Executive Summary
The Economic Impact and Functional Applications of Human Genetics and Genomics

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Produced by TEConomy Partners, LLC.
Report Authors: Simon Tripp and Martin Grueber

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Executive Summary

Modern life sciences and associated advancements in biopharmaceuticals, diagnostics, medical devices, and healthcare services have enabled unprecedented improvements in human health and longevity.

Perhaps nowhere has life science research advanced more in the modern age than through insights provided by genetics and genomics. This field is both fundamental in biological research—elucidating the basic code of life, DNA, upon which our form and function depend—and in enabling applied and translational discoveries across most diseases and health disorders.

This report examines and describes the positive impacts that are derived from modern human genetics and genomics science and its associated commercial and clinical applications on the nation's economy, society, and the health and well-being of individuals.

Twenty years after the completion of the Human Genome Project, there has been widespread expansion and application of human genetics and genomics technologies. Technologies for sequencing and for genome analysis have advanced quite spectacularly—to the extent that genome sequencing is now both fast and affordable. The technologies of genetics and genomics, and the research advancements they have enabled scientists to make, have now brought human genetics and genomics to a visible inflection point—a point in time where scientific discoveries are rapidly translating into clinical insights and significant human health and well-being advancements.

The Economic Impact of the Human Genetics and Genomics Sector

The U.S. economy has advanced on the back of scientific progress—progress that has enabled national leadership in diverse industries such as aerospace, energy, agriculture, transportation, advanced materials, information technology, and biotechnology. Continuing to strengthen the competitiveness of the U.S. economy requires ongoing expansion of the national capacity for innovation and the scientific and technological research and development (R&D) upon which innovation depends. Particularly important is leveraging science and innovation to give rise to new, fast-growing, advanced industries that spark economic growth and improved standards of living. Born out of federal investment in the Human Genome Project, the U.S. achieved early leadership in the genetics and genomics industry—leadership that has resulted in the growth of an important and dynamic economic sector.

Substantial U.S. economic activity, supporting a large volume of high-paying jobs across the nation, is generated from the performance of genetic and genomic research, the development and manufacturing of commercial genomic technologies, the broad range of diagnostics products and therapeutics on the

Figure ES-1: The Economic Impact of the Human Genetics and Genomics Sector in the United States

DIRECT EFFECT		INDIRECT EFFECT		INDUCED EFFECT		
Human Genetics & Genomics Focused Research Expenditures, Services, and Corporate Operations in the U.S.	+	Purchase of Secondary Inputs & Services from U.S. Suppliers and Vendors	+	Human Genetics & Genomic Supported Employees Spending Disposable Income in the U.S. Economy	=	Total Economic Impacts of Human Genetics & Genomics

$3.3B
FEDERAL RESEARCH

Federal research funding, using a conservative definition of what constitutes human genetics and genomics research, reached $3.3 billion in 2019, with most of this coming from NIH.

152,000
INDUSTRY JOBS

89,464 core private sector industry jobs and an estimated 62,710 additional extended industry jobs (related employment share from major pharmaceutical and medical testing/diagnostics companies).

850,000
TOTAL SUPPORTED JOBS

With a direct employment estimate of nearly 166,000 academic and industry jobs, human genetics and genomics supports more than 850,000 total jobs. Each direct human genetics and genomics job supports 4.12 additional jobs in the U.S. economy.

$265B
TOTAL ECONOMIC IMPACT

The direct economic activity generated by the human genetics and genomics industry exceeds $108 billion in 2019 and ultimately supports a total of more than $265 billion across the U.S. economy. Every $1.00 of direct human genetics and genomics activity generates an additional $1.45 in the U.S. economy.

$5.2B
DIRECT FEDERAL TAX REVENUES

The federal tax revenues of $5.2 billion generated by the direct operations of the human genetics and genomics domain alone surpasses the single year federal investment in human genetics and genomics of approximately $3.3 billion across all federal agencies.

4.75:1.00
FEDERAL RETURN ON INVESTMENT

In the simplest of terms, from a federal investment and revenue perspective, the overall economic impacts of U.S. human genetics and genomics generates a return on investment (ROI) of more than 4.75 to 1.00 ($3.3 billion in federal investment in human genetics and genomics – while the whole domain generates $15.5 billion in federal tax revenues).

