National Human Genome Research Institute

Department of Health and Human Services
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Fiscal Year 2019 Budget Request

Statement for the Record
Senate Subcommittee on Labor-HHS-Education Appropriations

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Mr. Chairman and Members of the Subcommittee:

Mr. Chairman and Members of the Committee: I am pleased to present the President's Fiscal Year (FY) 2019 budget request for the National Human Genome Research Institute (NHGRI) of the National Institutes of Health (NIH).

The Forefront of Genomics

NHGRI is, and always has been, at the forefront of genomics research. NHGRI led the U.S. contribution to the Human Genome Project, which was completed in 2003, and has since embarked on evermore ambitious endeavors, including the dissemination of genomic technologies, knowledge, and expertise throughout the NIH, into the private sector, and around the world. NHGRI accomplished this by driving cutting-edge research, developing new methods and approaches, and studying the impact of genomics on society with the goal of improving the health of all humans through genomic advances. The current pace of genomics is breathtaking, and we are approaching a transitional time in which there will be rapid uptake of genomics in medicine for prevention, diagnosis, and treatment of disease.

To prepare to lead the next phase of genomics, NHGRI officially launched a new strategic planning process in early 2018. This 2-year effort will generate a '2020 Vision for Genomics' and position the Institute to lead genomics research and its applications to human health into the next decade.

Our strong tradition of audacious thinking and effective strategic planning has led to advances that today are enabling some of the most high-profile initiatives in biomedical research. Examples include the NIH *All of Us* Research Program, which seeks to build the largest, most diverse dataset of its kind for health researchers, and the Cancer Moonshot initiative, which aims to accelerate cancer research and to improve our ability to detect, prevent, and treat cancer. The NHGRI-funded Electronic Medical Records and Genomics (eMERGE) Network, now in its third phase, has served as an invaluable pilot for precision medicine research studies, like *All of Us*, by developing the tools and approaches for using genomic information coupled with data in electronic medical records to study human health and disease, including prevention. The Cancer Genome Atlas (TCGA), equally funded by NHGRI and the National Cancer Institute (NCI), generated comprehensive maps of key genomic changes in 33 types of cancer and made all the generated data publicly available to the research community; this program provided a foundation upon which the molecular bases of cancer continue to be defined, revealing new approaches for cancer treatments. In addition, efforts like TCGA and the Cancer Moonshot heavily rely on the dropping costs of genome sequencing, which has been greatly facilitated by NHGRI's technology development research programs.

As noted earlier, the uptake of genomic medicine approaches will increase rapidly in the coming years, and NHGRI is committed to laying the groundwork for these changes. An example effort that will be underway in FY 2019, if funding allows, is the Clinical Sequencing Evidence-Generating Research Program (CSER), which aims to generate and analyze evidence for the use of genome sequencing in clinical care and to address barriers to genomic medicine implementation. This program has a targeted focus on recruiting ancestrally diverse and underserved populations, recognizing that the full benefit of genomic medicine will not be realized unless all of the diverse populations in the United States benefit equitably from genomic advances.

Compared to even a decade ago, genomics is now associated with a much greater breadth and depth of research activities. Furthermore, influenced by NHGRI's leadership, virtually every NIH Institute and Center now funds genomics research to some extent, and a significant amount of genomics research is funded beyond NIH. Recognizing that going forward, a majority of genomics research will be funded by others in the U.S. and internationally, NHGRI aims to identify, lead, and support areas of genomics that are paradigm-setting, that enable novel applications, and that expand the field - all with a focus on applications to human health and disease. In doing so, NHGRI will directly stimulate and achieve highly impactful and generalizable progress in genomics that will benefit the efforts of others for years to come.

Research

Our foundational work in technology development, coupled with new approaches for elucidating genome function, is fueling discoveries of how genomic variation relates to human health and disease; in turn, this knowledge is increasingly being applied to patient care through pilot projects that study the implementation of genomic medicine.

In FY 2019, if funding allows, NHGRI's longstanding Genome Sequencing Program will continue its fundamental work to identify genomic variants associated with disease and to provide resources for the research and clinical communities to discover the genomic underpinnings of disease. The Centers for Common Disease Genomics (CCDGs) are conducting an in-depth genomics study of roughly 10 common diseases, including cardiovascular disease and developmental disorders, to identify genomic variants that either increase or decrease risk associated with those diseases. Using the generated data, the sites intend to develop improved and novel analysis methods and study designs across the entire program. So far, the CCDG sites have generated over 50,000 whole-genome sequences and over 38,000 whole-exome sequences (the protein-coding portions of the genome); the size of such studies is needed to generate the statistical power that will allow reliable conclusions about these diseases to be derived.

Many of NHGRI's principal accomplishments have centered on unraveling the complexities of the genome and giving researchers open access to valuable data. For example, the Encyclopedia of DNA Elements (ENCODE) Project is creating a catalog of all the parts of the human genome that are functional (i.e., that play an active biological role). All of the generated ENCODE data are made freely available, providing every scientist rapid access to this unique and valuable information for their research. In fact, ENCODE's value in biomedicine can be readily appreciated by the widespread use of these data: there are more than 2,000 scientific publications from research groups that have used ENCODE data for their published work.

