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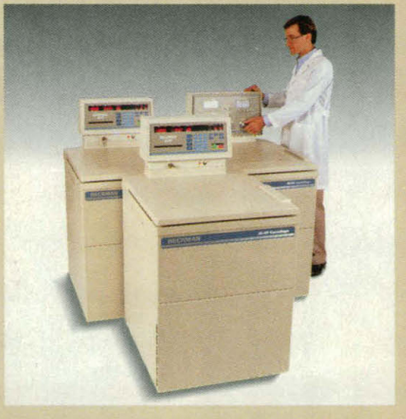

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SCIENCE

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COVER The development of most cancers seems to require a series of gene mutations, falling one after another like dominoes until a malignant tumor evolves. A new "domino" has been discovered: the gene that causes familial adenomatous polyposis (FAP), a hereditary condition that carries a high risk of colon cancer (see pages 661 and 665). The cover shows adenomatous polyps and the sequence analysis that led to identification of the FAP gene. Researchers are trying to use the FAP gene and other biomarkers to predict the risk of cancer (see special report on molecular epidemiology, page 612). [Illustration by Julie A. Cherry]

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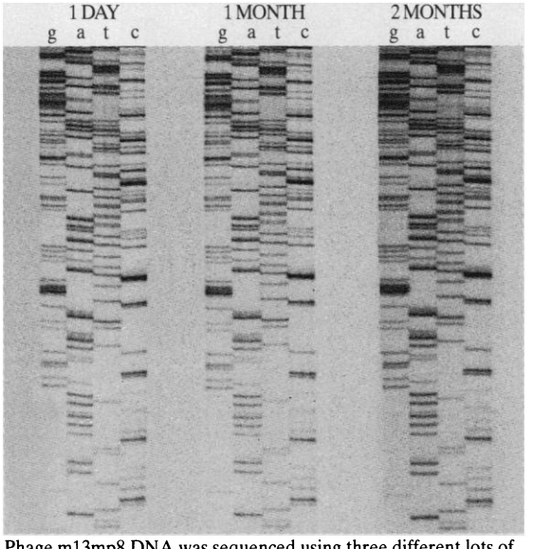

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This Week in SCIENCE

Stable phases

Buckminsterfullerene (C_{60}) will be valuable for the formation of electronic devices if it can be joined together with other materials. The prospects for developing stable heterostructures that consist of C_{60} as insulating material and superconducting layers of a material such as K_3C_{60} (an alkali-doped fullerene) now appear to be quite good (page 646). Such heterostructures could take the form of Josephson junctions, which are formed from two superconducting layers separated by an insulator, or quantum well structures, which are formed from layers of materials that have different electronic properties. Thin films of alkali-doped fullerenes were grown under ultrahigh vacuum conditions, and the stability of the resultant doped and undoped phases was analyzed. Poirier *et al.* report that when potassium or cesium is incorporated into thin films of C_{60}, stable junctions formed between the C_{60} phase and K_3C_{60} or Cs_3C_{60} phases. In contrast, K_6C_{60} and Cs_6C_{60} formed unstable junctions with C_{60}; fairly quickly the alkali migrated into the C_{60} phase to form a metallic phase.

Eruption potential

Yucca Mountain, Nevada, is under consideration as a burial site for high-level nuclear waste. One criterion for selecting a waste repository is that it remain stable for a minimum of 10,000 years. Yet Yucca Mountain has a history of volcanic eruptions, and young volcanic rocks (centers) of uncertain age are found in the mountains. The most recent activity in the region, which was at Lathrop Wells, was previously estimated from soil profile and geomorphic data to have occurred within the last 20,000 years. Turrin *et al.* have now reexamined the eruption potential of Lathrop Wells by dating this volcanic center with paleomagnetic and $^{40}Ar/^{39}Ar$ techniques (page 654). Their data indicate that the last activity at Lathrop Wells occurred about 140,000 years ago when there were two eruptions within 100 years of each other. If these dates are correct, then the area has evidently been volcanically stable for a period of time much longer than that required for safe storage of waste.

