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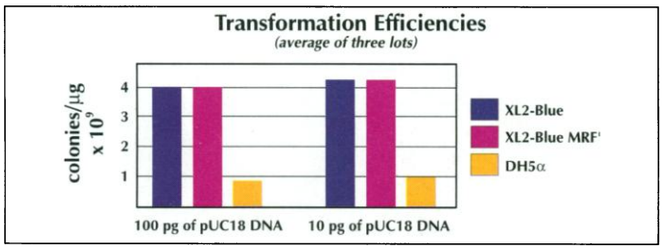

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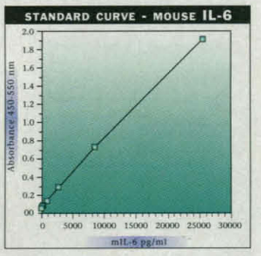

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ISSN 0036-8075
9 SEPTEMBER 1994
VOLUME 265
NUMBER 5178

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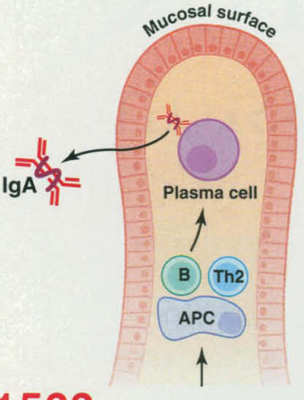


1522
New route for vaccines

MERCER RICHARDS/EARTHTRUST

1538
Illegal whaling gets marked

NEWS & COMMENT

NSF Gears Up for a Building Boom 1516
NIH Adds to the Facilities Boom 1517

USDA Holds Up Grants to Make a Political Point 1518

EPA Campaigns for Safer Chemicals 1519

Agreements Set Rules of the Road for Global Collaboration 1520

Ecologists Draft Plan to Dig in the Dirt 1521

RESEARCH NEWS

Triggering the First Line of Defense 1522

A New Way of Seeing Proteins in Motion 1525

Tuna Stocks: East Meets West 1525

Astronomers Gossip About the (Cosmic) Neighborhood 1526

Climate Modeling's Fudge Factor Comes Under Fire 1528

POLICY FORUM

Which Whales Are Hunted? A Molecular Genetic Approach to Monitoring Whaling 1538
C. S. Baker and S. R. Palumbi

PERSPECTIVES

Thumbs Up for Our Early Ancestors 1540
L. C. Aiello

Attractive Axon Guidance Molecules 1541
H. Baier and F. Bonhoeffer

ARTICLES

First Images of Asteroid 243 Ida 1543
M. J. S. Belton, C. R. Chapman, J. Veverka, K. P. Klaasen, A. Harch, R. Greeley, R. Greenberg, J. W. Head III, A. McEwen, D. Morrison. P. C. Thomas, M. E. Davies, M. H. Carr, G. Neukum, F. P. Fanale, D. R. Davis, C. Anger, P. J. Gierasch, A. P. Ingersoll, C. B. Pilcher

Catastrophes, Phase Shifts, and Large-Scale Degradation of a Caribbean Coral Reef 1547
T. P. Hughes

REPORTS

Simultaneous Observation of Columnar Defects and Magnetic Flux Lines in High-Temperature $Bi_2Sr_2CaCu_2O_8$ Superconductors 1552
H. Dai, S. Yoon, J. Liu, R. C. Budhani, C. M. Lieber

DEPARTMENTS

THIS WEEK IN *SCIENCE* 1505

EDITORIAL 1507
Risk Assessments of Low-Level Exposures

LETTERS 1509
Genetic Testing: J. A. Lowden; J. E. Cleaver • Mechanism of Scrapie Replication: P. T. Lansbury • Biodiversity Questions: P. R. Epstein and G. P. Chikwenhere; T. P. Young • Protein Configurations: J. E. Blalock

SCIENCESCOPE 1515

RANDOM SAMPLES 1529
Eight Get Medal of Science • Diet Chemistry • Recycling Elephants • Confluence of Interest

BOOK REVIEWS 1602
AIDS Epidemiology, reviewed by I. M. Longini Jr. • *The Explorers of Mars Hill*, J. Lankford • Other Books of Interest • Vignettes • Books Received

PRODUCTS & MATERIALS 1606

COVER

Hominid hand bones from Swartkrans Cave, South Africa. Comparative anatomy of the thumb, from *Paranthropus robustus* (about 1.8 million years ago), shows that this hominid could use tools. Other hominids found along with tools in deposits younger than 2.5 million years ago also evidently could use tools, but hominids that predate the appearance of tools lack the anatomical hallmarks of tool use. See page 1570 and the Perspective on page 1540. [Photo: Randall L. Susman]

Lattice Location of Trace Elements Within Minerals and at Their Surfaces with X-ray Standing Waves 1555
Y. Qian, N. C. Sturchio, R. P. Chiarello, P. F. Lyman, T.-L. Lee, M. J. Bedzyk

Reduction of Permeability in Granite at Elevated Temperatures 1558
D. E. Moore, D. A. Lockner, J. D. Byerlee

Grain Size–Dependent Alteration and the Magnetization of Oceanic Basalts 1561
D. V. Kent and J. Gee

Rapid Emplacement of Young Oceanic Lithosphere: Argon Geochronology of the Oman Ophiolite 1563
B. R. Hacker

Milankovitch Forcing of the Last Interglacial Sea Level 1566
T. J. Crowley and K.-Y. Kim

Carbon Dioxide Supersaturation in the Surface Waters of Lakes 1568
J. J. Cole, N. F. Caraco, G. W. Kling, T. K. Kratz

Fossil Evidence for Early Hominid Tool Use 1570
R. L. Susman

Requirement of Transcription Factor PU.1 in the Development of Multiple Hematopoietic Lineages 1573
E. W. Scott, M. C. Simon, J. Anastasi, H. Singh

