Mr. Chairman and Members of the Committee

I am pleased to present the Fiscal Year (FY) 2014 President's Budget request for the National Human Genome Research Institute (NHGRI). The fiscal year (FY) 2014 budget of $517,319,000 includes an increase of $5,061,000 above the comparable FY 2012 level of $512,258,000.

The Last Decade of Genomics Has Changed Biomedical Science

This year, we celebrate the tenth anniversary of the completion of the Human Genome Project (HGP). An ambitious scientific endeavor likened to biology's 'moon shot,' HGP catalyzed profound changes for many areas of biomedical research and beyond. To provide a perspective about these changes, it is illustrative to compare the 'state-of-the-art' at the beginning of HGP in 1990, at its completion in 2003, and now. To place these three time points in a cultural context, in 1990 Americans communicated by phone and fax; in 2003 it was email; and in 2013 it is the tweet.

Just as technology development has transformed routine communications (from the phone call to the tweet), it has been the cornerstone of the federal investment in genomics. During the HGP, it took 6-8 years of active sequencing and ~$1 billion to generate that first sequence of the human genome. In 2003, that same feat would have required 3-4 months and $10-50 million. Today, a human genome can be sequenced in ~1-2 days for a mere $3-5 thousand. As the time and cost have plummeted, the power of genomic strategies to advance research and the volume of generated genomic data have increased profoundly.

Why is this massive increase in capacity for data generation important? This extraordinary increase in data generation allows us to understand genome structure and function and through this knowledge to learn how genomes contribute to health and disease. For example, in 1990, we knew of ~50 genes that, when mutated, caused a human disease; in 2003 that number was almost 1,500; and today, it is nearly 3,000. Further, knowledge about the genomic basis for our responses to medications-an area of science called pharmacogenomics-has also grown steadily. In 1990, only four Food and Drug Administration (FDA)-approved drugs required labels that pointed out the relevance of a patient's genetic makeup for that medication; by 2003, this number had increased to 46; and today, it stands at 106. In fact, genomic contributions to medical research have been so substantial that fully half of the top ten '2012 medical breakthroughs' identified by *Time* reflected genomics accomplishments, and these were in large part supported and/or facilitated by NHGRI's research programs.
Although extraordinary progress has occurred over the past decade, much remains to be learned about the genome's role in biology and disease, and how to translate that knowledge to improve health outcomes. At the conclusion of HGP, we were but at the beginning of an exciting, but long journey to learn how to apply genomic information to improve health.

Learning from the Data Deluge

A major challenge for genomics research is the handling, analysis, and interpretation of the large volumes of genomic data now routinely generated. Solving this will require innovative infrastructure and novel methodologies. In FY 2014, NHGRI will support pioneering bioinformatics research across its research portfolio, from the use of cloud computing for efforts such as the 1000 Genomes Project to the development of novel clinical bioinformatics tools by the Clinical Sequencing Exploratory Research (CSER) program and the Electronic Medical Records and Genomics (eMERGE) Network, two flagship programs intended to study how to utilize an individual's genomic information in different clinical settings. Additionally, the Institute will provide key leadership within NIH for the Big Data to Knowledge (BD2K) initiative.

Consistent with NHGRI's 2011 strategic plan, the Institute's portfolio spans a continuum from basic research to study genomic structure and function, to translational research to discover the genomic basis for disease, through efforts to use genomics to increase the effectiveness of healthcare. The ENCyclopedia of DNA Elements (ENCODE) project, a key effort to identify the 'functional parts' within the human genome, published a landmark series of papers in 2012 reporting a catalog of functional elements within the human genome. The ENCODE catalog is like a GPS map for the human genome - just as by zooming in on a GPS map of the United States (to find the location of points of interests like banks and gas stations), the ENCODE catalog is now routinely used by researchers worldwide to zoom in on regions of interest in the human genome that are important for their studies. In FY 2014, NHGRI will begin to add another layer of knowledge to this map with the launch of the Genomics of Gene Regulation (GGR) initiative. GGR will fund research to decipher how genes are regulated and to understand how gene regulation affects the function of cells and tissues, human development, and disease.

In FY 2014, NHGRI also will continue advancing the discovery of the genomic bases of disease. For example, the search for genes that play a role in rare diseases will be accelerated through the work of NHGRI's Centers for Mendelian Genomics, as well as an extramural expansion of the highly successful NIH Undiagnosed Diseases Program. Through research programs such as the Large-Scale Genome Sequencing and Analysis Centers, the genomic underpinnings of common complex diseases, such as cancer, diabetes, autism, and Alzheimer's disease, will remain a focus within NHGRI's portfolio as well.

Implementing Genomic Medicine

With the increasing accessibility of genomic technologies, the utility of genomics is already being demonstrated in clinical areas such as pharmacogenomics, non-invasive prenatal testing, infectious disease diagnostics, and cancer. The largest class of drugs now with FDA-required pharmacogenomic information to guide use on their labels includes those used for the treatment of cancer. Further, genome sequencing to identify mutations in a tumor's DNA sequence is now commonplace in the research setting and beginning to be seen in the clinical setting. Current examples of genomics informing care include the widespread use of \textit{BRCA} testing in patients with familial risk.
factors for breast and ovarian cancer, the use of testing to predict breast cancer recurrence, and the use of genomic
diagnostic tests to determine the suitability of particular treatments such as trastuzumab (Herceptin®) use in breast
cancer, vemurafenib (Zelboraf®) use in melanoma, or crizotinib (Xalkori®) use in lung cancer.

In FY 2014, NHGRI also will continue extending its portfolio to investigate the methods and evidence needed to
integrate genomics as a standard component of clinical care. Both existing (e.g., CSER program) and new (e.g.,
Genomic Medicine Pilot Demonstration projects and the Genomic Sequencing and Newborn Screening Disorders
program) initiatives will be carried out by integrated research teams that include clinicians, scientists, and bioethicists.
These multi-disciplinary groups will examine the medical as well as the ethical, social, and legal issues involved with
making genomic data an essential, broadly accessible and broadly desirable element to inform clinical care. In FY
2014, the Institute will continue supporting research pertaining to the pursuit of genomic research and the realization
of genomic medicine, including protecting research participant privacy, determining when to return individual results,
and how to handle unanticipated, but clinically important, 'incidental findings'.

Through these and other programs, NHGRI will continue to lead the field of genomics in an effort to benefit the broad
biomedical research enterprise and to realize the goal of advancing human health through genomics research.

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

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**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 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.

Honors given to Dr. Green include a Helen Hay Whitney Postdoctoral Research Fellowship (1989-1990), a Lucille P.
Markey Scholar Award in Biomedical Science (1990-1994), induction into the American Society for Clinical
Investigation (2002), the Lilian M. Gilbreth Lectureship for Young Engineers at the National Academy of
Engineering (2001), an Alumni Achievement Award from Washington University School of Medicine (2005),
induction into the Association of American Physicians (in 2007), a Distinguished Alumni Award from Washington
University (2010), the Cotlove Lectureship Award from the Academy of Clinical Laboratory Physicians and
Scientists (2011), and the Wallace H. Coulter Lectureship Award from the American Association for Clinical
Chemistry (2012). He is a Founding Editor of the journal *Genome Research* (1995-present) and a Series Editor of
also Co-Editor of *Annual Review of Genomics and Human Genetics* (since 2005). Dr. Green has authored and co-
authored over 320 scientific publications.
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 initial efforts latter blossomed into a highly productive program in comparative genomics that provided important insights about genome structure, function, and evolution.

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. 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).

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