Mr. Chairman and Members of the Committee:

I am pleased to present the President's Fiscal Year (FY) 2010 Budget request for the National Human Genome Research Institute (NHGRI) of the National Institutes of Health. The FY 2010 budget includes $509,594,000, which is $7,227,000 more than the FY 2009 appropriation of $502,367,000.

NHGRI's budget request and its research projects are consistent with the President's multi-year commitment for Cancer.

Windfall of Discoveries of the Genetic Basis of Disease

The Nation's previous investments in the Human Genome Project (HGP) and the International HapMap Project have moved research forward into many diseases with unprecedented speed. HapMap-enabled genome-wide association studies (GWAS) identify a stunning number — over 130 in 2008 alone — of genetic factors associated with major causes of morbidity and mortality in the United States, such as autism, diabetes, cardiovascular disease, lung and prostate cancer, and inflammatory bowel disease. Identification of gene variants associated with disease raises the possibility of using genetic testing, in combination with family history information, to identify susceptible, pre-symptomatic subjects for screening and preventive therapies. It also provides key new understanding of the gene-environment interactions and biological pathways that lead to disease, thus providing new insights into treatment and prevention.

The Cancer Genome Atlas
Initiated in FY 2007, the Cancer Genome Atlas (TCGA) is a pilot project, jointly supported and led by the NHGRI and the National Cancer Institute (NCI) that applies a comprehensive, large-scale genomic analysis approach to cancer research. TCGA is designed to develop and test the complex scientific and technological approaches needed to identify the mutations and other genomic changes associated with various types of cancer. Three NHGRI-supported sequencing centers provide genomic sequencing capability for the TCGA. In FY 2008, the first major results of this pilot project were obtained for the most common form of brain cancer, glioblastoma multiforme (GBM). Another very exciting result was an unexpected observation that points to a potential mechanism of resistance to a common chemotherapy drug used for brain cancer. These first results from the TCGA pilot project represent an exciting indication of the value of the multi-dimensional analysis of the molecular characteristics in human cancer. In the next one to two years, the focus of TCGA will be on two other common cancers, squamous cell lung cancer and ovarian cancer, as well as further analysis of glioblastoma (brain cancer), as well as potential scale up to deal with many other forms of cancer.

Medical Sequencing

The NHGRI's medical sequencing program aims to drive continued technology improvement (lowering the cost of genome sequencing) and to produce data useful to biomedical research. Seven studies are currently underway to identify the genes responsible for several relatively rare, "single-gene" diseases and to survey the range of gene variants that contribute to certain common diseases. In FY 2008, a number of medical sequencing projects were initiated: 1) Sequencing the genomic regions identified in genome-wide association studies as containing genetic components underlying common diseases, such as diabetes, breast cancer, schizophrenia, or Crohn's disease; 2) Sequencing the genomes of important human pathogens, such as those that cause malaria and sleeping sickness, and their invertebrate vectors (in collaboration with the National Institute of Allergy and Infectious Disease (NIAID); and 3) The Cancer Genome Atlas project.

Personalized Genomic Medicine

In addition to basic research underway to support medical applications of genomics, two clinical genomics initiatives launched in FY 2007 are now in full stride. The first, ClinSeq, is a pilot study aimed at developing technological and procedural approaches to facilitate large-scale medical sequencing in a clinical research setting. The second, the Multiplex Initiative, is a study intended to provide genetic susceptibility testing for several common health conditions, such as cardiovascular disease and osteoporosis, to evaluate patients' reactions to the testing and receipt of results.

The 1000 Genomes Project

The 1000 Genomes Project builds on the human haplotype map developed by the International HapMap Project to produce a much more comprehensive view of genomic variation. In fact, it aims to find almost all the variants in the genome, including those that contribute to disease risk. The 1000 Genomes Project will map not only the single-letter differences in people's DNA, called single nucleotide polymorphisms (SNPs), but also will produce a high-resolution map of larger differences in genome structure called structural variants, which are rearrangements, insertions, deletions, or duplications of DNA segments. The importance of these structural variants has become increasingly clear from surveys completed in the past 18 months that demonstrate that differences in genome structure may play a role in susceptibility to such conditions as mental retardation and autism.

The project includes large-scale implementation of several new sequencing platforms to capitalize on the cost reductions emerging from evolving technologies, described in the journal Nature Biotechnology in October 2008. Using standard DNA sequencing strategies, the effort would likely cost more than $500 million. However, the cost of
the project is expected to be far lower to the program, — $30 million to $50 million — due to the project's pioneering implementation of new technologies.

Large Scale Sequencing

Currently, 197 genomes are either in the pipeline or have been completed by the NHGRI-supported large-scale sequencing centers, which are world leaders, renowned for their cost effective and high quality work. Completed in FY2009, the most recent study of a cow was an important development in agriculture that may lead to higher quality beef and milk production and possibly lower carbon dioxide emissions. Ongoing sequencing targets include several non-human primates, mammals, fungi, and multiple strains of yeast.

