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Human Genome news

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NCHGR Begins Unified Framework Map Effort

Expected to facilitate gene hunting

Investigators funded under the NIH National Center for Human Genome Research (NCHGR) Human Genome Program have begun a new, unified effort to develop a framework map of index markers for each chromosome of the human genome. Expected to take 2 to 3 years to complete, these maps will consist of an ordered set of special, high-quality index markers that will help scientists pinpoint genes or other genetic determinants more quickly. Once investigators narrow down a gene's location to an interval on the framework map, they can limit their search to the chromosome segment between the specific index markers.

Individual Investigators Assume Responsibility for Specific Chromosomes

"This is a crash program to get a series of really good markers out into the hands of the research community quickly so they can use them to go after genes," says James D. Watson, Director of NCHGR. "The plan is that the markers will go into a central repository where they will be available to everyone." The location of this repository is pending.

The concerted NCHGR effort to construct index maps grew out of a 1990 meeting of the NIH-DOE Joint Mapping Working Group.

This is a crash program to get a series of good markers to the research community quickly so they can use them to go after genes.
— James D. Watson

On March 22 in Salt Lake City, meeting participants noted that only a small fraction of the human chromosomes were well mapped. They identified as high priority the development of a framework map composed of about 300 highly polymorphic markers spaced 10 cM apart. The participants also agreed that the process would be speeded up by asking individual investigators to assume responsibility for seeing that the framework maps of specific chromosomes were completed.

The NIH Program Advisory Committee on the Human Genome approved the plan on June 18. A request for research project grant

In This Issue. . .

Genome News

NCHGR Index Marker Mapping Projects

NCHGR is supporting index mapping of the following human chromosomes, listed with the investigator responsible for each:

1 – Nicholas Dracopoli (Massachusetts Institute of Technology)

2, 6, 7, 8, 12, 14 – Helen Donis-Keller (Washington University in St. Louis)

3 – Sue Naylor (University of Texas Health Sciences Center)

4 – Jeff Murray (University of Iowa)

5, 16, 17 – Ray White (Howard Hughes Medical Institute and University of Utah)

9 – Dave Kwiatkowski (Massachusetts General Hospital)

10, 20 – Tim Keith (Collaborative Research, Inc.)

11 – Mike Litt (Oregon Health Sciences University)

13, 15 – Anne Bowcock (University of Texas Southwestern Medical Center)

18 – Conrad Gilliam (Columbia University)

19 – Jim Weber (Marshield Medical Research Foundation, Wisconsin)

22 – Jonathan Haines (Massachusetts General Hospital)

applications (RFAs) was issued shortly after, and grants have now been awarded (see box above).

The goal of the Human Genome Project for linkage mapping is to eventually develop a map on which DNA markers, each identified by a sequence tagged site, are spaced an average of 2 cM apart with no gaps greater than 5 cM. Framework maps of index markers are part of the plan to produce a highly detailed genetic linkage map of the human genome. Genetic linkage maps, which describe the order of and distance between markers and genes, are made by following the inheritance of traits in families. Because traits that are frequently inherited together are usually close together on a chromosome, researchers can use a nearby landmark that is easier to monitor to follow the inheritance of another trait.

About 2000 polymorphic human markers have been isolated, but 90% of these do not have high enough frequency of variation in the population to be incorporated into a framework map. In addition, their distribution is not evenly spaced throughout the genome. The currently available markers produce a map in which some regions contain a number of tightly clustered markers while other areas have few or none. The framework map will differ from existing linkage maps in that all markers will be particularly scientifically and medically useful. ◇

HGMIS Requests Information

Human Genome Management Information System (HGMIS) staff request information from our readers so we may compile useful resources, keep our subscribers more up to date on the genome project, maintain a current and inclusive calendar, and increase our knowledge and resources for use in constructing newsletter articles.

HGMIS would appreciate receiving notification about the following from investigators in the United States and abroad:

- Genome-related meetings (including those outside the United States), with dates, locations, and contact people's names, telephone and fax numbers, and e-mail addresses if available. We would also like to be on mailing lists to receive updates about planned meetings.
- Bibliographic citations and reprints of genome-related articles.
- Names and contact information for investigators working on each human and mouse chromosome as well as announcements of specific chromosome workshops for our calendar.

Send material to the address below:

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Oak Ridge National Laboratory
P.O. Box 2008
Oak Ridge, TN 37831-6050
615/576-6669, FTS 626-6669
Fax: 615/574-9888, FTS 624-9888
Internet: "bkq@ornl.gov"
BITNET: "bkq@ornlstc"

HGMIS staff wish to thank those who share this information with us for their cooperation and generosity. As always, we appreciate receiving comments and suggestions on how we can better serve our readers. ◇

Children's Hospital of Philadelphia Receives Human Genome Center Grant

The Children's Hospital of Philadelphia (CHOP), in collaboration with the University of Pennsylvania School of Medicine, has been awarded a $10-million, 5-year grant by the NIH National Center for Human Genome Research to establish a Human Genome Center. Under the leadership of principal investigator Beverly Emanuel and scientific director Robert L. Nussbaum, the new center will focus on the development of human chromosome 22 maps. The first hospital in the nation to be designated a genome center site, the CHOP center will receive $1,966,890 the first year. The research consortium will have collaborative components at the Fox Chase Medical Center and the DuPont Merck Pharmaceutical Company.

Abnormalities of chromosome 22, the smallest human chromosome, are associated with eight types of cancer and a number of birth defects. By studying the genes on chromosome 22, researchers can begin to understand the causes of these disorders. Investigators will use a variety of new technologies to locate some 300 anchor markers at regular intervals along the chromosome. They will also use yeast artificial chromosomes as cloning vectors to subdivide the chromosome into an ordered collection of DNA fragments. Once isolated, this set of fragments spanning the entire chromosome will be available to the scientific community for use in locating and isolating important genes.

"This Human Genome Center offers a great benefit to society by bringing scientists together to share technology in a cost-effective approach to research," Emanuel said. "Over the years, this collaboration should produce great health benefits for future generations of children and adults." ◇

Emanuel and Nussbaum Lead Research Consortium

Strausberg Heads NCHGR Technology Development Program

Leading the NIH National Center for Human Genome Research (NCHGR) search for new technologies is Robert L. Strausberg. Strausberg's recent selection for this critical staff position ended a nationwide search for a candidate with a broad perspective based on experience in both academia and the biotechnology industry. His task is to champion promising research proposals and to coordinate the burgeoning NCHGR technology development program.

As Director James D. Watson's Assistant for Technology Development, he will ensure that the need for rapid large-scale mapping and sequencing technology development is addressed. Strausberg will act as an advocate for researchers with unique and exciting ideas for new technologies and will foster the integration of these technologies into the NCHGR overall research plan.

In his additional role as Director of the Technology Development Program, Strausberg will be responsible for the management of grants to develop cost-effective large-scale DNA sequencing, focusing on reducing the cost. He will encourage multidisciplinary collaboration within large research projects and organize workshops and working groups for those interested in particular areas of technology development.

Strausberg also anticipates advising university and industry researchers about how to participate in the Human Genome Project. He plans to make a concerted effort to elicit suggestions from individuals on ways NCHGR can be more helpful in facilitating their research efforts. "Even if they currently have no background data, no track record, etc., I'm still eager to talk with those researchers who have novel ideas for large-scale sequencing and mapping. NCHGR wants to encourage innovation and fund projects with potential," he stated.

Strausberg received his Ph.D. in developmental biology from Ohio State in 1976 and later held a postdoctoral fellowship in biochemistry at Southwestern Medical School in Dallas. After serving as Assistant Professor of Biology at Southern Methodist University in Dallas, where his research focused on yeast molecular biology, Strausberg joined Genex Corporation. At Genex his research group was responsible for DNA sequencing and synthesis, cDNA and genomic cloning, and expression of foreign genes in yeast and *Escherichia coli*. ◇

Robert L. Strausberg
Director of the NCHGR
Technology Development
Program

NCHGR To Encourage Innovation

Genome News

Daniel W. Drell
Biologist
DOE Human Genome Program

DOE Program Names Drell to Staff

Daniel W. Drell recently joined Benjamin Barnhart and Marvin Stodolsky on the Human Genome Program staff of the DOE Office of Health and Environmental Research in Washington, D.C. His responsibilities as Biologist will include physical mapping and cDNA technologies; postdoctoral training programs; and ethical, legal, educational, and social issues in the use of data generated by genome research. He will also work with the NIH-DOE Joint Working Group on the Mouse and as liaison this summer to the NIH National Center for Human Genome Research.

