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Exchange

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DOE Holds First Human Genome Contractor/Grantee Workshop

Genome Data To Spark Expansion in Biological Research

At the first Contractor/Grantee Workshop for the DOE Human Genome Program, Benjamin J. Barnhart, Program Manager, told participants that data produced by the international human genome effort will impact the manner in which biological research is conducted and provide information needed for significant progress in many areas of research.

The meeting was held in Santa Fe, New Mexico, November 3 and 4, 1989, and the 150 attendees were audience to a total of 31 platform and 57 poster presentations representing each of the three major program areas: biological resources, instrumentation, and informatics capability development.

In addition to contractors and grantees, the workshop attracted staff from the DOE Office of Health and Environmental Research (OHER), the NIH National Center for Human Genome Research, the National Science Foundation, the U.S. Department of Agriculture, and the privately funded Howard Hughes Medical Institute (HHMI).

Charles R. Cantor, Director of the Lawrence Berkeley Laboratory (LBL) Human Genome Center and Chairman of the DOE Human Genome Coordinating Committee, told participants: "Technology will change dramatically; the key is implementation. I believe that the balance between the number of projects that are developing new technologies and the number of projects that are producing new map data is about right." He also said that progress in the Human Genome Project is on target—maybe ahead. Cantor congratulated Sylvia Spengler and her staff at LBL on their coordination of the meeting.

Workshop participants saw the meeting as useful in promoting the exchange of information and observed the spirit of cooperation

critically necessary for the successful completion of the genome project. Moreover, the workshop has led to close coordination of work, including interlaboratory meetings among the directors of national laboratory human genome projects, as well as among key investigators developing computational capabilities for handling and analyzing data in databases.

Barnhart stated in his opening remarks that human genome research for OHER is an outgrowth of four decades of work at the national laboratories. He said that OHER continues to address the technical problem of detecting infrequent human DNA

**Increased
Cooperation and
Coordination Result
from Workshop**

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DOE Contractor/Grantee Workshop

Newsletter Joint Sponsorship Announced by DOE and NIH

At the DOE Contractor/Grantee Workshop, Benjamin Barnhart, Manager of the DOE Human Genome Program announced that sponsorship of this newsletter will become a joint venture between the DOE Office of Health and Environmental Research and the NIH National Center for Human Genome Research beginning with the spring issue. Becoming a bimonthly publication, this newsletter will be renamed the *Human Genome News*. Produced by the Human Genome Management Information System (HGMS), the *Human Genome News* will assist the management of each agency's genome program by communicating issues relevant to human genome research to the public and by providing a forum for exchange of information to all individuals and agencies involved in genome research. Suggestions are welcome; please direct correspondence to the HGMS address at Oak Ridge National Laboratory. ♦

DOE Resource and Technology Development Objectives:

Physical Mapping, Sequencing Technologies, Informatics Capabilities

National Laboratory Gene Library Project Administered by LANL and LLNL

mutations induced by low levels of ionizing radiation and energy-related chemicals. Only when the total DNA sequence is elucidated – the long-term goal of the genome project – will a full understanding of the health effects of mutations be possible.

Barnhart specified three resource and technology development program areas and their related objectives that are being pursued by the DOE-sponsored genome program:

1. Physical mapping:
 - Development of more cost-effective methods for linear ordering of chromosomal DNA sequences.
 - Completion of linear ordering of cloned DNAs from chromosomes 16, 17, 19, 21, and X.
 - Construction of ordered DNA clones for additional chromosomes.
2. Sequencing technologies:
 - Development of innovative technologies for cost-effective and accurate sequencing.
 - Development of a technology transfer program.
3. Informatics capabilities:
 - Development of data management and networking tools.
 - Development of advanced algorithms for DNA sequence interpretation.

Highlights of Presentations

Map Production Efforts

Presentations indicated that research on the physical mapping of chromosomes is

progressing well. Many research groups engaged in physical mapping studies are using robotics and computer software and hardware to complete their analyses. Listed below are some highlights of physical mapping studies undertaken by DOE-funded researchers.

In his remarks as chairman for the chromosome mapping session, Lawrence Livermore National Laboratory (LLNL) Genome Project Director Anthony Carrano noted that the OHER-sponsored National Laboratory Gene Library Project (NLGLP) is carried out jointly by LLNL and Los Alamos National Laboratory (LANL). Larry Deaven (LANL) and Marvin Van Dilla (LLNL) spoke of their respective programs within the NLGLP. Investigators in the NLGLP begin with flow-sorter-purified chromosomes to produce chromosome-specific partial-digest human DNA libraries for studying the molecular biology of genes, studying and diagnosing genetic diseases, and constructing physical maps of chromosomes.

Over 2000 libraries and other materials have been distributed by the NLGLP to many laboratories that could not economically produce these materials themselves.

