# Human Genome news

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## DOE-NIH Retreat Improves Understanding

**Chromosome 16, 19 Contig Maps Estimated 60% Complete**

The NIH National Center for Human Genome Research (NCHGR) and the Human Genome Program of the DOE Office of Health and Environmental Research (OHER) held their second annual planning and evaluation retreat August 28–30 in Hunt Valley, Maryland. Members of the NIH-DOE Joint Subcommittee on the Human Genome participated, along with invited consultants from the scientific community. For a list of subcommittee members, see *HGN* 2(3): 7 (September 1990).

Representatives (listed in the table below) of various scientific disciplines and professional societies were invited to the meeting to share their views on the Human Genome Project.

The meeting, cochaired by Norton Zinder, Chairman of the NIH Program Advisory Committee on the Human Genome (PACHG), and Sheldon Wolfe, Chairman of the DOE Health and Environmental Research Advisory Committee (HERAC), was held to assess 5-year plan goals in view of progress made during the past year by NIH and DOE genome programs. The group also discussed the scientific community's reaction to the Human Genome Project, communication with the scientific community and congressional committees, budget projections, and evaluation of funding mechanisms to attain project goals.

NCHGR and OHER human genome program representatives presented updates on progress in genetic linkage mapping, physical mapping, informatics, DNA sequencing, and bioethics. Progress in mapping each chromosome was also discussed. Contig maps of chromosomes 16 and 19, being

**Scientific Discipline and Professional Society Representatives**

**Joan Bennett**, *Tulane University*
President, American Society for Microbiology

**Don Brown**, *Carnegie Institution*
Developmental geneticist

**David Cox**, *University of California, San Francisco*
American Society of Human Genetics

**Thomas Edgington**, *Scripps Clinic Research Institute*
President, Federation of American Societies for Experimental Biology (FASEB)

**Thomas Pollard**, *The Johns Hopkins University*
President, American Society for Cell Biology

**Howard Schachman**, *University of California, Berkeley*
Former FASEB President

## In This Issue...

## DOE-NIH Retreat

### Participants Recommend December 3 Subcommittee Meeting Topic:

- **Ways To Achieve Program Goals and Objectives**

developed at Los Alamos National Laboratory (LANL) and Lawrence Livermore National Laboratory (LLNL), respectively, were estimated to be about 60% complete.

OHER Associate Director David Galas noted that 75% of the DOE genome research budget is spent on programs in DOE national laboratories and the rest on directed research and technology development at U.S. universities or businesses. In contrast, NCHGR Deputy Director Elke Jordan stated that most NCHGR research dollars support projects at universities and businesses, funding a community historically tied to the NIH "R01" grant. NIH typically uses these grants to support smaller, nontargeted, investigator-initiated research projects.

Most consultants agreed that the Human Genome Project goals are achievable and should be pursued and that the 5-year plan is well thought out. The earlier cost estimates of $200 million per year recommended in the 1987 HERAC and the 1988 Office of Technology Assessment and National Research Council/National Academy of Sciences reports were reconfirmed, but inflation factors should be applied in estimating current and future budgets. Discussants said that the genome project has been the target of hostility because it was established at a time when research funds in some other areas had become hard to obtain. The average academic scientist may not fully understand the project and perceives it as a change from "traditional" NIH funding approaches.

NCHGR Director James Watson pointed out that NIH sponsors several well-received directed research programs, particularly in drug development for cancer and AIDS. Most basic research scientists are unaware, he said, that only about 55% of the NIH budget funds investigator-initiated grants. While such research is effective at generating new ideas, participants agreed that other funding mechanisms are often needed to develop those ideas into clinical applications or to coordinate resource sharing among large and small laboratories.

### Participants See Need for Directed Research Program To Meet Mapping Goals

Addressing ways for the federal agencies to achieve genome project goals, the group concluded that investigator-initiated grants alone probably would not meet the 5-year chromosome-mapping goals efficiently and economically and that they would be difficult to coordinate. Because of the variety of research carried out within the genome project, retreat participants supported a mixture of projects that include funding for:

- research centers,
- Program Announcements, and
- Requests for Applications.

Subcommittee members stressed that the scientific community needs to understand the difficulties faced by researchers who have recently completed postdoctoral training and are trying to compete in human genetics. The prohibitive cost of genetic research could lock young scientists out of the field. Accessible data and improved technologies acquired through the Human Genome Project are expected to empower capable scientists to pursue important research in human genetics.

Small, investigator-initiated grants can play a prominent role in technology development and in providing an entry point for small projects that have the potential to grow into larger ones, the group concluded. If deficit-reduction legislation causes severe budget cuts, the group recommended that these projects be prioritized rather than cut across the board.

Subcommittee members discussed the organization, management, and activities at the multidisciplinary DOE human genome centers. They noted the accomplishments being made in constructing physical maps of chromosomes 16, 19, and 21 and in developing supportive computational capabilities and innovative mapping and sequencing strategies and technologies.

Genome project staff members and consultants exchanged ideas about better ways to communicate with the greater scientific community. They felt that increased efforts should be made to show that the genome project "is going to do some terrific science." More exchange of information with professional societies and participation in their annual meetings were suggested. Consultants also stressed the importance of informing the research community about plans to sequence the genomes of model organisms, particularly those of yeast and *Escherichia coli*.

Human genome centers are important in outreach efforts, participants agreed, serving as hubs for the scientific community in several ways, including the sharing of reagents and resources generated by their research efforts. Informatics components should be designed to be useful to the greater scientific

*(see Retreat, p. 3)*

# New NIH Genome Centers Signal Milestone

Four new NIH human genome research centers have been established at U.S. universities to improve genome research technology and to develop complete genetic and physical maps of three human chromosomes and several mouse chromosomes. A private institution project mapping a fourth chromosome has been cofunded with DOE.

The 5-year genome center grants go to scientists at Washington University in St. Louis; the University of California, San Francisco (UCSF); the Massachusetts Institute of Technology (MIT) in Cambridge; and the University of Michigan, Ann Arbor. The project grant was awarded to The Salk Institute.

As hubs of the diverse NCHGR research program, the centers will be made up of several different but interrelated research projects. Centers will also serve as resources to outside scientists by providing them with newly developed research materials, opportunities to learn new techniques, and access to computer databases containing genome research results.

In announcing the National Center for Human Genome Research (NCHGR) grants, Health and Human Services Secretary Louis W. Sullivan said, "These centers signal an important milestone in the history of biomedical research. Technologies developed by genome project scientists will change the face of medical research well into the next century."

Over the past 2 years, NCHGR has been establishing a plan and organizing its research programs, says NCHGR Director James Watson. "With these new research centers, we have begun to do work we said we would do."

**Washington University, St. Louis**
First-year award $2,340,564

Under the direction of David Schlessinger and Maynard Olson, the Washington University Human Genome Center will use yeast artificial chromosome (YAC) technology, developed at this laboratory, to aid in the construction of complete maps of human chromosomes 7 and X. Chromosome 7 is believed to contain a total of about 5000 genes, including the cystic fibrosis gene and genes that control immune response. The X chromosome has also been the target of intensive study; genes for hemophilia A and B, diseases of the adrenal gland, fragile X syndrome, and color blindness are among those located on the X chromosome.