Drell, an honor graduate from Harvard College with a B.A. in biology, received his Ph.D. in immunology from the University of Alberta in Edmonton, Canada. He held postdoctoral positions at Sloan Kettering Institute, Rockefeller University, and Baylor College of Medicine. Drell then worked as a Staff Fellow in the Laboratory of Oral Medicine, NIH National Institute of Dental Research. He comes to DOE from the HLA Laboratory of the American Red Cross, after having served 2 years as Assistant Professor of Medicine at George Washington University Medical Center and Associate Director of its immunogenetics and immunochemistry laboratories.

Drell's past research has been in transplantation immunogenetics and tolerance and hybridoma production to a variety of antigens, including early mouse embryonic antigens, rabbit zona pellucida antigens, and antigens of human tumors. More recently, he has done research on the immunology of Type I diabetes mellitus and has worked on molecular biological methods of HLA-tissue typing. ◇

DOE Staff Now Numbers Three

Mouse Working Group Developing Strategies

The first meeting of the NIH-DOE Joint Working Group on the Mouse was held in Bethesda, Maryland, on May 6. Attendees were welcomed by Elke Jordan, Deputy Director, NIH National Center for Human Genome Research (NCHGR) and David Galas, Associate Director, DOE Office of Health and Environmental Research (OHER). Jordan indicated that the task of the working group is to help NIH and DOE determine the role of the mouse in the Human Genome Project and to develop a strategy for efficiently using the mouse to accomplish project goals [*HGN* **3**(1) 10 (May 1991)] as outlined in the 5-year plan.

The meeting opened with a discussion of the value of model organisms in the genome project. Several features make the mouse an important model organism:

- functional genes and other unique DNA probes can be efficiently analyzed and placed onto well-ordered genetic maps, which can be related to the genomes of humans and other species by exploiting conserved syntenic homologies;
- mutants can be generated to study gene function; and
- multigene traits, lethal mutations, and spontaneous mutations that may not be observed in humans can be studied more easily.

Strategies for completing the mouse genetic and physical maps are still evolving, but much progress has been made on the maps of simpler organisms. Physical maps of the intestinal bacterium *Escherichia coli*, the yeast *Saccharomyces cerevisiae*, and the nematode *Caenorhabditis elegans* are complete or nearly so, and sequencing of their genomes has begun. In addition, significant progress has been made in constructing a physical map of the fruit fly *Drosophila melanogaster*.

DOE and NIH agency representatives summarized research being conducted under the Human Genome Project.

Benjamin Barnhart, Manager, OHER Human Genome Program, stated that DOE has had a longstanding interest in studying model organisms through its Radiation Biology and Chemical Toxicology programs. Most recently, program emphasis has been on mechanistic studies (i.e., mechanisms of radiation and energy-related chemical damage causation). Currently, DOE annual support for the mouse is around $8 million; however, these projects, which include the large resources of mouse mutants at Oak Ridge National Laboratory and studies on mutagenesis, carcinogenesis, development, and reproduction, are not within the scope of the Human Genome Project.

Galas said that although NIH has more responsibility to support model organisms, DOE is exploring new ideas and examining how its national laboratories can respond

Next Mouse Working Group Meeting:
September 15,16

Topic:
Mouse Genetic Map

to the overall effort. He indicated that DOE intends to maintain some flexibility in supporting such projects. Discussion followed about ways to make national laboratory resources available to the general mouse scientific community.

Bettie Graham (NCHGR) reported that NCHGR support for 12 mouse-related research projects totals $5.3 million in FY 1991:

- ten investigator-initiated R01 research projects primarily to support genetic mapping,
- one R01 project to develop software tools that permit access to diverse databases, and
- one center grant to develop a complete physical map of the mouse genome.

To facilitate information exchange and to coordinate research findings, the mouse community has established 21 chromosome-specific committees, one for each of the 19 autosomes and the X and Y chromosomes [see *HGN* 3(1), 11 (May 1991)]. This varied representation was considered useful because several ideas would be allowed to flourish and, with time, a consensus could be reached on the best way to display map information. Committee reports will appear this year as a supplement to *Mammalian Genome*.

Verne Chapman (Roswell Park Cancer Center) summarized meetings in Princeton, New Jersey; the United Kingdom; and Annapolis, Maryland. He expressed pleasure that the mouse community has come together to agree on common research goals for the next 3 to 5 years and to cooperate with NIH and DOE in accomplishing genome project objectives. Mouse research goals:

- *Genetic Map* – Establish 320 reference loci spaced 5 cM apart on each chromosome.
- *Physical Map* – Develop a physical map of regions of particular genetic interest with the long-term goal of constructing an ordered set of recombinant clones spanning the whole genome.
- *Databases* – Collect, integrate, analyze, display, and disseminate mouse genomic information. Efforts will be made to work with the Genome Database at Johns Hopkins University to provide users with integrated mouse and human genome data.
- *Sequencing* – Sequence genome regions that are of biological interest (genes and other selected regions).

Joseph Nadeau (Jackson Laboratory) described several mouse mapping resources under development in the United States, Europe, and Japan, including

- dinucleotide repeats for genetic mapping;
- new methods and tools for analyzing data (such as a two-dimensional gel electrophoresis method being developed in Japan);
- yeast artificial chromosome and P1 vectors for constructing physical maps; and
- databases, including the object-oriented database being developed as part of the NCHGR mouse genome center led by Eric Lander at the Massachusetts Institute of Technology.

Working group members also discussed briefly what the mouse research community needs to do to make effective and efficient contributions to the Human Genome Project. These topics will be explored more fully in future meetings:

- maintenance of existing databases and development of additional ones;
- preservation and development of mouse resources (mapping panels, recombinant inbred strains, DNA, etc.);
- research support for constructing genetic and physical maps and for studying conserved synteny and gene function between mouse and human; and
- development and application of state-of-the-art technology. ◊

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

Mouse Working Group Contact:

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Mouse Workshop To Emphasize New Technologies, Other Areas

The Fifth International Mouse Genome Mapping Workshop will be held October 14–18 in Lunteren, the Netherlands. The program will concentrate on general strategies of genome analysis with emphasis on new technologies; logistical problems; sharing probes, oligonucleotides, and other resources; mouse models; biological resources; and informatics. Sufficient time will be allocated for individual chromosome committee meetings.

Abstracts of proposed presentations are required by August 1. Detailed information about the program, registration, facilities, accommodations, and transportation may be obtained from the workshop secretariat. Contact: Marlijn Sonne; Netherlands Cancer Institute, H4; Plesmanlaan 121; 1066 CX Amsterdam, the Netherlands; (Int.) 31/20-512-1990; Fax: (Int.) 31/20-617-2625. ◊

Genome News

JITF Reports Activities, Identifies Needs

The third meeting of the Joint Informatics Task Force (JITF) was held in San Francisco on March 14 and 15. Members attending were Dieter Soll (Chairman), George Bell, David Botstein, Elbert Branscomb, Nathan Goodman, Frank Olken, Sylvia Spengler, and Michael Waterman; liaison members included David Benton, James Cassatt, Steve Heller, Robert Robbins, and Keith Russell. [For a complete list of members and affiliations, see *HGN* **2**(1), 10–11 (July 1990) and **2**(2), 10 (September 1990).] Brief reports on current informatics activities were presented by NIH and DOE staff.

Task Force Recommends Workshops

Goodman and Branscomb reported on activities of the JITF ad hoc subcommittee on laboratory notebook software. The subcommittee, commissioned at the second meeting of JITF, recommended conducting workshops to foster open communication of genome informatics issues and information. Possible workshop topics include laboratory data management, data sharing and data submission to public databases, and research priorities and action items for the funding agencies and their biologically oriented advisory committees.

During the general discussion, several needs were identified for future consideration:

- Technical workshops at which operational laboratory data management software could be described and demonstrated for genome project investigators, center directors, and their information management specialists.
- Determination of requirements for supporting data in public mapping databases and addressing issues of representing data errors and confidence estimates in the public databases.
- Catalog of currently funded genome informatics research and development.
- Bibliography of published genome informatics work.
- Announcements of all genome project RFAs and RFPs in *Human Genome News*, as well as in the usual places of publication.

JITF Sees Need To Inform Review Panels of Data Management Criteria

Also discussed was the need to provide guidance to grant-review panels on criteria for data management components of large-scale mapping and sequencing projects. The task force enumerated several points for evaluation of proposed data management systems, specifying the need for adequacy in these areas:

- quality control, sample tracking, and overall project management;
- permanence, completeness, and data storage safety;
- data input/output rate (sufficient for the anticipated data entry and query load);
- genomics community access;
- data protection from unauthorized access or modification; and
- integration with related databases.