Glen Evans (The Salk Institute) reported on progress being made using a variety of physical mapping methods to construct a map of the distal tip of the long arm of chromosome 11. The map, developed in a collaborative effort with Peter Lichter's group at the Yale University School of Medicine, is already useful clinically.

Over 100 human genetic disorders have been localized to the 150-Mbp X chromosome. David L. Nelson (Baylor College of Medicine) reported his group's results for mapping the X chromosome using *Alu* polymerase chain reaction (PCR) mapping strategies. Pieter de Jong (LLNL) discussed the use of similar new *Alu* PCR methodologies for mapping chromosome 19.

Carrano reported that the LLNL automated fluorescence-based method for clone fingerprinting has been validated and coupled to software used for contig assembly, data storage, and graphical display of map information. The procedures are being successfully applied to the development of a cosmid and YAC contig map of chromosome 19. Of the 2200 cosmids processed for fingerprint analysis, over 900 are in contigs with an average contig length of about 3 cosmids.

DOE Contractor/Grantee Workshop

Ed Hildebrand (LANL) informed meeting attendees that nearly 70% of chromosome 16 has been fingerprinted with 2261 DNA clones in 389 contigs. One strategy being employed at LANL for physical mapping—the use of repeat sequences as nucleation sites—results in contig maps with landmarks that are useful for rapid integration of the genetic and physical maps.

Hong Fang (LBL) described the use of single-copy DNA probes—previously assigned to locations on the genetic map—as anchor points in physical mapping studies.

Informatics Presentations

Informatics is a term used to denote algorithms, databases, and hardware that support physical mapping and sequencing activities. This hardware and software—necessary for storing, retrieving, analyzing, and distributing data—must be available for the use of biologists as soon as possible. Genome projects generate computation problems in the following areas: image analysis, primary DNA and protein sequence analysis, prediction of tertiary structures of DNA and proteins, and database management and use.

Platform presentations on informatics were given on the following topics:

- new computer chips that will speed up sequence-matching queries [e.g., the biological information signal processor (BISP) now being implemented in 1- μ m CMOS technology] (Tim Hunkapiller, California Institute of Technology);
- methods to assess the reliability and quality of results produced by fingerprint mapping strategies (Elbert Branscomb, LLNL);
- development of techniques to predict the probability of overlap in a pair of cosmid clones for mapping fingerprint data (David Torney, LANL);
- management of digitized autoradiographic, confocal, and scanning tunneling microscopic data and implementation of a comprehensive chromosome-21 information system (William Johnston, LBL);
- establishment of more open communication between biologists and computer analysts (Ross Overbeek, Argonne National Laboratory); and

- a repository of well-characterized, cloned DNA segments to support gene structure and function studies and genomic mapping efforts for use by molecular biologists performing basic research (William Nierman, American Type Culture Collection).

New Approaches to Mapping, Sequencing, and Manipulating DNA

Mapping

Among presenters discussing new approaches to mapping and sequencing, Cassandra Smith (LBL) discussed end-game strategies for completing chromosome mapping in which actual sequence data including and adjacent to rare restriction enzyme cutting sites would serve as anchor points for further physical mapping activities.

Leonard Lerman (Massachusetts Institute of Technology) proposed a new mapping strategy that would exploit thermal stability differences between different domains within the DNA double helix.

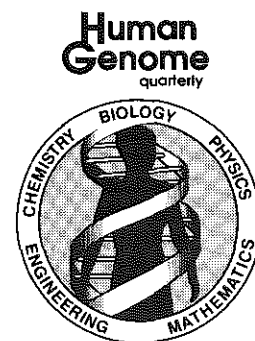
Sherman Weissman (Yale University Medical School) reported progress in developing selection and cloning methods to be used in conjunction with the new techniques for in situ hybridization and chromosome mapping.

Sequencing

Edward Yeung (Ames Laboratory) discussed a novel "indirect fluorescence" technique for detection of DNA bands during electrophoresis. The gel matrix fluoresces, but the DNA bands do not.

New sequencing technologies being developed in the DOE Human Genome Program were the subject of a number of presentations during this workshop and included:

- scanning tunneling microscopy (LBL, LLNL, Oak Ridge National Laboratory (ORNL), and University of New Mexico researchers);
- resonance ionization mass spectrometry sequencing using stable isotopes (Bruce Jacobson, ORNL/Atom Sciences, Inc.);
- single-molecule DNA sequencing by flow-cytometry (Richard Keller, LANL);
- sequencing with reusable libraries of oligonucleotide primers of length 8, 9, or 10 for cost effectiveness [William Studier, Brookhaven National Laboratory (BNL)];



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

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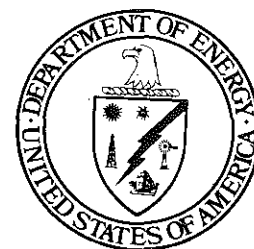
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DOE Contractor/Grantee Workshop

Second Contractor/Grantee Workshop To Be Held 18 to 24 Months After First Meeting

- computer-assisted multiple DNA sequencing methods (George Church, Harvard University Medical School);
- multiplex DNA sequencing and innovative large-scale sample processing methods (Robert Weiss, University of Utah Medical Center);
- methods for substantially increasing the reliability of a core DNA-sequencing step of the Sanger strategy, through genetic engineering of bacteriophage T7 DNA polymerase and modification of polymerase reaction conditions (Stanley Tabor, Harvard University Medical School); and
- oligonucleotide sequencing by hybridization (Radomir Crkvenjakov, Genetic Engineering Center, Belgrade, Yugoslavia).

