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DOE Ethical, Legal, and Social Issues Program Enters Its Third Year

Daniel Drell, DOE Office of Health and Environmental Research

In a significant departure from other previous large-scale scientific undertakings, the U.S. Human Genome Project specifically supports studies on ethical, legal, and social issues (ELSI) that can arise from the increasing availability of genetic information about individuals and populations. The decision to establish the DOE ELSI program, which is now in its third year, was spurred by the early realization that while human genome research itself does not pose any new ethical questions, use of the research data could raise very challenging issues. Among these issues are the ability to predict future disorders before any therapies or interventions are available; the privacy and confidentiality of genetic information with respect to employers, insurers, and others; and the possible misuse of genetic information for discriminatory purposes.

Studies Focus on Privacy

The DOE ELSI program, a complement to the program managed by the NIH National Center for Human Genome Research (NCHGR), focuses on the privacy and confidentiality of genetic information; this area includes the role of computers in assembling, storing, organizing, and manipulating genetic data. With NCHGR, DOE also seeks to educate the public in the use of genetic knowledge for informed decision making. During the past 2 years, the DOE Office of Health and Environmental Research (OHER) has spent more than 3% of its genome budget on the ELSI program.

An important feature of the U.S. Human Genome Project is the close cooperation and coordination between the DOE and NCHGR ELSI programs. As part of this collaboration, the first joint DOE-NIH ELSI grantee workshop will be held September 14–16 in Arlington, Virginia (see p. 3 for contact information).

Other collaborative activities include a major 2-year study conducted by the National Academy of Sciences Institute of Medicine on "Assessing Genetic Risks"; this research is expected to result in a report early in 1993. DOE and NIH are also working together on studies to (1) explore differences among state-supported genetic testing, screening, and counseling programs and (2) compare the use of genetic screening services and

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OHER Study To Assess Genetic Discrimination

genetic information in two communities with contrasting disease susceptibilities. Two additional cooperative ELSI activities are the National Study Conference on Genetics, Religion, and Ethics (convened in March in Houston, Texas) and a public television series, "Medicine at the Crossroads," produced by WNET/Thirteen in New York and scheduled for broadcast late this year.

OHER is supporting a study to assess the significance of genetic discrimination in various settings such as schools and workplaces. Repeated public meetings, congressional hearings, and a diversity of publications have indicated that the possibility of discrimination is one of the principal fears associated with the wider availability of genetic knowledge. A second investigation focuses on legal protections already available for genetic information, balancing public-health needs with respect for individual privacy.

In education, an area of great importance to OHER, two new projects are being started:

- Science teachers will participate in special workshops on genetics and its ELSI implications so that these teachers may become resources for further educational efforts in their communities. This work builds on an earlier OHER-funded project of the Biological Sciences Curriculum Study Group, which is preparing an educational module on genetics for all the estimated 55,000 high school science teachers in the United States.
- The WGBH Educational Foundation is receiving support to produce "The Secret of Life," a public television series scheduled for broadcast in 1993.

In the coming year, OHER will continue to refine the focus of its ELSI program toward the privacy and confidentiality of genetic information, emphasize education, and collaborate closely with NCHGR to avoid unnecessary duplication of effort. While important ELSI concerns accompany the Human Genome Project, the primary aim remains the enhanced health and well-being of each individual. The ELSI challenge is to conduct this effort as wisely and carefully as possible. ◊

ELSI Resources Available at LANL

A collection of resources on ethical, legal, and social issues (ELSI) related to the Human Genome Project is available at Los Alamos National Laboratory (LANL). Compiled by Michael Yesley over a 3-year period, these resources include a bibliography, a computer search service, and a collection of listed ELSI materials maintained at the General Law Library at LANL. Yesley, a staff attorney, conducts an ELSI program at the LANL Center for Human Genome Studies and assists in the administration of the DOE ELSI program.

The bibliography is a computer database of more than 2600 relevant scholarly and general books and articles identified for the LANL collection. The database also contains information such as keywords, multiple authors, and other names mentioned in the documents. Entries, which are generally limited at present to materials published in English, cover such topics as genetic privacy and discrimination in various settings; provision of genetic diagnosis and therapy; eugenics; genetic issues in reproduction; genetic counseling; Human Genome Project politics and administration; and commentary on legal questions, including intellectual property and forensics.

The materials can be selected rapidly and sorted according to a variety of parameters, such as chronological, alphabetical, topical, or any combination. Researchers are invited to use the ELSI collection by appointment at the LANL General Law Library. Requests for sorts and selections should be made to

- Michael R. Roth (Internet: "roth_michael_r@ofvax.lanl.gov") or Michael S. Yesley ("yesley_michael_s@ofvax.lanl.gov"); MS A187; Los Alamos National Laboratory; Los Alamos, NM 87545; 505/667-3766; Fax: 505/665-4424. ◊

¶ ELSI-Related Publication

AAAS, ABA Report Explores Ethical, Legal Aspects of Genetic Testing

The Genome, Ethics, and the Law: Issues in Genetic Testing is the report of a conference held at Berkeley Springs, West Virginia, on June 14–16, 1991, to explore the ethical and legal implications of advances in genetic testing. The papers in the book were presented at the meeting, which was cosponsored by the National Center for Human Genome Research and attended by scientists, ethicists, lawyers, health professionals, and representatives of other interested groups (e.g., the insurance industry and genetic disease associations). The report and the conference are part of a 2-year project of the National Conference of Lawyers and Scientists of the American Association for the Advancement of Science (AAAS) and American Bar Association (ABA) and the AAAS Committee on Scientific Freedoms and Responsibility. Free. [Contact: AAAS; 1333 H Street NW; Washington, DC 20005; 202/326-6600.] ◊

NIH-DOE Joint ELSI Working Group Holds First Public Forum

ELSI Insurance Task Force, Grantee Workshop, Other Activities Highlighted

Public Forum

The NIH-DOE Joint Working Group on Ethical, Legal, and Social Issues (ELSI) in human genome research held its first public forum on April 21 in Iowa City, Iowa. University of Iowa faculty members provided background information on genetics and the health and health policy implications of the Human Genome Project.

Genetics professionals and representatives of the public presented testimony; speakers included members of families affected by genetic disorders, state genetics coordinators, clinical genetics services providers, and clergy. Working group members were impressed by the breadth and depth of the testimony and discussion on providing access to and delivering genetic services, the need to protect the privacy of genetic information, and the risk of discrimination on the basis of genotype. Many speakers stressed the importance of involving affected families in ELSI program activities.

Task Force on Genetics and Insurance

The ELSI Task Force on Genetics and Insurance met March 23–24 and again May 31–June 1. At the March meeting, a subgroup charged with addressing alleged cases of insurance discrimination presented a series of background papers. The task force discussed state insurance regulations with a California State Insurance Commissioner's staff member and with experts in employment discrimination law and self-insured corporate benefit plans.

At the May 31–June 1 meeting the Insurance Task Force identified areas for further consideration. A subcommittee was formed to investigate the flow of genetic test information to insurance companies. Another group will study the nature of adverse selection, which occurs when applicants know they will become ill from a genetic disorder but conceal the test results and purchase large amounts of health insurance at a low premium. Although industry-wide actuarial data has taken into account the incidence of genetic conditions in the population, insurance companies maintain that adverse selection causes higher-than-expected claims payments. The insurance industry cites adverse selection in reserving the right to examine the results of applicants' genetic tests.

The Insurance Task Force drafted an outline for its final report, slated for May 1993, which will address many of these concerns.

Subcommittee reports will be heard at the next task force meeting, to be held in conjunction with the American Society of Human Genetics conference in San Francisco, November 9–10.

ELSI Grantee Workshop

The first NIH and DOE ELSI grantee workshop will be held on September 14–16 at the Radisson Mark Plaza Hotel in Arlington, Virginia. Attendance by all grantees is strongly encouraged. (Contact for workshop: Elinor Langfelder; see side column.)

NIH Cystic Fibrosis (CF) Studies Consortium

The NIH Cystic Fibrosis Studies Consortium, which was formed to foster cooperation among the eight CF investigative groups coordinated by NCHGR, met June 2–3. Discussions continued on informed consent, standardization of psychological measurement tools, and laboratory quality-control measures. The principal investigators of each of the eight cystic fibrosis testing and counseling studies reported on their progress in planning and developing educational materials and recruitment strategies. [See *HGN* **3**(5), 1–2 (January 1992).] ◊

Reported by Elinor J. Langfelder
ELSI Branch, NCHGR

Copies of the written testimony at the public forum are available on request from the National Center for Human Genome Research (NCHGR).

