NATIONAL HUMAN GENOME RESEARCH INSTITUTE

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Mission:
Since the completion of the Human Genome Project in April 2003, the National Human Genome Research Institute (NHGRI) has moved forward into the genomic era with a wide range of research initiatives aimed at improving human health. Examples of these new scientific projects include the HapMap, ENCODE, and a chemical genomics initiative. At the same time, the NHGRI has enhanced its Ethical Legal and Social Implications (ELSI) program, including the establishment of an extramural Centers of Excellence in ELSI Research (CEER) program and has further developed its intramural research program, including the creation of a new Social and Behavioral Research Branch. The NHGRI also continues to play an active role in the public policy debate surrounding issues of genomics and genetics, and to provide informational and educational resources to health care professionals, those with genetic disease, students, and the general public.

Selected Achievements and Initiatives:
The Human Genome Project: On October 21, 2004, a paper describing the essentially finished human genome sequence appeared in Nature. An international team of Human Genome Project collaborators converted the draft genome into a highly accurate form. This paper reported the results of that finishing process. The current genome sequence (Build 35) contains 2.85 billion nucleotides interrupted by only 341 gaps. It covers approximately 99 percent of the euchromatic genome and is accurate to an error rate of ~1 event per 100,000 bases. The remaining euchromatic gaps are resistant to all current sequencing methods. Notably, the human genome appears to encode only 20,000 to 25,000 protein-coding genes. The genome sequence will continue to serve as a firm foundation for biomedical research in the decades ahead.

Human Variation: Understanding how genetic variation is inherited in DNA haplotypes can provide considerable savings in time, effort, and cost in uncovering hereditary factors in disease. NHGRI has taken a leadership role in the development of the HapMap, a catalog of haplotype blocks and the single nucleotide polymorphisms (SNPs) that tag them. Researchers can use the HapMap to find the genes and variants that contribute to many diseases and, in addition, it will be a powerful resource for studying the genetic factors contributing to variation in individual response to disease, to drugs, and to vaccines.

The HapMap consortium had initially planned to identify an additional 3 million new SNPs to fill in areas where the density of SNPs in public databases was insufficient, but due to advances in technology the project has now identified more than 6 million new SNPs, for a total of 9 million. The consortium has completed the collection of samples and consent from 270 individuals from four populations (CEPH [U.S. residents with ancestry from Western and Northern Europe], Yoruba in Ibadan Nigeria, Han Chinese in Beijing, and Japanese in Tokyo). Eight research groups have performed genotyping for 890,916 SNPs in these samples as of September 2004. A phase I map will be available in early 2005, and achievement of the goals of the

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HapMap project is scheduled by the end of 2005. More information about HapMap is available at: www.hapmap.org.

ENCyclopedia Of DNA Elements (ENCODE): Following completion of the reference sequence, the next logical step was to characterize both the genes and intergenic elements that regulate gene expression, DNA replication, and chromosome structure. With the goal of identifying the precise location and function of all sequence-based functional elements in the genome, the NHGRI launched the ENCyclopedia Of DNA Elements (ENCODE) project. Grants were awarded in 2003 for the pilot phase, calling for application of existing technologies to a carefully chosen 30 megabases (roughly 1%), of the human genome. The pilot phase of the project is organized as an international consortium of computational and laboratory-based scientists.

Current technologies are not able to achieve all of the aims of even the initial phase of the ENCODE project. Therefore, at the same time that high-throughput efforts were being initiated using well-developed technologies, NHGRI launched a parallel effort to develop new technologies. The first set of grants to expand the repertoire of tools that can be applied to ENCODE or similar future projects was awarded in 2003. A second set of technology development grants was awarded in September 2004. It is envisioned that when an extensive "tool box" of technologies is available, it will be possible to annotate the entire human genome with information that will serve as a platform for more in-depth, detailed studies of biological function.

Ethical, Legal and Social Implications (ELSI) Research: Since its founding, the NHGRI has understood the need to analyze the ethical, legal, and social implications of genetic research and to address the issues they raise. The ELSI Research Program was established in 1990 as an integral part of the HGP. This program funds and manages research grants and education projects throughout the U.S. and supports workshops, research consortia, and policy conferences related to these projects. In particular, the ELSI program works to ensure the responsible use of genetic information, including appropriate prohibitions against the use of genetic information to discriminate against individuals. Guided by these research efforts, public policy can be implemented to ensure that advances in genetics and genomics are used for benefit and not for harm. The new CEER program will further facilitate the formulation and implementation of effective and equitable health and social policies related to genomic research.

Appropriations History
($ in thousands)

FY 2001	$382,112 (+13.9%)
FY 2002	$428,758 (+12.2%)
FY 2003	$464,995 (+8.5%)
FY 2004	$479,073 (+3.0%)
FY 2005	$488,608 (+2.0%)

Extramural Research Project Grants
(Includes SBIR/STTRs)

FY 2001	141
FY 2002	152
FY 2003	187
FY 2004	215
FY 2005	240

Success Rate — Research Project Grants

FY 2001	42%
FY 2002	34%
FY 2003	30%
FY 2004	23%
FY 2005	28%

Research Training Positions Supported

FY 2001	85
FY 2002	131
FY 2003	155
FY 2004	170
FY 2005	151

Research Centers

FY 2001	24
FY 2002	32
FY 2003	29
FY 2004	39
FY 2005	41