**University of California, San Francisco**
First-year award $2,240,242

Researchers headed by Richard Myers and David Cox will use a variety of techniques to complete a map of chromosome 4, which, at about 200 million nucleotides, is one of the largest chromosomes and is believed to contain genes for Huntington's and Alzheimer's diseases.

Using in situ hybridization, researchers will first construct a rough map of the chromosome and then fill in the details with landmarks prepared by other methods. The UCSF center will also have components at the University of Iowa and the Fox Chase Cancer Center in Philadelphia.

**Massachusetts Institute of Technology**
First-year award $2,178,552

Eric Lander (Whitehead Institute for Biomedical Research) will lead a consortium of 12 principal researchers at MIT, Whitehead, Harvard University, Princeton University, and Jackson Laboratories. They will construct highly detailed maps of mouse chromosomes 1, 11, and X, with the long-term goal of mapping the entire mouse genome. Because the mouse and human genomes are very similar, scientists have used mouse mutations as a model to study the effects of mutations on cell function, immunology, neurobiology, reproduction,

(see Centers, p. 4)

## NIH NCHGR Centers

- **Washington University**
  Chromosomes 7, X
- **UCSF**
  Chromosome 4
- **MIT**
  Mouse chromosomes 1, 11, X
- **University of Michigan**
  Mapping technology

## DOE Human Genome Program Centers

- **Lawrence Livermore National Laboratory**
  Chromosome 19
- **Lawrence Berkeley Laboratory**
  Chromosome 21
- **Los Alamos National Laboratory**
  Chromosome 16

## Cofunded DOE-NIH Project

- **The Salk Institute**
  Chromosome 11

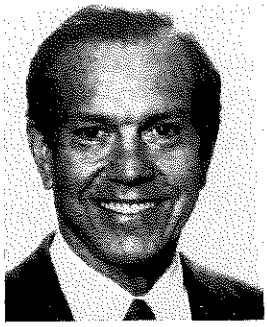
## Retreat *(from p. 2)*

community, and centers should continue to provide opportunities for interested scientists to train in newly developed technologies.

The meeting concluded with a report on activities supported by Human Genome Organisation (HUGO) Americas. The report was given by Charles Cantor of the DOE Lawrence Berkeley Laboratory (LBL), one of three HUGO vice presidents. HUGO is moving quickly to develop a prototype blueprint for coordinating single-chromosome mapping workshops. Retreat participants recommended that workshop chairs assemble annually to develop the best strategies for chromosome meetings. (For a more detailed article on HUGO, see page 4.) ◊

*Reported by Leslie Fink, Chief*
*Office of Human Genome Communication*
*NCHGR*

## Genome News



James B. Wyngaarden
Director
Human Genome Organisation

# Wyngaarden Named HUGO Director

James B. Wyngaarden was recently named to the newly created post of Director of the Human Genome Organisation (HUGO). He was officially confirmed by the HUGO Council at its September 7 meeting in Oxford, England.

In this position, Wyngaarden will help HUGO define its role in the genome project by overseeing HUGO international activities, guiding fund-raising, coordinating HUGO offices at the international level, and aiding in the identification of scientific areas of interest to HUGO, such as ethics and informatics.

Formerly Director of NIH, Wyngaarden will continue as foreign secretary of both the National Academy of Sciences and the Institute of Medicine (under the National Academy of Sciences charter). At Duke University, he is Professor of Medicine and Associate Vice-Chancellor for Health Affairs.

Wyngaarden is the recipient of many awards and honorary degrees. He is a member of the Board of Governors of the United States-Israel Binational Science Foundation, a Fellow of the Royal College of Physicians of London, and a member of the Royal Academy of Sciences of Sweden. ◊

## HUGO Americas Drafts Memorandum

The HUGO Americas ad hoc physical mapping advisory committee met in San Francisco on July 27 to formulate plans for HUGO Americas' approach to NIH and DOE for possible funding. The committee's memorandum stated that some desirable physical mapping roles for HUGO would be to:

- coordinate efforts on a chromosome-by-chromosome basis to minimize cost and promote sharing,
- coordinate HUGO efforts with Human Genome Mapping Workshop activities, and
- help select appropriate individuals to organize workshops and provide incentives for them to work through HUGO.

The memorandum states that HUGO would select or approve workshop chairs and assist in fund-raising and in organizing and running the meetings. The memorandum also established the following policies concerning workshops:

- Attendees are expected to share data and samples.
- Consensus data will go into a publicly accessible database.
- Workshops will deal with both genetic and physical data and be broadly representative of all ongoing work on the chromosome of interest.
- Scientists participating in international chromosome meetings will need to secure travel funds from sources in their own countries, except in unusual circumstances.
- A committee will be established to oversee the single chromosome mapping workshops officially sponsored by HUGO.

All three regional components of HUGO (Americas, Asia, and Europe) will probably organize workshops under HUGO sponsorship. To help HUGO Americas get started, the committee developed a proposal of policies and procedures for organizing workshops. The committee also drew up a tentative list of high-priority chromosome meetings likely to be held in the United States in the next 18 months. ◊

## Centers *(from p. 3)*

and behavior. The MIT center will prepare a YAC library as a resource for other scientists interested in studying the mouse genome.

**University of Michigan, Ann Arbor**
First-year award $1,560,942

A group led by Francis Collins will focus on improving technologies and speeding up the process of identifying disease genes "from clinic to base pair." The current long and arduous search for disease genes begins with collecting DNA from affected people and their relatives and continues through many difficult steps.

**The Salk Institute, La Jolla, California**

Glen Evans and his coworkers are mapping human chromosome 11 (project supported by NCHGR and DOE), to which 133 genes have been mapped, including those for Wilms' tumor, genitourinary defects, and mental retardation. Genes that play a role in several forms of cancer and allergies are also believed to be located on chromosome 11. ◊

# DOE Announces Contractor-Grantee Workshop

The second DOE Contractor-Grantee Workshop will be held February 17–20, 1991, in Santa Fe, New Mexico. The DOE Human Genome Coordinating Committee (HGCC) is organizing the workshop for the Human Genome Program of the Office of Health and Environmental Research to:

- foster exchange of information among participants in the DOE Human Genome Program,
- evaluate individual projects, and
- evaluate the DOE program as a whole.

Representatives from all grantee and contractor projects are expected to attend this workshop and to present project highlights either orally or through one or more posters. Registration for the anticipated 200 attendees will be from noon until 7:30 p.m. on Sunday, February 17, with an evening session at 8 p.m. The workshop will conclude with an evening session on Wednesday, February 20. Results of the workshop will be a major focus of the HGCC meeting on February 21.

Contractors and grantees should send one-page, single-spaced, titled abstracts of their DOE-funded genome research to Sylvia Spengler by January 15, 1991 (see box). More details on housing will be sent to contractors and grantees. ◊

**For more information on the DOE Contractor-Grantee Meeting, contact:**

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## DOE Program Appoints Cantor Principal Scientist

Charles R. Cantor has been appointed Principal Scientist for the DOE Human Genome Program. In this capacity, he will assist in the coordination of the program's scientific activities and advise the three DOE genome research centers, which are located at Lawrence Livermore National Laboratory (LLNL), Lawrence Berkeley Laboratory (LBL), and Los Alamos National Laboratory (LANL).

