Human Genome news

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Optical Mapping Offers Fast, Accurate Method for Generating Restriction Maps

New Approach Eliminates Electrophoresis, Is Amenable to Automation

Development of cheaper and faster technologies for large-scale genome mapping has been a major priority in the first 5 years of the Human Genome Project. Although many efforts have focused on improving standard gel electrophoresis and hybridization methods, a new approach using optical detection of single DNA molecules shows great promise for rapid construction of ordered genome maps based on restriction endonuclease cutting sites.[1–4]

Restriction endonucleases—enzymes that cut DNA molecules at specific sites in the genome—have played a major role in allowing investigators to identify and characterize various loci on a DNA molecule. Unlike maps based on STSs (a sequence-based landmark), restriction maps provide the precise genomic distances that are essential for efficient sequencing and for determining the spatial relationships of specific loci. Compared with hybridization-based fingerprinting approaches, ordered restriction maps offer relatively unambiguous clone characterization, which is useful for determining overlapping areas in contig formation, establishing minimum tiling paths for sequencing (coverage of a region), and characterizing genetic lesions with respect to various structural alterations.

Despite the broad applications of restriction maps, however, associated techniques for their generation have changed little over the last 10 years because of their reliance on tedious electrophoresis methods. Optical mapping of single DNA molecules represents the first practical nonelectrophoretic genomic-analysis approach toward producing ordered restriction maps.

Visualizing Gaps in a DNA Molecule

Ordered optical restriction maps were first constructed from yeast chromosomes by fluorescence microscopic imaging of stained DNA molecules treated with restriction enzymes.[1] In this method, individual fluorescently labeled DNA molecules were elongated on a microscope slide in a molten agarose flow containing restriction endonucleases. Resulting cleavage events were recorded by fluorescence microscopy as time-lapse digitized images; cut sites appeared as gaps that widened as DNA fragments relaxed (see figure at right). Fragment order was apparent throughout the procedure, and maps were constructed by measuring fragment sizes via relative fluorescence intensity or apparent length measurements. In addition to high throughput and high resolution, advantages of optical mapping include a very small sample size and the elimination of radioactive labeling required in conventional methods.

Modifications for Other Vectors

Improvements to the original optical mapping method now allow analysis of a wide range of such cloning vectors as cosmid, bacteriophage, P1, and YACs and produce accurate maps consisting of DNA fragments as small as 500 bp. These improvements include eliminating agarose and time-lapse imaging and fixing the elongated DNA molecules onto polylysine-treated glass surfaces. To analyze lambda clones, DNA samples have been fixed

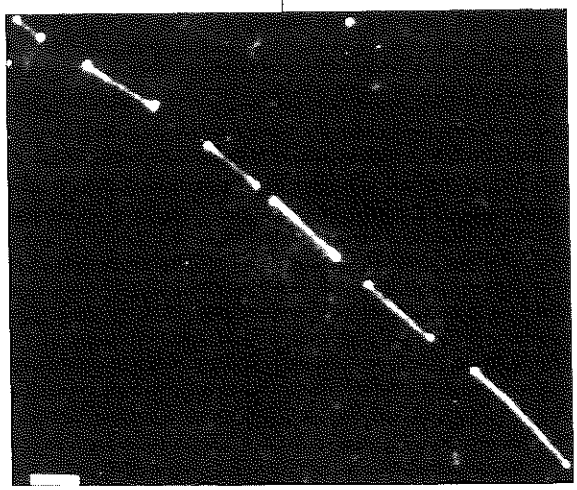

Image of a human chromosome 11 YAC clone (425 kb) cleaved by restriction endonucleases, stained with a fluorochrome, and visualized by fluorescence microscopy. (White bar at lower left corner represents 10 μm.)

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A longer review article on this topic by David Schwartz and his colleagues is in print in Issue 1 of *Genome Research*, published by Cold Spring Harbor Laboratory Press and available online, with downloadable video sequences of the technique in action (*http://www.cshl.org:80/journal/gr/supplement*).

onto derivatized glass surfaces by sandwiching them between a treated coverslip and glass slide. A cooled CCD camera was used to image molecules from 28 kb down to 800 bp[3]; more recent experiments have lowered the resolution limit to about 300 bp. Sizing errors are comparable to and in many cases lower than the rate achievable by agarose gel electrophoresis, depending on the number of molecules analyzed.

Generating YAC Maps

Although a large fraction of the human genome is covered by YAC contigs, few YAC restriction maps have been generated. Using optical mapping, ordered YAC restriction maps have been constructed,[4] with overall relative sizing errors comparable to routine pulsed-field gel electrophoretic analysis. Ordered restriction maps have now been generated for the human Beckwith-Wiedeman locus [with David Housman (Massachusetts Institute of Technology)], the *BRCA2* locus [with Stuart Fisher (Columbia University)], and the mouse olfactory locus [with Richard Axel (Columbia University)]. Optical maps are currently being generated from phage, cosmid, YAC, and BAC clones.

Large-Scale Genome Mapping

High-throughput approaches are being devised in anticipation of the vastly increased requirements for whole-genome analysis. Fully automated optical mapping approaches would require no human intervention between sample preparation and map construction and hold enormous promise for miniaturization. The advantages of optical mapping—high throughput and resolution, safety, and low cost—are likely to aid rapid progress in genome analysis and contribute significantly to the accelerating pace of the Human Genome Project as well as to efforts directed toward mapping human disease genes and other genetic alterations. *[David C. Schwartz (NCHGR grantee, New York University) and Akhtar Samad (Cornell Medical College)]* ◊

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☛ *Biological Resources*

Mapped Genomic Reagents Resource

More than 3200 human BACs and 250 PACs are now available from the Mapped Genomic Reagents Resource. The DOE-funded resource is headed by Julie Korenberg (Cedars-Sinai Medical Center and University of California, Los Angeles) and represents a collaboration with the two groups generating BAC and PAC libraries [Melvin Simon (California Institute of Technology) and Pieter de Jong (Roswell Park Cancer Institute)]. The project aims to establish an ordered sequenceable array of human BACs as a set of stable genome reagents that ultimately will be integrated with other vectors for sequencing, gene isolation, and molecular cytogenetic markers. Plans are to provide 24,000 BACs rapidly and cost-effectively as molecular cytogenetic markers, stable vectors for genome mapping and sequencing, and nucleation sites for contig construction. The mapped clones have also been provided to Thomas Hudson (Massachusetts Institute of Technology–Whitehead Institute) to establish STS assignments. Descriptions of the resource and associated database, reagent request form, and GIF illustrations of the genome-wide probe distribution can be found under "Integrated YAC/BAC/PAC Resource" (*http://www.csmc.edu/genetics/korenberg/korenberg.html*).◊

Coriell Cell Repositories

The National Institute of General Medical Sciences Human Genetic Mutant Cell Repository is requesting submission of blood or lymphoblastoid cell cultures from probands with well-documented phenotypes representing a variety of familial complex genetic disorders. In addition to familial cancers, complex disorders being sought include multiple sclerosis, epilepsy, Parkinsonism, hypertension, atherosclerosis, long QT syndrome, osteoporosis, asthma, rheumatoid arthritis, nonsyndromic hearing loss, neural tube defects, congenital heart disease, cleft lip and palate, fetal alcohol syndrome, morbid obesity, psoriasis, glaucoma, macular degeneration, cataracts, migraine, lupus erythematosus, Crohn's disease and other inflammatory bowel diseases, autism, dyslexia, attention deficit disorder, and Tourette's syndrome.

The National Institute on Aging Cell Repository has available for distribution cell cultures from three of the extended pedigrees used to clone the *AD3* gene for early-onset Alzheimer's disease. Affected and unaffected members of the Canadian Alzheimer's disease pedigree *FAD1*, the German *FAD2*, and the Italian *FAD4* are included in the collection. [Coriell Cell Repositories (800/752-3805 or 609/757-4848, Fax: -9737)].◊

DiGeorge Syndrome Region Cloned

Candidate Genes Identified

Researchers led by Beverly Emanuel and Marcia Budarf at Children's Hospital of Philadelphia have cloned a region of the chromosome 22 long arm containing a chromosomal breakpoint involved in DiGeorge syndrome (DGS) and have identified candidate genes spanning the breakpoint [*Nat. Genet.* **10,** 269–78 (July 1995)].

