Sequencing Groups Report Striking Results
Two Projects Reaffirm Value of Genomic Sequencing Approach

Major accomplishments achieved in two separate sequencing projects recently yielded the longest contiguous stretch of DNA sequence on record and the largest comparative sequence analysis of a biologically important region in humans. These results demonstrate the feasibility of large-scale sequencing projects and strongly support the value of whole-genome sequencing and comparative analysis of model organism and human sequence to identify human genes and provide insights into their organization, regulation, and function.

- Investigators led by Richard Wilson and Robert Waterston (Washington University, St. Louis) and John Sulston (Medical Research Council, Cambridge, U.K.) sequenced almost 2.2 Mb of the Caenorhabditis elegans genome [Nature 368, 32–38 (1994)].

- Researchers led by Ben Koop (University of Victoria) and Leroy Hood (University of Washington, Seattle) completed the sequence and comparative analysis of nearly 100 kb each of contiguous DNA from human and mouse genomic regions encoding T-cell receptors (TCRs) [Nature Genetics 7, 48–53 (1994)]. TCRs are cell surface molecules that play an important role in mammalian cellular immunity.

The C. elegans work was supported by the NIH National Center for Human Genome Research (NCHGR) and the U.K. Medical Research Council Human Genome Mapping Project. TCR analyses were funded by NCHGR and DOE genome grants to Hood and by a National Science and Engineering Research Council (Canada) operating grant to Koop, who began this work as a DOE Human Genome Distinguished Postdoctoral Fellow with Hood. Details of the two projects follow.

C. elegans Sequence

Wilson and colleagues reported on the first 3 years of their effort to determine the sequence of the 100-Mb C. elegans genome, which is slightly smaller than an average human chromosome. This project, made possible by years of intensive research that produced detailed genetic and physical maps of the six C. elegans chromosomes, is considered an important testing ground for sequencing human DNA on a large scale. Each half of the research consortium completed over 1 Mb of sequence from chromosome III, roughly 2% of the genome, and all sequences have been deposited in the publicly available C. elegans database, ACEDB.

The finished sequence is based on analysis of cosmid clones mapped to the chromosome by restriction digest fingerprinting and includes two 1-Mb cosmid contigs bridged by a yeast artificial chromosome (YAC) clone, with a 92-kb cosmid contig near the center of the YAC bridge [see HGN 4(2) 1–2 (May 1992)]. DNA templates for walking were obtained from 500 to 800 random phagemid and M13 subclones. After this initial random phase, site-specific oligonucleotide primers were used to extend sequences [see HGN 4(5) 1–2 (January 1993)]. Researchers
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Model-Organism Sequencing and Human Genome Project Goals

Systematic efforts to map, clone, and determine the entire DNA base sequence for several model organisms are considered crucial in developing strategies and tools for large-scale sequencing of the human genome. Human Genome Project short-term sequencing goals through 1998 include the following.

- Complete sequencing of *E. coli* and *S. cerevisiae* genomes by 1998 or earlier;
- Continue sequencing the *D. melanogaster* and *C. elegans* genomes, bringing the latter to near completion by 1998; and
- Continue side-by-side sequencing of biologically important regions in human and mouse.

Individual TCRs are made of two polypeptide chains, of which there are four different components (designated α, β, γ, and δ). Each component contains (1) a variable (V) region that is different for each receptor and responsible for specific recognition of foreign proteins and (2) a relatively invariant, constant (C) region for cell-surface attachment and other functions. The four components are encoded at three chromosomal loci in both the mouse and human genomes. Koop and Hood reported sequencing the C8 to Cox region of the α and δ TCR loci.

A comparison of sequences in this region revealed a high degree of similarity between corresponding mouse and human protein-coding and noncoding regions. These results suggest that the majority of the TCR region has been highly conserved through 80 million years of evolution, although only about 6% of the region contains gene-coding sequences. Until recently, many scientists believed that only 3% of the genome contained useful sequences that were embedded in vast stretches of noncoding "junk" DNA. Recent studies are challenging that view in favor of seeing chromosomes as information organisms with complex structural and gene-control systems. [Denise K. Casey, HGMIS]  

T-Cell Receptors

Koop and Hood sequenced and analyzed nearly 100 kb of contiguous sequence from nonvariable regions of the TCRα complexes in the human and mouse genomes. The goal of the project is to sequence and compare 5 to 6 Mb from these regions.

TCRs play a central role in regulating the mammalian cellular immune response. These glycoprotein molecules are embedded in the surfaces of T cells, where they recognize and bind to foreign protein fragments captured by a cell surface molecule that is part of the major histocompatibility complex (MHC). The fragments are produced by foreign substances, such as viruses or bacteria (for more details on TCR-MHC interactions, see box, p. 3).

Formation of the TCR-MHC-foreign protein fragment complex can stimulate target cell destruction by T cells or antibody production by B cells. Researchers believe inappropriate T-cell responses are the culprits in allergies and several different types of autoimmune diseases, such as arthritis and diabetes. Elucidation of TCR structures and their functions will yield insights into the regulation of the immune response.

Ideas for Articles?

*Human Genome News* staff asks Human Genome Project investigators to send ideas for newsletter articles on their research progress and available resources. See address on p. 12.
MHC Database Combines Map and Sequence Data

Investigators at the U.K. Imperial Cancer Research Fund (ICRF) have compiled much of the available human major histocompatibility complex (MHC) genetic and physical data into a publicly available database. MHCDB uses software developed for the Caenorhabditis elegans project to access, retrieve, and display MHC data. Information in release 1-0 includes:

- locations of over 100 genes and markers on the chromosome 6 genetic map and 69 yeast artificial chromosome (YAC) and 211 cosmid clones on the MHC physical map,
- 150 kb of genomic sequence with the exact location of gene structural elements such as exon-intron boundaries,
- elements such as promoters and repetitive elements,
- 294 cDNA sequences of polymorphic class I and class II MHC genes, and
- atomic coordinates of the class I HLA-A antigen.

MHCDB also has a tool for examining the antigen's structure from within the database and the ability to examine the variability of class I allele sequences within the three-dimensional structure of the class I antigen.

Other features will appear in future extensions to the core of ACEDB, the C. elegans database. These will include interfaces to sequence analysis software such as GRAIL, which detects coding regions in human sequences, and to the Pythia programs, which find repetitive elements and classify Alu repeats into Alu subfamilies. Information on Alu repeats can provide insights into MHC evolution.