The $1000 Genome

The NHGRI's continuing commitment to the development of innovative sequencing technologies, which reduces the cost and increases the speed of DNA sequencing, fuels the swift pace of genomic discoveries. In the past year, several groups have demonstrated the ability to work with individual DNA strands and read individual DNA bases. These two breakthroughs are being combined to deliver the ability to sequence DNA isolated directly from cells without any processing apart from purification. This is one technology with promise to achieve the goal of sequencing a genome for $1000 by 2014, NHGRI's original goal.

Genomic Function

The NHGRI supports research to identify and characterize the function of all parts of our genome and to understand their biological relevance. Efforts to uncover functional elements are not limited to the human genome, since understanding the genomes of other, "model," organisms also can give insight into the structure and function of the human genome.

Following a successful pilot project, the NHGRI implemented a full-scale ENCyclopedia of DNA Elements (ENCODE) Project in FY 2007 to examine the entire human genome for sequence-based functional elements. Concurrently, the NHGRI initiated modENCODE, which has similar goals for the analysis of the genomes of two important model organisms. This program will take advantage of the small, more manageable genomes of these organisms to unlock the function of the many genes they share with humans.

Ethical, Legal, and Social Implications

The NHGRI supports six Centers of Excellence in Ethical, Legal, and Social Implications (ELSI) Research. The Centers focus on issues surrounding large-scale genomics research and emerging genetic technologies. The NHGRI continues to support ELSI research as a core aspect of our research portfolio in an effort to anticipate and address the societal issues that will continue to arise as we learn ever more about the human genome and its contributions to human health and disease.

Moving Forward

The NHGRI recently began two new programs to harness genomic knowledge and technology to help patients whose needs are not met by existing scientific and medical programs. Launched in 2008, the Undiagnosed Diseases Program (UDP), jointly led by the NHGRI, the NIH Clinical Center, and the Office of Rare Diseases Research, focuses on the most puzzling medical cases referred to the NIH by physicians across the nation. The NIH Therapeutics for Rare and Neglected Diseases (TRND) Program, launched in FY 2009, builds upon the technology and strategies of high-throughput genomics to identify and shepherd novel therapeutics for diseases where the risks of failure are currently too high for the private sector, but the human need is too great to ignore. These conditions by definition either occur
in fewer than 200,000 Americans or in the developing world, limiting the profit motive for industry. UDP and TRND exemplify how the country can leverage the advances funded and developed by the NHGRI and the NIH to drive the development of more personalized, predictive, pre-emptive, and participatory diagnostic and therapeutic options, improving health outcomes for all Americans.

Alan E. Guttmacher, M.D.

Alan E. Guttmacher, M.D. is the Acting Director of the National Human Genome Research Institute of the National Institutes of Health and, since 2002, has also served as the Institute's Deputy Director. In those roles, he oversees the institute's efforts in advancing genome research, integrating the benefits of genome research into health care, and exploring the ethical, legal, and social implications of human genomics.

A pediatrician and medical geneticist, Dr. Guttmacher came to the NIH in 1999 as the Senior Clinical Advisor to the Director. He has also served as Director of NHGRI's Office of Policy, Communications and Education, leading the institute's efforts in advancing genome research, integrating the benefits of genome research into health care, and exploring the ethical, legal, and social implications of human genomics.

A pediatrician and medical geneticist, Dr. Guttmacher came to the NIH in 1999 as the Senior Clinical Advisor to the Director. He has also served as Director of NHGRI's Office of Policy, Communications and Education, leading the institute's involvement in educating both the public and health professionals about genomics and genomic healthcare. He has overseen NIH's involvement in The U.S. Surgeon General's Family History Initiative, an effort to encourage all Americans to learn about and use their families' health histories to improve health. Among Dr. Guttmacher's areas of expertise is the development of new approaches for translating the findings of the Human Genome Project into better ways of diagnosing, treating, and preventing disease. He has served as co-editor for a series of articles about genomic medicine that was published in the New England Journal of Medicine in 2002-2003 and is co-editing a similar series to appear there starting in early 2010.

Dr. Guttmacher came to the NIH from the University of Vermont, where he directed the Vermont Regional Genetics Center and Pregnancy Risk Information Service, the Vermont Cancer Center's Familial Cancer Program, and the Vermont Newborn Screening Program, founded Vermont's only pediatric intensive care unit, and was the principal investigator for an NIH-supported initiative that was the nation's first statewide effort to involve the general public in discussion of the Human Genome Project's ethical, legal, and social implications. He also had a busy practice in clinical genetics, conducted research, and taught.

A graduate of Harvard College and of Harvard Medical School, Dr. Guttmacher completed a residency in Pediatrics and a fellowship in Medical Genetics at Harvard and Children's Hospital of Boston. Among his honors was his election to the Institute of Medicine in 2004.

Last Reviewed: February 22, 2012