Named for endocrinologist Angelo DiGeorge, who first described the syndrome in 1965, the 22q11 microdeletion associated with DGS is believed to occur about once in 4000 to 5000 births. Children born with chromosome 22–deletion disorders share several characteristics, including cardiac defects, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia. Region 22q11.2 deletions may be implicated in a significant proportion of newborns with heart defects.

Although patients have many different deletion endpoints, researchers found that most have a 1.5-Mb deletion [the DiGeorge chromosomal region (DGCR)]. Deletion size has not been correlated with disorder severity. To identify candidate genes spanning the minimal region critical to DGS development, researchers studied a rare DGS individual with a balanced translocation between chromosomes 2 and 22. Gene transcripts were identified by direct screening of cDNA libraries, exon amplification, cDNA selection, and GRAIL sequence analysis. Attention is now focused on two genes located directly at the breakpoint; one of these codes for a protein that resembles the androgen receptor, suggesting a possible role in developmental regulation. A complete cosmid contig of DGCR has been constructed and is now being sequenced in collaboration with Bruce Roe (University of Oklahoma).◊

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Hudson Heads NCHGR Policy Office

Kathy Hudson has joined the NIH National Center for Human Genome Research (NCHGR) as Assistant Director for Policy Coordination. As head of the newly created Office for Policy Coordination, Hudson will be responsible for the Office of Communications, Office of Program Planning, and Office of Legislation.

Kathy Hudson

Before joining NCHGR, Hudson was Senior Policy Analyst in the Office of the Assistant Secretary for Health at the Department of Health and Human Services. She advised the Assistant Secretary on national health and science policy issues involving NIH. Before that, she was a Congressional Science fellow.

Hudson's training and professional experiences will provide focus and leadership in public policy and public affairs issues relating to NCHGR programs. She will coordinate NCHGR Ethical, Legal, and Social Implications activities.

Hudson received her B.A. in biology at Carleton College in Minnesota, M.S. in microbiology from the University of Chicago, and Ph.D. in molecular biology from the University of California, Berkeley. She has received numerous awards, including the Secretary's Special Recognition Award, Assistant Secretary for Health Special Recognition Award, and science fellowships from the Congressional Office of Technology Assessment and American Society for Microbiology.◊

Poll Shows Interest in Genetics

A new Harris telephone poll, conducted between April 6 and 9 for the nonprofit Center for Social and Legal Research in Hackensack, New Jersey, shows that the public is optimistic about the benefits but concerned about potential abuses of genetic testing and use of human DNA. Among 1000 adults nationwide, 56% said state DNA databases containing "genetic fingerprints" of all newborns would be "very" or "somewhat" acceptable, and 68% would be likely to ask doctors for genetic tests if they were available at a reasonable price. However, the overwhelming majority (86%) would be concerned if employers and insurers used genetic tests before deciding whether to hire or insure someone. Some 85% agreed that a national bioethics advisory commission should be established to advise and make recommendations on bioethical issues arising from human biology research.

Center president Alan Westin (Columbia University) said of the poll, "At a time of downsizing government and hostility to spending tax dollars, it is quite striking that more than 8 in 10 members of the public believe it would be valuable to have a government commission look into the uses of genetic testing and recommend protective policies."◊

News from Baylor

Genome Center Reports on Gene Studies

The following four items were reported in Issue 14 (May 1995) of the *Baylor Genome Center News* (*http://gc.bcm.tmc.edu:8088/newsletter/home.html*). To be placed on mailing list: *rossiter@bcm.tmc.edu.*

Chondrodysplasia Punctata (CDPX) Region. Investigators with Andrea Ballabio [formerly at Baylor College of Medicine (BCM) and now at the Telethon Institute of Genetics and Medicine (Milan)] have cloned the genomic region on the X chromosome where the gene for X-linked CDPX is assigned. From this region three adjacent genes, presumed from their structure to have sulfatase activity, have been isolated. Chondrodysplasia is a congenital defect of bone and cartilage development characterized by aberrant bone mineralization, severe underdevelopment of nasal cartilage, and short finger ends. CDPX is also implicated in a similar disorder known as warfarin embryopathy, a condition caused by the administration of warfarin (an anticoagulant drug) during a critical 6- to 9-week period of pregnancy. [*Cell* **81**, 15–25 (1995)]

X-Linked Ocular Albinism. Ballabio and Dick Lewis (BCM) have found an altered gene in the Xp22.3 region in patients with X-linked ocular albinism of the Nettleship-Falls type (OA1), a severe disorder affecting the eyes and the skin. [*Nat. Genet.* **10**, 13–19 (1995)]

Idiopathic Generalized Epilepsy (IGE). In searching for gene loci for IGE, Massimo Pandolfo, Pragna Patel, and coworkers at BCM and in Italy report that results of a study using nonparametric methods do not support linkage of IGE with chromosome 6 markers, as was suggested previously. Their results point to linkage to markers on the chromosome 8 long arm; this region is being investigated further in other IGE families. [*Hum. Molec. Genet.* **4**, 1201–7 (1995)]

Spinocerebellar Ataxia Type 1. Studies by Huda Zoghbi (BCM) and collaborators show that both the normal and expanded versions of the *SCA1* gene are translated and protein size is correlated with expansion size. Results showing that the proteins apparently have normal stability and distribution support the hypothesis of a novel harmful activity associated with the CAG coding region expansion. [*Nat. Genet.* **10**, 94–98 (1995)] ◊

Search Launcher Adds Features, Interface

New additions have been made to the BCM Search Launcher WWW page at *http://gc.bcm.tmc.edu:8088/search-launcher/launcher.html* [*HGN* 7(1), 12 (May–June 1995)]:

- Nucleic Acids Sequence Search Page has added BEAUTY-X, a BLASTX version of BEAUTY that adds sequence family membership and conserved and annotated domain information to BLAST searches.
- Gene Feature Search Page accesses servers that can search nucleic acid sequences for exons, introns, and open reading frames to determine the protein-coding potential of a DNA sequence (e.g., using GRAIL or GeneFinder).
- Sequence Utilities Page allows conversion between different sequence formats; and six-frame translation, reverse complementation, and restriction mapping of nucleic acid sequences.
- Protein Secondary Structure Prediction Page provides access to servers with applicable programs as well as launches to e-mail servers.
- Multiple Sequence Alignments Page has added BlockMaker from the Fred Hutchinson Cancer Research Center.

In addition, a new UNIX and Macintosh batch interface to the Search Launcher is now available. This program automatically reads multiple sequences from one or more input files, runs specified searches in the background (one at a time), then stores the results as individual HTML documents that can be read later using Mosaic or Netscape.

[Randall F. Smith, BCM] ◊

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NCHGR Newsletter Available

NCHGR Today, a four-page quarterly update on activities at the NIH National Center for Human Genome Research (NCHGR) Division of Intramural Research, includes information about NCHGR personnel, latest developments in genetic research, and upcoming events. [Free subscription: NCHGR Office of Communications (301/402-0911, Fax: -2218, *LeslieF@od.nchgr.gov*)] ◊

Fox Chase Team Wins Smithsonian Award

Innovative Computer Technology Enables "Virtual" Centers

A Fox Chase Cancer Center (FCCC) team led by Kenneth Buetow won the top science prize in the seventh annual *Computerworld* Smithsonian Awards Program. The team designed a computer technology that enhanced construction of a comprehensive human genetic map by the Cooperative Human Linkage Center (CHLC), a collaborative group composed of researchers at FCCC, University of Iowa, Harvard University, and Marshfield Medical Foundation. The work was funded by the NIH National Center for Human Genome Research.