To devote his efforts to these new responsibilities, Cantor has resigned his position as Director of the LBL Human Genome Center. He will continue to chair the DOE Human Genome Coordinating Committee and serve as a regional Vice President of the international Human Genome Organisation (HUGO).

"I am delighted to have this opportunity to play a central role in a program of historical importance for biology and medicine," said Cantor.

DOE Associate Director David J. Galas, Office of Health and Environmental Research, said, "The DOE genome program is indeed fortunate to have Charles Cantor take on this new program-wide role for scientific guidance and coordination. We look forward to working closely with him."

The genome research centers at LLNL, LANL, and LBL were established by DOE to construct physical maps of chromosomes and to develop the technology for mapping, sequencing, and deciphering this information.

Cantor headed the Human Genome Center at LBL, managed for DOE by the University of California, for 2 years. He will remain at Berkeley and, in addition to his broader role, serve in an advisory capacity to LBL Director Charles V. Shank.

"LBL is indebted to Dr. Cantor for his efforts on behalf of our Human Genome Center," said Shank. "As an internationally recognized expert in the fields of genetic mapping and sequencing, he is a valuable scientific resource, and I am pleased we will continue to have the benefit of his counsel."

Charles Cantor received his A.B. from Columbia University and his Ph.D. from the University of California, Berkeley. He was codeveloper with David Schwartz of the widely used pulsed-field gel electrophoresis technique [*Cell* **37** (1): 67–75 (1984)].

Cantor is a Guggenheim Fellow, Fellow of the American Association for the Advancement of Science, and an Alfred P. Sloan Foundation Fellow. In 1978 he received the Eli Lilly Award in Biological Chemistry and in 1985 an Outstanding Investigator Grant from the National Cancer Institute. He was elected to the National Academy of Sciences in 1988 and is a founding member of HUGO. ◊

Charles R. Cantor
Principal Scientist
DOE Human Genome Program

Genome News

# ELSI Working Group Targets Research, Policy Development Needs

The NIH-DOE Working Group on Ethical, Legal, and Social Issues (ELSI) related to data generated by the Human Genome Project held a workshop September 10–11 in Rockville, Maryland, to discuss research and policy development needs concerning the introduction of new genetic tests into clinical practice.

At its last meeting in February, the ELSI working group gave this topic high priority for NIH and DOE programs. They also identified several sets of professional and social policy issues whose impact will be significantly broadened by the expected acceleration of genetic test development and the increased number of people likely to become candidates for testing.

*Studies of genetic testing in clinical practice are given high priority.*

These issues include quality control of test development and performance, professional responsibilities of clinicians conducting tests, the psychological impact of genetic testing on patients and family members, confidentiality of and access to test results by third parties, and the cost of testing and counseling.

The working group sought to gain more information about these questions by focusing on the recently developed test for the cystic fibrosis (CF) gene. This test provides an important example because of the gene's relatively high frequency in the population and the clinical variability of CF. Protocols for integration of the CF test into medical practice could set important precedents for future genetic test development and use.

To identify research and policy development needs, the ELSI working group invited perspectives on the evolution of CF testing from several groups, including:

- scientists and clinicians involved with developing and evaluating the CF test;
- representatives of at-risk families; and
- experts on the ethical, legal, and social dimensions of genetic testing.

A session was devoted to a review of CF detection and to reports on trial CF testing programs in the United Kingdom and Denmark. Another session identified research and policy needs revealed by experience to date. The working group then met with members of NIH and DOE staff to discuss plans for implementing ideas raised at the workshop.

Identified research and policy development needs include:

- Studies to assess the psychosocial impact of testing (including risk perceptions among low- and high-risk populations and across ethnic or socioeconomic groups), outcome studies, and cost assessments.
- Analyses of mechanisms for ensuring quality control of tests performed and interpreted at different sites.
- Assessments of alternative professional qualifications necessary for performing and interpreting various genetic tests.
- Analyses to define standards for education before and counseling after the different diagnostic tests as they become available.
- Studies of insurance industry practices with respect to reimbursement for tests and the use of tests in underwriting policies.
- Comparative evaluations of confidentiality practices and policies adopted by existing genetic testing programs.
- Comparative assessments of the medical and community approaches to testing. ◇

**For further information about the ELSI workshop, contact:**

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**Ethical, Legal, and Social Implications Program**
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# Genetics, Ethics, and Human Values

The Council for International Organizations of Medical Sciences (CIOMS) held its 24th Round Table Conference in Tokyo and in Inuyama City, Japan, on "Genetics, Ethics and Human Values: Human Genome Mapping, Genetic Screening, and Therapy." The July 22–27 conference was held under the auspices of the Science Council of Japan and cosponsored by the World Health Organization and the United Nations Educational, Scientific, and Cultural Organization.

Fifth in the "Health Policy, Ethics, and Human Values: An International Dialogue" series, the meeting was cochaired by Eiji Inouye (Science Council of Japan, Tokyo) and by Alexander Morgan Capron (The Law Center, University of Southern California, Los Angeles).

CIOMS conferences provide international and interdisciplinary forums for the scientific and lay communities to exchange views on topics of immediate concern. Previous dialogues in the series, begun in 1984, have examined organ transplantation, genetic screening and counseling, health care of the elderly, lifestyles, and family planning.

Participants, who numbered 102, came from 24 countries. In addition to biomedical science and medicine, they represented a wide range of disciplines – sociology, psychology, epidemiology, law, social policy, philosophy, and theology – and brought with them experience in hospital and public health medicine, academia, private industry, and the executive and legislative branches of government.

Attendees explored a number of issues through presentations and discussions in plenary sessions and working groups. At the final session, they adopted the declaration, prepared by Capron, printed below as submitted by CIOMS. ◊

**To obtain copies of the proceedings when they are published later this year, contact:**

**Zbigniew Bankowski**
**Executive Secretary, CIOMS**
**c/o World Health Organization**
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**Switzerland**

## THE CIOMS INUYAMA STATEMENT

**I.** Discussion of human genetics is dominated today by the efforts now under way on an international basis to map and sequence the human genome. Such attention is warranted by the scale of the undertaking and its expected contribution to knowledge about human biology and disease. At the same time, the nature of the undertaking, concerned as it is with the basic elements of life, and the potential for abuse of the new knowledge which the project will generate have given rise to anxiety. The Conference agrees that efforts to map the human genome present no inherent ethical problems but are eminently worthwhile, especially as the knowledge revealed will be universally applicable to benefit human health. In terms of ethics and human values, what must be assured are that the manner in which gene mapping efforts are implemented adheres to ethical standards of research and that the knowledge gained will be used appropriately, including in genetic screening and gene therapy.