Protein folding

Protein G is a component of group G *Streptococci*; it is thought to play a part in the ability of these bacteria to evade immune responses of infected hosts. A portion of protein G, called the B1 domain, binds to the Fc portion of antibody molecules and interferes with the so-called "effector" activities of the antibodies that allow them to carry out their protective functions. Gronenborn *et al.* have studied the 56–amino acid structure of the B1 domain with high-resolution nuclear magnetic resonance spectroscopy (page 657). The domain has an unusual topology that has not been reported for any other protein. It has a four-stranded β sheet on top of which is a long helix. Almost all of the amino acids in B1 participate in hydrogen bonding, which is unusual: more typically, only 75% of the amino acids in proteins contribute to secondary structure. B1 has many hydrogen bonds stabilizing it but no disulfide bonds. In addition, the exterior of the domain is highly hydrophilic and the core is very hydrophobic. All of these features may figure in its unusual heat stability.

Identifying cancer genes

Genes that are closely associated with the development of colorectal cancer are being identified. The 5q21 region of the human chromosome was previously implicated in this disease; therefore, Kinzler, Nishisho, and others cloned and mapped several genes in the 5q21 region and then evaluated their relevance to the development of colorectal disease (pages 661 and 665). Specific mutations in genes APC and MCC were found to be associated with disease development in patients who develop colorectal cancers sporadically; one of these, APC, was mutated in patients with genetic predispositions to colorectal cancer (those with FAP or familial adenomatous polyposis, which is a precursor condition that leads to colorectal cancer, and the related Gardner's syndrome). As cancer researchers detect such cancer susceptibility genes and begin to understand how the genes interact with environmental carcinogens, they should be able to develop new biomarkers for identifying high-risk individuals. Developments in this growing field of molecular epidemiology, efforts to devise new clinical interventions to prevent disease in high-risk individuals, and ethical issues that are arising are discussed in a special report by Marx and Roberts (pages 612–616).

Epilepsy genes

El mice serve as models for certain types of human epilepsy. When the mice are about 3 months old they develop seizures that resemble those that occur in human epileptics, and seizures in both mice and humans can be controlled by the same anticonvulsive medications. A study by Rise *et al.* has clarified the genetic basis of the disease in mice, and this may simplify the search for epilepsy susceptibility genes in humans (page 669). The El mice were outcrossed with mice of normal strains and the progeny were backcrossed with appropriate parental mice. Seizure frequencies were recorded. One major gene was identified and mapped to chromosome 9; a minor modifier gene was identified on chromosome 2, and an interesting modifier was identified on chromosome 4; other suspect minor genes that may contribute to the epileptic phenotype were also identified. Chromosome 9 of the mouse is much like chromosome 3 of humans; many genes are similar and similarly linked. Therefore, it could prove fruitful to search in human chromosome 3 for a major epilepsy-associated gene. Epilepsy is, after stroke, the most common neurologic problem of humans.