According to Buetow, the technology created a "center without walls," establishing a new model for genome studies. Although such "virtual" centers have been used in other fields, it was a first for human genome research.

This computerized system helped researchers complete a high-density human linkage map—a short-term goal of the Human Genome Project—a year ahead of schedule [*Science* **265**, 1981–2144 (September 30, 1994) and *HGN* **6**(4), 1, 14–15 (November 1994)]. This map, along with others being developed in the Human Genome Project, will ultimately help improve diagnosis and prevention of disease by allowing researchers to pinpoint genetic characteristics linked with specific cancers, birth defects, and other hereditary and nonhereditary disorders.

The map was compiled from linkage data generated during the past decade by CHLC, Généthon, University of Utah, Yale University, and over 100 CEPH collaborators. The FCCC team created the common database to distribute data and maps within the project, with clients at each site communicating via the Internet with a centralized server maintaining the CHLC database. A number of graphic interface tools that work as distributed applications were also developed.

The winning technology, which was selected from 265 nominations, will occupy a permanent place in the Smithsonian Institution's research collection as part of the National Museum of American History exhibit "The Information Age: People, Information, and Technology." The awards program was begun in 1989 by *Computerworld* and the Smithsonian Institution to honor creative uses of information technology that benefit society and to identify these benefits for the general public. [Innovation Network Home Page: *http://innovate.si.edu*, CHLC Home Page: *http://www.chlc.org*] ◊

DOE Postdoctoral Fellows Named

DOE has announced the award of six 1995 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. Winners were chosen from a field of applicants who received their doctoral degrees after April 30, 1993.

Listed below are the name of each fellow, university of doctoral degree, host laboratory and research mentor, and research topic.

- **Evan Eichler** (Baylor College of Medicine): Lawrence Livermore National Laboratory, Harvey Mohrenweiser. Identification, organization, and characterization of zinc finger genes in a 2-Mb cluster on 19p12.
- **Kelly Ann Frazer** (University of California, San Francisco): Lawrence Berkeley National Laboratory, Eddie Rubin. In vivo complementation of the murine mutations grizzled, mocha, and jitteri.
- **Soo-in Hwang** (University of California, Berkeley): Lawrence Berkeley National Laboratory, Joe Gray. Positional cloning of oncogenes on 20q13.2.
- **James Labrenz** (University of California, Los Angeles): University of Washington, Seattle (UWS), Tim Hunkapiller. Error analysis of principal sequencing data and its role in process optimization for genome-scale sequencing projects.
- **Marie Ruiz-Martinez** [Northeastern University (NU)]: NU, Barry Karger. Multiplex purification schemes for DNA sequencing–reaction products: application to gel-filled capillary electrophoresis.
- **Todd Smith** (UWS): UWS, Leroy Hood. Managing the flow of large-scale DNA sequence information.

These fellows are the last to be appointed under this program. In the future, human genome researchers will be eligible for the Alexander Hollaender Distinguished Postdoctoral Fellowships, which offer appointments in the life, biomedical, and environmental sciences. The next application deadline is January 15, 1996. For information on this and other postdoctoral opportunities, see contact information on p. 11.◊

New EEOC Guidelines Clarify "Disability"

On March 15 the U.S. Equal Employment Opportunity Commission (EEOC) released official guidelines clarifying the meaning of "disability" as used in the Americans with Disabilities Act (ADA) of 1990. The guidelines extend ADA protection to individuals who experience employment discrimination based on genetic information related to illness, disease, or other disorders.

Referring to the ruling as a positive step, National Center for Human Genome Research director Francis Collins said, "The American people will receive the full medical benefit of genetic testing for predisposition to illness only when genetic discrimination barriers are lifted."

ADA defines a person with a disability as one who has a physical or mental impairment that substantially limits a major life activity, has a record of impairment, or is regarded as having an impairment. Employers who make adverse employment decisions based solely on genetic predisposition are regarding the individual as having an impairment, which is covered in the third part of the definition. Thus, these employers would be in violation of ADA. [Copies of ADA Guidelines: Write to EEOC; Office of Communications and Legislative Affairs; 1801 L St., NW; Washington, DC 20507] ◊

Chromosome 9 Workshop Produces New Maps

The Fourth International Workshop on Chromosome 9, held April 23–25 in Williamsburg, Virginia, was organized by Margaret Pericak-Vance (Duke University) and attended by 33 people from 7 countries. Sponsors included the U.K. Medical Research Council, DOE, NIH National Center for Human Genome Research, and the Human Genome Organisation (via a grant from the European Community).

Speaking of the meeting's success, A. Jamie Cuticchia [formerly Genome Data Base (GDB), now at Mitre Corporation] said, "The chromosome 9 workshop is noteworthy because for the first time on record every participant submitted data to GDB before the meeting. Recognizing that searchable data is critical in creating integrated maps, the chromosome 9 community required that *ALL* data be submitted in advance."

Continuing a previously effective format, individual participants made brief presentations of their interests and research highlights since the last meeting, and leaders of small working groups provided information on the latest findings. Chromosomal subgroups worked independently and then jointly to produce consensus physical and genetic maps. A new subsection on morbid anatomy was added to handle emerging correlations of mapped disorders with localized potential candidate genes. Selected meeting highlights follow.

Mapping

Global Map. The composite genetic linkage map was modified and updated during the meeting using a set of defined linkage data and SIGMA, a software program developed by Michael Cinkosky (formerly Los Alamos National laboratory, now at University of Utah Medical Center). Lack of telomeric markers continues to be a problem, but recent efforts have clarified the order of and distance between markers near each telomere; genetic distance in these regions has been reduced significantly as well. The map is most remarkable for uneven marker distribution, with several clusters of anonymous markers. This suggests that certain genomic regions have enhanced clonability properties, unusually high polymorphism rates among markers, low genetic-recombination rates, or a combination of these factors.

Morbid Anatomy. Six new Mendelian disease loci were identified by genetic linkage or physical mapping to chromosome 9. These are hyperglycinemia, isolated, nonketotic type 1 (GLDC); venous malformations (VMCM); familial melanoma (CDKN2); arthrogryposis (AMCD1); male pseudohermaphroditism (HSD17B3); and Osler-Rendu-Weber disease, type 1 (ENG).

Comparative Mapping. Publication of the results of 50 cross-hybridizations between products of human chromosome 9 and the mouse genome has provided a detailed comparative map. The chromosome now has known syntenies with eight segments derived from four mouse chromosomes. The information is sufficient for polarity determination in these homologous segments; none is astride the human centromere.

Resources

Hybrids. Allen Bale (Yale University) reported the submission of four hybrids containing defined 9q deletions to Coriell. Other hybrids, available from David Callen (Adelaide Children's Hospital), contain possibly useful breakpoints on chromosome 9 involving balanced translocations with chromosome 16.

Clones. The chromosome 9 cosmid library from Lawrence Livermore National Laboratory continues to be a valuable tool. A new section of the Chromosome 9 Home Page will include a list and free text information about cosmids in this library identified by the 300-microtitre–plate notation. New data or comments about the section should be sent to John Attwood (*john@mrc-hbgu.ucl.ac.uk*). A second chromosome 9 cosmid library has been constructed in the vector supercos [Murrell et al., *Genomics* **25**, 59–65 (1995)]. Some YACs from the chromosome 9–specific library constructed by MaryKay McCormick (Massachusetts General Hospital) are freely available, and others are distributed on a collaborative basis. In addition to the 160 or so cloned genes known on chromosome 9 and listed in GDB, 215 ESTs were added in the past year. The total of 330 ESTs presently identified includes 108 from Charles Auffray (Généthon). ESTs become increasingly valuable resources as the rate of EST mapping increases in genomic radiation hybrids.

Polymorphic Markers. GDB lists 341 polymorphic loci on chromosome 9. Of these, 286 are short tandem repeats (159 dinucleotides, 22 trinucleotides, and 105 tetranucleotides). Several new polymorphic markers were contributed at the meeting, including approximate map positions for 43 new tetranucleotide repeats from the Utah Marker Development Group (UMDG).