Another treasure trove of data for the biomedical research community was generated by the NHGRI-led Common Fund project GTEx (genotype-tissue expression), which began in 2008 and aimed to establish a database and accompanying tissue bank to allow scientists to study the relationship between genomic variation and gene expression. In October 2017, *Nature* published a collection of papers highlighting discoveries from the program. The analyses include data for thousands of tissue samples and demonstrated how gene regulation differs across individuals and tissue types.

NHGRI has also been building its portfolio in genomic medicine, piloting projects that seek to explore how to integrate genome sequencing within clinical care and begin to build an evidence base demonstrating its effectiveness. One example is the Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) program, which began in 2013 to study the opportunities and challenges in the use of genome sequencing for the care of newborns. NSIGHT has shown ways in which newborn sequencing can be critical for saving lives by increasing the speed of diagnosis. For example, one of our NSIGHT grantees, whose work was recently featured in *Time* magazine, is using genome sequencing to provide diagnoses and suggest treatment changes for critically ill infants in the neonatal intensive care unit in a timeframe that can make life-altering differences. [1] Notably, this group recently set a Guinness World Record for the fastest genomic diagnosis-19.5 hours.

Conclusion

As is clear from our research portfolio, NHGRI does more than fund the discovery of knowledge and create new technology-we have catalyzed cultural changes across biomedical research. We have demonstrated an unrelenting commitment to data sharing, our 'team science' approach has fostered a spirit of collaboration among scientists, and we have provided researchers with access to shared tools and data to transform genomic advances into health discoveries. As NHGRI delves into strategic planning in FY 2019 and beyond, we will collaborate with experts in the field to identify the cutting-edge areas across our diverse research domains that the Institute should champion and support in the coming decade. We will also continue to tackle the underrepresentation of minorities in genomics research to be sure that the knowledge gained through the federal investment in genomics benefits all.

NHGRI believes that advances in genomics research are transforming our understanding of human health and disease, and we are excited to continue accelerating breakthroughs, improving patient care, and advancing genomics in society.

[1] Park, A. (2017) Genetic Testing is Providing New Hope for Babies Born with Mysterious Ailments. *Time*. http://time.com/4951200/genetic-testing-providing-hope-babies-ailments/

Eric D. Green, M.D., Ph.D.

Director, National Human Genome Research Institute

Eric D. Green, M.D., Ph.D. is the Director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH), a position he has held since late 2009. NHGRI is the largest organization in the world solely dedicated to genomics research. Previously, he served as the NHGRI Scientific Director (2002-2009), Chief of the NHGRI Genome Technology Branch (1996-2009), and Director of the NIH Intramural Sequencing Center (1997-2009).

Born and raised in St. Louis, Missouri, Dr. Green received his B.S. degree in Bacteriology from the University of Wisconsin-Madison in 1981, and his M.D. and Ph.D. degrees from Washington University in 1987. During residency training in clinical pathology (laboratory medicine), he worked in the laboratory of Dr. Maynard Olson, where he launched his career in genomics research. In 1992, he was appointed Assistant Professor of Pathology and Genetics as well as a Co-Investigator in the Human Genome Center at Washington University. In 1994, he joined the newly established Intramural Research Program of the National Center for Human Genome Research, later renamed the National Human Genome Research Institute.

While directing an independent research program for almost two decades, Dr. Green was at the forefront of efforts to map, sequence, and understand eukaryotic genomes. His work included significant, start-to-finish involvement in the Human Genome Project. These efforts eventually blossomed into a highly productive program in comparative genomics that provided important insights about genome structure, function, and evolution. His laboratory also identified and characterized several human disease genes, including those implicated in certain forms of hereditary deafness, vascular disease, and inherited peripheral neuropathy.

As Director of NHGRI, Dr. Green is responsible for providing overall leadership of the Institute's research portfolio and other initiatives. In 2011, Dr. Green led NHGRI to the completion of a strategic planning process that yielded a new vision for the future of genomics research, entitled *Charting a course for genomic medicine from base pairs to bedside (Nature 470:204-213, 2011).* Since that time, he has led the Institute in broadening its research mission; this has included designing and launching a number of major programs to accelerate the application of genomics to medical care. With the rapidly expanding scope of genomics, his leadership efforts have also involved significant coordination with multiple components of the NIH, as well as other agencies and organizations.

Beyond NHGRI-specific programs, Dr. Green has also played an instrumental leadership role in the development of a number of high-profile efforts relevant to genomics, including the Smithsonian-NHGRI exhibition *Genome: Unlocking Life's Code*, the NIH Big Data to Knowledge (BD2K) program, the NIH Genomic Data Sharing Policy, and the U.S. Precision Medicine Initiative.

Last Updated: August 29, 2018