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Human Genome news

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DOE Holds Contractor-Grantee Workshop

Physical Mapping Efforts Going Well; Gels Increasing Sequencing Efficiency

The DOE Human Genome Program held its second Contractor-Grantee Workshop in Santa Fe, New Mexico, on February 17–20. More than 200 program-sponsored scientists attended the meeting, in addition to invited guests and industry representatives. DOE-supported human genome research projects are conducted at 7 DOE national laboratories (including its 3 human genome centers), 37 major universities, and 32 companies through collaborations and awards. Projects were represented by oral presentations or posters.

Charles R. Cantor and HGMIS gratefully acknowledge contributions to this article by Elbert W. Branscomb, Anthony V. Carrano, Leroy E. Hood, Robert K. Moyzis, and Robert J. Robbins.

Six platform sessions focused on the following:

- physical mapping progress,
- large DNA fragment cloning,
- strategies for preparing samples for efficient DNA sequencing,
- new methods for a variety of genome efforts,
- DNA sequencing instrumentation, and
- database and computer algorithm needs for existing or projected genome research.

David Galas, Associate Director, Office of Health and Environmental Research (OHER), spoke about the relationship between the Human Genome Program and other OHER programs. Michael Yesley [Los Alamos National Laboratory (LANL)] presented ethical, legal, and social issues pertaining to data produced in the genome project.

The general impression conveyed by most presenters was that physical mapping efforts are going well; chromosomes 16, 19, and portions of 11 are now well covered with large numbers of assembled contigs. Fluorescence in situ hybridization (FISH) is emerging as an extremely effective method for ordering cloned probes.

Fractionating DNA fragments is becoming much faster with capillary or thin gel slab electrophoresis. Informatics support for most physical mapping efforts and for large-scale DNA sequencing remains problematic, and more focus is needed on the immediate informatics needs of ongoing biology projects.

Many parallel efforts under way in cloning, informatics, mapping, and sequencing will further improve the technologies required for genomics. Program participants feel that this situation is healthy at present and that a few

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DOE Program Report Update

HGMIS is preparing the 1991 revision of the DOE *Human Genome 1989–90 Program Report.*

To update the report and accurately reflect DOE-funded genome research projects, HGMIS asks investigators to send abstracts, photographs, and figures. Investigators who have not already submitted this material are reminded to forward it to:

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Oak Ridge National Laboratory
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Oak Ridge, TN
37831-6050

approaches will emerge as those most likely to accelerate the project.

One theme that recurred frequently during the 3-day meeting was the rapid change in bottlenecks or rate-limiting steps, particularly in DNA-sequencing efforts. Advances in raw sequencing speed make automated production of DNA samples and melding of raw sequence reads increasingly important.

■ Physical Mapping

Generally, impressive progress continues in the construction of physical maps of selected human chromosomes. Yeast artificial chromosomes (YACs), though not without problems, are proving helpful in linking cosmid contigs or providing rapid initial coverage of a region.

The powerful new FISH technique is providing mapping data at several levels of resolution, extending from metaphase chromosomes. It offers a rapid and accurate method of regional clone assignment to a chromosome band. Barbara Trask [Lawrence Livermore National Laboratory (LLNL)] showed that much higher resolution mapping can be achieved with interphase cells; once markers are known to be close, their relative order can be determined and distances estimated in the 50-kb to 1-Mb range.

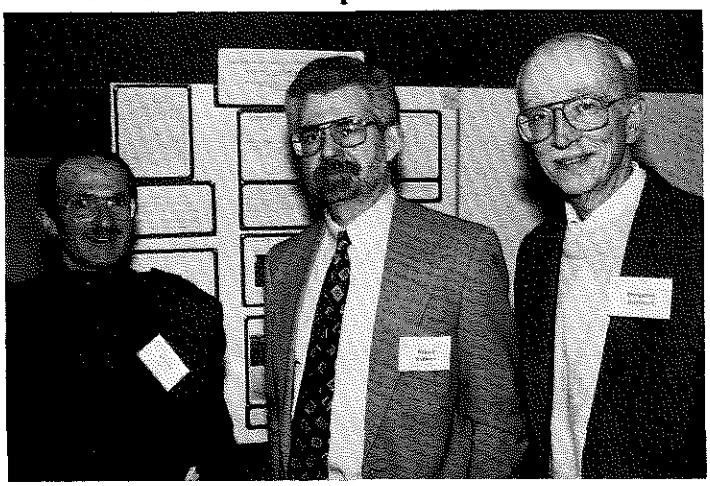
The presence of a selectable marker near the long-arm telomere of chromosome 16 made possible the construction of a set of hybrid cell lines particularly convenient for that chromosome. Grant Sutherland (Adelaide Children's Hospital, South Australia) explained this method and showed the usefulness of FISH in characterizing chromosomal rearrangements.

Glen Evans (Salk Institute) and collaborators have used a combination of methods in mapping chromosome 11. In constructing several multimegabase contigs of cloned DNA segments, Evans used a YAC as a hybridization probe against a filter array of cosmids to identify covered cosmids. Given the appropriate libraries, a series of overlapping clones for 1- to 2-Mb regions apparently can be isolated in a matter of weeks.

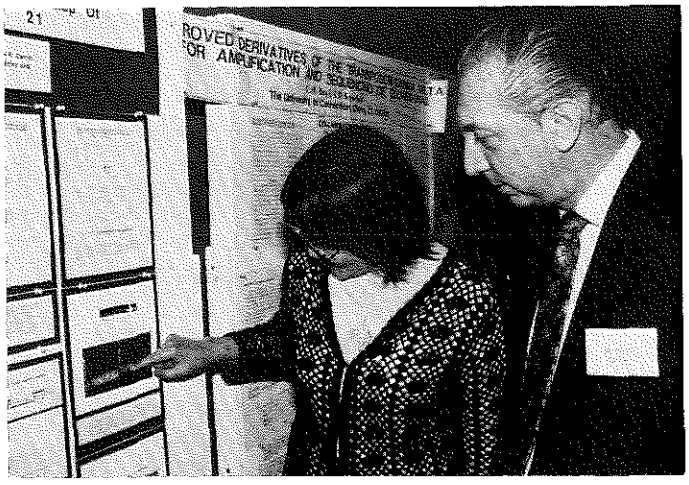
Both the chromosome 19 program at LLNL and that of chromosome 16 at LANL have collected about two-thirds of their chromosomes into cosmid contigs. A variety of very effective automated approaches are being used to expand and link these contigs. Existing maps are dense enough to be useful to investigators wishing to locate genes on these chromosomes; about 80% of randomly picked probes will fall on contigs or clones already mapped. To aid such studies, a series of anchor points has been established between the current genetic and physical maps. No clone-order discrepancies are evident between the two map types for either chromosome.

Excellent progress is being made with maps of X-chromosome regions. Thomas Caskey, David Nelson, and their coworkers (Baylor College of Medicine) are focusing on several areas that contain genes of interest rather than attempting to construct a complete

DOE Human Genome Program staff (l. to r.) Charles Cantor (Principal Scientist), Robert Robbins (Informatics Detailee to DOE from the National Science Foundation), and Benjamin Barnhart (Program Manager) view posters at the Contractor-Grantee Workshop.



Denan Wang (Lawrence Berkeley Laboratory Human Genome Center) explains her poster to DOE Human Genome Coordinating Committee (HGCC) member Anthony Carrano (Director, LLNL Human Genome Center).



map of this large chromosome. Caskey described the potency of using tandem simple sequence repeats as genetic markers.

In the next few years, nearly complete contig maps should be obtained on chromosomes 11, 16, 19, and X.

■ Large-Insert Cloning Vectors

Several groups reported new approaches toward large-insert cloning vectors:

- Peter Hahn and his colleagues (State University of New York, Syracuse) employed double-minute chromosomes as megabase-cloning vehicles.
- Jean-Michel Vos (University of North Carolina, Chapel Hill) suggested the Epstein-Barr virus as a cloning vehicle.
- Hiroshi Shizuya (Melvin Simon's laboratory, California Institute of Technology) described a new cloning system using *Escherichia coli* and its plasmid *F* factor.
- Philip Youderian (California Institute of Biological Research) discussed a set of "stealth" vectors that carry an S replicon, the *Salmonella* phage B-22 early region, and a chloramphenicol resistance determinant. The vectors can accept DNA inserts of several hundred kilobases, maintain them in a single copy, and then amplify them about 500-fold.

Gary Hermanson (Glen Evans' laboratory, Salk Institute) gave an interesting presentation on isolating the ends of YAC inserts by homologous recombination, a promising technique for walking within YAC libraries. Sherman Weissman (Yale University) reported on his group's efforts to achieve normalized cDNA libraries from human thymus. The research is proceeding well in setting the stage for large-scale sequence analysis of the corresponding cDNAs from various tissues.

■ DNA Sequencing Methodology

A goal of the Human Genome Project is to reduce DNA sequencing costs. While considerable attention has been given to data-collection instrumentation and data-analysis hardware and software, the scientists felt that more emphasis is needed on technologies that will reduce costs by increasing throughput and template quality.

A number of presentations dealt with transposon insertions to assist in DNA sequencing, thereby minimizing redundancy associated with shotgun cloning strategies. Douglas Berg (Washington University School of Medicine) and his group have exploited the bacterial Tn5*supF* transposon system by inserting a known 260-bp sequence into lambda clones to serve as the priming site for sequencing. This procedure eliminates the need to subclone large inserts, since sequencing could be accomplished directly from the lambda clone by primer walking from the inserted transposon. Claire Berg (University of Connecticut) described the use of transposon $\gamma\delta$(Tn1000) to sequence plasmid inserts. Robert Weiss and Raymond Gesteland (University of Utah) reported on applying this method to sequence plasmids containing 10-kb inserts. Their clone-pooling scheme is employed for rapid mapping of the transposon integration sites; the mapped transposons are then used as primer sites for multiplexed dideoxy sequencing.

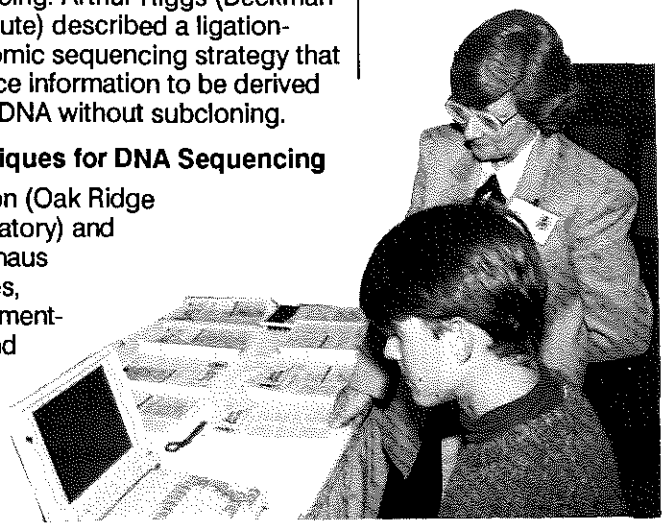
William Studier (Brookhaven National Laboratory) reported on priming DNA sequencing reactions by using sequences within the insert itself. George Church (Harvard Medical School) presented the status of his developments for computer-assisted multiplexed sequencing. Arthur Riggs (Beckman Research Institute) described a ligation-mediated genomic sequencing strategy that allows sequence information to be derived from genomic DNA without subcloning.