Review panels should be advised that other issues (e.g., hardware, operating system, or database management system) are to be considered only to the extent that they influence system adequacy and economy when evaluated according to the above criteria.

The remainder of the meeting was devoted to a wide-ranging discussion of methods for producing a report on the state of genome informatics for the NIH-DOE Joint Subcommittee on the Human Genome. Several broad issues were considered for inclusion in the report:

- enabling technologies,
- laboratory data management,
- public databases,
- networks and connectivity,
- human resources development,
- standards and guidelines, and
- review and funding.

In general, the report will attempt to be descriptive rather than normative and to provide sufficient detail to enable readers to assess the merits of the various approaches presented. The task force expects the audience for this report to include the joint subcommittee, federal agencies involved in the genome project, current and potential genome researchers, government officials, and the interested public.

The next meeting of JITF is tentatively scheduled for mid-November. ◊

Reported by David Benton
Assistant to the Director
for Scientific Data Management
NIH NCHGR

Genome News

HUGO Plans Single-Chromosome Workshops

Single-chromosome workshops are playing an increasingly important role in the international Human Genome Project. The Human Genome Organisation (HUGO) has made planning and running these workshops a central part of its activities.

HUGO offices in Bethesda (Maryland) and London now keep updated records related to single-chromosome workshop times and locations. The office staff can help with information about funding sources, and a common format for application to funding agencies is being worked out to ease the process of getting financial support.

HUGO requests workshop plans and contact information.

Persons who know of more contact people for the workshops listed or of plans for other workshops are asked to communicate this information to either of the HUGO offices listed at right and to HGMIS for inclusion in the calendar of genome events (see address, p. 2). ◇

CHROMOSOME	DATE	PLACE
2	October	Washington, D.C.
16	February 1992	Adelaide, Australia
13	Spring 1992	Sardinia
3	1992	Japan
19	1992	Netherlands
X	1992	Italy

CHROMOSOME MEETING CONTACTS*

2: N. Spurr [(Int.) 44-707-44444 x 353, Fax: (Int.) 44-707-49527]
16: E. Hildebrand [505/667-2793, Fax: 505/665-3024, E-mail: "hilde@flowvax.lanl.gov"]; G. Sutherland, [(Int.) 61-8/267-7284, Fax: (Int.) 61-8/239-0417]
13: A. Bowcock [214/688-3388, Fax: 214/688-8617]
3: Y. Nakamura [(Int.) 81-3/3918-0111 x 4501, Fax: (Int.) 81-3/3918-0342]
19: H. H. Ropers [(Int.) 31-80/61-40-17, Fax: (Int.) 31-80/542-151]
X: D. Toniolo [(Int.) 39-382/527-967, Fax: (Int.) 39-382/422-286]

*Additional contacts will be listed in later issues as they become known.

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179 Great Portland Street
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(Int.) 44-71/436-7178
Fax: (Int.) 44-71/436-1988

Meeting Reports

U.K. Genome Mapping Project Users' Meeting

The Medical Research Council (MRC) Human Genome Mapping Project (HGMP) held its Users' Meeting April 19 at the Royal College of Physicians in London. About 300 scientists attended the meeting, which included a discussion of HGMP and its resources, two scientific presentations, and a summary of national and international activities.

HGMP and Its Resources

Project Manager Tony Vickers (HGMP Resource Centre) stated that HGMP is entering the last year of a 3-year program. The budget has been relatively flat each year, with £4.5 million (about $8 million) budgeted for the final year. Future HGMP funding will be included in the MRC baseline budget, giving all U.K. researchers equal access to available funds.

Lewis Wolpert, Chairman of the HGMP Directed Programme Committee, stated that since its initiation, HGMP has spent £6.5 million (about $11.5 million) to support 54 grants; funds were divided equally between university researchers and MRC laboratory researchers. Thirty-three doctoral studentships have been supported, and senior fellowships are available.

The MRC strategy in the cDNA program is to sequence about 300 bases from each cDNA and to use a computer program to look for homologous sequences in databanks. Over 2000 cDNA clones have been analyzed, and about 700 clones partially sequenced; HGMP expects to have an additional 5000 new cDNAs sequenced by April 1992. The cDNA strategy is being pursued because funds are limited and HGMP considers these expressed genes to be the most biologically interesting part of the genome.

Possible uses for cDNAs were discussed:

- mapping sorted chromosomes or somatic cell hybrids,
- making global P1 libraries to fill gaps between cosmids and yeast artificial chromosomes,
- making gridded cDNA libraries, and
- stimulating additional sequencing.

The DNA Probe Bank is testing an oligonucleotide service. Current priorities include the acquisition of mouse minisatellite

HGMP To Pursue cDNA Strategy

For a description of the United Kingdom Human Genome Mapping Project, see *HGN* 2(6), 1–3 (March 1991).

Meeting Reports

MRC Users Meeting Hears Reports

- Mouse, pig, sheep projects
- HUGO
- EC
- Academia Europaea
- NCHGR

sequences from J. A. Todd's laboratory (John Radcliffe Hospital), 300 human C-A minisatellites, and sequences from index markers as they become available from the U.S. National Center for Human Genome Research (NCHGR).

Scientific Presentations

Todd discussed his work on microsatellites analyzed by polymerase chain reaction (PCR) for genetic mapping in the mouse. He is working with a mouse model of Type 1 insulin-dependent diabetes mellitus and has identified 233 mouse microsatellites, half of which come from cDNA sequences. The majority are dinucleotide repeats randomly distributed over the genome.

Nicola J. Royle (University of Leicester, U.K.) reported on the isolation of human telomere junction fragments by an anchor PCR strategy. She has identified a new family of minisatellites found in the proterminal region of some mouse and primate chromosomes.

Other National and International Activities

Bettie J. Graham (NCHGR) gave a presentation on the NCHGR program, stressing that the Human Genome Project is international in scope and that cooperation and collaboration are important to its success.

Diane McLaren (U.K. HGMP Secretariat) discussed the following recommendations from the European Science Foundation report on genome research:

- Agreement by national funding agencies on attitudinal consistency and expectations regarding the European Community (EC) and the Human Genome Organisation (HUGO).
- Integration and disciplined scientific planning and assessment in EC-sponsored genome research programs.
- Encouragement of HUGO to develop a framework for partnership between European efforts and those of other countries.
- Promotion of consolidated European involvement in the Genome Database (Johns Hopkins University) and in chromosome workshops.
- Development of shared facilities when they offer improved speed, reliability, and cost-effectiveness.
- Consideration of practical consequences of genome research (e.g., medical implications; better understanding of genetic diseases having a European distribution; and ethical, legal, and political issues).
- Incorporation of the European scientific community's ideas and enterprise.

Kay Davies (Oxford Institute of Molecular Medicine, U.K.) reported on the Academia Europaea, which was founded in 1988 and has about 1000 members representing medical sciences, humanities, and technical areas. The purpose of the organization is to suggest to European funding bodies the most promising work to be pursued. The Academia Europaea recently made the following recommendations about genome research:

- cDNAs should be sequenced rather than the entire genome.
- Comparative studies of model organisms are essential.
- The program should include other organisms, such as viruses, parasites, and plants.
- Funds should not be diverted from general research to support the genome program.
- Major countries should establish genome centers.
- Coordination with HUGO is important.

Bronwen Loder [EC and HUGO] reported on the EC Human Genome Analysis Program, which has been supported with about 15 million ECU (European currency units) over the past 2 years. She indicated that EC can expedite requests for chromosome-specific workshops and encouraged scientists to apply for support. Elizabeth Evans (HUGO) reminded participants that HUGO was established for investigators and recommended that they use its services.

Alan L. Archibald (U.K. Agricultural and Food Research Council) described a pig genome mapping project involving 16 laboratories in 8 European countries, which aims to develop low-resolution genetic and physical maps and a reference family panel. The following reasons were given for studying farm animals:

- They have large families, a short generation time, and a well-defined karyotype.
- They are excellent animals for studying quantitative trait loci.
- They have been used extensively as models in many biological experiments.

Pig genome research results so far include identification of 40 restriction fragment length polymorphisms, 10 variable number

(see MRC Users Meeting, p. 9)

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.

Second International Workshop on Chromosome 17

Thirty-six scientists from the United States, the United Kingdom, and Australia attended a workshop on chromosome 17 in Park City, Utah, on March 15–16. The workshop was sponsored by NIH and the U.K. Medical Research Council to compile chromosome 17 mapping and resource information and to coordinate sequence tagged site (STS) development and yeast artificial chromosome (YAC) screening efforts.