Direct Observation of Enzyme Activity with the Atomic Force Microscope 1577
M. Radmacher, M. Fritz, H. G. Hansma, P. K. Hansma

Detection of Endogenous Malondialdehyde-Deoxyguanosine Adducts in Human Liver 1580
A. K. Chaudhary, M. Nokubo, G. R. Reddy, S. N. Yeola, J. D. Morrow, I. A. Blair, L. J. Marnett

Control of Angiogenesis in Fibroblasts by p53 Regulation of Thrombospondin-1 1582
K. M. Dameron, O. V. Volpert, M. A. Tainsky, N. Bouck

Mutations in *aquaporin-1* in Phenotypically Normal Humans Without Functional CHIP Water Channels 1585
G. M. Preston, B. L. Smith, M. L. Zeidel, J. J. Moulds, P. Agre

Reduced Rate of Disease Development After HIV-2 Infection as Compared to HIV-1 1587
R. Marlink, P. Kanki, I. Thior, K. Travers, G. Eisen, T. Siby, I. Traore, C.-C. Hsieh, M. C. Dia, E.-H. Gueye, J. Hellinger, A. Guèye-Ndiaye, J.-L. Sankalé, I. Ndoye, S. Mboup, M. Essex

Analysis of Sequence Transfers Resembling Gene Conversion in a Mouse Antibody Transgene 1590
B. Xu and E. Selsing

Involvement of Nitric Oxide in the Elimination of a Transient Retinotectal Projection in Development 1593
H. H. Wu, C. V. Williams, S. C. McLoon

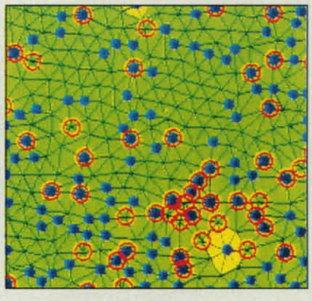
Activation of the Sphingomyelin Cycle Through the Low-Affinity Neurotrophin Receptor 1596
R. T. Dobrowsky, M. H. Werner, A. M. Castellino, M. V. Chao, Y. A. Hannun

TECHNICAL COMMENTS

Entropic Elasticity of λ-Phage DNA 1599
C. Bustamante, J. F. Marko, E. D. Siggia, S. Smith

Explicit and Implicit Learning and Maps of Cortical Motor Output 1600
M. A. Stadler; A. Pascual-Leone, J. Grafman, M. Hallett

1547
Causes of coral decline



1552
Pinned down

◩ Indicates accompanying feature

■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $92 ($50 allocated to subscription). Domestic institutional subscription (51 issues): $215. Foreign postage extra: Mexico, Caribbean (surface mail) $50; other countries (air assist delivery) $95. First class, airmail, student and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. **Printed in the U.S.A.**

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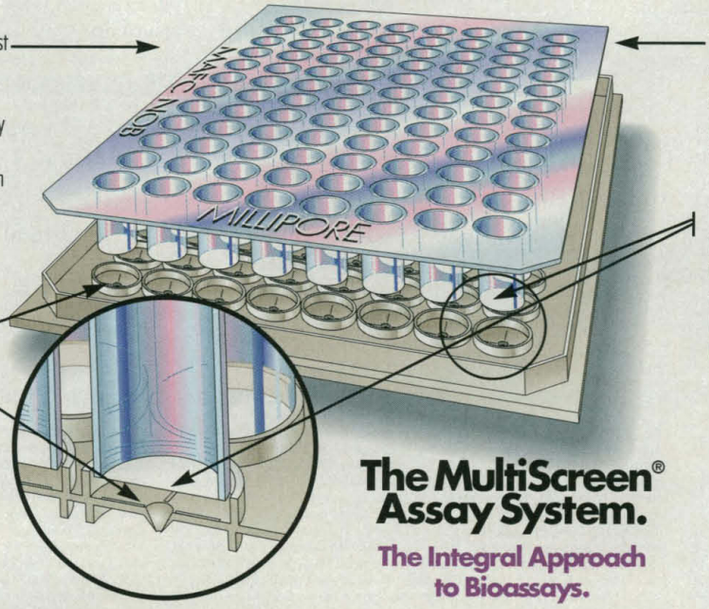

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edited by PHIL SZUROMI

Whale watching

Although whales continue to be hunted, only certain species can be taken legally. In a Policy Forum, Baker and Palumbi (p. 1538) present molecular genetics evidence that some of the commercially available whale products obtained from retail markets in Japan are from species whose hunting has been banned, such as fin and humpback whales. They argue that monitoring the products rather than just the catch is necessary to protect endangered whales.

Ravaged reefs

As recently as 1970, coral reefs nearly surrounded the island of Jamaica in the Caribbean Sea and served as a focus for the study of coral reef ecosystems and dynamics. In the past two decades, however, the reefs have degraded dramatically. In an Article, Hughes (p. 1547) describes the changes in the reefs and in the associated ecosystems and investigates the factors, including overfishing, pollution, and storms that led to the changes. Benthic algal communities rather than reefs now surround much of the island.

Back and forth

Bragg or coherent scattering in x-ray diffraction from a solid arises from a plane of atoms. If a crystal is aligned such that the scattered x-rays are reflected back along the path of the incident rays, then these two beams can interfere, and with careful alignment an x-ray standing wave can be set up. This standing wave propagates into the crystal, and atoms may absorb these x-rays and fluoresce. Qian *et al.* (p. 1555) used this standing wave technique to achieve very high sensitivity for the analysis of trace elements in a calcite crystal.