■ New Techniques for DNA Sequencing

Bruce Jacobson (Oak Ridge National Laboratory) and Heinrich Arlinghaus (Atom Sciences, Inc.) are implementing tin, iron, and

Sylvia J. Spengler, Executive Officer, HGCC, organized the DOE Contractor-Grantee Workshop in Santa Fe, New Mexico.

Reece Hart (Salk Institute) tries out the online DOE Human Genome Information Database, assisted by Beth Owens (HGMIS, Oak Ridge National Laboratory).



Lauren Sears and Ted Davis (New England Biolabs, Inc.) discuss strategies.

Genome News

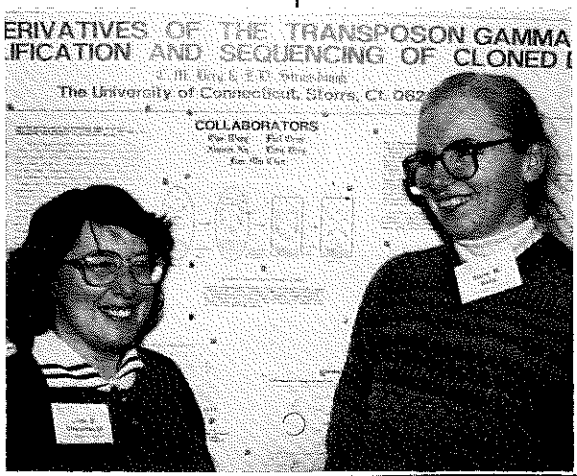
DOE Workshop Presentations Reflect Progress

Complete report, including abstracts, available on request from HGMIS (see request form, p. 24).

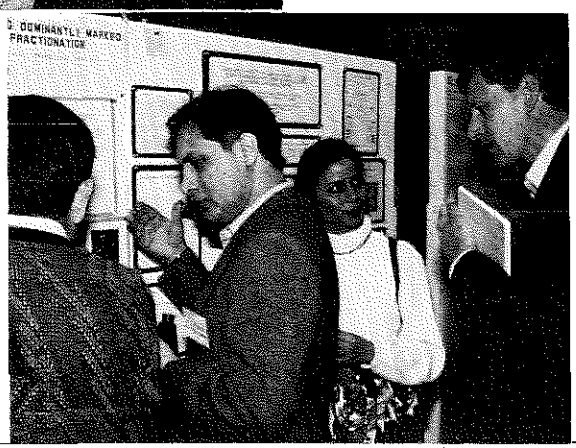
lanthanide isotopes as reporter groups for DNA sequencing. Sputter-Initiated Resonance Ionization Spectroscopy or Laser Atomization Resonance Ionization Spectroscopy (two forms of mass spectrometry used to assay these reporter groups), appear to have striking sensitivity and speed of analysis. The thin-layer capillary electrophoresis techniques reported by Barry Karger (Northeastern University) present notable opportunities for speeding up throughput in the analysis of DNA sequence fragments. The impressive data of Lloyd Smith (University of Wisconsin) suggested that thin-layer capillary gels will work effectively in sequencing-fragment separation and provide multiple-lane parallelism for DNA sequence analysis. The use of exonucleases and the ability to detect single nucleotides for the analysis of single DNA molecules are being advanced by Richard Keller's (LANL) group. (See associated article, p. 5.)

Several presentations were made on scanning tip microscopy. An outstanding one by Rodney Balhorn and Wigbert Siekhaus (LLNL) used scanning tunneling microscopy to reveal images of monolayers of adenine and thymine bases that are consistent with the known physical structure of these molecules.

Other presenters described methods for detecting DNA for either sequencing or mapping. Christopher Martin and Irena Bronstein (Tropix, Inc.) demonstrated the application of chemiluminescence in Sanger dideoxy sequencing protocols.



Linda Strausbaugh and Claire Berg (University of Connecticut) present their poster at the DOE Contractor-Grantee Workshop in Santa Fe, New Mexico.



Eliezer Huberman (Argonne National Laboratory), Raghbir Athwal (New Jersey Medical School), Arbansjit Sandhu (University of Medicine and Dentistry of New Jersey), and David Callen (Adelaide Children's Hospital) (l. to r.) enjoy discussions during a poster session.

This technique uses biotinylated primers in standard sequencing reactions. Richard Mathies and Alexander Glazer (University of California, Berkeley) demonstrated analytical miniaturized fractionations of fluorescing DNA fragments under a confocal laser microscope system.

Two novel methods are being developed as third-generation sequencing approaches. Joe Gray (LLNL) and coworkers are exploring the use of X-ray diffraction for DNA sequence analysis. Radoje Drmanac and Radomir Crkvenjakov (Argonne National Laboratory) described sequencing by hybridization: short oligomers (8 to 9 mers) with known sequence are hybridized to short fragments of DNA with unknown sequence. The collection of oligomers that hybridize to a fragment reveal the sequence. The group has successfully sequenced a small DNA segment and is now scaling up for practical applications.

■ Informatics

Presentations showed broad progress in applying computer technology to the Human Genome Project. Jim Fickett (LANL) and colleagues noted that the chromosome 16 map requires management of nearly a million data items, the bulk from fingerprinting about 4000 clones. With over 60% of chromosome 16 covered by cosmid contigs, attention is shifting to YACs, FISH, and sequence tagged sites (STSs) for closing intercontig gaps, thereby requiring extensions to the existing data system. Chris Fields (New Mexico State University) and colleagues described an automated system for screening candidate STS sequences and predicting good polymerase chain reaction priming sites on them.

Many posters and one presentation addressed the central computing problem of sequence matching. Eugene Lawler discussed a new dynamic programming method developed with William Chang (both at University of California, Berkeley) that is 4 or 10 times faster (using nucleotide or amino acid sequences, respectively) than the best previous dynamic programming algorithm.

Providing and controlling access to multiple data sources is a key challenge for genomic research. Thomas Slezak (LLNL) reported on some proof-of-concept tests that showed how controlled, multiple database access

(see DOE, p. 5)

LANL, Life Technologies Approve CRADA

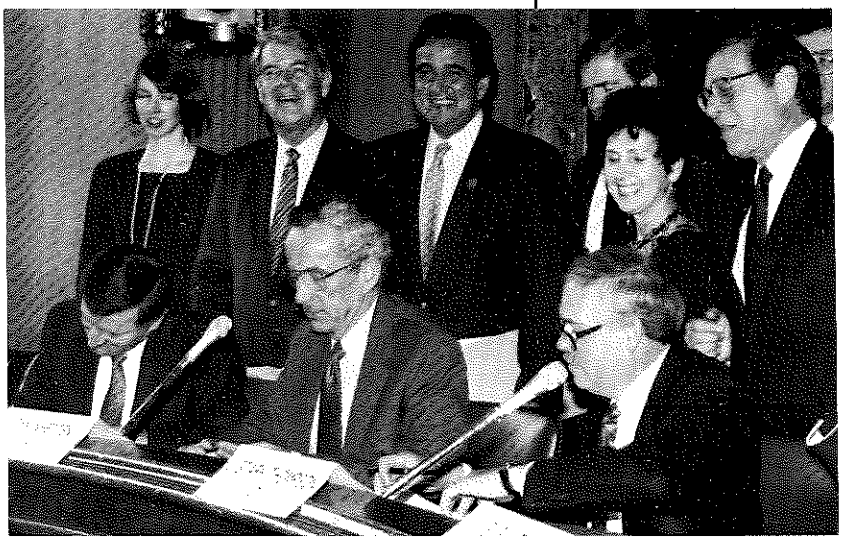
First for U.S. Human Genome Project

At a signing ceremony on March 21, representatives from Los Alamos National Laboratory (LANL) and Life Technologies, Inc., (LTI) approved a Cooperative Research and Development Agreement (CRADA), the first between a DOE human genome center and a private-sector corporation. This CRADA is also the first for LANL, for DOE defense-oriented laboratories, for the DOE Albuquerque operations office, and for the U.S. Human Genome Project.

The 3-year agreement calls for investigators from LANL and LTI to cooperate in developing faster and cheaper techniques for determining the base sequence of the human genome in much longer DNA fragments than now possible. This effort would be difficult for either team alone, and the collaboration promises to be fruitful for both parties. No money will change hands between the two organizations. LTI will have the first opportunity to license any products resulting from the joint effort and would pay royalties to LANL under such a license.

A mission of the DOE Human Genome Program is to transfer technologies developed in research laboratories to the private sector. This CRADA, an example of basic science and applied technology moving forward simultaneously, will set the stage for increased industry access to laboratory technology and will help government laboratories draw on private-sector resources.

In announcing the pact, Deputy Secretary of Energy W. Henson Moore said, "This agreement signifies a new partnership between government and industry researchers to work together to advance scientific knowledge and, equally important, to apply it in practical technologies to benefit the American people and the American economy."



W. Henson Moore, Deputy Secretary of Energy; John Whetten, LANL Associate Director for Energy and Technology; and J. Stark Thompson, LTI President and CEO, (seated l. to r.) signed the first CRADA of the Human Genome Project on March 21. Others participating are (l. to r.) Linda Stuntz, Deputy Under Secretary of Energy; Representative Joe Skeen (R-N.M.); Representative Bill Richardson (D-N.M.); Senator Jeff Bingaman (D-N.M.); Representative Constance Morella (D-Md.); and Senator Pete Domenici (R-N.M.).

The United States is considered outstanding in developing technology but not in transferring it from federal organizations to the private sector. An innovative response by Congress to the growing challenge of U.S. competitiveness, CRADAs are designed to make the laboratories more user friendly, facilitate technology transfer, and foster economic competitiveness by encouraging laboratory-industry partnerships.

In addition to providing an important vehicle to leverage research dollars, CRADAs help fulfill the vision of national laboratories solving complex, nationally important problems by demonstrating that investing in science can ultimately impact competitiveness. Several more CRADAs are now being planned, and DOE is committed to moving quickly and efficiently into future agreements.