Source: TEConomy Partners, LLC.

market that are derived from genomics knowledge and have pharmacogenomic associations, and the associated healthcare services that are delivered. The economic impact of the human genetics and genomics sector on the U.S. economy is assessed using the standard regional economics methodology of input-output analysis. The results demonstrate the growth of a powerful economic sector across the nation— a sector that has grown five-fold in its annual economic impact since 2010. Even more importantly, it is a sector that also generates robust functional impacts in terms of human health and well-being. Figure ES-1 summarizes some of the topline findings from the economic impact analysis.

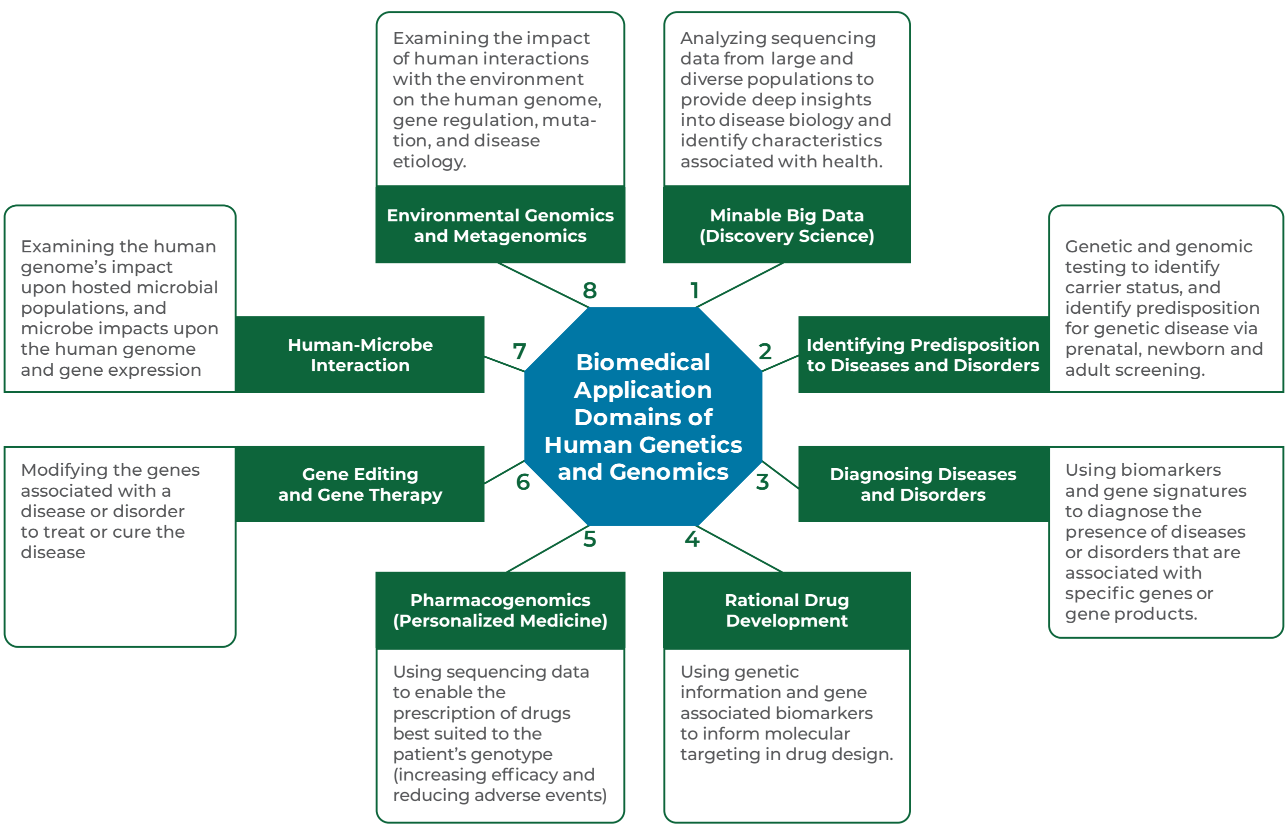
The sector also supports high wage jobs. Because it requires a well-educated and technically skilled workforce, direct jobs in the genetics and genomics sector pay more than $130,000 in annual total compensation (income and benefits) per worker, while the total jobs supported by human genetics and genomics economic activity (direct + induced) average greater than $81,000 in compensation per employee.

