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 800 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.

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.

Individual TCRs are made of two polypeptide chains, of which there are four different components (designated α, β, γ, 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 throughout 80 million years of evolution, although only about 6% of the region contains gene-coding sequences. Until recently, many scientists believed that only 9% 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 organelles with complex structural and gene-control systems. [Denise K. Casey, HGMIS]

DOE Human Genome Program Santa Fe Workshop Reminder

The fourth DOE Human Genome Program Contractor and Grantee workshop will be held November 13–17 in Santa Fe, New Mexico. At least one investigator from each funded project is expected to attend the entire meeting and represent the project at poster sessions. Some projects will also be represented in platform presentations.

Speakers will be notified by October 1.

To ensure inclusion in the program book, camera-ready abstracts are due no later than August 15 to Sylvia Spengler; Human Genome Program Operations; 459 Donner Laboratory; Lawrence Berkeley Laboratory; Berkeley, CA 94720 (510/486-4879, Fax: 5717, Internet: sylviaj@ux5.lbl.gov).

New HGMIS Address

The new address of the Human Genome Management Information System (HGMIS) is Oak Ridge National Laboratory; 1060 Commerce Park, MS 6480; Oak Ridge, TN 37830. Telephone and fax numbers and Internet address remain the same (615/576-6669, /574-9888, bkq@ornl.gov).

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 cosmids 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 Pithya programs, which find repetitive elements and classify Alu repeats into subfamilies.

Information on Alu repeats can provide insights into MHC evolution.

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 (viruses, 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 sentinels 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–foreign peptide complex is then recognized by surface molecules (T-cell receptors) found on "killer" T cells.

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), 8 (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(5), 6 (January 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 8(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: healthcare 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.

Genetics Specialties Highlighted in Booklet

Solving the Puzzle: Careers in Genetics is a 24-page booklet published by the Genetics Society of America and the American Society of Human Genetics. The booklet lists specialties in the field of genetics and profiles ten scientists whose occupations are based on genetics. [Contact: Genetics Society of America/American Society of Human Genetics; 9650 Rockville Pike; Bethesda, MD 20814-3998 (301/571-1825).]
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 1993 SCW reports, see p. 9.]

With the cooperation of Human Genome Organization Pacific, HGM 93 was organized by a committee that included Kenichi Matsubara (Osaka University (OU), Japan); Yusuke Nakamura and Haruo Sugano (Cancer Institute (CI), Japan); and Yoshiyuki Sakaki (University of Tokyo). Some 665 researchers from 25 countries attended the meeting, which was composed of a symposium joined by 14 invited speakers, 396 poster and 100 platform presentations, 7 chromosome-specific sessions, and 9 workshops.

The opening session of the workshop included reports on the status of the GDB Human Genome Data Base, which comprises the Genome Data Base (GDB) and Online Mendelian Inheritance in Man (OMIM). Kenneth Fasman, GDB informatics director, described future directions and the role of GDB in the proposed federation of genomic databases. Plans involve better integration with other databases, direct electronic data submission, improved physical map representation, and the development of a variety of modular graphics user interfaces to GDB, including a World Wide Web server. Peter Pearson, OMIM project director, described recent changes in OMIM editorial structure and plans for a structured phenotype database that would better integrate the contents of GDB and OMIM.

Genome Analysis and Medicine Symposium

This symposium opened with a session on genome program ethics worldwide. Victor McKusick (Johns Hopkins University (JHU)), Nancy Wexler (Columbia University), Alain Pompidou (European Parliament), and Hiraku Takebe (Kyoto University (KU), Japan) discussed activities in their respective countries and problems they have encountered, especially in education.

Mark Lathrop (CEPH) reported progress in identifying hypertension-susceptibility genes with rat models. Five chromosomal regions or genes were linked to various hypertension phenotypes observed in 4 kinds of models using over 150 mapped rat microsatellite markers. The chromosome 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 leukemia 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 EML 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 melanoma of soft tissue, EWS forms a hybrid gene with the ATF-1 (AMP dependent transcription factor 1) gene. Nakamura summarized the mutation analysis of the APC (adenomatous polyposis coli) gene in over 160 chromosomes 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)
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### Genome News

**Workshops on Selected Topics**

**COMPARATIVE MAP AND MODEL ORGANISMS.** About 1000 new cDNAs were sequenced and mapped to ordered arrays of yeast artificial chromosome (YAC) clones in *Caenorhabditis elegans* (Yui Kohara [National Institute of Genetics, Japan]). Leslie Lyons (National Cancer Institute) is using interspecific 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. Loeffer [Institute of Human Genetics, Germany]).

