

# HUMAN GENOME PROGRAM REPORT

## Part 1, Overview and Progress

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# MAJOR EVENTS IN THE U.S. HUMAN GENOME PROJECT AND RELATED PROGRAMS

1983

LANL and LLNL begin production of DNA clone (cosmid) libraries representing single chromosomes.

1984

DOE OHER and ICPEMC cosponsor Alta, Utah, conference highlighting the growing role of recombinant DNA technologies. OTA incorporates Alta proceedings into a 1986 report acknowledging value of human genome reference sequence.

1985

- \* Robert Sinsheimer holds meeting on human genome sequencing at University of California, Santa Cruz.  
At OHER, Charles DeLisi and David A. Smith commission the first Santa Fe conference to assess the feasibility of a Human Genome Initiative.

1986

Following the Santa Fe conference, DOE OHER announces Human Genome Initiative. With \$5.3 million, pilot projects begin at DOE national laboratories to develop critical resources and technologies.

1987

DOE advisory committee, HERAC, recommends a 15-year, multidisciplinary, scientific, and technological undertaking to map and sequence the human genome. DOE designates multidisciplinary human genome centers.

- \* NIH NIGMS begins funding of genome projects.

1988

- \* Reports by OTA and NAS NRC recommend concerted genome research program.  
HUGO founded by scientists to coordinate efforts internationally.

- \* First annual Cold Spring Harbor Laboratory meeting held on human genome mapping and sequencing.

DOE and NIH sign MOU outlining plans for cooperation on genome research.

Telomere (chromosome end) sequence having implications for aging and cancer research is identified at LANL.

1989

DNA STSs recommended to correlate diverse types of DNA clones.

DOE and NIH establish Joint ELSI Working Group.

1990

DOE and NIH present joint 5-year U.S. HGP plan to Congress. The 15-year project formally begins.

Projects begun to mark genes on chromosome maps as sites of mRNA expression.

R&D begun for efficient production of more stable, large-insert BACs.

1991

Human chromosome mapping data repository, GDB, established.

1992

- \* Low-resolution genetic linkage map of entire human genome published.

Guidelines for data release and resource sharing announced by DOE and NIH.

1993

International IMAGE Consortium established to coordinate efficient mapping and sequencing of gene-representing cDNAs.

DOE-NIH Joint ELSI Working Group's Task Force on Genetic Information and Insurance releases recommendations.

DOE and NIH revise 5-year goals [*Science* **262**, 43–46 (Oct. 1, 1993)].

- \* French Généthon provides mega-YACs to the genome community.

IOM releases U.S. HGP-funded report, "Assessing Genetic Risks."

GRAIL sequence interpretation service with Internet access initiated at ORNL.

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ADA	Americans with Disabilities Act
ANL	Argonne National Laboratory
BAC	bacterial artificial chromosome
cDNA	complementary deoxyribonucleic acid
CGAP	Cancer Genome Anatomy Project
DNA	deoxyribonucleic acid
DHHS	Department of Health and Human Services (NIH)
DOE	Department of Energy
EEOC	Equal Employment Opportunity Commission
ELSI	ethical, legal, and social issues
GDB	Genome Database
GRAIL	Gene Recognition and Analysis Internet Link
HERAC	Health and Environmental Research Advisory Committee
HGP	Human Genome Project, Human Genome Program
HUGO	Human Genome Organisation
ICPEMC	International Commission for Protection Against Environmental Mutagens and Carcinogens
IMAGE	Integrated Molecular Analysis of Gene Expression
IOM	Institute of Medicine (NAS)

## 1994

- \* Genetic-mapping 5-year goal achieved 1 year ahead of schedule.

Completion of second-generation DNA clone libraries representing each human chromosome by LLNL and LBNL.

Genetic Privacy Act, first U.S. HGP legislative product, proposed to regulate collection, analysis, storage, and use of DNA samples and genetic information obtained from them; endorsed by DOE-NIH Joint ELSI Working Group.

DOE Microbial Genome Program launched; spin-off of HGP.

LLNL chromosome paints commercialized.

SBH technologies from ANL commercialized.

DOE HGP Information Web site activated for public and researchers.

## 1995

LANL and LLNL announce high-resolution physical maps of chromosome 16 and chromosome 19, respectively.

- \* Moderate-resolution maps of chromosomes 3, 11, 12, and 22 maps published.

- \* First (nonviral) whole genome sequenced (for the bacterium *Haemophilus influenzae*).

Sequence of smallest bacterium, *Mycoplasma genitalium*, completed, displaying the minimum number of genes needed for independent existence.

- \* EEOC guidelines extend ADA employment protection to cover discrimination based on genetic information related to illness, disease, or other conditions.

## 1996

*Methanococcus jannaschii* genome sequenced; confirms existence of third major branch of life, the Archaea.

DOE-NIH Task Force on Genetic Testing releases interim principles.

- \* Integrated STS-based detailed human physical map with 30,000 STSs achieves an HGP goal.
  - \* Health Care Portability and Accountability Act prohibits use of genetic information in certain health-insurance eligibility decisions, requires DHHS to enforce health-information privacy provisions.
- DOE-NIH Joint ELSI Working Group releases guidelines on informed consent for large-scale sequencing projects.