Some of the projects listed above have the same goals but different modes of implementation. Multiple approaches are necessary (as recommended in the 1988 NRC report: *Mapping and Sequencing the Human Genome*) because many of the methodologies remain unproven for large-scale genome mapping and sequencing efforts.

Manipulating DNA

New methods presented for manipulating DNA included:

- development of a single-molecule counter—3 orders of magnitude more sensitive than conventional fluorescence-detection systems—for detecting DNA in sequencing gels (Richard Mathies, University of California, Berkeley);
- methylation of restriction recognition sites to create larger DNA fragments for mapping studies (Michael McClelland, California Institute of Biological Research);
- creation of synthetic endonucleases to recognize and map functionally important DNA regions (Betsy Sutherland, BNL);
- determination of conditions for selective cleavage of single-stranded DNA and RNA adjacent to hybridization sites (i.e., oligonucleotide-directed nucleases) (David Corey, LBL); and
- use of crossed oscillating electric and magnetic fields to yield high-resolution separations between DNA fragments (Gunter Hofmann, BTX, San Diego).

Hood Discusses Project Implementation

In his summary of the workshop, Leroy E. Hood (Director of the NSF Center for Integrated Protein and Nucleic Acid Chemistry and Biological Computation and Director of the Cancer Center at the California Institute of Technology) outlined the future course of the genome project.

He said that in the first five years, mapping and sequencing technologies should be developed, individual human chromosomes and the chromosomes of model organisms mapped, and small regions of human chromosomes and other genomes sequenced.

In the second five years, increased development should be pursued in the areas of technologies for large-scale mapping and sequencing, mapping studies, sequencing of small human chromosomes, and interpretation of sequence data. Hood also commented that the technologies "spun-off" from the genome project will be used for medical applications and to spur basic research.

In the final five years of the project, Hood proposed, the sequencing task should be completed, and intensive genome interpretation studies should be initiated. Scientists from many areas of biological research will be involved in sequence interpretation and in the identification of genes.

He further commented that, because of the interdisciplinary approaches needed in biological research, students should be mentored by representatives of many other disciplines such as computer science, chemical engineering, chemistry, English, and mathematics.

With the sequence data in hand, Hood related, the way in which biology is studied will be fundamentally reoriented. Research will proceed in the opposite direction from the traditional approach: investigators will begin with the DNA code for a gene and proceed "backward" to look for the function of that gene. Lexicons of protein structure motifs will be used to make generalizations and predictions of three-dimensional protein structure and, ultimately, to understand the function of proteins within the cell. ♦

*Written by Betty K. Mansfield
and Judy M. Wyrick
HGMIS, ORNL*

Sequencing Tasks Should Be Completed in 15 Years

Interagency Five-Year Human Genome Plan Submitted for Approval

To achieve the complementary goals and objectives of the two U.S. federal agencies having formal human genome programs, DOE and NIH have prepared an interagency five-year plan that describes synergistic, integrated approaches to facilitating coordination between the programs. In October 1988, the two agencies had signed a Memorandum of Understanding with these goals in mind.

The five-year plan was written in response to requests made to NIH from Congress for a report describing a comprehensive spending plan and optimal strategy for mapping and sequencing the human genome. At the invitation of NIH, DOE coauthored the report. The working group that drafted the document in the latter part of 1989 included six consultants representing the NIH Program Advisory Committee on the Human Genome, six representing DOE's Health and Environmental Research Advisory Committee (HERAC), and six other scientists selected at large, in addition to staff from each agency.

Endorsed by the advisory committees of the agencies, the five-year plan updates

previous reports on the U.S. Human Genome Project that were prepared by HERAC, the Congressional Office of Technology Assessment, and the National Research Council of the U.S. National Academy of Sciences. Anticipated annual updates of the plan will incorporate new developments and advances in genome research and technology.