**DNA POLYMERISM AND GENETIC MAPS.** Jeffrey Murray (University of Iowa) reported progress in the multicenter effort to develop a human genome map of over 1000 short tandem repeat polymorphisms, with emphasis on tri- and tetranucleotide repeats. Tera Matsie (University of Pittsburgh) developed Multimap, which enabled automatic construction of a linkage map of the human genome, including 654 markers. Melvin McNhmis (J-HU) identified 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]). Eichi 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 F- and 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 Genematica, an integrated data-management tool for genome sequencing projects (Yutaka Akiyama [KU]).

**DNA SEQUENCING.** Elson 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 Hatcitomi (University of Tokyo) used a vector containing double SfiI sites flanking the cloning site to generate 3' overlap. Satoshi Takahashi (Osaka 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 Hori (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 tri nucleotide repeats. Shih-Feng Tsai (National Yang-Ming Medical College, Taiwan) identified 326 *Drosophila melanogaster* cDNA clones containing CAP 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. Yui Tanaka (Ehime University, Japan) showed genetic evidence that variations at the cytchrome P450 debrisoquine (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 Hirschprung disease, MEN 2A (multiple endocrine neoplasias), 2A, or MEN 2B.

**cDNA.** Radoje Pmrnac (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 1000 tissue-specific cDNAs from human pancreatic islets, of which 443 represent novel sequences. Kousaku Okubo (OU) described "body mapping" on more than 6000 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 taxonomy classifications of genes identified by expressed sequence tag sequencing.

**NEW TECHNOLOGY.** Shirihi Hirose (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 Roizs (Institut Curie, France) proposed using the collection of 32-tp fragments generated by restriction digestion of genomic DNA, with *Bcfl* as a new type of STS for the human genome. Misao Ohki (National Cancer Center Research Institute, Japan) completed 101 restriction maps of 21q and 11q23.3 to qter. The multiple linking clones, together with this map, will serve as excellent tools for detecting chromosome rearrangements and deletions in these regions. [Kenichii Matsubara (OU, Japan) and Mitsuji Emi (CI, 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. 10C110; 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.

Contact: Betty Wolf, NCHGR; Bldg. 49, Rm. 4A38; 9000 Rockville Pike; Bethesda, MD 20892 (301/402-2012, Fax: -2440, Internet: wolfie@helix.nih.gov).

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 concrete representations for map information and construct a natural, geometric foundation for genome maps that can be used to define integrated mapping databases.

WILLIAM HAYE (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.
### Chromosome Editors*