Mapping Information

Genetic mapping

Genetic mapping data were presented for over 200 polymorphic markers. Pamela Fain and David Barker (University of Utah) presented a framework map that included 32 uniquely ordered markers (1000:1 odds). Peter O'Connell, Rose Plaetke, and Ray White (University of Utah and Howard Hughes Medical Institute) reported a framework map of 40 markers, 13 of which were common to the two maps. A total of 17 markers met the heterozygosity criteria for index markers (over 70%).

Fain and Richard Kouri (BIOS Corporation) have constructed crossover maps for all meioses in 40 Centre d'Etude du Polymorphisme Humain (CEPH) reference families in preparation for high-resolution genetic mapping using meiotic mapping panels.

Regional mapping

David Ledbetter (Baylor College of Medicine) described two YAC contigs in the Miller-Dieker lissencephaly syndrome region (MDS; 17p13.3). Several researchers agreed on a consensus localization of CMT1 (Charcot-Marie-Tooth disease locus) to a 6- to 10-cM interval in 17p11.2, distal to SMCR (Smith-Magenis syndrome locus) and markers D17S71 and D17S122 and proximal to markers D17S124 and D17S460. They were Philip Chance (University of Utah School of Medicine), Kelian Chen and Kenneth Fischbeck (University of Pennsylvania School of Medicine), Roger Lebo (University of California, San Francisco), Pragna Patel (Baylor College of Medicine), David Ross (University of Sydney, Australia), Charles Schwartz (Greenwood Genetics Center), and Jeff Vance (Duke University Medical Center).

In other reports, Kenneth Kidd (Yale University) described a 140-kb cosmid contig of a homeobox (HOX2) region and an 80-kb contig around the nerve growth factor receptor locus (NGFR). Ellen Solomon [Imperial Cancer Research Fund (ICRF)] related that several groups in the breast cancer consortium have confirmed genetic linkage between early-onset breast cancer and D17S74 in a subset of early-onset

(continued)

A more detailed report of resources and mapping information presented at the workshop will be published in *Cytogenetics and Cell Genetics.*

MRC Users' Meeting *(from p. 8)*

tandem repeats, and 10 microsatellite DNA fragments; physical mapping of 55 probes; and establishment of 100 new somatic cell hybrid lines. Investigators are evaluating a chromosome 1–specific library and developing a flow-sorted chromosome-specific library.

John Edwards (University of Oxford) spoke briefly on the New Zealand sheep map project, including plans to initiate collaborations with the U.K. genome initiative. ◊

Bettie J. Graham, Chief
Research Grants Branch
NIH NCHGR

Newsgroup Transfers to BIOSCI

The *Arabidopsis* Newsgroup, operated since July 1990 at Michigan State University, is now a part of BIOSCI at Genbank®. To send postings to the newsgroup, mail to the most convenient site:

Address	Location	Network
"arab-gen@genbank.bio.net"	United States	Internet/BITNET
"arab-gen@irlearn.ucd.ie"	Ireland	EARN/BITNET
"arab-gen@uk.ac.daresbury"	United Kingdom	JANET
"arab-gen@bmc.uu.se"	Sweden	Internet

Arabidopsis messages are also carried over USENET in the newsgroup bionet.genome.arabidopsis. USENET users can now post messages directly into the USENET newsgroup but should be sure to set the message distribution to "world" when prompted by the postnews software.

To resolve problems with the *Arabidopsis* newsgroup, contact the local BIOSCI node at one of the following addresses.

Address	Location	Network
"biosci@genbank.bio.net"	United States	Internet/BITNET
"biosci@irlearn.ucd.ie"	Ireland	EARN/BITNET
"biosci@uk.ac.daresbury"	United Kingdom	JANET
"biosci@bmc.uu.se"	Sweden	Internet

Note that there are separate e-mail addresses for the United Kingdom and Europe. One Swedish address is given for Europe. The remaining mail addresses are on the list at "genbank.bio.net". ◊

Meeting Reports

Chromosome 17 contact:
Pamela Fain
University of Utah
Salt Lake City, Utah 84108
801/581-5070
Fax: 801/581-6052

families. Jeff Hall (University of California) presented linkage data suggesting that a cancer-predisposing gene is distal to D17S74.

Resources

Somatic Cell Hybrids

A somatic cell hybrid panel developed by Ledbetter and coworkers has been deposited in the Human Genetic Mutant Cell Repository at the Coriell Institute in Camden, New Jersey. The panel consists of a chromosome 17-only hybrid and ten translocation or deletion breakpoints that divide the chromosome into ten intervals.

Four other somatic cell hybrid panels are available for chromosome 17, including chromosome-mediated gene transfer hybrids and radiation hybrids reported by Solomon and microcell hybrids and radiation hybrids reported by Robin Leach (University of Texas). Participants agreed that testing a common set of markers against all hybrids is essential to constructing a composite breakpoint map.

STSs

Sixty-two STSs are available for chromosome 17, including 40 from cloned genes, 7 from C-A repeats or other highly polymorphic loci, and 15 from other anonymous DNA markers. Participants agreed to avoid duplication of effort by sharing their plans to develop STSs and other freely available probes for reference markers.

YAC Screening Efforts

Principles and policies for a joint YAC screening effort were discussed. Groups at the University of Michigan (17q) and Baylor College of Medicine (17p) will perform initial screening using the Washington University YAC library, which will be merged with a chromosome 17 set of 36 YACs from Leiden University and the University of Pennsylvania. An advisory committee was appointed to monitor the screening effort.

Two other YAC libraries currently being developed for screening chromosome 17–specific sequences include the CEPH YAC library by White and Hans Albertsen at the University of Utah and a new YAC library by Tony Monaco and Hans Lehrach at ICRF in London.

A flow-sorted chromosome 17 cosmid library constructed by Dean Nizetic (ICRF) and Lehrach has been arrayed and stamped onto 2 high-density filters, each containing 10,000 cosmid clones. A general policy statement for use of these filters was distributed for comments and amendments. An array of cosmids made from flow-sorted material has also been prepared at Los Alamos National Laboratory.

Availability of Resources and Mapping Information

Participants agreed that all materials and resources presented at past and future workshops would be accessible to group members within 6 months of the workshop. YACs identified through the joint screening effort will be available immediately to all participants who contribute markers. A database and communication system for distributing information relating to the status of STS production and YAC screening will be developed during the coming year. ◇

Reported by Pamela Fain
University of Utah
Salt Lake City, Utah

Oak Ridge Exon Recognition System Online

Investigators in the Biology and Engineering Physics and Mathematics divisions at Oak Ridge National Laboratory are constructing an intelligent computational system to recognize and interpret genes and other biologically significant features in human DNA - sequence data. The first component of this gene recognition system is now accessible through Internet.

Gene Recognition and Analysis Internet Link (GRAIL), a simple user interface, allows users to e-mail DNA sequence files directly to the system and have an analysis automatically returned by e-mail. The current analysis includes potential protein-coding exon positions, with strand assignment and preferred reading frame, and statistical quality evaluation of each potential exon. Analysis turnaround time is generally only a few minutes for sequences less than 100 kb, and either single or multiple sequences may be submitted in each e-mail message.

Further rule-based interpretation of potential exons is planned soon, as are splice-junction analysis and automated database comparison of potential exons using the dynamic programming algorithm. Development of an expert system to facilitate automated computational assembly of recognized gene components and informatics-based interpretation is well under way and will be included in the system later. For system access, users should send an e-mail message to: "grail@ornl.gov" with the key word "register" in the first line as follows:

register, user name, user mailing address,
and user telephone number

The system will assign a user ID number and supply a help file with further instructions on supplying sequence data and interpreting system results. Send questions to:

Ed Uberbacher – "uber@msr.epm.ornl.gov"
Richard Mural – "m9l@stc.ornl.gov"

Fourth Mapping and Sequencing Meeting

The fourth annual meeting on Genome Mapping and Sequencing at Cold Spring Harbor, New York, was attended by more than 375 people. Held May 9–12, the meeting was designed to survey systematic efforts to analyze genomes of humans and a variety of model organisms.

It was partially supported by the National Center for Human Genome Research and organized by Charles Cantor (Human Genome Center, Lawrence Berkeley Laboratory), Maynard Olson (Washington University School of Medicine), and Richard Roberts (Cold Spring Harbor Laboratory). The following were among aspects of systematic genome analysis covered:

- biological insights into the molecular organization of chromosomes;
- applications to research on specific human diseases;
- experimental techniques;
- procedures for storing, analyzing, and communicating data; and
- methods of automating laboratory procedures.

As the number of large, long-term genome-analysis projects continues to increase, the annual meetings provide a much-needed forum for reporting progress and for discussing experience with various models for the scientific management of these projects. In the words of a veteran contributor to the field, this forum provides a regular, comprehensive overview of "where things stand."

