% of patients with metastatic cancer had access to an available targeted therapy.[13]

As cancers become resistant to first-, second-, and third-line treatments, patients can eventually run out of options. NGS is a critical part of the diagnostic and therapeutic pipeline. Identifying the mutations that help tumors escape treatment sets the stage for further drug development, ultimately providing patients a more seamless therapeutic path.

In the larger picture, there are dozens of diseases that have either no treatments or inadequate ones, including Alzheimer's disease, multiple sclerosis and many heart, lung, and liver conditions.

Inefficient drug development is part of the problem. In many cases, it takes more than 10 years and $2 to $4 billion – from inception through commercialization – to develop a single FDA-approved drug.[14] Even after rigorous early research and development, most of the drugs that enter human clinical trials fail to benefit patients and never make it to FDA approval.

Genomics has great potential to change this paradigm. In fact, the majority of FDA-approved drugs are now moving forward based on data that includes substantial genomic evidence.[15]

Companies are also refocusing on targets that are supported by human genetic data, an approach that has great potential to increase success rates.[16] Drug companies have learned that NGS is invaluable to validate therapeutic targets and the agents they have developed to modulate them.[17]

In addition, human genetic information can reveal side effects relatively early in the discovery process, providing important data to improve drug design.

NGS is also being used to create a new generation of companion diagnostic tests, which improve care by identifying which patients have the best chance to respond to specific drugs, fulfilling personalized medicine's long-term goal of precisely matching each patient with the most effective therapies.

Biopharma companies have long sought to overcome long development times and high costs, and NGS is part of the solution. Companies can use this data to design streamlined trials that simultaneously target predicted responder populations and identify unexpected responders outside the targeted groups.

Companies that embrace precision medicine, powered by NGS and related technologies, can improve the discovery process, speed clinical development timelines, and improve clinical trial success rates.[18,19]

The Struggle for Clinical Equity

Personalized medicine means having the right drug for the right patient at the right time. However, for that drug to even exist, it must be tested in relevant populations. Until recently, most clinical trials have primarily included people of European ancestry (see **Figure 3).** Without sufficient diversity early in drug development, mutations identified in one population might be irrelevant when treating people from other ethnic backgrounds.

One example is PIK3CA variations in metastatic breast cancer, which are more common in patients with white and Asian ancestry.[20] As a result, people in these groups have access to PIK3CA inhibitors, such as alpelisib. However, metastatic breast cancer in Black patients tends to lack this specific mutation and PIK3CA inhibitors don't effectively treat their disease. And since clinical studies have generally underrepresented Black populations, these patients may not have access to an effective alternative.

Without clinical trial equity, the quest for personalized medicine will always be incomplete.

NGS for Clinical Trials and Patient Care

As NGS becomes available at both centralized

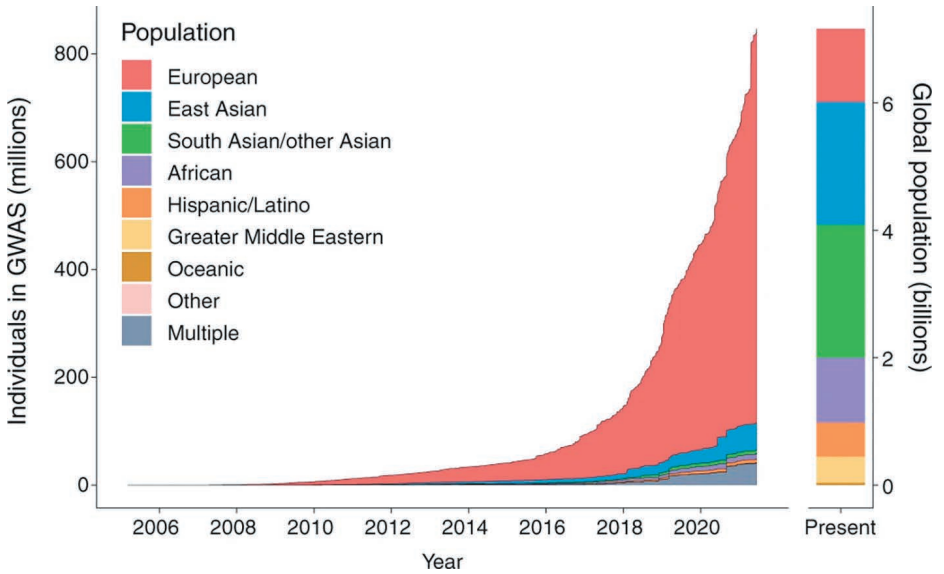

Figure 3: The search for equity applies to genomics research as well as clinical trials. As of June 2021, the vast majority (86%) of genomics studies have been conducted on individuals of European descent.