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<thead>
<tr>
<th>Committee</th>
<th>Name</th>
<th>Location</th>
<th>Fax</th>
<th>E-Mail</th>
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<tbody>
<tr>
<td>Chr. 1</td>
<td>Gail A.P. Bruns</td>
<td>Children's Hosp. Med. Ctr.</td>
<td>617/735-7588</td>
<td><a href="mailto:bruns@rascal.bwh.harvard.edu">bruns@rascal.bwh.harvard.edu</a></td>
</tr>
<tr>
<td></td>
<td>Nicholas C. Dracopoli</td>
<td>Natl. Inst. of Health</td>
<td>301/402-2170</td>
<td><a href="mailto:dracopol@helix.nih.gov">dracopol@helix.nih.gov</a></td>
</tr>
<tr>
<td></td>
<td>Nigel K. Spurr</td>
<td>Imperial Cancer Res. Fund, UK</td>
<td>+44-71/289-3802</td>
<td><a href="mailto:n.spurr@mahler.cl.pulnct.net">n.spurr@mahler.cl.pulnct.net</a></td>
</tr>
<tr>
<td>Chr. 2</td>
<td>Marshall Summar</td>
<td>Vanderbilt Univ.</td>
<td>615/343-9951</td>
<td><a href="mailto:marshall.summar@mcmillan.vanderbilt.edu">marshall.summar@mcmillan.vanderbilt.edu</a></td>
</tr>
<tr>
<td>Chr. 3</td>
<td>Susan Naylor</td>
<td>Univ. of Tex. Health Sci. Ctr.</td>
<td>210/567-8761</td>
<td>naylor@ thorin.uthsc.edu</td>
</tr>
<tr>
<td></td>
<td>Benjamin Carritt</td>
<td>Univ. Coll. of London</td>
<td>+44-71/387-3496</td>
<td><a href="mailto:b.carritt@ccc.ac.uk">b.carritt@ccc.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>Andreas Gal</td>
<td>Institut fur Humangenetik, GR</td>
<td>+49-451/500-4187</td>
<td><a href="mailto:gals@mailer.univ-berlin.de">gals@mailer.univ-berlin.de</a></td>
</tr>
<tr>
<td></td>
<td>Robert M. Gemmill</td>
<td>Eleanor Roosevelt Inst.</td>
<td>303/333-8423</td>
<td><a href="mailto:gemmill@thor.hsc.colonado.edu">gemmill@thor.hsc.colonado.edu</a></td>
</tr>
<tr>
<td></td>
<td>Yusuke Nakamura</td>
<td>Dept. of Biochem. Cancer Inst., JP</td>
<td>+61-3/3018-0342</td>
<td><a href="mailto:nakamura@ganr.z1.fca.or.jp">nakamura@ganr.z1.fca.or.jp</a></td>
</tr>
<tr>
<td>Chr. 4</td>
<td>G.-J. B. Van Ommen</td>
<td>Univ. of Leiden, NE</td>
<td>+31-71/276-075</td>
<td><a href="mailto:vanommen@ruif2.leidenuniv.nl">vanommen@ruif2.leidenuniv.nl</a></td>
</tr>
<tr>
<td></td>
<td>Kenneth H. Bueltow</td>
<td>Fox Chase Cancer Ctr.</td>
<td>215/728-3574</td>
<td><a href="mailto:k.bueltow@fccc.edu">k.bueltow@fccc.edu</a></td>
</tr>
<tr>
<td></td>
<td>Jeffrey C. Murray</td>
<td>Univ. of Iowa Hosp.</td>
<td>319/356-3347</td>
<td><a href="mailto:kmurray@blue.weg.uio.edu">kmurray@blue.weg.uio.edu</a></td>
</tr>
<tr>
<td>Chr. 5</td>
<td>John D. McPherson</td>
<td>Univ. of Calif., Irvine</td>
<td>714/725-3403</td>
<td><a href="mailto:john.d.mcpherson@uci.edu">john.d.mcpherson@uci.edu</a></td>
</tr>
<tr>
<td></td>
<td>Michelle LeBeau</td>
<td>Univ. of Chicago</td>
<td>312/702-3163</td>
<td><a href="mailto:mlebeau@mcis.bsd.uchicago.edu">mlebeau@mcis.bsd.uchicago.edu</a></td>
</tr>
<tr>
<td>Chr. 6</td>
<td>Howard M. Cann</td>
<td>Fondation Jean Dausset-CEPH, FR</td>
<td>+33-1/4018-0155</td>
<td><a href="mailto:howard@ceph.fr">howard@ceph.fr</a></td>
</tr>
<tr>
<td></td>
<td>R. Duncan Campbell</td>
<td>Univ. of Oxford, UK</td>
<td>+44-86/527-5729</td>
<td><a href="mailto:rdcampbell@molbiol.ox.ac.uk">rdcampbell@molbiol.ox.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>Andreas Ziegler</td>
<td>Inst. for Exp. Oncology and</td>
<td>+49-30/303-53778</td>