Defects and flux pinning

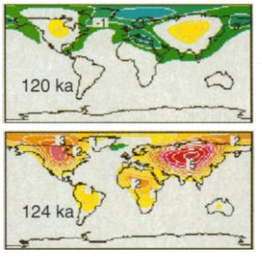
A superconductor can carry only so much current at a given temperature and remain a superconductor; the magnetic field caused by the flowing current disrupts the superconducting state. Also, in the high-temperature copper oxide superconductors, the magnetic flux lines resulting from flowing currents need to be pinned to defect sites; moving flux lines also lead to electrical resistance. Dai *et al.* (p. 1552) deliberately introduced columnar defects into $Bi_2Sr_2CaCu_2O_8$ superconductors by heavy-ion irradiation. They chemically etched these samples to identify the defect sites by scanning electron microscopy, and at the same time determined the structure of the flux line lattice by studying the distribution of magnetic iron clusters that were used to decorate the surface. They find that flux lines occupy only certain defect sites, suggesting that improvements in pinning may be possible.

Put in its place

Ophiolites are presumed pieces of oceanic crust and mantle that have been emplaced onto continents. Although studied for clues to the nature of mid-ocean ridges, their exact origins and evolution have been uncertain. By comparing dates from the Samail ophiolite in Oman and the metamorphic rocks underneath it, Hacker (p. 1563) suggests that this well-studied ophiolite was emplaced and cooled rapidly, within about 1 million years of its crystallization. The short time span implies that the ophiolite formed close to cold continental or oceanic crust, not in the middle of an ocean basin.

High seas

A key problem for understanding the effects of Earth's orbital variations on climate is the timing of high stands of sea level during the last interglacial period. Some recent studies seem to suggest that sea level crested several thousand years before the peak in solar insolation in the Northern Hemisphere approximately 126,000 years ago. The peak is complicated, however, because variations in insolation due to obliquity peaked



before those due to precession, rather than together as in the Holocene. Crowley and Kim (p. 1566) used a climate model to show that this complicated pattern of forcing can account for the early high sea-level stands.

Lost their lines

The diversity of mature blood cells has its origins in stem cells, which progress through a hierarchy of developmental intermediates. Scott *et al.* (p. 1573) found that mouse embryos that were homozygous for a mutation in the gene locus of the transcription factor PU.1, which was targeted to stem cells, died at a late gestational stage. Development of megakaryocytes and erythroid progenitors was normal, but progenitors of B and T cells, monocytes, and granulocytes were missing. These results suggest the existence of a lymphoid-myeloid multilineage progenitor that depends on *PU.1* expression.

p53 at the switch

Tumor cells must stimulate angiogenesis (the formation of new blood vessels) in order to grow and metastasize efficiently. Dameron *et al.* (p. 1582) show that in human fibroblasts, the switch from a nonangiogenic to an angiogenic phenotype coincides with loss of the tumor suppressor gene *p53*. This switch appears to be mediated through reduced production of thrombospondin-1, an inhibitor of angiogenesis whose expression is positively regulated by p53.

Less virulent

The two types of human immunodeficiency viruses, HIV-1 and HIV-2, differ in their geographic distributions; HIV-1 usually predominates, but in some areas, such as West Africa, HIV-2 is more prevalent. Fewer AIDS cases have been reported in West Africa than in Central and East Africa. Marlink *et al.* (p. 1587) surveyed HIV-1 and HIV-2 infection and disease in female sex workers in Senegal from 1985 to 1993. They found that HIV-2 is less virulent: 5 years after seroconversion, one-third of the women infected with HIV-1 had developed AIDS symptoms, whereas none of the women infected with HIV-2 were symptomatic. The rate of developing abnormal $CD4^+$ cell counts was also less for HIV-2 infection.

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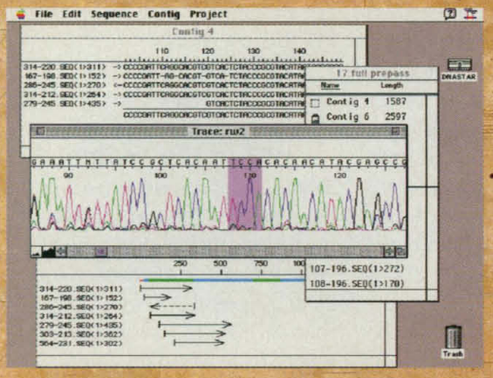

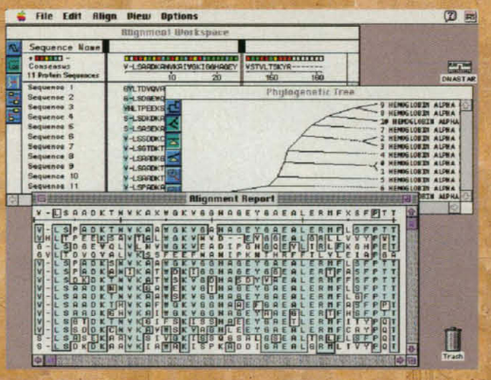

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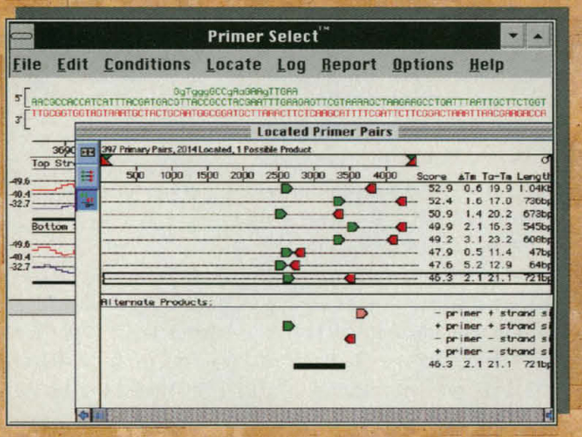

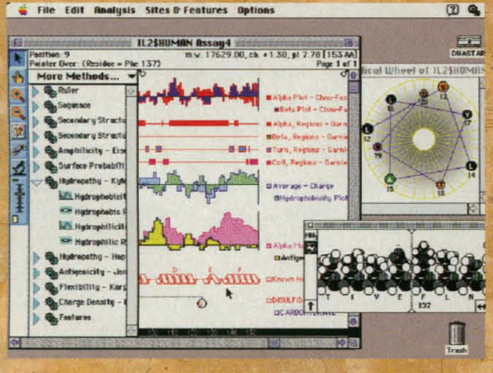

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- **Gerald Holton said so in *Science and Anti-Science***
- **Richard S. Nicholson said so in *Science* (vol. 261)**
- **Paul R. Gross and Norman Levitt said so in *Higher Superstition***

Formerly the attacks came from outside the academic and scientific disciplines. Increasingly, now, they come from within.

