Human Genome news

National Center for Human Genome Research
National Institutes of Health

A Forum For Human Genome Information Exchange

ISSN:1050-6101

Vol. 2, No. 6, March 1991

United Kingdom Human Genome Mapping Project Expands Activities

International Role Included in Objectives

New Funds to MRC for Coordination and Expansion of U.K. Genome Activities

In 1989 the U.K. Secretary of State for Education and Science awarded £11M ($21 million) to the Medical Research Council (MRC) for the initiation of a national Human Genome Mapping Project (HGMP) to coordinate and expand U.K. activities in human genome mapping and to provide a link with genome projects in other countries. Program objectives include giving the United Kingdom a role in international genome research and ensuring that the nation will benefit from medical and commercial applications of genome work.

The award supplements the £20M ($38 million) already committed to genetics research annually in the United Kingdom by MRC (£10M, or $19 million), other research councils, and medical research charities such as the Imperial Cancer Research Fund (ICRF) and The Wellcome Trust. The new funds are being distributed over a 3-year period from April 1989 to March 1992, after which £4.5M ($8.6 million) will be incorporated into the MRC annual funding baseline.

The U.K. project aims to have a balanced portfolio that reflects and exploits existing strengths; a few areas have been identified for strategic development. One example is that, instead of attempting large-scale sequencing or mapping, the U.K. program will concentrate on identifying and isolating as many genes as possible and characterizing them in biological terms. The assumption is that sequencing a few hundred bases of a cDNA would determine what kind of protein the gene codes for and how interesting the gene would be to investigators. This approach will indicate which genes have already been sequenced and avoid duplication of effort.

Success of the U.K. genome project depends on the consolidation of resources, emphasis on collaboration, and central coordination of the national effort in order to compete with major international teams.

Genome Project Components

The Human Genome Mapping Project consists of two major components – the Resource Centre and the Directed Programme of Research – supported by the Secretariat.

In This Issue...

Genome News

U.K. Human Genome Mapping Project

Project Management Committee

Dai Rees (Chair)
MRC

Martin Borrow
Guy's Hospital

Sydney Brenner
MRC, Molecular Genetics Unit

George K. Radda
MRC, Biochemical and Clinical Magnetic Resonance Unit

Lewis Wolpert
Middlesex Hospital Medical School

Tony Vickers (Project Manager)
MRC

Directed Programme Committee

Lewis Wolpert (Chair)
University College and Middlesex Hospital Medical School

Martin Bishop
MRC, Molecular Genetics Unit

Martin Bobrow
Guy's Hospital

Sydney Brenner
MRC, Molecular Genetics Unit

Roger Craig
ICI Pharmaceuticals

Malcolm Ferguson-Smith
Cambridge University

Peter Goodfellow
ICRF

Nicholas Hastie
MRC, Human Genetics Unit

Hans Lehrach
ICRF

Lucio Luzzatto
MRC/Leukemia Research Fund(LRF), Leukemia Unit

Mary Lyon
MRC, Radiobiology Unit

Susan Povey
MRC, Human Biochemical Genetics Unit

Christopher Rawlings
ICRF

Edwin Southern
Oxford University

John Sulston
MRC, Laboratory of Molecular Biology

Robert Williamson
St. Mary's Hospital Medical School

Tony Vickers (Project Manager)
MRC

The Project Management Committee oversees the Resource Centre and approves its budget; oversees the Directed Programme to ensure coordination with the center; and considers ethical, commercial, and other policy issues. The Resource Centre has a major role in effecting coordination.

Project Manager Tony Vickers has overall responsibility for the project, directs the Resource Centre, coordinates its activities with those of the Directed Programme, and represents U.K. genome mapping interests to the international community.

U.K. Resource Centre User Registration

Any U.K. academic researcher with relevant interests can register to use Resource Centre facilities without charge but must contribute information and materials in return. Other U.K. users and foreign investigators may be subject to restricted access and fees. For further information on Resource Centre services contact:

Christine Bates
U.K. Human Genome Mapping Project Resource Centre
Clinical Research Centre
Watford Road
Harrow, Middlesex HA1 3UJ
Telephone: (Int.) 44/81-869-3446
Fax: (Int.) 44/81-869-3807

Resource Centre

The Resource Centre acts as a national repository and site for systematic work, as well as a distributory and reference center for human and mouse cDNA libraries, yeast artificial chromosome (YAC) libraries, DNA probes, computing facilities, and relevant databases. The center is managed jointly by Ross Sibson (Biology) and Martin Bishop (Computing).

A number of existing YAC libraries are being transferred to the Resource Centre. The center makes cDNAs which, after partial sequencing, can be used as probes to find a gene's position on the YAC. Investigators can send their cDNAs to the center and receive the center's cDNAs for their own research. A significant number of genes could be identified and located by processing 100 cDNAs per week for 5 years.

In addition to the production of cDNA libraries and sequencing of new cDNAs, work at the center includes nonradioactive sequencing, hybridization screening, polymerase chain reaction screening, oligonucleotide synthesis, and in situ hybridization.

To help laboratory researchers with computer networking, advisors from the center are visiting laboratories to assist in establishing standard molecular biology software. In addition, the Resource Centre is developing the following informatics facilities:

- Computerization of data collection for the cDNA strategy.
- Online access to all standard databases and software packages.
- Incorporation of the Genome Data Base (GDB) from Johns Hopkins University for national and possibly European access.
- Computer training courses. For a full description of courses, contact Christine Bates at the Resource Centre (see lower box).

Directed Programme of Research

The Directed Programme selectively expands work in university departments, MRC establishments, and other institutions. The Directed Programme Committee (see upper box for members) works with the project manager to develop an overall operational strategy; identifies laboratories and solicits and evaluates proposals for

funding of appropriate research projects; awards short-term grants and contracts, studentships, and training fellowships; and funds conferences, workshops, and travel.

An early objective of the Directed Programme was to enhance relevant work by supporting research in three broad areas:

- General mapping of interesting genomic regions.
- Evaluation and design of enabling methodologies and equipment.
- Study of model organism genomes such as the mouse and the roundworm *Caenorhabditis elegans.*

While this work continues to be strongly supported, the major thrust of the Directed Programme is now focused on mapping cDNAs in collaboration with the Resource Centre. Data and materials generated with the cDNA strategy will be available to the community for further analysis, subject to publication in existing public domain databases.

The Directed Programme funds access to a variety of resources to complement Resource Centre activities, including the ICRF DNA probe bank (see upper box) recently transferred to the Resource Centre and the Human Cell Bank at the Centre for Applied Microbiology and Research at Porton, England. The Directed Programme has also obtained and tested the St. Louis and Imperial Chemical Industries YAC Libraries (Oxford/London).

Secretariat

The Secretariat, headed by Diane McLaren, administers project business, services the HGMP committees, and helps to establish international links and coordination with organizations such as the Human Genome Organisation and the Commission of the European Communities. Located at MRC headquarters, the Secretariat also organizes annual users meetings to inform the community on the progress of national and international genome initiatives.

Model Organism Studies

The U.K. genome project is focusing on two model genomes, the mouse and *C. elegans*, to complement its human genome work. A backcross between *Mus spretus* and *M. domesticus* has been set up at the Resource Centre to provide a DNA resource for physical mapping.

U.K. DNA Probe Bank

The U.K. DNA Probe Bank, funded by MRC, has been established at the HGMP Resource Centre in London. The Probe Bank's catalogue lists some 650 DNA probes, the majority of which have been assigned to chromosomes and will detect restriction fragment length polymorphisms. Probes will be distributed as aliquots of purified DNA.

The Probe Bank will serve two purposes:

- to supply DNA markers upon request and
- to isolate new DNA markers to bridge some of the gaps in current genetic maps.

To submit probes to the Probe Bank, groups should contact the HGMP Resource Centre for inclusion in the listings. A simplified listing of probes and a more comprehensive catalogue are available from the Resource Centre (see lower box, p. 2). ◇

Mapping cDNAs Is Major Thrust of U.K. Directed Programme

A joint project funded by MRC and the NIH National Center for Human Genome Research involves extensive pilot-scale sequencing of the *C. elegans* genome at the MRC Laboratory for Molecular Biology in Cambridge and Washington University Medical School in St. Louis. [see *HGN* 2(5), 1 (January 1991)]. ◇

Reported by Diane McLaren, Head
U.K. HGMP Secretariat
and
Denise Casey and Anne Adamson
HGMIS, ORNL

G-Nome News

Editors of *G-Nome News*, a quarterly newsletter produced by the U.K. Human Genome Mapping Project and funded by MRC, are calling for articles from the human genome community. *G-Nome News*, which has been in publication about 1 year, contains information in these general categories:

- U.K. project administration and management.
- Function of centralized resources, such as the Probe Bank.
- Technical articles.
- Contributions about genome research from laboratories around the United Kingdom.