When approved by each agency and submitted to Congress, the document will be distributed to everyone on the mailing list of this newsletter and will also be available to anyone requesting a copy. ◇

*Reported by Benjamin J. Barnhart, Manager
DOE OHER Human Genome Program*

**DOE and NIH
Coauthor
Coordination Plan**

Grant Application Notice

The DOE Office of Health and Environmental Research is inviting grant applications for the Human Genome Program. Research areas cover (1) technologies and resources for physical mapping; (2) advanced technologies for DNA sequencing; (3) data management systems; and (4) ethical, societal, and legal issues. Details on these research areas and on the application procedure will be published in the *Federal Register* in early March. Contact HGMIS for issue number. ◇

Robert Moyzis Named Director of LANL Center for Human Genome Studies

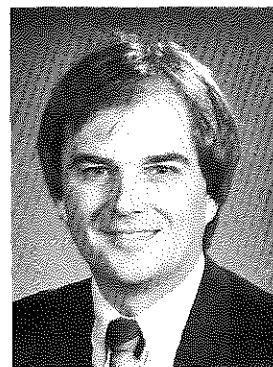
Robert K. Moyzis was named Director of the Center for Human Genome Studies at LANL in August 1989. In this capacity, he will also serve on the Human Genome Coordinating Committee (HGCC) of the DOE Human Genome Program. Moyzis replaced George I. Bell, Acting Director of the Center, whom he also replaced on the HGCC. Bell has returned to his management and research activities in the Theoretical Division at LANL.

Before his appointment as Director, Moyzis had served for 5 years as head of the LANL Genetics Group. He led the LANL physical mapping effort on chromosome 16 and received a Distinguished Performance Award from LANL for identifying and isolating the highly conserved functional human telomere—the region of DNA located at the ends of each human chromosome. This discovery, which resulted from Moyzis' research,

enables biologists to determine how and where chromosomes end and will provide physical orientation in constructing maps of the human genome.

Moyzis received his doctoral degree in molecular biology from the Johns Hopkins University in 1978. He graduated from Northeastern Illinois University in 1971 with degrees in biology and chemistry.

His memberships include the Human Genome Organisation, the American Association for the Advancement of Science, the Genetics Society, the American Chemical Society, and the American Society for Human Genetics. He is also an adjunct professor in the Cell Biology Department of the Cancer Research Center at the University of New Mexico. ◇



**Robert K. Moyzis, Director
Center for Human
Genome Studies
Los Alamos National
Laboratory
Member of HGCC**

Meetings and Workshops

Genome Sequencing Conference

Progress Reported in Automation of DNA Sequencing

Participants at the first annual Genome Sequencing Conference learned that many laboratories have begun sequencing projects. DNA sequencing techniques, both manual and automated methods, were the subject of much discussion. Held October 24–26 at The Barns of Wolf Trap Farm, near Washington, D.C., the meeting was organized and chaired by J. Craig Venter of NIH and C. Thomas Caskey of the Howard Hughes Medical Institute at the Baylor College of Medicine.

The program—consisting of 32 lectures, 2 panel discussions, and a poster session—was derived from reviewed abstracts. To

promote open discussion, the number of conference participants was limited to 150.

The Honorable Pete V. Domenici, United States Senator from New Mexico, spoke prior to a reception and dinner sponsored by Applied Biosystems, Inc. (ABI), at the Phillips Collection Gallery in Washington, D.C. He discussed the impact that DNA sequencing technology will have on this country's health care.

Throughout the conference, state-of-the-art DNA sequencing technology was examined and redefined. Presentations made on the relative merits of manual and automated

DNA sequencing demonstrated that the new automated methods have permitted the initiation of megabase sequencing projects. The general consensus was that manual sequencing methods were not likely to be useful for projects larger than those completed to date (200 kb); however, Fred Blattner (University of Wisconsin) indicated that he was using manual methods and would have the sequence of the *E. coli* chromosome nearly completed in one year.

New technologies (e.g., solid state and multiplex sequencing, as well as scanning tunneling microscopy) were also discussed. The consensus was that changes in DNA sequencing technology over the

next 5 years are more likely to be made by incremental improvements in current technologies rather than by the institution of new technologies. Clearly, DNA sequence determination is no longer the rate-limiting step in the data-gathering process (i.e., cloning, sequencing, and data entry); the limiting factor is now data analysis.

Contributing to this shift is the substantial progress made in the automation of sequencing reactions. A number of laboratories are currently using automatic workstations with



Gathered for discussion during the Genome Sequencing Conference at Wolf Trap were (l. to r.) Benjamin J. Barnhart (DOE Human Genome Program Manager), U.S. Senator Pete V. Domenici, Andy Bush (Domenici science staff), Jack McConnell (retired Director of Research, Johnson and Johnson), and conference organizer, J. Craig Venter (NIH). With Barnhart in the inset photograph is James D. Watson, Director of the NIH NCHGR.

Meetings and Workshops

robotic systems that can perform all steps involved in these reactions.

Several new approaches for preparing templates for DNA sequencing were discussed; most of them were based on some form of the polymerase chain reaction (PCR). A full discussion explored the use of PCR for direct sequencing of chromosomal DNA.