■ RUTH LEVY GUYER

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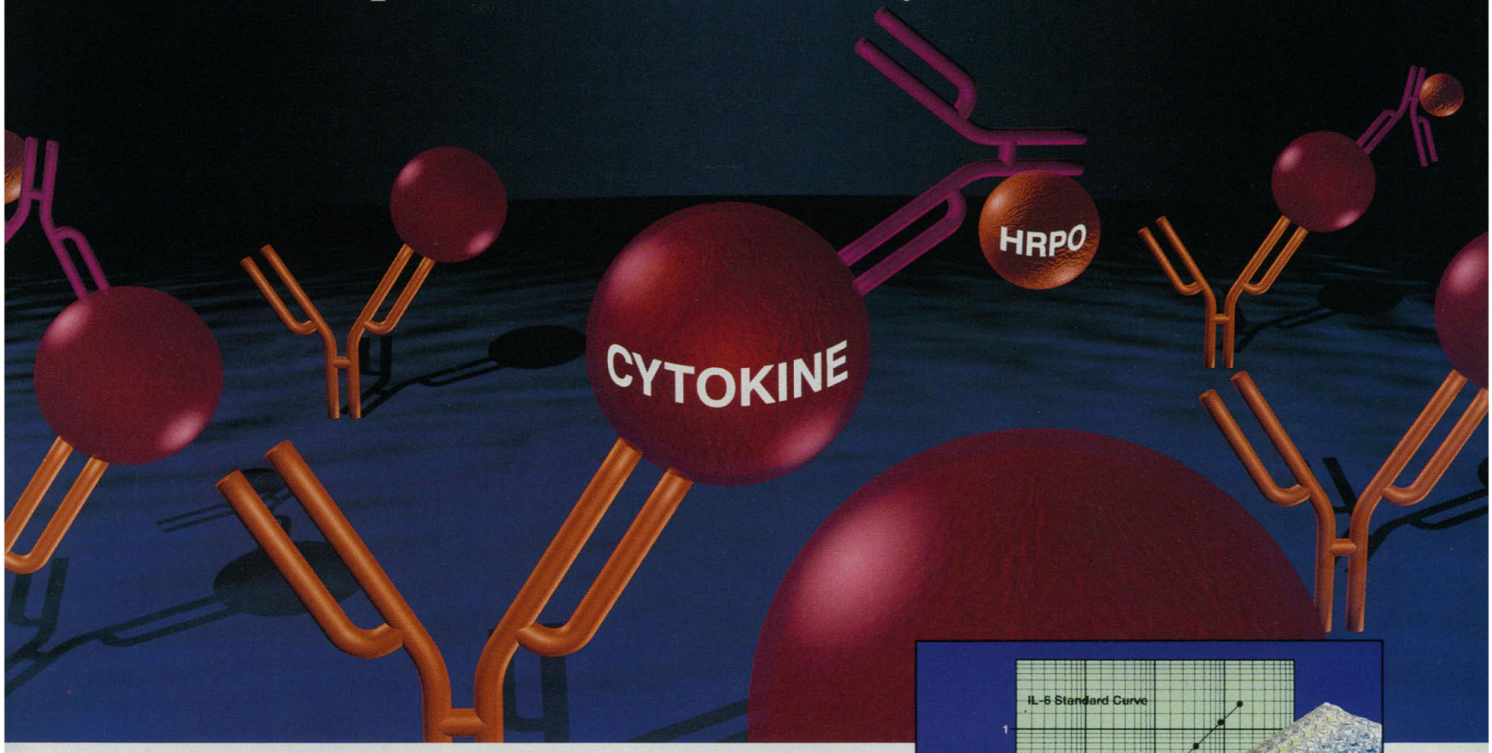

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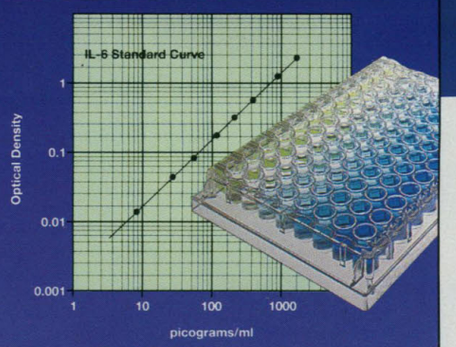

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SPECIAL TOPIC CHAIRPERSONS:

- **Tony Hunter, Salk Institue, ONCOGENES**
- **Richard Tullis, Synthetic Genetics EMERGING INNOVATIVE TECHNOLOGIES**
- **Darlene Roszak, Syngene Inc. NUCLEIC ACID AMPLIFICATION**
- **Frank Fujimura, Nichols Institute DETECTION, DIAGNOSTICS & GENETIC SCREENING**
- **Lyle Arnold, Genta APPLICATION OF ANTI-SENSE RNA**