MHCDB Information Online and in Print

MHCDB (release 1-0) is available online via the HGMP Clinical Research Centre, Harrow, U.K. (+44/81-869-3448, Fax: -3807, Internet: admin@hgmp.mrc.ac.uk). MHCDB users are encouraged to report errors and new data directly to ICRF at wn@duaseq.tif.icnet.uk. Additional information on the database can be found in "MHCDB—Database of the Human MHC," by William R. Newell, John Trowsdale, and Stephan Beck in Immunogenetics 40, 109–15 (1994).

MHCDB is funded by the European Economic Community's BioMed1 program.

What is Human MHC?

Much research has been devoted to studying genes and protein products of the human major histocompatibility complex, which occupies a 4-Mb stretch on the short arm of chromosome 6.

Residing in this area are genes responsible for cellular immunity—one of two main defenses evolved by vertebrates in their constant struggle to defend the body against the steady stream of microorganisms (v- ruses, bacteria, and other pathogens) that invade it. The body's other main defense is humoral immunity, which involves protein antibodies that are released into extracellular fluids and blood to fight foreign invaders.

Cellular Immunity

Cellular immunity is based on the interaction of MHC proteins found on surfaces of circulating cells and T lymphocytes (white blood cells that pass through the thymus gland during maturation). Produced in cells' endoplasmic reticulum, MHC proteins act as sentries in the war against intruders, recognizing them and identifying infected cells for destruction by specialized T cells. MHC proteins accomplish this task by capturing pieces of foreign proteins (peptides) they find within an infected cell and transporting them to the cell's surface. The MHC-specific T-cell receptors located on the cell interact with these proteins and activate the cell.

MHC proteins also promote the release of lymphokines by "helper" T cells. Lymphokines stimulate the body's overall immune response, including B-cell antibody production and activation of macrophages and other cells that participate in immune reactions. Loss of helper T cells, as occurs in HIV infection, results in immune-system failure.

"Self" Recognition

The ability to distinguish normal body constituents ("self") from everything else ("nonself") is based on individual differences in MHC proteins. When MHC genes were first cloned, researchers discovered that these proteins are exactly the same from cell to cell in each individual but differ markedly among people, more so than with most other proteins.

In humans, genes encoding proteins for self recognition are designated HLA (for human lymphocyte antigen). Scientists screening organ donors attempt to minimize the potential for rejection by matching patients with donors having the most similar HLA proteins.

Immune Disorders

Immune-system failures lead to loss of immune function, tumors, hyper-reactive conditions such as allergies, and autoimmune diseases such as arthritis and type 1 diabetes. Autoimmune diseases occur when the immune system mistakes the body's own proteins for intruders and marks healthy cells for destruction.

Researchers expect that a better understanding of how the MHC—foreign peptide complex binds to the T-cell receptor will one day lead to the development of new ways to fight transplant rejection and infectious and autoimmune diseases. These might include drugs that block binding sites or engineered receptors that can recognize features of pathogens with greater accuracy.

MHC Genomic Map

With 100 mapped genes, the human MHC is one of the most detailed areas of the human genome map. It is divided into three regions: class I (the 2-Mb telomeric region), class II (the 1-Mb centromeric region), and class III (the intervening megabase). The entire MHC has been cloned in YACs, and most regions are also represented in overlapping cosmid clones. Availability of these resources has led to the recent initiation of large-scale projects to sequence the MHC and to centralize much of the mapping and sequencing data in the MHC database. [Denise K. Casey, HGMSI]?
NACHGR Holds Tenth Meeting

The National Advisory Council for Human Genome Research was convened for its tenth meeting on January 24 in Washington, D.C., with Francis Collins, Director of the National Center for Human Genome Research (NCHGR), presiding. Harold Varmus, NIH Director, opened the meeting by discussing initiatives and policy issues under consideration at NIH.

One of these initiatives was the NIH intramural program review, which Varmus said was being conducted by a group of extramural advisors. The advisors' report was expected to recommend changes in the allocation of funds, scientific review processes, recruitment procedures, and physical setting. Varmus also announced that Howard Shachmann (University of California, Berkeley), the NIH ombudsman, will serve as the voice of the extramural community. He will meet scientists at universities around the country and bring their opinions of NIH back to the director.

A pilot program is under way to make the NIH peer-review system friendlier, fairer, and more efficient. In the revised system, study sections would quickly identify projects for more-detailed review and dismiss others. This rapid return would let applicants know when they need to rethink their proposals before they reapply. Varmus urged the council to examine grants closely and not rely solely on scores assigned by review panels.

Varmus reported that an Office of Science and Technology Policy forum, held at the end of January, would focus on the important roles of basic science and biomedical research. A series of panel discussions at the forum was to examine NIH embryo research. Varmus also discussed the issue of cDNA patenting.

Collins reported positive feedback on the new 5-year plan (Science, October 1, 1993). [Reprints of the Science article may be obtained from HGMIS; see p. 12 for address.] He also discussed the January Human Genome Organisation Summit Meeting in Houston [see HGN 6(1), 6-7 (May 1994)]. At the request of the council, Jerome Cox and David Benton (NCHGR) reported on informatics program status and concerns for the future. Council members raised key questions concerning the adequacy of system capacity for sequencing data, methods for improving communication among biologists and computer scientists, and ways of stimulating interest and training for the computer scientists needed to service database systems. A forum to address these questions and bring together scientists and informatics specialists was planned for the Cold Spring Harbor meeting in May.

Benton presented a concept paper for a program to foster the development of resources and specialized tools for genome research. These services would be supported through two mechanisms: P41 (Genome Research Resource Grant) and R24 (Genome Resource Development Grant). The council approved the concept with a few modifications.

Elizabeth Thomson (NCHGR) introduced for concept clearance an abstract on "Testing and Counseling for Heritable Breast, Ovarian, and Colon Cancer Risks," a proposed request for applications (RFA) [see HGN 6(1), 6-7 (May 1994)]. The council approved the RFA release with two qualifications: (1) studies associated with the RFA will be carried out in conjunction with research on the molecular and epidemiological basis of cancer-related genes and (2) genetic testing for heritable cancer risks is considered premature in the general population and should be used only in families where breast, ovarian, or colon cancer has already occurred. To complement the RFA, the council issued a statement on presymptomatic identification of cancer risk [see HGN 6(1), 6-7 (May 1994)].