Discussions at the conference indicated that the amount of DNA sequence information being added to databases is expected to increase dramatically in a very short time, and that the current mode of entry of new sequences into databases is inadequate. Two efforts under way will help to alleviate the problem: the GenBank® database is being restructured to facilitate input and access to sequence data, and the National Center for Biotechnology Information is integrating many different databases.

The topic of sequence distribution, both on a limited basis and for general use, elicited a strong debate about the period of time that sequencing laboratories should be allowed to retain generated sequences for in-house analysis before distributing them to databases. Most participants thought that a maximum of 1 year between sequence generation and dissemination is a reasonable working guideline until more experience is gained in information transfer.

The progress of current test projects, together with sequencing technology and computer/software advances, will be part of the agenda of the second annual Genome Sequencing Conference, scheduled for September 30 through October 3, 1990, in Hilton Head, South Carolina. ♦

*Reported by J. Craig Venter
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Communicative Disorders and Stroke
NIH*

Workshops on Large Insert Cloning and Chromosome X

Researchers Meet in Consecutive Sessions

Consecutive sessions of the Large Insert Cloning Workshop and the X-Chromosome Workshop were held in Houston, Texas, on December 12–14 and December 14–16. The meetings were sponsored by DOE and NIH.

Large Insert Cloning Workshop: YAC Technology Progressing

Considerable progress was reported in the construction and analysis of yeast artificial chromosomes (YACs). Several groups are using YACs from the libraries prepared in the Washington University laboratories of David Schlessinger and Maynard Olson, and broader distribution of the libraries is planned. In the new technology of YAC construction/introduction, two reports illustrated that careful optimization of yeast permeability conditions is essential to achieve high transformation frequencies. Two systems described for introducing larger fragments for *E. coli* hosts are:

1. Packaging and delivery of 100-kb recombinant DNAs accomplished with a prophage/bacteriophage P1-based system. The linear DNAs are circularized and maintained as single-copy plasmids, whose amplification can be induced.
2. A similar bacteriophage T4-based packaging system that can deliver recombinant DNAs in the 200-kb range.

X-Chromosome Workshop: Physical and Genetic Mapping Technologies Applied

Methodologies discussed at the X-Chromosome Workshop illustrated the broad array of physical and genetic mapping techniques now being used to refine the knowledge of chromosome structure and function.

Included in the program were the following: genetic mapping through family studies, production of hybrids with chromosome fragments, cosmid mapping, YAC mapping, and DNA sequencing and microcloning (the polymerase chain reaction amplification and cloning of DNAs derived from particular mitotic chromosome bands).

Hans Lehrach (Imperial Cancer Research Fund Laboratory, United Kingdom) reported progress in methods employed for characterizing clones by oligonucleotide probing. This methodology will contribute to ordering a library with a sixfold cosmid coverage of chromosome X.

In addition to research results, participants in the workshops also discussed sharing genetic resources and information. ♦

*Reported by Marvin Stodolsky
DOE OHER Human Genome Program*

**Robert M.
Cook-Deegan
(NIH NCHGR)
To Prepare
Extended Reports
on the Workshops
for Publication in
Genomics.**

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

Meetings and Workshops

Human Genome I

International Conference Describes Status of Genome Research, Cooperation

Human Genome I—the first in a series of international meetings—reported progress in efforts to map and sequence the human genome and to improve international cooperation in the Human Genome Project.

Attended by over 1300 scientists, science writers, and representatives of the commercial sector, the meeting was held October 2–4, 1989, in San Diego, California. Human Genome I was sponsored by the American Association for the Advancement of Science (publisher of *Science*) and the international Human Genome Organisation (HUGO).

Cochairs were Charles Cantor (Director of the DOE Human Genome Center at LBL) and Daniel Koshland (Professor of Biochemistry and Molecular Biology, University of California, Berkeley, and editor of *Science*). In addition to an excellent program of 31 platform talks and over 100 poster presentations, meeting attendees were able to view 80 commercial exhibits during the poster sessions.

In the keynote address, Cantor stated that the annual Human Genome meetings will provide an accounting of progress in the genome project to scientists, the public, and funding agencies. He also said that rapidly occurring advances in genetics research are facilitating the construction of genetic and physical maps of human and other genomes—the first task of the project.

Presentation Topics Demonstrate Diversification of Research

The selection of topics presented in platform talks and numerous poster presentations illustrates the diversification of genome research. Several of them pertained to the status of continuing research in genetic and restriction mapping, cloning techniques, ordered libraries, sequencing technologies, and societal implications of human genome research.

Methods presented in the area of technique innovations included in situ hybridization, PCR, radiation hybrids, rapid mapping, and automated contig mapping.

Studies covered on genomic regions of interest included cystic fibrosis (CF), the fragile X chromosome, telomeric and other repeating sequences, immunoglobulins, and T-cell receptors.