<td><a href="mailto:ziegler@mailer.univ-berlin.de">ziegler@mailer.univ-berlin.de</a></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transplantation Med., GR</td>
<td></td>
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</tr>
<tr>
<td>Chr. 7</td>
<td>Karl-Heinz Grzeschik</td>
<td>Med. Zentrum für Humangen., GR</td>
<td>+49-642/1/82920</td>
<td><a href="mailto:grzeschik@mailer.univ-berlin.de">grzeschik@mailer.univ-berlin.de</a></td>
</tr>
<tr>
<td></td>
<td>Lap-Chae Tai</td>
<td>Hosp. for Sick Children, CN</td>
<td>416/813-4931</td>
<td><a href="mailto:cjstate@sickkids.on.ca">cjstate@sickkids.on.ca</a></td>
</tr>
<tr>
<td>Chr. 8</td>
<td>Dennis T. Drayna</td>
<td>Mercator Genetics, Inc.</td>
<td>415/617-0883</td>
<td><a href="mailto:drayna@mercaton.com">drayna@mercaton.com</a></td>
</tr>
<tr>
<td></td>
<td>Stephen Wood</td>
<td>Univ. of British Columbia, CN</td>
<td>604/222-5348</td>
<td><a href="mailto:swood@unig.wisc.edu">swood@unig.wisc.edu</a></td>
</tr>
<tr>
<td>Chr. 9</td>
<td>Sue Povey</td>
<td>Univ. Coll. of London</td>
<td>+44-71/387-3496</td>
<td><a href="mailto:m.povey@hgmpr.mrc.ac.uk">m.povey@hgmpr.mrc.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>Jonathan L. Haines</td>
<td>Mass. General Hosp.</td>
<td>617/726-5736</td>
<td><a href="mailto:haines@helix.mgh.harvard.edu">haines@helix.mgh.harvard.edu</a></td>
</tr>
<tr>
<td>Chr. 10</td>
<td>Jen-I Mao</td>
<td>Collaborative Res., Inc.</td>
<td>617/891-5062</td>
<td><a href="mailto:mao@crick.com">mao@crick.com</a></td>
</tr>
<tr>
<td>Chr. 11</td>
<td>Veronica Van Heyningen</td>
<td>MRC Human Genetics Unit, UK</td>
<td>+44-31/343-2820</td>
<td><a href="mailto:vervan@hgu.mrc.ac.uk">vervan@hgu.mrc.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>Andrew P. Fainberg</td>
<td>Johns Hopkins Univ. Sch. of Med.</td>
<td>410/614-8189</td>
<td><a href="mailto:andyfein@welchlink.welch.jhu.edu">andyfein@welchlink.welch.jhu.edu</a></td>
</tr>
<tr>
<td></td>
<td>Carol Jones</td>
<td>Eleanor Roosevelt Inst.</td>
<td>303/333-8423</td>
<td><a href="mailto:andyfein@welchlink.welch.jhu.edu">andyfein@welchlink.welch.jhu.edu</a></td>
</tr>
<tr>
<td>Chr. 12</td>
<td>Ian W. Craig</td>
<td>Univ. of Oxford, UK</td>
<td>+44-86/527-5318</td>
<td>i <a href="mailto:craig@crc.ac.uk">craig@crc.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>Tobias Gedde-Dahl, Jr.</td>
<td>Univ. of Oslo, NW</td>
<td>+47-2/20-9593</td>
<td><a href="mailto:tobias.gedde-dahl@labmed.uio.no">tobias.gedde-dahl@labmed.uio.no</a></td>
</tr>
<tr>
<td></td>
<td>Raju Kucherlapati</td>
<td>Albert Einstein Coll. of Med.</td>
<td>718/823-6550</td>
<td><a href="mailto:kucherlo@aeom.yu.ca">kucherlo@aeom.yu.ca</a></td>
</tr>
<tr>
<td>Chr. 13</td>
<td>Dorothy Warburton</td>
<td>Columbia-Presb. Med. Ctr.</td>
<td>212/305-7436</td>
<td><a href="mailto:cul@cuccfsc.ccc.columbia.edu">cul@cuccfsc.ccc.columbia.edu</a></td>
</tr>
<tr>
<td></td>
<td>Aravinda Chakravarti</td>
<td>Case Western Reserve Univ.</td>
<td>216/368-5657</td>
<td><a href="mailto:aravinda@chiner.gene.cwru.edu">aravinda@chiner.gene.cwru.edu</a></td>
</tr>
<tr>
<td>Chr. 14</td>
<td>Diane W. Cox</td>
<td>Hosp. for Sick Children, CN</td>
<td>416/813-4931</td>
<td><a href="mailto:dcox@sickkids.on.ca">dcox@sickkids.on.ca</a></td>
</tr>
<tr>
<td></td>
<td>Tobias Gedde-Dahl, Jr.</td>
<td>Univ. of Oslo, NW</td>
<td>+47-2/20-9583</td>
