BIOLOGY PHYSICS MATHEMATICS ENGINEERING CHEMISTRY

Human Genome news

Sponsored by the National Institutes of Health and the U.S. Department of Energy

ISSN: 1050-6101

Vol. 5, No. 2, July 1993

Insurance Task Force Makes Recommendations

In May 1991 the Joint NIH-DOE Working Group on the Ethical, Legal, and Social Implications (ELSI) of Human Genome Research formed the Task Force on Genetic Information and Insurance to develop recommendations to prevent the negative impact of genetic information on access to insurance. The group was composed of physicians, biologists, geneticists and genetic counselors, lawyers, ethicists, and representatives from the insurance industry, associations of people with disabilities, and an organization of state governments. After meeting periodically for 2 years, the task force, cochaired by Thomas Murray (Case Western Reserve University) and Jonathan Beckwith (Harvard Medical School), presented its report to the working group on May 10 of this year. Following is a synopsis of the report's executive summary and the full text of the recommendations.

Synopsis of Executive Summary

One of the ironies in the current crisis in health care coverage is that developing more-accurate biomedical data could make things worse rather than better for those most in need. Knowledge useful in predicting the individual's likelihood of developing a particular disease opens the door to both the welcome preventive strategies and the unwelcome possibility of genetic discrimination. Injecting considerations about genetic risks into the current health care system could result in more-refined risk rating by insurers and greater difficulty in finding affordable health care coverage for large numbers of people. Access to health care might be denied or "preexisting" conditions excluded from coverage. Individuals might be compelled to provide genetic information as a condition of obtaining health care coverage, and information on genetic health risks may also include children, parents, siblings, and other relatives.

Affording special protection for genetic material and data is unlikely to provide a solution to these challenges. Genetic privacy should be vigorously protected, but other varieties of health-related information are equally sensitive. Because diseases are increasingly seen as having both genetic and nongenetic components, classifying health-related data as wholly genetic or nongenetic is difficult. Furthermore, as a practical matter, genetic and other materials are not segregated in medical records. The standard personal medical history, for example, is a rich source of genetic information. Policies intended to protect genetic privacy will need to address the privacy of health-related knowledge in general. The task force considered these factors carefully in making its recommendations.

Recommendations

In anticipation of fundamental reform in the financing and delivery of health care in the

Copies of the full report are available from:

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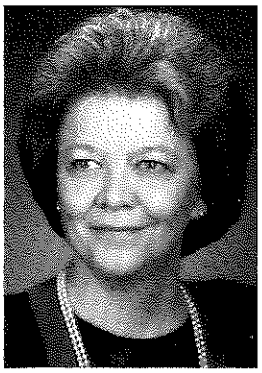
In This Issue. . .

Genome News

Elizabeth Thomson Joins NCHGR ELSI Branch



Elizabeth Thomson

Elizabeth Thomson, coordinator of statewide genetic counseling services at the University of Iowa from 1980 to 1993, has joined the Ethical, Legal, and Social Implications (ELSI) Branch of the National Center for Human Genome Research (NCHGR). Thomson will serve as coordinator of the research portfolio related to genetic testing, education, and counseling and manage the cystic fibrosis (CF) consortium. Eric Juengst, Acting Chief of the ELSI Branch, says that Thomson's extensive clinical background will be "invaluable to the ELSI program."

The ELSI Branch examines issues such as professional standards in introducing new genetic testing; informed consent in genetic research and testing; confidentiality of genetic test results; and fairness in the use of genetic information to avoid discrimination and social stigmatization. In her capacity as a genetic counselor and administrator, Thomson has had ample opportunity to observe directly the impact of genetic tests on individuals and families. "One goal of ELSI is to ensure that the benefits of developing genetic technologies are realized while potential risks are minimized," she said.

The CF consortium involves projects supported by the NIH National Institute of Child Health and Human Development, the National Center for Nursing Research, NCHGR, and National Institute of Diabetes and Digestive and Kidney Diseases. To assist in shaping standards of care and policies in the emerging field of genetic testing and counseling, the consortium serves as a prototype in the study of issues surrounding inherited diseases. The National Cancer Institute and NCHGR are cosponsoring a similar interdisciplinary evaluation of genetic diagnostic technologies in disorders such as breast, colon, and other forms of cancer.

Thomson will also be responsible for coordinating outreach efforts with professional and lay groups involved in the delivery of clinical genetic services. The NCHGR ELSI Branch has initiated discussions with professional societies and other health agencies to identify ways of dealing with the acute shortage of adequately trained genetic counselors. The branch has also organized activities with consumer groups such as the Alliance for Genetic Support Groups and individuals who have disabilities. These activities are designed to heighten the awareness of health professionals about consumer and disabilities issues.

Thomson received the B.S. degree in nursing from Coe College and the M.S. in preventive medicine and environmental health from the University of Iowa. She became the first genetic consultant for the Iowa State Department of Health in 1976 and was certified by the American Board of Medical Genetics in 1982. From 1986 to 1991, Thomson was Assistant Project Director of the Great Plains Genetic Services Network. A founding member of the International Society of Nurses in Genetics, Inc., Thomson also belongs to the American Society of Human Genetics, the American College of Medical Genetics, and the American Nurses Association. *[Sharon Durham, NCHGR]* ◊

Insurance *(from p. 1)*

United States, the Task Force on Genetic Information and Insurance offers the following recommendations. The recommendations concern health care coverage and should not be applied uncritically to other forms of insurance, such as life or disability income insurance.

1. Information about past, present, or future health status, including genetic information, should not be used to deny health care coverage or service to anyone.
2. The U.S. health care system should ensure universal access to and participation by all in a program of basic health services* that encompasses a continuum of service appropriate for the healthy to the seriously ill.
3. The program of basic health services should treat genetic services comparably to nongenetic services and should encompass appropriate genetic counseling, testing, and treatment within a program of primary, preventive, and specialty health care services for individuals and families with genetic disorders and those at risk of genetic disease.
4. The cost of health care coverage borne by individuals and families for the program of basic health services should not be affected by information, including genetic information, about an individual's past, present, or future health status.
5. Participation in and access to the program of basic health services should not depend on employment.
6. Participation in and access to the program of basic health services should not be conditioned on disclosure by individuals and families of information, including genetic information, about past, present, or future health status.
7. Until participation in a program of basic health services is universal, alternative means of reducing the risk of genetic discrimination should be developed. As one step, health insurers should consider a moratorium on the use of genetic tests in underwriting. In addition, insurers could undertake vigorous educational efforts within the industry to improve the understanding of genetic information.

*We use the phrase "program of basic health services" to describe the array of services that would be available to all after implementation of major health policy reforms, such as those being considered by the President's Health Policy Task Force. We explicitly reject all connotations of "basic" as minimal, stingy, or limited to such services as immunization and well-child care. A program of "basic" health services could encompass a broad range of care for those most in need.◊

DOE ELSI Program Emphasizes Education, Privacy

For the last 3 years, the DOE Human Genome Program, administered through the Office of Health and Environmental Research (OHER), has devoted 3% of its funding to the study of ethical, legal, and social issues (ELSI) surrounding data produced by modern genetic research. OHER has placed special emphasis on promoting public education about such research and on defining related privacy and confidentiality issues.

This commitment was prompted by the early realization that, although the potential benefits of human genome research are abundant, the availability and use of large volumes of genetic information will raise very challenging personal and social questions. Among these concerns are the ability to predict future illnesses well before any symptoms or medical therapies exist; the privacy and confidentiality of genetic information with respect to employers, insurers, direct marketers, banks, credit raters, and many others; the accessibility of large amounts of genetic information in data banks; and the possible discriminatory misuse of genetic information. One potential unwanted outcome of the Human Genome Project is that genome research and the wide use of genetic screening could promote a new genetic underclass and, therefore, a host of new societal conflicts.