Meiotic Breakpoints. Two groups reported algorithms concerned with defining meiotic breakpoints in the CEPH families. Steve Gerken (UMDG) aims to construct maps, and Attwood plans to produce a panel of well-supported breakpoints that can be used for rapid placement of new polymorphic markers. All breakpoints generated by Attwood are available via the Chromosome 9 Home Page (see sidebar for address), which contains an interactive form for requesting breakpoint details for any specified chromosomal region.

Community Goals

Specific community goals set at the workshop include (1) extending information on the ease of using genetic markers and (2) coordinating across numerous groups the refining of meiotic breakpoint mapping of many microsatellite markers.◊

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This article was excerpted from the electronic meeting report.

Chromosome 9 Workshop Information Available

Workshop reports, abstracts, maps, and figures are available by anonymous ftp (*ftp.gene.ucl.ac.uk* or *128.40.82.1*) in the subdirectory */pub/c9workshop/1995* or via the Chromosome 9 Home Page (*http://www.gene.ucl.ac.uk/chr9home.html*). An integrated chromosome 9 map can be found in the location database *LDB* (accessible via the chromosome 9 Home Page and *http://cedar.genetics.soton.ac.uk/public_html*). The map can also be obtained by anonymous ftp as the file */pub/chrom9/map* from *ftp://cedar.genetics.soton.ac.uk*. SIGMA is available via anonymous ftp (*ftp.ncgr.org*) and WWW (*http://www.ncgr.org/sigma/home.html*).

1996 Chromosome 9 Workshop Planned

A fifth workshop is tentatively planned for fall 1996 to bring various mapping issues to closure. Brandon Wainwright (Center for Molecular Biology and Biotechnology) will host the meeting in Brisbane, Australia, because of the number and diversity of chromosome 9 research groups there.

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Workshop Documents

http://probe.nalusda.gov:8000/acedocs/ace95/index.html

ACEDB Version 4.0 Debuts at Annual Meeting

Since its 1991 introduction for the *Caenorhabditis elegans* community, ACEDB has served as a data-management model for other research projects and has been adopted by a number of diverse organizations and individuals to maintain and distribute data on more than 40 genomes, including human, bovine, *Drosophila*, yeast, mycobacteria, *Arabidopsis*, grains, trees, and fungi. At the May 14–29 ACEDB conference and workshop in Geyserville, California, participants represented 10 countries, 4 continents, 38 organizations, 20 databases, and 19 organisms.

John McCarthy [Lawrence Berkeley National Laboratory (LBNL)] organized this year's meeting. Sponsors included DOE, NIH National Center for Human Genome Research, U.S. Department of Agriculture, National Science Foundation, and European Data Resource for Human Genome Research. Conference hardware and software were provided by LBNL, Digital Equipment, Sun Microsystems, Silicon Graphics, Network Computing Devices, Microsoft, and Stanford University.

The main goal of the 3-day conference, attended by about 70 people, was information exchange via tutorials, oral presentations, posters, online demonstrations, and discussions. Some 45 people stayed on for the 10-day workshop, whose goals were code development and consolidation, database building, documentation writing, interest-group discussions, and long-range planning. Investigators agreed to continue their collaborations after the meetings ended. For the first time, WWW was used extensively before, during, and after the conference and workshop to circulate instructions, document drafts, and meeting summaries.

Selected meeting highlights are described below; details are given in a series of WWW pages (see address in left column).

Meeting Highlights

- First public release of ACEDB version 4.0. Several curators converted their data models and databases to take advantage of new features, and programmers modified software modules to conform with version 4. During the workshop a number of bugs were identified and eliminated [report bugs to the ACEDB newsgroup (*acedb@net.bio.net*)]. The current release version is 4.1, available via ftp (*ncbi.nlm.nih.gov/repository/acedb*).
- Software enhancements to run multiple ACEDB clients for different databases, linked together via Perl scripts and HTTP servers [Doug Bigwood and John Barnett (National Agricultural Library {NAL}), Jeroen Coppieters (European Bioinformatics Institute), Jean Thierry-Mieg (Centre National de la Recherche Scientifique), and Steve Rozen (Massachusetts Institute of Technology)].
- Module for displaying multiple maps, including different levels (e.g., cytogenetic bands, STS locations, P1 clones, and DNA sequences) of the same region [Arun Aggarwal (LBNL)].
- Substantial progress on a prototype protein-sequence display module [Eric Sonnhammer (Sanger Centre)].
- HTML documentation for map display and sequence-assembly modules [Sam Cartinhour (Texas A&M and NAL), John Morris (Massachusetts General Hospital), and Kate Rice (Sanger Centre)]. The documentation working group recommended using HTML for all future ACEDB documentation.
- More than 20 different software tools listed for converting data to and from *.ace* files and various formats such as spreadsheets, Medline, and FASTA [Detlef Wolf (Integrated Genomic Database) and query tools working group].
- ACEDB conversion begun for Windows-NT by Richard Bruskiewich (University of British Columbia), Richard Durbin (Medical Research Council, U.K.), Thierry-Mieg, and others.

Future Meetings

The 1996 ACEDB conference and workshop will be held near Heidelberg, Germany, and hosted by Otto Ritter's group (Integrated Genomic Database Project). NAL will host the 1997 meeting, for which Bigwood and Dave Matthews (Cornell University) are cochairs.◊

☛ *ACEDB Application Examples*

Encyclopaedia of Drosophila 2.0

Of the many groups using ACEDB, the *Drosophila* Genome Project has made the greatest number of modifications to the program for their specialized needs. ACEDB was originally customized for use with *Drosophila* by Suzanna Lewis and Cyrus Harmon [Berkeley *Drosophila* Genome Project (BDGP)] to produce Flydb, the laboratory database of BDGP. MacAce, the Macintosh-compatible version of ACEDB, was written by Frank Eeckman (Lawrence Berkeley National Laboratory), Richard Durbin (Sanger Centre), and Harmon. This Macintosh version was further customized by Harmon and Lewis for the *Encyclopaedia of Drosophila (EofD)*, which is a joint product of BDGP (*http://fly2.berkeley.edu*) and FlyBase (*http://morgan.harvard.edu*). *EofD* displays published and unpublished BDGP data as well as data collected by FlyBase from the scientific literature and other genome projects. Since Release 1.0 became available in April, FlyBase and BDGP have distributed more than 1500 copies of the *EofD* CD-ROM, giving it the largest installed user base of any ACEDB implementation. Release 2.0 is now available on CD-ROM for the Macintosh ($15, including 36-page reference manual) and by ftp for the UNIX version. [Ordering information and computer requirements: *eofd-sales@morgan.harvard.edu*] ◊

Sanger Centre 22ace

The first release of the human chromosome 22 physical mapping database 22ace from the Sanger Centre is now available by ftp from *ftp.sanger.ac.uk* in the directory *pub/human/chr22/physical_map*. The database is implemented in version 4.1 of ACEDB. Details about ACEDB and the Chromosome 22 mapping group can be found on WWW (*http://www.sanger.ac.uk/hum22*). ◊

Agricultural Server

ACEDB acts as the back-end data server for all databases that are part of the USDA Agricultural Genome Information Server (*http://probe.nalusda.gov*). With release of the ACEDB aceserver, which can output ACEDB objects as Perl code, this programming language is being used to develop sophisticated cross-species database queries and draw data from molecular biology databases throughout the Internet.◊

Colloquy Explores Genetic Predisposition

An Interdisciplinary Colloquy on Genetic Predisposition, organized by Pilar Ossorio (University of California, Berkeley) and Michael Yesley (Los Alamos National Laboratory) and sponsored by the Ethical, Legal, and Social Issues (ELSI) component of the DOE Human Genome Program, was held last fall in Washington, D.C. The diverse group of invitees included scientists; DOE and NIH grantees and staff; consumer group representatives; social scientists; philosophers; members of the NIH-DOE Joint Ethical, Legal, and Social Implications Working Group; and a theologian.