OTHER PROGRAM FEATURES:
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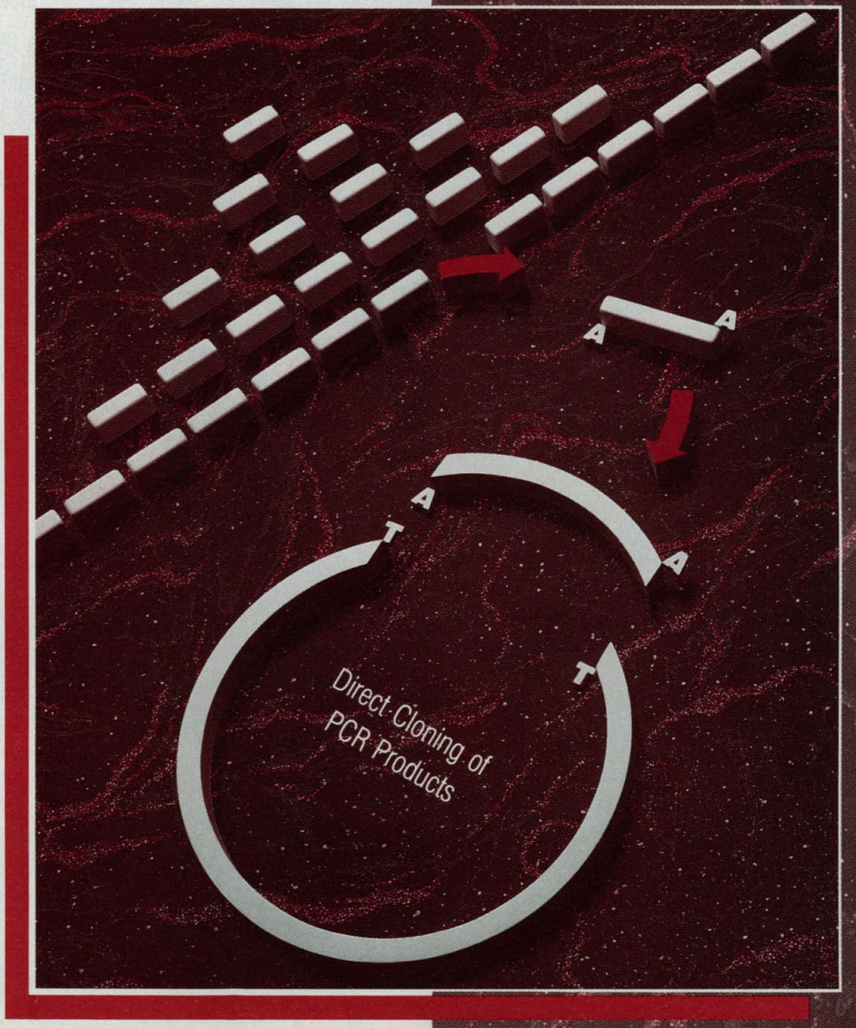