The NIH-DOE Joint Ethical, Legal, and Social Implications (ELSI) Working Group has been expanded to consider whether it should function as a deliberative body or promote development of the ELSI grant portfolio. The group has identified four high-priority policy issues: health-care reform, exclusionary testing and possible discrimination by employers, privacy of genetic information, and new genetic tests. Collins stated that the ELSI program is at a critical juncture with no other group stepping into this role, although establishment of a bioethics commission is under consideration by Congress.

Phillip Reilly (Shriver Center) discussed conflict-of-interest concerns surrounding grant awards and made several points about developing NIH guidelines.

Elke Jordan (NCHGR) announced the creation of new workshops to facilitate exchange with other NIH components. This mechanism is expected to be useful in supporting genetics projects that no one institute can fund alone.

The council reviewed 73 applications requesting almost $23 million. A total of 53 applications for over $12 million were recommended for approval.
Human Genome Mapping Workshop 93

The Human Genome Mapping Workshop 93 (HGM 93), held November 14–17, 1993, in Kobe, Japan, was the first of a new series of international genome workshops that are expected to succeed the former Human Gene Mapping Workshops (HGMs 1–11). Since HGMs ended in 1991, genome data have been collected, assembled, and edited at single-chromosome workshops (SCWs) and by chromosome editors at Chromosome Coordinating Meetings (CCMs). [For citations of databases, plans involve better integration with activities in their respective countries and some 2 marker was linked to elevated blood pressure in all 4 models, whereas the 11b hydroxylase marker on chromosome 7 was linked only in the Dahl hypertensive rat. William Cookson (University of Oxford) showed further linkage of asthma to 11q13 markers and suggested a subunit of the high-affinity receptor for IgE (IgE responsiveness) as a candidate gene. Francis Collins (NIH) summarized mutations in the NF1 gene found in neurofibromatosis type 1 patients. Only 6 of 56 mutations were the missense type, and most of the others involved gross gene rearrangements. The gene product, neurofibromin, was localized in the cytoplasm along a microtubule showing a network-like pattern.

Stefan Karlsson (NIH) described successful gene-replacement therapy for Gaucher disease in mice and monkey. Human protocols were recently approved, and clinical trials are underway at NIH. Janet Rowley (University of Chicago) reported that 95% of infantile acute leukemias cases with the 11q23 translocation have breakpoints within an 8-kb region of the MLL (mixed-lineage leukemia) gene, an observation that points to a chimeric gene fused to the 3' end of the AF4, AF9, or ENL gene. Gilles Thomas (Institut Curie, France) identified the SCH (schwannomin) gene as the target of NF2 (neurofibromatosis 2) mutations. Most germline mutations in NF2 patients and somatic mutations in meningiomas and schwannomas cause the synthesis of a truncated protein. In Ewing's sarcoma and peripheral neuroepithelioma, reciprocal translocation results in the formation of a hybrid gene containing the EWS gene and either the FLI-1 (Friend murine leukemia virus integration site) or ERG gene. In malignant melanomas of soft tissue, EWS forms a hybrid gene with the AFT-1 (CAMP dependent transcription factor 1) gene. Nakamura summarized the mutation analysis of the APC (adenomatous polyposis coli) gene in over 160 chromosom from patients and in sporadic cancers of the colon, stomach, and pancreas. The great majority of mutations resulted in truncation of the APC gene product, and 60% of the mutations for somatic cancers were clustered in a small part of the MCR coding region.

Chromosome-Specific Sessions
Seven sessions covered chromosomes, clinical disorders, neoplasia, and mitochondrial DNA. Senior chromosome editors reported data-assembly and editing results from CCM 93, which took place in Tsukuba, Japan, just before HGM 93; oral presentations followed on selected topics relevant to the chromosomes. The DNA committee reported compilation in GDB of 4183 genes, of which 3808 were cloned; over 2000 microsatellite markers including 350 tetra- or trinucleotide repeats; and 25,460 mapped D-segments.

(continued)
Workshops on Selected Topics

Comparative Map and Model Organisms

DNA Polymorphism and Genetic Maps

Cytogenetic Maps

Informatics

DNA Sequencing

Unusual Mechanisms

Polygenic Diseases

cDNA

New Technology

COMPARATIVE MAP AND MODEL ORGANISMS. About 1,000 new cDNAs were sequenced and mapped to ordered arrays of yeast artificial chromosome (YAC) clones in Caenorhabditis elegans [Yūji Kohara (National Institute of Genetics, Japan)]. Leslie Lyons (National Cancer Institute) is using interspecífic backcrosses between the Asian leopard and the domestic cat to construct a cat genetic map. The distal segment of mouse chromosome 2 was shown by fluorescence in situ hybridization (FISH) mapping to be in complete homology with human chromosome 20. Human counterparts of known mutations on mouse chromosome 2 were assigned to specific bands of human chromosome 20 [C. Loeßl (Institut für Humangenetik, Germany)].

DNA POLYMORPHISM AND GENETIC MAPS. Jeffrey Murray (University of Iowa) reported progress in the multicenter effort to develop a human genome map of over 100 core short tandem repeat polymorphisms, with emphasis on tri- and tetranucleotide repeats. Tara Matise (University of Pittsburgh) developed Multimap, which enabled automatic construction of a linkage map of the human genome, including 654 markers. Michel Mchnis (JHI) isolated new cDNAs containing polymorphic triplet repeats and mapped them by linkage analysis.

CYTOGENETIC MAPS. The FISH technique has been a powerful tool in evaluating CEPH and Genethon sequence tagged site (STS) YAC maps for contig integrity, chromosomal assignment, and the presence of chimeras [David Ward (Yale University)]. Eiichi Takahashi [National Institute of Radiological Sciences (NIRS), Japan] and Johji Inazawa (Kyoto Prefectural University of Medicine, Japan) constructed high-density human cytogenetic maps by using either direct R-banding FISH on prometaphase chromosomes or multicolor FISH on extended prophase chromosomes.

INFORMATICS. Two software programs were described for map and sequence analysis: SIGMA, a system for integrated genome map assembly [Michael Cinkosky (National Center for Genome Resources, Santa Fe, New Mexico)]; and Genematcher, an integrated data-management tool for genome sequencing projects [Yutaka Akiyama (KU)].

DNA SEQUENCING. Ellison Chen (Applied Biosystems) described using an ordered shotgun sequencing strategy in which YAC DNA was digested to 4- to 8-kb fragments and directly subcloned into plasmids for sequencing and subsequent mapping. Chen’s laboratory expects to sequence 1 Mb/year/one to two persons running automated equipment. In producing nested deletions of P1 (blood group) clones, Masahira Hatori (University of Tokyo) used a vector containing double SfiI sites flanking the cloning site to generate 3' overhangs. Satosh Takahashi (Mitsubishi Central Research Laboratory, Japan) discussed a high-throughput capillary-array gel electrophoresis system that uses multiple sheathflow and four-color detection with the goal of sequencing 1 Mb/week/machine.