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- **Elinor J. Langfelder**
  NIH NCHGR
  ELSI Branch
  Bldg. 38A, Rm. 617
  9000 Rockville Pike
  Bethesda, Md 20892
  301/402-0911
  Fax: 301/480-2770

Grantee Attendance at Workshop Is Strongly Encouraged

¶ ELSI-Related Publication

ELSI Seminar Series Essays Available

NCHGR cofunded a seminar series at the California Institute of Technology (Cal Tech) that addressed scientific and ELSI topics such as the social power of genetic information, DNA fingerprinting, informatics, and eugenics. *The Code of Codes: Scientific and Social Issues in the Human Genome Project,* edited by Daniel J. Kevles and Leroy Hood (Cal Tech), is a collection of essays by seminar participants. $29.95. (Available in bookstores or from Harvard University Press; 79 Garden Street; Cambridge, MA 02138-1499; 617/495-2480.) ◊

Genome News

Eric Juengst
Acting Director
NCHGR ELSI Branch

Healy Elevates NCHGR ELSI Program To Branch Status

The NIH Ethical, Legal, and Social Implications (ELSI) program of the National Center for Human Genome Research (NCHGR) was officially elevated to branch status on June 11 when NIH Director Bernadine Healy signed the *Federal Register* notice announcing the change. Eric Juengst was appointed Acting Chief of the ELSI Branch by NCHGR Acting Director Michael Gottesman. Juengst has served as Director of the ELSI program since it was first set up within the NCHGR Research Grants Branch.

This organizational change is expected to allow NCHGR to define explicitly the responsibilities of the ELSI program and its roles in carrying out the NCHGR mission. The ELSI Branch will have the following functions:

- Advise the NCHGR Director and Deputy Director on ethical, legal, and social implications of the NIH Human Genome Program and represent the directors at meetings where ethical concerns are discussed.
- Develop recommendations, guidelines, and policy options for the orderly introduction of information generated by human genome research into biomedical practice.
- Manage a portfolio of ELSI grants and develop requests for applications and program announcements focusing on the ELSI portion of the NIH Human Genome Program.
- Provide staff support for the ELSI Working Group of the NIH-DOE Joint Subcommittee on the Human Genome.
- Coordinate ELSI policy development with the NIH Science Policy Studies Center.
- Avoid duplication of effort by coordinating grant awards with agencies such as the National Endowment for the Humanities, the National Science Foundation, and DOE.
- Consult with other NIH programs regarding the ethical, legal, and social aspects of human genetics research. ◇

¶ ELSI-Related Publications

NRC Report Assesses DNA Typing Identification

The National Research Council Board on Biology recently released its report, funded in part by the NCHGR ELSI program, on the use of DNA fingerprinting in forensic science. *DNA Technology in Forensic Science* deals with questions regarding the applicability and appropriateness of DNA typing in personal identification. $24.95 plus $3 shipping. [National Academy Press; 2101 Constitution Ave. NW; Washington, DC 20418; 800/624-6242; in Washington area: 202/334-3313.] ◇

House Report Recommends Policy Commission for U.S. Human Genome Project

The House Committee on Government Operations has developed a report recommending the establishment of a federally chartered advisory commission to make ELSI policy for the U.S. Human Genome Project. Copies of *Designing Genetic Information Policy: The Need for an Independent Policy Review of the Ethical, Legal, and Social Implications of the Human Genome Project* (#102-478) are available free. [Contact: House Documents Room; Annex 2, Room B18; U.S. House of Representatives; Washington, DC 20515-6622; 202/225-3456.] ◇

OTA Surveys Genetic Screening in the Workplace

Medical Monitoring and Screening in the Workplace: Results of a Survey (1991), an 84-page background paper from the Office of Technology Assessment (OTA), draws upon the results of a 1989 survey about corporate practices and policies in medical and genetic monitoring and screening. The survey gathered information from chief health and personnel officers of 1500 U.S. companies, the 50 largest utilities, and the 33 largest labor unions.

Topics included applicants' health-insurance risk as a factor in hiring, periodic testing of employees who work in settings with known health risks, types and cost-effectiveness of examinations, accessibility to test findings, and employee rights in relation to genetic screening.

This paper focuses on data not presented in the 1990 OTA paper *Genetic Monitoring and Screening in the Workplace*, which was also compiled from the 1989 survey. OTA emphasizes that the survey does not address the question of whether genetic monitoring and screening are currently being used to determine eligibility for health insurance. $4.50. (Noncongressional users: Superintendent of Documents; U.S. Government Printing Office; Washington, DC 20402-9325; 202/783-3238. Congressional users: call 4-9241.) ◇

Genome News

New Mouse Chromosome Map Promises To Speed Gene Discoveries

Investigators reported in the June issue of *Genetics* the development of a new genetic map comprising easy-to-use markers on each mouse chromosome [*Genetics* **131**(2), 423–47 (June 1992)]. This accomplishment, supported by the NIH National Center for Human Genome Research, will greatly reduce the time required to identify and isolate mouse genes implicated in polygenic diseases such as cancer, diabetes, high blood pressure, and other inherited disorders. Because of extensive and well-characterized synteny maps between mouse and human, the map will help researchers find comparable human disease genes.

The new map, which consists of 317 markers spaced evenly along the 20 pairs of mouse chromosomes, was constructed by investigators from the Massachusetts Institute of Technology (MIT) Genome Center, the Whitehead Institute for Biomedical Research, and Rockefeller University. All the work was accomplished by two researchers in less than 18 months.

The markers used to construct the new map are a type of highly repetitive DNA sequence (simple sequence repeat, or SSR) that frequently varies in length, allowing investigators to track the inheritance of genes from one generation to the next.

According to the *Genetics* article, the new map satisfies criteria for the ideal genetic map, which should consist of markers that are (1) abundant and evenly distributed throughout the genome, (2) highly variable among individuals, (3) easy to trace, and (4) accessible to all scientists interested in using them. Eric Lander, Director of the MIT Genome Center, explains that variability, particularly among inbred strains where genetic differences are subtle, is especially important.

"Conventional mapping techniques are extremely powerful" in following linked traits in mouse strains that vary a great deal, says Lander, but the more the strains are related through inbreeding, the more difficult it becomes to follow linked traits with conventional methods. With coauthor William Dietrich, Lander and colleagues report that analysis of crosses between two inbred mouse strains reveals differences in SSR lengths at about half the marker positions, allowing inheritance in almost any cross to be followed in a straightforward manner.

Other advantages of the new map include

- identification of SSRs by the polymerase chain reaction (PCR), which – unlike conventional mapping techniques – is fairly easy to automate, and
- simple dissemination of genetic markers via publication of the short DNA sequences that flank each SSR. With these primers "in hand," an investigator can easily generate a marker of interest using PCR methods.

Markers on the new map will be "anchored" to those on the previous linkage maps; investigators will then be able to use SSRs to locate additional genes in the region in which they have already been working. The new map will thus provide a backbone for developing a much more detailed linkage map containing as many as 3000 SSR markers. ◇

Reported by Eve Nichols
Whitehead Institute for Biomedical Research
and
Leslie Fink
Office of Communications
NIH NCHGR

Marker Map To Aid in Finding Comparable Human Genes

All the markers will soon be available from

- Research Genetics
  2130 Memorial Parkway SW
  Huntsville, AL 35801
  800/533-4363
  Fax: 205/536-9016

For more information on the markers, see *HGN* 4(1), 3 (May 1992).

For more information on the map, contact:

- Eve Nichols
  617/258-5183
  Fax: 617/258-5061

¶ Journal Offers Mouse Reference Tool

Encyclopedia of the Mouse Genome I is a companion reference tool to the journal *Mammalian Genome*. The encyclopedia contains 532 pages of maps and commentaries, extensive genetic linkage information, summaries of cytogenetic data, mouse DNA clones and probes, the mouse map of paralogous genes, and a comparative mouse-human map. 1991. $49 separately; free with new personal subscription to journal. (Springer-Verlag New York, Inc.; Attn: Dean Smith; 175 Fifth Ave., New York, NY 10010; 212/460-1500 or 800/777-4643.) ◇

Reference Collection of Repetitive Sequences

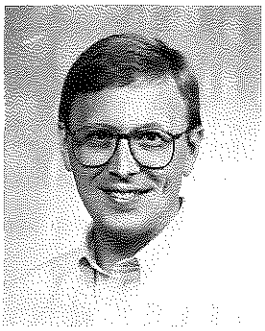
A reference collection of human repetitive elements, containing 53 "prototypic sequences" for each of the repetitive families discovered so far, has been compiled by Jerzy Jurka (Linus Pauling Institute). The collection is from DOE-sponsored studies in identification and analysis of novel families of repetitive elements. The prototypic sequences are published consensus sequences where possible or other representative sequences for families for which consensus sequences are unavailable. They represent high- and medium-reiteration-frequency interspersed repeats, long terminal repeats of endogenous retroviruses, alphoid repeats, telomere-associated repeats, and some miscellaneous repeats.

