

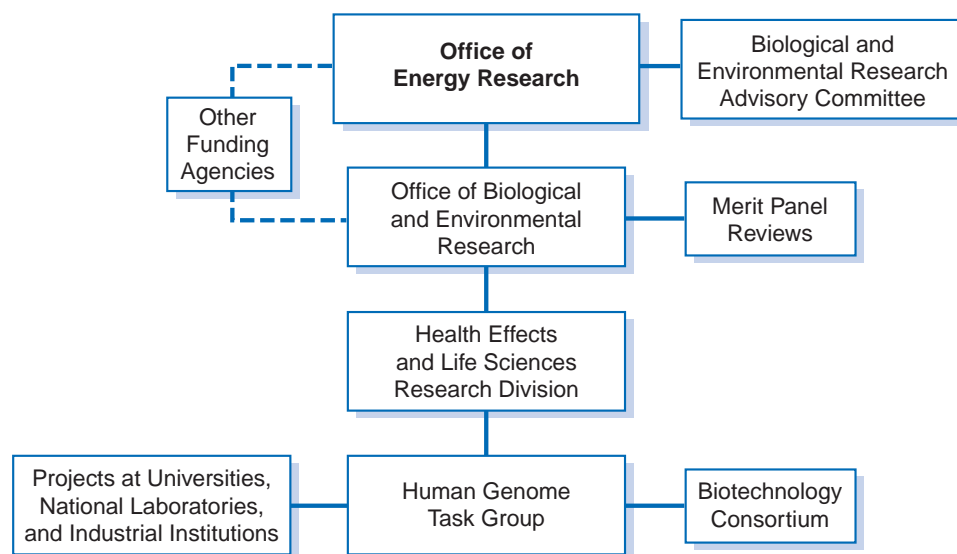
**T**he Human Genome Program was conceived in 1986 as an initiative within the DOE Office of Health and Environmental Research, which has been renamed Office of Biological and Environmental Research (OBER) (see chart below). The program is administered primarily through the OBER Health Effects and Life Sciences Research Division (HELSDRD), both directed by David A. Smith until his retirement in January 1996. Marvin Frazier is now Director of HELSRD, and OBER is led by Associate Director Aristides Patrinos, who also serves as Human Genome Program manager. Previous directors and managers are listed in the table below. OBER is within the Office of Energy Research, directed by Martha Krebs.

## DOE OBER Mission

Based on mandates from Congress, DOE OBER's principal missions are to (1) develop the knowledge necessary to identify, understand, and anticipate long-term health and environmental consequences of energy use and development and (2) employ DOE's unique scientific and technological capabilities in solving major scientific problems in medicine, biology, and the environment.

Genome integrity and radiation biology have been a long-term concern of OBER at DOE and its predecessors—the Atomic Energy Commission (AEC) and the Energy Research and Development Administration (ERDA). In the United States, the first federal support

See Appendix A, p. 73, for information on Human Genome Project history, including enabling legislation.



OHER Associate or Acting Directors		Human Genome Program Managers	
Charles De Lisi	1985	Benjamin J. Barnhart	1988
Robert W. Wood	1987	David A. Smith	1991
David J. Galas	1990	Aristides Patrinos	1996
Aristides Patrinos	1993		

Institutions Conducting DOE-Sponsored Genome Research	
DOE national laboratories	7
Academic institutions	28
Private-sector institutions	10
Companies, including Small Business Innovation Research	11
Foreign institutions (Russia, Canada, Israel)	7

## DOE Human Genome Task Group

Member	Specialty
<b>Chair: Aristides Patrinos</b> <b>Benjamin J. Barnhart</b> <b>Elbert Branscomb</b>	Physical sciences Genetics, Radiation biology Scientific Director, Joint Genome Institute
<b>Daniel W. Drell</b>	Biology, ELSI, Informatics, Microbial genome
<b>Ludwig Feinendegen</b> <b>Marvin Frazier</b> <b>Gerald Goldstein<sup>†</sup></b> <b>D. Jay Grimes<sup>†</sup></b> <b>Roland Hirsch</b> <b>Arthur Katz*</b> <b>Anna Palmisano*<sup>†</sup></b> <b>Michael Riches</b> <b>Jay Snoddy<sup>†</sup></b> <b>Marvin Stodolsky</b> <b>David G. Thomassen</b> <b>John C. Wooley</b>	Medicine, Radiation biology Molecular and cellular biology Physical science, Instrumentation Microbiology Structural biology, Instrumentation Physical sciences Microbiology, Microbial genome Physical sciences Molecular biology, Informatics Molecular biology, Biophysics Cell and molecular biology Computational biology

\*Joined, 1997.