<td><a href="mailto:tobias.gedde-dahl@labmed.uio.no">tobias.gedde-dahl@labmed.uio.no</a></td>
</tr>
<tr>
<td>Chr. 15</td>
<td>Timothy A. Donlon</td>
<td>Kapiolani Med. Ctr.</td>
<td>808/973-8350</td>
<td><a href="mailto:donlon@uhman.uhc.hawaii.edu">donlon@uhman.uhc.hawaii.edu</a></td>
</tr>
<tr>
<td></td>
<td>Cynthia C. Morton</td>
<td>Brigham and Women's Hosp.</td>
<td>617/738-6896</td>
<td><a href="mailto:mcmort@rascal.harvard.edu">mcmort@rascal.harvard.edu</a></td>
</tr>
<tr>
<td>Chr. 16</td>
<td>David F. Callen</td>
<td>Adelaide Children's Hosp., AU</td>
<td>+61-8204-7324</td>
<td><a href="mailto:dcallen@acade.adelauid.edu">dcallen@acade.adelauid.edu</a></td>
</tr>
<tr>
<td></td>
<td>Martin H. Breuning</td>
<td>Inst. of Human Genetics, NE</td>
<td>+31-71/276-075</td>
<td><a href="mailto:breuning@ruif2.leidenuniv.nl">breuning@ruif2.leidenuniv.nl</a></td>
</tr>
<tr>
<td></td>
<td>Norman Doggett</td>
<td>Los Alamos Nat. Lab.</td>
<td>505/665-3024</td>
<td><a href="mailto:doggett@gnome.lanl.gov">doggett@gnome.lanl.gov</a></td>
</tr>
<tr>
<td>Chr. 17</td>
<td>Pamela R. Fain</td>
<td>Univ. of Utah Res. Park</td>
<td>801/585-3232</td>
<td><a href="mailto:pam@summit.med.uth.edu">pam@summit.med.uth.edu</a></td>
</tr>
<tr>
<td></td>
<td>Ellen Solomon</td>
<td>Imperial Cancer Res. Fund, UK</td>
<td>+44-71/269-3469</td>
<td><a href="mailto:e_solomon@ictf.icnet.uk">e_solomon@ictf.icnet.uk</a></td>
</tr>
<tr>
<td>Chr. 18</td>
<td>Ad Geurts van Kessel</td>
<td>Univ. of Nijmegen, NE</td>
<td>+31-60/540-488</td>
<td><a href="mailto:antro_rv@aznvx1.azn">antro_rv@aznvx1.azn</a>,nl</td>
</tr>
<tr>
<td></td>
<td>Joan Overhouser</td>
<td>Thomas Jefferson Univ.</td>
<td>215/955-5393</td>
<td><a href="mailto:overha@calvin.jci.tju.edu">overha@calvin.jci.tju.edu</a></td>
</tr>
<tr>
<td>Chr. 19</td>
<td>Harvey Mohrenweiser</td>
<td>Lawrence Livermore Nat. Lab.</td>
<td>510/422-2282</td>
<td><a href="mailto:harvey@cea.llnl.gov">harvey@cea.llnl.gov</a></td>
</tr>
<tr>
<td></td>
<td>Keith J. Johnson</td>
<td>Charing Cross &amp; Westminster Med. Sch., UK</td>
<td>+44-61/846-7377</td>
<td>rgm600@uk.ac.1on.coxwms.s1</td>
</tr>
<tr>
<td>Chr. 20</td>
<td>Ingo Hansmann</td>
<td>Univ. Gottingen, GR</td>
<td>+49-551/339-303</td>
<td><a href="mailto:dshclot@wgdw1.dnet.gwdg.de">dshclot@wgdw1.dnet.gwdg.de</a></td>
</tr>
<tr>
<td></td>
<td>Tim P. Keith</td>
<td>Collaborative Res., Inc.</td>
<td>617/891-5062</td>
<td><a href="mailto:keith@cric.com">keith@cric.com</a></td>
</tr>
<tr>
<td>Chr. 21</td>
<td>Stylianos E. Antonarakis</td>
<td>Univ. of Geneva Med. Sch.</td>
<td>+44-22/702-5706</td>
<td><a href="mailto:sea@medsun.unige.ch">sea@medsun.unige.ch</a></td>
</tr>
<tr>
<td></td>
<td>David Patterson</td>
<td>Eleanor Roosevelt Inst.</td>
<td>303/333-8423</td>
<td><a href="mailto:davpat@druid.hsc.colonado.edu">davpat@druid.hsc.colonado.edu</a></td>
</tr>
<tr>
<td></td>
<td>Nobuyoshi Shimizu</td>
<td>Keio Univ. Sch. of Med., JP</td>
<td>+81-3/3351-2370</td>
<td><a href="mailto:shimizu@dnb.med.keio.ac.jp">shimizu@dnb.med.keio.ac.jp</a></td>
</tr>
<tr>
<td></td>
<td>Christine van Broeckhoven</td>
<td>Univ. of Antwerp, BG</td>
<td>+32-3/820-2541</td>
<td><a href="mailto:cvbroeck@reks.ua.ac.be">cvbroeck@reks.ua.ac.be</a></td>
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### 1993 Single Chromosome Workshop Reports Published