Specific information on the collection can be obtained now from "jurka@jmullins.stanford.edu", Fax: 415/327-8564. Later this year the collection will be deposited at the National Center for Biotechnology Information (NCBI) and other public-domain servers. (NCBI contact: 301/496-2475, Fax: 301/480-9241, Internet: "info@ncbi.nlm.nih.gov".) Reference: J. Jurka, J. Walichiewicz, and A. Milosavljevic, *J. Mol. Evol.*, in press. ◇

Genome News

Alu PCR: The Origins

By David L. Nelson



David L. Nelson
Associate Director
Human Genome Center
Baylor College of Medicine

This article is a personal account of events leading to the development of a technique for specifically identifying and amplifying only the human DNA sequences in hybrid cells and in yeast artificial chromosome (YAC), lambda, and cosmid clones. The author describes how insight and a bit of serendipity led to a creative application of the standard polymerase chain reaction (PCR) method, a procedure used to amplify a desired DNA sequence hundreds of millions of times in a matter of hours. *Alu* PCR, the application devised by Nelson and others, amplifies target sequences falling between segments of DNA that are repeated throughout the human genome. The *Alu* family of repetitive DNA sequences involves 150- to 300-bp segments containing sequence similarities, including a tetranucleotide that can be cleaved by the restriction enzyme *Alu* I. *Alu* repeats constitute nearly 10% of the total human genome.

Alu PCR was originally intended as a technique for identifying human DNA in human-rodent hybrid cells for a proposed reference human genome library. It has proved, however, to be an efficient approach to generating probes from laser microdissected or flow-sorted chromosomal regions. In addition, *Alu* PCR has facilitated clone ordering based on analysis of PCR patterns, thus making the identification of contiguous clones more efficient; this use has been extended to chromosome walking and expansion of established contigs. The use of PCR primers directed toward repeated DNA sequences has now been extended to include other repeated sequences and combinations of different types of repeated sequences.◊

—D. Casey, HGMIS

Alu PCR had its origins in January 1987 in Santa Fe, New Mexico, at one of the first meetings* on the Human Genome Project. Walter Gilbert, a keynote speaker, proposed something quite provocative: the development of a reference genome on which all investigators would work. This would allow sequence determination of a particular human genome rather than that of a hodgepodge collection of DNA samples produced by the preparation of recombinant libraries and cell lines.

Gilbert also suggested that the best genome for this purpose would be haploid; only one copy of each chromosome (and gene) would be represented, thus eliminating polymorphic variation between chromosomes. He recommended growing large quantities of a haploid tumor (an ovarian teratoma—I don't remember what was to become of the Y chromosome) and distributing the DNA to all genome researchers.

Gilbert's suggestion to begin anew in constructing chromosomal resources was unsettling. Having worked with David Housman [Massachusetts Institute of Technology (MIT)] as a graduate student, I was well schooled in the usefulness of somatic cell hybrid resources and was not ready to shelve them. (Somatic cell hybrids are produced by fusing together human and rodent cells. The preferential loss of human chromosomes during this process results in a hybrid cell with one to a few specific human chromosomes.) Using a standard cell lin eto reinvent all the hybrids and then isolating chromosome-specific sequences would be an arduous task.

My thoughts turned instead to the possibility of using the existing hybrids to identify clones in Gilbert's new reference library. I recalled a talk that Kary Mullis had given a month before at Baylor College of Medicine about PCR, which was then a new method on which Mullis had been working at Cetus Corporation. After Mullis's talk many of us spent inordinate amounts of time dreaming of new PCR applications.

"After Mullis's talk many of us spent inordinate amounts of time dreaming of new PCR applications."

This "PCR fever" generated many ideas that became reality at Baylor and elsewhere over the next couple of years. However, it took the trip to Santa Fe and Gilbert's talk to prompt me to consider *Alu* PCR. The question was simple: Was there a way to amplify only the human DNA in the hybrid cells to produce probes specific for human sequences? Having had extensive experience with the method developed by Housman and Jim Gusella (MIT) using human repeat sequences to identify specific human clones from hybrid cell libraries, I began to wonder whether the *Alu* repeat (the most common of the short interspersed repeat sequences) could be used to amplify only human sequences. Various schemes came to mind, most of them very convoluted and requiring vector sequence ligation to provide the second primer site for PCR. Amplifying the area between *Alu* repeats didn't occur to me until later.

On my return to Houston, I began to design primers for amplifying the target sequences ⇒

**"Exploring the Role of Robotics and Automation in Decoding the Human Genome" was held January 6–9, 1987, in Santa Fe, New Mexico.*

by PCR, gathering all the *Alu* repeats I could identify from the GenBank® sequence database and looking for regions of high homology between copies of human *Alu*. At first I paid no attention to the rodent *Alu*-equivalent sequences, assuming that since they did not cross-react in probe hybridization, they would not cross-amplify in PCR. When this assumption turned out to be wrong, I used a region unique to primate sequences that did not amplify rodent equivalents. Because we had no local oligonucleotide facility, I ordered the first *Alu* primer [designated TC (Tom Caskey)-65] from the central Howard Hughes Medical Institute facility in Boston.

"I realized just how lucky our first efforts had been, since without this initial success I probably would not have pursued further development of the method."

TC-65 arrived in about a month but remained in the freezer for over a year until PCR technology improved enough through the use of *Taq* polymerase and automated thermal cycling that I was finally ready to try it. Before those improvements, use of the Klenow fragment (a DNA polymerase) and manual shifting of tubes between water baths demanded too much bench bondage. In June 1988 our first try with the new protocol was rewarded—TC-65 provided human-specific amplification in hybrid cells. When most of the next primers I designed did not perform as well (because of cross-amplification with rodent sequences), I realized just how lucky our first efforts had been, since without this initial success I probably would not have pursued further development of the method.

By spring 1989 we had a very nice system for amplifying human sequences from hybrids and had begun to use it for cloned DNA as well. In April I presented a poster on our results at the second Cold Spring Harbor Genome Mapping and Sequencing meeting. To my surprise, Pieter de Jong of Lawrence Livermore National Laboratory presented a poster with very similar results. Later I learned that others had been working out similar primers directed to *Alu* for the same purpose, including Bryan Young [Imperial Cancer Research Fund (ICRF)] and Paul Goodfellow (University of British Columbia).

Today, use of *Alu* PCR and its variants has become standard practice for genomicists. Its usefulness as a specific identifier of human sequences extends from hybrid cells to YACs to clones in lambda and cosmid. It is also gratifying to see that the use I had originally envisaged is finally coming to fruition. The ability to use hybrid cell lines to probe "reference" libraries is demonstrated by the work of Tony Monaco (ICRF) and of Daniel Cohen's group at the Centre d'Etude du Polymorphisme Humain and Genethon; these researchers have identified chromosome- and region-specific YAC and cosmid clones by hybridization to *Alu* PCR products derived from somatic cell hybrids.

So, while Gilbert's idea of ovarian teratomas never caught on, the difficulty involved in producing high-quality YAC libraries (i.e., those having large-insert clones and a small number of chimeric clones) has made necessary the screening of a few "reference" genomes. Dissection of these total human libraries into chromosome- and region-specific sublibraries using somatic cell hybrids and *Alu* PCR is now a reality, and more interesting applications of PCR (and *Alu* PCR) are doubtless on the way. ◇

For more information on this topic, refer to

D. L. Nelson, S. A. Ledbetter, L. Corbo, M. F. Victoria, R. Ramirez-Solis, T. Webster, D. H. Ledbetter, and C. T. Caskey. "*Alu* Polymerase Chain Reaction: A Method for Rapid Isolation of Human Specific Sequences from Complex DNA Sources." *Proc. Natl. Acad. Sci. USA* **86**, 6686–90 (1989).