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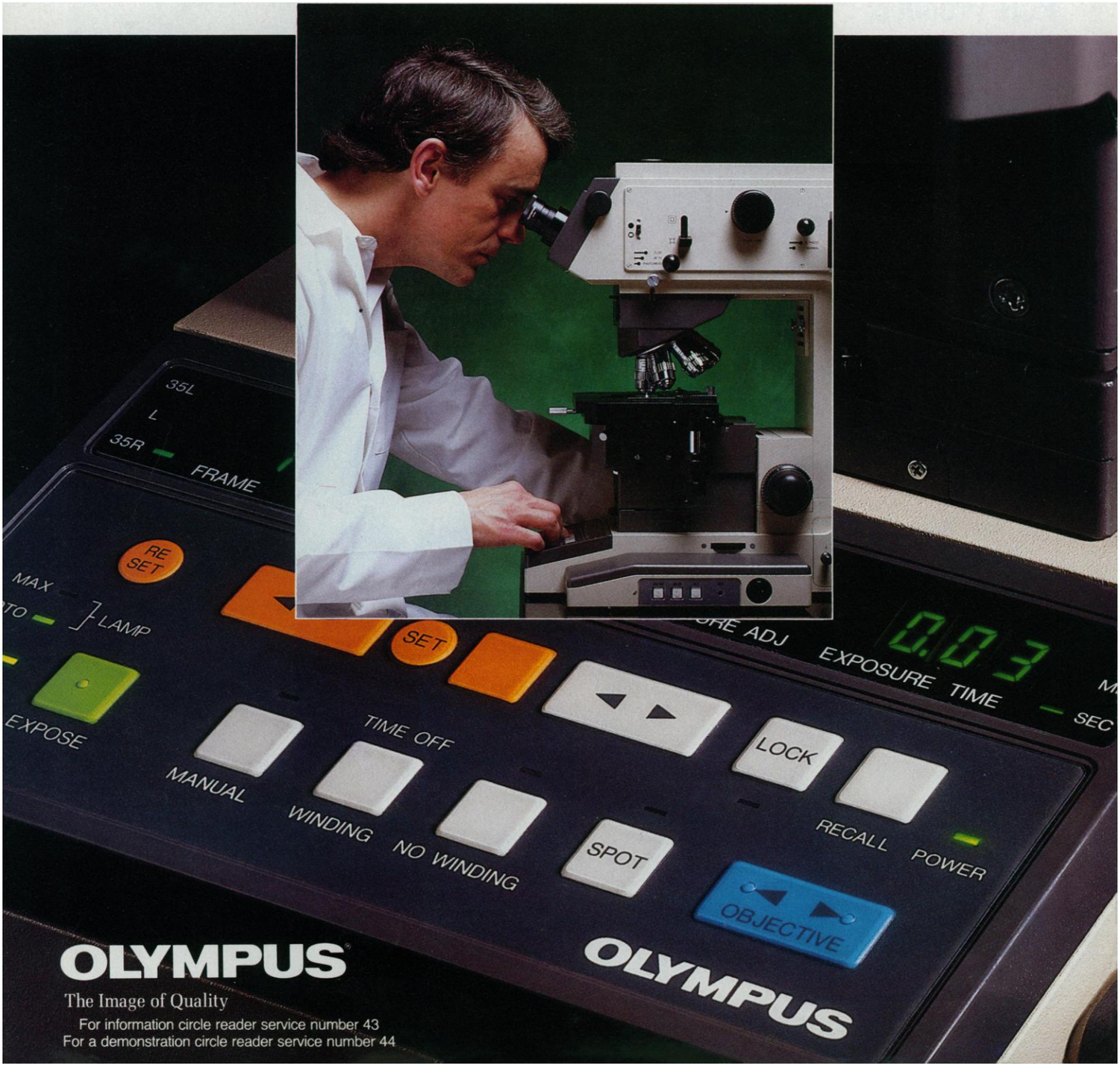

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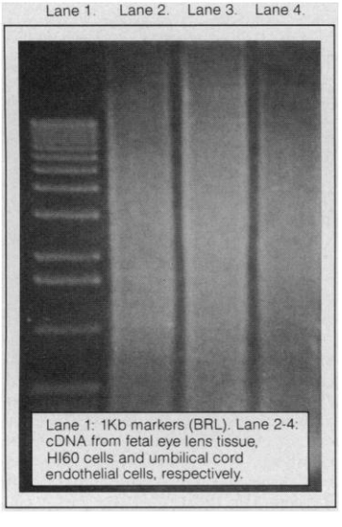