#### Reports Available at Press Time

**CHROMOSOME 3 (May 14–15)**

**CHROMOSOME 4 (July 10–11)**

**CHROMOSOME 6 (September 18–19)**

**CHROMOSOME 7 (May 20–22)**

**CHROMOSOME 8 (May 1-3)**

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**CHROMOSOME 9 (April 18-20)**

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**Genome News**

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**Group Hears Sociological, Philosophical, and Legal Perspectives**

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 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 GDB/OMIM login account at Johns Hopkins University (select Local Databases at the Main Menu and then Internet WWW Access).

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."

Resources

Tech Transfer. The Federal Biotechnology 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), 86 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)]

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; ordering 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.

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

UNITED STATES

- GDB User Support
  - Genome Data Bank
  - Johns Hopkins University
  - 2024 E. Monument Street
  - Baltimore, MD 21205-2100
  - 410/955-9705
  - Fax: 410/955-9704
  - Internet: help@gdb.org

- AUSTRALIA
  - Alex Reisner
  - ANGIS
  - Electrical Eng. Bldg. J03
  - University of Sydney
  - Sydney, N.S.W. 2006
  - Australia
  - +612-922-2048
  - Fax: -3847
  - Internet: reisner@angis.su.oz.au

- FRANCE
  - Philippe Dessain
  - Service de Bioinformatique
  - CNRS-INSERM
  - 7 rue Guy Moquet - BP6
  - 94801 Villejuif Cedex
  - France
  - +33/1455-9524
  - Fax: -5250
  - Internet: gwb@genev.sif.inserm.fr

- GERMANY
  - Otto Ritter
  - Molecular Biophysics Dept.
  - German Cancer Research Center
  - Im Neuenheimer Feld 280
  - D-6900 Heidelberg
  - Germany
  - +49/6221-42-2372
  - Fax: -2333
  - Internet: doks12.dkfz-heidelberg.de

- ISRAEL
  - Malma Prilusky
  - Bioinformatics Unit
  - Weizmann Institute of Science
  - 76100 Rehovot, Israel
  - +972-8-43456
  - Fax: -344113
  - Internet: isprilu@weizmann.weizmann.ac.il

- JAPAN
  - Mika Hirakawa
  - JICST GDB Center
  - Numajiri Sangyo Building
  - 783-12, Enakido
  - Tsukuba City, Ibaraki 305, Japan
  - +81/298-38-2965
  - Fax: -2956
  - Internet: mika@gdb.gdbnet.ad.jp

- NETHERLANDS
  - GDB User Support
  - CAOS/CAMM Center
  - Faculty of Science
  - University of Nijmegen
  - P.O. Box 6910
  - 6500 GL Nijmegen
  - Netherlands
  - +31/63-553911
  - Fax: -652977
  - Internet: post@caos.caos.kun.nl

- SWEDEN
  - GDB User Support
  - Biomedical Center
  - Box 570
  - S-751 23 Uppsala
  - Sweden
  - +46/18-174057
  - Fax: -524869
  - Internet: help@gdb.embnet.se

- UNITED KINGDOM
  - Christine Bates
  - Human Gene Mapping
  - Program Resource Center
  - CRC, Watford Road
  - Harrow, Middlesex HA1, 3UJ
  - United Kingdom
  - +44/81-869-3446
  - Fax: -3807
  - Internet: cbates@uk.ac.uk
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 physiologists, 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 agronomically 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-selection pressures. The plant's ancient art of antisense technology may take advantage of gene location to determine epigenetic DNA methylation events, which in turn will 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 length polymorphism and random amplified DNA, and the history of gene families. 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.

Mapping data from the Japanese program have been entered into two versions of an internal database called RiceBase, one version containing mostly cDNA information and the other physical map data.

International collaboration in rice mapping was encouraged by an informal workshop held in conjunction with the conference and cochaired by Susan McCouch (Cornell University) and Goufan Hong (Director, Chinese Rice Genome Program). Kurata indicated that the Japanese mapping data should be made public later this year and that 5' sequence data are available for several hundred markers. Over 4000 expressed sequence tag (EST) sequences for rice currently reside in the dbEST and GenBank databases. Pamela Ronald (University of California, Davis) announced the public availability of a variety of libraries, including bacterial artificial chromosomes and cosnids.

Physical Mapping

Physical mapping was highlighted again in the Arabidopsis workshop. Caroline Dean (John Innes Institute, U.K.) and Howard Goodman (Massachusetts General Hospital) reported that chromosomes 4 and 5 are nearing completion in the effort to integrate the two YAC and cosmid maps. A new YAC library developed by David Bouchez (Institut National de la Recherche Agronomique, France) should help in developing the integrated physical map. Michel Defenouil (National Scientific Research Center, France) reported that the project on ESTs has sequenced several thousand Arabidopsis cDNAs, which have been deposited in the public database.

QTL Experimental Design

Quantitative trait (QTL) analysis was examined with attention to experimental design. In a discussion of soybean cyst-nematode resistance, Dave Webb (Pioneer Hi-Bred) reported that one soybean introduction was found to have more resistance than any other tested. With the identification of three resistance loci, the effect of population size in selecting traits was tested. Large sample populations (minimum 200) were found to be essential in finding and mapping traits.