<sup>†</sup>Left OBER, 1997.

## Biotechnology Consortium

<b>Chair: Aristides Patrinos</b>	DOE Office of Biological and Environmental Research
<b>Charles Arntzen*</b> <b>Elbert Branscomb</b>	Cornell University Lawrence Livermore National Laboratory
<b>Charles Cantor</b> <b>Anthony Carrano</b>	Boston University Lawrence Livermore National Laboratory
<b>Thomas Caskey</b> <b>David Eisenberg</b> <b>Chris Fields<sup>†</sup></b> <b>David Galas</b> <b>Raymond Gesteland</b> <b>Keith Hodgson</b> <b>Leroy Hood</b> <b>David Kingsbury<sup>†</sup></b> <b>Robert Moyzis<sup>†</sup></b> <b>Mohandas Narla*</b> <b>Michael Palazzolo</b> <b>Melvin Simon*</b> <b>Hamilton Smith*</b>	Merck Research Laboratories University of California, Los Angeles National Center for Genome Resources Darwin Molecular, Inc. University of Utah Stanford University University of Washington, Seattle Chiron Pharmaceuticals University of California, Irvine Lawrence Berkeley National Laboratory Amgen, Inc. California Institute of Technology Johns Hopkins University School of Medicine
<b>Lloyd Smith</b> <b>Lisa Stubbs</b>	University of Wisconsin, Madison Lawrence Livermore National Laboratory
<b>Edward Uberbacher*</b> <b>Marc Van Montagu*</b> <b>Executive Officer:</b> <b>Sylvia Spengler</b>	Oak Ridge National Laboratory Ghent University, Belgium Lawrence Berkeley National Laboratory

\*Appointed after October 1996.

<sup>†</sup>Resigned, 1997.

Note: All members of the DOE Human Genome Task Group are ex-officio members of the Biotechnology Consortium.

for genetic research was through AEC. In the early days of nuclear energy development, the focus was on radiation effects and broadened later under ERDA and DOE to include health implications of all energy technologies and their by-products.

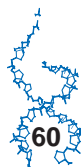
Today, extensive OBER-sponsored research programs on genomic structure, maintenance, damage, and repair continue at the national laboratories and universities. These and other OBER efforts support a DOE shift toward a preventive approach to health, environment, and safety concerns. World-class scientists in top facilities working on leading-edge problems spawn the knowledge to revolutionize the technology, drive the future, and add value to the U.S.

economy. Major OBER research includes characterization of DNA repair genes and improvement of methodologies and resources for quantifying and characterizing genetic polymorphisms and their relationship to genetic susceptibilities.

To carry out its national research and development obligations, OBER conducts the following activities:

- Sponsors peer-reviewed research and development projects at universities, in the private sector, and at DOE national laboratories (see box, p. 59).
- Considers novel, beneficial initiatives with input from the scientific community and governmental sectors.
- Provides expertise to various governmental working groups.
- Supports the capabilities of multi-disciplinary DOE national laboratories and their unique user facilities for the nation's benefit (p. 61).

Human Genome Program resources and technologies are focused on sequencing the human genome and related informatics and supportive infrastructure (see chart and tables, p. 62). The genomes of selected microorganisms are analyzed under the separate Microbial Genome Program.



# Major DOE User Facilities and Resources Relevant to Molecular Biology Research

*Although the genome program is contributing fundamental information about the structure of chromosomes and genes, other types of knowledge are required to understand how genes and their products function. Three-dimensional protein structure studies are still essential because structure cannot be predicted fully from its encoded DNA sequence.*

*To enhance these and other studies, DOE builds and maintains structural biology user facilities that enable scientists to gain an understanding of relationships between biological structures and their functions, study disease processes, develop new pharmaceuticals, and conduct basic research in molecular biology and environmental processes. These resources are used heavily by both academic and private-sector scientists.*

*Other important resources available to the research community include the clone libraries developed in the National Laboratory Gene Library Project and distributed worldwide, the GRAIL Online Sequence Interpretation Service, and the Mouse Genetics Research Facility.*