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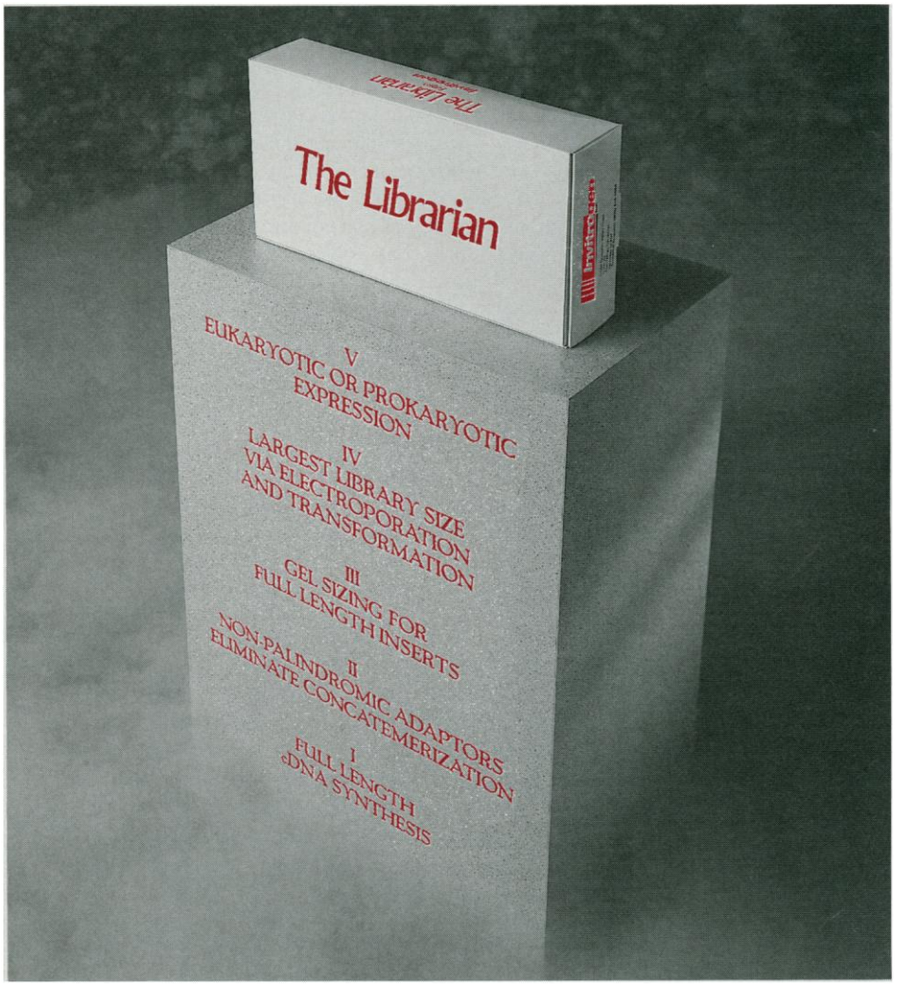

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SCIENTIFIC PROGRAM

MONDAY, OCTOBER 21

8:30 am-12:00 pm SESSION I — INFORMATICS

ELBERT BRANSCOMB: Lawrence Livermore National Laboratory – "Managing Genomic Data for the Research Community's Benefit"

EDWARD UBERBACHER: Oak Ridge National Laboratory – "Intelligent Methods for DNA Sequence Feature Recognition and Intepretation"

MINORU KANEHISA: Kyoto University – "Knowledge Information Processing for Genome Analysis"

CHRIS RAWLINGS: Imperial Cancer Research Fund – "Integrating Genome Information: A Knowledge-based Approach"

ROSS OVERBEEK: Argonne National Laboratory – "Setting up an Effective Query Capability: A Radical Proposal"

JULIO CELIS: Aarhus University – "Human 2-D Gel Protein Databases: Linking Protein and DNA Information"

12:00 pm-4:00 pm LUNCH/WORKSHOPS/EXHIBITS/POSTERS

4:00 pm-7:15 pm SESSION II — MODEL ORGANISMS

JOSEPH NADEAU: The Jackson Laboratory – "Encyclopedia of the Mouse Genome and the Database Integration Problem"