The OHER ELSI component is independent of but complementary to the ELSI activities of the human genome program managed by the NIH National Center for Human Genome Research (NCHGR). To avoid unnecessary duplication of effort, OHER and NCHGR have initiated a number of collaborative activities: the Joint ELSI Working Group, which periodically consults with NIH and DOE program staff and assists in ELSI program coordination; the Joint DOE-NIH ELSI Grantee-Contractor Workshop held in September 1992 in Arlington, Virginia [See *HGN* **4**(5), 5–6 (January 1993)]; and some projects described below that are jointly supported by OHER, NCHGR, other agencies and organizations, and commercial companies. One such collaborative effort, just concluding, is a major study by the Institute of Medicine entitled "Assessing Genetic Risk," which reviews issues arising from the introduction of new genetic tests into medical practice in the near future.

Education To Promote Public Understanding

In keeping with its commitment to education, DOE OHER is supporting a set of exhibits on genetics and the Human Genome Project at the San Francisco Exploratorium; linked to these exhibits will be a DNA-extraction demonstration and a lecture series on ELSI. Paula Gregory (University of Michigan) and Debra Collins (University of Kansas) are conducting workshops for high school science teachers in molecular genetics, biotechnology methods, and societal implications inherent in genome research. Some workshop laboratory exercises are based on the OHER-funded Biological Sciences Curriculum Study (BSCS) *Mapping and Sequencing the Human Genome: Science, Ethics, and Public Policy* (mailed to U.S. high school biology teachers).

Joseph McInerney (Colorado College), the principal investigator for the BSCS module, has begun work on another unit focusing on genetic database design and utility and the effects of accumulating large amounts of information in computer-accessible form. This module, which will include software, is also intended for distribution to high school biology teachers throughout the United States.

Several OHER-funded ELSI projects that have concluded or are nearing completion should be yielding results soon. In April the four-part documentary series "Medicine at the Crossroads" was broadcast on WNET; a WGBH series "The Secret of Life" is scheduled for four consecutive evenings beginning September 26 on U.S. public television stations (check local listings).

Genetic Privacy Issues

The OHER ELSI program is focusing on a broad range of genetic privacy issues from the perspectives of several disciplines, including philosophy, social science, and law. Through grants and commissioned papers, the program supports both analytical and empirical research projects, most of which involve comparative studies. These studies contrast such factors as attitudes toward genetic privacy in different populations; the need for appropriate measures to protect genetic information in various

Education Opportunities

- Exhibits
- Demonstrations
- Lectures
- Workshops
- Science Module
- Documentaries
- Judges' Deskbook

Multidisciplinary Studies Support Analytical and Empirical Research

Genome News

States Increase Efforts To Regulate Use of Genetic Information

contexts; and evolving policies of private institutions and state, federal, and foreign governments in this area.

Multidisciplinary research teams are customarily involved in grants related to genetic privacy. Collaboration among disciplines is also encouraged by periodic meetings for research discussions among principal investigators and commissioned-paper writers. The objective of these collaborations is to promote a comprehensive approach to issues and methodologies and assist policymakers in determining appropriate protection mechanisms for personal genetic information. OHER-funded projects and papers on genetic privacy are described briefly below.

A philosophical study of privacy, with particular attention to genetic information, will provide a conceptual foundation for analyzing and resolving issues of genetic privacy [Madison Powers (Georgetown University)]. Another study will relate existing social science work on privacy to anticipated genetic privacy issues [Alan Westin (Columbia University)]. This study will also examine current privacy-protection measures, debates over the need to update privacy protection, and implications for social and legal policies to deal with expected future genetic testing and applications of genetic data.

Ongoing empirical studies compare (1) attitudes toward genetic information in different cultural contexts [Troy Duster (University of California, Berkeley)] and (2) ethical and social facets of genetic screening programs mandated in various states [Ralph Trottier (Morehouse School of Medicine)]. Both studies will explore privacy concerns of the affected populations. Another empirical study by Marvin Natowicz and Carol Barash (Shriver Center) is examining genetic discrimination experienced by individuals in dealing with social institutions such as employers, insurers, and schools. Results of the studies may indicate a need to protect against certain disclosures or uses of genetic information.

A recently completed survey by Philip Reilly (Shriver Center) has found that state legislative efforts to regulate the use of genetic information are increasing, particularly in employment and insurance, but major gaps and deficiencies in statutory coverage persist. Another survey by Reilly showed that life insurance companies are more interested in obtaining existing genetic test information than in performing tests on applicants. Company ratings based on genetic conditions reflect a considerable degree of subjectivity rather than actuarial data.

A study by Frank Grad (Columbia University Law School) is examining the rationale for the protection of genetic information, balancing the individual's right to confidentiality against the values of disclosure to protect public health and the interests of blood relatives and intended spouses. Franklin Zweig (George Washington University) is leading an 18-month effort to produce a judges' reference book for cases involving genetic testing and gene therapy.

Two new studies focus on the growing practice of banking individuals' DNA or genetic data in forensic, academic, military, and commercial settings [Reilly; George Annas (Boston University Law School)]. These studies involve empirical research on the handling of privacy in these settings and analysis to develop and refine proposed policies and guidelines.

A commissioned paper by Lori Andrews (American Bar Foundation) will explore genetic privacy in the context of familial responsibilities. Another paper will compare protection of personal data under civil and common law in foreign countries and the relevant declarations of several international organizations [Bartha Knoppers (University of Montreal)].

Efforts have begun for communicating issues identified in these studies to public policymakers so foreseeable problems surrounding the availability of genetic information can be avoided. *[Daniel W. Drell, OHER Human Genome Program, and Michael S. Yesley, Los Alamos National Laboratory]* ◊

U.K. HGMP Encourages CAD Access

The Chromosome Abnormality Database (CAD) was initiated 2 years ago by the U.K. Human Genome Mapping Program (HGMP) under the guidance of the U.K. Association of Clinical Cytogeneticists. Maintained by Simon Mercer, CAD contains over 40,000 records of human acquired and constitutional chromosome abnormalities. These records, some of which go back 20 years, were contributed by more than 40 U.K. cytogenetic laboratories.

The database is designed to provide a research and clinical resource that will link the gene-mapping community with local cytogenetic laboratories. CAD furnishes researchers with access to chromosome breakpoints that might not have been studied before and to frozen material and cell lines maintained by many local laboratories and by the Human Cell Bank at Porton Down, England. At present, the database collects only from U.K. cytogenetic laboratories and other similar U.K. institutions.

Although CAD is available online via the U.K. HGMP Clinical Resource Center, Mercer will conduct complex searches and searches for investigators without network access. His address is CAD; Oxford Medical Genetics Laboratories; Churchill Hospital; Headington, Oxford OX3 7LJ; England (+ 44/865-226003, Fax: -226006, Internet: *simon@bioch.ox.ac.uk*).◊

Future Directions of Human Genome Project Considered

The NIH National Center for Human Genome Research (NCHGR) held a meeting in Hunt Valley, Maryland, April 23–24 as part of its process for developing a research plan for the next phase of the Human Genome Project. The meeting was intended to (1) appraise project accomplishments likely to be achieved by the end of the initial 5-year phase; (2) generate creative and novel ideas for building on this progress to meet long-range goals; and (3) consider ways in which the project can most effectively and broadly benefit present and future research in biology and medicine. Participants included members of the genome research community and of disciplines most likely to use the technology generated by the Human Genome Project.