C. Breukel, J. Wijnen, C. Tops, H. v/d Klift, H. Dauwerse, and P. Meera Khan. "Vector-*Alu* PCR: A Rapid Step in Mapping Cosmids and YACs." *Nucleic Acids Res.* **18**(10), 3097 (1990).

A. R. Brooks-Wilson, P. N. Goodfellow, S. Povey, H. A. Nevanlinna, P. J. de Jong, and P. J. Goodfellow. "Rapid Cloning and Characterization of New Chromosome 10 DNA Markers by *Alu* Element-Mediated PCR." *Genomics* **7**, 614–20 (1990).

F. E. Cotter, G. M. Hampton, S. Nasipuri, W. F. Bodmer, and B. D. Young. "Rapid Isolation of Human Chromosome-Specific DNA Probes from a Somatic Cell Hybrid." *Genomics* **7**, 257–63 (1990).

S. A. Ledbetter, D. L. Nelson, S. T. Warren, and D. H. Ledbetter. "Rapid Isolation of DNA Probes Within Specific Chromosome Regions by Interspersed Repetitive Sequence Polymerase Chain Reaction." *Genomics* **6**, 475–81 (1990).

A. P. Monaco, V. M. Lam, G. Zehetner, G. G. Lennon, C. Douglas, D. Nizetic, P. N. Goodfellow, and H. Lehrach. "Mapping Irradiation Hybrids to Cosmid and Yeast Artificial Chromosome Libraries by Direct Hybridization of *Alu*-PCR Products." *Nucleic Acids Res.* **19**(12), 3315–18 (1991).

D. L. Nelson, "Interspersed Repetitive Sequence Polymerase Chain Reaction (IRS PCR) for Generation of Human DNA Fragments from Complex Sources." *Methods: A Companion to Methods in Enzymology* **2**(1), 60–74 (1991).

I. M. Chumakov, I. Le Gall, A. Billault, P. Ougen, P. Soularue, S. Guillou, P. Rigault, H. Bui, M-F. De Tand, E. Barillot, H. Abderrahim, D. Cherif, R. Berger, D. Le Paslier, and D. Cohen. "Isolation of Chromosome 21–Specific Yeast Artificial Chromosomes from a Total Human Genome Library," *Nature Genetics* **1**(3), 222–25 (1992).

David L. Nelson is Associate Director for the Human Genome Center, Baylor College of Medicine, where his Alu-PCR research was funded by both DOE and NIH. Director of the Baylor genome center is Thomas Caskey.

Genome News

Report Card Summaries for Individual Chromosomes:

- Sequence
- Contigs
- Genes
- Linkage Maps
- STSs

Genome Report Card Summarizes Progress

The Genome Report Card, a summary prepared by the National Center for Human Genome Research (NCHGR), presents an overview of progress made toward the 5-year chromosome mapping and DNA sequencing goals of the U.S. Human Genome Project. The report card is based on data from the GDB™ Human Genome Data Base, GenBank®, and primary publications. Additionally, genetic linkage map information is derived from the Human Genome Mapping Workshop 10 (HGM 10), the Centre d'Etude du Polymorphisme Humain (CEPH), and the NCHGR Index Map project.

The following information is reported for each human chromosome:

- **Sequence.** The total number of kilobase pairs of DNA sequenced is shown in "bins" that represent sequence localized to (1) a single cytogenetic band, (2) a chromosomal region larger than a band but smaller than or equal to a chromosome arm, or (3) the chromosome, but not to a specific arm or band. The total amount of sequence localized to the chromosome and the approximate degree of completion are indicated. The percentage-completed figure is based on an estimate of the total amount of DNA in each chromosome. These data are taken from GDB and GenBank.
- **Contigs (if available).** Published overlapping clone contigs of 1 Mb or more or ordered sets of contigs essentially covering a chromosomal region of 1 Mb or more are diagramed. The total length of contigs localized to the chromosome is shown, and an estimate of the percentage of the chromosome covered by contigs is provided. The percentage-completed figure is based on an estimate of the total amount of DNA in each chromosome. Data are from primary publications.
- **Genes.** Total number of mapped genes is shown. The percentage-completed number is based on an estimate of 100,000 genes in the human genome and assumes that genes are distributed proportionate to chromosome length. Data are from GDB.
- **Linkage maps (if available).** Sex-averaged linkage maps are shown. CEPH consortium maps are as published; index maps are as

(see Report Card, p. 9)

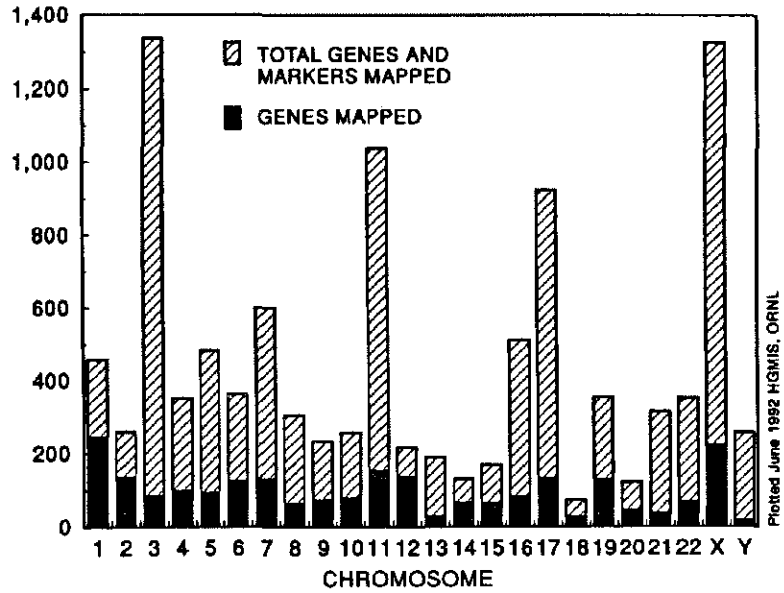
Genome Data Base (GDB) Statistics Show Genes and Markers Mapped*

This figure depicts the total number of genes and markers entered into GDB as of May 1 and assigned to specific chromosomes. Types of markers include D-segments (arbitrary DNA segments of unknown function), fragile sites (points on chromosomes that are seen as breaks or gaps on metaphase preparation), and breakpoints (chromosomal breaks induced by radiation, chemical, or other methods). Current mapping statistics may be obtained from GDB via anonymous FTP by downloading two files:

- loci_chr.<date>.asc
- gdb_obj.<date>.asc.

Date is in the format YYMMDD. To request a guide to FTP access, contact GDB User Support (see box, p. 9).

Data used in preparing this graph are from the GDB™ Human Genome Data Base (database outline); Johns Hopkins University; Baltimore, Maryland. Date cited: May 1, 1992. ◇



*Approximately 3050 genes and markers in GDB have not been assigned to chromosomes.

GDB™ Software Problems, Requests Should Be Directed to User Support

To allow GDB to be more responsive to the needs of the research community, GDB staff requests that users contact User Support directly to

- report software bugs and
- request enhancements.

Communicating with User Support allows GDB to track and solve problems systematically and to process and evaluate suggestions on new features for the system. GDB requests that users be as specific and detailed as possible when reporting bugs or suggesting enhancements, particularly in explaining the usefulness of requested new features. ◊

New Fax Number for GDB

The new fax number for GDB User Support in Baltimore is 410/614-0434.

Report Card *(from p. 8)*

reported to NCHGR by the investigators; HGM 10 maps are those published by the Human Genome Mapping Workshop 10 Linkage Committee; and EUROGEM maps are those published by the EUROGEM consortium. High-resolution and framework maps will be added as they become available.

- **STSs.** All unique anonymous DNA segment markers that can be assayed with polymerase chain reaction primers are included. Data are from GDB.

The March 1992 edition of the Genome Report Card constitutes the information baseline with which future data can be compared to assess progress. (Copies of the booklet are available from Office of Communications; NIH NCHGR; Building 38A, Room 617; Bethesda, MD 20892; 301/402-0911; Fax: 301/480-2770.) ◊

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.

GDB and OMIM Training Course Schedule

Two comprehensive hands-on training courses on the use of GDB and OMIM are being scheduled in Baltimore and other locations:

- The general course for scientific users provides a basic understanding of the databases and the relationships among the different types of data.
- The course for users with editing privileges includes instructions on adding, modifying, and deleting GDB data.