Francisco Ayala (University of California, Irvine) reviewed the meeting's purpose, which was to explore genetic predisposition from multiple perspectives and identify points of agreement and disagreement, questions for future discussions, and areas for policy development. Genetic predisposition was chosen as the topic because of its interdisciplinary relevance.

Referring to the nature-nurture controversy, Ayala discussed heritability and the extent to which genes and environment determine a particular trait. He said heritability is usually defined incorrectly as the contribution of genes to a trait, whereas a correct definition would be the contribution of genetic variation to phenotypic variation. Ayala pointed out that heritability can vary drastically from 0 to 100% for the same trait in the same organism. To illustrate his point, he used examples from biomass studies of a cinquefoil plant under varying natural conditions.

In his presentation on Gene Expression in Context, Chris Fields (National Center for Genome Resources) suggested looking at other disciplines for more precise concepts about genetic predisposition. He raised questions about the nature of genes and inheritance and suggested that a long-term, multigenerational view is needed when genetics is discussed.

Fields continued that experiments on model organisms in controlled environments don't reveal much about the range of gene expression and phenotypic variation in a natural setting. For the last 20 to 25 years, molecular biologists have used homogeneous model organisms and have studied biological mechanisms in controlled environments. Extrapolating from laboratory organism studies to the heterogeneous human population is not always possible.

Fields emphasized the need for scientific measurements and for a language that describes the level of complexity both in environmental action and in gene or other biological mechanisms. He believes biology is in a position analogous to that of physics in the last century, when a great deal of progress and optimism were prevalent but the conceptual foundation was only a year or two away from being completely rebuilt. He thinks biology is ready for a new foundation that couples the theory of evolution, which underlies all biological thinking, to the mechanisms of gene expression in a cellular, developmental, and environmental context.

Dorothy Nelkin (New York University) illustrated predisposition concepts that appear in popular culture. Beliefs in biological determinism from earlier this century are perpetuated today in the idea of genetic predisposition. A common theme is that people are not responsible for behavior because it is predestined by their genes. This theme also appears in discussions of alcoholism and other addictions, including smoking, overeating, and gambling. Now, Nelkin finds, some popular stories suggest that success and failure are encoded in genes. Popular assumptions about genetic predisposition oversimplify the complexities and contingencies expressed in scientific descriptions of these concepts. Deterministic assumptions about genetic predisposition are especially striking in American society, Nelkin said, where the very foundation of the democratic experiment is based on the improvability, indeed the perfectibility, of all human beings.

In his presentation on Genetic Predisposition and the Practice of Medicine, Eric Juengst (Case Western Reserve University) contrasted the metaphors of fortune teller and weather forecaster. He suggested that genetic predictions are probabilistic, like weather forecasting, and will vary according to local environment.

Juengst used illustrations to explain how people think about predisposition in the clinical setting and how patients see themselves. The major ways of understanding how people think about genetic disease and its social implications flow from two 19th-century models: "constitutional predisposition" and "specific causation." Environmental conditions may or may not be important in gene expression.

The group extensively discussed each presentation and the meaning of predisposition.

Summary

Participants recommended follow-up studies and discussions on predisposition and such related topics as informed consent, screening, and people's reactions to test results.◊

¶ Magazine on Biophotonics

Biophotonics International is a new bimonthly magazine designed to provide the latest information on photonic products and systems to researchers and industries that are using photonic technology in medical or biotechnological products and procedures. The magazine will address solutions for both clinical and research applications. [Laurin Publishing Co.; Pittsfield, MA (413/499-0514, Fax: /442-3180, *photonics@mcimail.com*)] ◊

Genome News

☆☆Notice to DOE Contractors and Grantees

The fifth DOE Human Genome Program Contractor and Grantee workshop will be held January 28–February 1, 1996, 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. Registration and abstracts are due October 6 to Sylvia Spengler; Human Genome Program Coordination; 459 Donner Laboratory; Lawrence Berkeley National Laboratory; Berkeley, CA 94720 (510/486-4879, Fax: -5717, *sylviaj@ux5.lbl.gov*).◊

New HGMIS Telephone, Fax Numbers

The HGMIS area code has changed from 615 to 423.

New numbers:

- 423/576-6669
- Fax: /574-9888

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 Lockheed Martin Energy Systems, Inc., for the U.S. Department of Energy, under Contract DE-AC05-84OR21400.◊

Genome News

Human Genome news

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

Human Genome Management Information System
Oak Ridge National Laboratory
1060 Commerce Park, MS 6480
Oak Ridge,TN 37830
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http://www.ornl.gov/TechResources/Human_Genome/home.html

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Using RH Mapping, Rhserver To Incorporate Human ESTs, STSs with Linkage Maps

Meiotic linkage maps consisting of highly polymorphic, PCR-based markers spanning the human genome have had a tremendous impact on the positional cloning of human disease genes in recent years. The availability of cDNA sequences representing the majority of human genes promises to have an equally dramatic impact on human genetic research over the next few years. Efficient strategies for using cDNA sequence information to identify human disease genes will incorporate partial human cDNA sequence STSs with meiotic linkage maps. However, despite recent technical advances in both physical and genetic mapping, determining the order and distance between large numbers of DNA markers at the 0.5- to 1-Mb resolution level remains a difficult task.

The Stanford Human Genome Center (SHGC) has generated a set of 83 "whole-genome" radiation hybrids (RHs) that has proven very useful for producing high-resolution maps integrating human cDNAs with meiotically ordered polymorphic markers. Each hybrid retains about 18% of the entire human genome with an average fragment size of 4 Mb. Scoring 6000 random markers on this RH set should result in a map of the entire human genome averaging 500-kb resolution, with around 50% of all markers ordered with odds better than 1000:1. To date, 975 markers on the Généthon meiotic linkage map have been placed on the RH set at SHGC.

Given that certain human chromosomal fragments show instability over time and in different hybrid passages, SHGC is carrying out all mapping studies using a single large batch of hybrid DNA prepared and distributed to the scientific community by Research Genetics. Peter Goodfellow (University of Cambridge, U.K.) and Jean Weissenbach (Généthon) have used a lower dose of X rays to generate a second independent set of RH DNAs, distributed as GENEBRIDGE 4 by Research Genetics. These two reagent sets should allow many different laboratories around the world to integrate data in much the same way that DNA from the common set of CEPH families is used to generate an integrated human meiotic linkage map.

To facilitate integration of cDNA markers and meiotic linkage markers, SHGC has established an automated e-mail server for RH mapping information. Rhserver allows scientists who have scored an STS of interest on the SHGC RH panel to determine which of the Généthon markers map near their STS. Submitted typing information is subjected to a "two-point" statistical analysis, and rhserver returns a list of markers that link to the subject marker with a LOD score of 6.0 or higher. The list includes linked markers, LOD score of each link, and distance in centirays between linked markers. For this RH set, one centiray is equal to about 30 kb.

Based on the scoring of 313 STSs derived from cDNA sequences, investigators have found that any random marker has a 50% chance of linking with a LOD of 6 or higher to one of the framework markers; this link will represent a valid map assignment more than 97% of the time. As the number of SHGC-scored markers increases, so will the probability of linkage.