**Argonne National Laboratory**  
Advanced Photon Source

**Brookhaven National Laboratory**  
High-Flux Beam Reactor  
National Synchrotron Light Source  
Protein Structure Data Bank  
Scanning Transmission Electron Microscope

**Lawrence Berkeley National Laboratory**  
Advanced Light Source  
Center for X-Ray Optics  
National Energy Research Scientific Computing Center

**Lawrence Livermore National Laboratory**  
National Laboratory Gene Library Project

**Los Alamos National Laboratory**  
National Flow-Cytometry Resource  
National Laboratory Gene Library Project  
Neutron-Scattering Center

**Oak Ridge National Laboratory**  
GRAIL, Online Sequence Interpretation Service  
Mouse Genetics Research Facility

**Pacific Northwest National Laboratory**  
Environmental Molecular Sciences Laboratory

**Stanford University**  
Synchrotron Radiation Laboratory

# Human Genome Program

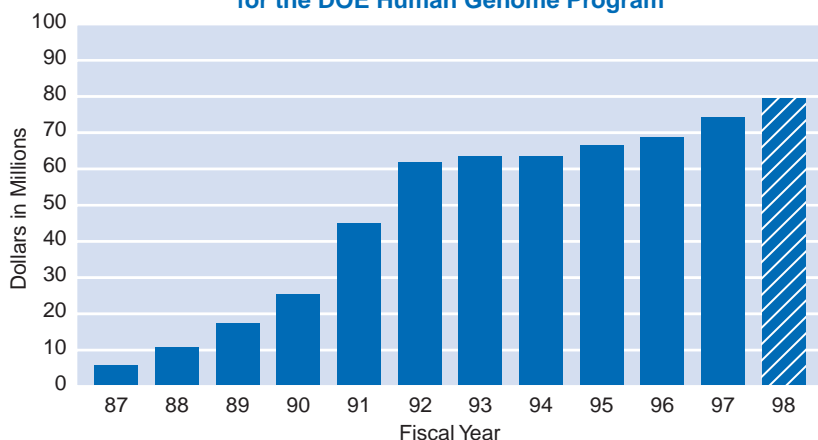
## Coordination and Resources

Program coordination is the responsibility of the Human Genome Task Group (see box, p. 60), which, beginning in 1997, includes Elbert Branscomb, the Joint Genome Institute's Scientific Director. The task group is aided by the Biotechnology Consortium (which succeeded the former Human Genome Coordination Committee; see box, p. 60) to foster information exchange and dissemination. The task group administers the DOE Human Genome Program and its evolving needs and reports to the

Associate Director for Biological and Environmental Research (currently Aristides Patrinos). The task group arranges periodic workshops and coordinates site reviews for genome centers, the Joint Genome Institute, databases, and other large projects. It also coordinates peer review of research proposals, administration of awards, and collaboration with all concerned agencies and organizations.

The Biotechnology Consortium provides the OBER Associate Director with external expertise in all aspects of genomics and informatics and a mechanism by which OBER can keep track of the latest developments in the field. It facilitates development and dissemination of novel genome technologies throughout the DOE system, ensures appropriate management and sharing of data and resources by all DOE contractors and grantees, and promotes interactions with other national and international genomic entities.

**Operating Expenditures and FY 1998 Projected Budget for the DOE Human Genome Program**



**Human Genome Program Fiscal Year Expenditures (\$M)**

Year	Operating	Capital Equipment	Construction	Total
1996	68.3	5.6	5.7	79.6
1997	73.9	6.0	1.0	80.9
1998*	79.9	5.2	0.0	85.1

\*Projected expenses.

**Human Genome Program Operating Funds Distribution in FY 1996 (\$K)**

FY 1996	Mapping	Sequencing	Sequencing Technology	Informatics	ELSI	Administration	Totals	%
DOE Laboratories	8,980	11,015	11,128	6,840	313	2,783 *	41,059	60.1
Academic	6,671	4,368	3,257	6,178	642	4	21,120	30.9
Nonprofit	563	0	467	2,783	1,311	38	5,162	7.5
Federal	0	0	0	0	0	1,000 **	1,000	1.5
<b>Total</b>	<b>16,214</b>	<b>15,383</b>	<b>14,852</b>	<b>15,801</b>	<b>2,266</b>	<b>3,825</b>	<b>68,341</b>	
% of Total	23.8	22.5	21.7	23.1	3.3	5.6	100	

\*Includes DOE laboratories' nonresearch costs but not U.S. government administration or SBIR.