Fatumo, S., Chikowore, T., Choudhury, A. et al. A roadmap to increase diversity in genomic studies. Nat Med 28, 243–250 (2022). https://doi.org/10.1038/s41591-021-01672-4

Alicia R. Martin, Masahiro Kanai, Yoichiro Kamatani, Yukinori Okada, Benjamin M. Neale, and Mark J. Daly, Current clinical use of polygenic scores will risk exacerbating health disparities, Nat Genet., 2019 Apr; 51(4): 584–591, online 2019 Mar 29. https://www.nature.com/articles/s41588-019-0379-x

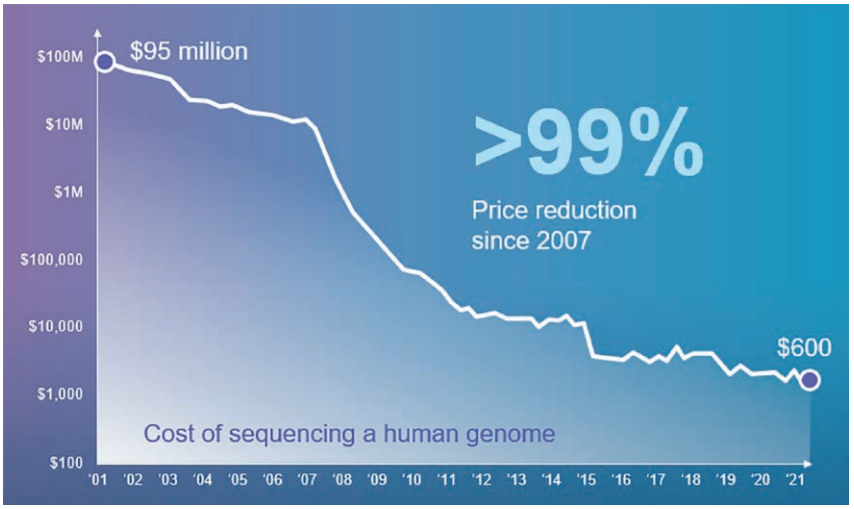

Figure 4: The cost of sequencing the human genome has fallen more than 90% in the past 20 years. https://www.genome.gov/sequencingcosts

laboratories and health systems, more patients will have opportunities to participate in precision clinical trials. Another way genomics can accelerate drug discovery is by identifying more eligible patients. NGS helps companies select the right trial participants based on the genetics behind their disease. Sequencing can identify which patients have the potential to be strong responders, slow responders, and non-responders, as well as revealing other pharmacological traits.

As a greater proportion of patients gain access to sequencing, NGS can identify the most appropriate patients for each clinical study, potentially reducing the risks of failure, study costs, and time to market. All these efforts improve the efficiency of drug development and can contribute to reduced drug costs and development timelines for diseases that may not have been prioritized by the biotech and pharmaceutical industry.

Once precision medicines requiring NGS-based testing are approved, shortening the gap between biopsy and NGS results will empower physicians to prescribe targeted drugs more rapidly or enroll patients in promising trials.

NGS Fuels Global Partnerships

Ongoing collaborations between life sciences companies, governments, academic institutions, and pharmaceutical companies continue to drive discovery and show how NGS is improving our understanding of human biology and disease and improving patient care.

Australia's Precision Oncology Screening Platform Enabling Clinical Trials (PrOSPeCT) program is sequencing 20,000 cancer patients, many with clinically challenging cancers.[22] The project offers patients better access to comprehensive genomic testing. If no approved therapy is available, this program also helps patients enroll in clinical trials.

This gives patients greater access to emerging therapies and provides biopharma companies a more efficient mechanism to fill their trials. By guiding the use of established therapies and boosting clinical trial enrollment, this initiative will expand scientific understanding of global genomic diversity.