These attacks are dangerous:

- They undermine public confidence
- They alter directions of research
- They affect funding
- They subvert the standards of reason and proof

> *...alternative sciences or parasciences by themselves may be harmless enough except as one of the opiates of the masses, but...when they are incorporated into political movements they become a time bomb waiting to explode. We have recently been watching just such a possibility in the United States.*
>
> — **Gerald Holton**

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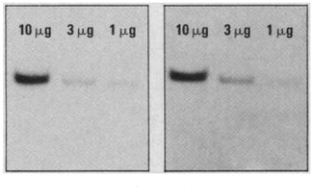
The Boehringer Mannheim Genius™ System makes sensitive scientific procedures equally as swift and safe. In hours—not days—probes prepared with the Genius System can detect single copy genes in as little as 1 μg of DNA in a genomic Southern blot, and are guaranteed to detect 0.03 pg of DNA in a direct dot blot.



Parallel human genomic Southern blots demonstrate the high sensitivity and low background provided by the Genius System (right, 12-min. exposure) compared to probes prepared with ^{32}P (left, 3-day exposure).

Like traditional radioactive methods, the Genius System provides specific and reliable detection of target sequences. But unlike other nonradioactive methods, the Genius System uses a unique antibody-based protocol that minimizes background interference, maximizes the signal-to-noise ratio, and produces your results faster.

Safety and sensitivity combined

Every time you make a Southern blot or dot/slot blot, screen a library or conduct an *in situ* hybridization with radioactive methods, you expose yourself and those around you to the risks of radiation. Every time you use the Genius System to perform these same procedures, you receive the assured safety that only nonradioactive products provide, along with guaranteed sensitivity and specificity.

Sensitivity to your needs

Boehringer Mannheim's user-training programs and technical support personnel can help make your conversion to nonradioactive DNA labeling and detection procedures smooth and trouble-free. Contact your Boehringer Mannheim representative or call 1-800-262-4911 (514-686-7141 in Canada).

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GENIUS™
SYSTEM

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What's the least you can expect from Pharmacia Biotech automated DNA sequencing?

Choice

R1709

The last thing you want automation to do is restrict your choices. So when we designed ALF™, our automated DNA sequencer, we made sure that it gave you maximum choice – in chemistry, in methodology, in data presentation. One important example of the choice it offers is the ability to use labelled or unlabelled primers, an economical way of dealing with the need for a variety of primers.

With its ease of use, speed of operation, choice of chemistries and the ability to present raw as well as processed data, ALF ensures that you get the choices you need for the results you want.

Which means that when it comes to choosing a DNA sequencer, go for the one that gives you choice.

Pharmacia Biotech puts time on your side.

Pharmacia Biotech

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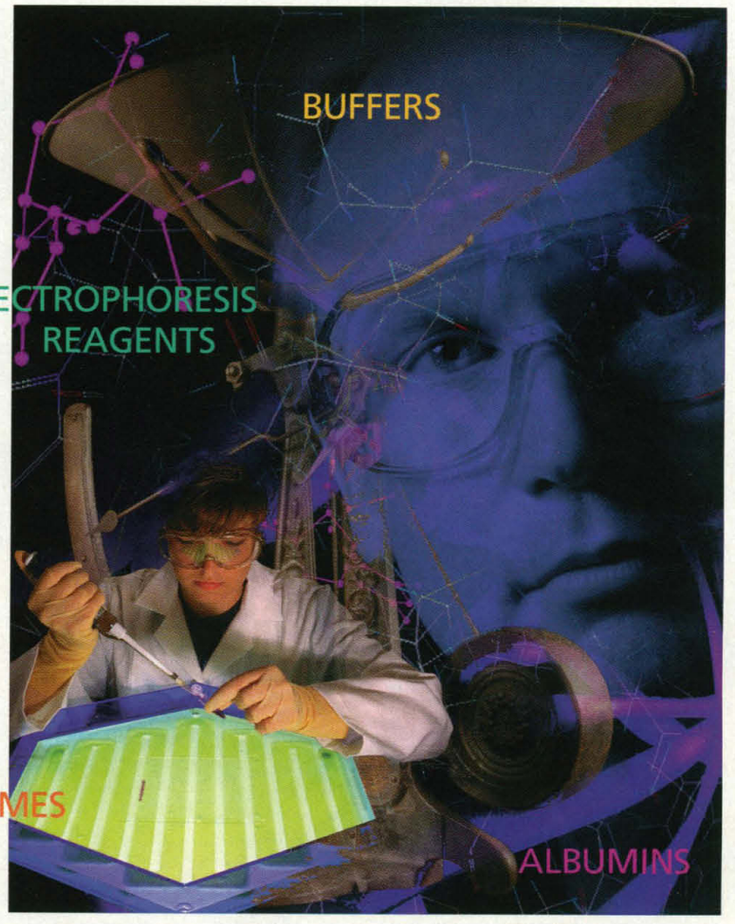

What distinguishes a chemical company: First and foremost - service; which is Sigma's approach to supporting the future of research. Should technical questions arise, a Sigma specialist is available to assist you with the use or application of our 33,000-plus products. In addition - quality; every one of Sigma's products is thoroughly assayed in state-of-the-art analytical laboratories using the most demanding analytical criteria.