Class frequency and location will be determined by demand (schedule below). Courses are free, but attendees must pay their own travel and lodging expenses. Hotel information and directions will be mailed with registration materials.

As interest in GDB continues to grow, organizations around the world will offer training that requires access to GDB in Baltimore. Notifying GDB User Support about planned training activities will enable the staff to ensure database availability by scheduling maintenance and repairs at other times.

CONTACT FOR GDB USER SUPPORT:
410/955-7058, press 4 after greeting;
Fax: 410/614-0434;
Internet: "help@welch.jhu.edu".

PLANNED EXHIBITIONS

- ASHG, San Francisco, Calif., Nov. 10–12.

Course	Dates
BALTIMORE	
Editing	Sept. 13–15
General User	Sept. 21–22
General User	Nov. 23–24
LONDON (HARROW)	
Editing	Aug. 17–18
Editing	Aug. 19–20
General User	Aug. 21
SAN FRANCISCO	
Editing	Nov. 6–7
General User 1-day course for ASHG meeting attendees	Nov. 8

USER SUPPORT OFFICES

United States

GDB User Support
Welch Medical Library
1830 E. Monument Street,
Third Floor
Baltimore, MD 21205
410/955-7058
Fax: 410/614-0434
Internet:
"help@welch.jhu.edu"

The Help Line is staffed from 9 a.m. to 5 p.m. EST for information on accounts, technical support, data questions, and training courses. 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: 800/736-1130.

United Kingdom

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Meeting Reports

Fifth Cold Spring Harbor Meeting on Genome Mapping and Sequencing

Encouraging Results, Promising Technology Presented

Reports of encouraging results and promising technology were presented May 6-10 at the fifth annual Cold Spring Harbor Laboratory (CSHL) meeting on Genome Mapping and Sequencing. Organized by Richard Myers (University of California, San Francisco), David Porteous (Western General Hospital, U.K.), and Richard Roberts (CSHL), the workshop featured descriptions of advances in sequencing and mapping projects on the genomes of a variety of organisms. Progress was presented in several informatics programs that could benefit genome research in any organism.

MIT Reports on Nearly Complete Chromosome Y Map

A highlight of the meeting was the presentation by David Page's group [Massachusetts Institute of Technology (MIT)] of the nearly finished map of the euchromatic segment of the Y chromosome. The strategy used was to retrieve yeast artificial chromosomes (YACs) by sequence-tagged-site content and order them under a panel of chromosome Y deletions.

CEPH Develops Large-Insert YAC Resource

Another important result was presented by Daniel Cohen (Centre d'Etude du Polymorphisme Humain), who announced the development of a library of YAC clones having an average insert size larger than 1.2 Mb. This large-insert YAC resource, which will facilitate rapid expansion of YAC contigs, will be broadly available this fall.

Other mapping efforts are proceeding rapidly:

- physical maps of chromosomes 21, 22, and X are among the most detailed of the human chromosomes;
- nearly 1000 polymorphic markers have been mapped genetically in the mouse by Eric Lander's group at the MIT Genome Center; of these, about 750 are PCR-typable SSLP markers (see article, p. 5); and
- other groups are constructing maps for a number of important organisms, including *Dictyostelium*, *Schizosaccharomyces pombe*, and the dog.

In the realm of sequencing, great progress is being made in the roundworm *Caenorhabditis elegans* and the yeast *Saccharomyces cerevisiae*. The entire sequence of yeast chromosome 3 has been determined. Interestingly, many more genes are being found from the DNA sequence of these organisms than had been predicted from previous genetic and biochemical studies. Automated sequencing is becoming increasingly fast and accurate, and Roberts estimated that megabase sequencing projects at a reasonable cost will soon be possible. Ben Koop of Leroy Hood's team (California Institute of Technology) presented comparisons of sequences of the mouse and human T-cell receptor region.

Several advances in gel-based sequencing technology were reported. A Fourier transform method for identifying and reducing noise from fluorescence signals was described by Bruce Roe (University of Kansas). C. Turmel (Xerox Research Center, Canada) and coworkers have improved fragment band separations in the 500 + base range by implementing pulsed-field techniques. The team led by Wilhelm Ansorge (European Molecular Biology Organization, Heidelburg) is now interrogating DNA fractionation gels with multiple lasers, allowing coincident fractionations of samples with different fluor labels.

The first blind sequencing of DNA by oligonucleotide hybridization methods was announced by Radomir Crkvenjakov and Radoje Drmanac (Argonne National Laboratory). Mitch Eggers (Houston Advanced Research Center) described a design for quantitation of DNA fragments hybridized to oligonucleotide arrays utilizing underlying microelectronics. Progress in the gas-phase suspension of oligonucleotides for use in sequencing by mass spectroscopy was reported in Lloyd Smith's (University of Wisconsin) laboratory.

A session was held on database systems to support mapping projects, and several databases were available for demonstration. The National Center for Biological Information has incorporated the cDNA EST database from the laboratory of Craig Venter (NIH) into a DBEST database, promising several added query services [see *HGN* **3**(6), 17 (May 1992)]. Several strategic applications of sequence interpretation systems were reported. ◊

Reported by Nathaniel C. Comfort
Science Writer
Cold Spring Harbor Laboratory

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

Second International Workshop on Human Chromosome 16

The Second International Workshop on Human Chromosome 16 was held in Adelaide, South Australia, February 26–28 and was attended by 40 participants, including 23 from 7 overseas countries. The meeting was sponsored by NIH, DOE, and the National Health and Medical Research Council of Australia and organized by Ed Hildebrand [Los Alamos National Laboratory (LANL)] and Grant Sutherland [Adelaide Children's Hospital (ACH), Australia].

Physical Mapping

The use of an extensive, recently developed mouse-human somatic cell hybrid panel having an average distance of 1.6 Mb between adjacent breakpoints has greatly increased the resolution of the human chromosome 16 cytogenetic-based physical map. The map includes many Centre d'Etude du Polymorphisme Humain DNA markers, as well as cosmids fingerprinted with repetitive sequences and assembled into contigs by the Los Alamos genome center. Radiation hybrid panels for chromosome 16 have been constructed by Isabella Ceccherini (Instituto G. Gaslini, Genova, Italy) and Michael Siciliano (M. D. Anderson Cancer Center) for mapping and cloning particular regions.

Raymond Stallings and Norman Doggett (LANL) presented data showing that contigs representing 15% of chromosome 16 have now been physically mapped using either the hybrid cell panel or fluorescence in situ hybridization (FISH) techniques [David Ward (Yale University)]. This percentage will increase rapidly as sequence tagged sites are constructed from the contig ends, facilitating somatic cell hybrid panel mapping. Contig gaps will be closed by using yeast artificial chromosomes (YACs) from both total genomic and flow-sorted chromosome 16–specific YAC libraries. The construction of YAC contigs on chromosome 16 is progressing, especially in such areas of biological interest as the genes for polycystic kidney disease (PKD1) and Batten disease (CLN3) and in the vicinity of two fragile sites (FRA16A and FRA16B). Combined use of the somatic cell hybrid panel, cosmid contigs, and YACs provides a powerful approach for cloning or mapping specific chromosomal regions.

Peter Harris (Medical Research Council, Oxford) has now cloned both telomeres of chromosome 16, enabling the extent of the physical maps to be defined.

Genetic Mapping

Helen Kozman (ACH) presented a chromosome 16 genetic map that consists of 62 polymorphic markers, including most of the previously published restriction fragment length polymorphism markers. The sex-averaged map is 162 cM long (131 cM in males, 198 cM in females) and shows excess male recombination at the telomeres and excess female recombination on each side of the centromere.

A number of polymerase chain reaction (PCR)–based $(AC)_n$ microsatellite markers are being incorporated into this genetic map. Marker isolation and high-resolution multipoint mapping are progressing in the vicinity of PKD1 and CLN3, efforts that should allow refined localization and positional cloning of these two disease genes.

John Mulley (ACH) compiled a list of 19 index markers for chromosome 16, including 10 PCR-formatted markers and 10 markers with a heterozygosity greater than 0.7.

Genes

A total of 82 genes have now been located on chromosome 16, with 8 new assignments since HGM 11. Three new disease-gene localizations were reported at the workshop.

Two patients with Rubinstein-Taybi syndrome (dysmorphic facies, broad thumbs, big toes, and mental retardation) were reported to have a reciprocal translocation involving the short arm of chromosome 16. Martijn Breuning (Leiden University, Netherlands) reported that 6 of 24 patients with this syndrome were found by FISH to have submicroscopic deletions.