The meeting clearly demonstrated rapid growth in effective activity in the field. Although real novelty surfaces infrequently, the power of experimental approaches is increasing dramatically. These gains arise from incremental improvements in base technologies and from the evolution of more effective ways to combine and apply them.

Perhaps the best indication of progress is the rapidity and effectiveness with which genome analysis advances are being applied to important biological problems.

For example, the story behind the most striking biological advance reported at the meeting—the molecular definition of the fragile X site—differs markedly from that of previous successes in cloning genetic-disease genes. The fragile X syndrome, the most common heritable form of mental retardation, encompasses a bizarre combination of genetic, cytogenetic, and phenotypic effects whose genetic behavior is strikingly non-Mendelian. Both chromosomal imprinting and hypermutability appear to be important in the etiology of this disease.

The power of experimental approaches is increasing dramatically.

Three different research groups reported success in defining the fragile site. The successful laboratories were all able to identify and then clone the fragile site's DNA by systematic methods; no reliance on end-game serendipity marked this search as it had many earlier searches for disease genes. Cooperation by major genome centers in providing rapid access to yeast artificial chromosome clones and the increased resolving power of fluorescent in situ hybridization to metaphase chromosomes both played critical roles. Broad evidence indicates that the challenge in identifying mutated genes in human genetic disease has shifted from recovering disease-locus DNA to developing proof that a particular candidate gene is the one whose mutant alleles cause disease. ◇

Written by Maynard Olson
Washington University School of Medicine

Cold Spring Harbor Meeting Demonstrates Rapid Growth

Attendees Hear Reports on Fragile X Site

COLD SPRING HARBOR SESSIONS AND CHAIRPERSONS

Genome Organization
M. L. Pardue
Massachusetts Institute of Technology

Large DNA Cloning
D. J. Portcous
Medical Research Council, Edinburgh

***Alu*-PCR and Other Methods**
W. Szybalski
University of Wisconsin

Informatics
S. Brenner
Medical Research Council, Cambridge, U.K.

Polymorphisms and Linkage Methods
H. Donis-Keller
Washington University, Missouri

Sequencing/Automation
L. Smith
University of Wisconsin

Large-Scale Mapping Projects
G. Evans
Salk Institute for Biological Studies

Interesting Loci
R. Myers
University of California, San Francisco

Meeting Reports

Conference on Legal and Ethical Issues

Conference proceedings will be available this fall. Conference notebooks, video tapes, and audio tapes may be obtained now.

Contact:

Cathy Tanenbaum
Health Law and Policy Institute
University of Houston Law Center
Houston, TX 77204-6381
713/749-3872
Fax: 713/749-2395

On March 7–9 the Health Law and Policy Institute of the University of Houston sponsored the conference "Legal and Ethical Issues Raised by the Human Genome Project." Underwritten by a grant from the NIH National Center for Human Genome Research, the conference was a large and successful interdisciplinary meeting to explore the ethical, legal, and social implications of using data produced by the Human Genome Project. Over 230 people from North America, Europe, and Asia attended. Presenters and major topics discussed are listed below.

Human Genome Project Overview

Genome mapping and sequencing, technology issues in genome research, clinical applications, and legal challenges.

Presenters: Victor McKusick (Johns Hopkins University Hospital), Charles Cantor (Lawrence Berkeley Laboratory), Thomas Caskey (Baylor College of Medicine), and Alexander Capron (University of Southern California Law Center).

Human Reproduction

Possible limitation by law of the right to procreate, genetic screening and the treatment of newborns, and the effect of genome project data on malpractice litigation.

Presenters: John Robertson (University of Texas Law School), Ellen Wright Clayton (Vanderbilt University School of Law), and Lynn Fleisher (Sidley and Austin).

Confidentiality of Genetic Information in the Clinical Setting

The legal right to medical confidentiality and the effect of genetic information on human identity.

Presenters: Michael Conneally (Indiana University Medical Center), Harold Edgar (Columbia University School of Law), and Dan Brock (Brown University).

Commercial and Practical Applications of Genome Information

Copyright and patent issues, domestic and international technology transfer, and DNA forensics.

Presenters: Iver Cooper (Browdy and Neimark), Geoffrey Karney (Dickstein, Shapiro, and Morin), and Robyn Nishimi (Office of Technology and Assessment, U.S. Congress).

Genetic-Based Discrimination in Employment and Insurance

Presenters: Mark Rothstein (Health Law and Policy Institute), Rob Bier (American Council of Life Insurance), and Thomas Murray (Case Western Reserve University School of Medicine).

Other Speakers and Topics

Alan Weisbard (University of Wisconsin Medical School) was the conference summarist.

Robert Bazell (NBC News) emphasized the need for scientists and health policy experts to become involved in ensuring that the public is provided with accurate and timely information.

Other speakers included NBC News Science Correspondent Robert Bazell and U.S. Representative Mike Andrews (D-Texas). Bazell spoke of the difficult but important task of informing the public about genome issues. Noting the limitations of network television reporting, Bazell emphasized the need for scientists and health policy experts to become involved in ensuring that the public is provided with accurate and timely information. Andrews addressed the role of Congress in funding and in enacting legislation to deal with legal issues arising from availability of genome project information. ◇

Reported by Mark Rothstein
Health Law and Policy Institute
University of Houston Law Center
Houston, Texas 77204-6381

Ethical, Legal, and Social Issues (ELSI) Handbook Available from NIH

The National Center for Human Genome Research announces the availability of a handbook, *Program on Ethical, Legal, and Social Implications of Human Genome Research: A Guide for Applications.* This handbook is designed to assist ELSI applicants in tailoring their proposals to forms designed for biology researchers. It describes the NIH review process from application preparation through funding and gives advice on avoiding problems previously encountered by applicants. Copies of the handbook may be obtained by contacting Elinor Langfelder at 301/496-7531. ◇

Georgetown University Forum on Issues in the Diagnosis of Genetic Disease

Nearly 200 federal employees, academics, manufacturers, laboratory personnel, journalists, and others met April 18–20 in Washington, D.C., to discuss the technical, regulatory, and societal issues associated with the biotechnology used in diagnosing genetic disease. The following organizations sponsored the meeting, which was the first open forum to debate technical and regulatory questions:

- Georgetown University Department of Community and Family Medicine,
- NIH National Center for Human Genome Research,
- Food and Drug Administration,
- NIH National Institute of Child Health and Human Development, and
- Health Industry Manufacturers Association.

Six panels covered a wide range of topics, focusing on sets of key questions in each session. The first session dealt with principles of molecular biology, tests used in detection of genetic disease, and strengths and limitations of the tests. A later panel stressed the federal role in regulating laboratories involved with DNA testing and presented quality assurance requirements as applied to the laboratories. Panelists included representatives of the College of American Pathologists, the New York State Health Department (licenser of the laboratories), the Council of Regional Networks, and Collaborative Research, Inc.

Consumers and genetic counselors discussed the impact of new tests, conceptions of risk, and the best ways to communicate information. Panelists debated the merits of the cystic fibrosis test as a prototype for introducing tests into clinical medicine. The final panel was composed of ethicists, lawyers, a health maintenance organization provider, and third-party payers; they addressed issues related to the social, ethical, and legal aspects of availability of new genetic information and debated the problems of insurance coverage, the potential for discrimination, and possible remedies.

At the final session each panel's moderator presented recommendations on key issues. These recommendations, along with panel summaries and presenters' abstracts, are contained in the final report (see box above). ◇

Reported by Susann Wilkinson
Georgetown University School of Medicine

To obtain a copy of the report, send a $13.50 check payable to Georgetown/ DNA to:
Susann Wilkinson
Department of Community and Family Medicine
Georgetown University School of Medicine
3750 Reservoir Road, NW
Kober-Cogan 218
Washington, DC 20007

Catalogue of DNA Materials

¶The second edition (1991) of the *ATCC Recombinant DNA Materials Catalogue* lists over 1350 different recombinant DNA items available from ATCC, including cloning vectors; hosts for transformation and transfection (animal cell lines and microorganisms); clones from animal, bacterial, fungal, yeast, plant, viral, and viroid genomes; libraries; *Saccharomyces cerevisiae* genomic clone maps; and other useful information.