> Research Genetics, Inc. [800/533-4363 (U.S. and Canada), Fax: 205/536-9016, *http://www.resgen.com*]

Rhserver will be updated periodically to reflect additional scoring information from SHGC. All scoring information sent to rhserver by other laboratories is confidential and is not examined or retained by SHGC. For scientists who wish to carry out additional analyses not provided by rhserver, raw scoring data for the framework markers is available by ftp from *shgc.stanford.edu* or from the EBI RHdb below. To receive the current set of instructions for using rhserver, send an empty e-mail (no message body) with a subject line of *info* to *rhserver@shgc.stanford.edu. [David R. Cox, Stanford University School of Medicine]* ◊

☛ *Informatics Resources*

EBI Releases RHdb

The European Bioinformatics Institute (EMBL outstation, Hinxton) has announced the release of RHdb, a new database for radiation hybrid mapping raw data. Flat files (ASCII text) are accessible at *ftp://ftp.ebi.ac.uk/pub/databases/RHdb* or *http://www.ebi.ac.uk:80/RHdb* in *exp.dat* (experimental conditions), *panel.dat* (panel information), and *rh.dat* (raw mapping data). Data submissions: see format at *http://www.ebi.ac.uk/RHdb*; database questions: *datalib@ebi.ac.uk* with *rhdb* on the subject line.◊

Haplotyping Programs Available

The haplotyping programs SIMCROSS and SIMWALK, developed by Daniel Weeks and colleagues (University of Oxford and University of Pittsburgh), are now available in the *pub* directory by anonymous ftp (*ftp://watson.hgen.pitt.edu/pub*). These are programs to generate optimal haplotype configurations on general pedigrees by using a likelihood-based approach for correctly taking intermarker recombination fractions into account. [Contact: Daniel Weeks (Fax: 412/624-3020 or +44-1865/742-196, *dweeks@watson.hgen.pitt.edu* or *daniel.weeks@well.ox.ac.uk*)] ◊

GDB Forum

Enhancements to GDB Web Server

- **The WWW GDB Browser Locus Detail** provides links to mammalian homology data from Jackson Laboratory. The browser is available via the GDB Home Page (*http://gdbwww.gdb.org/*).
- **The Probe Library Location Query** allows searching for probes at specific plate, row, and column locations within a selected library. Links to this query are available from the GDB Browser and the Probe Query form.
- **Monthly lists of all new GDB citations** include those entered through Medline retrievals and literature scanning by GDB staff. The lists, organized by chromosome, link to detailed information for each citation. "Citations Relevant to GDB" is under "GDB Data Submission and Related Information," located on the GDB Home Page.
- **The GDB Web server** in Baltimore has been modified to use a new file structure. As a result, the URLs for this server have changed, and users are advised to modify their links. The GDB Web mirror sites already use the new file structure and are not affected by this change.◊

Data Submitted to GDB

This summer, a significant amount of mapping and reagent data was loaded into GDB electronically, either through direct submission by researchers or by download and processing of public data by GDB staff.

During the 1-month period between July 19 and August 18, submission of 5387 PCR probes, 6100 clone probes, and 4983 D-segments boosted GDB totals for each object by 17%, 2%, and 7%, respectively.

Below are samples showing sites from which data was received and GDB submission numbers. For information about submitted data, use the Submission ID Query available from the GDB Browser on any GDB Web server. [Data-submission questions: *data@gdb.org*]

Some Data Sources and GDB I.D. Numbers

Généthon	G00-598-851
Washington University	G00-600-051
dbEST	G00-601-421
IMAGE consortium	G00-615-188
European Bioinformatics Institute	G00-618-869
Whitehead Institute (MIT)	G00-626-152

¶ Electronic Journal on Molecular Biology

GENE-COMBIS, part of the journal *Gene*, is a new online electronic journal devoted to computing problems that arise in the molecular biology field. Edited by Michael Ashburner (University of Cambridge) and Nathan Goodman (Whitehead Institute), GENE-COMBIS includes online articles, alerting service, discussion forum, user directory, and recommended software. It links to other bibliographical references and databases for rapid, direct submission and retrieval of sequences and source codes mentioned in the articles. Anonymous peer reviews are included with the papers, which are published on WWW 8 to 10 days after approval by the editors and later in hard copy in *Gene*.

The service is directly available to scientists at institutes that maintain a hard-copy subscription to *Gene*. Individual subscription charges for others will be waived for the first year of operation (ending July 31, 1996), but a unique identifier is required for access to all components. This identifier is obtained through a subscription application (follow the option "access registration") from the GENE-COMBIS Home Page (*http://www.elsevier.nl/locate/genecombis* and *http://www.elsevier.com/locate/genecombis*). ◊

GDB Access Via WWW

The GDB Web server is available directly at the following URLs:

- **United States** *http://gdbwww.gdb.org/*
- **Australia** *http://morgan.angis.su.oz.au/gdb/docs/gdbhome.html*
- **France** *http://www.infobiogen.fr/gdbwww/*
- **Germany** *http://gdbwww.dkfz-heidelberg.de/*
- **Israel** *http://inherit1.weizmann.ac.il/gdb/docs/gdbhome.html*
- **Japan** *http://gdb.gdbnet.ad.jp/gdb/docs/gdbhome.html*
- **Netherlands** *http://www-gdb.caos.kun.nl/gdb/docs/gdbhome.html*
- **United Kingdom** *http://www.hgmp.mrc.ac.uk/gdb/docs/gdbhome.html*

Other GDB node with WWW server in English:

- **Sweden** *http://www.bmc.uu.se/Computing-Dept.html*

GDB User Support, Registration, Training

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. The Help Line in Baltimore is staffed from 9 a.m. to 5 p.m. EDT 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.

"GDB/OMIM and Genomic Data on the Internet" classes will be held in Baltimore on December 4–5. Courses related to GDB and OMIM are also offered at some of the nodes. Contact the appropriate User Support office for details.

User Support Offices

UNITED STATES
GDB User Support
Genome Data Base
Baltimore, Maryland
410/955-9705
Fax: /614-0434
help@gdb.org

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+ 31/80-653391
Fax: -652977
post@caos.caos.kun.nl

SWEDEN
GDB User Support
Biomedical Center
Uppsala, Sweden
+ 46/18-174057
Fax: -524869
help@gdb.embnet.se

UNITED KINGDOM
Administration
HGMP Resource Centre
Cambridge, U.K.
+ 44/1223-494511
Fax: -494512
admin@hgmp.mrc.ac.uk

Next *HGN* To Highlight Progress

On October 1, the Human Genome Project will celebrate its fifth anniversary. To commemorate this event, the next issue of *HGN* will highlight progress made over the last 5 years in achieving project goals.◊

Calendar of Genome Events*

October 1995

28–Nov. 1. Symp. on Computer Appl. in Med. Care: Toward Cost-Effective Clinical Computing; New Orleans [AMIA, 301/657-1291, Fax: -1296, *denise@amia2.amia.org, http://amia2.amia.org*]

November 1995

5–7. 5th Intl. Workshop on Identification of Transcribed Sequences; Marseilles, France (abs. deadline: Aug. 15) [N. Matthews, 303/333-4515, Fax: -8423, *nanm@druid.hsc.colorado.edu*]

5–8. 3rd Intl. Conf. on Automation in Mapping & DNA Sequencing; Berkeley, CA [M. Field, 510/486-6386, Fax: -5548, *mofield@lbl.gov*]

9. Richard Roberts; Rockville, MD [TIGR/NIST Distinguished Speakers Series, D. Hawkins, 301/838-3501, Fax: -0209, *dhawkins@tigr.org, http://www.tigr.org*]

9–11. 4th Conf. on Molec. Nanotechnology; Palo Alto, CA [Foresight Institutes, 415/324-2490, Fax: -2497, *foresight@cup.portal.com, ftp://ftp.parc.xerox.com/pub/nano/nano4.html*]

12–16. 9th Intl. Mouse Genome Conf.; Ann Arbor, MI (abs. deadline: Aug.1) [D. Miller, 716/845-4390, Fax: -8169, *dmiller@mcbio.med.buffalo.edu*]

13–14. 4th Intl. Workshop on Human Chromosome 16; Leiden, Netherlands [M. Breuning, +31-71/276-048 or -293, Fax: -075, *breuning@rullf2.leidenuniv.nl*]

13–15. IBEX '95; San Francisco [BioExpo, 713/529-1616, Fax: -0936, *iei@mail.infohwy.com*]