The second disease localization was reported by Dan Kastner (NIH, Bethesda). Familial Mediterranean Fever, an autosomal recessive disorder characterized by acute attacks of fever with sterile peritonitis, pleurisy, or synovitis, was genetically mapped to the chromosome 16 short arm. Linkage disequilibrium between different ethnic groups strongly suggests the presence of at least two mutant alleles with different clinical manifestations.

Resolution of Cytogenetic Chromosome 16 Physical Map Increased

A complete report of the Chromosome 16 meeting, in addition to abstracts of poster presentations, will be published in *Cytogenetics and Cell Genetics*.

⇒

Meeting Reports

Human Genome news

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

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Chromosome 16 Meeting Contact:
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  Internet: "ceh@telomere.lanl.gov"

The third new disease assignment was a gene for late-onset familial breast cancer presented by Rachel Giles (University of California, Berkeley). A number of families that do not demonstrate linkage to the assigned chromosome 17 gene showed tentative linkage to DNA markers on the chromosome 16 long arm.

Anne-Marie Cleton-Jansen (Leiden University) and Hitoshi Tsuda (National Cancer Institute, Tokyo) showed that loss of heterozygosity in breast tumors involved at least two and probably three regions of the chromosome 16 long arm. Of particular interest was the revelation that the region of heterozygosity loss on the distal tip of the chromosome 16 long arm coincides with the probable location of the late-onset familial breast cancer gene.

Stephen Reeders (Yale University) presented an update on cloning the autosomal dominant polycystic kidney disease (PKD1), which was mapped to a 700-kb CpG island–rich segment on the tip of the chromosome 16 short arm. Progress has been difficult because the region is extremely gene rich, with at least 23 identified genes now being analyzed.

Batten disease (juvenile-onset neuronal ceroid lipfuscinosis CLN3) has been mapped to 16p12. A high-resolution linkage map has been constructed within this region, and the genetic location of CLN3 is being refined. An informal consortium was established to facilitate the exchange of materials and the identification of additional microsatellite repeats in the Batten disease region.

Comparative Mapping

Gerd Scherer (University of Freiburg, Federal Republic of Germany) and Jenny Marshall Graves (La Trobe University, Australia) compiled comparative data on mapping loci in the mouse and human genomes. While human serum albumin (HSA) 16q markers are all syntenic on MNU8, the locations of HSA 16p markers have been found to be distributed among four mouse chromosome 16s; this is in contrast to cattle where all HSA 16p markers are syntenic. Participants agreed to make a concerted effort to obtain gene probes on human chromosome 16; Breuning will distribute the probes to groups interested in comparative mapping.

Informatics and Resource Availability

As maps have become more complex, the need has grown for new software to aid in mapping, data management, and the map assembly process at the laboratory and committee levels. Two prototype systems were described: (1) CHROMINFO, designed in Reeders' laboratory, and (2) SIGMA, developed by Michael Cinkosky and James Fickett (LANL).

All new data are being entered into the Genome Data Base. Summary tables listing reference markers, genes, and disease loci are available by sending e-mail to "bioserve@genome.lanl.gov" with the single word "chromosome-16" in the text field.

Extensive discussions took place on resource availability and sharing among laboratories; participants proposed that all reagents be made available to the research community when the manuscript characterizing the reagents is accepted for publication. Many reagents are available on request from their originators, although sharing is limited by the cost and logistics of preparation and distribution. Where possible, reagents will be made available through such existing repositories as the American *Type Culture* Collection in Rockville, Maryland.

To further mapping objectives and to support and expedite studies of human biology and biomedical technology applications, future workshops will continue to facilitate cooperation and collaborations by providing a forum for introducing new information and reagents. The next workshop on chromosome 16 will be held in the United States in the fall of 1993. ◇

Reported by David F. Callen
Adelaide Children's Hospital
and
Ed Hildebrand
Los Alamos National Laboratory

New Numbers for Baylor Newsletter

The new numbers for contacting the *Baylor Genome Center News* are 713/798-5669, Fax: 713/798-5386. ◇

Second Bioethics Seminar

The Second Bioethics Seminar: Ethical, Legal, and Social Issues in Human Genome Research took place March 20–21 in Fukui, Japan. Over 200 participants from Japan and 13 other countries attended the meeting, which was held under the auspices of the Fukui Medical School and the Study Group on Human Genome Research of the Japanese Ministry of Education. The event was cosponsored by the United Nations Educational, Scientific, and Cultural Organization; the World Health Organization; and other groups.

Speaker abstracts were provided in English and Japanese, and simultaneous translation occurred during the sessions. In lectures and panel discussions, 12 foreign scientists and 30 Japanese speakers from various fields of natural and social science discussed the status of human genome research in Japan; the historical background of bioethics, clinical application, and social issues in medical genetics; the responsibility of scientists; and the results of an international opinion survey. The scientific portion of the meeting was followed by a lecture for the general public.

Contact: Norio Fujiki; Department of Internal Medicine and Medical Genetics; Fukui Medical School; Matsuokacho, Fukui Pref., 910-11, Japan; (Int.) 81/776-61-3111, ext. 2297; Fax: (Int.) 81/776-67-8100. ◊

Documents Provided Free by NIH NCHGR

In addition to the Genome Report Card (p. 8), the following documents are available at no charge from the National Center for Human Genome Research (NCHGR) Office of Communications: Bldg. 38A, Room 617; 9000 Rockville Pike; Bethesda, MD 20892; 301/402-0911, Fax: 301/480-2770.

- **The Human Genome Project: New Tools for Tomorrow's Health Research** is a 19-page booklet that explains the basic science of the Human Genome Project, reviews its history, and briefly assesses progress.
- **Funding Opportunities for the Human Genome Project** lists all the program announcements and information statements related to NCHGR funding in support of the Human Genome Project.
- **Index Marker Catalog** lists index-quality markers and interim maps available as of March of this year. Characterized by a heterozygosity of at least 70%, the markers include restriction fragment length polymorphisms and markers based on microsatellites or other DNA sequences. The catalog, an interim summary of the index marker/framework map project [see **HGN 3**(2), 1–2 (July 1991)], includes information on accessing the markers and using them to localize genetic markers to specific intervals. ◊

For Your Information

U.S. Genome Research Funding Guidelines

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

NIH National Center for Human Genome Research (NCHGR)

Application receipt dates:

- R01, P01, R21, R29, P30, P50, K01,* and R13 grants – February 1, June 1, and October 1.
- Individual postdoctoral fellowships and institutional training grants – January 10, May 10, and September 10.
- Small Business Innovation Research Grants (SBIR: firms with 500 or fewer employees) – April 15, August 15, and December 15.
- Research supplements for underrepresented minorities – applications are accepted on a continuing basis.
- Requests for Applications (RFAs) – receipt dates are independent of the above dates. Notices will appear in **HGN** and other publications.

*Expedited review possible. Check with NCHGR staff during application development phases.

Program announcements are listed in the weekly **NIH Guide for Grants and Contracts**,* which is available by

- Hard-copy subscription – call 301/496-7441.
- Remote login via modem to NIH Grant Line – call John James, 301/496-7554.
- Listserver computer network subscription – call Dottie Baker, 919/966-5625; BITNET: "pjones@uncvx1.bitnet" or Internet: "jones@samba.acs.unc.edu".

*Expanded statements of RFAs listed in the NIH grants guide may be obtained from either of the two electronic sources or from NIH NCHGR in Bethesda, Maryland (301/496-0844).

DOE Human Genome Program

Special Research Grants: Program Notice 92-13
Solicitations for technology research proposals were announced in the April 23 issue of the **Federal Register** [**57**(79), 14833–34 (1992)] and in issues of **Science** and other publications. The DOE Office of Health and Environmental Research (OHER) of the Office of Energy Research invites applications for the development and implementation of automated mapping and advanced sequencing technologies and informatics/computational/interpretive capacities that are broadly supportive of the Human Genome Program. Formal proposals due August 7. For more information, contact

- David Smith, OHER, ER-72 (GTN), DOE Office of Energy Research, Washington, D.C. (301/903-6488).