The authority to enter into CRADAs was extended to DOE contractor-operated laboratories through the National Competitiveness Technology Transfer Act of 1989,

DOE *(from p. 4)*

can be achieved by using client-server architecture found in most commercial, multiuser database systems. Peter Pearson (Johns Hopkins University) described the public database efforts under way with the Genome Data Base (GDB) project (sponsored by the Howard Hughes Medical Institute). He also discussed collaborations with LANL and LLNL for sharing physical mapping data and the possibility of researchers viewing laboratory-generated map data in the information-rich context of GDB. ◊

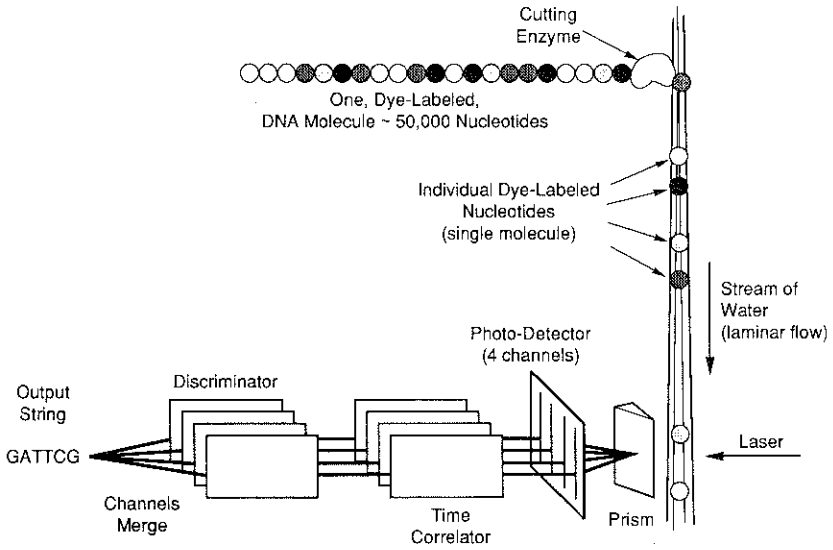
Genome News

LTI Says CRADA Will Increase Research Pace

DNA Rapid Sequencer being developed by LANL and LTI. If successful, the technology will allow sequencing of 50,000-bp DNA fragments at 1000 bp/s.

cosponsored by New Mexico Senators Pete Domenici and Jeff Bingaman. "Human gene mapping holds tremendous potential for improving the quality of life for so many," said Domenici, who envisioned research partnerships among the laboratories, businesses, and universities to work on projects such as human genome, high-temperature superconductivity, and semiconductors.

The research described in the agreement will use an LTI-modified DNA polymerase to label a single DNA strand with four different fluorescent, base-specific tags; an exonuclease is then used to cut the labeled nucleic acid base pairs from the DNA (see figure). To determine the DNA base sequence, the individual labeled bases are induced to fluoresce in one of four colors as they pass sequentially through a focused laser beam. The bases can be identified and counted by a sensitive photodetector.



The most commonly used commercial sequencing methods can handle only short DNA fragments of about 500 bp. If this new technology proves successful, researchers will be able to sequence fragments at least 100 times longer. A team of LANL researchers, led by Richard Keller and funded by the DOE Human Genome Program, will offer expertise in physical chemistry, detection technologies, instrumentation, and DNA handling to bring to fruition a novel DNA sequencing technique patented by several LANL scientists.

The LTI scientists, led by John Harding since 1989, will concentrate on developing the new enzymes and modified nucleotides essential for sequencing DNA with the new technology. Harding's research efforts have centered on creating new tools and applying existing ones to analyze and map mammalian genomes.

Council on Competitiveness Urges Action To Strengthen Performance

The United States' once-commanding lead in the critical technologies driving economic growth and national security is being challenged by international competition, according to a new report by the Council on Competitiveness.

Gaining New Ground: Technology Priorities for America's Future is the result of a 2-year effort guided by a group of technology experts from industry, universities, and labor from around the country. The report is based on an analysis of 94 technologies in 9 major economic sectors that together account for sales of more than $1 trillion.

The report lists several key findings, including the following:

- The critical generic technologies that will drive economic growth and competitiveness over the next decade already exist, and industry needs to improve its ability to convert them into marketable products and services.
- U.S. leadership in many critical technologies has been slipping and, in some cases, has been lost altogether. Other countries are systematically achieving leadership in many critical technologies.
- America's research universities constitute a great national asset, but their focus on technology and competitiveness is limited.

The report concludes that, unless the nation acts to enhance its position in critical generic technologies, the U.S. ability to compete will erode further, with serious consequences for jobs, economic growth, and national security. The report recommends a series of actions for government, industry, and universities to strengthen the country's performance. One recommendation is that technological leadership become a national priority.

The Council on Competitiveness is a nonprofit coalition of chief executives from leading businesses, organized labor, and higher education, whose goal is to improve the ability of U.S. industry and its workers to compete in world markets.

Full copies of the report may be obtained for $20. ◊

Contact:
Council on Competitiveness
900 17th Street NW, Suite 1050
Washington, DC 20006
202/785-3990

"It's high risk, high payoff. If we can make it work, it will improve sequencing rates by several orders of magnitude. We're shooting for about 1000 base pairs a second, compared with current commercial sequencing rates of less than 10,000 base pairs a day," Keller said. The projected rate of 1000 bp/s is derived from enzymatic rates of cleavage and rates of detection.

Through its BRL and GIBCO brands, LTI is a leading supplier worldwide of molecular biology and cell and tissue culture products to academic and industrial laboratories involved in genetic and other basic biology research. The company, headquartered in Gaithersburg, Maryland, has commercialized many enzymes and several modified nucleotides and now develops an average of 400 new products each year.

LTI President and Chief Executive Officer J. Stark Thompson stated, "We are confident that our agreement with Los Alamos will lead to the development of products that will significantly move forward the pace of human genome research. An added benefit is that these results will strengthen the nation's biotechnology industry in the world marketplace."

Operated by the University of California for DOE, LANL was founded in 1943 during World War II as part of the Manhattan Project. Historically, the defense-oriented national laboratories have focused on national security issues, but now their technical base is recognized for contributions in other important complex technological areas. ◇

Reported by Anne Adamson
HGMIS, ORNL

For more information on the LANL-LTI CRADA, contact:

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Moore Calls Tech Transfer Critical to Future

On January 24, W. Henson Moore, Deputy Secretary of Energy, spoke before the DOE Technology Transfer Seminar in Washington, D.C. Some of his remarks are excerpted and summarized in the article below.

The DOE science and technology mission, which encompasses fundamental research, technology development, and technology transfer, is critical to our nation's future. If fundamental research is the starting point, technology transfer must be the finish line. To fulfill our science and technology mission, we must ensure that knowledge moves efficiently up the chain from basic science to precompetitive technology and into the commercial marketplace.

This new emphasis on science and technology has come about for two reasons:

- Technology is the key to economic growth and global competitiveness in the 21st century. Economic growth is based on the development of new technology, and new technology is derived from basic research. In recent years the United States has fallen behind in applying research for economic benefit.
- Technology is vital to reconciling our need for energy with our commitment to a cleaner, healthier environment.

We have seen the enormous value of cutting-edge technology in the recent war in the Middle East – a testament to the quality of U.S. science and technology when they are consistently supported. We must all begin to work toward an equally high level of consistent support for nondefense research and development. We must promote an integrated process that encourages the natural evolution of basic science into precompetitive technologies, then into commercial systems, products, and jobs.

DOE, one of six federal agencies that account for almost all government R&D, has enormous resources to accomplish this mission. We have some 35,000 scientists and engineers, 14,000 trained technicians, and a budget of $6 billion this year, about equally divided between defense and nondefense. We must maximize the use of human and financial resources to accomplish technology transfer.

To achieve a dynamic, constructive working partnership between government and industry, we must first get the work of our laboratories better known. Second, we need to stop *talking* technology transfer and start *doing* it.

The key characteristics of such a partnership are a more-efficient negotiating process, localized decision making, and flexibility within a consistent framework. Other benefits of this strengthened partnership between government and industry are the following:

- increased use of joint R&D planning groups, more cost sharing, and expanded mechanisms for introducing the concept of market pull into DOE-funded research;
- improved intellectual property protection;
- streamlined administrative processes, like those in the new CRADAs, to speed the negotiation and approval of agreements; and
- increased interaction among researchers.

Modern technology, much like modern information, is extremely fragile and short-lived. ◇

"If fundamental research is the starting point, technology transfer must be the finish line."
— W. Henson Moore

Genome News

NIH Discusses cDNA Role with Invited Group

The NIH Human Genome Program emphasizes the construction of complete genetic and physical maps of the genomes of human and selected model organisms and development of new technology and information systems to manage mapping and sequencing data. Sequencing entire genomes will begin when the cost of sequencing is substantially below current cost.

The NIH National Center for Human Genome Research (NCHGR) explored the usefulness of cDNA isolation and analysis in helping to achieve the Human Genome Project's 5-year goals. This examination comes in light of the attention being given to cDNAs by human genome programs in the United Kingdom, some European countries, and more recently by DOE. A small group (see participants' list below) that included members of the Program Advisory Committee on the Human Genome met December 2, 1990, in Bethesda, Maryland, to discuss the role cDNAs might play in the NIH Human Genome Program.

The group identified the following advantages of pursuing cDNA studies:

- cDNAs are a source of sequence tagged site (STS) markers and can be used to identify potential candidate genes.
- A central goal of the Human Genome Project will be to identify stretches of DNA coding for proteins, and biologists would benefit more if they had this information sooner rather than later.
- Some model systems, such as *Escherichia coli, Caenorhabditis elegans*, and *Drosophila melanogaster*, have physical maps that are complete or nearly so. Studies of these genomes are at a point where cDNA research could make a significant contribution to understanding the biology of these organisms, thereby increasing their value as models for human studies.

The group cautioned that this is a research area not previously envisioned as part of the 5-year goals. If cDNA studies are supported, the group suggested the following considerations:

- Long-term Human Genome Project goals should not be compromised for short-term payoffs. Full-scale pursuit of cDNAs may result in dilution of effort for quick biological returns.
- Problems with current cDNA libraries include structure and quality, correction for super abundance, achievement of full-length cDNAs, detection of alternate transcripts, and localization on the physical map.

Participants suggested that NCHGR pursue development of technology with the following objectives:

- To identify all coding regions in a large segment of genomic DNA.
- To construct and order high-quality, tissue-specific, full-length cDNA libraries.

The group also indicated that many cDNAs have been well characterized by biologists working in areas other than the Human Genome Project. They suggested that mechanisms be developed to facilitate identification of STSs on these cDNAs and mapping of these cDNAs to chromosomes. The group recommended that NCHGR collaborate with other NIH components on this project. (See announcement of RFA HG-91-02, p. 19.) ◇

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

MEETING PARTICIPANTS

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Glen Evans
Salk Institute for Biological Studies

Bettie Graham
NIH NCHGR

Mark Guyer
NIH NCHGR

Daniel Hartl
Washington University School of Medicine

Elke Jordan
NIH NCHGR

Robert Moyzis
Los Alamos National Laboratory

Maynard Olson
Washington University School of Medicine

Philip Sharp
Massachusetts Institute of Technology

Edwin Southern
University of Oxford

Sherman Weissman
Yale University

Norton Zinder
Rockefeller University

NCHGR Advisory Council Holds First Session

The National Advisory Council for Human Genome Research held its first meeting in Bethesda, Maryland, on January 22. Council members (listed below) reviewed grants and were oriented on NIH procedures.