This summary article highlights major points that were discussed at the meeting, which was not intended to achieve consensus or establish final priorities. An executive summary and a set of more-detailed minutes will be submitted to the NIH-DOE planning group responsible for formulating the plan for the next phase of the genome project, beginning with fiscal year 1994.

Considerations

Genetic Mapping. Many meeting participants said linkage mapping should continue to be an important goal. As the high-resolution (2- to 5-cM) map is "completed," continued improvement in the type and quality of informative markers will be necessary. Linkage maps will continue to be important for a number of studies, they said, such as mapping disease genes, identifying the genetic basis for complex diseases, and studying variables that affect recombination itself. In addition, telomeres for each chromosome need to be cloned and included in linkage maps. A number of participants also stated that physical maps are the best way to help fill gaps in linkage maps, particularly as the resolution of linkage maps increases.

Physical Mapping. Attendees suggested that a sequence tagged site (STS) map with 200- to 300-kb resolution would be as useful as the current goal of 100-kb resolution. Improved technology, such as much bigger clones and contigs than originally anticipated, make the lower-resolution map as valuable as the higher-resolution one.

Specifying a particular cloning or vector system for achieving physical mapping goals is not important at this time, those present said. In the next phase of the genome project, high-resolution physical maps containing sequencing information will be more important than a sequence-ready clone collection because vector technology for sequencing may change. Planners should expect that chromosome maps will continue to develop in a "bimodal" way, with some genomic regions mapped in greater detail than others. Differences in detail will primarily reflect the degree of annotation, not resolution.

Attendees also suggested that individual scientific communities need to be more involved in distributing resources generated by the genome project, especially physical mapping resources. Investigators in user communities, who will be the beneficiaries of such resources, must mount concerted efforts to help obtain necessary financial and organizational support, including opportunities for commercial distribution.

Sequencing. Participants gave strong support to proceeding with the complete sequencing of human and model-organism DNA as identified in the initial 5-year plan. They agreed that the overall technical goal is to build systems that can permit the rapid sequencing of various genomes at a reasonable cost. Such improved technology is important because the ensuing biological questions will demand comparisons between genomes of different species or individuals. Model-organism research is critical, and determining genomic sequence for most model organisms is now cost-effective.

Sequencing the mouse genome should not be viewed in the same context as other model organisms, participants said. Instead, mouse and human DNA should be sequenced side by side to take advantage of comparisons and provide guidance in areas such as noncoding sequence. If the technologies developed are robust enough to sequence the human genome efficiently, sequencing the mouse genome should not significantly increase the effort.

Those present affirmed that NCHGR should maintain its focus on developing technology for large-scale sequencing.

Participants Pursue Project Ideas and Possible Directions Beyond 1994

Mouse and Human DNA Should Be Sequenced Side by Side, Say Participants

Genome News

Expanded Disease-Gene Mapping Increases Importance of Addressing ELSI Concerns

Significant investment in 1993 instrumentation might "lock in" this technology and inhibit development of more-efficient methodologies for the future. Systems need to be investigated for integrating front-end sample preparation with data collection and back-end analysis.

Attendees also noted that the technology for accurate, full-length cDNA sequencing shares some important similarities and differences with that needed for genomic sequencing. The genome project should be neutral, they said, on sequence production from genomic DNA versus full-length cDNA, as long as data quality is good, information content is high, and tracts of contiguous sequence are long. In contrast, big differences were considered to exist between expressed sequence tag (EST) generation and genomic sequencing. Some groups will continue to gather short sequences from many expressed sequences, thus effectively maximizing the identification of expressed genes. Development of strategies for rapid, efficient incorporation of existing ESTs into STS-based physical maps should, however, be considered.

Ethical, Legal, and Social Implications. Participants observed that anticipating and addressing ethical, legal, and social implications (ELSI) of genome research will become more important as disease-gene mapping expands and improved sequencing technology makes available more-refined molecular diagnostics. The major challenge in this area is the effective integration of ELSI research results into professional and public policymaking on genetic issues. An initial step would be to conduct a "meta-analysis" of the ELSI portfolio to draw out policy-oriented findings. A second step would be to work with appropriate professional and lay constituencies to create and communicate viable policy options.

Some of those present stated that the genomics community can be particularly helpful in facilitating ELSI policy development in areas such as intellectual property and commercialization and the responsible transition from basic research to clinical applications of genetic findings. Increased interaction should be fostered among ELSI researchers, constituencies, and the "bench" genomics community, so that well-informed views can be articulated.

Attendees felt that solutions to some issues will bring others to the surface. Health care reform efforts, for example, may inhibit genetic discrimination by insurers but exacerbate genetic-privacy issues by making medical records more accessible within the health care system. Public policy approaches to these issues can take advantage of other related work such as the Americans with Disabilities Act or efforts to preserve the privacy of medical records.

Participants agreed that education in genetics and associated issues is of paramount importance for both the general public and health care professionals. In addition to funding public education, influencing national science education policy should be an ELSI goal.

As policymaking on genetic issues spreads farther into professional and governmental spheres, better methods will be needed for disseminating ELSI research information. One approach suggested was an accessible topical database to provide users with information relevant to clinical and public policymaking.

Some future issues that will expand the range of ELSI perspectives were noted. For example, international DNA-sampling projects require cross-cultural sensitivity to the social implications of genetic identity; the psychosocial impact of new reproductive genetic tests must be assessed for people with disabilities; and responsible reporting of genetic study results means working with both the media and groups of people affected by the information. Outreach efforts to appropriate academic, professional, and lay communities will be important in launching initiatives in these areas.

New Genome Project Goals. In setting priorities for using the available budget, participants encouraged NCHGR and DOE to choose the *feasible* over the *desirable* to get the job done. At the same time, they stated, the Human Genome Project can and should provide leadership, expertise, and coordination for research efforts beyond the central goals of mapping and sequencing the genome. The research community must emphasize the efficiency of annotating maps and studying gene function on a chromosome-wide or genome-wide scale rather than in genomic regions of interest for specific diseases. Attendees encouraged NCHGR to pursue coordination among NIH institutes and other agencies for funding such projects.◊

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.◊

NCHGR Sequencing Workshop Studies Goals, Technology, Training

The National Center for Human Genome Research (NCHGR) sponsored a workshop on April 20–21 in Washington, D.C., to evaluate progress toward DNA sequencing goals established in the first 5-year plan and to begin planning for the next 5 years. Information from the workshop will be considered in developing future goals. The meeting was attended by NIH and DOE genome program staff, genome scientists, and representatives from the commercial sector, national laboratories, and universities.

Participants discussed the likelihood of meeting current 5-year goals for sequencing; the interface between mapping and sequencing within the overall program; programmatic balance among evolutionary technology development, revolutionary technology research, and production sequencing; development, implementation, and exportation of new technology; balance of genomic and cDNA sequencing and mapping; and training related to sequencing.

Below is a brief summary of discussion points and attendees' recommendations toward the 1998 sequencing and technology-development goals for the Human Genome Project. The next 5-year plan will span fiscal years 1994–98.

Sequencing. The project is expected to meet the 1995 goal of 20 Mb of model-organism sequence but probably not the goal of 10 Mb of human sequence. Attendees felt that the greatest impact of the genome project will come from sequence, sequence-derived information, and associated new technologies. Basic biological research will be the greatest beneficiary of these products. Where possible, sequencing efforts should be closely coordinated for human DNA and syntenic regions in the mouse. By 1998 (the 15-year project's midpoint), 175 Mb of model-organism DNA and 100 Mb of combined mouse and human DNA should have been sequenced, participants said. The combined capacity of all large-scale sequencing centers should be 100 Mb per year of documented high-quality finished sequence, with projected cost-efficiency of $0.25 per base pair.