Deadlines for receipt of copy for quarterly editions are: Winter, January 10; Spring, April 9; Summer, July 10; and Autumn, October 10. Newsletter articles, written or on disk (any format) can be transmitted to Nigel Spurr at the following:

Nigel Spurr, ICRF
Clare Hall Laboratories
Blanche Lane
South Mimms, Potters Bar
Hertfordshire, EN6 3LD, U.K.
Fax: (Int.) 44/707-49527
E-mail: ("NSPURR@UK.AC.ICRF")

Genome News

DOE-NIH Joint Subcommittee Hears Reports

Informatics, ELSI, and Sequencing Working Groups Describe Progress

Next Scheduled DOE-NIH Joint Subcommittee and PACHG Meetings Set for June 25

The DOE-NIH Joint Subcommittee on the Human Genome convened in Bethesda, Maryland, on December 3, 1990, with Sheldon Wolff and Norton Zinder presiding. Reports were heard from the joint working groups on DNA sequencing; informatics; and ethical, legal, and social issues. Representatives of international groups and other U.S. agencies were also present to describe the progress of their respective genome programs. [For a list of subcommittee members and their affiliations, see *HGN* **2**(3), 7 (September 1990).]

Joint Informatics Task Force (JITF)

[For a list of members, see *HGN* **2**(2), 10 (July 1990).]

David Benton [National Center for Human Genome Research (NCHGR)] reported on the JITF meeting (November 30–December 1, 1990), which addressed the Human Genome Project need for public databases containing map and sequence data (see article, p. 8). Benton stated that JITF has developed a number of guidelines concerning the establishment of genome data resources.

The JITF report prompted a discussion of various informatics issues. Several participants noted that the complexity of currently available physical mapping data necessitates an experimental approach to database development and a period during which experience can be acquired. Mark Pearson (Du Pont) noted that three major database projects—the Genome Data Base at Johns Hopkins University, GenBank® at Los Alamos National Laboratory, and GenInfo at the NIH National Center for Biotechnology Information—are developing products that will be available this year and are attempting to integrate their operations and to facilitate access to these databases.

Maynard Olson (Washington University) noted at least three levels at which databases enter into the human genome program and cautioned against trying to develop a uniform technical standard that crosses these diverse settings:

- Public databases where information has been gathered from the literature and from long-term user submissions.
- More specialized databases (e.g., physical mapping databases for model organisms) that have a very high information content but are of interest to fewer people.
- Operational databases generated by investigators on the front lines of information gathering.

NIH-DOE Working Group on Ethical, Legal, and Social Issues (ELSI)

Nancy Wexler (Columbia University and Hereditary Disease Foundation) discussed the September 10, 1990, ELSI meeting [see *HGN* **2**(4), 6 (November 1990)]. Wexler noted that additional funding sources are needed because pilot testing programs will involve costly service components such as DNA analysis, as well as educational efforts to explain the importance of such programs to other agencies. She emphasized that the question of introducing new genetic screening tests will extend beyond cystic fibrosis (CF) as genetic linkages for other disorders are discovered.

Phillip Sharp (Massachusetts Institute of Technology) remarked that the national institutes having an interest in CF might help support pilot screening programs, and Robert Katz (NIH National Institute of Diabetes and Digestive and Kidney Diseases) suggested discussing the issue with the institutes involved in CF research.

The question of whether the Human Genome Project should fund pilot genetic-screening programs was discussed at length. While participants agreed that CF offers a paradigm for conducting and evaluating such programs, they expressed concern that the genome project might be expected to fund pilot programs for every genetically linked disease. Wexler predicted

Subcommittee, PACHG Recommendation Supports CF Pilot Testing

The subcommittee and PACHG formulated a draft message to NIH Acting Director William Raub. This message stated that the two groups recognize the importance of evaluating CF genetic testing as a precedent for introducing new genetic tests that will result from the Human Genome Project and emphasized the immediate need for funding mechanisms to support CF research-based pilot testing. The draft message contained the recommendation that NCHGR take a leadership role in developing these mechanisms.

that although different pilot programs for individual diseases may be necessary at first, the need for research on these programs will decrease as experience is gained and standards of delivery are developed (see box, p. 4).

Mapping Index Markers

Mark Guyer (NCHGR) provided an update on efforts to establish the framework genetic linkage map of index markers that had been described by the mapping working group. He reported that applications received in response to the NCHGR July 1990 Request for Applications would be reviewed by the NIH National Advisory Council for Human Genome Research and awards made early in 1991.

Information on the developing framework map was provided in the subcommittee meeting notebooks. The information was based on presentations given at a meeting in Cincinnati, Ohio, on October 16, 1990. The number of markers, their identification, and their availability were summarized for each chromosome. Approximately 95% of the markers listed are in the public domain.

Guyer also mentioned two chromosome-specific workshops held since the June 1990 subcommittee and NIH Program Advisory Committee on the Human Genome (PACHG) meetings:

- the chromosome 19 workshop in August [see *HGN* **2**(4), 11 (November 1990)] and
- the chromosome 5 workshop in September [see *HGN* **2**(4), 13 (November 1990)].

He added that a second round of workshops is planned for chromosomes 3, 11, 17, 21, 22, and X.

International Efforts

Human Genome Organisation (HUGO)

Director James B. Wyngaarden described the primary goals of HUGO:

- to assist in human genome research coordination;
- to foster collaboration among scientists to prevent unnecessary competition or duplication;
- to coordinate human genome research with parallel studies in model organisms;
- to facilitate exchange of data and biomaterials;
- to promote technology transfer through training programs; and
- to encourage consideration of ethical, social, legal, and commercial issues.

HUGO has over 333 members representing more than 25 countries and is establishing offices in Bethesda, Maryland; Europe; and Japan. [For more information and a list of officers, see *HGN* **2**(2), 6 (July 1990) and **2**(4), 4 (November 1990).]

Wyngaarden stated that HUGO had established subcommittees, similar to the joint NIH-DOE working groups, to deal with ethical, legal, and social issues; informatics; intellectual property; mouse gene mapping; and genetic and physical mapping of the human genome. He noted that HUGO is currently involved in activities related to its initial mission of coordinating chromosome-specific workshops. Wyngaarden announced that a HUGO Council meeting in Oxford, England, on January 7 would explore the idea of identifying a conference center where these workshops might be conducted and where the computer facilities necessary for information exchange might reside. He reported that plans are proceeding smoothly for the 11th International Workshop on Human Gene Mapping to be held in London in August (see "HGM 11," p. 11).

Commission of the European Communities (CEC)

Bronwen Loder (CEC and HUGO) announced that the first phase of the CEC human genome program, whose objectives are similar to those of the U.S. project, began in June 1990 with a 2-year budget of approximately $20 million. She noted that this figure represents new money to be spent entirely on the human genome and that model organism research is being supported in other ways. She added that the second phase of the program, scheduled to begin in June 1992, is likely to receive considerably more funding than the first phase.

Loder reported that the following contracts for central facilities have been awarded:

- Provision of DNA membranes for genetic mapping projects (Centre d'Etude du Polymorphisme Humain).
- Distribution of probes to laboratories conducting genetic mapping (U.K. DNA Probe Bank).
- Distribution of cosmid libraries.
- Construction and distribution of cDNA libraries.

HUGO, CEC Give Reports

To receive minutes of PACHG and Subcommittee Meetings, contact:
Office of Communications
NIH NCHGR
Bldg. 38A, Room 617
Bethesda, MD 20892
301/402-0911
Fax: 301/480-2770

Genome News

NIH-DOE Joint Subcommittee and PACHG June Meetings To Focus on Informatics

Loder stated that cDNA sequencing is an important part of the European program, accounting for roughly 10% of the budget. She noted that contracts will be established this year with the data resource center at the German Cancer Center in Heidelberg and with five laboratories that will provide a yeast artificial chromosome screening service. The CEC program has requested proposals for projects in contig mapping, development of new mapping and sequencing technologies, and informatics.

Loder added that applications have also been requested for pilot studies on development and assessment of low-cost, efficient methods for specific diagnosis of severe genetic defects. The training component of the CEC program will soon be announced, and a committee on ethical, legal, and social issues will be established by formal action of the commission.

Other International Programs

Diane McLaren (Medical Research Council, London) described the U.K. Human Genome Mapping Project (see article, p. 1) and Michele Durand (Science Attaché, French Embassy) presented information about the French human genome research program that began early this year [see *HGN* **2**(5), 12 (January 1991)].