In the applications area, presentations were given on single-gene diseases

(on the X chromosome), multigene diseases, unstable DNA sequences, informatics—interpreting the DNA sequence, sex determination, and human evolution.

Francis Collins (Howard Hughes Medical Institute, University of Michigan Medical Center), codiscoverer of the CF gene with Lap-Chee Tsui (The Hospital for Sick Children, Toronto), described the strategies employed in the arduous task of locating and cloning the CF gene. He remarked that since CF is a high-frequency, single-gene disease, the CF gene was relatively easy to locate, compared to genes responsible for multigenic diseases. He stated that had sets of overlapping DNA clones—products resulting from the DOE Human Genome Program—been available during the quest for the CF gene, the task would have been completed two years earlier.

Several speakers discussed the organization of human genome efforts in other countries. Victor McKusick (Johns Hopkins University School of Medicine), then President of HUGO, described the role of HUGO in the Human Genome Project and the rapid accumulation of genetic map data—the first step toward a basic understanding of disease genes.

Nobel laureate James Watson, Director of the Cold Spring Harbor Laboratory and Director of the NIH NCHGR, in addition to the NIH genome program, discussed:

- the benefit of the genome project to society;
- the necessity for cooperation among all biologists; and
- the need for international support to accomplish the tasks of mapping, sequencing, and interpreting human genome data.

Charles Cantor described DOE's mandate from which ensued the need to determine and interpret the DNA sequence directly: to be able to detect low-frequency mutations that result from ionizing radiation and energy production by-products. He said some DOE areas of expertise include:

- coordinating large projects,
- designing and integrating computer and other system components for use in research projects, and
- transferring these technologies to the commercial sector.

Overlapping DNA Clones To Speed Gene Identification

New Techniques Applied to Genomic Regions

Meetings and Workshops

Cantor called for merging the DOE and NIH committees that have overlapping missions—for example, creating joint informatics and ethics task forces to conduct the respective studies of the computing needs and societal implications of the genome project.

The closing overview talk was given by Nobel laureate Renato Dulbecco (The Salk Institute), an early proponent of the genome project [*Science* 231, 1055–1056 (1986)]. He said that although all of biology is connected by evolution as evidenced by striking similarities at all levels of organization, there is a limit to what can be learned from the study of other species. He reasoned that to understand the biology of humans, true human characteristics must be studied; therefore, the Human Genome Project must exist. "To get a deep understanding of function of the [human] genome," he said, "the sequence becomes essential." He also contended that the "big science/cottage industry" question is not appropriate for the genome project; individual research groups, while maintaining their own interests, have been pulled together to complete this proj-

ect. "The whole is greater than the sum of its parts," Dulbecco stated.

Dulbecco outlined a scenario for biological research after more of the genome data becomes available. Start with the sequence, he said, and look at gene expression in a systematic manner—cell type by cell type—so that the mechanisms that control development and differentiation can be uncovered. "Antibodies could be made to synthetic polypeptides," he claimed; "it is conceivable to determine the tertiary structure of proteins." The genome project will impact other fields of research with the design of new drugs. Dulbecco affirmed that there are great opportunities to apply genome project results in cancer research.

A comment made by Cantor earlier in the meeting provided the consensus statement: "Rather than compromising the future of biology, the Human Genome Project is ensuring it." ♦

*Written by Betty K. Mansfield
HGMIS, ORNL*

Cantor Calls for Joint DOE/NIH Task Forces on Computing Needs and Societal Implications

Human Genome Organisation Elects New Officers, Members

The Human Genome Organisation (HUGO), whose role in the worldwide human genome project is to coordinate international efforts, elected new officers for 1990 and 20 new members on December 3, 1989. Charles R. Cantor, Director of DOE's Human Genome Center at LBL and Chairman of the DOE Human Genome Coordinating Committee, was elected regional Vice President for North America.

The new President of HUGO is Sir Walter Bodmer, Director of the United Kingdom's Imperial Cancer Research Fund Laboratory. The other two Vice Presidents and their respective regions are Andrei D. Mirzabekov (Director, Institute of Molecular Biology of the Academy of Sciences in the Soviet Union), Eastern Europe; and Kenichi Matsubara (Director, Institute for Molecular and Cellular Biology, Osaka University, Japan), Asia.