**II.** Public concern about the growth of genetic knowledge stems in part from the misconception that while the knowledge reveals an essential aspect of humanness, it also diminishes human beings by reducing them to mere base pairs of deoxyribonucleic acid (DNA). This misconception can be corrected by education of the public and open discussion, which should reassure the public that plans for the medical use of genetic findings and techniques will be made openly and responsibly.

**III.** Some types of genetic testing or treatment not yet in prospect could raise novel issues – for example, whether limits should be placed on DNA alterations in human germ cells because such changes would affect future generations, whose consent cannot be obtained and whose best interests would be difficult to calculate. The Conference concludes, however, that for the most part present genetic research and services do not raise unique or even novel issues, although their connection to private matters such as reproduction and personal health and life prospects and the rapidity of advances in genetic knowledge and technology accentuate the need for ethical sensitivity in policymaking.

**IV.** It is primarily in regard to genetic testing that the human genome project gives rise to concern about ethics and human values. The identification, cloning, and sequencing of new genes without first needing to know their protein products greatly expand the possible scope for screening and diagnostic tests. The central objective of genetic screening and diagnosis should always be to safeguard the welfare of the person tested: test results must always be protected against unconsented disclosure, confidentiality must be ensured at all costs, and adequate counselling must be provided. Physicians and others who counsel should endeavour to ensure that all those concerned understand the difference between being the carrier of a defective gene and having the corresponding genetic disease. In autosomal recessive conditions, the health of carriers (heterozygotes) is usually not affected by their having a single copy of the disease gene; in dominant disorders, what is of concern is the manifestation of the disease, not the mere presence of the defective gene, especially when years may elapse between the results of a genetic test and the manifestation of the disease.

**V.** The genome project will produce knowledge of relevance to human gene therapy, which will very soon be clinically applicable to a few rare but very burdensome recessive disorders. Alterations in somatic cells, which will affect only the DNA of the treated individual, should be evaluated like other innovative therapies. Particular attention by independent ethical review committees is necessary, especially when gene therapy involves children, as it will for many of the disorders in question. Interventions should be limited to conditions that cause significant disability and not employed merely to enhance or suppress cosmetic, behavioural or cognitive characteristics unrelated to any recognized human disease.

**VI.** The modification of human germ cells for therapeutic or preventive purposes would be technically much more difficult than that of somatic cells and is not at present in prospect. Such therapy might, however, be the only means of treating certain conditions, so continued discussion of both its technical and its ethical aspects is therefore essential. Before germ-line therapy is undertaken, its safety must be very well established, for changes in germ cells would affect the descendants of patients.

**VII.** Genetic researchers and therapists have a strong responsibility to ensure that the techniques they develop are used ethically. By insisting on truly voluntary programmes designed to benefit directly those involved, they can ensure that no precedents are set for eugenic programmes or other misuse of the techniques by the State or by private parties. One means of ensuring the setting and observance of ethical standards is continuous multidisciplinary and transcultural dialogue.

**VIII.** The needs of developing countries should receive special attention to ensure that they receive their due share of the benefits that ensue from human genetic research. In particular, methods and techniques of testing and therapy that are affordable and easily accessible to the populations of such countries should be developed and disseminated whenever possible. ◊

Meeting Reports

# Genome Sequencing Conference II

**Genome Sequencing Conference III**
**September 22–25, 1991**
**Hyatt Regency,**
**Hilton Head,**
**South Carolina**

**Cochairs:**
**Craig Venter**
**Leroy Hood**

The Genome Sequencing Conference II, cochaired by J. Craig Venter (NIH National Institute of Neurological Disorders and Stroke) and Walter Gilbert (Harvard University), was held September 30–October 3 at Hilton Head, South Carolina. Sponsors of the conference (see box) included federal agencies and commercial organizations.

The first full day of the meeting, October 1, marked the official implementation of the DOE-NIH 5-year plan for the national Human Genome Project. The meeting, attended by some 200 people, provided an excellent forum for exchanging ideas among researchers and developers of hardware and software.

James Watson [Director, NIH National Center for Human Genome Research (NCHGR)] emphasized that mapping and sequencing model organisms is necessary now to prepare for human genome sequencing, even though the same technologies may not be used to sequence the human genome. He urged his audience to "go home and publish sequence" and said that simply endorsing the genome project is not enough. Watson also stated that because of important commercial and research applications, new sequence data should be released as soon as it is ascertained to be correct.

David Galas [DOE Associate Director, Office of Health and Environmental Research (OHER)] underscored the consensus that automating present sequencing technology to its projectable limits would be sufficient to accomplish the short-term sequencing goal of 3 billion base pairs. He said that novel technologies, described in some high-risk proposals, will be needed to reach more advanced, longer-term goals.

Galas also announced that the DOE physical mapping effort will include establishment of a master set of cDNAs for deriving sequence tagged sites (STSs)—important because the STSs will be placed on sites actively being transcribed in the genome.

Venter described his work in obtaining STSs from 30,000 human brain cDNAs. These "expressed sequence tags" (ESTs), along with their first 400 clones, will be available from a new category in GenBank® and from the American Type Culture Collection (ATCC), respectively.

**Conference Sponsors**

- NIH National Center for Human Genome Research (NCHGR)
- DOE Office of Health and Environmental Research (OHER)
- NIH National Institute of Neurological Disorders and Stroke
- Applied Biosystems, Inc.
- Cray Research, Inc.
- E. I. du Pont de Nemours and Company
- Pharmacia LKB Biotechnology

## HIGHLIGHTS

A number of groups are working on projects that will optimize the automation and scaleup of laboratory apparatus and data analysis capability, such as the following:

- special-purpose computer chips for detecting sequence alignments and pattern matching in large databases;
- parallel processors programmed to identify regions of local sequence similarity;
- software for integrating data handling throughout the sequencing process;
- design innovations for commercial sequencing equipment and robotic workstations;
- coupling PCR and sequencing reactions by addition of dideoxy terminators and end-labeled primers.

Progress reported by several laboratories in completing cosmid and larger-size sequencing projects included:

- 240 kb from chromosomes 4 and 19,
- over 100 kb from mouse and human T-cell receptor loci,
- 2 *Caenorhabditis elegans* cosmids, and
- continuing increase in *Escherichia coli* genome data.

There was general agreement that sequencing reactions and gel scanning have been successfully automated and that progress is being made in automating the front-end steps of mapping, cloning, and template preparation; contig assembly using computer algorithms is now the rate-limiting step. Participants also discussed strategies for gap closure and for resolving ambiguities caused by repetitions or polymorphisms.

Attendees agreed that software development is needed for transferring data between units of laboratory equipment, for inputting data, and for storing and analyzing massive amounts of raw sequence data. One speaker noted that sequence-analysis software packages sometimes require different formats of GenBank®, with each format using over 100 Mbytes of disk space. Some

participants at the meeting called for cooperation among software developers, because as GenBank® increases in size, the demand for user disk space will become particularly acute.

Several speakers discussed error sources, propagation during assembly, and effects on sequence analysis. Some investigators working with prokaryotes projected error rates of only .00001%, but the general consensus was that errors of .01 to .001% would be acceptable and achievable at a reasonable cost for a first pass through the whole genome. As technology advances, regions of interest could be resequenced with a higher degree of accuracy at reduced costs.