Special Research Grants: Program Notice 92-14
OHER invites applications for special research grants to support activities on Ethical, Legal, and Social Issues (ELSI) that may arise from the use of data resulting from the Human Genome Project [**Fed. Reg.**, **57**(78), 14710–11 (April 22, 1992)]. These activities include (1) conducting multidisciplinary empirical research on privacy as it pertains to genetic information, (2) preparation and dissemination of educational materials to enhance public understanding of both the scientific and ELSI aspects of the Human Genome Project, and (3) planning and implementing conferences focused on relevant issues. Applicants are urged to discuss proposals with

- Daniel Drell, OHER (301/903-4742, Fax: 301/903-5051, Internet: "drell@mailgw.er.doe.gov"). Proposals due August 7.

SBIR Grants
DOE also invites small business firms to submit grant applications addressing the human genome topic of SBIR programs, which are designed to strengthen innovative firms in areas of research and development and to contribute to the growth and strength of the nation's economy. The human genome topic emphasizes instrumentation development for automated clone processing, improvements in DNA sequencing technologies, and enhanced sequence data storage and processing capabilities. Next submission date: fall 1992. For more information, contact

- Samuel Barish; SBIR Program Manager, ER-16; DOE; Washington, DC 20585; 301/903-5707.

Human Genome Distinguished Postdoctoral Fellowships
Next deadline: February 1, 1993. For further information, see **HGN 3**(3), 5 (September 1991) or contact

- Linda Holmes, Oak Ridge Associated Universities: 615/576-4805. ◊

Calendar of Genome Events*

August

11. Advances in Genetic Information: Public Policy Issues for State Governments; Miami Beach, FL [K. Marshall, 606/231-1882, Fax: -1858]

16–21. Ninth International Biotechnology Symposium & Exhibit; Crystal City, VA [Am. Chem. Soc. (ACS), 202/872-6286, Fax: -6128]

18–23. Molecular Genetics of Bacteria & Phages; Cold Spring Harbor, NY [Cold Spring Harbor Laboratory (CSHL), 516/367-8346, Fax: -8845]

26–30. Mouse Molecular Genetics; CSHL, Cold Spring Harbor, NY [see contact: Aug. 18–23]

September

2–6. Cancer Cells: Genetics & Molecular Biology of Breast Cancer; CSHL, Cold Spring Harbor, NY [see contact: Aug. 18–23]

7–11. Eighth Workshop on Molecular Genetics of the Mouse; Dourdan, France [J.-L. Guenet, (Int.) 33/1-4568-8555, Fax: -8639]

10–14. *First International **E. coli** Genome Meeting; Madison, WI [M. Ellingson, 608/262-2755, Fax: -5487]

13–15. Third International Workshop on Human Chromosome 11; San Diego, CA [G. Evans, 619/453-4100, ext. 279, Fax: /558-9513]

14–16. ELSI Grantee Workshop; Washington, DC [E. Langfelder, 301/402-0911, Fax: /480-2770]

17. NCHGR Lecture Series: Genetic Dissection of Complex Traits; Bethesda, MD [C. Dahl, 301/402-0838]

17–20. Third International Workshop on Chromosome 22; Philadelphia, PA [B. Emanuel, 215/590-3856, Fax: -3764]

18–20. Chromosome 12 Gene Mapping Workshop; Oxford, England [R. Gemmill, 303/333-4515, Fax: -8423 or I. Craig, (Int.) 44/865-275-327, Fax: -318]

20–21. *National Advisory Council for Human Genome Research; Bethesda, MD [J. Ades, 301/402-2205, Fax: -2218]

20–23. Chromosome 13 Workshop; Dallas, TX [A. Bowcock, 214/688-3896, Fax: -8617]

22–26. Gene Therapy; CSHL, Cold Spring Harbor, NY [see contact: Aug. 18–23]

23–24. The Birth of Bioethics; Seattle, WA [Continuing Medical Education, 800/869-2633 or 206/543-1050, Fax: -3195]

25–26. Winding Your Way Through DNA; San Francisco, CA (symposium full) [V. McDougle, 415/476-6714, Fax: -4099]

26–30. Genome Sequencing and Analysis IV; Hilton Head, SC [S. Wallace, 301/480-0634, Fax: -8588]

October

5–6. *Protecting Human Subjects in Research Involving Families: Points to Consider; Bethesda, MD [see contact: Sept. 14–16]

7–9. "The Impact of Molecular Medicine on Clinical Practice" at the Anglo-American Conference; London, England [W. O'Reilly, 212/371-1150, Fax: -1151]

9–11. Genetic Factors in Crime: Findings, Uses, and Implications; College Park, MD [D. Wasserman, 301/405-4753, Fax: /314-9346]

11–15. Sixth International Mouse Genome Conference; Buffalo, NY [V. Chapman, 716/845-5840, Fax: -8169]

14–17. Human Genome '92: The Human Genome Project International Conference; Nice, France [Am. Assoc. for the Advancement of Science (AAAS), 202/326-6461, Fax: /289-4021]

15. NCHGR Lecture Series: Genosensors: Microfabricated Devices for Automated DNA Sequence Analysis; Bethesda, MD [see contact: Sept. 17]

17–21. First International Conference on Mathematical and Computational Analysis of the Human Genome and Its Mutation Load; Szeged, Hungary [Human Genome Research Ltd., (Int.) 36/62-23855, Fax: -23844]

November

4–6. Third Meeting of Mammalian Genetics and Development Workshop; London [S. Rastan, (Int.) 44/81-869-3266, Fax: -3270]

4–8. Genetics of Cancer; Hilton Head, SC [Am. Assoc. for Cancer Research (AACR), 215/440-9300, Fax: -9313]

6–8. Chromosome 2 Workshop; Half Moon Bay, CA [S. Naylor, 512/567-3842, Fax: -6781]

6–8. Human Genome Project: Impact, Implications, and Issues; San Francisco, CA [B. Leopold, 215/872-7608, Fax: -1192]

9–10. ELSI Insurance Task Force; San Francisco, CA [see contact: Sept. 14–16]

9–11. Plant Genome I; San Diego, CA (abstract deadline: Oct. 1) [D. Scherago, 212/643-1750, Fax: -1758]

9–13. 42nd Annual Meeting of the American Society of Human Genetics (ASHG); San Francisco, CA [M. Ryan, 301/571-1825, Fax: /530-7079]

11. Planning meeting at ASHG for the First International Chromosome 8 Workshop ; San Francisco, CA [D. Drayna, 415/266-1413, Fax: -2739]

12–13. Impact of Molecular Genetics on the Treatment of Genetic Diseases; Bethesda, MD [R. Abizaid, 301/230-0052, Fax: -0054]

15–17. *Chromosome Coordinating Meeting 1992; Baltimore, MD [P. Pearson, 410/955-9705, Fax: -0054]

December

7. *DOE Human Genome Coordinating Committee; Bethesda, MD

7–8. DOE/NIH Joint Subcommittee on the Human Genome; NIH Program Advisory Committee on the Human Genome; Bethesda, MD [see contact: Sept. 20–21]

January 1993

5–8. Biotechnology Computing Track of the 26th Hawaiian International Conference on System Sciences; Kauai, HI [L. Hunter, 301/496-9300, Fax: -0673, Internet: "hunter@nlm.nih.gov"]

17–22. "Advances in Gene Technology: Protein Engineering and Beyond" at the 1993 Miami Bio/Technology Winter Symposia; Miami Beach, FL [S. Black, 305/547-3597, Fax: /324-5665]

24–25. *National Advisory Council for Human Genome Research; Bethesda, MD [see contact: Sept. 20–21]

February 1993

1–6. Oncogenes and Anti-Oncogenes in Cell Differentiation, Development, and Human Cancer; AACR, Big Sky, MT [see contact: Nov. 4–8]

7–11. *Third DOE Contractor-Grantee Workshop; Santa Fe, NM (abstract deadline: Nov. 1) [S. Spengler, 510/486-4879, Fax: -5717]

15–19. *15th Annual Conference on the Organization & Expression of the Genome; Lorne, Victoria, Australia [S. Easteal, (Int.) 61/6-249-4719, Fax: -4712

March 1993

6–8. Chromosome 20 Workshop; Paris, France [C. Smith, 510/643-6376, Fax: -1188]

April 1993

12–18. 1993 Keystone Symposia Meetings: Gene Therapy; Keystone, CO [Keystone Symposia, 303/262-1230, Fax: -1525]

12–18. 1993 Keystone Symposia Meetings: Genetically Targeted Research & Therapeutics-Antisense & Gene Therapy; Keystone, CO [see contact: April 12–18, above]

May 1993

9–12. Fourth Annual X Chromosome Workshop; St. Louis, MO [M. Thomas, 314/362-7259, Fax: -1232]

14–15. Fourth International Workshop on Chromosome 3; Groningen, Netherlands [C. Buys, (Int.) 31/50-632-925, Fax: -947]

16. Chromosome 3 & Cancer; Groningen, Netherlands [see contact: May 14–15]

16–17. *National Advisory Council for Human Genome Research; Bethesda, MD [see contact: Sept. 20–21]

19–22. 84th Annual Meeting of AACR; Orlando, FL [see contact: Nov. 4–8]

20–22. Chromosome 7 Gene Mapping Workshop; Marburg, Germany [K.-H. Grzeschik (Int.) 49/6421-28-4080, Fax: -5630]

June 1993

Second International Workshop on Chromosome 6; Berlin, Germany [A. Ziegler, (Int.) 49/30-303-52617, Fax: (Int.) -53778]

21–22. DOE/NIH Joint Subcommittee on the Human Genome; NIH Program Advisory Committee on the Human Genome; Bethesda, MD [see contact: Sept. 20–21]

*Attendance at meetings listed with asterisk is either limited or restricted. Dates may change; check with contact person.