Modeled after the European Molecular Biology Organisation, HUGO elects members based on scientific distinction in areas relevant to the genome project. Two DOE HGCC members, Cantor and Leroy E. Hood, serve on HUGO's governing body—the

HUGO Council. The other three HGCC members—Anthony V. Carrano, C. Thomas Caskey, and Robert K. Moyzis—are also HUGO members. Of the original 220 members of HUGO, 7 are located in genome research centers within DOE national laboratories, and 2 are members of the DOE Health and Environmental Research Advisory Committee. ♦

HGM10 Plotbooks, Diskettes, and Proceedings Available

The "Plotbook" and diskettes based on data compiled and integrated at the Tenth International Workshop on Human Gene Mapping (HGM10), which was held at Yale University in June 1989, are now available. They are produced as a joint effort of the HGM10 Yale University organizers and staff and the Human Gene Mapping Library (HGML) staff, who are supported by the Howard Hughes Medical Institute (HHMI). HHMI and the NIH grant that supported HGM10 have underwritten the printing and duplication costs. Distribution fee for each is \$20.00. Checks payable to "Yale University-HGM10 Plotbook" should be sent to: HGML, Attention: Plotbooks; 25 Science Park; New Haven, CT 06511.

Human Gene Mapping 10 (ed. K. K. Kidd, H. P. Klinger and F. H. Ruddle), an 1150-page compilation of 29 expert committee reports and 700 abstracts of HGM10, is available for \$156.00 from S. Karger Publishers, Inc., Farmington, CT 06085. ♦

Meetings and Workshops

Consecutive Meetings Bring Diverse Groups Together

Participants See Need for Interdisciplinary Effort

Genes and Machines, Chapter II

An international symposium and workshop, MacroMolecules, Genes and Computers, was held August 13–18 in Waterville Valley, New Hampshire. Some 200 people, including mathematicians, computer scientists, molecular biologists, and geneticists, attended the conference. Deemed a great success by those participating, Genes and Machines, Chapter II was sponsored jointly by the NIH National Library of Medicine and the Molecular Biology Computer Research Resource at the Dana-Farber Cancer Institute/Harvard School of Public Health. Support for the meeting also came from the NIH Division of Research Resources and a number of commercial companies.

Two central themes emerged:

1. Familiarity with a broad range of topics is needed for complete understanding of the information encoded in the human genome.
2. There is a need for complex analysis tools and methodologies and for database support.

Topics covered by the 43 invited speakers were organized into the following sessions:

- Molecular-Molecular Recognition;
- Regulatory Signal Transduction Networks;
- Comparative Sequence Analyses;
- Function Pattern Correlate Identification;
- Genomic Organization; Databases: Interconnection, Utility and Management; and
- Future Directions.

Along with the more than 4 days of presentations, two afternoon workshops provided participants with hands-on opportunities to use new hardware and software. ◇

*Reported by Karen D. Gruskin
Baylor College of Medicine*

*and Temple F. Smith
Molecular Biology Computer Research Resource
Dana-Farber Cancer Institute/Harvard School
of Public Health*

BIO-MATRIX '89: Conference on the Matrix of Biological Knowledge

Integration of Databases Proposed

BIO-MATRIX '89, the third Bio-Matrix symposium, began with the last session of the MacroMolecules, Genes and Computers Workshop and continued to August 20 at Waterville Valley, New Hampshire. BIO-MATRIX '89 convened to explore the implementation of the Bio-Matrix concept and to foster the necessary interchange among the various computer science and biological disciplines. Bio-Matrix proponents see a pressing need to integrate all biological databases into a cohesive whole that would be interfaced to a knowledge base containing a structured representation of biological information. Seventeen speakers presented talks on topics related to the achievement of these goals to the 65 biologists and computer scientists attending the meeting.

As an outgrowth of this meeting, George Mason University, with the support of the National Science Foundation and NIH, will sponsor the International Meeting: Bioinformatics, Integration of Organismic and Molecular Data Bases and Use of Expert Systems in Biology on July 9–11 in Fairfax, Virginia. ◇

*Reported by Randall F. Smith
Molecular Biology Computer Research Resource
Dana-Farber Cancer Institute/Harvard School
of Public Health*

To become a member of the Bio-Matrix network and receive the Bio-Matrix newsletter, send a \$25 annual registration fee (\$10.00 for students) to: Santa Fe Institute: Bio-Matrix Project; 1120 Canyon Road; Santa Fe, NM 87501 Phone: (505) 984-8800; FAX: (505) 982-0565; E-mail: andi@dfi.santafe.edu. Requests to be added to the Bio-Matrix electronic mailing list should be sent to:

BIO-MATRIX-REQUEST@BIONET-20.BIO.NET.(Internet) or
BIO-MATRIX-REQUEST%BIONET-20.BIO.NET@CUNYVM (bitnet).