\*\*DOE contribution to the international Human Frontiers Neurosciences Program.

## Communication

The DOE Human Genome Program communicates information in a variety of ways. These communication systems include the Human Genome Management Information System (HGMIS), projects in the Ethical, Legal, and Social Issues (ELSI) Program, electronic resources, meetings, and fellowships. Some of these mechanisms are described below. For more details, see Research Highlights, ELSI projects, p. 18.

## HGMIS

HGMIS provides technical communication and information services for the DOE OBER Human Genome Program Task Group. HGMIS is charged with (1) helping to communicate genome-related matters and research to contractors, grantees, other (nongenome project) researchers, and other multipliers of information pertaining to genetic research; (2) serving as a clearinghouse for inquiries about the U.S. genome project; and (3) reducing research duplication by providing a forum for interdisciplinary information exchange (including resources developed) among genetic investigators worldwide.

HGMIS publishes the newsletter *Human Genome News*, sponsored by OBER. Over 14,000 *HGN* subscribers include genome and basic researchers at national laboratories, universities, and other research institutions; professors and teachers; industry representatives; legal personnel; ethicists; students; genetic counselors; physicians; science writers; and other interested individuals.

HGMIS also produces the DOE *Primer on Molecular Genetics*; a compilation of ELSI abstracts; and reports on the DOE Human Genome and Microbial Genome Programs, contractor-grantee workshops, and other related subjects.

Electronic versions of the primer and other HGMIS publications are available via the World Wide Web. HGMIS also

initiates and maintains other related Web sites (see DOE Electronic Genome Resources section below and DOE Web Sites at right).

In addition to their print and online publishing efforts, HGMIS staff members answer questions generated via Web sites, telephone, fax, and e-mail. They also furnish customized information about the genome project for multipliers of information (contact: Betty Mansfield at 423/576-6669, Fax: /574-9888, [mansfieldbk@ornl.gov](mailto:mansfieldbk@ornl.gov)).

## DOE Electronic Genome Resources

**Web Sites.** The DOE Human Genome Program Home Page displays pointers to other programs within OBER and the Office of Energy Research. Links are made to additional biological and environmental information and to HGMIS, Genome Database, and other sites.

HGMIS initiates and maintains the searchable Human Genome Project Information Web site. This site contains more than 1700 text files of information for multidisciplinary technical audiences as well as for lay persons interested in learning about the science, goals, progress, and history of the project. Users include almost all levels of students; education, medical, and legal professionals; genetic society and support group members; biotechnology and pharmaceutical industry personnel; administrators; policymakers; and the press.

The site also houses a section of frequently asked questions, a quick fact finder, *Primer on Molecular Genetics*, all issues of *Human Genome News*, DOE Human Genome Program and contractor-grantee workshop reports, *To Know Ourselves*, historical documents, research abstracts, calendars of genome events, and hundreds of links to genome research and educational sites. More than 1000 other Web pages link to this site, resulting in more than 100,000 text file transfers each month. This

## DOE Web Sites

**DOE Human Genome Program**  
[http://www.er.doe.gov/production/ober/hug\\_top.html](http://www.er.doe.gov/production/ober/hug_top.html)

**OBER**  
[http://www.er.doe.gov/production/ober/ober\\_top.html](http://www.er.doe.gov/production/ober/ober_top.html)

**Office of Energy Research**  
<http://www.er.doe.gov>

**Human Genome Project Information**  
<http://www.ornl.gov/hgmis>

**HGP and Related Meetings**  
<http://www.ornl.gov/meetings>

**Courts**  
<http://www.ornl.gov/courts>



Heritage: Human Genome Project Information

http://www.ornl.gov/hgmis/

## Human Genome Project Information

Welcome! Explore this site for information about Human Genome Project. Officially begun in 1990, a multidisciplinary U.S. effort has among its primary estimated 80,000 human genes.

- Scientists and researchers: Explore our technical
- All other visitors: Begin your search below.

Both technical and nontechnical sites are funded by Human Genome Program (DOE HGP).