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Dog-eared, rumpled & the "most frequently used" scientific journal.

According to a report in the May 1994 edition of *Welch Library Issues,* SCIENCE tops the list of the most frequently used journals in one of the largest biomedical collections in the world: The William H. Welch Medical Library, Johns Hopkins University School of Medicine. Four times a year for a two-week period the Welch Library staff tracks the usage of scientific and medical journals in the library. According to the data collected from 1990 to March of 1994, SCIENCE received 1,953 uses. That's over 100 more uses than the second most used journal listed.

Each week 160,000 subscribers around the globe turn to SCIENCE for the most important leading-edge research and the latest scientific news stories. No wonder copies of SCIENCE in libraries look a bit dog-eared and rumpled. SCIENCE is the journal scientists turn to first.

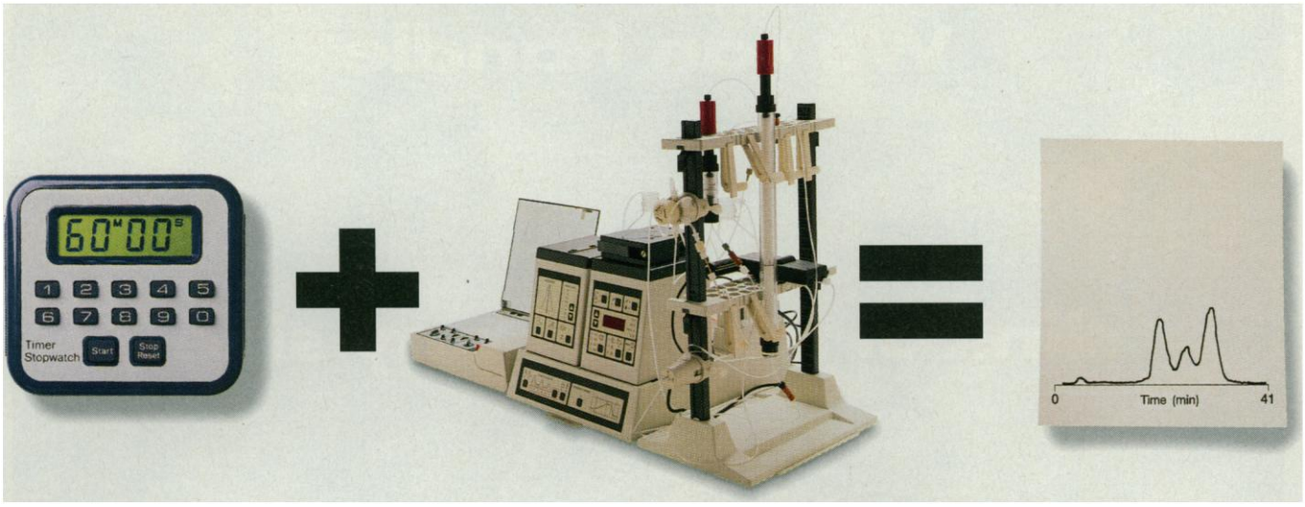
SCIENCE

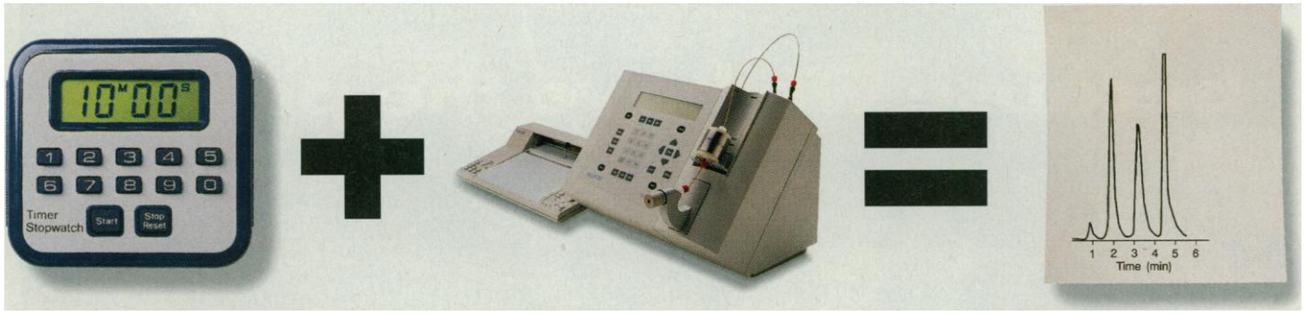
Most frequently used journals

in the William H. Welch Medical Library, Johns Hopkins University School of Medicine

SCIENCE	**1,953**
JAMA	*1,846*
New England Journal of Medicine	*1,765*
Journal of Biological Chemistry	*1,646*
Nature	*1,614*
Lancet	*1,577*
Proceedings of the National Academy of Sciences of the USA	*1,331*
Cell	*1,024*
American Journal of Physiology	*739*
Cancer	*731*
American Journal of Epidemiology	*667*
Journal of Immunology	*661*
Brain Research	*652*
Cancer Research	*647*
Annals of Internal Medicine	*615*