The council advises the Director of NIH, the Secretary and the Assistant Secretary for Health of the Department of Health and Human Services, and the Director of the National Center for Human Genome Research (NCHGR) on the conduct of human genome research, training, and information dissemination related to the Human Genome Project.

The council also provides final review of applications submitted to NCHGR for research or training grants and cooperative agreements and recommends approval for projects that show promise. ◇

Next NCHGR Advisory Council Meeting: June 7

ADVISORY COUNCIL MEMBERS:

Francisco J. Ayala
University of California, Irvine; population geneticist; National Academy of Sciences member; Chairman of the Board of Basic Biology of the National Research Council.

David Botstein
Stanford University School of Medicine; author of numerous scientific papers on genetics and molecular biology; member of several editorial boards and advisory committees; member of the NIH Program Advisory Committee on the Human Genome, 1988–90.

K. Danner Clouser
Pennsylvania State University College of Medicine; philosopher, educator, and biomedical ethicist; member of numerous advisory boards; Founding Fellow of The Hastings Center.

Francis S. Collins
University of Michigan and Howard Hughes Medical Institute; physician and molecular geneticist noted for the recent isolation of the cystic fibrosis and neurofibromatosis type 1 genes.

Jerome R. Cox
Washington University; computer scientist with special knowledge in database management and design; consultant and chair of numerous computer science and biomedical research boards and advisory committees.

Norman Davidson
California Institute of Technology; biologist; faculty member since 1946; California Scientist of the Year (1980).

Joe W. Gray
Lawrence Livermore National Laboratory; biomedical scientist; author of numerous publications on flow cytometry systems and cell cycles.

Hiliary H. Holloway
New Atlantic Bank and counsel at the law firm of Marshall, Dennehey, Warner, Colemann, and Goggin; member of the National Board of Directors of the United Negro College Fund; recipient of the Martin Luther King, Jr., Award.

Kay Jamison
Johns Hopkins School of Medicine; clinical psychologist; active with lay organizations that represent individuals with mental illness.

Dorothy Nelkin
New York University; interdisciplinary social scientist whose work has focused on the role of science in public policy and on public understanding of science; author of *Selling Science: How the Press Covers Science and Technology*.

Shirley M. Tilghman
Princeton University; molecular biologist and developmental geneticist; member of several advisory committees.

Keith R. Yamamoto
University of California, San Francisco; biochemist and biophysicist; National Academy of Sciences member; expert in gene organization, expression, and function.

NIH PACHG Appoints New Members, Chair

Stanford biochemist and molecular biologist Paul Berg will succeed Norton D. Zinder (Rockefeller University) as Chair of the National Center for Human Genome Research (NCHGR) Program Advisory Committee on the Human Genome (PACHG). He will also serve with Sheldon Wolff (University of California) as Cochair of the DOE-NIH Joint Subcommittee on the Human Genome. Berg and two other new members, Diane Smith and Robert Tjian, join PACHG for 4-year terms.

Berg is currently Director of the Beckman Center for Molecular and Genetic Medicine in Palo Alto, California, and professor of biochemistry at Stanford University School of Medicine.

Among his many honors are California Scientist of the Year (1963), the Albert Lasker Basic Medical Research Award, the Nobel Prize in Chemistry, and the National Medal

(see PACHG, p. 10)

Paul Berg, Chair
NCHGR Program
Advisory Committee
on the Human Genome

Genome News

DOE-NIH Establish Mouse Working Group

For meeting minutes or additional information on the DOE-NIH Mouse Working Group, contact:

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Fax: 301/480-2770

A new joint working group has been established by the DOE-NIH Joint Subcommittee on the Human Genome to advise the committee on near-term and future research priorities and needs in mouse genomic research as it relates to goals of the Human Genome Project. All human genome joint working groups have the following general responsibilities:

- facilitate implementation of 5-year-plan goals;
- establish research priorities;
- identify research, training, and technical needs; and
- coordinate U.S. research activities with those of other countries, especially Europe and Japan.

The 5-year plan states that the study of model organisms is essential to interpreting data obtained in studies of humans and to understanding human biology. For this reason, the plan continues, the Human Genome Project will support mapping and sequencing of the genomes of a select number of nonhuman organisms. The laboratory mouse is considered one of the most useful model organisms.

The mission and agenda of the NIH-DOE Joint Working Group on the Mouse will be defined at its first meeting, scheduled for May 6 in Bethesda, Maryland. The group plans to meet twice yearly in the Washington area. ◇

DOE-NIH Mouse Working Group:

Verne Chapman
Roswell Park Cancer Institute

Neal Copeland
NCI-Frederick Cancer Research and Development Center

Frank Constantini
Columbia University

William Dove
University of Wisconsin, Madison

Joe Nadeau
Jackson Laboratory

Roger Reeves
Johns Hopkins University School of Medicine

Janet Rossant
Mt. Sinai Hospital

Oliver Smithies
University of North Carolina, Chapel Hill

Richard Woychik
Oak Ridge National Laboratory

PACHG *(from p. 9)*

of Science. His memberships include the National Academy of Sciences, the American Academy of Arts and Sciences, the Institute of Medicine, and the French Academy of Sciences. Berg coauthored the recently published reference text *Genes and Genomes* (see abstract, p. 18)

Diane C. Smith, who replaces outgoing committee member Jaime Carbonell (Carnegie-Mellon University), is an engineer and mathematician who has been working in the field of computer science since 1972. After serving on the computer science faculty at the University of Utah, she joined the Computer Corporation of America as Vice President for Advanced Information Technology. Smith is currently manager of technology development for the Custom Systems Division of the Xerox Corporation.

Robert Tjian replaces David Botstein (Stanford University School of Medicine). Tjian brings broad experience in the areas of molecular and cellular biology to the committee, with a specific focus in the field of virology and regulation of gene transcription. He has been an investigator at Howard Hughes Medical Institute since 1987 and professor in the Department of Biochemistry, University of California, Berkeley, since 1982. His awards include the Pfizer Award for Enzymology in 1983 and the Milken Family Medical Foundation Cancer Research Award in 1988.

The 12 PACHG members are selected by Department of Health and Human Services (DHHS) Secretary Louis W. Sullivan. PACHG gives advice on research directions and goals of the Human Genome Project to the DHHS Assistant Secretary for Health, the NIH Director, and the NCHGR Director.

See *HGN* **2**(3), 7 (September 1990) for a complete list of PACHG members. ◇

To receive minutes of PACHG and NIH-DOE Joint Subcommittee Meetings, contact:

Office of Communications
NIH NCHGR
Bldg. 38A, Room 617
Bethesda, MD 20892
301/402-0911
Fax: 301/480-2770

Workshop on Mouse Genome Mapping

The Fourth International Workshop on Mouse Genome Mapping, held November 4–8, 1990, in Annapolis, Maryland, brought together a community of scientists interested in mapping the mouse genome. The work of chromosome committees began in Annapolis, and their reports are being prepared for publication in *Mammalian Genome* in 1991.

Workshop participants defined common research goals for mapping the mouse genome that reflect the unique strengths and value of the mouse as an experimental genetic system. These goals include development and dissemination of the following:

- saturated genetic maps based on well-spaced reference loci,
- physical maps of selected chromosome segments, and
- mouse genomics databases.

■ Genetic Mapping

Goals: *Establishment of about 160 to 320 reference loci spaced 5 to 10 cM apart on each chromosome.* Ideal reference loci have the following characteristics:

- inexpensive and easy to type,
- highly variable among laboratory strains as well as diverse *Mus* species,
- universally available as markers typed by polymerase chain reaction (PCR) assays as well as Southern blotting,
- derived from expressed genes, and
- conserved between humans and mice.

Such sets of reference loci will provide universal cross-reference points for mapping specific genes of interest and a framework for high-resolution mapping of specific chromosomal regions.

Results: *Unambiguously ordered multilocus maps of extended linkage groups, with adjacent markers spaced no more than 20 cM apart, for all chromosomes.* The maps are composed largely of named genes identified by recombinant DNA probes in Southern blotting assays. Hundreds of genes are being placed each year. Saturated maps now exist for most segments of the X chromosome, estimated to be 80 cM in length; over 50 ordered DNA markers are spaced no more than 5 cM apart. Extended regions of chromosomes 1, 2, 3, 16, and 17 are similarly well mapped. Physical mapping studies have already confirmed the accuracy of some maps.

Several crucial gaps in these maps are now being addressed. Strategies for identifying centromeres and telomeres are being developed, and new approaches for identifying polymorphic anonymous DNA segments should yield large numbers of widely distributed new markers. DNA variants associated with several telomeres have been identified, and a satellite probe, specific for the centromeres of laboratory-strain mouse chromosomes, seems likely

Mouse Chromosome Committees

CHROMOSOME NUMBER	CHAIR AND COCHAIRS
1	**Michael Seldin**, Duke University Medical School **Beverly Paigen**, Jackson Laboratory
2	**Linda Siracusa**, Thomas Jefferson University **Catherine Abbott**, University College, London
3	**Miriam Meisler**, University of Michigan, Ann Arbor **Michael Seldin**, Duke University Medical School
4	**Jeffrey Friedman**, Rockefeller University **Konrad Huppi**, NIH National Cancer Institute (NCI)
5	**Christine Kozak**, NIH National Institute of Allergy and Infectious Diseases **Dennis Stephenson**, Roswell Park Cancer Institute
6	**Rosemary Elliott**, Roswell Park Cancer Institute **Nathan Bahary**, Rockefeller University
7	**Eugene Rinchik**, Oak Ridge National Laboratory **Steve Brown**, St. Mary's Hospital Medical School, London
8	**Jeffrey Ceci**, Frederick Cancer Research and Development Center, NCI **Jo Peters**, Medical Research Council
9	**David Kingsley**, Frederick Cancer Research and Development Center, NCI
10	**Ben Taylor**, Jackson Laboratory **Monica Justice**, Frederick Cancer Research and Development Center, NCI
11	**Arthur Buchberg**, Thomas Jefferson University **Sally Camper**, University of Michigan, Ann Arbor
12	**Peter D'Eustachio**, New York University Medical Center
13	**Monica Justice**, Frederick Cancer Research and Development Center, NCI **Dennis Stephenson**, Roswell Park Cancer Institute
14	**Joseph Nadeau**, Jackson Laboratory
15	**Beverly Mock**, NIH National Cancer Institute
16	**Roger Reeves**, Johns Hopkins School of Medicine **Muriel Davisson**, Jackson Laboratory
17	**Lee Silver**, Princeton University
18	**Muriel Davisson**, Jackson Laboratory
19	**Jean-Louis Guenet**, Institut Pasteur
X	**Steve Brown**, St. Mary's Hospital Medical School, London **Philip Avner**, Institut Pasteur
Y	**Eva Eicher**, Jackson Laboratory

Genome News

Copies of the workshop program and abstracts are available from:

Verne Chapman
Department of Molecular and Cellular Biology
Roswell Park Cancer Institute
Elm and Carlton Streets
Buffalo, NY 14263
716/845-5840
Fax: 716/845-8169

to provide a genetic tag for centromeres as genetic loci in interspecies backcrosses.