- Students! Quick answers here - Human Genome
- Project History, Goals, and Progress
- Understanding the Basics: The Science Behind It
- Teachers: Resources and Funded Education Proj
- Genetic Support Groups
- How the New Genetics May Affect You
- What's New In the Project? ( = September 11)
- Publications
  - Primer on Molecular Genetics: Basic Guide
  - To Know Yourself: A Review of Genetics Project
  - Your Genes, Your Choices, a book desc science behind it, and the ethical, legal, and project. Also mirrored on this site.
  - Human Genome News Newsletter
  - Other Publications: DOE Program Reports &
- Gateways To Other Resources: HGP and Geneti

http://www.ornl.gov/production/other/hg\_top.html

U.S. Department of Energy  
Office of Energy Research  
Office of Biological and Environmental Research

## Human Genome Program

The Human Genome Program of the Department of Energy is focused on reaching the goals of the U.S. Human Genome Project in cooperation with the extramural division of the National Human Genome Research Institute of the National Institutes of Health. The U.S. project is part of a larger international endeavor to characterize the genomes of humans and several model organisms. Other genome programs include the DOE microbial genome program, a project to characterize microbes of environmental or industrial interest.

The DOE Human Genome Program includes research projects at universities, DOE genome centers, DOE-owned national laboratories, and other research organizations.

### An Introduction

The U.S. Human Genome Project (HGP) is the national coordinated 15-year effort to characterize all the human genetic material—the genome—by improving existing human genetic maps, constructing physical maps of entire chromosomes, and ultimately determining the complete sequence of the deoxyribonucleic acid (DNA) substrate in the human genome. Parallel studies are being carried out on selected model organisms to facilitate the interpretation of human gene function. The ultimate goal of the U.S. project is to discover all of the more than 50,000 human genes and render them accessible for further biological study.

Vital and very active genome research is also being pursued by researchers and science funding agencies outside the United States. In addition to the NIH National Human Genome Research Institute, there are other genome programs in the United States, including a genome program of the Department of Agriculture. A directed microbial genome program is also supported by the DOE Office of Biological and Environmental Research to create an infrastructure for characterizing microbes of industrial or environmental interest.

Current technology could be used to attain the objectives of the HGP, but the cost and time required would be unacceptable. For this reason, a major feature of the first 10 years of the project is to optimize existing methods and develop new technologies to increase efficiency in DNA mapping and sequencing 10 to 20-fold. The genome will eventually be sequenced using continually evolving technologies and revolutionary methods.

Information obtained as part of the HGP will dramatically change almost all biological and medical research and expand the vocabulary of current genetic knowledge. In addition, both the methods and the data developed as part of the project are likely to benefit investigations of many other genomes, including a large number of commercially important plants and animals. In a departure from most scientific programs, research is also funded on the ethical, legal, and social implications (ELSI) of the data produced by the HGP.

Heritage: Human Genome Project Information: Research

http://www.ornl.gov/hgmis/research.html

## Human Genome Project Research

Welcome! Explore this site for U.S. Human Genome Project progress, research, and resources. Visit our less technical site for history of the project, education materials, and ethical, legal, and social issues. Both web sites are funded by the U.S. Department of Energy Human Genome Program (DOE HGP).

### Latest News

- News ( = October 8, 1997)
  - Information on the 1997 DOE Human Genome Program Contractor-Grantee workshop available.
- Funding and Training ( = September 11, 1997)

### Publications

- Calendars
  - Meeting Calendar
  - Training Calendar
  - Meetings Web Site
- Human Genome News newsletter
- U.S. DOE Program Reports and Workshop Abstracts

### Research Topics

- Sequencing Research
- Mapping Research
- Instrumentation Research
- Informatics Research
- Ethical, Legal, and Social Issues (ELSI) Research
- U.S. Research Centers
- Goals for Human Genome Project Research (revised 5 Year Plan)

### Finding More Info

- Links to the Genetic World: Links World-Wide ( = July 1997)
- Contacts for the Human Genome Project
- Contacts for this web site

Search this web site

Understanding the Internet and Web: a brief tutorial for new web users.  
Site Stats and Credits; Disclaimers, links to clip-art sources, web awards, and statistics about this web site.

This Web site is maintained by the Human Genome Management Information System (HGMIS) for the U.S. Department of Energy Human Genome Program. HGMIS is an information resource at Oak Ridge National Laboratory. The site is being continuously updated and HGMIS appreciates your input. Send questions or comments to [caswell@ornl.gov](mailto:caswell@ornl.gov), and URL updates or Web questions to [mantina@ornl.gov](mailto:mantina@ornl.gov).