UNUSUAL MECHANISMS. Tada-aki Horii (NIRS, Japan) and Hidehisa Yamagata (OU) presented genetic evidence for the presence of founder chromosomes in the Japanese population affected by Fragile X syndrome and myotonic dystrophy, two disorders caused by expansion of unstable trinucleotide repeats. Shin-Feng Tsai (National Yang-Ming Medical College, Taiwan) identified 326 Drosophila melanogaster cDNA clones containing CAG or CAA repeats, the majority of which are novel sequences. Yoshihiro Jinno (Niigata University, Japan) developed a screening strategy to detect imprinted genes. This strategy is based on using mRNA from hydatidiform mole, an androgenetic product in which transcripts of maternally expressed genes are absent. Ichiro Takahashi (National Institute of Health, Japan) identified a 100-kD protein that binds specifically to RNA of XIST (X-inactivation–specific transcript) gene. The interaction of this protein with XIST RNA may be involved in the X-inactivation process.

POLYGENIC DISEASES. Eric Lander (Massachusetts Institute of Technology) presented an overview of cancer and diabetes as complex diseases. Yūji Tanaka (Eliz University, Japan) showed genetic evidence that variations at the cytokrome P450 diebrisoquine (CYP2D6) gene may be a predisposing factor to Parkinson’s disease. Ann Pulver (JHU) genotyped 240 polymorphisms in 39 families to show the potential linkage of schizophrenia to 22q12-q13.1 (LOD score 2.82); schizophrenia is known to be genetically heterogeneous. Phenotypic diversity of mutations occurring in a single gene was highlighted by Giovanni Romeo (Gasolini Institute, Italy), who showed different mutations in an RET protooncogene causing Hirschsprung disease, MEN 2A (multiple endocrine neoplasia), 2A, or MEN 2B.

cDNA. Radoeje Pirmannac (Argonne National Laboratory) and Sebastian Meier-Ewert (Imperial Cancer Research Fund, U.K.) described cataloguing 60,000 human brain and 10,000 human embryo cDNAs. Partial sequence information was obtained by using short oligonucleotide probes (6-, 7-, and 8-mers) for hybridization to high-density filter grids of cDNAs and automatically scoring the signals. Jun Takeda (University of Chicago) characterized 1,000 tissue-specific cDNAs from human pancreatic islets, of which 443 represent novel sequences. Kousaku Oiko (OU) described “body mapping” on more than 6,000 distinct genes in 20 different tissues. In this strategy, the abundance of gene transcript in each cell or tissue is measured by sequencing 3' ends of cDNAs on a large scale. Chris Fields (The Institute for Genomic Research) developed the Expressed Gene Anatomy Database (EGAD). EGAD maintains relational data on sequence, gene expression, and sequence classifications of genes identified by expressed sequence tag sequencing. Anne Marie Poustaika (German Cancer Research Center), Osamu Onodera (Nigata University, Japan), and Yoshikazu Ishida (Tokai University, Japan), respectively, identified and mapped new region-specific cDNAs from the Xq27.3-qter, Xq24-qter, and distal 4p regions. Their methods included cDNA selection by magnetic capture from ordered cosmids and YACs, Alu polymerase chain reaction (PCR) on hncDNA from somatic cell hybrids, and single-primer PCR on laser-microdissected chromosomes.

NEW TECHNOLOGY. Shinji Hirokane (Institute of Physical and Chemical Research, Japan) compared spot patterns generated by the restriction landmark genomic scanning method to contig formation of YAC clones derived from a single chromosome-specific YAC library. Gerard Roizés (INSERM, France) proposed using the collection of 32-tp fragments generated by restriction digestion of genomic DNA, with BcgI as a new type of STS for the human genome. Misao Ohki (National Cancer Research Institute, Japan) completed 110 restriction maps of 21q and 11c23.3 to qter. The non-redundant clones, together with this map, will serve as excellent tools for detecting chromosome rearrangements and deletions in these regions. Kenichi Matsubara (OU, Japan) and Mitsuru Emi (Cl, Japan)
NCHGR Intramural Program Reaches Out

The Division of Intramural Research of the National Center for Human Genome Research (NCHGR) was established in 1993 to study genes that cause diseases, including cancer, and to focus on medical genetics, clinical gene-therapy research, and the development of clinical diagnostic tests. With a broader scope than the U.S. Human Genome Project, which is composed of the NCHGR extramural and DOE genome programs, the intramural program also complements and fosters collaboration with other NIH research efforts in human molecular genetics, structural biology, and gene therapy.

To make information about the latest advances available to scientists and others outside NIH, the intramural program has established education and outreach activities, including the following.

Genetics Education Program: Designed to increase knowledge among teachers, students, policymakers, news media personnel, health-care professionals, and the general public about human gene-mapping and cloning technologies, cancer genetics, and gene therapy. Director Paula Gregory said of the program, "We hope to give people the knowledge they need to understand genetics so they can make informed and responsible decisions about how they will use genetic technologies in their lives."

Through a variety of formats, including courses and hands-on workshops, Gregory teaches DNA science and helps teachers learn creative and effective ways to communicate this information to their students. Several programs are aimed at cultivating minority participation in genome research, including a short course for faculty from minority colleges and universities.

Program staff also maintain a comprehensive computer listing of genetics education programs throughout the country; prepare informational brochures, slide sets, and videos; coordinate mentor programs among genome scientists and local college and high school faculty; work with state and national teacher organizations; and publish and distribute a national newsletter on genetics for educators. A workshop for science and medical writers is planned for September 30 on the NIH campus in Bethesda.

Contact: Paula Gregory, NCHGR; Bldg. 10, Rm. 10C100; 9000 Rockville Pike; Bethesda, MD 20892 (301/496-3978, Fax: -7157, Internet: edcore@helix.nih.gov).

Visiting Investigator Program (begins January 1, 1995): Allows tenured or tenure-track university scientists to use NCHGR resources for 3 to 12 months. Visiting investigators can learn new technologies, conduct research collaborations, or pursue sabbatical research in genetic diseases; gene transfer; cancer genetics; development of diagnostic techniques; clinical gene therapy; medical genetics; and ethical, legal, and social implications of genomic research. Betty Wolf, Director of the Visiting Investigator Program, says, "This program is designed to respond to the increasing need for access to new technologies among the genetics community and to encourage implementation of such technologies when investigators return to their home institution."