Novel uses of oligonucleotides as probes or as PCR primers have dramatically increased the number of polymorphic loci available while reducing the time and genomic DNA consumed in doing the assays. Some combination of strategies seems likely to provide the markers needed to fill the remaining gaps in the genetic map. Other strategies exploit cross hybridization of mouse genomic DNA with human variable number tandem repeat probes and with randomly chosen oligomer sequences. Other methods appear likely to define numerous useful polymorphisms throughout the mouse genome.

Elegant in situ hybridization experiments suggest that many repeated sequence classes that are widely distributed over the genome may tend to concentrate in regions corresponding to Giemsa bands. This biased distribution raises the intriguing possibility that in the course of pushing genetic maps to closure, much will be learned about the physical organization of mammalian chromosomes and perhaps about the evolution of the organization as well.

■ Physical Mapping

Goals: *Physical analysis of regions of particular genetic interest, with the long-term goal of an ordered set of recombinant clones spanning the whole genome.*

Results: *Availability of physical maps spanning megabase regions near loci of interest.* These data, together with the growing number of yeast artificial chromosome (YAC) clones centered on genes of interest, suggest that resources already available for large-scale cloning and mapping may be sufficient to assemble large parts of the desired long-range DNA map of the mouse genome. Use of YACs to attack genomic regions of special interest is rapidly becoming routine.

Simultaneously, significant technology development is taking place. Improved methods were reviewed for screening high-density filters of YAC libraries and for generating and interpreting fingerprinting data for YAC clones.

A particular advantage of using the mouse as an experimental system is a series of deletion mutations centered on several genes known to play crucial roles in early development and in neural function. These deletion resources will be useful in the long-range physical mapping of several regions of the mouse genome.

■ Databases

Goals: *Collection, integration, analysis, display, and dissemination of mouse genomic information.*

Results: *An impressive collection of databases recording gene mapping results, molecular clones and probes, and physical mapping data.* Specific modifications were discussed to ensure that each database can continue to accommodate data flow and store increasing amounts of raw data (e.g., recombination fractions and haplotypes) as well as derived interpretations (e.g., linkage maps). Work is under way to create methods for integrating and displaying these data in interactive systems that draw simultaneously on several data sources. Also, efforts are being made in conjunction with the Genome Data Base project to provide users with ready access to integrated mouse and human genomic information.

■ Conclusion

Elaboration of a mouse genome map based on DNA markers is well under way. Based on visible mutations and biochemical markers, numerous points of cross reference to the classical map have been established. The use of several mouse species and genetically defined inbred strains has yielded highly informative genetic mapping resources that have been especially valuable in mapping functional genes.

Thus, the usefulness of comparing mouse with human genetic and physical maps has increased as more mouse genes have been mapped and as experimental models of human hereditary disease have been identified. The ability to define, map, and manipulate mouse genes makes the species a unique laboratory resource for studying the genetics of biologically and medically important traits. ◇

Reported by Verne Chapman
Roswell Park Cancer Institute,
Peter D'Eustachio
New York University Medical Center,
and
Joseph Nadeau
Jackson Laboratory

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.

Meeting Reports

Second X Chromosome Workshop

The second X Chromosome Workshop, funded by the U.K. Medical Research Council, was held at St. Catherine's College, Oxford, on January 5–7. Some 70 participants heard short presentations of new mapping data and then divided into four groups to construct physical and genetic maps and to compile a table. The table indicates where contigs are available and which laboratories have yeast artificial chromosome (YAC) clones of interest. Copies of the table, which has been submitted to *Genomics*, are available on request from Kay Davies (see box, upper right). A summary of the reference markers is presented in the figure at lower right.

Although a complete genetic map of the X chromosome has been available for some time, it was based largely on markers with restricted information potential. Several microsatellite markers along the chromosome now indicate that a higher-resolution map will soon be available; 12 Mb of the short-arm telomere have been mapped by pulsed-field electrophoresis [Christine Petit (Institut Pasteur); Andrea Ballabio (Instituto G. Gaslini)], and an equivalent map has been constructed for the long-arm telomere [Anne-Marie Poutska (German Cancer Research Center); Hans Lehrach (Imperial Cancer Research Fund {ICRF})]. Researchers are currently assembling YAC contigs to complement these studies.

Important contributions were made to the characterization of sequences expressed from inactive X chromosomes and mapped in the region containing the putative inactivation center [Ballabio; Huntington Willard (Stanford University School of Medicine); Philip Avner (Institut Pasteur)]. Methylation differences close to the fragile site in individuals expressing the phenotype were separately reported by the laboratories of Jean-Louis Mandel (Institute National de la Sante et de la Recherche Medicale) and Davies.

Mapping resources for the X chromosome were discussed. Several groups are screening YAC libraries to complete a contig map of the chromosome [Thomas Caskey (Baylor College of Medicine); Centre d'Etude du Polymorphisme Humain; Lehrach; Robert Nussbaum (University of Pennsylvania School of Medicine); David Schlessinger (Washington University School of Medicine); Michele D'Urso (International Institute of Genetics and Biophysics)]. Ordered cosmid libraries are proving a valuable resource [Lehrach; David Bentley (Guy's Hospital)].

The chromosome was divided into intervals by well-characterized somatic cell hybrid breakpoints, which may be used as common reference points on the map [Peter Goodfellow (ICRF); Willard]. Most chromosome regions are being actively mapped both genetically and physically because a disease locus of interest exists in most intervals.

The Genome Data Base [Peter Pearson (Johns Hopkins University)] was accessible during the meeting so participants could input data and reference the database.

The third X Chromosome Workshop, to be organized by Daniela Toniolo (Consiglio Nazionale delle Richerche) and Michele D'Urso, will be held in Italy in 1992. ◊

Reported by Kay Davies
Institute of Molecular Medicine
and
Ian Craig
University of Oxford

X Chromosome contact:

Kay Davies
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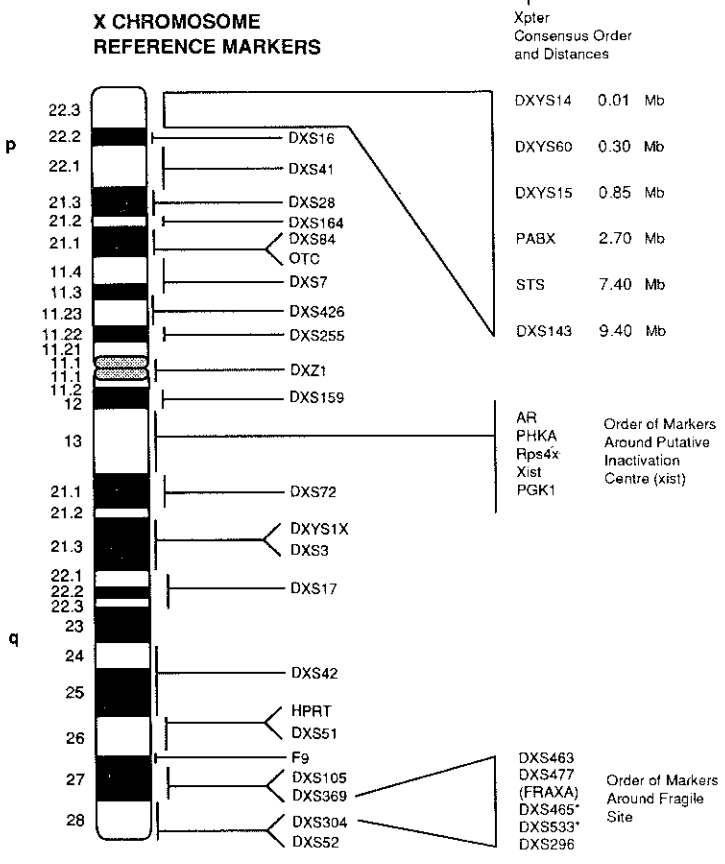
United Kingdom

Reference marker positions based on the X-chromosome committee report from HGM10.5 (Oxford) and modified to include information presented at the workshop. This information concerns physical ordering and map positions for the Xpter region together with the order of markers around the putative inactivation center and the fragile site (contributors acknowledged in text).



*Probes for these Loci detect (by PFGE) methylation differences in males expressing the fragile site at Xq27.3 (see text)

Resources

Nonprofit Resource Centers Facilitate Mapping

Researchers Can Readily Compare Results Obtained with Well-Characterized Cell Cultures and DNA Samples

Investigators in the international Human Genome Project and others often rely on centralized sources of cell lines and DNA to facilitate mapping. For nominal fees, these nonprofit sources offer reliable, well-characterized cell cultures and DNA samples that enable comparison of results from different laboratories. In addition, individual laboratories are spared costly and time-consuming storage and distribution and are given access to the latest resources.

Repository services include collection, authentication, amplification, storage, and distribution of cells and DNA, including management of updated information on all holdings. Several repositories also maintain databases on results obtained using their resources. Access to some of the resources may be limited.

U.S. CENTERS

Two major U.S. resource centers are the American *Type Culture* Collection (ATCC) in Rockville, Maryland, and the Coriell Institute for Medical Research in Camden, New Jersey. ATCC, a private, nonprofit organization, maintains the most diverse existing collection of microorganisms and cell lines, including bacteria, fungi, protozoa, viruses, metazoan cell lines, and DNA recombinants. Coriell houses the world's largest collection of human cells and offers somatic cell hybrid resources.

Other important resource facilities include the National Cell Culture Center and the Jackson Laboratory. The newly established National Cell Culture Center in Minneapolis, Minnesota, provides large-scale mammalian cell culture services. Jackson Laboratory, located in Bar Harbor, Maine, offers mouse strains, mutations, and mouse DNA resources.

These centers are under contract to various federal agencies to provide resources to or serve as repositories for the research community.

ATCC Catalogue

The fourth edition of the ATCC/NIH *Repository Catalogue of Human and Mouse DNA Probes and Libraries* (1990) lists materials deposited at ATCC as part of the DNA repository. Also enumerated are related materials from the ATCC molecular biology collection and Patent Culture Depository.