Venter, reading a statement prepared by Applied Biosystems, Inc. (ABI), announced that an agreement had been reached between the company and the scientific community that relies heavily on ABI sequencing hardware and software. ABI will enter into written licensing agreements with individual laboratories to provide access to data file formats to those wishing to develop the sequencing software for their research. If such software is useful to the scientific community and is distributed, the researchers will include text in the software to indicate that the ABI proprietary file format is for research purposes only and not to be used in any commercial product.

Two informative evening discussions were held simultaneously – one on sequencing instrumentation and the other on software requirements of large-scale sequencing projects. Informal presentations at the instrumentation workshop included:

- PCR techniques for preparing templates from single- and double-stranded DNA;
- advances in automated sample preparation;
- a method for direct transfer of DNA to membranes during sequencing electrophoresis;
- rapid sequencing using high-voltage, low-Joule-heating capillary gel electrophoresis; and
- commercial sequencing equipment available from Pharmacia LKB Biotechnology and ABI.

Software workshop participants discussed software problems and development of some general solutions that could be implemented at many different project sites. During the discussions, there was general agreement that the evolving databases should be designed to increase the portability of data and to provide additional data fields (for specific sequence data) that will allow for:

- estimation of error rates,
- correlation of cDNA and amino acid sequences,
- correlation to physical and genetic maps, and
- inclusion of information on cell types that express given sequences.

Participants predicted the development of global databases that can be queried by scientists searching for answers to basic biological questions (e.g., understanding eukaryotic gene expression, developmental biology, disease etiologies, and protein function). Representatives from the computing community requested that detailed descriptions of the needs of molecular geneticists be specified; when such specifications stabilize, further software development can commence.

Another area for cooperation between the scientific communities concerns the development of sequence assembly programs, some of which are being written by academic computer scientists who may not have resources for software customer support. One solution suggested was to turn the programs over to the commercial sector for further development, documentation, distribution, and customer support.

Jane Peterson (NIH NCHGR) reported that the September 29 meeting of the DOE-NIH Working Group on Sequencing focused on reducing costs and developing models for cost assessment in scaleup projects.

A more detailed report on the conference, containing lists of speakers and their topics, can be obtained from HGMIS (see masthead, this page). (See related article, "The Genome Project and the Pharmaceutical Industry," a satellite meeting to Genome Sequencing Conference II, p. 10). ◇

*Reported by Kathleen H. Mavournin*
*and*
*Betty K. Mansfield*
*HGMIS, Oak Ridge National Laboratory*

Human Genome news

This newsletter is intended to facilitate communication among genome researchers and to inform persons interested in genome research. Suggestions and contributions are invited.

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Meeting Reports

# The Genome Project and the Pharmaceutical Industry

A group of prominent scientists met with pharmaceutical industry representatives to discuss the Human Genome Project's impact on health care at a September 30 satellite meeting to Genome Sequencing Conference II (see p. 8). The meeting was convened to:

- inform industry representatives about the project and its rapid rate of development and
- encourage private industry to translate project data into pharmaceuticals and diagnostics for improving health care.

In his opening remarks, Mark Pearson (E. I. du Pont de Nemours and Company) said that mapping genes and other markers leads to identification of disease loci; sequencing DNA identifies drug targets; and knowledge of molecular mechanisms allows rational design of a new generation of therapeutics.

## Identified Genes are Potential Targets for Drug Intervention

J. Craig Venter (NIH National Institute of Neurological Disorders and Stroke) pointed out that the 50,000–100,000 genes to be identified by the Human Genome Project are potential targets for pharmacological intervention. The drug industry will therefore be the first group to begin applications-oriented interpretation of genome data.

In generating this data, the Human Genome Project is continuing the basic biological research agenda started in the 1940s of understanding function by studying structure. Technical advances are making possible the complete molecular dissection of genes so that their functions and interactions can be clarified, noted Robert Cook-Deegan.

The genome project is now considered to be feasible because of the development of and improvements in sequencing technologies, recombinant DNA techniques, restriction fragment length polymorphism mapping methodologies, and the polymerase chain reaction. Walter Gilbert (Harvard University) pointed out that published DNA sequence (human and nonhuman) has been increasing annually by 60% since 1975. At that rate, he predicted, an amount equivalent to a human genome will be sequenced by the year 2000.

Francis Collins (University of Michigan) noted that deducing the origins of some single-gene diseases required years of work. The underlying causes of multigenic diseases—such as heart disease, diabetes, high blood pressure, and cancer—will be even more difficult to decipher. Genome project data, he asserted, will lead scientists to an understanding of the etiologies of these diseases. The pharmaceutical industry, by applying these data, can play a major role in alleviating the effects of these multigenic diseases or in eradicating them.

Scientists present agreed that the Human Genome Project will revolutionize the study of medicine and stimulate the creation of the next generation of drug therapies. Pearson suggested that new modalities, including viruses and structural elements that recognize precise cell surfaces, could be used to target drugs to disease-affected tissues without affecting the rest of the body.

Drug therapies currently are far less than 100% effective, in part because of individual genetic differences; sequence data will elucidate these variations to allow improved precision in the design of drugs and drug trials and in the prescription of therapeutics. Gilbert said that patient response to drug therapies would be predictable and that side effects could be anticipated and minimized.

Michael Hogan (Triplex Pharmaceuticals) noted that some members of the industry are demonstrating that it will be possible to proceed directly from DNA sequence data to pharmaceutical development without waiting until the end of the genome project. In a revolutionary approach to drug design, information from project databases will allow the design of oligonucleotide drugs that directly bind to target DNA duplexes. Oligonucleotides would occupy the major groove in the target duplex and could modulate transcription of that region.

Leroy Hood (California Institute of Technology), Eric Lander (Massachusetts Institute of Technology), Gilbert, and Pearson spoke of using DNA sequence databases to predict 3-dimensional protein structure and function. A finite number of structural motifs (4000–10,000) based on sequence homologies are believed to dictate protein function; this information can be used to design therapeutics that work at the protein level, a traditional avenue of drug design.

*(see Pharmaceuticals, p. 11)*

This newsletter is prepared at the request of the DOE Office of Health and Environmental Research and the NIH National Center for Human Genome Research by the Biomedical and Environmental Information Analysis Section of the Health and Safety Research Division at Oak Ridge National Laboratory, which is managed by Martin Marietta Energy Systems, Inc., for the U.S. Department of Energy, under Contract DE-AC05-84OR21400.

# Chromosome 19 Workshop

The Chromosome 19 Workshop in Charleston, South Carolina, August 3–5, was attended by about 30 scientists from the United States, Canada, and Europe. First drafts of consensus linkage and physical maps were developed. The sessions are described below.

### GENETIC AND PHYSICAL MAPPING

**Myotonic Dystrophy (DM) Research.** Robert Korneluk (Children's Hospital of Eastern Ontario) reported that the DM gene is localized to about 1 cM on chromosome 19q. In collaboration with researchers at Lawrence Livermore National Laboratory (LLNL), he successfully used cosmids to "walk" toward the gene. Allen Roses (Duke University Medical Center) briefly described the DM working group, comprising eight institutions in the United States and the United Kingdom. His group is comparing gene expression in the muscles of normal vs DM patients and has located several markers on the distal end of chromosome 19 with a somatic cell hybrid panel. Ann Saunders (Duke University Medical Center) has mapped the comparable DM mouse locus to about an 8-cM region of chromosome 7.