To better understand the genetic drivers behind common diseases, the SG100K project, Singapore's Precision Health Research will sequence 100,000 people from diverse Asian backgrounds.[23] This three-year project will investigate the genetic factors that influence cancer, diabetes, hypertension, and other conditions affecting Asian populations.

Similarly, Our Future Health, one of the UK's largest research programs, is studying how the genome and other factors can help prevent, detect, and treat a variety of conditions.[24] Our Future Health seeks to enroll 5 million participants, making it the largest population genetic health program in the world.

These are only a few examples of major, collaborative efforts to sequence large populations to better understand the relationship between genetics and health across diverse populations. The data from these and other studies will continue to empower life sciences companies as they develop new diagnostics and therapies.

Solving the Big Data Problem

Developing instruments and assays that precisely read a patient's genome is important, but to truly personalize medicine, we must accurately and efficiently analyze the data to generate novel insights.

Given the massive amount of NGS data being generated on large populations, machine learning and other artificial intelligence approaches are becoming essential tools to analyze the molecular variations that drive diseases, predict how patients will respond to specific treatments, and help providers create the most effective care plans. By identifying patterns in data generated from large population studies, like the ones cited in the section above, scientists and clinicians can apply that knowledge to improve care.

As genomic databases become larger and more complex, researchers are finding creative ways to separate signal from noise to transform raw data into useful knowledge. As these technologies evolve and migrate into the clinic, physicians will need user-friendly interfaces that communicate the most actionable information and provide decision support. Like the sequencers themselves, these tools will have to be fast, easy to use, and incredibly reliable to support rapid adoption.

Data management is critically important because sequencers will continue to improve and produce more information. The movement from small panels to CGP will generate significantly more information. And, as the cost of sequencing continues to decrease, whole genome analysis of tumors and patients will become standard of care for some cancers. In addition, multi-omic approaches (combining DNA, RNA, methylation, and/or protein analyses) will also produce significant data. Researchers will have to find ways store, transfer and analyze these ever-growing databases. Of course, these richer multi-omic datasets should also help improve the quality of insights derived (better signal to noise).

To keep pace and continuously innovate, labs are embracing a variety of artificial intelligence approaches. In one case, researchers are using deep learning to predict aberrant splicing variations in RUGDs.[25] These non-coding genomic variations may contribute to many of these diseases, but they are difficult to detect with current methods. Deep learning could help provide answers for thousands of patients and their families.

With the $100 genome within reach, whole-genome sequencing may become the assay of choice to understand the genetic drivers of disease. Adopting a data handling infrastructure that is ready to meet this challenge is essential to leverage inexpensive NGS technology to its full potential.

Looking Forward: Better Diagnosis and Treatment

Fundamental discovery research is providing new insights into the molecular mechanisms that cause

disease, as well as identifying potential therapies that hit more molecular targets. NGS is helping accelerate the drug discovery pipeline through improved drug design and precision clinical trials.

On the clinical side, the growing expansion of NGS capabilities is accelerating clinicians' ability to diagnose patients, identify the most precise treatments and continuously track treatment efficacy.

Ultimately, any comprehensive disease prevention strategy will include NGS to understand each individual's risk of disease and the best means to protect them. Current drug discovery efforts are often focused (justifiably) on extending the therapeutic chain – providing expanded options for patients with advanced disease to extend their lives. The next frontier in patient care shifts focus upstream, both for novel drugs and advanced diagnostic methods.

Ideally, early detection through liquid biopsies and other technologies will open earlier treatment windows for a wide range of diseases, helping maintain health rather than simply treat disease. When early detection becomes commonplace, diseases with historically poor outcomes will become more manageable. The goal is to intercept disease early and improve patient's quality of life.

As sequencing and data analytics continue to improve, these technologies will generate other clinical benefits. NGS is both comprehensive and indication agnostic. Genomic analysis will provide more precise information about each patient's unique situation, including their comorbidities, and will consider all possible indications. Genomics will help clinicians better comprehend the connections between the body's major systems, such as cardiovascular, respiratory, metabolic, and inflammatory, helping them address disease even more holistically.