The Functional Impacts of Human Genetics and Genomics

The speed and affordability of gene sequencing and advanced genomic data analytics have helped produce deep biomedical insights and innovations, which are being combined with advancements in biopharmaceuticals, diagnostics, and other medical technologies that leverage genomic information. An evident tipping point has been achieved where the utility of genomics and wide-spread use of sequencing is clearly advantageous for significantly enhancing human health outcomes. As this report highlights, the functional application of human genetics and genomics to clinical healthcare is now a daily reality in some medical fields (e.g., cancer diagnosis and treatment) and is increasingly front-and-center in neurological, psychiatric, gastrointestinal, immunologic, rheumatologic, dermatologic, pain management, and other application areas of clinical medicine. It is also fundamental to advancements being made in the diagnosis and treatment of a wide range of rare diseases and disorders—helping to end the diagnostic odysseys of millions of patients afflicted with rare diseases that have been difficult to diagnose and sparsely served in terms of available treatments.

In reviewing the functional applications of human genetics and genomics, the authors find that the positive impacts being generated are highly diverse—generated within eight major domains

Figure ES-2: Functional Biomedical Impact Domains (Applications) of Human Genetics and Genomics



Source: TEConomy Partners, LLC.

of activities impacting human health. These are summarized and briefly described in Figure ES-2.

The eight domains identified in Figure ES-2 are already having profound impacts in advancing clinical health sciences and health outcomes. Each of these areas is profiled briefly below and detailed further in the full body of the report.

1. Minable Big Data (Discovery Science)

Advancements in high-speed gene sequencing technologies have facilitated the assembly of exabytes[1] of genomic information that can be analyzed (assisted by highly advanced and automated analytical systems) for unique insights into genome structure and function and the association of gene variants with human diseases and health disorders. It is anticipated that by 2025 more than 60 million patients will have had their genome sequenced in a healthcare context.[2] Access to extremely large volumes of sequenced individuals provides a rich platform for important scientific discovery and for advancing the identification and classification of genomic variant pathogenicity (variants associated with causation of disease). Both science and technological capabilities are now at the point where the analysis of genomic and phenomic big data provides a powerful pathway forward for biomedical discovery and clinical applications to improve human health.

2. Identifying Predisposition to Diseases and Disorders

One of the primary research and clinical applications of human genetics and genomics is identification of the potential predisposition for individuals to develop specific diseases or health disorders. Modern genetic screening for such predispositions divides into three key categories: 1) carrier screening, which tests a prospective parent for the presence of gene variants that have been shown to be associated with risk of passing down a hereditary disorder (thereby helping to inform family planning and associated decisions); 2) pre-natal and post-natal testing, which focuses on testing for genetic predisposition to disease in the fetus or in newborns; and, 3) child and adult testing.

Information provided by predisposition screening enables patients and their physicians to make informed healthcare decisions, plan follow-up health monitoring strategies, and identify strategies for care using evidence-based clinical best practices.

3. Diagnosing Disease, Rare Diseases, and Disorders

Whole genome and whole exome sequencing are increasingly being used in clinical practice to facilitate the diagnosis of diseases or health disorders. In addition to the many common chronic diseases (such as heart disease, diabetes, cancer, etc.), approximately 7,000 rare diseases have been recognized[3] and have historically been a significant challenge to diagnose. Rare diseases, by their inherent nature of being rare, present diagnostic challenges because so few physicians have encountered them. Often, these diseases may present symptoms seen in other, more common diseases, resulting in an understandable misdiagnosis and inappropriate treatment strategies being adopted. Patients, and their families, may embark on long "diagnostic odysseys", seeing dozens of practitioners, undergoing multiple tests and procedures, enduring fruitless attempts at treatment over many years without ever getting a definitive, accurate diagnosis. Genetic and genomic testing provides a pathway to solving this dilemma in multiple diseases and disorders impacting many thousands of patients.

Collectively, rare diseases have a significant population impact, with approximately 1 in 10 individuals having a rare disease (estimated at between 25-30 million patients in the U.S. and 350 million worldwide).[4] Modern genetic and genomic diagnostic tools, informed by

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1 An exabyte = 10006 bytes (1,000,000,000,000,000,000 bytes).
2 Birney, Ewan. "Luminaries Share Their Thoughts on Advances in 'Omics Over the Past Five Years." C*linical Omics Magazine,* vol. 6, no. 2, March-April 2019.
3 National Center for Advancing Translational Sciences, Genetic and Rare Diseases Information Center. "FAQs About Rare Diseases." https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases. Accessed 12 May 2021.
4 Ibid.