Contact for catalogue:
800/638-6597 or 301/881-2600
Fax: 301/321-5826
Repository information:
Donna Maglott, 301/231-5586
Fax: 301/770-1541

■ ATCC

Since 1925 ATCC has maintained and distributed biological resource material to the international research community. It offers the following traditional material:

- 13,630 bacterial strains,
- 24,780 strains of filamentous fungi and yeasts,
- 1005 protozoan type cultures,
- 1485 animal and plant viruses, and
- over 3000 human and other animal cell cultures.

ATCC recently added a collection of recombinant DNA probes, clones, and libraries; approximately 400 new probes and 5 to 10 new libraries will be added annually. A description of several useful ATCC mapping resources follows.

DNA Probes and Libraries Repository

In 1985 the NIH National Institute of Child Health and Human Development (NICHD) established an international Repository of Human and Mouse DNA Probes and Libraries within ATCC. Repository functions include the following activities:

1. DNA Probes; Clone and Genomic Collections. Repository staff obtain, amplify, and distribute over 100 probes detecting restriction fragment length polymorphisms (RFLPs). They also maintain clone and genomic repositories from known genes independent of RFLP detection.

- The clone repository—over 1640 human and 155 mouse clones—contains discrete sequences distributed throughout the human and mouse genomes. Clones specific to each human chromosome and most mouse chromosomes are available. Restriction analysis is used to verify the structure of all clones received. A photograph of the ATCC restriction digest gel and a sample of the ATCC clone preparation are returned to the depositor for confirmation before the clone is distributed as transformed bacteria or bacteriophage. Clones with human inserts may also be available as purified DNA. The NICHD contract mandates that 300 human and 100 mouse clones be added annually.
- The genomic repository was established in 1988 to maintain a collection of clones constituting a complete genome. Its primary function is to develop and evaluate methods and instrumentation needed to maintain a human genome repository. These methods include automated DNA preparation; clone verification; data maintenance and analysis; and

sample storage, recovery, and distribution. Currently available are 850 clones from the *Saccharomyces cerevisiae* genome (provided by Maynard Olson's Washington University Laboratory), organized in about 180 different contigs.

2. National Laboratory Gene Library Project (NLGLP) Resources. Sixty chromosome-specific gene libraries constructed at Lawrence Livermore National Laboratory (LLNL) and Los Alamos National Laboratory (LANL) are preserved and distributed by ATCC. [*HGN* **2**(1), 12–13 (May 1990)].

3. Information Management/Database. Catalogues, information sheets, and a menu-driven online database describe the repository's holdings. For information on database access, see box at right.

4. DNA Primers. ATCC offers predesigned oligonucleotide primers for in vitro amplification of human DNA, including oligonucleotide pairs for 50 polymorphic loci. Product sheets give information on primers, including allele sizes, gene name, cytogenetic location, and sequence.

Other ATCC Mapping Resources

ATCC offers over 3000 well-characterized cell lines and hybridomas through five different government-sponsored collections, thus providing a valuable resource for studying gene expression. About 80 species are represented, with the majority of cultures being human, lower primate, or laboratory animal in origin. [Contact: Technical Collection Specialist, 301/231-5553.]

ATCC Repository Database Access

Use of the menus requires emulation of a VT100 terminal (8 data bits, a stop bit, full duplex, parity none) and a 1200-baud modem. Log on is automatic after calling 301/881-4909 and answering the prompts with the word "common" followed by return/enter. Telephone service is the only charge.

■ Coriell Institute for Medical Research

Located on the campus of the University of Medicine and Dentistry of New Jersey, the Coriell Institute is a nonprofit biomedical research institute that establishes, characterizes, stores, and distributes over 7000 cell lines worldwide. Coriell has provided cells to scientists around the world for 18 years and in 1990 began offering DNA samples.

Three major NIH cell repositories housed at Coriell compose the world's largest collection of human cells:

- Human Genetic Mutant Cell Repository of the National Institute of General Medical Sciences, founded in 1972;
- Aging Cell Repository of the National Institute on Aging, created in 1974; and
- National Cell Repository (NCR) of the National Institute of Mental Health. Established in 1990, NCR facilitates research on the genetic components of manic depression, Alzheimer's disease, and schizophrenia. This repository is expected to add 6000 cell lines by 1993 and to achieve a total of 7500 additional lines by 1995.

The three repositories above, in addition to smaller collections on cancer, diabetes, and other diseases, are collectively known as the John T. Dorrance, Jr., International Cell Science Center. Richard Mulivor is the director.

Cell Lines. All cell lines, which are derived from samples collected worldwide, are screened to confirm species of origin and for mycoplasmas and other contaminants, are well characterized, and are clinically documented. An extensive bibliographic database and abstracts of literature citations documenting culture characterizations are also maintained.

Human Cultures. Coriell maintains cell cultures (derived from human fibroblasts, lymphoblasts, and amniotic fluid) that represent over 400 genetic diseases and 800 chromosomal aberrations. Virus-transformed fibroblast cultures and cultures from apparently normal individuals are also available.

To aid linkage analysis studies, Coriell offers cultures from multigenerational family groups; databases are being maintained by several contributors of samples. Within the collections are samples from affected individuals and families (including non-affected members) with cystic fibrosis, fragile X-linked mental retardation, Huntington's disease (from the Venezuelan pedigree), retinitis pigmentosa, and major affective disorder (from the Amish pedigree). Utah pedigrees were contributed by Ray White and collaborators at the Howard Hughes Medical Institute (HHMI) in Utah.

Somatic Cell Hybrids: Cultures and DNA. Human/rodent somatic cell hybrids are available as cultures and purified DNA. For details on their mapping panel, see box, p. 16. Coriell also offers DNA from monochromosomal hybrids for human chromosomes 2–9, 11–14, 16–19, 21, 22, X, and Y, as well as DNA from hybrids

Coriell Houses World's Largest Human Cell Collection

Resources

retaining 3 or fewer human chromosomes in a variety of combinations.

[Contact for Coriell collections: Richard Mulivor, 609/757-9697. Catalogue: 800/752-3805 or 609/757-4848, Fax: 609/964-0254.]

■ National Cell Culture Center

The National Cell Culture Center offers customized services for large-quantity production of animal cells and secreted proteins. By providing access to state-of-the-art cell culture instrumentation and techniques, this new program addresses the needs of the small research laboratory as well as those of larger collaborative groups. The center provides cells in suspension and monolayer cultures in quantities ranging from 25 to 150 L. In addition, cell-secreted products such as monoclonal antibodies are available in quantities of 1 to 100 g.

The National Cell Culture Center addresses needs of small research laboratories as well as those of larger efforts.

Human/Rodent Somatic Cell Hybrid Mapping Panel Available from Coriell

The National Institute of General Medical Sciences (NIGMS) Human Genetic Mutant Cell Repository has Mapping Panel No. 1 DNA samples available for distribution. The panel consists of DNA isolated from 18 human/rodent somatic cell hybrids retaining from 1 to 19 human chromosomes. Fifteen samples were isolated from human/mouse somatic cell hybrids resulting from the fusion of male human fibroblasts (IMR-91) with the thymidine kinase-deficient mouse cell line (B-82). The panel is completed with DNA isolated from three monochromosomal hybrids retaining human chromosomes 9, 16, and X.

The panel has been characterized by the following:

- G-banded chromosome analysis;
- in situ hybridization analysis using biotinylated total human DNA to detect human chromosomes, human/rodent translocated chromosomes, and human chromosome fragments; and
- Southern blot hybridization.

Probes were used for the short and long arms of all human chromosomes except 10, 13, 14, 15, 20, and 21, all of which were analyzed with long-arm probes only. The panel consists of 50 μg of DNA from each hybrid and 100 μg of DNA from each of three parental human and rodent cell lines.

Contact: Human Genetic Mutant Cell Repository; Coriell Institute for Medical Research; 401 Haddon Avenue; Camden, NJ 08103; [800/752-3805 in the United States; 609/757-4848 from other countries; Fax: 609/964-0254].

Sponsored by NIH National Center for Research Resources, this service is available to researchers throughout the United States and Canada. The Scientific Advisory Committee selects and prioritizes requests; preference is given to NIH-supported projects. Researchers are charged only for consumable materials and a portion of labor costs for each project. [Application form or additional information: Mark Hirschel, director, 800/325-1112, Fax: 612/786-0915.]

■ Jackson Laboratory

Located in Bar Harbor, Maine, Jackson Laboratory maintains a widely diverse collection of genetically defined mice for basic research and for studies of genetic and developmental factors underlying a variety of disorders. Over 700 different mutations and 1000 different strains and sets of recombinant inbred strains and congenic strains are regularly used for mapping studies by scientists worldwide. These are available through the laboratory's Foundation and Special Mouse Stocks, Mouse Mutant Resource, and Robertsonian Chromosome Resource.

The Mouse DNA Resource offers genomic DNA (from splenic extracts) from inbred, congenic, and mutant-bearing mouse strains. [Contact: Marie Ivey, 207/288-3371, ext. 1395.]

The Genetic Information Resource compiles and distributes information on the laboratory's numerous mouse strains and mutants (e.g., genetic linkage data that can be visualized directly or on chromosome maps), specific gene typing for given strains, literature references, and phenotypic characteristics of strains. In addition, the GBASE database maintains information about mouse loci, allelic characterization of inbred strains, and genetic maps.

INTERNATIONAL CENTERS

■ U.K. DNA Probe Bank

Funded by the Medical Research Council as part of the U.K. Human Genome Mapping Project Resource Centre, the probe bank offers some 650 DNA probes free to the U.K. research community. Foreign investigators may be subject to fees and restricted access [*HGN* **2**(6), 1–3 (March 1991)]. [Contact: Christine Bates, (Int.) 44/81-869-3446, Fax: (Int.) 44/81-869-3807.]

■ European Cell Bank

The European Cell Bank consists of two components serving gene mappers in the United Kingdom and Europe:

- European Collection of Animal Cell Cultures Human Cell Bank, housed at the Public Health Laboratory Service (PHLS) at Porton (United Kingdom), prepares and distributes lymphoblastoid and other cell lines. Many lines have constitutional chromosomal rearrangements with breakpoints useful for human gene mapping. Foreign investigators may have restricted access to some materials. [Contact: B. Bolton, PHLS Centre for Applied Microbiology and Research, (Int.) 44/0980-610391, Fax: (Int.) 44/0980-611315.]
- Department of Cell Biology and Genetics at Erasmus University (Rotterdam) banks fibroblast lines, with particular emphasis on inborn errors of metabolism. [Contact: V. Cleijer, (Int.) 31/10-408-7223, Fax: (Int.) 31/10-408-7200.]

■ Centre d'Etude du Polymorphisme Humain (CEPH)

The mission of CEPH, established in Paris in 1983 as a nonprofit institution, is to facilitate construction of human genetic linkage maps of each chromosome by using DNA polymorphisms. CEPH coordinates international gene-mapping efforts for collaborating researchers in laboratories in North America, Europe, South Africa, Japan, and Australia.