To achieve the goals of sequencing the human genome and the genomes of selected model organisms, attendees suggested that funding for DNA sequencing and technology development should shift to more than $100 million per year. Commitment to long- and short-term training is also needed for future staffing and to encourage new scientists to enter production-sequencing projects. Although the information derived from sequencing full-length cDNAs is considered valuable, this approach is currently too expensive because of several problems, including normalization and the quality of cDNA libraries. In addition, large-scale cDNA mapping technology is not yet considered to be cost-effective.

Mapping-Sequencing Interface. The shift of funds from a mapping emphasis to a sequencing emphasis should begin now, according to participants. "Sequence-ready maps" or sequence substrates should be generated in production-sequencing groups to ensure maximum usefulness of the product. Because of concern over map quality, some attendees felt that two colinear maps within any region are needed to validate accuracy. The construction of a 100-kb-resolution map based on sequence tagged sites (STSs) is recommended for preparing state-of-the-art, sequence-ready substrates in conjunction with large-scale sequencing efforts.

Technology Development. The NCHGR program should continue to invest moderate levels of funds in high-risk, high-payoff technologies that seem a long way from large-scale implementation. Parallel development and testing of multiple approaches and strategies is critical. Each large-scale sequencing program should have both technology development and production sequencing, although the balance between these elements may vary. Emphasis was placed on integrated modular systems that can afford complete automation of the sequencing process. Identifying the most costly steps and targeting them for technology development is crucial.

Transfer and Exportability. Grant applications for technology development should include plans for transfer and exportability. An infrastructure may need to be established to facilitate distribution of information and technology transfer among laboratories. To prevent overlap and make better use of information obtained by each individual

Attendees:
- **NIH and DOE Genome Staffs**
- **National Laboratory, Private-Sector, University Representatives**

1995 Model Organism DNA Sequencing Goal Expected To Be Met

Genome News

Infrastructure Needed for Transfer of Information and Technology

group, more coordination is needed among centers and individuals who are developing technology. The project needs to connect with the users of genome information to ensure development of the most-useful products, such as repositories of materials or user software. NCHGR may be able to facilitate coordination through meetings or a newsletter.

Systems Integration. Systems integration and sequencing informatics are critical areas in which technology must be advanced to drive down costs and improve production within tasks such as mapping or sequencing. Planned improvements in ABI 373 hardware are projected to increase sequencing throughput in the gel electrophoresis and raw-sequence-acquisition steps of the overall process by 32-fold within the next 5 years.

From this discussion, participants achieved consensus on multiple critical points, which they suggested should be considered as 1998 goals for the Human Genome Project:

- By 1998, 175 Mb of model-organism DNA and 100 Mb of combined mouse and human DNA should have been sequenced.
- Efforts to sequence human DNA and the syntenic regions in mouse should be closely coordinated, where possible.
- The combined capacity of all large-scale sequencing centers in 1998 should be 100 Mb per year of documented high-quality finished sequence with a projected cost-efficiency of $0.25 per base pair at that time.
- Substantial support should be given to innovative and high-risk technological developments as well as improvements in current methodologies to meet the needs of the genome project as a whole.
- Critical areas of focus for technology development are systems integration and sequencing-associated informatics.
- For sequencing purposes, the goal of an STS-based map of 100-kb resolution is optimal to allow for preparation of state-of-the-art sequence-ready substrates in conjunction with large-scale sequencing efforts.
- Funding for DNA sequencing/technology development should shift to more than $100 million per year.◊

✍ Correction to Contact Information

In "Genome Centers Promote Collaboration" [*HGN* 4(6), 6 (March 1993)], contact information for Jeffrey Murray (University of Iowa) should be 319/356-3508, Fax: /335-6970, Internet: *jeff-murray@umaxc.weeg.uiowa.edu* ◊

NCHGR Supports Pre- and Postdoctoral Training

■ **PA- 92-21**

NCHGR reminds the scientific community that funds are available to support research training at three career levels: (1) predoctoral training through institutional training grants, (2) individual postdoctoral fellowships for advanced training in genomic analysis, and (3) senior fellowships for established scientists who wish to acquire new skills relevant to genomic research. Training is also encouraged in areas related to the NCHGR Ethical, Legal, and Social Implications (ELSI) program. Participation is limited to U.S. citizens or permanent residents.

Receipt dates for institutional training grant applications remain September 10, January 10, and May 10. New receipt dates for individual fellowship applications are August 5, December 5, and April 5. Specific information on each program may be obtained from the following people.

- Individual postdoctoral fellowships, Elise Feingold (301/496-7531, BITNET: *fey@nihcu,* Internet: *fey@cu.nih.gov*).
- Institutional training grants, Bettie Graham (301/496-7531, BITNET: *b2g@nihcu*, Internet: *b2g@cu.nih.gov*).
- ELSI program, Eric Juengst (301/402-0911, BITNET: *ejs@nihcu*, Internet: *ejs@cu.nih.gov*).◊

NCHGR Holds YAC Library Workshop

The NIH National Center for Human Genome Research supported a workshop January 29–31 in Herndon, Virginia, to discuss problems associated with constructing yeast artificial chromosome (YAC) libraries. Major advances in molecular genetics over the past few years can be attributed to the use of YAC cloning, and the availability of a number of large YAC libraries has facilitated genome research on humans as well as on the mouse and other model organisms. Despite these marked successes, a number of problems remain, among the most frustrating of which is the difficulty in constructing YAC libraries, even by experienced investigators.

The workshop was organized by Daniel Cohen (Centre d'Etude du Polymorphisme Humain/Genethon), Eric Green (Washington University), and Rodney Rothstein (Columbia University). The group of 25 investigators with expertise in large DNA cloning, yeast biology, and/or YAC cloning discussed experiences and shared protocols. Presentations and discussions were organized into sessions on (1) DNA purification and construction of ligation mixes, (2) yeast transformation, (3) YAC vectors and yeast hosts, and (4) plans for future studies.

No single "consensus" protocol will provide large numbers of clones on a consistent basis.

Sustained Commitment Required

Almost every aspect in the multistep construction of YAC clones was discussed in detail. In many cases, attendees agreed on a particular procedure or reagent, while markedly different experiences were reported for other steps. One important conclusion emerging from the workshop was that no single "consensus" protocol will provide large numbers of clones on a consistent basis. Attendees generally agreed that success in achieving consistent results requires a long, sustained commitment over many months and the willingness to perform numerous parallel controls to test different steps in the overall process.

An example of this commitment is the careful attention required in preparing and handling yeast spheroplasts. All investigators are using adaptations of the spheroplast-transformation protocol originally described by Peter Burgers (Washington University School of Medicine) in *Analytical Biochemistry* **163**:391 (1987). At the workshop, Burgers presented unpublished data demonstrating the dramatic effect of slightly altered polyethylene glycol (PEG) concentrations on the transformation efficiency of large DNA molecules. His data indicated that titrating the optimal concentration for transformation is important for each new batch of PEG.

Simon Foote (Whitehead Institute) described his method for establishing and maintaining optimal spheroplasting in the construction of a YAC library enriched for DNA from the human Y chromosome. MaryKay McCormick (Los Alamos National Laboratory) discussed her use of frozen spheroplasts in making YAC clones.

Definitive solutions to problems of YAC chimerism and instability are not yet available, although several promising lines of investigation are under way. In the characterization of libraries constructed with recombination-deficient yeast strains, preliminary data is encouraging.

Electronic Newsgroup Established

As a result of the workshop, an electronic newsgroup has been established to provide a forum for topics related to the preparation, analysis, and use of YACs. Information about alternative host strains, YAC stability, and problems with reagents used in YAC library construction will be transmitted rapidly to all subscribers. A diverse group of investigators using YACs is expected to participate in the newsgroup, which is distributed from the BIOSCI computer (*net.bio.net* on the Internet). Distribution may later include USENET if usage grows sufficiently.