Updated: August 1997

*The DOE Human Genome Program and Human Genome Project Information Web sites offer both general and scientific audiences thousands of text files and links for comprehensive coverage of all aspects of genome research worldwide. See text (pp. 63 and 65) for further details.*

HGMIS site has received a Four-Star designation from the Magellan Group and the Editor's Choice Award from LookSmart.

Genome-project and related meetings are listed at a Web site (see box, p. 63), through which users can register and submit research abstracts. Another listed related site discusses issues at the critical intersection of genetics and the court system. This Web page is part of a project to educate and prepare the judiciary for the coming onslaught of cases involving genetic issues and data.

**Newsgroup.** The Human Genome Program Newsgroup operates through the BIOSCI electronic bulletin board network to allow researchers worldwide to communicate, share ideas, and find solutions to problems. Genome-related information is distributed through the newsgroup, including requests for grant applications, reports from recent scientific and advisory meetings, announcements of future events, and listings of free software and services (*gnome-pr@net.bio.net* or <http://www.bio.net>).

## Postdoctoral Fellowships

OBER established the Human Genome Distinguished Postdoctoral Research Program in 1990 to support research on projects related to the DOE Human Genome Program. Beginning in FY 1996, the Human Genome Distinguished Postdoctoral Fellowships were merged with the Alexander Hollaender Distinguished Postdoctoral Fellowships, which provide support in all areas of OBER-sponsored research. Postdoctoral programs are administered by the Oak Ridge Institute for Science and Education, a university consortium and DOE contractor. For additional information, contact Linda Holmes (423/576-3192, [holmesl@ornl.gov](mailto:holmesl@ornl.gov)) or see the Web site (<http://www.ornl.gov/ober/hollaend.htm>).

## Human Genome Distinguished Postdoctoral Fellows

Names of past and current fellows in genome topics are given below with their research institutions and titles of proposed research. For 1996 research abstracts, refer to Index of Principal and Coinvestigators on p. 71 in Part 2 of this report.

**1994 Mark Graves** (Baylor College of Medicine): Graph Data Models for Genome Mapping

**William Hawe** (Duke University): Synthesis of Peptide Nucleic Acids for DNA Sequencing by Hybridization

**Jingyue Ju** (University of California, Berkeley): Design, Synthesis, and Use of Oligonucleotide Primers Labeled with Energy Transfer-Coupled Dyes

**Mark Shannon** (Oak Ridge National Laboratory): Comparative Study of a Conserved Zinc Finger Gene Region

**1995 Evan Eichler** (Lawrence Livermore National Laboratory): Identification, Organization, and Characterization of Zinc Finger Genes in a 2-Mb Cluster on 19p12

**Kelly Ann Frazer** (Lawrence Berkeley National Laboratory): In Vivo Complementation of the Murine Mutations Grizzled, Mocha, and Jitteri

**Soo-in Hwang** (Lawrence Berkeley National Laboratory): Positional Cloning of Oncogenes on 20q13.2

**James Labrenz** (University of Washington, Seattle): Error Analysis of Principal Sequencing Data and Its Role in Process Optimization for Genome-Scale Sequencing Projects

**Marie Ruiz-Martinez** (Northeastern University): Multiplex Purification Schemes for DNA Sequencing-Reaction Products: Application to Gel-Filled Capillary Electrophoresis

**Todd Smith** (University of Washington, Seattle): Managing the Flow of Large-Scale DNA Sequence Information

## Alexander Hollaender Distinguished Postdoctoral Fellows in Genome Research

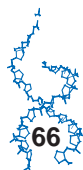
**1996 Cymbeline Culiati** (Oak Ridge National Laboratory): Cloning of a Mouse Gene Causing Severe Deafness and Balance Defects

**Tau-Mu Yi** (Laboratory of Structural Biology and Molecular Medicine, Los Angeles): Structure-Function Analysis of Alpha-Factor Receptor

**1997 Jeffrey Koshi** (Los Alamos National Laboratory): Construction, Analysis, and Use of Optimal DNA Mutation Matrices

**Sandra McCutchen-Maloney** (Lawrence Livermore National Laboratory): Structure and Function of a Damage-Specific Endonuclease Complex

*The laser-based flow cytometer developed at DOE national laboratories enables researchers to separate human chromosomes for analysis.*  
[Source: Los Alamos National Laboratory]





**T**he U.S. Human Genome Project is supported jointly by the Department of Energy (DOE) and the National Institutes of Health (NIH), each of which emphasizes different facets. The two agencies coordinate their efforts through development of common project goals and joint support of some programs addressing ethical, legal, and social issues (ELSI) arising from new genome tools, technology, and data.