Plant Genome Research

Reports from U.S. agencies were given by Stephen Heller [U.S. Department of Agriculture (USDA)] and Mary Clutter [National Science Foundation (NSF)]. Heller stated that the goal of the USDA plant genome research program is to facilitate the genetic improvement of plants by locating important genes and markers on chromosomes, determining gene structure, and transferring genes to improve performance. He referred to a Request for Proposals [*Federal Register* **55**, 49380 (November 27, 1990)] calling for research in three areas: (1) generation of broad maps of agronomic and forest species with 25-cM gaps, (2) intense mapping and characterization of chromosomal trait regions, and (3) development of new technologies for mapping and sequencing.

Heller noted that the USDA program's FY 1991 budget allocation amounts to $14.674 million in new money, of which $11 million will be used for competitive grants and $3.674 million (a line item to the Agricultural Research Service) for the operational expenses of the Office of Plant Genome Mapping, initial mapping activities, database and electronic communications, prototype data analysis of two major crop species and one forest tree species, and laboratory robotics development. A portion of the Agricultural Research Service funds will also be used to help support the NSF *Arabidopsis* project [see *HGN* **2**(3), 13 (September 1990)].

Clutter stated that the NSF FY 1991 budget includes $5 million in new money for the first year of the *Arabidopsis* genome project.

Mouse Genome Research

Following these presentations, James Watson (Director, NIH NCHGR) raised the question of establishing an NIH-DOE joint working group on mouse genome research. Guyer stated that participants in the Fifth International Mouse Workshop (November 4–8, 1990, Annapolis, Maryland) discussed a unified effort to develop mouse genetic and physical maps. He added that the mouse research community had requested that a working group be formed to help coordinate research and to develop a policy for mouse genomics in the United States. ◊

Project To Profile U.S. Biotechnology Faculty

An ambitious new project undertaken by the North Carolina Biotechnology Center will catalog all U.S. academic faculty working full time on biotechnology research. The project has received the support of three major funding agencies – NIH, National Science Foundation, and U.S. Department of Agriculture – as well as seven professional societies. The information gathered will be published this year in a computer database and as a directory, both for use by a wide variety of researchers, government agencies, and companies.

A broad definition of biotechnology will be used to include all research relating to cell biology, molecular biology, and genetics and involving new techniques such as recombinant DNA, monoclonal antibodies, and protein engineering. Research in a number of fields, including health care, agriculture, chemicals, and the environment, will be covered. For more information, call: 919/541-9366. ◊

To request a questionnaire, contact:

Biotechnology Research Faculty Profile
Biotechnology Information Division
North Carolina Biotechnology Center
P.O. Box 13547
Research Triangle Park, NC 27709

Respond via modem to:
USDA Bulletin Board, 800/624-2723

NIH PACHG Says Mapping Projects Indicate High-Quality Science

The NIH Program Advisory Committee on the Human Genome (PACHG) met on December 3, 1990, in Bethesda, Maryland, with Norton Zinder presiding. The meeting included funding reports, a presentation on intellectual property rights, and scientific presentations on large-scale mapping projects. [For a list of PACHG members and their affiliations, see *HGN* **2**(3), 7 (September 1990).]

Zinder, in commenting on the scientific presentations, said they were indicative of the high-quality science being conducted under the auspices of the NIH human genome program.

Elke Jordan [Deputy Director, National Center for Human Genome Research (NCHGR)] briefly reviewed budget information and lists of grants awarded since FY 1990. She indicated that a substantial amount of the budget increase granted in 1991 would be spent on the research centers program and that additional funds have been allocated for research project grants and other components.

Intellectual Property Rights

Alice Martin—specialist in intellectual property rights at the law firm of Arnold, White, & Durkee, certified medical geneticist, and member of the American Bar Association—provided an overview of the intellectual property that will be generated by the project (e.g., DNA sequences, technological developments, and databases). She described the types of mechanisms available to protect intellectual property—patents, copyrights, trademarks, and trade secrets—and summarized protection extent, enforcements, and advantages and disadvantages associated with each of these mechanisms.

Martin also explored the philosophical issue of whether legal protections for intellectual properties generated by genomic research are against the public interest. She provided examples of different approaches by inventors of various biological products and techniques. Legally protected intellectual property affords advantages, such as royalties that can be used to fund additional research, and gives opportunities for inventors to retain some control over the use of their inventions.

Addressing the question of the patentability of life forms and DNA sequences, Martin indicated that the U.S. Patent and Trademark Office uses three criteria in deciding whether or not to issue a patent: the invention must be new; must be nonobvious based on the prior art (i.e., the body of knowledge accumulated in the inventor's field of expertise); and must be useful.

She added that, although life forms or products that occur in nature cannot be patented, modifications of these life forms or products (e.g., isolated or purified DNA segments, clones, or cDNAs) may be patentable. Martin anticipated that the major difficulty in patenting DNA sequences will be in proving that they are nonobvious when technology and methods for generating sequences become widely used.

Elaborating on U.S. patent law, Martin discussed the experimental-use exception to property rights, whereby an individual can make or use a patented item as long as commercial gain is not intended. She also delineated some of the differences between U.S. and European patent laws and noted that efforts to make the two systems more compatible are in progress.

Martin concluded by stating that no new laws will be needed to address intellectual property issues related to the Human Genome Project, but she emphasized that an understanding of intellectual property rights will be essential in avoiding potential legal problems among inventors, collaborators, and funding agencies. She remarked that it might be appropriate for PACHG and DOE to form a joint working group on intellectual property issues to ensure that the rights of all parties are clearly stated and to stay abreast of public opinion and congressional actions.

Presentations on Mapping Projects

Five grantees delivered scientific presentations on major mapping projects supported by NCHGR:

- David Schlessinger (Washington University) discussed yeast artificial chromosome-based mapping of human chromosomes X and 7 and of other targeted portions of the genome.

(see PACHG, p. 8)

PACHG Told Understanding of Intellectual Property Rights Is Essential

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.

Genome News

JITF Discusses Map and Sequence Databases

Database Presentations

- Genome Data Base, Welch Medical Library, Johns Hopkins University
  Peter Pearson and Richard Lucier
- Lawrence Livermore National Laboratory Human Genome Center
  Elbert Branscomb
- Los Alamos National Laboratory (LANL) Center for Human Genome Studies
  James Fickett
- GenInfo Backbone Sequence Database, National Center for Biotechnology Information
  David Lipman
- "Electronic Data Publishing" Model, GenBank®, LANL
  Paul Gilna and Michael Cinkosky
- Priority Area Research Project on Genome Informatics, Japanese Human Genome Project
  Minoru Kanehisa (Kyoto University)
- European Molecular Biology Laboratory Data Library
  Graham Cameron

The second Joint DOE-NIH Informatics Task Force (JITF) meeting, November 30–December 1, 1990, addressed the Human Genome Project need for public databases containing mapping and sequencing data. Discussions were organized around presentations on existing map and sequence databases by representatives from data-housing facilities. Several presentations focused on the evolution, current status, and future development plans of data repositories (see box).

Other speakers were Scott Tingey (Du Pont) and Brian Hauge (Massachusetts General Hospital). Tingey discussed the Molecular Breeding Program (plants) and offered some solutions to the problems of storing vast quantities of laboratory data in accessible forms. Hauge described the progress and database requirements of the *Arabidopsis* genome mapping program.

Guidelines Established

The task force concurred on the following guidelines for establishing genome data resources:

1. Mapping databases are most naturally organized as organism-specific consensus map databases containing all genetic and physical mapping data that are significantly useful to the biomedical community.
2. Centralized consensus databases should provide direct or indirect access to the supporting data.
3. Central databases and project-supporting databases should be implemented using software and hardware systems that adhere to industry standards. Currently, these are the commercial relational database management systems using client-server architecture; they run on Posix-compliant computers connected to the research Internet and are capable of supporting communication with the Transmission Control Protocol/Internet suite of protocols (TCP/IP).
4. Public-use databases must provide a stable, documented Application Program Interface, so that third parties may develop interface software to the data. Public-use databases should use a standard system for representing typographic information (e.g., italics and superscripts) where it has important scientific meaning. Standard Generalized Markup Language is one such standard.
5. Public-use databases must be designed to support differential data accessibility among authorized users.
6. Data suppliers should be encouraged to estimate confidence limits of data or consensus elements, and these limits should be represented in the database.
7. The databases should maintain a history of database changes, such as an audit trail or set of editorial citations.

JITF Working Groups

The four JITF working groups made brief reports on their work. The action items that follow were included in the reports or resulted from them.