DOE and NCHGR issue guidelines on use of human subjects for large-scale sequencing projects.

- \* *Saccharomyces cerevisiae* (yeast) genome sequence completed by international consortium.

Sequence of the human T-cell receptor region completed.

Wellcome Trust sponsors large-scale sequencing strategy meeting in Bermuda for international coordination of human genome sequencing.

## 1997

DOE forms Joint Genome Institute for implementing high-throughput sequencing at DOE HGP centers.

- \* NIH NCHGR becomes NHGRI.
- \* *Escherichia coli* genome sequence completed.
- Second large-scale sequencing strategy meeting held in Bermuda.
- \* High-resolution physical maps of chromosomes X and 7 completed.

*Methanobacterium thermoautotrophicum* genome sequence completed.

*Archaeoglobus fulgidus* genome sequence completed.

- \* NCI CGAP begins.

- \* DOE had limited or no involvement in this event.

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LANL	Los Alamos National Laboratory
LBNL	Lawrence Berkeley National Laboratory
LLNL	Lawrence Livermore National Laboratory
MGP	Microbial Genome Project
MOU	Memorandum of Understanding
mRNA	messenger ribonucleic acid
NAS	National Academy of Sciences
NCHGR	National Center for Human Genome Research (NIH)
NCI	National Cancer Institute (NIH)
NHGRI	National Human Genome Research Institute (NIH)
NIGMS	National Institute of General Medical Sciences (NIH)
NIH	National Institutes of Health
NRC	National Research Council
OHER	Office of Health and Environmental Research
ORNL	Oak Ridge National Laboratory
OTA	Office of Technology Assessment
R&D	Research and Development
SBH	sequencing by hybridization
STS	sequence tagged site
YAC	yeast artificial chromosome





# Preface

**M**ore than a decade ago, the Office of Health and Environmental Research (OHER) of the U.S. Department of Energy (DOE) struck a bold course in launching its Human Genome Initiative, convinced that its mission would be well served by a comprehensive picture of the human genome. Organizers recognized that the information the project would generate—both technological and genetic—would contribute not only to a new understanding of human biology and the effects of energy technologies but also to a host of practical applications in the biotechnology industry and in the arenas of agriculture and environmental protection.

Today, the project's value appears beyond doubt as worldwide participation contributes toward the goals of determining the human genome's complete sequence by 2005 and elucidating the genome structure of several model organisms as well. This report summarizes the content and progress of the DOE Human Genome Program (HGP). Descriptive research summaries, along with information on program history, goals, management, and current research highlights, provide a comprehensive view of the DOE program.

Last year marked an early transition to the third and final phase of the U.S. Human Genome Project as pilot programs to refine large-scale sequencing strategies and resources were funded by DOE and the National Institutes of Health, the two sponsoring U.S. agencies. The human genome centers at Lawrence Berkeley National Laboratory, Lawrence Livermore National Laboratory, and Los Alamos National Laboratory had been serving as the core of DOE multidisciplinary HGP research, which requires extensive contributions from biologists, engineers, chemists, computer scientists, and mathematicians. These team efforts were complemented by those at other DOE-supported laboratories and about 60 universities, research organizations, companies, and foreign institutions. Now, to focus DOE's considerable resources on meeting the challenges of large-scale sequencing, the sequencing efforts of the three genome centers have been integrated into the Joint Genome Institute. The institute will continue to bring together research from other DOE-supported laboratories. Work in other critical areas continues to develop the resources and technologies needed for production sequencing; computational approaches to data management and interpretation (called informatics); and an exploration of the important ethical, legal, and social issues arising from use of the generated data, particularly regarding the privacy and confidentiality of genetic information.

Insights, technologies, and infrastructure emerging from the Human Genome Project are catalyzing a biological revolution. Health-related biotechnology is already a success story—and is still far from reaching its potential. Other applications are likely to beget similar successes in coming decades; among these are several of great importance to DOE. We can look to improvements in waste control and an exciting era of environmental bioremediation, we will see new approaches to improving energy efficiency, and we can hope for dramatic strides toward meeting the fuel demands of the future.

In 1997 OHER, renamed the Office of Biological and Environmental Research (OBER), is celebrating 50 years of conducting research to exploit the boundless promise of energy technologies while exploring their consequences to the public's health and the environment. The DOE Human Genome Program and a related spin-off project, the Microbial Genome Program, are major components of the Biological and Environmental Research Program of OBER.

DOE OBER is proud of its contributions to the Human Genome Project and welcomes general or scientific inquiries concerning its genome programs. Announcements soliciting research applications appear in *Federal Register*, *Science*, *Human Genome News*, and other publications. The deadline for formal applications is generally midsummer for awards to be made the next year, and submission of preproposals in areas of potential interest is strongly encouraged. Further information may be obtained by contacting the program office or visiting the DOE home page (301/903-6488, Fax: -8521, [genome@oer.doe.gov](mailto:genome@oer.doe.gov), URL: [http://www.er.doe.gov/production/ober/hug\\_top.html](http://www.er.doe.gov/production/ober/hug_top.html)).

Aristides Patrinos, Associate Director  
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U.S. Department of Energy  
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