E-mail subscription requests should be sent to *biosci@net.bio.net* only; no special computer commands are necessary. Messages to be posted, announcements, and queries about YAC construction should be sent to *yac@net.bio.net*. Investigators constructing YAC libraries or using YAC clones are encouraged to participate in this electronic newsgroup for rapid submission of important unpublished information about YAC cloning. *[Eric Green, Washington University School of Medicine]* ◊

YAC Library Construction Tackled:

- **DNA Purification**
- **Transformation**
- **Vectors and Hosts**
- **Future Studies**

Genome News

1993 DOE Postdoctoral Fellowships Announced

The DOE Office of Health and Environmental Research has announced that three people have accepted Human Genome Distinguished Postdoctoral Fellowships for 1993. The winners will conduct research for up to 2 years at DOE and university laboratories that have substantial research efforts supported by the DOE Human Genome Program. Fellows have the opportunity to attend contractor-grantee and professional meetings, where they can interact with other investigators.

Names of the 1993 fellows and their majors, graduate institutions, host laboratories, and research plans are given below.

- **JEFFREY ELBERT**, chemistry (Northwestern University), will work with Gilbert Brown at Oak Ridge National Laboratory to develop labels for DNA sequencing.
- **JOHN KECECIOGLU**, computer science (University of Arizona), will develop algorithms for sequence analysis with Dan Gusfield at the University of California, Davis.
- **MARK NEFF**, genetics (University of Virginia), will work with Jasper Rine at Lawrence Berkeley Laboratory to characterize the genetic basis of dog behavioral traits through linkage maps.

These fellowships carry a stipend of $37,500 for the first year and $40,500 the second. The fellowship program is administered by the Science and Engineering Education Division of the Oak Ridge Institute for Science and Education [P.O. Box 117; Oak Ridge, TN 37831-0117 (615/576-9934, Fax: -0202)].

The next application deadline is February 1, 1994. ◊

1991, 1992 Fellows at DOE Contractor-Grantee Workshop

The 1991 and 1992 Human Genome Distinguished Postdoctoral fellows found many opportunities for discussion at the DOE Contractor-Grantee Workshop, held in February 1993 in Santa Fe, New Mexico. From left are Michael Smith, Julia Parrish, David Lever, Rhett Affleck, Janet Warrington, William Bruno, and Xiaohua Huang. Fellows not attending were Carol Soderlund and Harold Swerdlow.

NCHGR Establishing Genome Science and Technology Centers

■ **PA-93-091**

NCHGR is establishing GESTEC (Genome Science and Technology Centers), a reformulated, flexible program of research support. GESTEC is designed to develop technologies for large-scale generation of mapping and sequencing information, improved informatics solutions to data management, and better methods of annotating maps and sequences. Applications are invited for new and continuing large-scale, multidisciplinary projects to finish the first 5-year goals of the Human Genome Project and address further project needs.

Grants in the GESTEC program may be supported by Specialized Center Grants (P50) or Program Project Grants (P01). The P50 mechanism will be used for broader, more-complex, multidisciplinary programs and P01 for projects that support a minimum of three research components with a well-defined central research focus.

Written and telephone inquiries are strongly encouraged, and NCHGR welcomes the opportunity to clarify any issues or questions from potential applicants. The full program announcement and GESTEC grant proposal guidelines should be requested before the application is prepared.

Contacts for inquiries: Jane Peterson (GESTEC program) and Robert Strausberg (DNA sequencing/technology development); NCHGR; Bldg. 38A, Room 610; NIH; Bethesda, MD 20892 (301/496-7531).◊

GDB 5.1 Includes Accession Numbers

Genome Data Base (GDB) Version 5.1, to be released this summer, will feature:

- **IDENTIFIERS.** Unique, unchanging, artificial external identifiers for all types of database entries (e.g., locus, probe, map, polymorphism, mutation, and citation) will provide rapid retrieval of individual data items without very specific queries.
- **CITATIONS OF GDB SUBMISSIONS.** Authors can use accession numbers as a convenient reference to a body of submitted data, and readers can retrieve all data related to the article. This feature is especially useful for major mapping studies, in which very large amounts of data are submitted to the database.
- **DOCUMENTATION OF GDB SUBMISSIONS.** Journal editors can require, as many do with GenBank® and EMBL sequence data, that authors submit data to the database and include accession numbers in their manuscripts. A number of editors have already agreed in principle to support this effort, which will help ensure timely submissions to GDB.

A detailed description of how to use accession numbers will be available online in the Release Notes under *News*.◊

GDB, OMIM Now on WAIS

GDB and Online *Mendelian Inheritance in Man* (OMIM) are now available on Wide Area Information Servers (WAIS) with *help* files that describe how to search them effectively.

GDB WAIS includes specialized databases for locus, map, probe, polymorphism, mutation, citation, and contact data. Searching provides detailed information on the primary data type and links to other kinds of data displayed in tabular form. Accession numbers allow additional searches for details about the linked entries, and a combined database returns entries from all individual databases. GDB WAIS is updated weekly during off-peak hours. OMIM WAIS, a single database of OMIM documents, is updated daily at 9 a.m. EST.◊

☛ *IMPORTANT NOTICE*

Sometime in August, Internet addresses for all GDB services will change to the domain *gdb.org*. For example, the technical support address will become *help@gdb.org*, and the Computational Biology Gopher server currently on *merlot.welch.jhu.edu* will be addressed as *gopher.gdb.org*. The precise date of the switchover and a complete list of new Internet addresses will be posted on the BIOSCI newsgroups and on the main login screens at Baltimore and GDB remote sites worldwide. Further information will be contained in the September issue of *HGN*. ◊

GDB USER SUPPORT, REGISTRATION

To become a registered user of GDB and OMIM, contact one of the User Support offices listed at right (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, OMIM Training Schedule

Comprehensive hands-on training courses on the use of GDB and OMIM will have at least one computer workstation for two participants. Registrants will receive at least 3 weeks notice if insufficient registration causes class cancellation.

The general course for scientific users provides a basic understanding of the databases and relationships among different types of data.

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.

COURSE REGISTRATION INFORMATION

Contact U.S. GDB User Support Office (at top right).

COURSE SCHEDULE

General User Classes will be held in Baltimore on July 26–27, September 27–28, and December 6–7. No editing classes are scheduled.

SCHEDULED EXHIBITIONS

17th International Congress of Genetics, Birmingham, U.K., Aug. 15–21.

ASHG, New Orleans, Oct. 5–9.

USER SUPPORT OFFICES

UNITED STATES
GDB User Support
Genome Data Base
Johns Hopkins University
2024 E. Monument Street
Baltimore, MD 21205-2100
410/955-7058, Fax: /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 and training courses, technical support, and data questions. Calls received after hours will be forwarded to the appropriate voice mail and returned as soon as possible. To obtain a user's local SprintNet (Telenet) number for locations within the United States: 800/736-1130.

UNITED KINGDOM
Christine Bates
Human Gene Mapping Program Resource Center
CRC, Watford Road
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+ 44/81-869-3446, Fax: -3807
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+ 49/6221-42-2372, Fax: -42-2333
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+ 61/2-692-2948, Fax: -3847
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NETHERLANDS
GDB User Support
CAOS/CAMM Center, Faculty of Science
University of Nijmegen
P.O. Box 9010
6500 GL NIJMEGEN, Netherlands
+ 31/80-653391, Fax: -652977
Internet: *post@caos.caos.kun.nl*

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

Resources

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:

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Bethesda, MD 20892
301/402-0911, Fax: /480-1950
Internet: *lsf@cu.nih.gov*

National Center for Human Genome Research

¶ NCHGR Documents

The following documents, updated for 1993, are available from the NIH National Center of Human Genome Research (NCHGR); Office of Communications; Bldg. 38A, Room 617; 9000 Rockville Pike; Bethesda, MD 20892 (301/402-0911, Fax: /480-2770).