(see JITF, p. 9)

PACHG *(from p. 7)*

- Glen Evans (Salk Institute for Biological Studies) discussed a project to produce a physical map of human chromosome 11 and to develop computer software for manipulating the map.
- Richard Myers (University of California, San Francisco Medical School) reported on efforts to construct high-resolution genetic and physical maps of human chromosome 4. The project includes components at the University of Iowa and the Fox Chase Cancer Center.
- David Ward (Yale University Medical School) described research to map clones on human chromosomes 1, 3, 5, 9, 10, 11, 16, and X using fluorescent in situ hybridization to guide the preparation of genetic linkage or long-range restriction maps.
- Francis Collins (University of Michigan Medical School) presented an overview of the goals of his project to develop advanced technology in genetic and physical mapping and DNA sequencing. ◇

ELSI Working Group Examines Progress

The NIH-DOE Working Group on the Ethical, Legal, and Social Issues (ELSI) related to mapping and sequencing the human genome met on January 7–8 in Crystal City, Virginia. The purpose of the meeting was to examine progress in policy development on three sets of professional and public policy issues identified as high priority for the NIH-DOE ELSI program:

- protecting the confidentiality of genetic information;
- facilitating responsible integration of new genetic tests into clinical practice; and
- promoting fairness in genetic information use, especially by insurers and employers.

Privacy Issues Addressed

Madison Powers (Georgetown University) spoke on legal protection of confidentiality and privacy, including the Federal Privacy of Genetic Information Bill (H.R. 5612, 101st Congress, 2nd Session) introduced by Representative John Conyers, Jr., D-Michigan. Powers described the current network of federal, state, and regulatory protections and identified gaps in the ability to maintain medical record confidentiality.

Mark Rothstein (University of Houston) addressed the implications of the Americans with Disabilities Act (ADA) in the use of genetic information for employment screening. He concluded that ADA provides discrimination protection to

(see ELSI, p. 10)

HIAA Representative Gives Insurance Industry's Views

JITF *(from p. 8)*

Data Requirements Working Group

The group will concentrate on mapping data; Lipman recommended establishing connections with model organism mapping data projects. Branscomb was appointed liaison to the Human Genome Organisation committee on physical mapping data.

Connectivity and Infrastructure Working Group

The group's aim was reported to be fostering capability and not mandating actions; it recognized that the Internet TCP/IP protocol suite is the U.S. connectivity standard. The working group recommended that all genome centers and genome data resources be Internet accessible and that the funding agencies provide connection guidance and support. The group pointed out that network resource availability would create a second cycle of demand from individual researchers; NIH and DOE should expect this demand to increase and be prepared for it.

Training Working Group

Although DOE, NIH, and the National Science Foundation (NSF) have separate genome and computation fellowships, the working group stressed that the Human Genome Project has an opportunity to make a real impact on interdisciplinary computation and biology training by designing a fellowship that would be available at a number of levels: predoctoral, postdoctoral, and mid-career. Another short-term goal of the working group is the development of a summer course in genome informatics for investigators whose primary training is in biology.

Long-Term Needs Working Group

The need for analytical tools and genome informatics training was discussed. The group noted that NSF has taken the lead in biocomputing training. Frank Olken (Lawrence Berkeley Laboratory) pointed out that the Human Genome Project should support basic research in database theory, because advances in database theory and practice are necessary to achieve project goals. Lipman suggested that the cost for such research would be less than that for one genome center, and that Human Genome Project administrators need to be aware of current research and to encourage computer scientists to meet the project's database requirements.

Prior to its next meeting (tentatively scheduled for March 14–15), JITF plans to organize a workshop on laboratory support databases and associated software to develop a requirement specification for a general laboratory support tool. ◇

Reported by David Benton
NIH NCHGR
and
Robert Robbins
NSF/DOE

JITF Plans To Organize Database Workshop

David Benton is Assistant to the Director for Scientific Data Management at NCHGR.

Robert Robbins is Program Director for Database Activities in the Biological, Behavioral, and Social Sciences at NSF; he is assisting DOE in genome informatics and computational activities through the courtesy of NSF.

Genome News

ELSI *(from p. 9)*

ELSI Working Group To Form Insurance Task Force

disease-gene carriers and to those suffering from genetic disabilities. Rothstein shared the recommendations he made to the Equal Employment Opportunity Commission for developing regulations that would make these protections explicit.

Lori Andrews (American Bar Foundation) discussed several avenues for stimulating model legislation at the state level and for providing input into federal regulation development. Patricia King (Georgetown University Law Center) agreed to assume responsibility for coordinating further initiatives in this area.

Genetic Testing and Insurance

Jude Payne [Health Insurance Association of America (HIAA)] presented the insurance industry's views on using genetic tests in underwriting practices. She concluded that no particular genetic test is likely to be cost-effective enough to use as a routine insurance screen; however, if medical screening increases, insurers will have to decide whether to include such information in their underwriting decisions. She announced the formation of an HIAA working group on genetic testing to help develop industry policy over the coming months.

Margaret Anderson [Office of Technology Assessment (OTA)] discussed a survey of insurance companies that is a component of an upcoming OTA cystic fibrosis (CF) study. This study will assess the significance of genetic information in current underwriting practices and clarify the plans and policies of individual insurance companies with respect to genetic information.

Philip Reilly (Eunice Kennedy Shriver Center for Mental Retardation) discussed the need for research on insurance issues and the role of state insurance regulation in protecting against unfair use of genetic information by insurers. Because much U.S. health insurance is provided by self-insuring large employers not governed by state laws regulating commercial firms, legislation may need to be extended to cover these self-insurance plans.

The ELSI working group plans to help coordinate initiatives in this area by forming an Insurance Task Force that will include representatives from the insurance industry, corporate benefit plans, consumer and health groups, and scholars actively researching these issues. Tom Murray (Case Western Reserve University) will serve as chair.

Genetic Services and Medical Practice

ELSI staff reported on several initiatives that evolved from the September 1990 ELSI workshop, which focused on issues related to the clinical introduction of new genetic tests. Together, these initiatives (listed below) should help establish a sound professional foundation for the provision of emerging genetic services; the working group will follow them closely.

- National Center for Human Genome Research (NCHGR) has taken a lead role in organizing an NIH-wide response to the need for pilot studies on how best to deliver DNA-based carrier testing for CF.
- NCHGR and DOE have initiated a major study by the National Academy of Sciences and the Institute of Medicine to help assess and establish standards of care and quality-control mechanisms for the delivery of new genetic services.
- Neil Holtzman (Johns Hopkins School of Medicine) informed the group about his NCHGR-supported study of primary-care physicians' preparedness for handling various aspects of genetic testing.
- Robyn Nishimi (OTA) discussed the upcoming OTA project on screening for CF. The project goal is to use CF testing as a model for policy issues that will arise as new genetic tests are integrated into medical practice. ◇

Reported by Eric T. Juengst, Director NCHGR Ethical, Legal, and Social Implications Program

Public Education

In addition to the substantive issues outlined in the article above, one high-priority activity for the working group is to promote public education and the discussion of Human Genome Project issues. As part of this effort, NCHGR is contributing to the funding and DOE is considering cosponsorship of a public television series, "The Future of Medicine," whose objective is to examine the philosophical, social, and scientific significance of medicine in human life.

Because data produced by the Human Genome Project will affect the practice of medicine, the working group seeks to make accessible to the public the scientific basis of the project and its ethical, legal, and social implications. Attending the workshop were the series' producers from WNET (New York City) and the British Broadcasting Corporation, who updated the working group on their progress and requested advice on how to improve their message and delivery. The series is slated to air in the 1992–93 season. ◇

NCHGR, Health Groups Share Perspectives

On January 14, the NIH National Center for Human Genome Research (NCHGR), the Alliance of Genetic Support Groups, and Research! America presented "The Human Genome Project: New Tools for Tomorrow's Health Research." The program was developed especially to familiarize members of voluntary health associations with Human Genome Project goals and to address questions about how genome research will improve hereditary disease research. The half-day program at the NIH campus in Bethesda, Maryland, featured speakers who shared their experiences, perspectives, and predictions about various aspects of the project and its contribution to human genetic research.

In opening remarks to the 90 patient advocates who attended, NIH Acting Director William Raub highlighted the universal application of the Human Genome Project's scientific developments. He explained that high-resolution chromosome maps, yeast artificial chromosome technology, sequence tagged sites, and new sequencing technologies will enhance the range of NIH efforts to "determine the protein product [and] to identify the chromosome and the exact location of genes on the chromosome. As the Human Genome Project develops, the interplay between our [national] institutes' missions will become ever stronger. The wisdom of this organized, up-front investment in mapping and then sequencing will pay off many times over in the specific disease areas that make up the constituent interests of the NIH."

Thomas Caskey (Baylor College of Medicine) emphasized the importance of Human Genome Project goals to develop:

- genetic and physical maps,
- new methods to identify genes, and
- technology for transfer of research information to laboratories and individuals.

He also stressed the structuring of these scientific advances into a socially acceptable framework and pointed out that the realization of these goals will be a "significant boost" to patients and families with inherited diseases.

