National Human Genome Research Institute

Department of Health and Human Services
National Institutes of Health

Fiscal Year 2015 Budget Request

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

April 2, 2014

Eric D. Green, M.D., Ph.D.
Director, National Human Genome Research Institute

Mr. Chairman and Members of the Committee

I am pleased to present the Fiscal Year (FY) 2015 President's Budget request for the National Human Genome Research Institute (NHGRI). The FY 2015 budget of $498,451,000 reflects an increase of $1,323,000 above the enacted FY 2014 level of $497,128,000.

The research funded and conducted by NHGRI in FY 2015 will continue to unlock the secrets of life's DNA code. We still have much to discover with regard to how the three billion DNA bases of the human genome influence our physical and biochemical characteristics - and, in turn, our health. While we continue to reveal all the information encoded by DNA, we have started pursuing clinical applications of genomic knowledge and implementing genomic medicine.

Understanding how the structure and function of the human genome relates to health and disease will be essential for the implementation of genomic medicine. Among the knowledge to be gained is how the ~20,000 genes in the human genome are turned on and off at the appropriate times and in the appropriate places; this is largely the role of regulatory elements within the genome that act like 'dimmer switches' controlling lights. Through the Institute's Encyclopedia of DNA Elements (ENCODE) Project, a more detailed inventory of these regulatory elements is emerging. In FY 2015, the Genomics of Gene Regulation (GGR) initiative will begin to investigate the choreography of these different elements in different cells and tissues. Many of the elements that ENCODE has identified and GGR will characterize play a role in human diseases and traits, underscoring the foundational value of these projects.

More than 25 million Americans suffer from rare diseases, cumulatively more than those afflicted with cancer. While the genomic bases for just over 5,000 rare diseases have been established - the majority of those established since the end of the Human Genome Project - the causal genes for an estimated 2,000-4,000 additional rare diseases remain to be identified. To investigate the latter, NHGRI's Centers for Mendelian Genomics Program is harnessing powerful DNA-sequencing technologies to analyze patients' genomes on an unprecedented scale en route to establishing the genomic underpinnings of these remaining rare disorders. The resulting discoveries offer the promise of ending the diagnostic odyssey of afflicted patients as well as insights about the diseases that may lead to new therapeutic approaches.

In FY 2015, NHGRI will also focus on more common, but more genomically complex, diseases - those diseases that reflect great public health burdens. One such disease, cancer, is fundamentally a disease of the genome. Hence, NHGRI has been collaborating with the National Cancer Institute in developing The Cancer Genome Atlas (TCGA) since 2006, studying the genomes of different types of tumors and cataloging the discovered genomic aberrations. In FY 2015, TCGA will reach the milestone of analyzing 10,000 tumor samples, revealing many new insights about cancer.

Similarly, NHGRI has partnered with the National Institute on Aging to pursue the largest genomics study of Alzheimer's disease to date. The Alzheimer's Disease Sequencing Project (ADSP) is sequencing and analyzing the genomes of several hundred Alzheimer's patients to help identify the genomic factors contributing to this complex disease, which affects as many as five million Americans aged 65 and older.

Investigators throughout the biomedical research enterprise - well beyond the study of genetic diseases - are now incorporating genomic analyses into their research. A major catalyst for this dissemination has been NHGRI's unparalleled Advanced DNA Sequencing Technology Program, the successes of which have led to a phenomenal drop in the cost of DNA sequencing[1], enabling many more investigators to incorporate genomic analyses into their research. However, these researchers have a widespread and urgent need for improved analytical tools for analyzing DNA sequence data. To address this, NHGRI has created the Genome Sequencing Informatics Tools (GS-IT) program. Like the Institute's development of cutting-edge innovations in DNA sequencing, GS-IT is creating pioneering robust data-analysis tools for studying genomes.

To become a reality, genomic medicine needs refined approaches for using genomic information to improve health outcomes. For instance, in FY 2015, the Implementing Genomics Into Clinical Practice (IGNITE) Network will test methods for disseminating genomic medicine strategies more widely. IGNITE investigators will be initially studying the use of genomic risk information for treating kidney disease, the utility of family health history, and the use of genomic information for selecting appropriate medications. In another effort, NHGRI is partnering with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development to support the Newborn Sequencing in Genomic Medicine and Public Health (NSIGHT) Program, which is examining the potential for genome sequencing to improve the care of newborns.

Pilot programs such as IGNITE and NSIGHT, in addition to other large genomics projects, are only valuable if the generated knowledge diffuses through the medical establishment. To help healthcare professionals become competent with genomic information in delivering patient care, NHGRI is working with the National Center for Biotechnology Information to develop the Clinical Genome Resource (ClinGen), which will provide a curated knowledgebase of clinically relevant genomic variants. ClinGen will be freely available to clinicians, researchers, and professional organizations developing clinical practice guidelines, helping to usher in larger-scale implementation of genomic medicine.

To capitalize on the genomics research funded by NHGRI and other NIH institutes for medicine, the next generation of scientists and clinicians must be equipped with the skills to lead their fields during the 21st century. In FY 2015, new institutional training programs and individual career awards in genomics research and in genomic medicine will develop leaders in those respective fields, including the provision of cross-training in associated disciplines such as bioethics and data science.

Another of NHGRI's educational efforts targets the general public. The Institute collaborated with the Smithsonian Institution's National Museum of Natural History to create the exhibition *Genome: Unlocking Life's Code*. Privately funded, this widely acclaimed exhibition is expected to be visited by more than 3.5 million people before the end of FY 2015. In addition, a series of nine public engagement programs are being produced; these events will remain accessible via the web to complement the exhibition as it travels North America over the next five years.

As described above, NHGRI's genome sciences portfolio will continue to explain the role of the genome in human traits and disease, while its genomic medicine portfolio will apply that knowledge to improve human health. The Institute will ensure that information about genomic advances is disseminated to scientists and healthcare professionals as well as the general public, and that the technologies and generated knowledgebase will continue to be a growth engine for our economy [2].

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

National Human Genome Research Institute
Bethesda, Maryland

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 dedicated solely to genomics research, and aims to advance human health through 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). 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, including significant, start-to-finish involvement in the Human Genome Project.

Now, as Director of NHGRI, Dr. Green is responsible for providing overall leadership of the Institute's research portfolio and other initiatives; this requires significant coordination with other NIH components and funding agencies and research organizations. 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).*

---

[1] Technology: The $1,000 Genome - *Nature,* March 20, 2014

[2] The Impact of Genomics on the U.S. Economy [unitedformedicalresearch.com]

Posted: August 12, 2014