This 240-page catalogue is mailed free to U.S. researchers; foreign researchers are charged a modest mailing fee. Contact: ATCC/Marketing, NR74; 12301 Parklawn Drive; Rockville, MD 20852; 800/638-6597 or 301/881-2600, Fax: 301/321-5826. ◇

Massachusetts Developing Regional Speakers' Bureau

The Massachusetts Genetics Program of the Massachusetts Department of Public Health, in collaboration with the Massachusetts Human Genome Task Force, is planning to develop a New England regional speakers' bureau to meet the growing number of requests from educational, religious, medical, and industrial organizations for lecturers, panelists, and experts in human genome research. Speakers may include M.D.'s, Ph.D.'s, researchers, genetic counselors, consumers, members of families with genetic disease, clergy, ethicists, social workers, nurses, educators, business executives, venture capitalists, and others who can discuss some aspect of the potential impact of data produced by human genome research.

Persons who wish to participate as speakers in this program may obtain a questionnaire from Robin J. R. Blatt at the address below. The returned form will be summarized into a standardized format, collated, and incorporated into a speakers' bureau guide, which will then be distributed to interested individuals and organizations. This speakers' bureau may serve as the beginning of a directory that could eventually be expanded both nationally and internationally. ◇

Robin J. R. Blatt, Education Coordinator
Massachusetts Genetics Program
Massachusetts Department of Public Health
150 Tremont Street
Boston, MA 02111
617/727-5121, Fax: 617/723-1659

Meeting Reports

Human Genome news

National Center for Human Genome Research

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

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Genetic Counseling: Ethics, Values, and Professional Responsibilities

The Center for Biomedical Ethics and the Department of Human Genetics of the University of Minnesota conducted a meeting on April 18–20 to address the impact of data produced in the Human Genome Project on the norms that guide genetic counseling practice. Several issues were raised at the meeting, which was cosponsored by the NIH National Center for Human Genome Research.

A current primary goal for genetic counselors is to support client autonomy by providing complete genetic information in a nondirective way so the values of the client, not those of the professional, guide reproductive decision making. Value neutrality has long served as a guide for conveying information about the diagnosis of potentially devastating and incurable genetic conditions. Because such reproductive decisions profoundly impact family life, the values of those who will live with the consequences are given primacy.

The first challenge is to determine whose values will guide decision making in future genetic counseling.

The Human Genome Project is likely to expand medical technologies that will enable

- presymptomatic diagnosis of individuals carrying specific disease genes,
- identification of multigene defects involved in common diseases such as heart disease and diabetes, and
- identification of individual susceptibility and environmental factors that interact with genes to produce disease.

These new kinds of information will challenge the norm of nondirective counseling, raising questions of who provides and who receives information and how it is conveyed. As technologies make genetic information more accessible, society must decide how to use the information.

Meeting participants identified the following questions that society needs to address:

- What is a genetic disease and for which conditions will clients be offered screening?
- What will be the counselor's role in protecting confidentiality and opposing genetic discrimination?
- Who will provide genetic counseling services? In what setting will they be offered? Will primary practitioners become the first-line genetic counselors? Will the volume of available information foster the development of single-gene or subspecialty counselors? What skills and preparation will be needed by future counselors?
- What level of certainty should be achieved before counselors share DNA diagnostic information with people potentially affected by a specific genetic condition?
- Should ancillary information, such as nonpaternity or disorders in which the phenotypic effects are unknown, be shared with clients?
- Should susceptibility information be conveyed in a prescriptive way that encourages lifestyle changes to reduce risk?
- Should a public health intervention model supersede the current mode of nondirectiveness when genetic technology provides the possibility for cure or eradication of specific genetic diseases?
- Who will be the client—the individual, the family, or society at large?
- Should genetic counselors become their clients' advocates to counteract public health and economic pressures that threaten individual autonomy?

With data from the Human Genome Project increasing rapidly, problems arising from the application of new genetic knowledge in clinical practice must be addressed. The first challenge is to determine whose values will guide decision making in future genetic counseling. ◇

Reported by Dianne Bartels
Center for Biomedical Ethics
University of Minnesota
Minneapolis, MN 55455
612/625-4917, Fax: 612/626-6800

NTIS Offers Technology Transfer Information

The *1991 Catalog of Products and Services* of the National Technical Information Service (NTIS), which is part of the U.S. Department of Commerce, lists a number of resources and publications designed to aid the transfer of technology from federal laboratories to the private sector. Selected catalog listings related to technology transfer are excerpted below.

Specify number and title when ordering.

- Information: 703/487-4780.
- Sales desk: 800/553-6847 or 703/487-4800.
- Periodicals subscriptions: 703/487-4630; other items: 703/487-4650.

Prices given are double outside the United States, Mexico, and Canada, unless stated otherwise.

Federal Research in Progress (FEDRIP) Database

The FEDRIP Database summarizes 120,000 current U.S. government–funded research projects, allowing determination of progress in specific areas before publication in technical reports or journals. Database content focuses on health, physical sciences, agriculture, engineering, and life sciences information from ten different government departments and agencies, including DOE.

FEDRIP may be searched through DIALOG, 1/800/334-2564. Batch searching and selective dissemination of information services are available through NERAC, Inc., 203/872-7000. Free search guide (Booklet PR-847/817): 703/487-4650.

Publications

Emerging Technologies: A Survey of Technical and Economic Opportunities, prepared by the Technology Administration of the Department of Commerce, identifies 12 technologies offering market potential in 4 commercial areas that are expected to create markets for an estimated $1 trillion in sales by the year 2000. The four areas are life sciences applications, advanced materials, electronics and information systems, and manufacturing systems. The report also lists actions that might be taken by U.S. industry and government to spur commercial development of these technologies. 62 pp. $17. Order No. PB90-216557CAU.

Science and Technology Resources in U.S. Industry, a book compiled by the National Science Foundation, explores and summarizes American industrial science and technology resources in terms of two important parameters of innovation: R&D activities and employment and use of scientists, engineers, and technicians. This report examines how a country's competitive position will be largely determined by the quality of its investment in human and capital scientific and technological resources. 111 pp. $23. Order No. PB90-107194CAU.

Center for the Utilization of Federal Technology (CUFT)

CUFT publications inform U.S. industry of federal laboratory inventions and technologies that have commercial potential or are at a breakthrough stage. Most of these inventions may be licensed through CUFT, which offers exclusive, coexclusive, and nonexclusive licenses, depending upon the technology and market conditions. For more information about licensing, call CUFT at 703/487-4738. Publications may be ordered from NTIS.

The weekly *Government Inventions for Licensing Abstract Newsletter* describes new inventions produced in federal laboratories, many of which offer business opportunities and require little development before they are ready to market. Annual index. $235 per year; $340 outside the United States, Canada, and Mexico.

(continued)

STIS Provides NSF Publications Access

The National Science Foundation (NSF) Science and Technology Information System (STIS), a new electronic dissemination system, provides easy access to NSF publications including *Bulletin*, program announcements, *Guide to Programs*, telephone directory, and many others. Full text can be searched online and copied; password registration is unnecessary, and connect time is free.

Access Via Internet or Modem

STIS may be accessed on Internet by using either of the following commands: "telnet stis.nsf.gov" or "telnet 128.150.195.40". To copy a publication, an Internet user can request delivery by e-mail, conduct an anonymous file transfer protocol session, or print material from a screen display. Modem access (if long distance, telephone charges apply) is available at 1200-, 1400-, and 9600-baud rates. To copy a publication, material can be printed from screen or the full text can be downloaded using the Kermit protocol. [Director, STIS; NSF Office of Information Systems; Room 401; 1800 G Street, N.W.; Washington, DC 20550; 202/357-7555.] ◇

Resources

The annual *Catalog of Government Inventions Available for Licensing* includes more than 1000 inventions in 43 subject areas. Provided are a detailed summary of each item, information on the inventor and on obtaining background material, and subject and inventor indexes. 1990 catalog, $54. Order No. PB91-100206CAU. Issues from previous years are available.

Monthly issues of the NTIS *Tech Notes* contain 100 selected fact sheets on the latest and best U.S. government–developed technologies and know-how provided by federal laboratories run by DOE, the Department of Defense, National Aeronautics and Space Administration, and National Institute of Standards and Technology. Focusing on the most practical results, *Tech Notes* provides concise, illustrated announcements describing new processes, instruments, materials, equipment, software, services, and techniques, as well as contact addresses and telephone numbers. Subscribers receive a free copy of the annual *Federal Laboratory Technology Catalog*, described below. $175 per year.

Summarizing the material in *NTIS Tech Notes*, the *Federal Laboratory Technology Catalog* describes more than 1000 processes, instruments, materials, equipment, software, services, and techniques. Contact information and subject index provided. 1990 Catalog, $42 for nonsubscribers to *NTIS Tech Notes*. Order No. PB91-100198CAU. Issues from previous years are available.