Genome Marker Catalog. The latest edition, which reflects the remarkable increase in the number of highly informative markers, lists 4 times more index-quality markers and interim maps than the March 1992 catalog. 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)], also contains information on accessing the markers and using them to localize genetic markers to specific intervals.

Genome Report Card. This publication provides a yearly overview of progress toward Human Genome Project mapping and sequencing goals. For each human chromosome, the report card lists the number of mapped genes, genetic marker locations, number of sequence tagged sites, contig length and position, and the number of base pairs of sequenced DNA. Data in the 1993 report card are presented in a simplified format that includes 1992 totals for comparison.

Funding Opportunities for the Human Genome Project. A listing is provided of all the program announcements and information statements related to NCHGR funding in support of the Human Genome Project.

The Human Genome Project: New Tools for Tomorrow's Health Research. This 19-page booklet, published in September 1992, explains the basic science of the Human Genome Project, reviews its history, and briefly assesses progress.◊

dbEST Database for Expressed Sequence Tags

Accumulation and analysis of expressed sequence tags (ESTs) have become an important component of genome research. EST data are used to identify gene products; study tissue differentiation, development, and molecular evolution; and accelerate human gene cloning.

dbEST, the National Center for Biotechnology Information (NCBI) special resource for ESTs, contains more than 20,000 sequences from major model organisms and other species. NCBI accepts direct bulk data submissions, issues GenBank® accession numbers, and receives input via daily updates from Los Alamos National Laboratory, European Molecular Biology Laboratory, and DNA Data Base of Japan. Because up to 70% of new ESTs cannot be characterized by homology with known sequences, a special system based on a BLAST function library has been developed for automatic and continual reannotation. This is accomplished by periodic rescreening of all ESTs against general-purpose nucleotide and protein sequence databases.

Submitted information and results of analyses are stored in a relational database and made available to the public in a variety of forms. Data may be searched using the BLAST Internet and e-mail servers, and full reports on ESTs may be obtained from *est_report@ncbi.nlm.nih.gov* (type *help* in the message body and leave the subject line blank). Sequences from dbEST are also included in a new EST division of GenBank. A FASTA-formatted version of all sequences in dbEST (with descriptive header lines) is available for anonymous ftp from the Data Repository at NCBI (*ncbi.nlm.nih.gov*). Full reports on ESTs also contain information on the availability of physical DNA clones (e.g., American *Type Culture* Collection numbers and ordering information). *[Mark Boguski, NCBI]* ◊

Repetitive-Element Searching

Pythia Version 1.5 is available for analysis of repetitive elements in human DNA. Pythia performs the following three DNA sequence analysis tasks.

- Identification of DNA element repetitions by comparing DNA sequences with the updated reference collection of repetitive elements maintained by Jerzy Jurka (Linus Pauling Institute) [see *HGN* 4(2), 5 (July 1992)]. The repetitive regions are recognized using the algorithmic significance method of Aleksander Milosavljevic (Argonne National Laboratory) [*Proc. First Int. Conf. Intelligent Syst. Mol. Biol.* (1993), in press].
- Identification of subfamily membership of *Alu* sequences by aligning DNA sequences against the *Alu* consensus and by identifying bases in a set of positions that are diagnostic for individual *Alu* subfamilies [*J. Mol. Evol.* **32**, 105–21 (1991)]. The subfamilies were originally reconstructed using the minimal-length-encoding method [*Mach. Learn. J.* **12**(1–3), 69–87 (1993)].
- Identification of simple DNA regions consisting of tandem repeats and similar repetitive patterns. The regions are recognized using the algorithmic-significance method [*Comput. Appl. Biosci.* **9**(4) (1993), in press].

The programs can be accessed via electronic mail or obtained in Sun Sparcstation executable form (compiled under Sun OS 4.1.2). For instructions on using the e-mail server, send the word *help* in the subject line to the Internet address *pythia@anl.gov*; to obtain the software, type *software* in the subject line. *[Aleksandar Milosavljevic, Argonne National Laboratory (708/252-7860, Fax: -3387, Internet:* milosav@anl.gov*) and Jerzy Jurka, Linus Pauling Institute (415/327-4864, Internet:* jurka@jmullins.stanford.edu*)]* ◊

Human Chromosome Workshops

Chromosome 8

The First International Human Chromosome 8 Workshop was held May 2–4 at the University of British Columbia, Vancouver, Canada. The conference, which was attended by 23 participants from Australia, Europe, and North America, was supported by CGAT/CTAG (Canadian Genome Analysis & Technology Program, Programme Canadien de Technologie & d'Analyse du Genome) as well as by NIH, DOE, and agencies in other participating countries.

Genetic Maps. Stephen Daiger (University of Texas, Houston) reported that 17 laboratories had submitted data on 142 systems representing 117 different loci. The Centre d'Etude du Polymorphisme Humain consortium map, which will include data submitted by the workshop deadline, is in the error-checking stage and is expected to be submitted for publication by early fall.

Physical Maps. Physical mapping of LGCR (Langer-Giedion chromosome region) continues. Hermann-Josef Lüdecke (Institut für Humangenetik, Universitätsklinikum, Essen, Germany) reported sequence tagged sites from an 8q24.1 microdissection library. Dan Wells (University of Houston) announced the construction of yeast artificial chromosome contigs for the same region.

Disease Loci. Three new disease loci assignments were reported. Kamel Ben Othmane (Duke University) described a recessive form of CMT (Charcot-Marie-Tooth disease) in Tunisians that maps to 8q. Robin Leach (University of Texas, San Antonio) reported a family with benign neonatal epilepsy (EBN2) mapping to 8q. Multiple exostoses (MEX) in some families maps to LGCR. Genetic heterogeneity in MEX was noted by Susan Blanton (University of Virginia, Charlottesville), with the majority of families segregating the EXT1 locus on 8q24.

Resources. Construction of new radiation hybrid cell panels was announced by a number of laboratories, while extension of an existing cell hybrid panel was reported by Michael Wagner (University of Houston).

A second workshop, to be held in Oxford, England, in September 1994, will be organized by Nigel Spurr (Imperial Cancer Research Fund). *[Stephen Wood, University of British Columbia, Internet:* swood@unixg.ubc.ca*]* ◊

Chromosome 9

The Second International Workshop on Human Chromosome 9 was held April 18–20 in Chatham, Massachusetts. The meeting was attended by 66 participants, and 53 abstracts were presented.

Physical and Genetic Maps. Index marker and Centre d'Etude du Polymorphisme Humain consortium maps for the chromosome were discussed in detail. High-resolution mapping efforts resulting from disease-gene searches were described for several regions. These regions include 9p22 [near the interferon gene cluster, both A and B (IFN or IFNA)], site of melanoma-susceptibility and tumor-suppressor genes involved in leukemia, melanoma, lung cancer, and glioma pathogenesis; 9q22 (near D9S12), site of the ESS1 (multiple self-healing squamous epithelioma) and NBCCS (nevoid basal cell carcinoma syndrome) loci; and 9q34, which is near ABO (blood group locus), and site of one tuberous sclerosis locus (TSC1).

Disease Loci. Additional disease genes mapped to chromosome 9 in the past year include cartilage-hair hypoplasia (CHH) on 9p12-13; FACC (Fanconi's anemia, group C) on 9q22; and familial dysautonomia (DYS) on 9q31-32.