Source: Welch Library Issues, May 1994, Volume 6, Number 3





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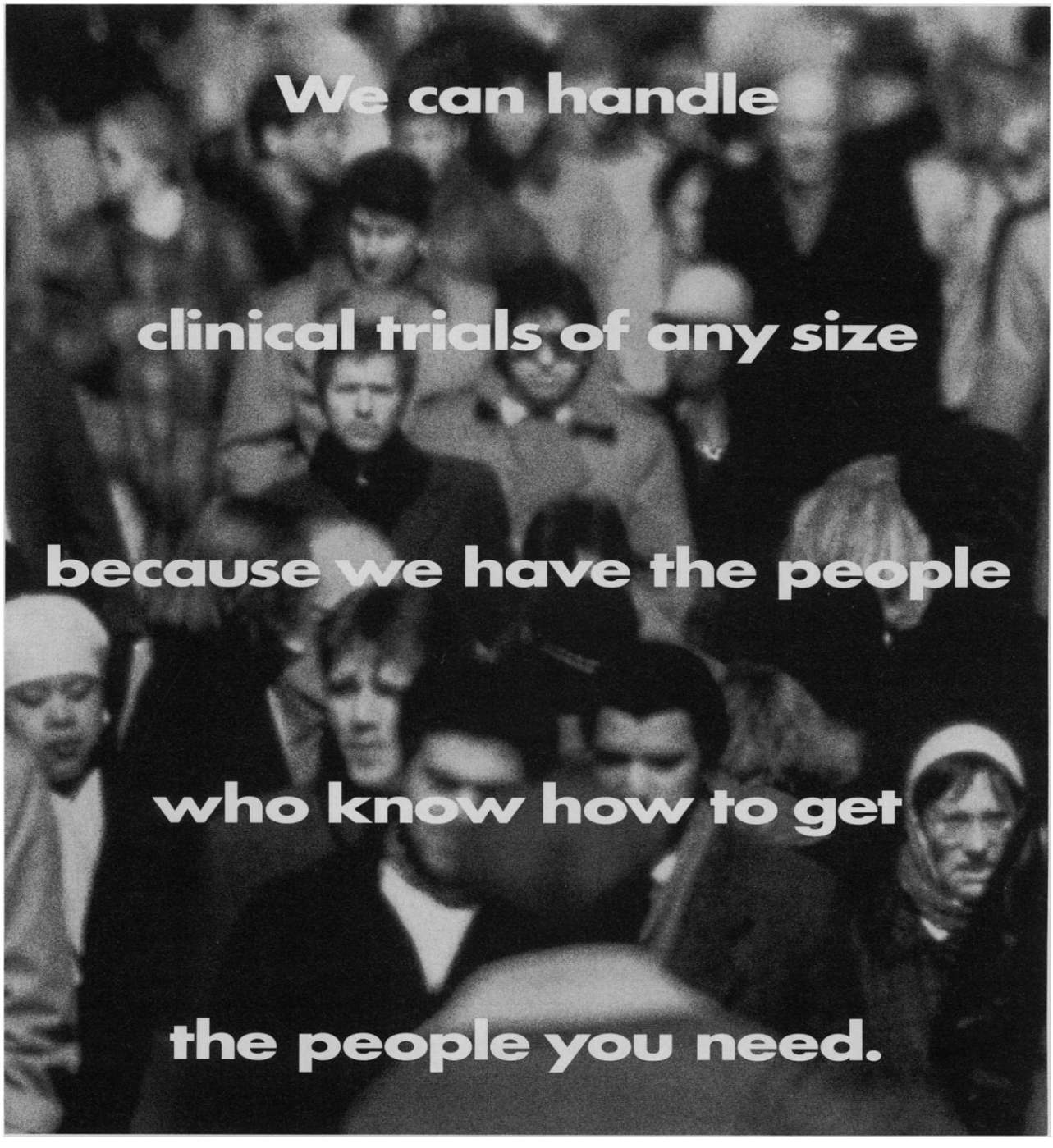

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Don't let small sample dialysis get out of hand.

Take control with the new Pierce Slide-A-Lyzer™ Dialysis Cassettes!

Load a sample for dialysis easier and faster than ever with this revolutionary new system. The new Pierce Slide-A-Lyzer™ Dialysis Cassette replaces the mess and hassles of conventional tubing with a more convenient, more effective approach.

1.

No more boiling, soaking, tying, or clamping - all you need is a syringe to load and remove your sample from these ready-to-use, disposable cassettes. The exclusive cassette design gives you total sample control, good surface-to-volume ratio and consistently reliable sample recovery. For even greater convenience, use the accessory Buoys to float your sample during dialysis, and as a bench-top cassette stand during loading and recovery.

2.

Pierce Slide-A-Lyzer™ Cassettes have a 0.5 - 3.0 ml sample capacity, 10,000 molecular weight cut-off, and are ideal for routine dialysis of protein, nucleic acid and carbohydrate samples.

3.

Product #	Description	U.S. Price
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66430	**Slide-A-Lyzer™ Buoys, 10 pack**	$12
66490	**Slide-A-Lyzer™ Syringe and 18G Needle Accessories, 10 pack** Contains: 10 each of 5 cc single-use, sterile, polypropylene syringes with Luer-Lok® tips and single-use, sterile, 18-gauge, 1" needles compatible for use with the Slide-A-Lyzer™ Dialysis Cassette. Ideal for nucleic acid applications.	$9

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Eighteenth Annual Symposium

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"Molecular Evolution and Biotechnology"

Presentations of the Ciba Drew Award in Biomedical Research will be made to:

Thomas R. Cech, PhD
University of Colorado
Boulder, CO
"Catalytic RNA: Mechanism and Structure"

Albert Eschenmoser, PhD
ETH–Zurich
Switzerland
"Toward a Chemical Etiology of the Natural Nucleic Acids"