**Progress at LLNL.** Anthony Carrano described the strategy for long-term physical mapping in which cosmid contigs are created by automated fluorescence-based fingerprinting. Some 60% of chromosome 19 is now covered by cosmid contigs. Gaps are being closed by extension of existing contigs with yeast artificial chromosomes (YACs) or other cosmids. Orientation and distance between contigs is performed by integration with the genetic map and by fluorescence in situ hybridization.

*(see Chromosome 19, p. 12)*

## Pharmaceuticals *(from p. 10)*

A concern of attendees was that medical education in genetics lags far behind current knowledge. Delineating disease etiologies has evolved from an early emphasis on transmitted diseases to the current stress on diseases with origins in intermediary metabolism. Participants agreed that medical schools should teach future doctors about the genetic causes of disease.

Some researchers suggested that drug companies may be slow to apply information gained through the Human Genome Project to the introduction of new pharmaceuticals and other medical technologies. Large companies, they said, may be burdened by high costs, past successes, and an overpowering bureaucracy. Pearson stated that molecular genetics will provide tools for finding new drugs; he is optimistic that a cooperative atmosphere will flourish among industry leaders in this search. Others speculated that smaller, venture-capital firms may be first to apply genome project information to important applications in the health-care field. Gilbert stated that the pharmaceutical companies that apply the information first will produce the most benefits for themselves and for health care.

The meeting was sponsored by Parke-Davis Pharmaceutical Research Division of Warner Lambert and organized by Venter and Jack B. McConnell (retired Director of Research, Johnson & Johnson). Cochairs were Venter and Pearson. The meeting, which featured 7 speakers, was attended by nearly 70 pharmaceutical and genome project representatives. ◇

*Reported by Betty K. Mansfield*
*HGMIS, Oak Ridge National Laboratory*

## HGM 10.5 Meeting

Human Gene Mapping Workshop (HGM) 10.5 was held September 6–10 in Oxford, England, and provided a successful test of the first version of the Genome Data Base (GDB) developed at The Johns Hopkins University.

HGM committee chairs and cochairs for each chromosome became familiar with the system's capabilities and, with the computing team, entered a significant amount of new mapping data into the database: 225 new genes and 1946 new DNA segments were added, representing increases of 14% and 66%, respectively, over the map produced after HGM 10 at Yale University in June 1989. In addition, 842 literature references were added. Participants agreed that the computing system worked well and that GDB provided straightforward and user-friendly access to the mapping data for editing purposes.

Workshop HGM 11 will be held August 18–22, 1991, in London. To be placed on the mailing list for announcements and further information, write to:

- Michael Probert, HGM 11 Office
  Imperial Cancer Research Fund
  P.O. Box 123, Lincoln's Inn Fields
  London WC2A 3PX, England ◇

## Meeting Reports

**Proceedings will be published in *Genomics* and on the Human Genome Newsgroup electronic bulletin board. For obtaining access to the newsgroup, see *HGN* 2(1): 10 (May 1990).**

## Chromosome 19 *(from p. 11)*

Pieter de Jong discussed the flow-sorted chromosome 19 cosmid library of about 10,000 clones, and Emilio Garcia reviewed the construction of a chromosome 19 YAC library. De Jong described making and extending contigs by using *Alu*-PCR, in which primer pairs corresponding to *Alu* repeats are used to help determine the overlap between cosmid clones with similar sequences.

Harvey Mohrenweiser described "seeding contigs," a method of assembling cosmids into contigs using dispersed-middle-repetitive repeat elements, and Anne Olsen explained the assembly of contigs for the carcinoembryonic antigen immunoglobin superfamily locus. Elbert Branscomb detailed the use of relational databases and graphical browsing tools to examine contig data. A mechanism was discussed to allow external users access to these tools.

**Progress at Various Laboratories.** Keith Johnson (Charing Cross and Westminister Medical School) discussed malignant hyperthermia, which is triggered by inhalation anesthesia. In humans, the gene is probably located near 19q13.2–13.3 and appears to be large. The homologous chromosome in the mouse genome is chromosome 7.

David Saltman (Stanford University School of Medicine) discussed molecular characterization of translocation breakpoints in human leukemia and lymphoma. In acute leukemia patients, genes E2A and lyl-1 are known to exist at translocation breakpoints on 19p. By in situ hybridization, lyl-1 was localized between 19p13.1 and 13.2, and E2A was localized at 19p13.3.

Hubertus Smeets (University Hospital, Nijmegen, the Netherlands) presented a physical map of 19q13 (APOC2-ERCC region) developed using contour-clamped homogeneous electric field gels. Eleven new probes have been mapped in this region of about 2 kb.

Nancy Jenkins (NIH National Cancer Institute) discussed the mouse genetic map, where resolution averages 3 cM. Regions of mouse chromosomes 11, 17, 9, 8, and 7 are homologous to human chromosome 19. Using a rapid new system, this group maps new probes in about 7 days.

### RESOURCES AND TECHNIQUES

Bronya Keats (Louisiana State University Medical Center) described her committee's effort to standardize the presentation of linkage maps, encouraging uniform reporting for each locus mapped. Keats said that there is not enough data yet to develop a framework map of chromosome 19.

James Weber (Marshfield Medical Research Foundation) discussed his polymorphic markers, based on simple sequence repeats (CA or GT), which are very informative, uniformly distributed in the genome, and abundant, occurring about every 10 kb. He has typed 14 markers on the long arm of chromosome 19.

Michael Siciliano (University of Texas M. D. Anderson Cancer Center) described somatic cell hybrids (hamster-human) used for the human chromosome 19 cDNA mapping and DM project. He also reported on work with cDNAs, including a series of four primers used to identify splice donor sites. Using one of them, Siciliano identified the ERCC1 gene sequence in a somatic cell hybrid panel. These polymorphic cDNAs can be used for sequence-tagged sites and can form a database for candidate disease genes. David Brook (Massachusetts Institute of Technology) reported on several radiation-reduction somatic cell hybrid lines and described his "exon trap" to identify genomic DNA.

### Need for Future Collaboration

Carrano concluded the meeting by reiterating the need for future collaboration. Workshop participants apportioned responsibility for future projects (see box) and agreed to meet once or twice a year, depending on how rapidly new data are generated. ◇

*Reported by Bettie J. Graham, Chief*
*Research Grants Branch*
*NIH NCHGR*
*and*
*Anthony V. Carrano, Director*
*LLNL Human Genome Center*

**Future Chromosome 19 Projects**

- Finalization of the genetic, physical, and composite maps constructed at the meeting.
- Construction of a consensus framework contig map from information provided by workshop attendees.
- Compilation of a list of somatic cell hybrids and mapping panels.
- Construction of comparative maps of human chromosome 19 and homologous regions in mouse chromosomes.
- Assembly of data for an STS map.
- Coordination of the pulsed-field gel mapping data.
- Development and circulation of guidelines for sharing resources.
- Publishing of proceedings.