Resources. New chromosome 9 resources include an arrayed cosmid library [Pieter de Jong (Lawrence Livermore National Laboratory)], a YAC library [MaryKay McCormick (Los Alamos National Laboratory)], and an extensive collection of trapped exons [Alan Buckler (Massachusetts General Hospital)]. These resources complement existing radiation hybrid panels [Cynthia Jackson (Brown University and Rhode Island Hospital)] and translocation cell lines [Malcolm Ferguson-Smith (Cambridge University)]. *[David J. Kwiatkowski, Brigham and Women's Hospital, Boston, Internet:* kwiatkowski@calvin.bwh.harvard.edu*]* ◊

A chromosome 9 anonymous ftp server has been established by John Attwood (University College, London; *john@mrc-hbgu.ucl.ac.uk*). The address *diamond. gene.ucl.ac.uk* (128.40.82.1) may be used to download chromosome 9 workshop abstracts, figures, and reports (to be published later in *Cytogenetics and Cell Genetics*). An electronic mailing list has also been arranged for the chromosome 9 community.

Need more information on topics related to HGP?

Call *Human Genome News* staff at 615/576-6669.

Calendar of Genome-Related Events* (acronyms, p. 16)

August

15–21. 17th Int. Congress of Genetics; Birmingham, UK [D. Smith, +44/21-414-5888, Fax: -3850]

17–22. MacroMolecules, Genes, and Computers: Chap. Three; Waterville Valley, NH [D. Madden, 415/570-6667, ext. 8803, Fax: /572-2743, Internet: *dawn@apldbio.com*]

24–29. Molecular Genetics of Bacteria & Phages; Cold Spring Harbor, NY [CSHL, 516/367-8346, Fax: -8845]

29–Sept. 3. *Artificial Intelligence and the Genome at IJCAI '93; Chambery, France [J.-G. Ganascia, + 33/1-44-27-4723, Fax: -7000, Internet: *ganascia@laforia.ibp.fr*]

September

8–12. Eukaryotic DNA Replication; CSHL [see contact: Aug. 24–29]

9–10. ELSI Working Group Meeting and CF Consortium; Bethesda, MD [E. Thomson, 301/402-0911, Fax: -1950]

9–13. *E. Coli* Genome Meeting; Madison, WI [M. Ellingson, 608/262-2755, Fax: -3453]

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

20–24. 11th Australian Biotechnology Assoc. Conf.; Perth [J. Sargeant, Fax: +61/9-310-3505, Internet: *mgkjones@murdoch.edu.au*]

27–29. Fetal Cells in Maternal Blood: Prospects for Noninvasive Prenatal Diagnosis; Arlington, VA (poster deadline: June 1) [NYAS, 212/838-0230, Fax: -5640]

October

2–4. 3rd Int. Transcribed Sequence Workshop; New Orleans [U. Hochgeschwender, 301/402-1769, Fax: -2140]

2–5. NSGC 12th Annual Education Conf.; Atlanta (application deadline: April 15) [B. Leopold, 215/872-7608, Fax: -1192]

5–9. ASHG 43rd Annual Meeting; New Orleans (abstract deadline: June 1) [M. Ryan, 301/571-1825, Fax: /530-7079]

10–11. 2nd Int. Genetic Epidemiology Society Meeting; New Orleans [LSU, 504/568-5272, Fax: -3920]

13–16. DNA: The Double Helix. Forty Years: Perspective and Prospective; NYAS, Chicago (poster deadline: July 2) [see contact: Sept. 27–29]

21–22. Law and Science at the Crossroads: Biomedical Technology, Ethics, Public Policy, and the Law; Boston [SULS, 617/573-8627, Fax: /248-0648]

23–27. Genome Sequencing and Analysis Conf. V; Hilton Head, SC [S. Wallace, 301/216-9567, Fax: /977-7233]

November

5–6. First Genetic Marker—Blood Group Research, "Race," and Disease: 1900–1950; Indianapolis [W. Schneider, 317/274-3811, Fax: -2347]

7–10. Electrophoresis '93; Charleston, SC (paper deadline: June 1) [J. Cunningham, 301/898-3772, Fax: -5596]

7–11. MGC 93; Hamamatsu, Japan [K. Moriwaki, +81/559-75-0771, Fax: -6240]

7–11. Molecular Approaches to Cancer Immunotherapy Conf.; Asheville, NC (registration deadline: Aug. 2) [AACR, 215/440-9300, Fax: -9313]

9–13. Interactions of Cancer Susceptibility Genes and Environmental Carcinogens; Lyon, France [AACR/IARC Conf., 215/440-9300, Fax: -9313 or +33-7/273-8485, Fax: -8575]

10–12. *CCM 93; Tsukuba, Japan [N. Shimizu, +81/333-53-1211, ext. 2721, Fax: -51-2370]

14–17. HGM 93; Kobe, Japan [HGM Secretariat, +81/6-454-4811, Fax: -4711]

15–19. Nanometer Scale Biotechnology: DNA Nanoconstructions at the 1993 AVS Natl. Symposium; Orlando, FL [D. Manos, 804/221-3525, Fax: -3540]

17–19. Engineered Animal Models; San Francisco [CHI, 617/487-7989, Fax: -7937]

18–20. Beyond DNA Probes; San Diego [Scherago Int., 212/643-1750, Fax: -1758]

20–21. Healthcare Financing in a Changing World; Washington, DC [J. Weiss, 800/336-GENE]

December

8–9. Mathematical and Statistical Aspects of DNA and Protein Sequence Analysis; London [Sci. Mtgs. Sec., +44/71-839-5561, ext. 278, Fax: -930-2170]

13–15. Genome Informatics Workshop IV; Yokohama, Japan [HGC, Fax: +81/3-3440-6173, Internet: *workshop@ims.u-tokyo.ac.jp*]

January 1994

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

24–27. BioEast '94; Washington, DC [Bioconferences Int., 301/652-3072, Fax: -4951]

24–27. Plant Genome II; San Diego [see contact: Nov. 18–20]

31–February 5. Molecular Genetics of Progression and Metastasis; AACR, Big Sky, MT [see contact: Nov. 7–11]

February 1994

5–10. Advances in Gene Technology: Molecular Biology and Human Genetic Disease at the 1994 Miami Bio/Technology Winter Symposia; Fort Lauderdale, FL [S. Black, 305/547-3597, Fax: /324-5665]

7–11. Int. Conf. on Comparative Gene Mapping in Terrestrial and Aquatic Vertebrates; Oslo [H. Lewin, 217/333-5998, Fax: /244-5617 or O. Lie, +47/22-96-47-82, Fax: -86]

28–Mar. 2. Human Genome Project: Commercial Implications; CHI, San Francisco [see contact: Nov. 17–19]

March 1994

3–4. Gene Transcription-Based Therapeutics; CHI, San Francisco [see contact: Nov. 17–19]

April 1994

24–28. First World Congress on Computational Medicine, Public Health, and Biotechnology; Austin, TX (abstract deadline: Nov. 1) [Compmed 1994, 512/471-2472, Fax: -2445, Internet: *compmed94@chpc.utexas.edu*] ◊

Training Calendar**

August

1–6. Short Course on Molecular Diagnostics, Counseling, and the Human Genome Project; Ann Arbor, MI [D. Baker, 313/763-2933, Fax: -4692]

8–20. Molecular Evolution; MBL, Woods Hole, MA (application deadline: June 1) [D. Chrysler, 508/548-3705, ext. 401]

9–13. Cell Culture Technique; LTI, Germantown, MD [L. Kerwin, 800/952-9166, Fax: 301/258-8212]

12–13. Clinical Application of PCR; West Haven, CT [BTP, 800/821-4861, Fax: 515/232-8306]

12–13. *Tissue In Situ Hybridization; Oncor, Inc., Gaithersburg, MD [M. Williams, 800/776-6267, Fax: 301/926-6129]

16–20. *†‡Genome Technology and Its Implications; Ann Arbor, MI [P. Gregory, 313/747-2738, Fax: /763-4692]

17–20. Plant Biotechnology Methods; Penn State Biotech. Institute, University Park, PA [P. Phillips, 800/833-5533, Fax: 814/863-1357]

21–22. Molecular Biology and Recombinant DNA Technology; Chicago [ACS, 800/227-5558, Fax: 202/872-6336]

22–Sept. 2 *Experimental Genetics of the Laboratory Mouse; Jackson Lab., Bar Harbor, ME [P. Mobraaten, 207/288-3371, ext. 1376]

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*Attendance at meetings listed with asterisk is either limited or restricted. Dates may change; check with contact person.
**Dates and course status may change, and courses may also be offered at other times and places; check with contact person.
†NCHGR-funded event.
‡DOE-funded event.