Extraordinary advances in genome research are due to contributions by many investigators in this country and abroad. In the United States, such research (including nonhuman) also is funded by other federal agencies and private foundations and groups. Many countries are major contributors to the project through international collaborations and their own focused programs. Coordinating and facilitating these diverse research efforts around the world is the aim of the nongovernmental international Human Genome Organisation.

Some details of U.S. and worldwide coordination are provided below.

### U.S. Human Genome Project: DOE and NIH

In 1988 DOE and NIH developed a Memorandum of Understanding that formalized the coordination of their efforts to decipher the human genome and thus “enhance the human genome research capabilities of both agencies.” In early 1990 they presented Congress with a joint plan, *Understanding Our Genetic Inheritance, The U.S. Human Genome Project: The First Five Years (1991–1995)*. Referred to as the Five-Year Plan, it contained short-term scientific goals for the coordinated, multiyear research project and a comprehensive spending plan. Unexpectedly rapid progress in mapping prompted early revision of the original 5-year goals in the

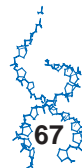
fall of 1993 [*Science* **262**, 43–46 (October 1, 1993)]. Current goals, which run through September 30, 1998, are listed on page 5; text of both 5-year plans is accessible via the Web (<http://www.ornl.gov/hgmis/project/hgp.html>).

DOE and NIH have adopted a joint policy to promote sharing of genome data and resources for facilitating progress and reducing duplicated work. (See Appendix B: DOE-NIH Sharing Guidelines, p. 75.)

### ELSI Considerations

NIH and DOE devote at least 3% of their respective genome program budgets to identifying, analyzing, and addressing the ELSI considerations surrounding genome technology and the data it produces. The DOE ELSI component focuses on research into the privacy and confidentiality of personal genetic information, genetics relevant to the workplace, commercialization (including patenting) of genome research data, and genetic education for the general public and targeted communities. The NIH ELSI component supports studies on a range of ethical issues surrounding the conduct of genetic research and responsible clinical integration of new genetic technologies, especially in testing for mutations associated with cystic fibrosis and heritable breast, ovarian, and colon cancers.

In 1990, the DOE-NIH Joint ELSI Working Group was established to identify, address, and develop policy options; stimulate bioethics research; promote education of professional and lay groups; and collaborate with such international groups as the Human Genome Organisation (HUGO); United Nations Educational, Scientific, and Cultural Organization; and the European Community. Research funded by the U.S. Human Genome Project through the joint working group has produced policy recommendations in various areas. In May 1993, for



example, the DOE-NIH Joint ELSI Working Group Task Force on Genetic Information and Insurance issued a report with recommendations for managing the impact of advances in human genetics on the current system of healthcare coverage. In 1996, the working group released guidelines for investigators on using DNA from human subjects for large-scale sequencing projects. The guidance emphasizes numerous ways to preserve donor anonymity [see Appendix C, p. 77, and the World Wide Web (<http://www.ornl.gov/hgmis/archive/nchgrdoe.html>)].

In 1997, following an evaluation, the two agencies modified the ELSI working group into the ELSI Research and Program Evaluation Group (ERPEG). ERPEG will focus more specifically on research activities supported by DOE and NIH ELSI programs.

## Other U.S. Programs

The potential impact of genome research on society and the rapid growth of the biotechnology industry have spurred the initiation of other genome research projects in this country and worldwide. These projects aim to create maps of the human genome and the genomes of model organisms and several economically important microbes, plants, and animals.