Nancy Wexler (Hereditary Disease Foundation and Columbia University), explaining the value of placing markers on chromosomes to help pinpoint genes, stressed the staggering amount of DNA ultimately to be sequenced. "It's essential that this task be done in an organized and coordinated manner," she said. "Each individual voluntary association couldn't begin to tackle a project like this." She said the Human Genome Project offers tremendous opportunities for collaboration among scientists in all fields in helping to complete the fine details of the human genome picture, so that all genetic diseases might one day be understood.

In anticipation of future genetic testing and screening programs, Robert Murray (Howard University School of Medicine) recounted the unfortunate errors that were made when testing for sickle cell anemia began in the 1970s. He suggested that future testing programs do the following:

1. Educate the population to be tested about the disease and the possible implications of positive results.
2. Involve members of that community in the development of conditions under which the test would be given and interpreted.
3. Be sensitive to social stigmatization.
4. Educate the community at large so it can understand the true implications of a positive test result.

(see Perspectives, p. 12)

HGM 11 Set for London, August 18–22

The 11th International Workshop on Human Gene Mapping (HGM 11) will be held August 18–22 in London. As a transition from earlier workshops, the first 2 days will include talks and workshop sessions on topics such as the genetic map, physical map, mapping panels, probe resources, and loci of particular interest. The final 2 days will consist of open discussion meetings on these and other topics and of plenary scientific talks by invited speakers on major issues in gene mapping.

Attendance is limited and priority will be given to authors of accepted abstracts. Deadline for receipt of abstracts is April 15 (see box for contact information). ◇

Reported by Jane Crowther
Imperial Cancer Research Fund

Jane Crowther
HGM 11 Office H
Imperial Cancer Research Fund
P.O. Box 123
Lincoln's Inn Fields
London WC2A 3PX, U.K.
(Int.) 44-71/269-3389, Fax: 44-71/430-1787,
E-mail: "HGMINFO@UK.AC.ICRF.HGM"

NCHGR Encourages Hereditary Disease Groups To Volunteer for Family Studies

Genome News

Locations of Other NCHGR Centers:

- Washington University, St. Louis
- University of California, San Francisco
- Massachusetts Institute of Technology, Cambridge
- University of Michigan, Ann Arbor

Baylor, Utah Receive NCHGR Center Grants

The NIH National Center for Human Genome Research (NCHGR) has awarded two 5-year Human Genome Research Center grants to teams at the Baylor College of Medicine in Houston and the University of Utah in Salt Lake City. These two additions bring to six the total number of NCHGR-supported genome research centers.

Centers form the foundation of the diverse NCHGR research program and 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. Funds for these two new centers will provide "core facilities" that will enable genome researchers to carry out the goals of the Human Genome Project.

University of Utah (first year: $2,076,272). Led by geneticists Raymond Gesteland and Raymond White, the Utah center will focus on developing high-quality DNA markers to add to the genetic linkage map of human chromosomes 16, 17, and a portion of 5 and to help connect the genetic and physical maps. Investigators expect to generate about 640 markers each year and, in collaboration with a group at the University of Alberta in Edmonton, Canada, will also develop more rapid DNA sequencing methods.

The Utah center will include a computer component to perform genetic and statistical analyses to link information about inherited diseases to specific chromosomes and genes. Mapping technology developed at the Utah center will be available to other gene hunters through collaborations.

Baylor College of Medicine (first year: $1,833,621). Led by Thomas Caskey, the Baylor genome center will seek to improve DNA sequencing technology while developing a physical map of human chromosomes X and 17 and a genetic linkage map of chromosome 6. Investigators will collect DNA samples from patients with inherited diseases and, with special computer programs, attempt to locate disease genes on cloned yeast artificial chromosomes, focusing on large DNA regions known to contain genes responsible for diseases. ◊

Reported by Leslie Fink, Chief NCHGR Office of Communications

Perspectives *(from p.11)*

NCHGR Ethical, Legal, and Social Implications Program Director Eric Juengst offered an overview of NIH efforts to anticipate cultural and social implications of new and more accurate genetic tests that will be developed as genome research is translated into medical practice. He noted the following NCHGR program functions:

- To support social and scientific research into the identification of potential social problems and ways to address them.
- To develop public policy options to safeguard the confidentiality of genetic information.
- To educate health professionals and the lay public about issues raised by new genetic information.

Following individual presentations, the speakers formed a panel to answer and comment on many thought-provoking questions from the audience. Members of hereditary disease groups were invited to participate in the Human Genome Project by volunteering for family studies, which form the heart of disease-gene mapping, and by providing feedback to ensure that the ELSI program fits the public's needs.

In closing, Nancy Wexler explained that isolating a disease gene would not mean an "instant panacea," but she speculated about the kinds of prevention and treatment approaches that might be taken after the gene is discovered. She said that rapidly advancing technology is providing encouragement that eventually all genes will be located. While members of hereditary disease groups may sometimes feel discouraged and alone, she said, they should realize that together they can be a tremendously powerful constituency. The Human Genome Project provides a way for them to combine forces to achieve their individual goals more rapidly. ◊

Reported by Sandy O'Connor NCHGR Office of Communications

FASEB Journal Features Genome Research

The January issue of *The FASEB Journal* focuses on worldwide genome research. It contains articles on topics such as the origins of the U.S. Human Genome Project; current mapping trends; DNA sequencing; molecular studies of human genetic disease; information management; ethical, legal, and social issues related to availability of genome data; the Human Genome Organisation; and genome efforts in Japan, Europe, Latin America, and the U.S.S.R. ◊

NCHGR Involves Minorities in Activities

NIH recognizes the need to increase the number of the underrepresented minority scientists participating in biomedical and behavioral research as a means of addressing a potential research labor shortage in the 21st century. The National Center for Human Genome Research (NCHGR) is committed to this goal, in addition to realizing the importance of having all scientists contribute to research progress. Because genomic research is a relatively new scientific discipline and NCHGR a new component of NIH, the center has the opportunity to approach this initiative in creative ways.

The center plans the following efforts to encourage participation of minority scientists and institutions:

1. Educate the scientific community about the genome program and about opportunities at all career levels.
2. Increase the number of trained minority researchers through a variety of research training and career development programs.
3. Provide opportunities for minority students to pursue research projects.

Education

During the past year, NCHGR has informed the broader scientific community of its programmatic interests through announcements in the *NIH Guide to Grants and Contracts* and through presentations at annual meetings of professional societies. In exploring ways to reach more minority scientists, NCHGR is doing the following:

- Working with the Minority Biomedical Research Support and Minority Access to Research Careers programs to include within their annual meetings a minisymposium on the Human Genome Project.
- Cooperating with Research Center in Minority Institutions investigators to develop a series of genome-related proposals for consideration by NIH [see *HGN* 2(3), 8 (September 1990)].

Training

Training opportunities will be available to minority scientists at all career levels—from high school students to established scientists—through programs such as the Minority High School Student Research Apprentice Program, the National Research Service Award, the Senior Fellowship Award, and the Special Emphasis Research Career Award. The NCHGR minority initiative will stress training for new scientists, opportunities for established scientists to develop additional skills, and more intensive training for those who wish to change fields.

The center has developed a Minority Institution Travel Award Program to give support to students and faculty from minority institutions to attend workshops, conferences, and courses relating to genomic research.

Research Projects

Over the next 3 years, the center plans to identify a core of minority students and established scientists interested in genomic research as a career and to work with them to develop individual action plans. For identified students and scientists, NCHGR will:

- Support travel to discuss training, proposals, and research plans with genome researchers; to attend courses and workshops; and to make short-term laboratory stays.
- Arrange seminars on grant writing.
- Monitor activities on a quarterly basis to ensure that the objectives of the plan are being achieved.
- Provide project developmental funds to allow investigators to spend time in laboratories learning new techniques, to purchase supplies and equipment, or to obtain release time to pursue new research ideas.

Ultimately, the expectation is that minority investigators will obtain support through the regular NIH grant mechanisms.

NCHGR plans to develop relationships with minority students and investigators that will make them an integral part of the larger community of human genome researchers. These associations will facilitate collaborations and provide timely access to the latest techniques, information, and resources.

The center also encourages its grantees to identify minority students and faculty members and encourage their participation in the Human Genome Project by making laboratory opportunities available and by acting as consultants or mentors on research projects. Individuals who would like to know more about the NCHGR initiative for minority scientists should contact Bettie J. Graham at 301/496-7531. ◇

Reported by Bettie J. Graham, Chief
NCHGR Research Grants Branch

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.