> The ability to tailor a drug regimen to a specific genetic code that is truly personalized to that specific DNA double helix has been a dream of researchers, physicians, and patients alike. Advances in precision medicine, specifically around the genome…are making this dream a reality."
>
> **Kristen Ciriello Pothier. *Personalizing Precision Medicine*. A Global Voyage from Vision to Reality. John Wiley & Sons, Inc., 2017.**

scientific advancements in identifying gene variants associated with specific diseases, are providing clear diagnostic benefits. By deploying genetic and genomic testing, up to and including whole genome sequencing, diagnostic odysseys may be ended for many patients—not only providing a pathway to appropriate treatment but also reducing significant waste in the healthcare system and the associated costs of incorrect diagnosis. Even if no treatment is available, peace of mind can result through simply having an "answer" and being able to end the costly hunt for diagnosis. It has been noted that "this is clearly the most powerful diagnostic tool ever developed for the millions of children with rare diseases."[5]

4. Rational Drug Development

Rational drug development uses genetic and genomic information to advance the development of new biopharmaceuticals to treat diseases. Biomarkers (genes or gene products) are providing molecular targets for purposefully designed drugs that are engineered to bind to targets. The application of genetics and genomics to drug development has resulted in multiple clinical successes, with specific examples highlighted in this report. Biopharmaceutical companies are now able to use genetic and genomic information to target the trials of their pharmaceutical and biologic molecules to patients who have been preselected through the presence of biomarkers (often genetic). This has the potential to advance more drugs successfully to market since they are more likely to demonstrate efficacy in their trials by virtue of being rationally targeted.

It is also notable that progress in genetics and genomics has enabled pharmaceutical research to increasingly address rare diseases—helping to rebalance biopharmaceutical research in terms of work on chronic diseases versus rare diseases.

5. Precision Medicine and Targeted Therapeutics (Pharmacogenetics)

Having an ability to sequence a patient's whole genome rapidly and cost-effectively has opened the door to a new paradigm in healthcare termed "precision medicine" whereby an individual's genetic profile is used to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. The discipline of "pharmacogenetics" (also "pharmacogenomics") has developed as a field of research and, increasingly, clinical practice, that addresses the genetically determined variation in how individuals respond to specific drugs in terms of differences in dose requirement, efficacy, and the risk of adverse drug reactions (ADRs). It is increasingly being employed to help physicians select the "right drug and the right dose" for a patient based on their genome (assuming there is statistically significant clinical information linking a drug to specific gene variants in terms of efficacy and side effects). Currently, pharmacogenetics is improving health outcomes along three primary paths:

5 Kingsmore, Stephen. "Luminaries Share Their Thoughts on Advances in 'Omics Over the Past Five Years." *Clinical Omics Magazine,* vol. 6, no. 2, March-April 2019.

- Selection of the therapeutic (among multiple choices) that is likely to prove most efficacious based on the patient's genome and a drug's proven efficacy for their specific genotype.
- Ruling-out a therapeutic (among multiple choices) based on the patient's genome and a drug's potential for unacceptable adverse side effects given their specific genotype.
- Development of an optimized drug dosage for a patient based on their genotype's influence on the rate at which they will metabolize the drug.

Cancer is perhaps the most well-recognized cluster of disease for which genetic tests may impact drug selection and dosing; however, analysis of U.S. Food and Drug Administration (FDA) data shows that pharmacogenetic associations are also in place for multiple chronic diseases and conditions, covering applications in major categories such as cardiovascular disease, gastroenterological diseases and disorders, infectious diseases, neurological diseases and disorders, psychiatric conditions, and rheumatologic diseases. Pharmacogenetic associations now span a range from relatively rare diseases, such as Tourette's syndrome and Tardive dyskinesia, to common conditions, such as hypercholesterolemia and depression. There are more than 100 drugs for which the associations are now listed by the FDA.