ANDRE GOFFEAU: Catholic University of Louvain – "The European Plan to Sequence the Yeast Genome: Progress Report"

KUNIO ISONO: Tohoku University – "Neurogenetics of Taste in *Drosophila*"

FOTIS C. KAFATOS: Harvard University/IMBB, Crete – "Integrated Maps of the *Drosophila* Genome"

EUGENE RINCHIK: Oak Ridge National Laboratory – "Fine-structure Functional and Physical Mapping of Germline Deletions in the Mouse"

CHRIS SOMERVILLE: DOE Plant Research Lab, Michigan State University, "The Arabidopsis Genome Project"

TUESDAY, OCTOBER 22

8:30 am-12:00 pm SESSION III — POLITICS

WALTER BODMER: Imperial Cancer Research Fund – "HUGO"

CHARLES R. CANTOR: DOE Human Genome Project – "U.S. Department of Energy"

MARK GUYER: National Institutes of Health – "Index Markers"

KENICHI MATSUBARA: Osaka University – "The Japanese Genome Project as of 1991"

BRONWEN LODER: Commission of the European Communities – "The EC Human Genome Analysis Programme"

12:00 pm-4:00 pm LUNCH/WORKSHOPS/EXHIBITS/POSTERS

4:00 pm-7:15 pm SESSION IV — PHYSICAL MAPS: CAN THEY BE COMPLETED?

GLEN EVANS: Salk Institute – "Physical Maps of Human Chromosomes"

HANS LEHRACH: Imperial Cancer Research Fund – "Of Mice and Men: The Global Analysis of the Mammalian Genome"

DAVID SCHLESSINGER: Washington University (St. Louis) – "Yeast Artificial Chromosome-based Mapping of 50 Mb of the Human X Chromosome (Xq24-qter)"

ANTHONY CARRANO: Lawrence Livermore National Laboratory – "A Chromosome 19 Physical Map"

ROBERT MOYZIS: Los Alamos National Laboratory – "Physical and Functional Mapping of the Human Genome"

WEDNESDAY, OCTOBER 23

8:30 am-12:00 pm SESSION V — METHOD DEVELOPMENT

RONALD W. DAVIS: Stanford University – "Sequencing the Yeast Genome"

WACLAW SZYBALSKI: McArdle Laboratory, University of Wisconsin – "Sequencing of Eukaryotic Genomes Without Cloning"

PIETER J. DEJONG: Lawrence Livermore National Laboratory – "A New Approach for Completing Contig Maps Using Alu-PCR"

LLOYD M. SMITH: University of Wisconsin – "High-speed DNA Sequencing in Ultrathin Gels"

DAVID WARD: Yale University – "Gene Mapping by Fluorescence In Situ Hybridization"

12:00 pm-4:00 pm LUNCH/WORKSHOPS/EXHIBITS/POSTERS

4:00 pm-7:15 pm SESSION VI — HUMAN LANDMARKS

PETER GOODFELLOW: Imperial Cancer Research Fund – "Chromosome Fragmentation Techniques"

ANTHONY MONACO: Imperial Cancer Research Fund/University of Oxford – "Genome Analysis of the Human X Chromosome"

GRANT R. SUTHERLAND: Adelaide Children's Hospital – "The Fragile X: A Novel Genetic Element"

L. L. CAVALLI-SFORZA: Stanford University – "Diversity and the Origin of Races"

MARY-CLAIRE KING: University of California, Berkeley – "Genetic Analysis of Breast Cancer in Families"

All speakers listed have been confirmed. Others will be added later.