For Your Information

23–27. Advanced Recombinant DNA Methodology; Rockville, MD [ATCC, 301/231-5566, Fax: /770-1805]

30–Sept. 3. DNA-Protein Interactions; LTI, Germantown, MD [see contact: Aug. 9–13]

September

8. Intro. to PCR; BTP, Los Angeles [see contact: Aug. 12–13]

9–10. *Intro. to Molecular Cytogenetics; Oncor, Inc., Gaithersburg, MD [see contact: Aug. 12–13]

9–10. Quantitative RNA-PCR; BTP, Los Angeles [see contact: Aug. 12–13]

13–14. Basic Cloning & Hybridization Techniques; BTP, Los Angeles [see contact: Aug. 12–13]

13–17. Data Banks and Computer Support of the Human Genome Project; Moscow [V. Tsitovich, Fax: +7-095/135-14-05, Internet: *tsitov@imb.msk.su.internet*]

15–17. Basic Cytogenetic Techniques & Applications; ATCC, Rockville, MD [see contact: Aug. 23–27]

16–17. Clinical Applications of PCR; BTP, Los Angeles [see contact: Aug. 12–13]

20–23. PCR Methodology; Columbia, MD [Exon-Intron, Inc., 410/730-3984, Fax: -3983]

26–29. The Secret of Life; 9–11 p.m. on PBS [check local listings]

27–Oct. 1. Advanced Linkage Course; Zürich, Switzerland [K. Montague, 212/960-2507, Fax: /568-2750]

October

1. NSGC: The ABCs of Cancer Genetics; Wallingford, PA [B. Leopold, 215/872-7608, Fax: -1192]

2–4. Identification of Transcribed Sequences Workshop; New Orleans (abstract deadline: July 1) [K. Gardiner, 303/333-4515, Fax: -8423]

4–8. Recombinant DNA Technologies I; LTI, Germantown, MD [see contact: Aug. 9–13]

4–8. RNA Isolation and Characterization; Exon-Intron, Inc., Columbia, MD [see contact: Sept. 20–23]

8–11. Recombinase Mediated Genome Reorganization; ASBMB, Keystone, CO [G. Goodenough, 301/530-7010, Fax: -7014]

11–14. PCR Techniques; Lake Tahoe, NV [CATCMB/CUA, 202/319-6161, Fax: -4467]

11–14. Recombinant DNA Methodology; CATCMB/CUA, Lake Tahoe, NV [see contact: Oct. 11–14, above]

11–16. Recombinant DNA Technologies II; LTI, Germantown, MD [see contact: Aug. 9–13]

12–15. DNA Fingerprinting; ATCC, Rockville, MD [see contact: Aug. 23–27]

13–26. †Advanced In Situ Hybridization & Immunocytochemistry; Cold Spring Harbor, NY (application deadline: July 15) [CSHL, 516/367-8346, Fax: -8845]

14–27. †Analysis & Genetic Manipulation of YACs; CSHL (application deadline: July 15) [see contact: Oct. 13–26]

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 under-represented 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 during application development phases.

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

- Hard-copy subscription: call 301/496-7441.
- Electronic version (E-Guide): Access through one of the following methods.
  1. Institutional Hubs. A designee receives automatic updates and distributes them locally to researchers. To use this NIH-preferred method, send a message naming the responsible person to Rebecca Duvall (BITNET: *q2c@nihcu*, Internet: *q2c@cu.nih.gov*).
  2. NIH Grant Line (also known as DRGLINE). User reads electronic bulletin board for weekly updates. Connection is through a modem, and files can be transmitted rapidly via BITNET or Internet. For more information, contact John James (301/496-7554 or BITNET: *zns@nihcu*).

*Full text 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

Solicitations for proposals were announced in the *Federal Register* **58**(30), 8746–48 and in *Science* and other publications. Proposals were due on July 15.

For funding information or general inquiries, contact the program office via

- 301/903-6488, Fax: -8521, or Internet: *#genome%er@mailgw.er.doe.gov* or *genome@oerv01.er.doe.gov*

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 research and development and to contribute to the growth and strength of the nation's economy. For more information on SBIR grants, contact

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

National SBIR conferences: Washington, DC (October 13–15,); Seattle, WA (November 15–17); Houston, TX (April 26–28, 1994). Conference Hotline: 407/791-0720.

1994 Human Genome Distinguished Postdoctoral Fellowships

Deadline: February 1, 1994. For further information, contact

- Linda Holmes, Oak Ridge Institute for Science and Education (615/576-4805).◊

22–25. Epigenetic Modifications of the Genome; ASBMB, Keystone, CO [see contact: Oct. 8–11]

24–25. 4th Keck Symposium on Computational Biology; Pittsburgh (registration deadline: Sept. 7) [L. Jarzynka, 412/624-6978, Internet: *jarzynka@cs.pitt.edu*]

November

3–12. †Essential Computational Genomics for Biologists; CSHL (application deadline: July 15) [see contact: Oct. 13–26]

11–14. *RLGS Method Training Course; Tsukuba, Japan (application deadline: July 31) [Y. Hayashizaki, +81/298-36-9145, Fax: -9098] ◊

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3. ___ DOE *Human Genome 1991–92 Program Report.*
4. ___ *Primer on Molecular Genetics.* (Included in program report above. Extracted as separate document for educational use.)

CALENDAR ACRONYMS

AACR Am. Assoc. for Cancer Res.
ACS Am. Chem. Soc.
ASBMB Am. Soc. for Biochemistry & Molecular Biology
ASHG Am. Soc. of Human Genetics
ATCC Am. *Type Culture* Coll.
AVS Am. Vaccum Soc.
BTP Biotechnology Training Programs
CATCMB/CUA Ctr. for Advanced Training in Cell and Mol. Biology/Catholic Univ. of Am.
CCM Chromosome Coordinating Meeting
CF cystic fibrosis
CHI Cambridge Healthtech Institute
CSHL Cold Spring Harbor Lab.
GDB/OMIM Genome Data Base/Online *Mendelian Inheritance in Man*
ELSI Ethical, Legal, and Social Implications
HGC Human Genome Center
HGM Human Genome Mapping
IARC Int. Agcy. for Res. on Cancer
IJCAI Int. Joint Conf. on Art. Intell.
LSU Louisiana State Univ.
LTI Life Technologies, Inc.
MBL Marine Biological Laboratory
MGC Mouse Genome Conference
NSGC Natl. Soc. of Genetics Counselors
NYAS NY Acad. of Sci.
RLGS Restriction Landmark Genomic Scanning
SULS Suffolk Univ. Law School

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