6. Gene Editing and Gene Therapy

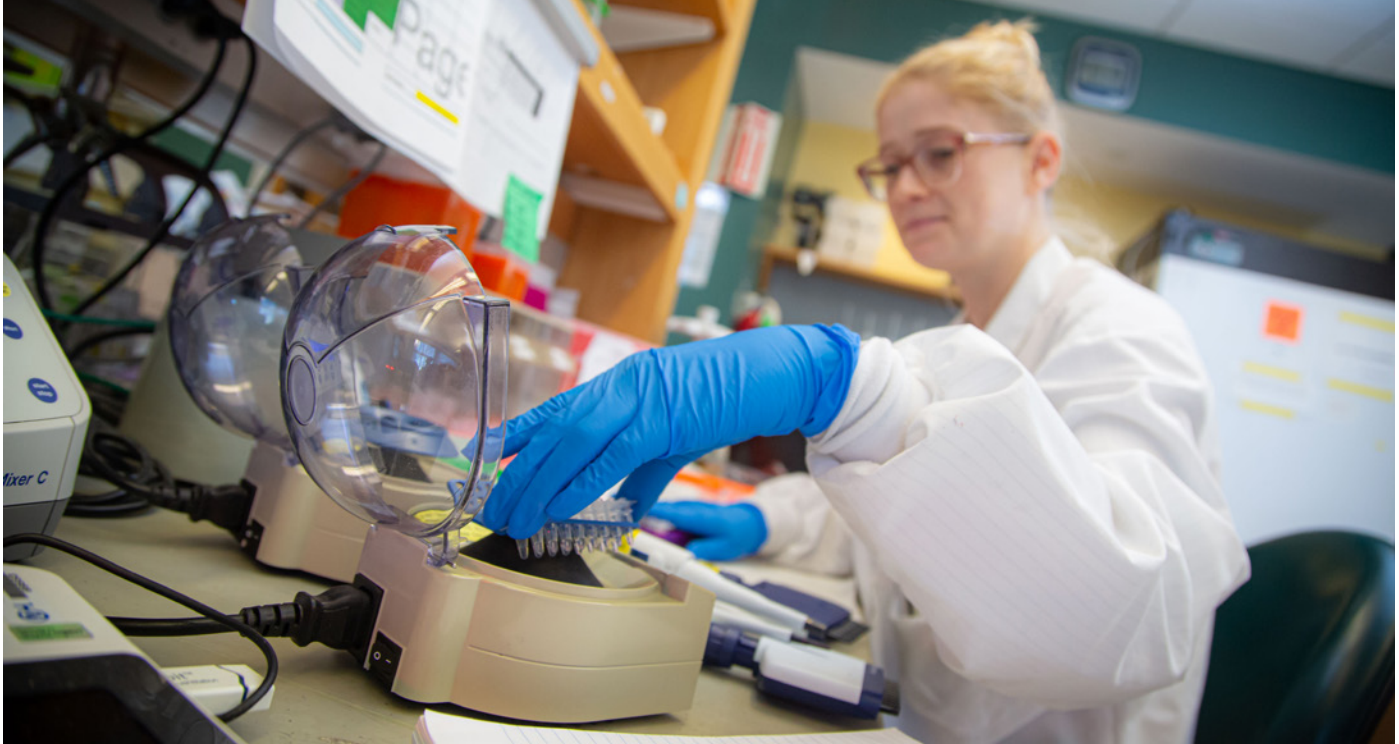
As noted above, genetic and genomic advancements are elucidating gene variant associations with the predisposition for disease, providing enhanced diagnosis of diseases, and providing increasingly effective pathways for therapeutics and disease treatment. Another developing approach is to use the expanding knowledge of gene variants associated with disease to provide targets for potential modification of a patient's genes themselves—modification that has the goal of treating, and potentially curing, the target disease through what is termed gene editing or gene therapy. Ultimately, gene editing and gene therapy represent new pathways to the treatment and curing of diseases, but these approaches are still in the early stages of clinical application.[6] Part of the caution in clinical application arises from a need for further study of the potential for off-target gene edits (mutagenesis) to occur in non-targeted genes and for unintended mosaicism to occur. Despite these challenges, there are several important gene therapies that have successfully advanced through clinical trials, helping to treat a series of previously untreatable rare diseases. It is a promising field for ongoing advancement.

7. Human-Microbe Interactions

Each of us is host to communities of trillions of microbes. Microbes serve important functions for humans, for example aiding our digestion and the breakdown of micronutrients, defending us from pathogenetic microbes, and priming our immune system. Recent research has shown that we have a symbiotic two-way genetic interaction with microbes, with microbes impacting our genes and gene expression, and human genotype impacting the make-up of the microbial communities we host.

While microbes play an important positive role in our health, many microbes are pathogenic, being the causative agents for human infectious diseases. Research is finding that individual genomes can be associated with resistance or susceptibility to certain infectious diseases, and the recent COVID-19 pandemic, coinciding with the current significant volumes of patients for which genome sequences are available, has enabled significant clinical study of genome effects on viral susceptibility and resistance.