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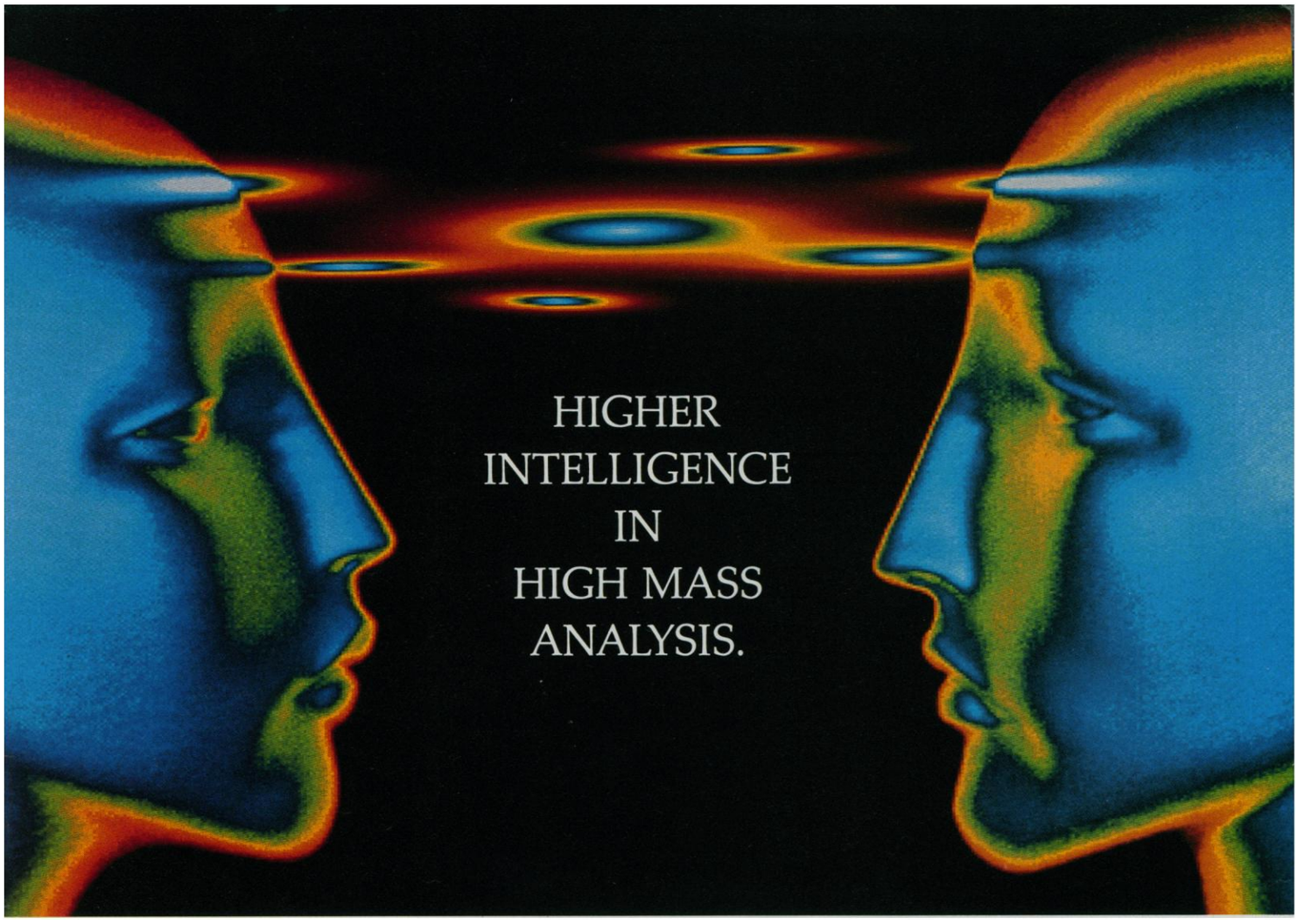

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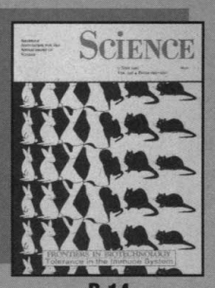

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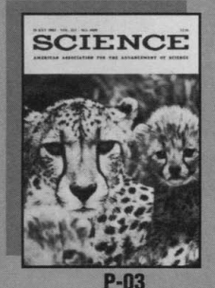

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