Managing Editor
Betty K. Mansfield

Editors/Writers
Anne E. Adamson
Denise K. Casey
Kathleen H. Mavournin
Joe L. Rich

Production Manager/Editor
Judy M. Wyrick

Production Assistants
K. Alicia Davidson
Larry W. Davis
Laura N. Yust

Special Thanks to:
John S. Wassom
Brad L. Whitfield

Correspondence Address:
Betty K. Mansfield
ORNL
P.O. Box 2008
Oak Ridge,TN 37831-6050

Phone: 615/576-6669
FTS 626-6669

Fax: 615/574-9888
FTS 624-9888

BITNET: "BKQ@ORNLSTC"
Internet: "BKQ@ORNL.GOV"

Sponsors:

Benjamin J. Barnhart
DOE Program Office
Germantown, MD
301/353-5037, FTS 233-5037
Fax: 301/353-5051
FTS Fax: 233-5051

Leslie Fink
NIH National Center for Human Genome Research
Bethesda, MD
301/402-0911
Fax: 301/480-2770

Genome News

HUGO Sees Innovation Thriving in European Research

HUGO Europe Meets in Frankfurt

At the first Human Genome Organisation (HUGO) meeting held in Europe, some 200 scientists from 16 countries assembled December 10–12, 1990, in Frankfurt, Germany, to discuss European genome research. Innovation was seen to be thriving in the broad range of methodological developments and applications presented.

The meeting, marking the first time that a German federal or private institution has contributed to a HUGO activity, was largely supported by the Federal Ministry of Research and Technology; the German Society for Chemical Equipment, Chemical Engineering, and Biotechnology (DECHEMA); and the European Community (EC).

The program of 38 oral and 49 poster presentations was planned to bring together scientists in medicine, molecular biology, and informatics and to foster interaction with national and European policymakers. Trends and strategies in genome research were the subjects of round-table discussions.

Several speakers reported attempts to create easily accessible data centers with internationally accepted data transfer standards; computer experts stated that future systems will have to be more flexible. Participants were impressed by the speed of degenerate homology searches using a massively parallel Active Memory Technology distributed-array processor with the Needleman-Wunsch-Sellers algorithm, as presented by Andrew Coulson (University of Edinburgh).

A. Goffeau (EC, Brussels) reported on EC funding in European genome research. The coordinated effort of 35 laboratories to sequence yeast chromosome III with standard nonautomated methods is almost complete. Within a 250-kb region, 196 open reading frames have been found: 19 already known; 25 homologous to known genes; 16 probable membrane proteins; and 136 temporary one-membered sets.

Fumihiko Matsuda of Tasuka Honjo's laboratory (Kyoto, Japan) described an impressive large-scale analysis of nine independent yeast contigs involving some 5.5 Mb and 71 V_H antibody genes that exhibited quite varied gene density within the contigs, from 21 V_H genes in one 380-kb region to 2 V_H genes in another region of 1.1 Mb. (V_H refers to the immunoglobulin heavy chain variable gene regions.)

A novel inverse polymerase chain reaction protocol from André Rosenthal (Medical Research Council, Cambridge) has been effective in short sequencing excursions or walks from any known sequence tagged site (STS) to the next restriction site of choice, currently with a range limited to about 4 kb [A. Rosenthal and D. S. C. Jones, *Nucleic Acids Res.* **18**(10), 3095 (May 25, 1990)].

The chromosomal physical-microdissection techniques of Bernhard Horsthemke (Institute for Human Genetics, Essen) and G. Senger (Institute for Human Genetics, Erlangen) were compared with the laser techniques of Bertrand Jordan (National Institute of Health and Medical Research, Marseilles) and K. O. Greulich (University of Heidelberg), along with examples of subsequent small-fragment cloning. A novel development by Greulich involves optical "pincers" to lift up and isolate the dissected chromosomal segment.

A technical breakthrough by A. Perrin (Pasteur Institute) that holds promise for future practical application is the characterization of an ultrarare-cutter restriction enzyme (18-bp recognition site). It would be valuable in combination with small, transposable elements or retroviruses for introducing unique cut sites into complex genomes [C. Monteilhet et al., *Nucleic Acids Res.* **18**(16), 1407–1413 (March 25, 1990)].

K. H. Grzeschik (University of Marburg), on behalf of those involved in genetic counseling, expressed the preference that STSs be derived from highly polymorphic regions rather than from cDNAs or highly conserved sequences, an approach designed to lead more directly to candidate genes.

Richard Benson (Center for Human Genetics and Biomedical Ethics, Leuven) reviewed ethical questions related to the Human Genome Project. He concluded that, while human genome research is not ethically neutral, a project that can make a unique contribution to the advancement of human health is not merely "something that would be nice to do," but ethically imperative. ◊

Reported by John Collins
National Biotech Research Center, Germany

Conference organizers

- **Walter Bodmer**
  Imperial Cancer Research Fund, London
- **Edwin Southern**
  University of Oxford
- **Glauco Tocchini-Valentini**
  University of Rome
- **Mark Lathrop**
  Centre d'Etude Polymorphisme Humain, Paris
- **Karl-Heinz Grzeschik**
  University of Marburg, Germany
- **Albert Driesel**
  DECHEMA Institute, Frankfurt
- **John Collins**
  National Biotech Research Center (GBF), Braunschweig

Workshop on International Cooperation for the Human Genome Project: Ethics

The Second Workshop on International Cooperation for the Human Genome Project: Ethics, sponsored by Fundacion Banco Bilbao Vizcaya and organized by Fundacion Valenciana de Estudios Avanzados, was held in Valencia, Spain, on November 12–14, 1990. Highlights of some of the many papers are given below.

The presentation by Eric Lander (Whitehead Institute for Biomedical Research and Massachusetts Institute of Technology) set the theme of the workshop. He said that gene mapping is the best way to find cures for genetic disorders, but the hiatus between the ability to predict and the ability to cure, as well as society's impatience in wanting to use research results prematurely, will raise challenging ethical questions.

Hans-Martin Sass (Ruhr University, Germany) described a rancorous debate occurring in Germany, where alternative groups have challenged genetic diagnostics as eugenic public health policy and bioethics as intended merely to gain acceptance of risky technologies.

Several speakers on religious considerations focused on differing attitudes toward reproductive intervention. The Catholic and Islamic speakers rejected any use of in vitro fertilization. The Jewish and Protestant speakers rejected absolute prohibitions and insisted, instead, on evaluation to ensure benefit and prevent misuse of genetic technology.

Eric Juengst [Director, Ethical, Legal, and Social Implications (ELSI) Program, NIH National Center for Human Genome Research] suggested that stigmatization and fatalism may be avoided by interpreting genetic risk markers in terms of contingencies, rather than predispositions, to emphasize the ability to protect individuals through non-genetic interventions.

Theodore Friedmann (Center for Molecular Genetics, University of California, San Francisco) observed that the question of appropriate target conditions and traits will become increasingly difficult. Albert Jonsen (University of Washington, Seattle) predicted that genetic information will reshape the traditional doctor-patient relationship, focusing more attention on family than individual, and creating presymptomatically diagnosed "unpatients" for whom no therapy is yet available.

Regarding the use of genetic information, John Fletcher (University of Virginia) reported international consensus on what guidelines for human geneticists should be. Dorothy Nelkin (New York University) advised paying heed to popular beliefs about genetic information in promoting its use. Neil Holtzman (Johns Hopkins School of Medicine) noted that individual autonomy can be reduced by screening and that public expectations need to be aligned with the limits of genetics.

Mark Rothstein (University of Houston Law Center) discussed the conflicting interests of individuals, employers, and society in preemployment screening. G. W. de Wit (Erasmus University, Rotterdam) argued that genetic information will be useful to insurers only in the case of single-gene diseases and, in such case, equality of information between insurer and insured must be enforced, at least for life and disability insurance.

Helen Donis-Keller (Washington University) described a commercial arena in which uniform laboratory standards have not been set and noted that competition does not necessarily produce high-quality results. Norman Fost (University of Wisconsin) discussed several issues related to carrier testing.

Daniel Kevles (California Institute of Technology) suggested that eugenics may continue to mislead, not for lack of good intentions, but simply because conclusions are scientifically wrong. Benno Muller-Hill

(see Ethics Workshop, p. 16)

Chromosome Meetings

Human Genome News wishes to publish notice of upcoming individual chromosome meetings in its "Calendar of Genome Events." Brief summaries of the meetings are also requested.

Please call the Human Genome Management Information System (HGMIS) for information on submitting meeting reports. Send pertinent calendar information, including the name and telephone number of a contact person, to the HGMIS address shown on page 20. ◇

Meeting Reports

Drosophila Genome Meeting

A workshop on *Drosophila* genome research, held in Madison, Wisconsin, on August 3–5, 1990, was cosponsored by the National Center for Human Genome Research (NCHGR) and the University of Wisconsin Graduate School. The meeting's goals included consideration of the following:

- the current state of *Drosophila* genome analysis,
- possible goals of *Drosophila* genome research, and
- possible strategies for achieving these goals.