Researchers and clinicians rely on innovative genomic tools to help them decipher complex biology and improve patient care. Through sequencers, sequencing tests, data innovations and other technologies, NGS technologies are helping them succeed and leading the way to personalized medicine. We look forward to the day when inexpensive NGS delivers personalized care for everyone, everywhere. JoPM

References

1. Cercek A, Lumish M, Sinopoli J, et al. PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer. N Engl J Med. 2022;386(25):2363-2376. doi:10.1056/NEJMoa2201445
2. McDermott DF, Atkins MB. PD-1 as a potential target in cancer therapy. Cancer Med. 2013;2(5):662-673. doi:10.1002/cam4.106
3. Groisberg R, Subbiah V. Immunotherapy and next-generation sequencing guided therapy for precision oncology: What have we learnt and what does the future hold?. Expert Rev Precis Med Drug Dev. 2018;3(3):205-213. doi:10.1080/23808993.2018.1480898
4. Chen M, Zhao H. Next-generation sequencing in liquid biopsy: cancer screening and early detection. Hum Genomics. 2019;13(1):34. Published 2019 Aug 1. doi:10.1186/s40246-019-0220-8
5. Early cancer detection: How to find cancer early. Galleri. https://www.galleri.com/multi-cancer-early-detection. Accessed August 6, 2022. Illumina acquired GRAIL in 2021 and the company is being held as a separate entity, overseen by an independent trustee, pending the completion of the European Commission's merger review.
6. Yang XA. Editorial: Next Generation Sequencing (NGS) for Rare Diseases Diagnosis. Front Genet. 2021;12:808042. Published 2021 Dec 23. doi:10.3389/fgene.2021.808042
7. Fitz's story. RCIGM. https://radygenomics.org/case-studies/fitzs-story/. Published April 20, 2022. Accessed August 6, 2022.
8. Autologous gene therapy for Artemis-deficient SCID – full text view. Full Text View – ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03538899. Accessed August 6, 2022.
9. Sweeney NM, Nahas SA, Chowdhury S, et al. Rapid whole genome sequencing impacts care and resource utilization in infants with congenital heart disease [published correction appears in NPJ Genom Med. 2021 May 26;6(1):39] [published correction appears in NPJ Genom Med. 2021 May 26;6(1):38]. NPJ Genom Med. 2021;6(1):29. Published 2021 Apr 22. doi:10.1038/s41525-021-00192-x
10. Adepoju P. African coronavirus surveillance network provides early warning for world. Nat Biotechnol. 2022;40(2):147-148. doi:10.1038/d41587-022-00003-3
11. Dookie N, Khan A, Padayatchi N, Naidoo K. Application of Next Generation Sequencing for Diagnosis and Clinical Management of Drug-Resistant Tuberculosis: Updates on Recent Developments in the Field. Front Microbiol. 2022;13:775030. Published 2022 Mar 24. doi:10.3389/fmicb.2022.775030
12. Rare disease day: Frequently asked questions. Rare Disease Day: Frequently Asked Questions. https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf. Accessed August 8, 2022.
13. Marquart J, Chen EY, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Benefit From Genome-Driven Oncology [published correction appears in JAMA Oncol. 2018 Oct 1;4(10):1439]. JAMA Oncol. 2018;4(8):1093-1098. doi:10.1001/jamaoncol.2018.1660
14. Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. JAMA. 2020;323(9):844–853. doi:10.1001/jama.2020.1166
15. Ochoa D, Karim M, Ghoussaini M, Hulcoop DG, McDonagh EM, Dunham I. Human genetics evidence supports two-thirds of the 2021 FDA-approved drugs. Nat Rev Drug Discov. 2022;21(8):551. doi:10.1038/d41573-022-00120-3
16. Nelson MR, Tipney H, Painter JL, et al. The support of human genetic evidence for approved drug indications. Nat Genet. 2015;47(8):856-860. doi:10.1038/ng.3314
17. Stitziel NO, Kathiresan S. Leveraging human genetics to guide drug target discovery. Trends Cardiovasc Med. 2017;27(5):352-359. doi:10.1016/j.tcm.2016.08.008
18. Hubaud A, Singh AP. Genetics in Drug Discovery. Trends Genet. 2021;37(7):603-605. doi:10.1016/j.tig.2021.04.001
19. Nelson MR, Tipney H, Painter JL, et al. The support of human genetic evidence for approved drug indications. Nat Genet. 2015;47(8):856-860. doi:10.1038/ng.3314
20. Goel N, Kim DY, Guo JA, Zhao D, Mahal BA, Alshalalfa M. Racial Differences in Genomic Profiles of Breast Cancer. JAMA Netw Open. 2022;5(3):e220573. Published 2022 Mar 1. doi:10.1001/jamanetworkopen.2022.0573
21. Roshanthi K. Weerasinghe, Ryan Meng, Alexa K. Dowdell, et al. Identification of clinically actionable biomarkers via routine comprehensive genomic profiling across a large community health system. Journal of Clinical Oncology 2022 40:16_suppl, e15035-e15035
22. $185 million investment to fast-track treatments for rare and 'untreatable' cancers. Omico. https://www.omico.com.au/news/185-million-investment-to-fast-track-treatments-for-rare-and-untreatable-cancers/. Published March 18, 2022. Accessed August 9, 2022.
23. SG100K to sequence 100,000 Singaporeans. Precision Health Research Singapore (PRECISE). https://www.npm.sg/collaborate/partners/sg100k/. Accessed August 9, 2022.
24. Our Future Health. https://ourfuturehealth.org.uk/research-programme/. Accessed August 9, 2022.
25. Predicting splicing from primary sequence with deep learning. Illumina. https://www.illumina.com/science/genomics-research/articles/predict-splicing-primary-sequence-deep-learning.html. Accessed August 19, 2022.