Partial funding of salary support and all funding for research-related expenses while at NIH are available to visiting investigators. Proposal extensions to 1 year are preferred so that research objectives may be accomplished. Applications are accepted throughout the year, with selection based on potential or demonstrated excellence in a clinical or research discipline.

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DOE Announces 1994 Human Genome Distinguished Postdoctoral Fellows

DOE has announced that four people have accepted 1994 Human Genome Distinguished Postdoctoral Fellowships to conduct research for up to 2 years at university or DOE laboratories. These fellowships were initiated by DOE to develop tools, technologies, and resources for deciphering the molecular nature of the human genome and to support related research. Listed below are the name of each fellow, university and discipline of doctoral degree, host laboratory and research mentor, and research plans.

MARK GRAVES (University of Michigan, Computer Science)
BAYLOR COLLEGE OF MEDICINE, CHARLES LAWRENCE: Examine novel and concise representations for map information and create a natural, graph-theoretic foundation for genome maps that can be used to define integrated mapping databases.
WILLIAM HAWE (Northwestern University, Chemistry)
DUKE UNIVERSITY, MICHAEL PIRRUNG: Explore a new methodology for sequencing the human genome with a spatially addressable array of DNA analogs by using light-directed immobilized polymer synthesis.

JINGYUE JU (University of Southern California, Chemistry)
UNIVERSITY OF CALIFORNIA, BERKELEY, RICHARD MATHIES: Investigate new types of dye labels for multiplex detection of DNA in sequencing, polymerase chain reaction, and other procedures.
MARK SHANNON (University of Tennessee, Life Sciences)
OAK RIDGE NATIONAL LABORATORY, LISA STUBBS: Explore the structural and functional relationship between a human chromosome 19q13.2 region and the homologous region of mouse chromosome 7, and develop a method for generating targeted deletions to scan the mouse genome for essential functional units.

Fellows receive a stipend of $37,500 the first year and $40,500 the second. The program is administered by the Science and Engineering Education Division of the Oak Ridge Institute for Science and Education (P.O. Box 117; Oak Ridge, TN 37831-0117 [615/576-9934, Fax: /241-5219]). Applications for the next awards are due February 1, 1995.0
### Genome News

#### Chromosome Editors

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*Chromosome editors, an international panel recommended by their peers and appointed by the Human Genome Organisation's Human Genome Mapping Committee, review information submitted for inclusion in GDB. They are responsible for validating data and providing guidance in moving information from the community to the public database. Senior editors are shown in **boldface.**

### 1993 Single Chromosome Workshop Reports Published

**Reports Available at Press Time**

**CHROMOSOME 3** (May 14–15)

**CHROMOSOME 4** (July 10–11)

**CHROMOSOME 5** (September 18–19)

**CHROMOSOME 7** (May 20–22)

**CHROMOSOME 8** (May 1–3)

**CHROMOSOME 9** (April 18–20)

**CHROMOSOME 10** (June 10–12)

**CHROMOSOME 18** (July 18–20)

**CHROMOSOME 20** (September 6–8)

**CHROMOSOME 21** (May 23–24)

ELSI Working Group Explores Privacy Issue

The NIH-DOE Joint Working Group on the Ethical, Legal, and Social Implications (ELSI) of Human Genome Research met April 21–22 in Bethesda, Md., to conduct a workshop on the privacy of genetic information and develop a knowledge base from which to formulate policy recommendations. The workshop was organized by Michael Yesley [DOE's Los Alamos National Laboratory (LANL)]. Several NIH and DOE grantees who are studying genetic-information privacy from sociological, philosophical, and legal perspectives were invited to report on their preliminary results, and other commentators with expertise in information privacy or discrimination contributed additional analysis.

Third-Party Knowledge
Health-information privacy is an important topic during this period when health-care reform is being actively discussed, and the use of genetic information raises particularly difficult practical and philosophical problems related to access and disclosure. Third parties such as insurers, employers, adoption agencies, and educational institutions may feel they need to access genetic data that might have predictive or diagnostic value, while others feel that such access could lead to discrimination. Some proposed legislation, such as the Fair Health Information Practices Act of 1994 (H.R. 4077), focuses specifically on privacy concerns by attempting to establish a legal framework of fair practices for health information and to regulate its access, disclosure, and use. In discussions about such laws, George Annas (Boston University) suggested that genetic information should be regulated during sample collection and when it is stored, disclosed, and used.

Genetic Privacy in the Family
Because particular genes are more often shared by family members, genetic information on one person may also pertain to parents, siblings, and other relatives. For example, individuals who test positive for the allele associated with Huntington's disease must have one parent who also carries the same allele (except in rare cases of spontaneous mutations). Attendees asked, Does genetic privacy make sense when considered in the context of family?

Troy Duster (University of California, Berkeley) is investigating the interpretation and communication of genetic information in families of different cultural and socioeconomic backgrounds. He presented preliminary conclusions: (1) women are most often charged with communicating genetic information within families; (2) genetic testing during pregnancy is less likely to be perceived as threatening or stigmatizing if seen as routine rather than directed toward "at-risk" families; (3) men in all the socioeconomic and cultural groups studied are more likely to deny genetic conditions; and (4) family members are most likely to communicate about genetic conditions during a pregnancy and immediately following the diagnosis of a child.

Other grantees have been studying legal precedents for either protecting or disclosing genetic information among family members and the philosophical and legal basis for intrafamilial obligations. Aside from the parent-child relationship, no strong basis is apparent for such obligations. In the U.S. legal system, disclosure between spouses is not required, and physicians are allowed to override patient confidentiality only to avert a life-threatening situation or public peril. These points should be considered when asking whether genetic privacy may be breached: What is the harm to be averted? Will disclosure actually avert the harm? Is disclosure the only way?

DNA Databanks
DNA databanks, which can be any collection of cells or tissues, are another source of concern. Interest in forensic DNA databanks is growing, with 19 states having laws that authorize the collection of samples from convicted felons; 13 states have begun such collections. Jean McEwen and Philip Reilly (Shriver Center) reported widespread uncertainty about the types of sample releases that are legally or ethically prohibited. In the absence of clear guidelines, the temptation is to use samples collected for a purpose such as identification for a completely different purpose such as research. The joint working group is currently using information generated from grantee research to develop a set of guidelines that will help ensure confidentiality of databank materials. [Pilar Ossorio, LANL]
Proposed GDB 5-Year Work Plan Available

Documentation describing the proposed GDB 5-year work plan is available via World Wide Web (WWW), including discussions of GDB and its roles in the federation of genomic databases and in the revised NIH-DOE 5-year plan. Additional documents describing GDB's proposed design for Version 6 will also be available soon to enable the user community to provide feedback during the design phase.