Calendar of Genome Events*

April	3	DOE Human Genome Coordinating Committee; Pasadena, CA
	3-5	"Panel on the Human Genome Project" at the Fifth International Conference on Statistical and Scientific Database Management; Charlotte, NC; [Z. Michalewicz (704) 547-4873, FAX: (704) 547-2352]
	4-5	DOE Workshop on Application of Mass Spectrometry to DNA Sequencing; Seattle, WA
	10-13	The First International Conference on Electrophoresis, Supercomputing, and the Human Genome; Tallahassee, FL [D. Burnette (904) 644-1010, FAX: (904) 644-0098]
	18-20	Genes, Proteins and Computing: International Conference on Computing in Molecular Biology; Chester, United Kingdom [A. Bleasby (Int.) 44-0925-603348, FAX: (Int.) 44-0925-603195]
	30-May 1	National Research Council, Computer Science and Technology Board, Computing and Molecular Biology Workshop; Washington, DC
May	2-6	Genome Mapping and Sequencing Conference; Cold Spring Harbor, NY
	25	"Panel on Database Issues of the Human Genome Project" at the 1990 International Conference on Management of Data; Atlantic City, NJ [R. Pecherer (505) 665-1970]
June	10-13	Development of Physical Methods for Mapping the Human Genome (Meeting and Workshop); Mt. McKinley Park, AK
	18	NIH Program Advisory Committee on the Human Genome; Bethesda, MD [C. Mohan (301) 496-0844]
	19	Joint DOE/NIH Advisory Subcommittees; Bethesda, MD
	19	DOE Human Genome Coordinating Committee; Bethesda, MD
	30-July 3	Combined 1990 Meeting of the International and American Electrophoresis Societies; Washington, DC; abstract deadline: April 1 [AES (615) 327-7064, FAX: (615) 327-7078]
July	9-11	International Meeting: Bioinformatics, Integration of Organismic and Molecular Data Bases, and Use of Expert Systems in Biology; Fairfax, VA; abstract deadline: April 1 [H. Morowitz (703) 323-2262, FAX: (703) 764-4725]
	18-21	Genetics Societies of America and Canada Joint Meeting; San Francisco, CA; abstract deadline: April 6 [J. Francese (301) 571-1825, FAX: (301) 530-7079]
	22-27	CIOMS 24th Conference - Genetics, Ethics and Human Values: Human Genome Mapping, Genetic Screening and Genetic Therapy; Tokyo, Japan
August	27-30	"Symposium on Mapping and Sequencing" at the 1990 National American Chemical Society Meeting-Analytical Division; Washington, DC; [L. M. Smith (608) 263-2594]
	28-29	DOE/NIH Five-Year Plan Update Workshop; Cold Spring Harbor, NY
September	6-11	International Workshop on Human Gene Mapping (HGM 10.5); Oxford, United Kingdom
	30-Oct. 3	Genome Sequencing Conference II; Hilton Head, SC; abstract deadline: July 15 [S. Wallace (301) 480-0634, FAX: (301) 480-8588]
October	22-24	Human Genome II: An International Conference on the Status and Future of Human Genome Research; San Diego, CA; abstract deadline: Aug. 15 [Scherago Assoc., Inc., (212) 730-1050, FAX: (212) 382-3725]
November	12-14	Mapping and Sequencing the Genome: New Opportunities/New Dilemmas - The Ethical Issues; Monte Picayo, Spain

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

Acronym List

Acronyms listed were chosen because they were either used in the text or 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.

AES	American Electrophoresis Society	LBL*	Lawrence Berkeley Laboratory, Berkeley, Calif.
ANL*	Argonne National Laboratory, Argonne, Ill.	LLNL*	Lawrence Livermore National Laboratory, Livermore, Calif.
ASHG	American Society of Human Genetics	NAS	National Academy of Sciences (U.S.)
ATCC	American Type Culture Collection	NCBI†	National Center for Biotechnology Information (NLM)
BISP	Biological information signal processor	NCHGR†	National Center for Human Genome Research (NIH)
BNL*	Brookhaven National Laboratory, Upton, N.Y.	NIH†	National Institutes of Health
CF	Cystic fibrosis	NLGLP*	National Laboratory Gene Library Project (LANL, LLNL)
CIOMS	Council for International Organizations of Medical Sciences	NLM†	National Library of Medicine (NIH)
DHHS	Department of Health and Human Services (U.S.)	NRC	National Research Council (NAS)
DNA	Deoxyribonucleic acid	NSF	National Science Foundation
DOE	Department of Energy (U.S.)	OER*	Office of Energy Research
HERAC*	Health and Environmental Research Advisory Committee	OHER*	Office of Health and Environmental Research (OER)
HGCC*	Human Genome Coordinating Committee	ORNL*	Oak Ridge National Laboratory, Oak Ridge, Tenn.
HGMIS*	Human Genome Management Information System (ORNL)	OTA	Office of Technology Assessment (U.S. Congress)
HGML	Human Gene Mapping Library (HHMI)	PAC†	Program Advisory Committee (NIH)
HHMI	Howard Hughes Medical Institute	PNL*	Pacific Northwest Laboratory, Hanford, Wash.
HUGO	Human Genome Organisation [international]	STS	Sequence-tagged site
ICRF	Imperial Cancer Research Fund	USDA	U.S. Department of Agriculture
LANL*	Los Alamos National Laboratory, Los Alamos, N.M.	YAC	Yeast artificial chromosome

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