The 1990/91 *Directory of Federal Laboratory and Technology Resources* is a guide to hundreds of federal laboratories willing to share their expertise, equipment—and sometimes even their facilities—to aid U.S. research efforts. It contains detailed summaries, addresses, and telephone numbers of 1100 resources; descriptions of 90 technical information centers; a complete list of the more than 300 federal laboratory technology transfer offices; a contact name, address, and telephone number for each entry; and indexes by subject, state, federal laboratory, and agency. $59.95. Order No. PB90-104480CAU. ◊

Genome Publications

¶As time and space permit, *Human Genome News* will publish information about selected books and journals that may be of interest to our readers. This is not a comprehensive list, and announcements will be taken from material at hand. We welcome news from authors and publishers about new and upcoming publications relevant to genome research.

Another publication announcement is on p. 13.

"Human Gene Mapping 10.5," *Cytogenetics and Cell Genetics*, Volume 55, Nos. 1–4 (1990), is a 786-page special issue devoted to the proceedings of the Oxford conference held September 5–10, 1990. The status of each human chromosome and other aspects of chromosome mapping are organized in a consistent format in individual chapters. [United States: S. Karger Publishers; P.O. Box 529; Farmington, CT 06085; 203/675-7834, Fax: 203/675-7302. Europe: S. Karger AG, Allschwilerstrasse 10 P.O. Box, CH-4009 Basel, Switzerland; (Int.) 41/61-306-1111, Fax: 41/61-306-1234.

Genetic Maps (Fifth Edition), edited by Stephen J. O'Brien (National Cancer Institute), furnishes comprehensive comparative data on the genetic organization of different species. The new edition is published in two formats: a series of six paperback books, each containing a variety of genetic maps from one group of organisms ($27 per book); and a cloth-bound reference volume that includes the complete collection of maps from all 129 species listed. 1990, $150. [Cold Spring Harbor Laboratory; Fulfillment Department, LM90; 10 Skyline Drive; Plainview, NY 11803-9729; United States, except New York State: 1/800/843-4388; all other locations: 516/367-8423; Fax: 516/367-8432.]

Shaping Genes: Ethics, Law, and Science of Using Genetic Technology in Medicine and Agriculture by Darryl R. J. Macer (University of Tsukuba, Japan) contains chapters on

HHMI Publishes Book on Genome Research

¶The Howard Hughes Medical Institute in Bethesda, Maryland, published in May a softcover book, *Blazing a Genetic Trail* (56 pages). Written in nontechnical language, the report contains articles on such topics as the successful search for the cystic fibrosis gene, the usefulness of mice and large human families to medical geneticists, a young investigator's quest for the genetic cause of his own disease, and the future of genetic research.

A limited number of copies are available free of charge. Requests from teachers have priority. Order: Howard Hughes Medical Institute; Communications Office; 6701 Rockledge Drive; Bethesda, MD 20817-9866; 301/571-0330 or contact HGMIS at the address on p. 2. ◊

For Your Information

such topics as general ethical concerns, medical ethics, animal rights, applied genetic engineering, genetic screening and selection, human gene therapy, human genetic engineering, selective human breeding, and bioethics for the future. 1990, United States, $18; United Kingdom, £10. [Eubios Ethics Institute; 31 Colwyn Street; Christchurch, New Zealand or P.O. Box 125, Tsukubagakuen; Ibaraki 305, Japan.]

Computer Applications for Molecular Biologists, Volume 1, a 77-page handbook of biotechnology software reports, contains useful microcomputing information. The book's reviews of programs and comprehensive software packages that focus on a single problem can serve as a guide for anyone planning to purchase laboratory software. Complete names and addresses of manufacturers and suppliers are provided. 1991, $45. [Mary Ann Liebert, Inc.; 1651 Third Avenue; New York, NY 10128; 1/800/654-3238 or 212/289-2300.]

The following four books are available from Academic Press, Book Marketing Department; 1250 Sixth Avenue; San Diego, CA 92101-4311; United States and Canada, 1/800/321-5068; Fax: 1/800/235-0256.

PCR Protocols: A Guide to Methods and Applications, edited by Michael A. Innis, David H. Gelfand, and John J. Sninsky (Cetus Corporation) and Thomas J. White (Hoffmann-LaRoche, Inc.), is a 482-page laboratory manual for making PCR work. 1990, comb-bound, $39.95; casebound, $79.

Molecular Biology Labfax (1991), edited by T. A. Brown (University of Manchester Institute of Science and Technology), is one of a series of books that bring together key data for a major subject in a single volume. The detailed compendium contains information on bacteria and bacteriophages, chemicals and reagents, radiochemicals, restriction and methylation, DNA and RNA modifying enzymes, cloning vectors, genomes and genes, electrophoresis, hybridization analysis, centrifugation, and safety. 322 pages. 1991, $49.95.

Recombinant DNA Methodology, edited by Ray Wu (Cornell University), Lawrence Grossman (Johns Hopkins University), and Kivie Moldave (University of California, Santa Cruz) is a 760-page volume in the *Selected Methods in Enzymology* series. 1989, comb-bound, $49.95.

Recombinant DNA Laboratory Manual, by Judith W. Zyskind and Sanford I. Bernstein (San Diego State University). 195 pages. 1989, comb-bound, $24.95. ◊

U.S. Genome Research Funding Information

Note: Investigators wishing to apply for NIH 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

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 Innovation 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. Notices will appear in *HGN* and other publications.

  Program announcements are listed in issues of the weekly *NIH Guide for Grants and Contracts*, which are available 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; BITNET: "pjones@uncvx1.bitnet" or Internet: "jones@samba.acs.unc.edu".

  Expanded statements of 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 issue of *Science*, and in other publications. Investigators whose preproposals are accepted for programmatic relevance are notified to submit a formal proposal by August 9.

For further information, contact the program office via

301/353-5037 or FTS 233-5037; Fax: 301/353-5051 or 233-5051
Internet: "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. Next submission date: spring 1992. For more information, contact

Samuel Barish; SBIR Program Manager, ER-16; DOE; Washington, DC 20585; 301/353-5707.

Human Genome Distinguished Postdoctoral Fellowships
Next deadline: February 1, 1992. For further information, see *HGN* **2**(3), 11 (September 1990) or contact

Oak Ridge Associated Universities: 615/576-4805. ◊

Calendar of Genome Events*

August	12–16	**STM 1991 International Conference**; Interlaken, Switzerland [*C. Gerber, (Int.) 41/1-724-8645, Fax: (Int.) 41/1-724-3223*]
	16–17	**1991 NORD Patient/Family Conference**; Baltimore, MD [*NORD, 203/746-6518*]
	18–22	**11th International Workshop on Human Gene Mapping (HGM 11)**; London [*J. Crowther, (Int.) 44/71-269-3389, Fax: (Int.) 44/71-430-1787*]
	20–25	**Molecular Genetics of Bacteria and Phages**; CSHL, Cold Spring Harbor, NY (application required); [*CSHL, 516/367-8346, Fax: 516/367-8845*]
September	1–6	**Fourth European Conference on Spectroscopy of Biological Molecules**; York, U.K. [*R. E. Hester, (Int.) 44/904-432557, Fax: (Int.) 44/904-432516*]
	3–6	**Panel Discussion on Genome Mapping at the 17th International Conference on Very Large Databases**; Barcelona, Spain [*N. Kamel, 904/392-2687*]
	4–5	***DOE/NIH Advisors Retreat**; Half Moon Bay, CA
	10–13	**Second International Workshop on Human Chromosome 22**; Montreal, Canada [*G. Rouleau, 514/934-8094 or 937-6011, Fax: 514/937-3532*]
	11–12	***NIH/DOE Joint Working Group on Ethical, Legal, and Social Issues**; Washington, DC [*E. Juengst, 301/496-7531, Fax: 301/480-2770*]
	14–15	**The Human Genome Project: A Public Forum**; Alexandria, VA [*J. Weiss, 1/800/336-GENE or 202/331-0942*]
	15–16	***NIH-DOE Joint Working Group on the Mouse**; Boston, MA
	18–21	**14th Congress of the International Society of Forensic Haemogenetics**; Mainz, FRG [*P. Schneider, (Int.) 49/6131-172688 or -392118, Fax: (Int.) 49/6131-393183*]
	20	***National Advisory Council for Human Genome Research**; Bethesda, MD
	22–25	**Genome Sequencing Conference III**; Hilton Head, SC [*S. Wallace, 301/480-0634, Fax: 301/480-8588*]
October	5	**International Gathering of Networks of Support Groups**; Washington, DC [*see contact: Sept. 14–15*]
	6–11	**8th International Congress of Human Genetics**; ASHG, Washington, DC [*M. Ryan, ICHG, 301/571-1825, Fax: 301/530-7079*]
	7–9	***DOE Human Genome Program Proposal Review Panel**; Washington, DC
	14–18	**Fifth International Workshop on Mouse Genome Mapping**; Lunteran, the Netherlands [*M. Sonne, (Int.) 31/20-512-1990, Fax: (Int.) 31/20-617-2625*]
	18–19	**The Societal Impact of Human Genetic Engineering**; Oak Ridge, TN [*N. Brown, 615/483-4357*]
	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*]
	26	**Science and Journalism III. Genes and Human Behavior: A New Era?** Boston, MA [*J. Beckwith, 617/432-1920*]
November	8–9	**Justice and the Human Genome**; Chicago, IL [*Conference Registrar: 312/996-5225, Fax: 312/996-5227*]
	13–15	***Genome Research Review Committee**; Bethesda, MD
	20–22	**Bioinformatics in the 90s**; Maastricht, the Netherlands [*J. Franklin, (Int.) 31/2993-72751, Fax: (Int.) 31/2993-72877*]
January 1992	3–4	***NIH Program Advisory Committee on the Human Genome**; Irvine, CA
	3–4	**Joint NIH-DOE Subcommittee on the Human Genome**; Irvine, CA [*C. Mohan, 301/496-0844, afternoons*]
	5	***DOE Human Genome Coordinating Committee**; Irvine, CA
	7–10	**"Biotechnology Computing Minitrack" at the Hawaii International Conference on System Sciences-25**; Kailua-Kona, HI [*L. Hunter, 301/496-9300, Fax: 301/496-0673, E-mail: "hunter@nlm.nih.gov"*]
	25–Feb. 1	**Keystone Symposia Meeting: Molecular Mechanisms in DNA Replication & Recombination**; Taos, NM (abstract deadline: Sept. 25) [*Keystone Symposia, 303/262-1230, Fax: 303/262-1525*]