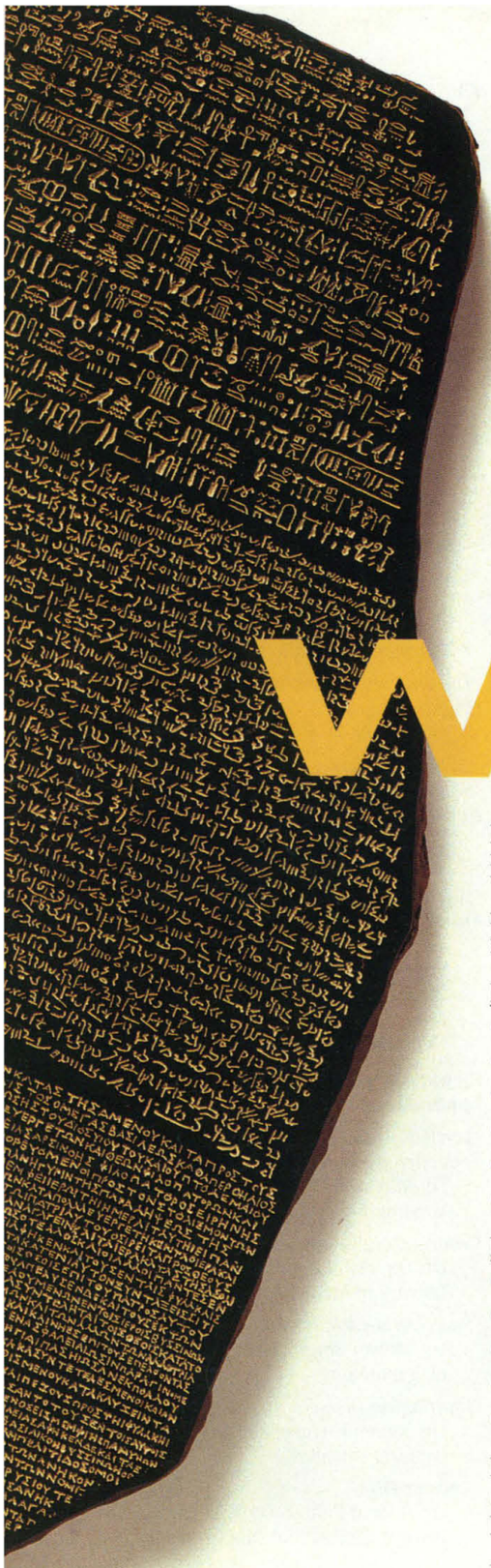
Manfred Eigen, PhD
Max Planck Institute
Göttingen, Germany
"Molecular Diagnostics and Evolutionary Biotechnology"

The proceedings will be introduced and moderated by:

George deStevens, PhD
Research Professor of Chemistry
Drew University

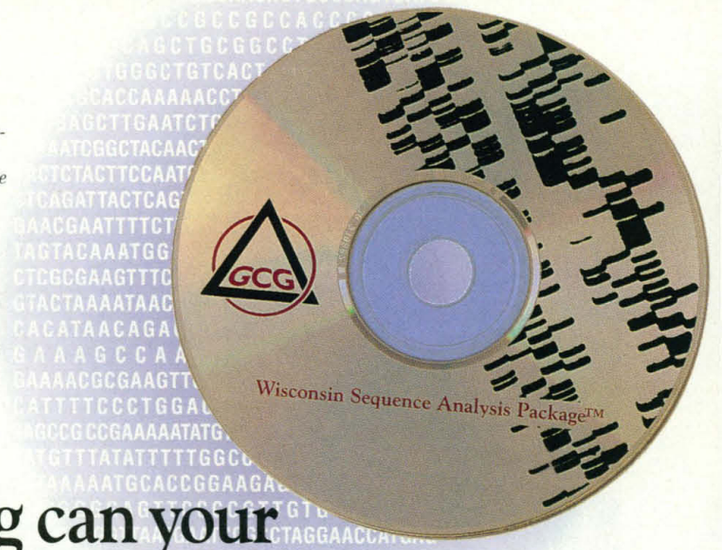
Baldwin Gymnasium
William and Carol Simon Forum and Athletic Center
Madison, NJ 07940
Tuesday, 11 October 1994
1:30 pm-5:30 pm

Address inquiries to:
George deStevens, PhD, Frontiers in Biomedical Research
Drew University, Madison, New Jersey 07940



For over 1,000 years the art of reading ancient Egyptian hieroglyphics was lost to the world. Then, in 1799 the Rosetta Stone was discovered. It was the key to unlocking the language of hieroglyphics.

The Wisconsin Sequence Analysis Package provides you with the key to discovering information in a language even older than hieroglyphics: DNA, the language of life.



How long can your research afford to wait?

When trying to decipher a complex language, certain tools are necessary for quick, successful interpretation.

The **Wisconsin Sequence Analysis Package** developed by Genetics Computer Group (GCG) is a complete sequence analysis package, handling database searching, sequence comparison, secondary structure prediction, sequence assembly and much more. And **Digital's Alpha AXP** computers give the Wisconsin Package the power you need to work in a field where new sequences are added to the databases at a rate of over 250,000 residues per day.

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Dr. P. Marcus, P. Betts and Dr. M. Sekellick, University of Connecticut Biotechnology Center

Project: First isolation of the chicken interferon gene. Journal of Interferon Research 14:83-91, 1994.
Accession number: U07868

Software: Wisconsin Sequence Analysis Package

Computer: Digital Alpha AXP 3000 Model 500

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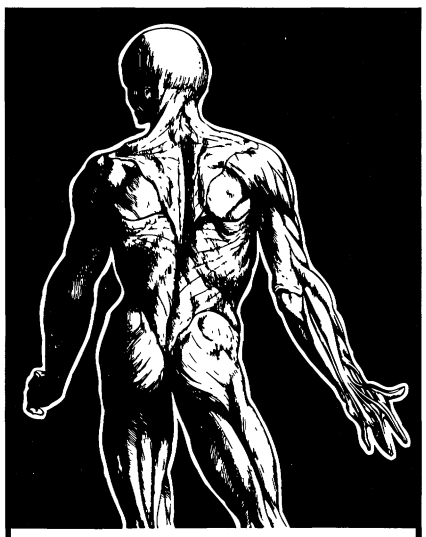

HUMAN GENOME 1994

THE GENES AND BEYOND

THE INTERNATIONAL CONFERENCE

OCTOBER 2–5, 1994

THE WASHINGTON RENAISSANCE HOTEL WASHINGTON, D.C.