6 It should be noted that the discussion of gene editing and gene therapy pertains to modifying non-hereditable (somatic) genes—changes to an individual's genes that will only affect the individual being treated but not the genes of future generations. There is ongoing discussion and public debate about the potential use of gene editing to make heritable genetic changes (changes to the germline). Such genome edits would result in changes to an individual's DNA being passed to their progeny and subsequent generations. At the present time, the general consensus of leading organizations in medical genetics, genetics research, and genetic counseling is that genome editing which culminates in human pregnancy should not be undertaken, and that further research is required into the scientific, clinical, and ethical implications of germline editing.



Genomics in the COVID-19 Pandemic

Genomics rapidly assumed crucial roles in COVID-19 research and clinical care in areas such as: (1) the deployment of DNA and RNA sequencing technologies for diagnostics, tracking of viral isolates, and environmental monitoring; (2) the use of synthetic nucleic acid technologies for studying SAR- CoV-2 virulence and facilitating vaccine development; (3) examination of how human genomic variation influences infectivity, disease severity, vaccine efficacy, and treatment response; (4) the adherence to principles and values related to open science, data sharing, and consortia based collaborations; and (5) the provision of genomic data science tools to study COVID-19 pathophysiology. The growing adoption of genomic approaches and technologies into myriad aspects of the global response to the COVID-19 pandemic serves as another important and highly visible example of the integral and vital nature of genomics in modern research and medicine.

Eric D. Green, et al. “Perspective: Strategic Vision for Improving Human Health at the Forefront of Genomics.” Nature, vol. 586, no. 29, October 2020.

8. Metagenomics and Environmental Genomics

There exists a vast network of interactions between individual genomes and other biological and environmental systems. Each of us walks a slightly different path through life, experiencing different influences upon our physiology in terms of the food we eat, the amount of sun we expose ourselves to, the environments we experience in our jobs, the pathogens that we by chance encounter, etc. Any and all of these and more may be subtly changing (mutating) letters in our genome or periodically influencing gene regulation or expression. Metagenomics is the field of genomics that investigates these interactions and their effects.

Obviously, the human genome is highly complex. Add to that all the genomes in the environment with which one may come into contact, and the enormity of the subject comes into focus. Large-scale sequencing programs are, however, providing a rich resource of data for scientists to mine in metagenomic studies.

Conclusion

The fields of human genetics and genomics are having profound positive impacts not only in terms of biomedical discovery, but also in terms of the clinical practice of medicine—working to improve the lives for millions of patients and demonstrating great promise for future highly positive contributions to human health and well-being worldwide.

As the eight functional domains for human health application of genetics and genomics illustrate, this field of science (and the expanding industry associated with it) generates a profound impact on biomedical research and the practice of clinical healthcare. In addition to applications in human medicine and wellness, there are also several non-medical human applications of genetics and genomics, including forensic science, anthropology and genealogy, evolutionary biology, and paternity testing. These are also highlighted in the report.

It is readily evident that, as fundamental genomic knowledge has expanded, the enhanced understanding of genetic mechanisms generated, in concert with access to rich whole exome and genome datasets (and associated reference compendia of human gene variants), has opened the door to a new era of discovery and progress in medicine. The impacts of these advancements are now increasingly reverberating across medicine, a fact highlighted by Eric Green, the Director of the National Human Genome Research Institute (NHGRI), and colleagues who note that:"

> *With insights about the structure and function of the human genome, and ever improving laboratory and computational technologies, genomics has become increasingly woven into the fabric of biomedical research, medical practice, and society. The scope, scale, and pace of genomic advances so far were nearly unimaginable when the human genome project began; Even today, opportunities beyond their initial expectations, with many more anticipated in the next decade.*[7]

While generating these positive functional impacts is the raison d'etre for pursuing the advancement of human genetics and genomics, it has also had the very positive spillover effect of building a powerful science- and technology-based economic sector for the U.S.—a sector that supports over 850,000 jobs across the nation and generates a $265 billion economic impact in terms of U.S. economic output. The continued innovation in human genetics and genomics is expanding the stock of knowledge upon which our continued advancement depends and shows great promise to continue to do so long into the future. The field represents a particularly strong example of how investing in fundamental and applied science generates robust economic, social, and individual benefits for humankind.

7 Green, Eric D., et al. "Perspective: Strategic Vision for Improving Human Health at the Forefront of Genomics." *Nature*, vol. 586, 29 Oct. 2020.

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