The need for large sample populations was emphasized also by Karl Lark (University of Utah, Salt Lake City), who reported that specialized statistical methods and graphing
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 way 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 WWW servers and includes information on the following:

- YEAST ARTIFICIAL CHROMOSOME (YAC) DATA SEARCHES: data generated at BCM, CEPH-Ganathon, and Massachusetts Institute of Technology.
- BIOLOGIST’S CONTROL PANEL: easy access to database searches and various libraries and literature.
- GENOME CENTER COMPUTING HELP: answers to frequently asked questions and help on topics related to computing.
- Mosaic can be obtained by anonymous ftp from ftp.ncsa.uiuc.edu, 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.imgen.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)

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<td>31–Sept. 2</td>
<td>**Autom. In Mapp. and DNA Sequencing: Hinxton, UK [Sanger Ctr., D. Cooper, +44-22/349-4957, Fax: +4919, Abs. submiss.: <a href="mailto:densei@sanger.ac.uk">densei@sanger.ac.uk</a>]</td>
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<td>31–Sept. 4</td>
<td>Mouse Mol. Genet.; Cold Spring Harbor, NY [CSHL, 516/367-8346, Fax: -8845, <a href="mailto:meetings@chil.org">meetings@chil.org</a>]</td>
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**September**

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<th>1–3</th>
<th>**2nd Intl. Chromosome 14 Workshop; Oxford, UK [J. H. Edwards or S. Craig, +44-68/627-5314, Fax: -5318, <a href="mailto:c14@bich.ox.ac.uk">c14@bich.ox.ac.uk</a>]</th>
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<td>3–5</td>
<td>4th Nordic Genome Workshop; Helsinki, FN, L. Petten, Fax: -0474-4496, <a href="mailto:hpdol@hfd.fi">hpdol@hfd.fi</a></td>
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<td>8–13</td>
<td>10th Int. Conf. on Methods in Protein Struct. Anal.; Snowbird, UT [Baylor Coll. of Med., M. Atassi, 713/798-6050, Fax: 796-8040]</td>
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<td>16–18</td>
<td>2nd Intl. Chromosome 8 Workshop; Oxford, UK [N. Spurr, +44-71/269-8346, Fax: -3802, <a href="mailto:nspurr@nialicr.cncto.uk">nspurr@nialicr.cncto.uk</a> or R. Leach, 210/557-6947, Fax: -6781]</td>
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<td>17–21</td>
<td>Intl. Genome Sequencing and Anal. Conf. VI; Hilton Head, SC (abs. deadline: June 29) [D. Hawkins, 301/869-9056, Fax: -9777-2723, <a href="mailto:seqconf@biorx.org">seqconf@biorx.org</a>]</td>
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<td>20</td>
<td>Delivering DNA: the Future of Mol. and Med.; Institution; Bethesda, MD [P. Gregory, 301/496-3978, Fax: -7157, <a href="mailto:edcore@helix.nih.gov">edcore@helix.nih.gov</a>]</td>
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<td>21–25</td>
<td>Gene Therapy; CSHL [see contact: Aug. 31–Sept. 4]</td>
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**26–28** | Chromatin Struct. & Gene Expression; Madrid [CIMB, Gonzalez, +34-1/435-4420, Fax: -576-3201] |

**October**

| 2–5 | Hum. Genome 94: The Genes and Beyond; Washington, DC (abs. deadline: July 1) [G. Griffin, 703/671-1400, Fax: -7695] |
| 6–9 | DIMACS Workshop Combinatorial Algorithms for Mapp. & Sequencing; Piscataway, NJ [P. Pavzner, 814/863-3599, Fax: -865-3176, pavzner@cse.psu.edu] |
| 9–12 | GSA 1994 Annu. Meet.; Pacific Grove, CA [see contact: Aug. 16–21] |
| 12–14 | Nat. SBIR Conf.; Washington, DC [see SBIR Grants, p. 15] |
| 14–17 | 2nd Intl. Workshop on Hum. Chromosome 7; Tokyo [L.-C. Tsui, 416/813-6015, Fax: +4931, cdata@stidika.on.con] |
| 15–18 | 13th Annu. NSGC Educ. Conf.; Montorl. [B. Leopold, 510/872-7606, Fax: -1192] |
| 16–18 | 4th Intl. Id. of Transcribed Sequences Workshop; Montreal (abs. deadline: August 15) [ERI, N. Matthews, 303/333-4515, Fax: -8423] |
| 16–20 | Transcriptional Control of Cell Growth and Differentiation; Chatham, MA [AACR Special Conf., 215/440-9300, Fax: -9313] |
| 18–22 | 44th ASHG Annu. Meet.; Montreal [M. Ryan, 301/547-1825, Fax: -530-7079] |
| 24–28 | 3rd Intl. Conf. on Nanometer-Scale Sci. and Technol. in conjunction with the 41st AVS Natl. Symp.; Denver [C. Marrian, 202/767-3150, Fax: -4998] |
| 28–31 | ASBMB Fall Symp.: Oligonucleotide Selection and Mol. Diversity; Lake Tahoe, CA [ASBMN, 301/530-7010, Fax: -7014] |