16–17. 3rd Intl. Workshop on Human Chromosome 12 Mapping; Leuven, Belgium [P. Marynen, +32-16/34-5891, Fax: -5997, *peter.marynen@med.kuleuven.ac.be*]

18. Chromosome 12 Genes in Human Cancer; Leuven, Belgium [see contact: Nov. 16–17]

30–Dec. 1. Exploiting Transgenic Technology for Commercial Development; San Diego [IBC, 508/481-6400, Fax: -7911]

December 1995

2–6. Molecular Basis of Gene Transcription; San Diego [AACR, J. Ruben, 215/440-9300, Fax: -9313]

3–6. **HUGO Comparative Genome Organisation Workshop; Queensland, Australia [HUGO Americas, 301/654-1477, Fax: /652-3368, *hugo@gdb.org*]

3–7. 3rd UNESCO Human Genome Conf.; New Delhi [S. Matsui, +33-1/45-68-3887, Fax: /45-67-2639]

7–8. Applied Molecular Evolution; IBC, La Jolla, CA (abs. deadline: Nov. 9) [see contact Nov. 30–Dec. 1]

8–9. DNA Databanks & Repositories; Birmingham, AL [AFIP/ARP, 800/577-3749, Fax: 301/427-5001, *came@email.afip.osd.mil*]

9–13. ASCB; Washington, DC [K. King, 301/530-7153, Fax: -7139, *ascbinfo@ascb.faseb.org, gopher://gopher.faseb.org:70/11/Societies/ASCB*]

10–12. Genome Informatics 1995; Yokohama, Japan (abs. deadline: Oct. 13) [N. Tomioka, Fax: +81-3/5449-5434, *workshop@ims.u-tokyo.ac.jp*]

14. Hamilton Smith; TIGR/NIST, Rockville, MD [see contact: Nov. 9]

January 1996

3–6. Pacific Symp. on Biocomputing; Kohala Coast, HI (early reg.: Oct. 2) [L. Hunter, 301/496-9300, Fax: -0673, *hunter@nlm.nih.gov* or T. Klein, 415/476-0663, Fax: /502-1755, *klein@cgl.ucsf.edu, http://cgl.ucsf.edu/psb/psb.html*]

11. Florence Haseltine; TIGR/NIST, Rockville, MD [see contact: Nov. 9]

14–18. Plant Genome IV; San Diego (PG I, II, and III abs.: *http://probe.nalusda.gov:8000*) [Scherago Intl., 212/643-1750, Fax: -1758, *scherago@biotechnet.com*]

15–18. BioEast '96; Washington, DC [BioConf. Intl., 301/652-3072, Fax: -4951]

28–Feb. 1. 5th DOE HGP Contractor-Grantee Workshop; Santa Fe, NM (abs. deadline: Oct. 6) [S. Spengler, 510/486-4879, Fax: -5717, *sylviaj@ux5.lbl.gov*]

February 1996

5–6. NIH Natl. Advisory Council for Human Genome Res.; Washington, DC [J. Ades, 301/402-2205, Fax: -2218, *ja51b@nih.gov*]

5–6. Intellectual Property Issues: Critical Challenges for Biomedicine and Genomics; Santa Fe, NM [CHI, 617/487-7989, Fax: -7937, *chi@world.std.com, http://www.xensei.com/conferences*]

10–14. **MBWS-96: Advances in Gene Technol.–Therapeutic Strategies & Molecular Medicine; Ft. Lauderdale, FL (abs. deadline: Nov. 10) [MBWS, 800/miagene, Fax: 305/324-5665, *mbws@mednet.med.miami.edu*]

10–16. Molecular Mechanisms in DNA Replication & Recombination; Taos, NM [Keystone Symp., 303/262-1230, Fax: -1525]

15. James M. Wilson; TIGR/NIST, Rockville, MD [see contact: Nov. 9]

March 1996

4–6. 3rd Annual HGP: Commercial Implications; CHI, San Francisco [see contact: Feb. 5–6]

11–14. 3rd ACMG and 27th MOD; San Antonio, TX [S. Robinson, 301/571-1825, Fax: -1895, *srobinson@acmg.faseb.org*]

14. Bruce Stillman; TIGR/NIST, Rockville, MD [see contact: Nov. 9]

15–17. Chromosome 5 Workshop; Manchester, U.K. [M. Dixon, Tel/Fax: +44-161/275-5620, *mdixon@fs2.scg.man.ac.uk*]

18–20. Single Chromosome 4 Mapping Workshop; Bochum, Germany [O. Riess, +49-234/700-3831, Fax: /709-4196, *riessoby@rz.ruhr-uni-bochum.de*]

21–23. Genetics Revolution: A Catalyst for Education and Public Policy; Dallas [M. Mays, 214/659-5328, Fax: -5171, *memays@dcccd.edu*]

22–24. HGM 96; Heidelberg, Germany [HUGO Europe, Secretariat, +44-171/935-8085, Fax: -8341]

24-27. Electrophoresis '96; Atlanta (abs. deadline: Oct. 15) [D. Wiley, 800/627-0629, Fax: 913/843-1274, *dwiley@allenpress.com*]

*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.

April 1996

11. Neal Lane; TIGR/NIST, Rockville, MD [see contact: Nov. 9]

21–26. Molecular Cytogenetics; Barga, Italy [GRC, 401/783-4011, Fax: -7644, *grc@grcmail.grc.uri.edu*]

27–May 1. 37th Annual *Drosophila* Res. Conf.; San Diego (abs. deadline: Dec. 1) [S. Bernstein, 619/594-5629, Fax: -5676, *sbernst@sunstroke.sdsu.edu, http://morgan.harvard.edu/dros-conf.html*]

May 1996

8–12. 1996 Genome Mapping and Sequencing Meeting; Cold Spring Harbor, NY [CSHL, 516/367-8346, Fax: -8845, *meetings@cshl.org, http://www.cshl.org*]

20–21. NIH Natl. Advisory Council for Human Genome Res.; Washington, DC [see contact: Feb. 5–6]

Training Calendar*

November 1995

15-25. DNA Sequencing: Adv. Approaches, Automated Methods, and Analysis; EMBL, Heidelberg, Germany [W. Ansorge, +49-6221/387-355, Fax: -306, *ansorge@embl-heidelberg.de*]

December 1995

4-5. GDB/OMIM and Genomic Data on the Internet; Baltimore [see p.9]

6-8. **Computer-Assisted Molecular Design Course; San Francisco (early reg.: Sept. 1) [N. MacKenzie, 415/476-1913, Fax: /502-4690, *nlmk@cgl.ucsf.edu, http://mdi.ucsf.edu*]

January 1996

8-12. **Advanced Linkage Course; New York [K. Montague, 212/960-2507, Fax: /568-2750, *km165@columbia.edu, http://linkage.cpmc.columbia.edu*]

Extended calendars and a list of organizations offering training are available at *http://www.ornl.gov/TechResources/Human_Genome/home.html* or from HGMIS (see p. 8 for contact information).

For Your Information

☛ Software, Database Resources

Stanford University

CENSOR Software. Jerzy Jurka and Paul Klonowski (Stanford University) have added CENSOR software to the Pythia program developed by Aleksander Milosavljevic (Argonne National Laboratory) and Jurka. This addition should speed up and facilitate identification, analysis, annotation, and removal (censoring) of repetitive DNA from sequences. To run online CENSOR, send *help* message to *pythia@anl.gov*. The original software is available from the National Center for Biotechnology Information (NCBI, *ftp://ncbi.nlm.nih.gov/repository/repbase/software*).