Phil Febbo, MD

Phil Febbo, MD was appointed as Chief Medical Officer in March 2018. In this role, he is responsible for developing and executing the Company's medical strategy to accelerate genomic testing into healthcare practice. Dr. Febbo has a successful track record of translational research, clinical excellence, and for embedding molecular insights into clinical care.

Immediately before joining Illumina, Dr. Febbo served as CMO of Genomic Health. Prior to his five years at Genomic Health, Dr. Febbo was a Professor of Medicine and Urology at theUniversity of California, San Francisco (UCSF), where his laboratory focused on using genomics to understand the biology and clinical behavior of prostate cancer, and his clinical practice focused on genitourinary oncology.

Before joining the faculty of UCSF, Dr. Febbo worked at Duke University Medical Center's Institute of Genome Sciences and Policy. He completed his internal medicine residency at the Brigham and Women's Hospital, and his fellowship in oncology at the Dana-Farber Cancer Institute. After which he was an Attending Physician inthe Genitourinary Oncology Center at Dana-Farber, Instructor at Harvard Medical School, and a post-doctoral fellow in Dr. Todd Golub's laboratory at Dana-Farber, as well as the Whitehead Institute Center for Genomic Research of MIT (now the Broad Institute).Throughout his career, Dr. Febbo has served as a primary investigator for the Translational Research Program of The Alliance, an NCI-supported cooperative group, where his work focused on incorporating biomarkers into large clinical trials.

Dr. Febbo holds a Bachelor of Arts degree in Biology from Dartmouth College and an M.D.from UCSF.

Joydeep Goswami, PhD

Joydeep Goswami is Chief Strategy and Corporate Development Officer, where he is responsible for driving planning, strategic partnerships and acquisitions. He is also Interim Chief Financial Officer.

Most recently, Joydeep served as the President of Thermo Fisher Scientific's Clinical Next-Generation Sequencing (NGS) and Oncology business unit, where he oversaw efforts that drove the adoption of NGSin clinical oncology, research and reproductive health. He has held senior leadership roles across the pharma/biotech, diagnostics and research tool continuum, previously serving at companies such as Life Technologies and Invitrogen, in addition to Thermo Fisher Scientific. He has led teams across various functions, including sales, marketing, R&D and other support functions. Joydeep served as President, Asia Pacific and Japan while at Thermo Fisher Scientific and created the Stem Cells and Regenerative Medicine Business Unit at Invitrogen. Additionally, he spent five years at McKinsey, where he specialized in strategy for pharmaceutical, medical technology and technology companies.

Joydeep holds his MS, PhD in Chemical Engineering, an MBA from MITand a Bachelor's degree in Chemical Engineering from the Indian Institute of Technology.