# First International Workshop on Human Chromosome 5

Twenty-nine scientists from eight countries gathered at St. Mary's Hospital Medical School in London September 4–5 for the First International Workshop on Human Chromosome 5, sponsored by the NIH National Center for Human Genome Research, the DOE Human Genome Program, the U.K. Medical Research Council, and GeneLabs, Inc.

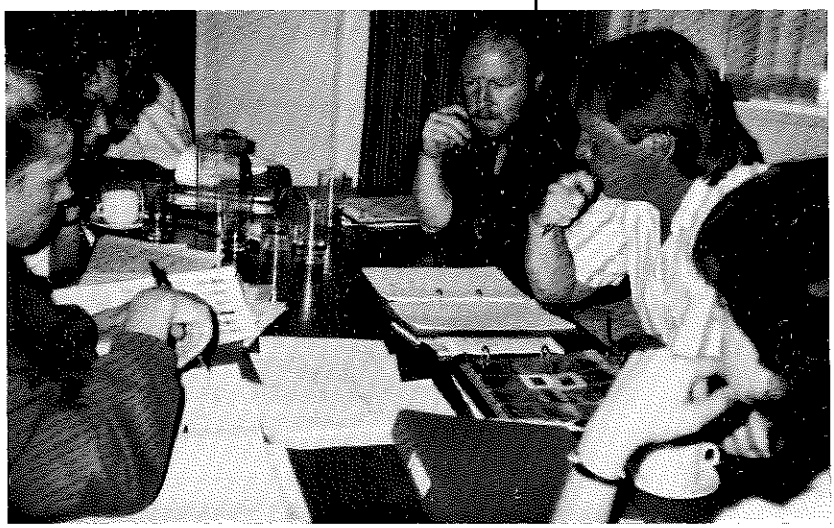
Objectives of this intensive, 2-day workshop were to update the chromosome 5 consensus map and reference marker assignment, to assess resources available now or needed for future mapping efforts, and to provide input to the Chromosome 5 Committee of the Human Gene Mapping Workshop (HGM 10.5) held in Oxford September 6–11.

### Genetic and Physical Mapping

Localization of spinal muscular atrophy (SMA) and familial adenomatous polyposis (FAP) genes were discussed. New linkage data placed the gene for diastrophic dysplasia (DTD) – a craniofacial dysplasia – on 5q. A large amount of new 2-point linkage data made possible the ordering of markers over much of the long arm.

Substantial progress in physical mapping was reported for chromosome 5, considering its large size. Many new markers have been placed by in situ hybridization; most are concentrated on the distal part of 5q, which seems to be rich in growth-factor and receptor genes. Detailed physical maps were presented for areas containing growth-factor genes (IL3, CSF2, IL4, and IL5) and the FAP region. An extensive collection of hybrids was reported containing translocations at 5p, which will provide a valuable resource for continued mapping in this region.

Consensus physical and genetic maps showed many informative markers, both restriction fragment length polymorphisms and microsatellites, mostly on 5q. Participants saw a clear need for more highly informative markers of the variable number of tandem repeat or microsatellite type but were pleased that most useful reference markers are freely available. Often probes that were best mapped physically had not been as well mapped genetically, and conversely. Attendees proposed that reference probes be mapped both ways by the next workshop and felt that a good start was made in providing a set of informative reference markers spanning chromosome 5. ◊



**Workshop participants at the First International Workshop on Human Chromosome 5 prepare a consensus map of the interleukin gene cluster. Pictured l. to r. around the table are Elena Frolova (Shemyakin Institute, Moscow), Wilma Neuman (University of Chicago), Michael Lovett (GeneLabs), David McElligot (The Salk Institute), and Fran Lewitter (Brandeis University).**

*Reported by*
*Carol A. Westbrook*
*Department of Medicine*
*University of Chicago*
*and*
*Robert T. Williamson*
*St. Mary's Hospital*
*Medical School*
*University of London*

**Follow-up Projects for Chromosome 5**

- **Workshop Summary**
  To include lists of available resources (e.g., hybrids, probes, and libraries); will be prepared and distributed to participants.
- **List of Reference Markers**
  Prepared during working sessions; will be proposed for inclusion in the HGM-10.5 report for chromosome 5.
- **Composite Genetic and Physical Maps**
  Will be refined, updated, and submitted for publication.
- **Newsletter For Chromosome 5**
  Will soon begin circulation to continue the spirit of collaboration; coordinated by Carol Westbrook.

## NCHGR Invites Grant Applications

The National Center for Human Genome Research (NCHGR) invites applications for assistance awards to support feasibility studies using advanced DNA sequencing technology to accomplish large-scale sequencing projects at a higher rate and lower cost than currently possible.

Application deadline is December 3. To discuss research objectives and obtain application information, contact Jane L. Peterson; Chief, Research Centers Branch; NCHGR; Building 38A, Room 610; National Institutes of Health; Bethesda, MD 20892; (301) 496-7531, E-mail: jp2@nihcu.bitnet or jp2@cu.nih.gov. ◊

## Calendar of Genome Events*

| | | |
|---|---|---|
| November | 16 | **Computer-Aided Genetic & Protein Engineering**; live via satellite at various locations [*Digital Equipment Corp., (800) 227-5558, ext. 31*] |
| | 20 | **"Part I: Mapping the Human Genome,"** panel discussion at Understanding the New Issues in Genetics; Baltimore [*RSVP line, (301) 328-8000*] |
| December | 3 | **NIH Program Advisory Committee on the Human Genome**; Bethesda, MD [*C. Mohan, (301) 496-0844*] |
| | 4 | **Joint DOE-NIH Subcommittee on the Human Genome**; Bethesda, MD |
| | 4 | **DOE Human Genome Coordinating Committee**; Bethesda, MD |
| | 8 | **Review of the United Methodist Church Genetic Science Task Force Report**; Oak Ridge, TN |
| | 10–12 | **HUGO Meeting on Genome Analysis: From Sequence to Function**; Frankfurt, Germany [*DECHEMA Meetings Office, HUGO, Fax: (Int.) (49-69) 756-4201*] |
| January 1991 | 8–11 | **"Biotechnology Computing Minitrack"** at the **Hawaii International Conference on System Sciences–24**; Kailua-Kona, HI [*L. Hunter, (301) 496-9300, Fax: (301) 496-0673*] |
| | 27–Feb. 1 | **Bio/Technology Magazine Winter Symposium – Advances in Gene Technology: The Molecular Biology of Human Genetic Disease**; Miami Beach, FL [*The Miami Bio/Technology Winter Symposia, (800) 624-4363, Fax: (305) 324-5665*] |
| February | 17–20 | DOE Contractor/Grantee Workshop; Santa Fe, NM [*Sylvia Spengler, (415) 486-4943, Fax: (415) 486-5717*] |
| | 24–28 | **"Special Mini-Track on Artificial Intelligence Applications to Molecular Biology"** at **The Seventh IEEE Conference on Artificial Intelligence Applications**; Miami Beach, FL [*D. Searls, (215) 648-2146*] |
| March | 19–21 | **"Development and Application of Electrophoresis Techniques in Molecular Biology"** sessions at the **International Electrophoresis Society Meeting**; Washington, DC [*J. Cunningham, (301) 898-3772, Fax: (301) 898-5596*] |
| | 24–28 | **Mathematical Analysis of the Human Genome: DNA Sequence to Protein Structure**; Santa Fe, NM [*S. Spengler, (415) 486-4943, Fax: (415) 486-5717*] |
| Spring | TBA | **Public Forum on the Human Genome Project**; San Francisco [*Alliance of Genetic Support Groups, (800) 336-4363*] |
| May | 15–18 | **"Genetic-Related Symposia"** at the **82nd Annual Meeting of the American Association for Cancer Research**; Houston [*M. Foti, (215) 440-9300, Fax: (215) 440-9313*] |
| | 8–11 | **Genome Mapping and Sequence Conference**; Cold Spring Harbor, NY |

*Attendance at meetings listed without contact information is by invitation only.