In addition to investigators from the *Drosophila* community, the workshop was attended by representatives of the *Caenorhabditis elegans* genome project and by experts in sequencing technology and biocomputing. Because of the important issues raised and the limited number of workshop participants, attendees published a summary report of the proceedings. Readers may request a copy of the summary report from HGMIS at no charge.

Participants gave several reasons for their view that *Drosophila* research should be given a high priority in the allocation of funds for the genome initiative:

- Well-designed sequencing projects targeted on any of several loci on the *Drosophila* genome are likely to yield important, easily interpretable, and scientifically useful data to the research community as a whole.
- Many complex biological processes in humans are also found in *Drosophila*, and sequence analyses of selected regions of its genome are likely to provide important clues to the genetic control of analogous processes in humans.
- *Drosophila* is unique in that the polytene chromosomes already provide a high-resolution physical map to which the molecular map may be easily aligned.
- The P element and similar transposons promise to be powerful tools for enhancing genetic research and are likely to provide new methods for accessing other organisms' DNA for physical mapping and sequence analysis.
- The *Drosophila* genome's size allows reasonable expectation of a complete sequence analysis.

The workshop included reports from current and proposed *Drosophila* genome projects, discussions of genome analysis work being done on *C. elegans* and *Escherichia coli*, reports on current initiatives to manage information and strain maintenance and distribution, and a description of advanced sequencing technologies.

Reported by William S. Reznikoff
Department of Biochemistry
University of Wisconsin

Drosophila Workshop Recommendations

- Configure ongoing genome projects so that they share information with each other and with the *Drosophila* community.
- Place high priority on the development and maintenance of informatics systems.
- Initiate annual workshops, which will include *Drosophila* researchers not directly involved in genome programs, to help disseminate the fruits of the project and refine priorities reflecting the genome community's changing needs.

Workshop To Develop Paper on Database

The 32nd Annual *Drosophila* Research Conference in Chicago will include a March 23 workshop, chaired by Dan Lindsley (University of California, San Diego), to give updates on the *Drosophila* genome project and to develop a community position paper on computerizing the *Drosophila* database.

Contact: Anne Marie Langevin, 301/571-1825

Ethics Workshop *(from p. 15)*

(Genetics Institute, University of Cologne, Germany) argued for the sole right of the individual to know his or her genotype. William Bartholome (University of Kansas) called for the establishment of mechanisms to control the application of new genetic knowledge.

Conference speakers generally did not question the value of the Human Genome Project but expressed concern about genetic information uses and called for further ethical inquiry and public education.

The conference concluded with the presentation to Queen Sofia of the "Valencia Declaration on Ethics and the Human Genome Project," summarizing the participants' deliberations. ◇

Written by Michael S. Yesley
Coordinator, ELSI Activities
DOE Human Genome Program
Los Alamos National Laboratory

Human Genome Project Publications Win Awards

A poster, a program report, and a newsletter produced by the Human Genome Management Information System (HGMIS) at Oak Ridge National Laboratory were winners in the 1991 Society for Technical Communication/East Tennessee Chapter (STC/ETC) competition. The poster and program report are sponsored by the Human Genome Program of the DOE Office of Health and Environmental Research, and the newsletter is jointly supported by DOE and the NIH National Center for Human Genome Research.

Experts from the Delaware Valley STC chapter and other outside judges evaluated some 38 entries in the Technical Art Competition and 113 entries in the Technical Publications Competition on the basis of how well they fulfilled their function as technical communication publications. Winners of the Distinguished Technical Communication Award, the highest given, were automatically entered in the STC international competition to be held April 14–17 in New York City.

Distinguished Technical Communication Awards

- **Arts Competition** – Design Graphics and Presentation category: a poster, "DOE Human Genome Management Information System."
- **Publications Competition** – House Organs category: *Human Genome News*.

Merit Award

- **Publications Competition** – Periodic Activity Reports category: *Human Genome 1989–1990 Program Report*.

STC, with over 14,000 members in more than 120 chapters, is the world's largest professional organization devoted to the art and science of technical communication and one of the fastest growing professional societies. A network linking technical communicators all over the world, the purpose of STC is to keep both entry-level and veteran communicators aware of the latest trends in technical communication.

The newsletter staff wishes to thank those who have contributed articles and our sponsoring agencies' staffs, who have offered excellent suggestions and advice. ◇

U.S. Genome Research Funding Information

Note: Investigators wishing to apply for NIH or USDA funding are urged to discuss their projects with agency staff before submitting formal proposals. DOE requires no prior discussion on preproposals.

NIH National Center for Human Genome Research (NCHGR)

Application receipt dates:

- R01, P01, R21, P30, P50, and R13 grants – February 1, June 1, and October 1.
- Individual postdoctoral fellowships and institutional training grants – January 10, May 10, and September 10.
- Small Business Innovative Research Grants (SBIR: firms with 500 or fewer employees) – April 15, August 15, and December 15.
- Requests for Applications (RFAs) – receipt dates are independent of the above dates.

Program announcements are listed in issues of the weekly *NIH Guide for Grants and Contracts*, which may be obtained by:

- Hard copy subscription – call 301/496-7441.
- Remote log-in via modem to NIH Grant Line – call John James, 301/496-7554.
- Listserver computer network subscription – call Dottie Baker, 919/966-5625. Send E-mail requests to "pjones@uncvx1.bitnet" or "jones@samba.acs.unc.edu" (Internet).

Expanded statements of the RFAs listed in the NIH grants guide may be obtained from either of the two electronic sources or from NIH NCHGR in Bethesda, MD (301/496-0844).

DOE Human Genome Program

Solicitations for proposals were published in the February 20 issue of the *Federal Register*, in the February 22 *Science*, and in other publications. Investigators whose preproposals are accepted for programmatic relevance are notified to submit a formal proposal.

E-mail inquiries on Internet may be addressed to:

- "genome@oerv01.er.doe.gov"

SBIR Grants. DOE also invites small business firms to submit grant applications addressing the human genome topic of SBIR programs, which are designed to strengthen innovative firms in areas of research and development and to contribute to the growth and strength of the nation's economy. The human genome topic emphasizes instrumentation development for automated clone processing, improvements in DNA sequencing technologies, and enhanced sequence data storage and processing capabilities.

Selected firms may receive up to $50,000 to explore the feasibility of their ideas. In a second phase, up to $500,000 will be available to individual firms to support those ideas judged highest in potential for meeting program objectives. For a copy of the DOE solicitation, issued on December 7, 1990, contact: Samuel Barish; SBIR Program Manager, ER-16; DOE; Washington, DC 20585; 301/353-5707.

- SBIR grant application receipt date: March 7.

Human Genome Distinguished Postdoctoral Fellowships. Next deadline, winter 1992. ◇

Calendar of Genome Events*

March	19–21	**"Development and Application of Electrophoretic 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*]
April	4–5	*Chromosome 3 Meeting; Denver, Colorado; no abstract required [*Bob Gemmill, 303/333-4515*]
	8–9	***The Genetic Prism: Understanding Health and Responsibilities**; Berkeley, CA [*P. Boyle, 914/762-8500*]
	10–11	***Chromosome 21 International Workshop**; Denver, CO [*D. Patterson, 303/333-4515*]
	12	**Technological, Ethical, Legal, and Public Policy Implications of the Emerging Genetic Knowledge**; Oklahoma City, OK [*T. Bole, 405/271-2111*]
	18–20	**Conference on Biotechnology and the Diagnosis of Genetic Disease: An Assessment Forum on the Societal, Technical, and Regulatory Issues**; Arlington, VA [*S. Wilkinson, 202/687-5391*]
	18–20	***Genetic Counseling: Ethics, Values, and Professional Responsibilities**; Minneapolis, MN [*Meetings proceedings available from D. Bartels, 612/625-4917*]
	22–24	**"Workshop on Social Issues in Human Genome Research"** at **FASEB 1991**; Atlanta, GA [*E. Juengst, 301/496-7531*]
	29–30	**Ninth Annual ATCC Biotechnology Patent Conference**; Washington, DC [*P. Burke, 301/231-5524, Fax: 301/231-5826*]
May	8–12	***Genome Mapping and Sequencing Conference**; Cold Spring Harbor, NY
	15–17	**Nordic Genome Workshop**; Visby, Gotland Island, Sweden [*U. Pettersson, (Int.) 46/18-17-40-00, Fax: (Int.) 46/18-52-68-49*]
	15–18	**Genetics-Related Symposia** at the **82nd Annual Meeting of the American Association for Cancer Research**; Houston , TX [*M. Foti, 215/440-9300, Fax: 215/440-9313*]
	16	Symposium on **"Ethical Issues in Genetic Research in Psychiatry"** at the **American Psychiatric Association Annual Meeting**; New Orleans, LA [*P. Turgeon, 202/682-6170*]
June	1–5	**8th International *C. elegans* Meeting**; Madison, WI [*Registration: Memorial Union Conference Office, 608/262-2755; Technical: P. Anderson, 608/263-8429*]
	2–4	***Human Genome Research in an Interdependent World**; Bethesda, MD [*D. Wikler, 608/263-6287*]
	14–16	***Ethical and Legal Implications of Genetic Testing**; Berkeley Springs, WV (some papers to be published) [*E. Broughman, 202/326-6614/6600*]
	25	NIH Program Advisory Committee on the Human Genome; Bethesda, MD [*C. Mohan, 301/496-0844, afternoons*]
July	13	**Symposium on Social Issues in Human Genome Research** at the **International Society for the History, Philosophy, and Social Studies of Biology Conference**; Evanston, IL [*P. Stewart, 703/231-7687; Fax: 703/231-9307*]
	14–18	***Workshop at AAAI-91 Conference: AI Approaches to Classification and Pattern Recognition in Molecular Biology**; Anaheim, CA; [*M. Noordewier, 201/932-3698*]
	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, 512/471-2472, Fax: 512/471-2445, E-mail: "xxvb742@utchpc.bitnet" or "xxvb742@morpheus.chpc.utexas.edu"*]
	29–Aug. 2	***Gordon Research Conference on Molecular Genetics**; Newport, RI [*Gordon office, 401/783-4011, Fax: 401/783-7644*]
August	18–22	**11th International Workshop on Human Gene Mapping (HGM 11)**; London [*J. Crowther, (Int.) 44-71/269-3389, Fax: 44-71/430-1787*]