This documentation can be accessed directly from the GDB Home Page via WWW (URL http://gdbwww.gdb.org) or through a GDB/OMIM login account at Johns Hopkins University (select Local Databases at the Main Menu and then Internet WWW Access).\*1

GDB 5.4 Provides Easy Output, Submission Numbers

In GDB Version 5.4 released this summer, output report generation has added an easy one-step way to output search results. Tool-Basic Output has a single screen for defining the report and sending it once by e-mail. Users can still define reports to save and run multiple times by using Tool-Full Output.

Each group of GDB objects submitted as a set now has a GDB identification number in addition to the individual numbers given to each object. Users can retrieve submission numbers through the GDB ID manager and see summary information by selecting View-Submission.

A detailed description of how to use Basic Output and other new features will be available online in "Release Notes" under "News."\*2

Resources

Tech Transfer. The Federal Bio-Technology Transfer Directory, by Ronald A. Rader and Sally A. Young, lists all federal biomedical and biotechnology-related inventions, patents and patent applications, and technology transfers from 1980 through 1993. Some 2800 detailed abstracts, organized by agency or laboratory, describe 2100 inventions, 900 patent licenses, 510 cooperative research and development agreements (CRADAs), 85 inventions shared with other organizations, and 140 biological materials transfers. Over 570 inventions and 110 CRADAs involve genetic technologies, gene sequencing, or cloning. Information is included about licensees and CRADA collaborators, their development activities and strategic partnerships, and the status of products and technologies in process. Extensive indexes. 678 pp., 1994. [Information or order: Biotechnology Information Institute; 1700 Rockville Pike, Suite 400; Rockville, MD 20852-1631 (301/424-0255, Fax: -0257).] \*2

Software Catalogue. The Genethon Catalogue of Molecular Biology Programs lists software of interest to molecular biologists. Each entry includes domain, such as phylogeny or multiple aligned sequence; author; contact; licensing; system; and language, such as Fortran or C. "Hotlines" provide additional information and a software description. Programs are included for UNIX, VMS, and Sun systems but not for microcomputers. The catalogue is accessible through WWW at the URL http://www.genethon.fr/exterieur/bio_catalog_resume.html. \*2

GDB USER SUPPORT, REGISTRATION

To become a registered user of GDB and OMIM, contact one of the User Support offices listed below (a user may register to access both Baltimore and a remote node). Questions, problems, or user-registration requests may be sent by telephone, fax, or e-mail. User-registration requests should include name, institutional affiliation, and title (if applicable), street address (no P.O. box numbers), telephone and fax numbers, and e-mail address.

The Help Line in Baltimore is staffed from 9 a.m. to 5 p.m. EST for information on accounts and training courses, technical support, and data questions. Calls received after hours will be forwarded to the appropriate voice mail and returned as soon as possible. To obtain a user’s local SprintNet (Telenet) number for locations within the United States: 800/776-1130.

GDB, OMIM Training Schedule

"GDB/OMIM and Genomic Data on the Internet" classes will be held in Baltimore on Sept. 19–20 and Nov. 14–15. This course offers thorough coverage of the structure, content, and roles of GDB and OMIM; discusses the strengths and weaknesses of various interfaces for searching the data; and explores related genomic resources available worldwide on the Internet. In addition to using GDB and OMIM application software, participants will learn how to retrieve phenotype, mapping, and sequence data with tools such as ftp, e-mail, Gopher, and the WWW hypertext browser NCSA Mosaic. Contact the U.S. GDB User Support Office.

User Support Offices

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Plant Genome Research Begins a New Voyage of Discovery

Plant Genome II was held January 24–27 in San Diego. The conference, which attracted 553 participants from 22 countries, featured applications of genome mapping and analysis to solve existing problems and uncover answers to fundamental questions about plant genomes and their evolution.

According to Steven Oliver (University of Manchester, U.K.), the taxonomy of gene function will soon be essential in efficiently identifying new genes. This new age of research, which he compared to another voyage of Darwin’s *Beagle*, will require a multidisciplinary approach with the collaboration of physicists, geneticists, biochemists, and plant breeders. James Cook (U.S. Department of Agriculture (USDA), Agricultural Research Service (ARS), and Cooperative State Research Service) reinforced Oliver’s message by pointing out that now is the time to bring plant breeders together with molecular biologists to search for agriculturally important genes.

New Insights

The study of plant genome structure and organization can lead to interesting discoveries as highlighted by Richard Flavell (John Innes Institute, U.K.). Understanding the role of epigenetic regulation, gene order, and in situ homology sequence searching will ultimately advance the practical application of biotechnology. As a result of having to protect themselves from foreign DNA, plants have developed strategies—including gene silencing—to cope with transposon-sequence pressures. The plant’s ancient art of antisense technology may take advantage of gene location to determine epigenetic DNA methylation events, which in turn would regulate gene expression. Flavell pointed out that concerted evolution in the long term helps to maintain high levels of conservation across the chromosome in both sequence and gene order or synteny.

Progress in Rice

Nori Kurata (National Institute of Agrobiological Resources, Japan) described a genetic map of the rice genome with 1400 restriction fragment length polymorphism and random amplified polymorphic DNA markers. Over 7500 clones, of which 1800 are of known function, have been sequenced from callus tissue at different developmental stages. Kurata reported construction of a rice cDNA expression map that includes information on tissue specificity, distribution of isozyme genes, gene families, and such functionally related genes as ribosomal protein genes and the histone gene family.

Physical mapping in the Japanese program will focus on identifying economically important genes. High priority is being given to chromosomes 1, 4, 6, and 11. A number of important resistance genes are known to reside on 6.
are needed to identify many important loci. Specifically, Lark identified interacting traits in epistasis. One height trait measured individually had no effect but, when interacting with another plant height QTL, could account for 25% of the variation. The basis of Lark’s technique is to use large populations and to conduct pairwise comparisons of loci in plants with extreme phenotypes. After the results are graphed, epistatic interactions are identified. According to Thomas Cheesbrough, (South Dakota State University, Brookings), this type of analysis will be essential in studying the genes of such metabolic pathways as oil production because each enzyme is highly dependent on gene products of the entire metabolic chain.