## Calendar of Genome Events*

| | | |
|---|---|---|
| July | 22–26 | **"High Performance Computing in Biology and Medicine"** and **"Computational Molecular Biology and Genetics"** at the **13th IMACS World Congress on Computation and Applied Mathematics**; Dublin[*M. Witten, USA, (512) 471-2457, Fax: (512) 471-2445, E-mail: xxv6742@utchpc*] |
| August | 18–22 | **11th International Workshop on Human Gene Mapping (HGM 11)**; London [*M. Probert, (Int.) (44-71) 269-3052, Fax: (44-71) 430-1787*] |
| | 25–31 | **XXII International Conference on Animal Genetics**; East Lansing, MI [*R. Bull, (517) 355-4616, Fax: (517) 353-5436*] |
| September | 22–25 | **Genome Sequencing Conference III**; Hilton Head, SC [*S. Wallace, (301) 480-0634, Fax: (301) 480-8588*] |
| October | 6–11 | **8th International Congress of Human Genetics**; Washington, DC [*ICHG, (301) 571-1825, Fax: (301) 530-7079*] |
| | 21–23 | **Human Genome III: The International Conference on the Status and Future of Human Genome Research**; San Diego [*Scherago Assoc., Inc., (212) 382-1921*] |

*Attendence at meetings listed without contact information is by invitation only.

## Training Calendar: Workshops and Coursework

| | | |
|---|---|---|
| November | 13–16 | **Basic Cloning Techniques**; Ames, IA (also offered Dec. 11–14 in Miami; Feb. 19–22/91 in Norton, MA) [*S. Chance, (515) 232-8306*] |
| | 26–30 | **Transfection Techniques**; Gaithersburg, MD [*G. Tinney, (301) 921-2250*] |
| December | 3–4 | **Short Course on Modern Methods in the Purification and Analysis of Biopolymers for Biotechnology and Genetic Analysis: Liquid Chromatography and Capillary Electrophoresis**; Iselin, NJ [*J. Cunningham, (301) 898-3772, Fax: (301) 898-5596*] |
| | 7 | **DNA Amplification by PCR**; New Orleans (also offered Dec. 11 at Melbourne, FL; Dec. 18 at Houston; Jan. 10/91 at San Diego; Jan. 16/91 at Los Angeles; and March 18/91 at Norton, MA) [*see contact: Nov. 13-16*] |
| | 10–14 | **Recombinant DNA Techniques**; Gaithersburg, MD [*see contact: Nov. 26-30*] |
| | 18–21 | **IBI Recombinant DNA Workshop**; Middletown, CT [*L. Salen, (800) 243-2555 or (800) 786-5600*] |
| January 1991 | 3–5 | **Polymerase Chain Reaction in Molecular Biology**; Washington, DC [*Catholic University of America, (202) 319-6161, Fax: (202) 319-5721*] |
| | 7–11 | **Recombinant DNA Methodology: Lecture/Demonstration/Hands-on Demonstration**; (also offered March 4–8/91) Washington, DC [*see contact: Jan. 3-5*] |
| | 7–11 | **Basic Cell and Tissue Culture**; Washington, DC [*see contact: Jan. 3-5*] |

## Acronym List

Acronyms listed were chosen because they were either used in the text or are relevant to the human genome research community. Listed in parentheses after an organization is the branch of government or the organization to which it is responsible.

*Denotes U.S. Department of Energy organizations.
†Denotes U.S. Department of Health and Human Services organizations.

| | |
|---|---|
| **ABI** | Applied Biosystems, Inc. |
| **AIDS** | acquired immune deficiency syndrome |
| **ATTC** | American Type Culture Collection |
| **bp** | base pair |
| **cDNA** | complementary DNA |
| **CF** | cystic fibrosis |
| **CIOMS** | Council for International Organizations of Medical Sciences |
| **cM** | centimorgan |
| **DHHS** | Department of Health and Human Services (U.S.) |
| **DNA** | deoxyribonucleic acid |
| **DM** | myotonic dystrophy |
| **DOE** | Department of Energy (U.S.) |
| **DTD** | diastrophic dysplasia |
| **ELSI*†** | DOE-NIH Working Group on Ethical, Legal, and Social Issues |
| **EST** | expressed sequence tag |
| **FAP** | familial adenomatous polyposis |
| **GDB** | Genome Data Base (HHMI) |
| **HERAC** | Health and Environmental Research Advisory Committee |
| **HGCC*** | Human Genome Coordinating Committee |
| **HGM** | Human Genome Mapping |
| **HGN*†** | **Human Genome News** |
| **HGMIS*** | Human Genome Management Information System (ORNL) |
| **HHMI** | Howard Hughes Medical Institute |
| **HUGO** | Human Genome Organisation [International] |
| **LANL*** | Los Alamos National Laboratory, Los Alamos, N.M. |
| **LBL*** | Lawrence Berkeley Laboratory, Berkeley, Calif. |
| **LLNL*** | Lawrence Livermore National Laboratory, Livermore, Calif. |
| **MIT** | Massachusetts Institute of Technology |
| **NCHGR†** | National Center for Human Genome Research (NIH) |
| **NCI†** | National Cancer Institute (NIH) |
| **NCRR†** | National Center for Research Resources (NIH) |
| **NIH†** | National Institutes of Health |
| **NLGLP*** | National Laboratory Gene Library Project (LANL, LLNL) |
| **NSF** | National Science Foundation |
| **OER*** | Office of Energy Research |
| **OHER*** | Office of Health and Environmental Research (OER) |
| **ORNL*** | Oak Ridge National Laboratory, Oak Ridge, Tenn. |
| **PACHG†** | Program Advisory Committee on the Human Genome (NIH) |
| **PCR** | polymerase chain reaction |
| **PNL*** | Pacific Northwest Laboratory, Hanford,Wash. |
| **RFLP** | restriction fragment length polymorphism |
| **SMA** | spinal muscular atrophy |
| **STS** | sequence tagged site |
| **UCSF** | University of California, San Francisco |
| **YAC** | yeast artificial chromosome |

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*Comments:*

**Human Genome Management Information System**

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