CONFERENCE AGENDA

SUNDAY, OCTOBER 2

Welcoming Reception

MONDAY, OCTOBER 3

Plenary Session I: Genome Analysis – The New Frontier

"Human Gene Identification by Positional Cloning"
Dr. Francis Collins, National Center for Human Genome Research

"Genetic Basis of Human Colorectal Cancer"
Dr. Bert Vogelstein, Johns Hopkins Oncology Center

"Mapping Genes and Genomes: Genetic Dissection of Complex Traits"
Dr. Eric Lander, Whitehead Institute/ MIT

"Human Genome Diversity"
Dr. Mary Claire King, University of California, School of Public Health

"Manipulating Cancer Genes in the Mouse"
Dr. Harold Varmus, National Institutes of Health

"Intellectual Property: DNA and its Offspring"
Dr. Kate Murashige, Morrison & Foerster

"Presymptomatic Diagnosis of Self and Progeny"
Dr. C. Thomas Caskey, HUGO

Concurrent Sessions

M1 *"New Methods of DNA-Based Diagnosis"*
Dr. Stephen P.A. Fodor, Affymetrix, Inc.

M2 *"Human Gene Identification"*
Dr. Kay E. Davies, Institute of Molecular Medicine, University of Oxford

M3 *"Social and Scientific Issues in Genetic Testing"*
Dr. Nancy Wexler, Hereditary Disease Foundation

M4 *"Gene Therapy"*
Dr. Inder M. Verma, The Salk Institute

TUESDAY, OCTOBER 4

Plenary Session II: Development and Signal Transduction

Special Guest: Donna Shalala, U.S. Department of Health and Human Services

"MYOD & Myogenesis"
Dr. Harold Weintraub, Fred Hutchinson Cancer Research Center

"Genome Analysis in the Mouse"
Dr. Shirley M. Tilghman, Princeton University

"Pax: Genes for Mice and Men"
Dr. Peter Gruss, Max Planck Institute of Biophysical Chemistry, Germany

"From an Interferon Clone to the Regulation of Oncogenesis"
Dr. Tadatsugu Taniguchi, Institute for Molecular and Cellular Biology, Osaka University

"C. elegans Genome Project"
Dr. Richard Wilson, Washington University Medical School

"Small GTPases – Switching on Biological Responses"
Dr. Alan Hall, MRC Laboratory for Molecular Cell Biology, U.K.

Concurrent Sessions

T1 *"Gene Targeting"*
Dr. Elizabeth Robertson, Harvard University

T2 *"Sequence to Function"*
Dr. Temple F. Smith, Biomolecular Engineering Research Center, Boston University

T3 *"Education and the Human Genome Project"*
Dr. Paula Gregory, National Center for Human Genome Research, NIH

T4 *"Chromatin Structure and the Regulation of Gene Expression"*
Dr. Gary Felsenfeld, Laboratory of Molecular Biology, NIH

WEDNESDAY, OCTOBER 5

Plenary Session III: Mapping

"Toward the Ultimate Generation of an Integrated Map of the Human Genome"
Dr. Daniel Cohen, C.E.P.H., France

"Application of High Resolution Genetic Maps to Studies of Common Disorders"
Dr. Jeffrey C. Murray, University of Iowa

"Yeast Genome Project"
Dr. André Goffeau, Université Catholique de Louvain, Unité de Biochimie Physiologique

"The Drosophila Genome Project – a Progress Report"
Dr. Gerald M. Rubin, University of California

"Status and Prospects for the Complete Human Genome Sequence"
Dr. Richard A. Gibbs, Baylor College of Medicine

"High Speed DNA Sequencing: Present and Future Technologies"
Dr. Lloyd M. Smith, University of Wisconsin

"Towards a Complete Set of Human Genes"
Dr. J. Craig Venter, The Institute for Genomic Research

Plenary Session IV: Mapping and Applications

"Vertically Integrated Mapping and Sequencing of Human DNA"
Dr. Maynard Olson, University of Washington School of Medicine

"Interpreting Genes and Genomes"
Dr. David J. Lipman, NIH, National Library of Medicine

"Some Applications of a Genome Library"
Dr. Melvin Simon, California Institute of Technology

"Huntington Disease"
Dr. James F. Gusella, Massachusetts General Hospital

"Ancient DNA"
Dr. Svante Pääbo, Zoologisches Institut, Universitat Munchen

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THE INTERNATIONAL CONFERENCE ON THE HUMAN GENOME PROJECT

OCTOBER 2-5, 1994 ■ WASHINGTON, D.C.

CONFERENCE REGISTRATION FORM

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2. A check payable to Global Trade Productions, Inc. must accompany this form. Correct fees must be received to be registered.
3. Your name and organization will appear exactly as you indicate on the form below.
4. PRINT OR TYPE ALL INFORMATION REQUESTED.

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Is this your first Human Genome Conference?

❑ Yes ❑ No

If not, how many have you attended?

❑ 1 ❑ 2-5 ❑ more than 5

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Title _____

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❑ Please check here if you have a disability that requires auxiliary aids during the Conference. Describe your special needs: _____

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_____

(We'll contact you prior to the Conference.)

CONCURRENT SESSIONS

To aid us in planning, please check the sessions you are most likely to attend. You are not committed to these specific sessions. (See Preliminary Agenda for presentation titles.)

Monday, October 3	Tuesday, October 4
❑ M1	❑ T1
❑ M2	❑ T2
❑ M3	❑ T3
❑ M4	❑ T4

Please check if you will attend the Welcoming Reception, Sunday, October 2.

❑ Yes ❑ No

Please check if you plan to submit an abstract.

❑ Yes ❑ No

REGISTRATION OPTIONS

Mark your selection(s) below by circling the appropriate fee.

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❑ Monday ❑ Tuesday ❑ Wednesday

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