*Attendance at meetings listed with asterisk is either limited or restricted.

Calendar of Genome Events*

September	14–15	**The Human Genome Project: A Public Forum**; Alexandria, VA [*G. Bowles, 804/924-9477, Fax: 804/982-3650*]
	18–21	**14th Congress of the International Society of Forensic Haemogenetics**; Mainz, FRG [*P. Schneider, (Int.) 49/6131-172688/392118, Fax: (Int.) 49/6131-393183*]
	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**; ASHG, Washington, DC; abstract deadline: April 1 [*M. Ryan, 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, CA [*Scherago Assoc., Inc., 212/730-1050, Fax: 212/382-1921*]

*Attendance at meetings listed with asterisk is either limited or restricted.

Training Calendar: Workshops and Coursework

March	18	**DNA Amplification by PCR: Hands-On Training in Molecular Biology Laboratory Techniques**; BTP, Norton, MA (also offered at other times and locations) [*S. Chance, 515/232-8306 1:00–5:00 p.m. CST*]
	18–22	**Transfection Techniques**; LTI, Germantown, MD (also July 29–August 2) [*G. Tinney, 800/828-6686, Ext. 7,13 or 301/921-2250, Fax: 301/258-8212*]
	19–22	**Basic Cloning Techniques**; Norton, MA [*see contact: Mar. 18*]
April	2–5	**Linkage and Chromosome Mapping/Sequence Analysis**: Courses at U.K. Human Genome Mapping Project Resource Centre; Harrow, England (later dates also offered) [*C. Bates, (Int.) 44/81-869-3446, Fax: (Int.) 44/81-869-3807*]
	8–12	**Recombinant DNA Techniques I**; LTI, Germantown, MD (also May 6–10, July 8–12, September 16–20) [*see contact: Mar. 18–22*]
	8–22	**Cloning & Analysis of Large DNA Molecules**; Cold Spring Harbor, NY) [*CSHL, 516/367-8343, Fax: 516/367-8845*]
	15–19 & 22–26	**Recombinant DNA: Techniques and Applications**; ATCC, Rockville, MD [*D. Drabkowski, 301/231-5566, Fax: 301/770-1805*]
May	7–10	**RFLP Analysis: Hands-On Training in Molecular Biology Laboratory Techniques**; New Orleans, LA [*see contact: Mar. 18*]
June	3–8	**cDNA Library Workshop**; LTI, Germantown, MD (also October 7–12) [*see contact: Mar. 18–22*]
	10–15	**Recombinant DNA Techniques II**; LTI, Germantown, MD (also July 15–20, September 23–28) [*see contact: Mar. 18–22*]
	24–28	**Principles of Flow Cytometry: Hands-On Training in Molecular Biology Laboratory Techniques**; Ames, IA [*see contact: Mar. 18*]
July	1–21	**Molecular Cloning of Neural Genes**; Cold Spring Harbor, NY (application for attendance required) [*see contact: Apr. 8–22*]
	5–13	**DNA-Related Methods in Human Genetics: YAC Cloning in Genome Analysis**; London [*P. Faik, (Int.) 44/71-403-6998*]
	22–Aug. 2	**Short Course in Medical and Experimental Mammalian Genetics**; Jackson Laboratory, Bar Harbor, ME [*J. Musetti, 207/288-3371, ext. 1253, Fax: 207/288-5079*]
	23–Aug.12	**Yeast Genetics**; Cold Spring Harbor, NY (application for attendance required) [*see contact: Apr. 8–22*]
	23–Aug.12	**Advanced Molecular Cloning and Expression of Eukaryotic Genes**; Cold Spring Harbor, NY (application for attendance required) [*see contact: Apr. 8–22*]
August	5–12	**Genetic Approaches to Human Disease Using DNA Markers**; Cold Spring Harbor, NY [*see contact: April 8–22*]
October	8–21	**Analysis and Genetic Manipulation of YACS**; Cold Spring Harbor [*see contact: Apr. 8–22*]
	27–Nov. 5	**Essential Computational Genomics for Molecular Biologists**; Cold Spring Harbor [*see contact: Apr. 8–22*]

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.

AAAI	American Association for Artificial Intelligence
ASHG	American Society of Human Genetics
ATCC	American **Type Culture** Collection
BTP	Biotechnology Program
cDNA	complementary DNA
CEC	Commission of the European Communities
CF	cystic fibrosis
DECHEMA	German Society for Chemical Equipment, Chemical Engineering and Biotechnology
DNA	deoxyribonucleic acid
DOE	Department of Energy (U.S.)
EC	European Community
ELSI	Ethical, Legal, and Social Issues/ Implications
FASEB	Federation of American Societies for Experimental Biology
GBF	National Biotech Research Center (Germany)
GDB	Genome Data Base (HHMI, Johns Hopkins University)
HGCC*	Human Genome Coordinating Committee
HGM 11	11th Human Gene Mapping Workshop
HGMIS*	Human Genome Management Information System (ORNL)
HGMP	Human Genome Mapping Project (U.K.)
HGN*†	**Human Genome News**
HHMI	Howard Hughes Medical Institute
HIAA	Health Insurance Association of America
HUGO	Human Genome Organisation [International]
ICRF	Imperial Cancer Research Fund (U.K.)
IMACS	International Association for Mathematics and Computers in Simulation
JITF*†	Joint Informatics Task Force
LANL*	Los Alamos National Laboratory, Los Alamos, N.M.
LBL*	Lawrence Berkeley Laboratory, Berkeley, Calif.
LLNL*	Lawrence Livermore National Laboratory, Livermore, Calif.
LRF	Leukemia Research Fund (U.K.)
LTI	Life Technologies, Inc.
MRC	Medical Research Council (U.K.)
NCHGR†	National Center for Human Genome Research (NIH)
NIH†	National Institutes of Health
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.
OTA	Office of Technology Assessment
PACHG†	Program Advisory Committee on the Human Genome (NIH)
PCR	polymerase chain reaction
RFA	Request for Applications
RFLP	restriction fragment length polymorphism
SBIR	Small Business Innovative Research
STC/ETC	Society for Technical Communication/ East Tennessee Chapter
STS	sequence tagged site
TCP/IP	Transmission Control Protocol/Internet suite of protocols
USDA	U.S. Department of Agriculture
YAC	yeast artificial chromosome

HGMIS MAILING ADDRESS
Betty K. Mansfield
Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, TN 37831-6050

Comments:

Human Genome Management Information System

Subscription/Document Request (Vol. 2, No. 6)

1. ___ **Human Genome News**
   ___ New Subscriber ___ Change of Name/Affiliation/Address ___ Drop Name from mailing list
2. ___ **Human Genome Information Database**
3. ___ **DOE Human Genome 1989–90 Program Report**
4. ___ **Understanding Our Genetic Inheritance, The U.S. Human Genome Project: The First Five Years, FY 1991–1995 (Joint DOE-NIH 5-Year Plan)**

Please type or print. Enclose previous newsletter address label or business card, if possible.

Name: _____ **Phone:** _____
(First) (MI) (Last)

Affiliation: _____

Mailing Address (business or home, please circle): _____

_____

_____

E-Mail Address: _____ **Fax:** _____