Repbase. The Repbase database for screening human repetitive DNA sequences was published and released electronically in 1992 with DOE support. Reference collections by Jurka's group now contain 434 prototypic examples and consensus sequences for rodents, other mammals, nonmammalian vertebrates, invertebrates, and plants. Only the human reference collection is being updated regularly. In addition to complex repeats, the group has compiled the 67 most abundant simple repeats and, with NCBI support, 38 collections of known repeats present but not necessarily annotated in GenBank primate sequences. Repbase is accessed through the NCBI address above. Jurka (*jurka@gnomic.stanford.edu*) would like to receive user comments on CENSOR and Repbase.◊

Jackson Laboratory

The following two resources are supported by NCHGR through a grant to Janan Eppig. [Information: Mouse Genome Informatics User Support (207/288-6445, *mgi-help@informatics.jax.org*)]

Encyclopedia of the Mouse Genome. The *Encyclopedia of the Mouse Genome*—a software tool that provides a graphic display of mouse chromosome maps—runs on a Macintosh, Sun, or DEC Alpha workstation. Data files include the most current Chromosome Committee reports and Massachusetts Institute of Technology mouse genetic maps. The encyclopedia can also interact with the Mouse Genome Database (MGD).

Current versions of the software (1.0A13 for Macintosh, 3.0A2 for UNIX) and data files can be downloaded from WWW using the "Encyclopedia of the Mouse Genome" link on the Mouse Genome Informatics Home Page (*http://www.informatics.jax.org*). Instructions are also provided to configure Netscape and Mosaic for MGD and encyclopedia interaction.

MGD. (*http://www.informatics.jax.org*) and a mirror site for the European research community (*http://mgd.hgmp.mrc.ac.uk*) are now available on WWW. Improvements in Release 2.0 include a PostScript map tool for making printouts of mouse genetic maps; an option to view composite data sets for recombinant inbred strains; and access to Michael Festing's (University of Leicester, U.K.) "Listing of Inbred Strains."

In addition, changes to MGD query forms include a banner at the top of each form providing "buttons" for easier navigation within MGD. The Mammalian Homology query form has been redesigned, and the fields "Modification Date" and "Accession number" have been added to several query forms. Bibliographic records now include abstracts, if available, and the Citations query form includes an "Abstract" field to search for citations containing specified text in the abstracts. Finally, the Mouse Genetic Marker Information query form enables users to specify a "Type" of marker or to search by "Cytogenetic Band" location. ◊

U.S. Genome Research Funding

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

NIH National Center for Human Genome Research (NCHGR)

Program announcements listed in *NIH Guide for Grants and Contracts* (*gopher.nih.gov* and *http://www.nih.gov* or 301/496-0844). Bracketed numbers below refer to application due dates.
[1] February 1, June 1, and October 1;
[2] April 5, August 5, and December 5;
[3] May 10; [4] on a continuous basis; and
[5] May 1 and November 15.

Program Categories

Research

- Ethical, legal, and social implications (ELSI) of human genome research, Fellowships (PA 92-21) [1].
- Genome science and technology centers (PAR 94-044) [1].
- Informatics (PA 92-59) [1].
- New and improved technologies for genomic research and analysis (PA 94-045) [1].
- Pilot projects or feasibility studies for genomic analysis (PAR 94-046) [1].

Training

- Courses related to genomic analysis (PA 91-88) [1].
- Individual postdoctoral and senior fellowships in genomic analysis and technology (PA 92-21) [2].
- National research service awards:
  - Institutional training grants in genomic science for predoctoral and postdoctoral trainees (PA 94-085) [3].
  - Individual predoctoral student fellowships for disabled (PA 95-028) [5] and minorities (PA 95-029) [5].
- Special emphasis research career awards in genomic research (PA 91-89) [1].

Special Programs

- Minority institution travel awards (PA 91-17) [4].
- Research supplements for underrepresented minorities and disabled [4].

NCHGR: 301/496-7531, Fax: /480-2770

- ELSI: *Elizabeth_Thomson@nih.gov* or 301/402-4997.
- Genetic linkage mapping, annotation, and single-chromosome workshops: *Elise_Feingold@nih.gov*
- Informatics: *David_Benton@nih.gov*
- Large-scale mapping, sequencing of human and mouse genomes: *Jeff_Schloss@nih.gov* or *Jane_Peterson@nih.gov*
- Physical mapping technology, training, and special programs: *Bettie_Graham@nih.gov*
- Sequencing technology development, technology transfer, nonmammalian model organisms: *Carol_Dahl@nih.gov* or *Robert_Strausberg@nih.gov*

DOE Office of Health and Environmental Research (OHER) Human Genome Program

- Contact for funding information or general inquiries: *genome@er.doe.gov* or 301/903-6488.
- Relevant documents: *http://www.er.doe.gov/production/oher/hug_top.html*

Alexander Hollaender Distinguished Postdoctoral Fellowships

Research opportunities in energy-related life, biomedical, and environmental sciences, including human genome, global change, and supporting disciplines.
Next deadline: January 15, 1996

- Contact: Barbara Dorsey, Oak Ridge Institute for Science and Education (615/576-9975, Fax: /241-5219)

Small Business Innovation Research (SBIR) Grants

DOE and NIH invite small business firms (less than 500 employees) to submit grant applications addressing the human genome topic of SBIR programs. The two agencies also support the Small Business Technology Transfer (STTR) program to foster transfers between research institutions and small businesses. Contacts:

- Kay Etzler; c/o SBIR Program Manager, ER-16; DOE; Washington, DC 20585 (301/903-5867, Fax: -5488). DOE SBIR due March 1, 1996; STTR, early 1996.
- Bettie Graham (see contact, NCHGR). NIH SBIR due April 15, August 15, and December 15. STTR, December 1.

National SBIR/STTR conferences: Salt Lake City, UT (October 30–November 1); Dallas, TX (April 29–May 1, 1996). Conference hotline: 407/791-0720; electronic registration: 203/379-9427.◊

EUCIB Database on WWW

The European Collaborative Interspecific Backcross (EUCIB) provides resources for a high-resolution genetic map that will form the basis for constructing a complete physical map of the mouse genome. The MBx database, which supports the mapping effort by storing mouse, locus, and probe data, is now available on WWW (*http://www.hgmp.mrc.ac.uk/MBx/MBxHomepage.html*).◊

Chromosome 19 SCW Interest Sought

Keith Johnson (University of Glasgow) would like to hear from anyone interested in participating in a Chromosome 19 workshop in spring 1996 (+44-141/330-5101, Fax: -4877, *gbga98@udcf.gla.ac.uk*).◊

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3. ___ DOE *Human Genome 1993 Program Report* DOE *Primer on Molecular Genetics* (see *http://www.gdb.org/Dan/DOE/intro.html*)

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SELECTED ACRONYMS

AACC Am. Assoc. for Clinical Chem.
AACR Am. Assoc. for Cancer Res.
AAI Am. Assoc. of Immunologists
ACMG Am. Coll. of Medical Genet.
AFIP/ARP Armed Forces Inst. of Pathol./Am. Registry of Pathol.
AMIA Am. Med. Informatics Assoc.
ASBMB Am. Soc. for Biochem. & Mol. Biol.
ASCB Am. Soc. for Cell Biol.
ASHG Am. Soc. for Hum. Genet.
ASIP Am. Soc. for Investigative Pathologists
BAC bacterial artificial chromosome
BIO Biotechnology Industry Organization
CHI Cambridge Healthtech Inst.
CSHL Cold Spring Harbor Lab.
EMBL European Mol. Biol. Lab.
EST expressed sequence tag
FASEB Fed. of Am. Soc. for Exptl. Biol.
GDB/OMIM Genome Data Base/Online *Mendelian Inheritance in Man*
GRC Gordon Res. Conf.
HGM Human Genome Meeting
HGP Human Genome Project
HUGO Hum. Genome Org.
IBC Intl. Bus. Communications
IBEX Intl. Biotechnol. Expo
LTI Life Technologies, Inc.
MBWS Miami Bio/Technol. Winter Symp.
MOD March of Dimes
OHER Office of Health and Environmental Research
PAC P1 artificial chromosome
STS sequence tagged site
TIGR/NIST The Inst. for Genome Res./Natl. Inst. of Standards and Technol.
USDA U.S. Department of Agriculture
WWW World Wide Web
YAC yeast artificial chromosome

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