Reference Panel. The main premise of CEPH is that collaborative research on DNA from the same families will result in earlier completion of the human genetic linkage map. CEPH provides its collaborators with free, high-quality cellular DNA samples from a panel consisting of DNA from 40 large families (each with at least 6 children) with no known genetic diseases. Collaborators use their own probe and restriction enzyme combinations to determine the genotypes of various DNA polymorphisms for the entire panel. All data are sent to the CEPH database.

Database. The CEPH database, containing genotypes for all tested genetic markers (mostly DNA polymorphisms), consists of a collaborative portion and a public portion. The collaborative database, available only to CEPH investigators, includes unpublished and published data. Published data are later moved to the CEPH public database (available to the general scientific community). Unpublished data can be released to the public database after 2 years. [To receive the database, available on a 5.25-in. disk, and a book of LOD scores and recombination-frequency estimates for syntenic markers in the database, write to CEPH; 27 rue Juliette Dodu; 75010 Paris, France.]

Consortium Linkage Maps. CEPH investigators construct consortium maps of each chromosome, using published data from the database. The first such map, of chromosome 10, was recently published [*Genomics* **6**, 393–412 (1990)] with a mean distance of 11 cM between genetic markers. The second consortium map, of chromosome 1, was published in April [*Genomics* **9**, 686–700 (1991)] with a mean genetic distance of 6.7 cM. To provide resources for constructing higher-resolution maps (perhaps 1 to 2 cM), CEPH is enlarging its reference panel to include 61 families.

Probe Collections. A project being developed in collaboration with ATCC is the construction of probe kits for the mapped genetic markers on CEPH consortium maps. Sponsored by NIH National Center for Research Resources, this project aims to enhance the use of the CEPH consortium genetic linkage map by enabling researchers to localize disease-determining and other interesting genes.

[Contact for CEPH: Howard Cann, Fax: (Int.) 33/1-40-18-01-55 (Paris).]

■ Japanese Cancer Research Resources Bank

The Japanese Cancer Research Resources Bank, established to facilitate cancer research, includes cell and gene repositories. Resources are available to qualified investigators associated with certain medical, research, or educational organizations. [Contact: Katsuyuki Hashimoto; Gene Repository Section; National Institute of Health; 10-35, Kamiosaki 2-Chome; Shinagawa-ku, Tokyo 141; (Int.) 81/03-444-2181, ext. 304, Fax: (Int.) 81/03-446-6286.] ◇

Reported by Denise Casey
HGMIS, ORNL

DNA and Cell Repository Services:

- **collection**
- **authentication**
- **storage**
- **distribution**

CEPH Coordinates Collaborators' Gene Mapping Using Its Family Reference Panel

Resources

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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Genome Literature Abstracts

¶As time and space permit, *Human Genome News* will publish information about selected new 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.

Genome Analysis, a new series of books on genome structure and function, reviews some of the latest findings, methods, and ideas in human and animal genetics. Edited by Kay Davies (University of Oxford) and Shirley Tilghman (Princeton University) and published every 4 to 6 months, each volume focuses on one broad theme. Volume I, *Genetic and Physical Mapping* is now available; forthcoming titles include *Gene Expression and Its Control* and *Genes and Phenotypes*. $40 per volume. [Cold Spring Harbor Laboratory; Fulfillment Department, LM90; 10 Skyline Drive; Plainview, NY 11803-9729; United States, except New York State: 800/843-4388; all other locations: 516/367-8423; Fax: 516/367-8432.]

Molecular Cloning: A Laboratory Manual (Second Edition) has tripled in size and grown to three volumes since it was first published in 1982. The 1989 manual describes not only manipulations of recombinant DNA, but also the reasons for particular steps and the principles underlying the methodology. Three-volume set, plastic comb binding, $115. One-volume, clothbound reference edition, $225. [Cold Spring Harbor Laboratory (see entry above).]

Genes and Genomes by Maxine Singer (Carnegie Institution of Washington) and Paul Berg (The Beckman Center for Molecular and Genetic Medicine, Stanford University) was written to capture the sense of discovery, understanding, and anticipation that has followed the recombinant DNA breakthrough. Part I reviews the field of molecular genetics in the early 1970s; Part II examines the logic, concepts, and general practices of gene cloning and the characterization and manipulation of DNA; Part III presents the major take-home messages of the new experimental paradigm; Part IV introduces the upcoming companion Volume II, a sampling of case studies of genetic systems that have been especially illuminated by the recombinant DNA approach. Over 700 illustrations are included. Casebound with jacket, $52. [Marketing Director, University Science Books; 20 Edgehill Road; Mill Valley, CA 94941.]

DNA Science: A First Course in Recombinant DNA Technology by David A. Micklos (Cold Spring Harbor Laboratory) and Greg A. Freyer (Columbia University) is a laboratory text that introduces the theory, practice, and applications of recombinant DNA technology. Written in a semijournalistic style and designed to be read from cover to cover, the book presupposes no prior experience by student or instructor. Paper, $29.95. [Published by Cold Spring Harbor Laboratory Press and Carolina Biological Supply Company (CBSC). Order from CBSC, 2700 York Road; Burlington, NC 27215; 919/584-0381 or 800/334-5551; North Carolina only: 800/632-1231].

Genetic Monitoring and Screening in the Workplace, an Office of Technology Assessment (OTA) report, resulted from a 1989 OTA survey of some 2000 companies and unions to determine which of them used genetic monitoring or screening tests of workers or job applicants. The report discusses the survey, ethical and legal concerns, and two central policy issues identified by OTA: (1) the federal government's role in the regulation, oversight, or promotion of genetic monitoring and screening tests and (2) the adequacy of federally sponsored research on the relationships between genes and the environment. Full report (052-003-01217-1), $12. [Superintendent of Documents; U.S. Government Printing Office; Washington, DC 20402-9325; 202/783-3238.] Report summaries, free. [OTA, U.S. Congress; Washington, DC 20510-8025; 202/224-8996.]

Human Gene Mapping Techniques by Helen Donis-Keller (Washington University School of Medicine) is a step-by-step guide to designing a mapping project, identifying a gene's chromosomal location, developing high-resolution physical and genetic maps, and cloning the gene. With a major emphasis on genetic linkage mapping, this book presents gene-mapping strategies for researchers who have some experience with molecular biology and gene-cloning techniques. 1990. $39.95. [Stockton Press; 15 East 26th Street; New York, NY 10010; United States, except New York: 800/221-2123; New York: 212/481-1334; Fax: 212/779-9479.] ◇

New Technologies To Detect All Genes and Coding Regions in Genomic DNA

RFA HG-91-02

The National Center for Human Genome Research invites applications for research grants to support the development of either of the following:

- new technologies or research strategies capable of detecting all coding sequences and/or genes in genomic DNA; or
- more general and efficient methods of preparing, isolating, and characterizing libraries of intact cDNAs.

Project emphasis will be on experimental rather than computational approaches.

Timetable

- Letter of Intent receipt (recommended but not required for application): June 17.
- Application receipt: July 15.
- Initial Review Group review: February 1992.
- Earliest funding: April 1992.

For more information or a complete copy of the RFA, contact: Bettie J. Graham, Chief; Research Grants Branch; NIH NCHGR; Building 38A, Room 612; Bethesda, MD 20892; 301/496-7531; BITNET: "b2g@nihcu.bitnet"; Internet: "b2g@cu.nih.gov" ◇

Human Genome Program Developmental Grants (P20)

RFA HG-91-04

The National Center for Human Genome Research announces the availability of nonrenewable developmental grants (P20) to provide support to groups of outstanding investigators who wish to undertake the following:

- develop interdisciplinary research collaborations and strategies,
- obtain preliminary results that demonstrate feasibility, and
- develop a research plan addressing a major research goal of the Human Genome Project.

The plan would be used as the application basis for a program project (P01) or center grant (P50).

Timetable

- Letter of Intent receipt: May 9 and September 14.
- Application receipt: July 9 and November 14.

To obtain the full RFA and instructions, contact: Jane L. Peterson, Chief, Research Centers Branch; NIH NCHGR; Building 38A, Room 610, Bethesda, MD 20892; 301/496-7531, Internet: "jp2@cu.nih.gov" ◇

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 (see notices at left and on next page).

  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; 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 due August 9. Further information can be obtained via:

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.

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 more information, contact: Samuel Barish; SBIR Program Manager, ER-16; DOE; Washington, DC 20585; 301/353-5707. Next submission date: spring 1992.

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

Oak Ridge Associated Universities: 615/576-4805 ◇

For Your Information

Studies of Testing, Counseling for Cystic Fibrosis Mutations

■ **RFA HG-91-01**

Assistance awards are available for studies of the clinical delivery of individual and family educational and counseling services related to DNA-based testing for the genetic mutations that cause cystic fibrosis. The following NIH institutions invite applications:

- National Center for Human Genome Research (NCHGR),
- National Institute of Child Health and Human Development,
- National Center for Nursing Research, and
- National Institute for Diabetes and Digestive and Kidney Diseases.

This RFA is intended to solicit research projects that can be used to identify clinical practices that best increase patient understanding of disease-gene carrier testing and test results. Practices should also protect individuals and families from test-related psychological harm, stigmatization, and discrimination. Appropriate topics include education before testing, counseling after testing, optimum test settings, levels of understanding and interest among different populations, recordkeeping and disclosure policies, and test accuracy and cost-effectiveness.

Timetable

- Letter of Intent receipt (recommended but not required for application): May 1.
- Application receipt: June 7.
- Initial and council reviews: July–September.
- Earliest award: September 30.

For additional information or a copy of the complete RFA, contact:

Eric T. Juengst, Director; Ethical, Legal, and Social Implications Program; NIH NCHGR; Building 38A, Room 614; Bethesda, MD 20892; 301/496-7531; Internet: "ejs@cu.nih.gov" ◇

Genome-Related Tutorials Offered

Mathematical Sciences

The Societal Institute of the Mathematical Sciences (SIMS) will conduct a tutorial on the mathematical sciences in genomic analysis on August 4–24 at Stanford University. Participants will explore how quantitative methodologies can be used effectively in genomic analysis, particularly in connection with the Human Genome Project. Topics will include fragment assembly, informatics, pattern analysis of molecular sequences, and DNA and protein structure predictions. Several days of background lectures will prepare participants for the later presentations of senior tutorial faculty.

The tutorial is supported by a grant from the National Center for Human Genome Research. Funds are available to qualified participants for travel and living expenses while at Stanford. The tutorial will be held again in the summer of 1992 on the East Coast. ◇

Contact:
Societal Institute of the Mathematical Sciences
97 Parish Road South
New Canaan, CT 06840
203/966-1008
Fax: 203/972-6069

Ethical Implications

"Genomic Information: Ethical Implications," an intensive, advanced-level course, will be held November 4–8 at the University of Washington, Seattle. Partly sponsored by the National Center for Human Genome Research, the course will include an introduction to relevant methods and issues in bioethics for scientists and an introduction to the scientific and clinical features of the genome project for bioethics/humanities scholars. The workshop aims to promote discussion and sound analysis of the ethical and social issues that will arise from data produced in the genome project.