Mapping Technologies
Mapping technologies were featured in several talks and posters throughout the conference. Perry Cregan (USDA, ARS) and others reported continued success with simple sequence repeats, which are small sequence patterns that are repeated at variable lengths. The variable length of the repeats provides a tool needed by crop breeders and geneticists to identify variations. Amplified fragment length polymorphism (AFLP), a related new technology, was reported by Pieter Vos and Marc Zabeau (KeyGene, Netherlands). AFLP will provide markers for map regions that other markers have not bridged successfully. The AFLP technique has the capacity to exploit multiple forms of variation within the genome. The new technology described by Vos is still a long way from direct application by plant breeders. [Susan McCarthy, USDA]

Pig Gene-Mapping Coordination Effort Grows

Last year the Cooperative State Research Service of the U.S. Department of Agriculture designated a group of Iowa State University (ISU) scientists, headed by Max Rothschild, to coordinate U.S. efforts to find individual genes that control pig reproduction, disease resistance, and physical traits. The cooperative project is focused on producing a consensus pig gene map, enlarging the public gene-mapping database, fostering communication and resource sharing among researchers, and working closely with the pig industry.

Producing a useful gene map is expected to take several years and involve a number of U.S. scientists and laboratories; about 700 genes and markers have been mapped to date. Reference family DNA is being made available to researchers, and some 150 published microsatellite markers have been produced and distributed to requesting laboratories. Published data are being added to the pig database USPIGBASE [Information: mfrothsc@iastate.edu; for WWW, http://www.public.iastate.edu/~pigmap].

The bimonthly newsletter Pig Genome Update and a computer discussion group are available for all animal gene mappers. To enroll for the discussion group, send e-mail address to angenmap@iastate.edu. [Max Rothschild, ISU]

Genome News

HGN Renewal Request

This is the last issue for U.S. subscribers who have not responded to HGN’s request for renewal. In lieu of the renewal form that appeared in the March issue, readers may send a copy of their mailing label marked with “RENEW” and needed corrections.

Find Errors in HGN?

Please contact Human Genome News staff so we may correct them for our readers. Fax: 615/574-9888 Internet: bkq@ornl.gov

Resources: BCM Genome Center Adds More Services

WWW Server
A World Wide Web (WWW) server at the Baylor College of Medicine (BCM) Genome Center distributes genome information being discovered at BCM and other centers. X Mosaic, a browsing tool that originated at the National Center for Supercomputing Applications, gives access to the BCM server and includes information on the following:

- YEAST ARTIFICIAL CHROMOSOME (YAC) DATA SEARCHES: data generated at BCM, CEPH-Ganathion, and Massachusetts Institute of Technology.
- BIOLOGIST’S CONTROL PANEL: easy access to database search and various libraries and literature.
- GENOME CENTER COMPUTING HELP: answers to frequently asked questions and help on topics related to computing.

X Mosaic can be obtained by anonymous ftp from ftp.ncbi.nlm.nih.gov, and the file README first supplies further instructions. The Mosaic software is in the directory /Web. X Mosaic will display on X-window devices such as X terminals, UNIX workstation consoles, and Mac running MacX. Current versions of Mosaic for the Macintosh and PC Windows do not support all features necessary to use the forms on the BCM WWW server.

The uniform resource locator (URL) for the BCM Genome Center is http://kiwi.ingen bcm.tmc.edu:8088. Questions and comments should be addressed to gc-help@gc.bcm.tmc.edu. [Joanna Power and Bob Cottingham, BCM]

Mouse YAC Screening Service

The Baylor Cloning Core Laboratory has received and prepared for multistep PCR screening a collection of about 53,000 mouse YAC clones. The collection includes 40,000 clones from Steve Brown (St. Mary’s Hospital Medical School, U.K.) and 13,000 from Hans Lehrach (Imperial Cancer Research Fund, U.K.). Because the funding for this effort is very limited, the Baylor laboratory will furnish DNA samples and clones but will not conduct PCR and gel analyses. The amount of sample sent will depend on estimated screening needs and availability, and costs for overnight shipping will be paid by the recipient. [Contact for further information and request form – Fax: 713/798-5366 or -8597, Internet: yaclab@bcm.tmc.edu]
Calendar of Genome-Related Events* (acronyms, p. 16)

**September**

1-3, **2nd Int'l Chromosome 14 Workshop;** Oxford, UK [J. H. Edwards or S. Craig, +44-68/527-5314, Fax: -5318, c14@bionch. ox.ac.uk]

2-5, **20th World Congress of Hematologists;** Berlin, Germany

2-7, **5th Nencki Institute Symposium on Neuroendocrinology;** Warsaw, Poland

2-7, **13th CBMB Symposium;** Charlotte, NC [see contact: Sept. 7]

4-8, **More info;** 1994 Yeast Galactol. and Mol. Biol. Meet.; Seattle, WA [GSA, Ed Quinones, 301/571-1625, Fax: -576-7079]

9-12, **1st Int'l Symp. on Human Chromosome 14;** Research Triangle Park, NC [J. H. Edwards or S. Craig, +44-68/527-5314, Fax: -5318, c14@bionch. ox.ac.uk]

21-25, **4th Nordic Genome Workshop: Helsinki, Finland (abs. deadline: June 30) [see contact: Sept. 7]**

22-24, **4th Int'l Workshop on Hum. Chromosome 14;** Tokyo [see contact: Sept. 7]

24-28, **4th Int'l Workshop on Hum. Chromosome 14;** Tokyo [see contact: Sept. 7]

24-28, **5th NWCI Symposium on Chromosome 14;** Seattle, WA [see contact: Sept. 7]

29-30, **5th NWCI Symposium on Chromosome 14;** Seattle, WA [see contact: Sept. 7]

30, **5th NWCI Symposium on Chromosome 14;** Seattle, WA [see contact: Sept. 7]

**October**

2-5, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

21-25, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

28-30, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

14-17, **Int'l Conference on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

22-25, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

25-28, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

Training Calendar*

7, **Intro. to PCR;** Los Angeles (also offered Nov. 14) [see contact: Sept. 7]

8, **Intro. to Mol. Cytogenet.;** New York (also offered Nov. 14) [see contact: Sept. 7]

8-9, **Intro. to Mol. Cytogenet.;** New York (also offered Nov. 14) [see contact: Sept. 7]

**November**

6-10, **2nd South-North Hum. Genome Conf.;** Beijing, CH [see contact: Sept. 7]

6-10, **8th Int'l Mouse Genome Conf.;** London [see contact: Sept. 7]