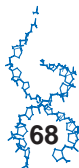
- The DOE Microbial Genome Program, begun in 1994, is producing complete genome sequence data on industrially important microorganisms, including those that live under extreme environmental conditions. The sequences of several microbial genomes have been completed. [[http://www.er.doe.gov/production/ober/EPR/mig\\_top.html](http://www.er.doe.gov/production/ober/EPR/mig_top.html)]
- In 1990, the National Science Foundation, DOE, and the U.S. Department of Agriculture (USDA) initiated a project to map and sequence the genome of the model plant *Arabidop-*

*sis thaliana*. The goal of this project is to enhance fundamental understanding of plant processes. In 1996, the three agencies began funding systematic, large-scale genomic sequencing of the 120-megabase *Arabidopsis* genome, with the goal of completing it by 2004, with DOE support through the Office of Basic Energy Sciences. [<http://pgec-genome.pw.usda.gov/agi.html>]

- USDA also funds animal genome research projects designed to obtain genome maps for economically important species (e.g., corn, soybeans, poultry, cattle, swine, and sheep) to enable genetic modifications that will increase resistance to diseases and pests, improve nutrient value, and increase productivity.
- The Advanced Technology Program (ATP) of the U.S. National Institute of Standards and Technology promotes industry-government partnerships in DNA sequencing and biotechnology through the Tools for DNA Diagnostics component. DOE staff participates in the ATP review process (see box, p. 22). [<http://www.atp.nist.gov>]
- In 1997 the NIH National Cancer Institute established the Cancer Genome Anatomy Project (CGAP) to develop new diagnostic tools for understanding molecular changes that underlie all cancers (<http://www.ncbi.nlm.nih.gov/ncicgap>). DOE researchers are generating clone libraries to support this effort.

## International Collaborations

The current DOE-NIH Five-Year Plan commends the “spirit of international cooperation and sharing” that has characterized the Human Genome Project and played a major role in its success. Cooperation includes collaborations among laboratories in the United States



and abroad as well as extensive sharing of materials and information among genome researchers around the world. The DOE Human Genome Program supports many international collaborations as well as grantees in several foreign institutions.

Collaborations involving the DOE human genome centers include mapping chromosomes 16 and 19, developing resources, and constructing the human gene map from shared cDNA libraries. These libraries were generated by the Integrated Molecular Analysis of Gene Expression (called IMAGE) Consortium initiated by groups at Lawrence Livermore National Laboratory, Columbia University, NIH National Institute of Mental Health, and Généthon (France).

Investigators from almost every major sequencing center in the world met in Bermuda in February 1996 and again in 1997 to discuss issues related to large-scale sequencing. These meetings were designed to help researchers coordinate, compare, and evaluate human genome mapping and sequencing strategies; consider new sequencing and informatics technologies; and discuss release of data.

## Human Genome Organisation

Founded by scientists in 1989, HUGO is a nongovernmental international organization providing coordination functions for worldwide genome efforts. HUGO activities range from support of data collation for constructing genome

maps to organizing workshops. HUGO also fosters exchange of data and biomaterials, encourages technology sharing, and serves as a coordinating agency for building relationships among various government funding agencies and the genome community.

HUGO offers short-term (2- to 10-week) travel awards up to \$1500 for investigators under age 40 to visit another country to learn new methods or techniques and to facilitate collaborative research between the laboratories.

HUGO has worked closely with international funding agencies to sponsor single-chromosome workshops (SCWs) and other genome meetings. Due to the success of these workshops as well as the shift in emphasis from mapping to sequencing, DOE and NIH began to phase out their funding for international SCWs in FY 1996 but encouraged applications for individual SCWs as needed. In 1996, HUGO partially funded an international strategy meeting in Bermuda on large-scale sequencing. Principles regarding data release and a resources list developed at the meeting are available on the HUGO Web site (<http://hugo.gdb.org/hugo.html>).

Membership in HUGO (over 1000 people in more than 50 countries) is extended to persons concerned with human genome research and related scientific subjects. Its current president is Grant R. Sutherland (Adelaide Women and Children's Hospital, Australia). Directed by an 18-member international council, HUGO is supported by grants from the Howard Hughes Medical Institute and The Wellcome Trust.

## Countries with Genome Programs

Countries with genome programs or strong programs in human genetics include Australia, Brazil, Canada, China, Denmark, European Union, France, Germany, Israel, Italy, Japan, Korea, Mexico, Netherlands, Russia, Sweden, United Kingdom, and United States.

*Los Alamos National Laboratory researchers Peter Goodwin and Rhett Affleck load a sample of fluorescently labeled DNA into an ultrasensitive flow cytometer used to detect single cleaved nucleotides. [Source: Lynn Clark, LANL]*