Fifteen participants from each discipline will be selected. Women and minorities are especially encouraged to apply, and two fee waivers are available. Applications are due July 19. This workshop will also be offered June 15–19, 1992. ◇

Contact:
Inge Boulanger
Department of Medical History and Ethics, SB-20
University of Washington School of Medicine
Seattle, WA 98195
206/543-5447

Calendar of Genome Events

May	15–18	**Symposium on the Human Genome Project** at the **82nd Annual Meeting of the American Association for Cancer Research**; Houston , TX [*M. Foti, 215/440-9300, Fax: 215/440-9313*]
	16	**"Ethical Issues in Genetic Research in Psychiatry"** symposium at the **American Psychiatric Association Annual Meeting**; New Orleans, LA [*P. Turgeon, 202/682-6170*]
	27–29	***Second International Chromosome 11 Physical Mapping Workshop**; Paris [*G. Evans (U.S.), Fax: 619/558-9513 or C. Junien (Int.) 33/1-42-24-1357*]
June	1–5	**8th International *C. elegans* Meeting**; Madison, WI [*Registration: 608/262-2755; Other information: P. Anderson, 608/263-8429*]
	2–4	**Human Genome Research in an Interdependent World**; Bethesda, MD [*D. Wikler, 608/263-6287*]
	7	***National Advisory Council for Human Genome Research**; Bethesda, MD
	14–16	***Ethical and Legal Implications of Genetic Testing**; Berkeley Springs, WV [*E. Broughman, 202/326-6614/6600*]
	24	***NCHGR Grantees Meeting**; Lister Hill Center, Bethesda, MD
	25	***NIH Program Advisory Committee on the Human Genome**; Bethesda, MD [*C. Mohan, 301/496-0844, afternoons*]
	25	**Joint NIH-DOE Subcommittee on the Human Genome**; Bethesda, MD [*see contact: June 25*]
	25	***DOE Human Genome Coordinating Committee**; Bethesda, MD
	25–29	**Ethical and Pastoral Care Issues in Genetics**; Washington, DC [*F. Seydel, 202/687-8810*]
July	7–10	**March of Dimes Clinical Genetic Conference: Developmental and Genetic Disorders of the Central Nervous System**; Vancouver, BC [*March of Dimes Birth Defects Foundation, 914/428-7100*]
	13	**"Social Issues in Human Genome Research"** symposium 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*]
	14–19	***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 [*A. Cruickshank, 401/783-4011, Fax: 401/783-7644*]
August	12–16	**STM 1991 International Conference**; Interlaken, Switzerland; preregistration deadline: June 10 [*C. Gerber, (Int.) 41/1-724-8645, Fax: (Int.) 41/1-724-3223*]
	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); abstract deadline: June 11 [*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*]
	10–13	**Second International Workshop on Human Chromosome 22**; Montreal, Canada [*G. Rouleau, 514/934-8094 or 937-6011, Fax: 514/937-3532*]
	14–15	**The Human Genome Project: A Public Forum**; Alexandria, VA [*J. Weiss, 800/336-GENE or 202/331-0942*]

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

Calendar of Genome Events*

September (cont.)	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**; NIH, 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, Netherlands [*M. Sonne, (Int.) 31/20-512-2516, 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*]

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

Training Calendar: Workshops and Coursework

May	29–31	**Expression of Recombinant DNA in Eukaryotic Systems**; CUA, Washington, DC [*M. Miller, 202/319-6161, Fax: 202/319-5721*]
June	3–7	**Recombinant DNA Techniques**; Rochester Institute of Technology, NY (also June 10–14 and Nov. 18–22) [*C. Miller, 716/475-5977*]
	3–8	**cDNA Library Workshop**; LTI, Germantown, MD (also October 7–12) [*G. Tinney, 800/828-6686, Ext. 713 or 301/921-2250, Fax: 301/258-8212*]
	5–7	**Recombinant DNA Methodology**; Exon-Intron, Inc., Columbia, MD (also offered July 8–12, Aug. 7–9, Sept. 9–13, and other times) [*Exon-Intron, 301/730-3983*]
	10–14	**Recombinant DNA/Cytogenetic Approaches to Genetic Disease and Gene Mapping**; CUA, Washington, DC [*see contact: May 29–31*]
	10–14	**Genetic Toxicology**; Gordon Research Conferences, New London, NH [*A. Cruickshank, 401/783-4011, 401/783-3372, Fax: 401/783-7644*]
	10–14	**Tissue Culture and Hybridoma Techniques**; Rochester Institute of Technology, NY (also Nov. 18–22) [*see contact: June 3–7*]
	10–15	**Recombinant DNA Techniques II**; LTI, Germantown, MD (also July 15–20, September 23–28) [*see contact: June 3–8*]
	11–14	**Basic Cloning Techniques**; BTP, St. Louis, MO (also offered June 18–21 at Colorado Springs, CO; July 9–12 at New York, NY; and other dates and locations) [*S. Chance, 515/232-8306, 1:00–5:00 p.m. CST*]
	17–21	**Plant Molecular Biology**; Gordon Research Conferences, Andover, NH [*see Gordon contact: June 10-14*]
	17–21	**Recombinant DNA/PCR for Diagnosis of Microbial and Neoplastic Disease**; CUA, Washington, DC [*see contact: May 29–31*]
	18–19	**Clinical Diagnosis using PCR and Hybridization Analysis**; BTP, San Diego, CA [*see contact: June 11–14*]

Training Calendar

June (cont.)	24–28	**Principles of Flow Cytometry: Hands-On Training in Molecular Biology Laboratory Techniques**; BTP, Colorado Springs, CO [*see contact: June 11–14*]
July	1–5	**Linkage and Chromosome Mapping/Sequence Analysis**: Courses at U.K. Human Genome Mapping Project Resource Centre; Harrow, England (also offered July 8–12, July 15–19) [*C. Bates, (Int.) 44/81-869-3446, Fax: (Int.) 44/81-869-3807*]
	5–13	**DNA-Related Methods in Human Genetics: YAC Cloning in Genome Analysis**; London [*P. Faik, (Int.) 44/71-403-6998*]
	8	**DNA Amplification by PCR**; BTP, New York, NY (also offered July 22 at St. Louis, MO and other dates and locations) [*see contact: June 11–14*]
	8–12	**Protein and Nucleic Acid Separation Techniques**; CUA, Washington, DC [*see contact: May 29–31*]
	8–12	**Recombinant DNA Techniques I**; LTI, Germantown, MD (also Sept. 16–20, Nov. 11–15) [*see contact: June 3–8*]
	15–19	**Molecular & Genetic Basis for Cell Proliferation**; Gordon Research Conferences, Meridan, NH [*see contact: June 10–14*]
	16–19	**RFLP Analysis**; BTP, Houston, TX (also offered July 23–26, Aug. 6–9, and other locations and times) [*see contact: June 11–14*]
	16–19	**Advanced Topics in Recombinant DNA**; Exon-Intron, Columbia, MD [*see contact: June 5–7*]
	22–26	**Biological Structure & Gene Expression**; Gordon Research Conferences, Plymouth, NH [*see contact: June 10–14*]
	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*]
	29–31	**PCR Methodology**; Exon-Intron, Columbia, MD [*see contact: June 5–7*]
	29–Aug. 2	**Molecular Genetics**; Gordon Research Conferences, Newport, RI [*see contact: June 10–14*]
August	4–24	**Tutorial on the Mathematical Sciences in Genomic Analysis** [*SIMS, 203/966-1008, Fax: 203/972-6069*]
	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
	13–16	**RNA Isolation and Characterization**; Exon-Intron, Columbia, MD [*see contact: June 5–7*]
September	16–19	**GeneWorks**; Mountain View, CA (Registration deadline: Sept. 3) [*IntelliGenetics, Inc., 415/962-7300*]
October	8–21	**Analysis and Genetic Manipulation of YACS**; CSHL, Cold Spring Harbor; application deadline: July 15 [*CSHL, 516/367-8346, Fax: 516/367-8845*]
	14–16	**PCR Techniques**; CUA, Lake Tahoe, NV [*see contact: May 29–31*]
	27–Nov. 5	**Molecular Genetics of Fission Yeast**; CSHL, Cold Spring Harbor (application deadline: July 15) [*see contact: Oct. 8–21*]
	27–Nov. 5	**Essential Computational Genomics for Molecular Biologists**; Cold Spring Harbor (application deadline: July 15) [*see contact: Oct. 8–21*]
November	4–8	**Genomic Information/Ethical Implications**; Seattle, WA (application deadline: July 19) [*I. Boulanger, 206/543-5447*]
	11–14	**PC/Gene**; Mountain View, CA (Registration deadline: Oct. 28) [*see contact: Sept. 16–19*]

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 Training Programs
CBSC	Carolina Biological Supply Company
cDNA	complementary DNA
CEPH	Centre d'Etude du Polymorphisme Humain
CRADA	Cooperative Research and Development Agreement
CSHL	Cold Spring Harbor Laboratory
CUA	Catholic University of America
DHHS	Department of Health and Human Services (U.S.)
DOE	Department of Energy (U.S.)
FISH	flourescence in situ hybridization
GDB	Genome Data Base (HHMI, Johns Hopkins University)
HGM	Human Gene Mapping Workshop
HGMIS*	Human Genome Management Information System (ORNL)
HGN*†	**Human Genome News**
HHMI	Howard Hughes Medical Institute
HUGO	Human Genome Organisation [International]
ICHG	International Congress of Human Genetics
IMACS	International Association for Mathematics and Computers In Simulation
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.
NCI†	National Cancer Institute (NIH)
NCR	National Cell Repository
NCHGR†	National Center for Human Genome Research (NIH)
NICHD†	National Institute of Child Health and Human Development (NIH)
NIGMS†	National Institute of General Medical Sciences (NIH)
NIH†	National Institutes of Health
NLGLP*	National Laboratory Gene Library Project (LANL, LLNL)
NSF	National Science Foundation
OER*	Office of Energy Research
OHER*	Office of Health and Environmental Research (OER)
ORNL*	Oak Ridge National Laboratory, Oak Ridge, Tenn.
OTA	Office of Technology Assessment (U.S. Congress)
PACHG†	Program Advisory Committee on the Human Genome (NIH)
PCR	polymerase chain reaction
PHLS	Public Health Laboratory Service (U.K.)
RFLP	restriction fragment length polymorphism
SBIR	Small Business Innovation Research
SIMS	Societal Institute of the Mathematical Sciences
STM	scanning tunneling microscope
STS	sequence tagged site
YAC	yeast artificial chromosome

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