**November**

| 4–6 | Nordic Genomic Initiative Workshop: Cloning of Large DNA Fragments; Olof [H. Prydz, +47-22/65-57-54, Fax: -694-130] |
| 4–8 | 3rd Intl. E. coli Genome Meet.; Woods Hole, MA [MBL, M. Riley, 508/548-7007 ext. 612, Fax: -540-6002, mrsley@whoi.mbl.edu] |
| 5–9 | 18th Annu. Symp. on Comput. Appl. in Med. Care; Washington, DC [AMIA, G. Mutnik, 301/857-1291, Fax: -1296, amicia@camix.sunford.edu] |

| 6–10 | 2nd South-North Hum. Genome Conf.; Beijing, CH [G. Bernardi, +39-1/1326-5824, Fax: 14427-7971, bernardi@einst2.fir] |
| 6–10 | 8th Intl. Mouse Genom Conf.; London [S. Brown, +44-71/772-1252, Fax: -706-3272, s.brown@smi.ac.uk] |
| 9–11 | 9th Intl. Workshop on Chromosome 21; Tsukuba-city, JP [N. Shimizu, Tal/Fax: +81/3-3351-2370, shimiza@dmn.med.keio.ac.jp] |
| 13–17 | 4th DOE Genome Contractor-Grantee Workshop; Santa Fe, NM [S. Spangler, 510/46-4379, Fax: -5717, sylviaj@w3.1bl.gov] |

14–16 | Computational Approaches in the Anal. and Eng. of Proteins; CIMB, Madrid [see contact: Sept. 29–28] |
| 14–18 | Supercomput. 94: Conf. on High Performance Comput. and Commun.; Washington, DC (poster deadline: Aug. 1) [Supercomput. 94, 515/264-4074, Fax: -0828, info@sc94.aneslab.gov] |
| 20–22 | Intl. Symp. on Genomic Imprinting; Florence, IT [M. Uzielli, +39-55/666-2931, Fax: -2916] |

Training Calendar*

**September**

| 7 | Intro. to PCR; Los Angeles (also offered Nov. 14) [BTP, S. Chance, 800/821-4861, Fax: 603/659-4708] |
| 8–9 | Intro. to Mol. Cytogenet.: Metaphase and Interphase Chromosomes; Galtenshires, MD [Oncor, Inc., 800/556-6267, Fax: 301/626-6129] |
| 8–9 | Quantitative RNA-PCR; BTP, Los Angeles (also offered Nov. 15–16) [see contact: Sept. 7] |
| 12–13 | Basic Cloning & Hybridization Tech.; BTP, Los Angeles (also offered Nov. 17–18) [see contact: Sept. 7] |
| 12–16 | Recombinant DNA Methodol.; Columbia, MD [Exon-Intron, Inc., 410/730-3984, Fax: -3983] |
| 12–16 | DNA Protein Interactions; Germantown, MD [LTI, 800/952-9166, Fax: 301/258-6212] |
| 15–16 | Clin. Appl. of PCR; BTP, Los Angeles [see contact: Sept. 7] |
| 19–20 | GDB/OMIM and Genomic Data on the Internet courses; Baltimore [GDB User Support, 410/555-9705, Fax: -014-0434, help@gdb.org] |
| 19–23 | Signal Transduction/Protein Phosphorylation; LTI, Germantown, MD [see contact: Sept. 12–16] |

*Dates and meeting status may change; courses may also be offered at other times and places; check with contact person.

**Attendance is either limited or restricted.
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).]

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 oertp01.er.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 Etzler; c/o SBIR Program Manager, ER-16; DOE; Washington, DC 20585 (301/903-5687, Fax: -5488).
- Bettie Graham; Bldg. 38A, Rm. 610; NIH; 9000 Rockville Pike; Bethesda, MD 20892 (301/496-7531, Fax: /408-2770).


November


2-7. Computational Genomics; CSCHL (Appl. deadline: July 15) [see contact: Oct. 13-26]

4-5. DNA Databases & Repositories; St. Paul [AFIP/ARP, 301/427-5231, Fax: -5501, lowther@email.afip.osd.mil]

January 1995

9-13. **Adv. Linkage Course; New York (appl. deadline: Nov. 10) [see p.18; K. Monague, 212/960-2507, Fax: /888-2750, BITNET: ort@mysp]

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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1. **Human Genome News**  
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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.
CIBM Ctr. for Inf. Meth. in Biol.
CSHL Cold Spring Harbor Lab.
DOE Dept. of Energy
ERI Eleanor Roosevelt Inst.
FVEA Fundacion Valenciana de Estudios Avanzados
GDB/OMIM Genome Data Base/Online Mendelian Inheritance in Man.
GSA Genet. Soc. of Am.
LTI Life Technologies, Inc.
MBL Marine Biological Lab.
NSGC Natl. Soc. of Genet. Counselors
SBIR Small Bus. Innovation Res.

**HGN Renewal Request**

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