Training Calendar: Workshops and Coursework*

August

2–14. Molecular Evolution; Marine Biological Laboratory (MBL), Woods Hole, MA [F. Dwane, 508/548-3705, ext. 216]

3–7. *Nucleic Acid and Protein Sequence Analysis Workshop; Pittsburgh, PA [N. Blankenstein, 412/268-4960, Internet: "blankens@a.psc.edu"]

6–7. Molecular Cytogenetics: Chromosome In Situ; Oncor, Inc., Gaithersburg, MD (also offered Oct. 1–2 and Dec. 10–11) [M. Williams, 800/776-6267, Fax: 301/926-6129]

10–14. RNA Isolation and Characterization; Exon-Intron, Inc., Columbia, MD [Workshop Coordinator, 410/730-3984, Fax: -3983]

10–15. cDNA Library Techniques; Germantown, MD (also offered Nov. 2–6) [Life Technologies, Inc. (LTI), 800/952-9166 or 301/921-2250, Fax: /258-8212]

11–14. Recombinant DNA Techniques; New Brunswick, NJ [Office of Continuing Professional Education, 908/932-9271, Fax: -8726]

16–21. Computer-Integrated Laboratory: A Hands-On Experience in Lab Automation; Blacksburg, VA (also offered Dec. 6–11) [Am. Chem. Soc. (ACS), 202/872-4508, Fax: -6336]

17–18. GDB/OMIM Training Courses [see schedule, p. 9]

17–18. PC/GENE; IntelliGenetics (IG), Mountain View, CA [S. Maulik, 415/962-7300, Fax: -7302]

19–21. Recombinant DNA for Chemists (ACS); Washington, DC [see contact: Aug. 16–21]

24–27. †Partnerships in Teaching Biotechnology: Human Genome Technology Workshop; Ann Arbor, MI (also offered Aug. 28–29) (classes full) [P. Gregory, 313/764-8050, Fax: -4133]

24–28. Advanced Recombinant DNA Methodology; Rockville, MD (also offered Dec. 14–18) [Am. **Type Culture** Collection (ATCC), 301/231-5566, Fax: /770-1805]

24–28. DNA-Protein Interactions; LTI, Germantown, MD (also offered at later dates) [see contact: Aug. 10–15]

September

9–11. Cloning & Hybridization Analysis of PCR Products; Biotechnology Training Programs (BTP), Los Angeles, CA (also offered Dec. 16–18 in Gainesville, FL) [S. Chance, 800/821-4861]

14–15. Clinical Diagnosis using PCR & Hybridization Analysis; BTP, Los Angeles, CA [see contact: Sept. 9–11]

14–17. PCR Methodology; Exon-Intron, Inc., Columbia, MD [see contact: Aug. 10–14]

14–18. Recombinant DNA Techniques I; LTI, Germantown, MD (also offered at later dates) [see contact: Aug. 10–15]

16. Introduction to PCR; BTP, Los Angeles, CA (also offered Dec. 15 in Gainesville, FL) [see contact: Sept. 9–11]

21–26. Recombinant DNA Techniques II; LTI, Germantown, MD (also offered at later dates) [see contact: Aug. 10–15]

30. Capillary Electrophoresis; New Brunswick, NJ [see contact: Aug. 11–14]

30–Oct. 2. Basic Cytogenetics; ATCC, Rockville, MD [see contact: Aug. 24–28]

October

5–9. Cell Culture Techniques; LTI, Germantown, MD (also offered at later dates) [see contact: Aug. 10–15]

8–21. †Analysis & Genetic Manipulation of YACs; Cold Spring Harbor, NY [CSHL, 516/367-8343, Fax: -8845]

9–22. †Molecular-Cell Biology Techniques: Advanced In Situ Hybridization and Immunocytochemistry; CSHL, Cold Spring Harbor, NY [see contact: Oct. 8–21]

12–14. PCR Techniques; Lake Tahoe, NV [Ctr. for Advanced Training in Cell and Molecular Biology/Catholic Univ. of Am. (CATCMB/CUA), 202/319-6161, Fax: -5721]

12–14. Recombinant DNA Methodology (CATCMB/CUA); Lake Tahoe, NV [see contact: Oct. 12–14]

18–Nov. 1. Carolina Workshops on cDNA and Gene Expression; Chapel Hill, NC [W. Litaker, 919/966-1730, Fax: -6821]

19–23. †Advanced Linkage Courses; Zürich, Switzerland (application deadline: Aug. 25) [K. Montague, 212/960-2507, Fax: /568-2750]

26–27. Future Technologies for DNA Analysis; Bethesda, MD [Armed Forces Institute of Pathology (AFIP), 301/427-5231, Fax: -5001]

26–30. Recombinant DNA: Techniques & Applications; ATCC, Rockville, MD (also offered Feb. 22–26, 1993) [see contact: Aug. 24–28]

26–Nov. 4. †Essential Computational Genomics for Biologists; CSHL, Cold Spring Harbor, NY [see contact: Oct. 8–21]

27–Nov. 9. Molecular Genetics, Cell Biology & Cell Cycle of Fission Yeast; CSHL, Cold Spring Harbor, NY [see contact: Oct. 8–21]

November

3–6. PCR Applications/Cycle DNA Sequencing; ATCC, Rockville, MD (also offered Mar. 2–5, 1993) [see contact: Aug. 24–28]

7–8. Future of DNA Sequence Analysis Workshop; Oslo, Norway [H. Prydz, (Int.) 47/2-95 87 54, Fax: -69 41 30]

9–13. Recombinant DNA Methodology; Exon-Intron, Inc., Columbia, MD [see contact: Aug. 10–14]

11–12. Advanced Data Banks; IG, Mountain View, CA [see contact: Aug. 17–18]

December

8–11. DNA Fingerprinting; ATCC, Rockville, MD [see contact: Aug. 24–28]

AAAS Am. Assoc. for the Advancement of Science.
AACR Am. Assoc. for Cancer Research
ACS Am. Chemical Soc.
AFIP Armed Forces Institute of Pathology
ASHG Am. Soc. of Human Genetics
ATCC Am. **Type Culture** Collection
BTP Biotechnology Training Programs
CATCMB/CUA Center for Advanced Training in Cell and Molecular Biology/Catholic Univ. of America
CSHL Cold Spring Harbor Laboratory
ELSI Ethical, Legal, and Social Issues
IG IntelliGenetics
LTI Life Technologies, Inc.
MBL Marine Biological Laboratory
NCHGR National Center for Human Genome Research

8–11. Molecular Modeling: Methods and Techniques (ACS); Athens, GA [see contact: Aug. 16–21]

January 1993

11–15. †Advanced Linkage Courses; New York, NY (application deadline: Nov. 16) [see contact: Oct. 19–23]

Deadline for Submissions to Newsletter

Calendar. Items for the *Human Genome News* (*HGN*) Calendar of Genome Events or Training Calendar should be submitted by mail or fax to reach HGMIS by the third week of the month in which the previous newsletter was published: for example, the third week of September for the November issue and the third week of November for the January newsletter. *Human Genome News* is published in January, March, May, July, September, and November. See page 12 for the HGMIS fax number and address.

Meeting Reports. In addition to these advance calendar listings, *HGN* staff welcomes reports on past chromosome workshops and sequencing, mapping, informatics, and ELSI meetings. ◇

*Dates and course status may change, and courses may be offered at other times and places; check with contact person.
†NCHGR-funded event.

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