9-11, **5th Int'l Symp. on Human Chromosome 21;** Toronto [see contact: Sept. 7]

13-17, **4th DOG Genome Contractor-Grantee Workshop;** Santa Fe, NM [see contact: Sept. 7]

15-17, **Int'l Conference on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

18-22, **Intro. to PCR;** Los Angeles (also offered Nov. 14) [see contact: Sept. 7]

26-28, **Chromatin Struct. & Gene Expression;** Madrid [CIMB, Gonzalez, +34/1-435-4240, Fax: -435-4240]

28-30, **5th Int'l Symp. on Human Chromosome 14;** Tokyo [see contact: Sept. 7]

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NCHGR Supports Training at Three Career Levels

The NIH National Center for Human Genome Research (NCHGR) reminds the scientific community that funds are available to support multidisciplinary research training at three career levels: (1) predoctoral training through institutional training grants, (2) postdoctoral fellowships for advanced training in genomic analysis through institutional training grants or individual fellowships, and (3) individual senior fellowships for established scientists who wish to acquire new skills relevant to genomic research. Positions expanded under the institutional training grants allow predoctoral, postdoctoral, and short-term training.

NCHGR also supports training in areas of interest to the ethical, legal, and social implications program and strongly emphasizes interdisciplinary training.

Application Receipt Dates
- Individual fellowships: April 5, August 5, and December 5.

[Contact for additional information: Bettie Graham (301/496-7531, Internet: bettie.graham@occhost.nlm.nih.gov).]

U.S. Genome Research Funding Guidelines

Note: Investigators wishing to apply for funding are urged to discuss their projects with appropriate agency staff before submitting proposals.

NCHGR National Center for Human Genome Research (NCHGR)

Application receipt dates:
- P01, P03, R21, R29, P30, P50, K01, and R18 grants – February 1, June 1, and October 1.
- Individual postdoctoral fellowships – April 5, August 5, and December 5.
- Small Business Innovation Research Grants (SBIR: firms with 500 or fewer employees) – April 15, August 15, and December 15.
- Research supplements for underrepresented minorities – applications are accepted on a continuing basis.
- Requests for applications (RFAs) – receipt dates are independent of the above dates. Notices will appear in HGN and other publications.

"Expected review possible. Check with NCHGR during application development phases.

Program announcements are listed in the weekly NIH Guides for Grants and Contracts," which is available electronically through one of the following methods.
- Gopher (gopher.nih.gov).
- Institutional Hubs. A designee receives automatic updates and distributes them locally to researchers. Send a message naming the responsible person to BITNET: q2c@niheu or Internet: q2c@cu.nih.gov.
- NIH Grant Line (also known as DRGLINE): Electronic bulletin board updated weekly. Connection is through a modem (301/402-2221), and files can be transmitted rapidly via BITNET or Internet. The Grant Line is also accessible by Telnet to gopher.nlm.nih.gov. When connection is open, type VT100. At the INITiALS prompt, type BBS and at the ACCOUNT prompt, type CCSR. For more information, contact John James (301/594-7270, Fax: -7384).

Full text of RFAs listed in the NIH grants guide may also be obtained from NIH NCHGR in Bethesda, Maryland (301/496-0844).

DOE Human Genome Program

For funding information or general inquiries, contact the program office via
- 301/903-6489 or Internet: genome@er.doe.gov. Relevant documents are available by ftp to oehp01.doe.gov in directory genome.

SBIR Grants

DOE and NIH invite small business firms to submit grant applications addressing the human genome topic of SBIR programs, which are designed to strengthen innovative firms in research and development and contribute to the growth and strength of the nation's economy. For more information on human genome SBIR grants, contact:
- Kay Etzioni; c/o SBIR Program Manager, ER-16; DOE; Washington, DC 20585 (301/903-5667, Fax: -5488).
- Bettie Graham; Bldg. 36A, Rm. 610; NIH; 9000 Rockville Pike; Bethesda, MD 20892 (301/496-7531, Fax: /406-2770).

National SBIR conferences: Washington, DC (October 12–14); San Jose, CA (November 14–16); Chicago, IL (April 26–28, 1995). Conference Hotline: 407/791-0720.

November

1–14. Mol. Genet., Cell Biol., & Cell Cycle of Fission Yeast; CSFL (Appl. deadline: July 15) [Cold Spring Harbor Lab., 516/687-8345, Fax: -8845, meetings@cshl.org]

17–20. Recombinant DNA Technol. & DNA Sequencing: Lake Tahoe, NV [CATCMB/CUA, M. Miller, 202/519-6161, Fax: -4467, millerw@cua.edu]


17–21. Recombinant DNA Tech. I; LTI, Germantown, MD [see contact: Sept. 12–16]

18–31. Adv. in situ Hybridization and Immunocytochem.; CSHL (Appl. deadline: July 15) [see contact: Oct. 13–26]

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 Sciences 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.
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2. ___ Reprint of "A New Five-Year Plan for the U.S. Human Genome Project" (Science, October 1, 1993) by Francis Collins and David Galas
3. ___ DOE Human Genome 1993 Program Report ___ DOE Primer on Molecular Genetics

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SELECTED ACRONYMS
AACR Am. Assoc. for Cancer Res.
AMIA Am. Med. Informatics Assoc.
AFIP/ARP Armed Forces Inst. of Pathol./Am. Registry of Pathol.
ASHG Am. Soc. of Human Genet.
ASBMB Am. Soc. for Biochem. & Mol. Biol.
AVS Am. Vacuum Soc.
BTP Biotechnol. Train. Programs
CEPH Centre d'Etude du Polymorphisme Humain
CFF Cystic Fibrosis Found.
CMB Ctr. for Intl. Meet. on Biol.
CSHL Cold Spring Harbor Lab.
DIMACS Discrete Mathematics & Comp. Sci.
DOE Dept. of Energy
ERS Eleanor Roosevelt Inst.
FVEA Fundacion Valenciana de Estudios Avanzados
GBD/OMIM Genome Data Base/Online Mendelian Inheritance in Man.
GSA Genet. Soc. of Am.
LTI Life Technologies, Inc.
MBL Marine Biological Lab.
NIH Natl. Inst. of Health
NSGC Natl. Soc. of Genet. Counselors
SBIR Small Bus. Innovation Res.

HGN Renewal Request
This is the last issue for U.S. subscribers who have not responded to HGN's request for renewal. In lieu of the renewal form that appeared in the March issue, readers may send a copy of their mailing label marked with "RENEW" and needed corrections.

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