*Attendance at meetings listed with asterisk is either limited or restricted. Dates may change; check with contact person.

Training Calendar: Workshops and Coursework*

August	4–24	**Tutorial on the Mathematical Sciences in Genomic Analysis;** Stanford, CA [*SIMS, 203/966-1008, Fax: 203/972-6069*]
	5	**DNA Amplification by PCR;** BTP, Philadelphia, PA (also offered Aug. 12 in Madison, WI; Aug. 26 in Birmingham, AL; Sept. 16 in Los Angeles, CA; and other dates and locations) [*S. Chance, 515/232-8306, 1:00–5:00 p.m. CST*]
	5–9	**Nucleic Acid and Protein Sequence Analysis Workshop for Biomedical Researchers;** Pittsburgh Supercomputing Center, Pittsburgh, PA [*N. Kiser, 412/268-5206 or 1/800/222-9310 (PA), 1/800/221-1641 (U.S. outside PA); Internet: "kiser@a.psc.edu", BITNET: "kiser@cpwpsca.bitnet"*]
	6–9	**Basic Cloning Techniques;** BTP, Philadelphia, PA (also offered Aug. 13–16 in Madison, WI; Aug. 27–30 in Cleveland, OH: Sept. 17–20 in Los Angeles, CA; and other dates and location) [*see contact: Aug. 5*]
	6–9	**RFLP Analysis;** BTP, Madison, WI (also offered Aug. 27–30 in Birmingham, AL; Oct. 15–18 in Ames, IA) [*see contact: August 5*]
	12–16	**Cell Culture Techniques;** LTI, Germantown, MD (also offered December 2–6) [*G. Tinney, 1/800/828-6686, 301/921-2250, Fax: 301/258-8212*]
	13–16	**RNA Isolation and Characterization;** Exon-Intron, Columbia, MD [*Exon-Intron, 301/730-3983*]
	19–23	**Advanced DNA-Protein Techniques;** LTI, Germantown, MD [*see contact: Aug. 12–16*]
September	16–19	**GeneWorks;** Mountain View, CA (Registration deadline: Sept. 3) [*IntelliGenetics, Inc., 415/962-7300*]
	16–20	**Recombinant DNA Techniques I;** LTI, Germantown, MD (also offered Nov. 11–15) [*see contact: Aug. 12–16*]
	23–28	**Recombinant DNA Techniques II;** LTI, Germantown, MD (also offered Nov. 18–23 and Dec. 16–21) [*see contact: Aug. 12–16*]
	24–27	**PCR Technology;** ATCC, Rockville, MD (also offered Nov. 19–22) [*C. Mills, 301/881-2600, Fax: 301/770-2587*]
	30-Oct. 2	**Freezing & Freeze-Drying of Microorganisms;** ATCC, Rockville, MD [*see contact: Sept. 24–27*]
October	7–12	**cDNA Libraries Techniques;** LTI, Germantown, MD [*see contact: Aug. 12–16*]
	8–21	**Analysis and Genetic Manipulation of YACs;** CSHL, Cold Spring Harbor, NY [*CSHL, 516/367-8346, Fax: 516/367-8845*]
	10–23	**Macromolecular Crystallography;** CSHL, Cold Spring Harbor, NY [*see contact: Oct. 8–21*]
	14–16	**PCR Techniques;** CUA, Lake Tahoe, NV [*M. Miller, 202/319-6161, Fax: 202/319-5721*]
	27–Nov. 5	**Molecular Genetics of Fission Yeast;** CSHL, Cold Spring Harbor, NY [*see contact: Oct. 8–21*]
	27–Nov. 5	**Essential Computational Genomics for Molecular Biologists;** CSHL, Cold Spring Harbor, NY [*see contact: Oct. 8–21*]
	28–Nov. 1	**Recombinant DNA: Techniques and Applications;** ATCC, Rockville, MD (also offered Nov. 4–8) [*see contact: Sept. 24–27*]
	28–Nov. 15	**Carolina Workshop on Molecular Techniques for Human/Mammalian Genome Analysis;** Chapel Hill, NC (application deadline: Sept. 1) [*W. Litaker, 919/966-1730, Fax: 919/966-6821*]
November	4–8	**Genomic Information/Ethical Implications;** Seattle, WA [*I. Boulanger, 206/543-5447*]
	11–14	**PC/Gene;** Mountain View, CA (Registration deadline: Oct. 28) [*see contact: Sept. 16–19*]
December	3–5	**Cytogenetics: Techniques & Applications;** ATCC, Rockville, MD [*see contact: Sept. 24–27*]
March 1992	2–17	**Carolina Workshop on Yeast Molecular Genetics;** Chapel Hill, NC (application deadline: Feb. 1, 1992) [*see contact: Oct. 28–Nov. 15*]

*Dates may change; check with contact person.

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.

ANL*	Argonne National Laboratory, Argonne, Ill.
ASHG	American Society of Human Genetics
ATCC	American **Type Culture** Collection
BTP	Biotechnology Training Programs
CHOP	Children's Hospital of Philadelphia
cDNA	complementary DNA
CEPH	Centre d'Etude du Polymorphisme Humain
cM	centimorgan
CSHL	Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.
CUA	Catholic University of America
CUFT	Center for the Utilization of Federal Technology (NTIS)
DOE	Department of Energy (U.S.)
EC	European Community
ECU	European Currency Unit
ELSI	Ethical, Legal, and Social Issues
FEDRIP	Federal Research in Progress Database
GRAIL	Gene Recognition and Analysis Internet Link (ORNL)
HGM	International Workshop on Human Gene Mapping
HGMIS*	Human Genome Management Information System (ORNL)
HGMP	Human Genome Mapping Project (U.K.)
HGN*†	**Human Genome News**
HHMI	Howard Hughes Medical Institute
HLA	histocompatibility antigens
HUGO	Human Genome Organisation [International]
ICRF	Imperial Cancer Research Fund (U.K.)
JITF	Joint Informatics Task Force
kb	kilobase
LANL*	Los Alamos National Laboratory, Los Alamos, N.M.
LBL*	Lawrence Berkeley Laboratory, Berkeley, Calif.
LLNL*	Lawrence Livermore National Laboratory, Livermore, Calif.
LTI	Life Technologies, Inc.
MRC	Medical Research Council (U.K.)
NCI†	National Cancer Institute (NIH)
NCHGR†	National Center for Human Genome Research (NIH)
NIH†	National Institutes of Health
NORD	National Organization for Rare Disorders
NSF	National Science Foundation (U.S.)
NTIS	National Technical Information Service (U.S. Department of Commerce)
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
SBIR	Small Business Innovation Research
SIMS	Societal Institute of the Mathematical Sciences
STIS	Science and Technology Information System (NSF)
STM	scanning tunneling microscopy
STS	sequence tagged site
YAC	yeast artificial chromosome

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