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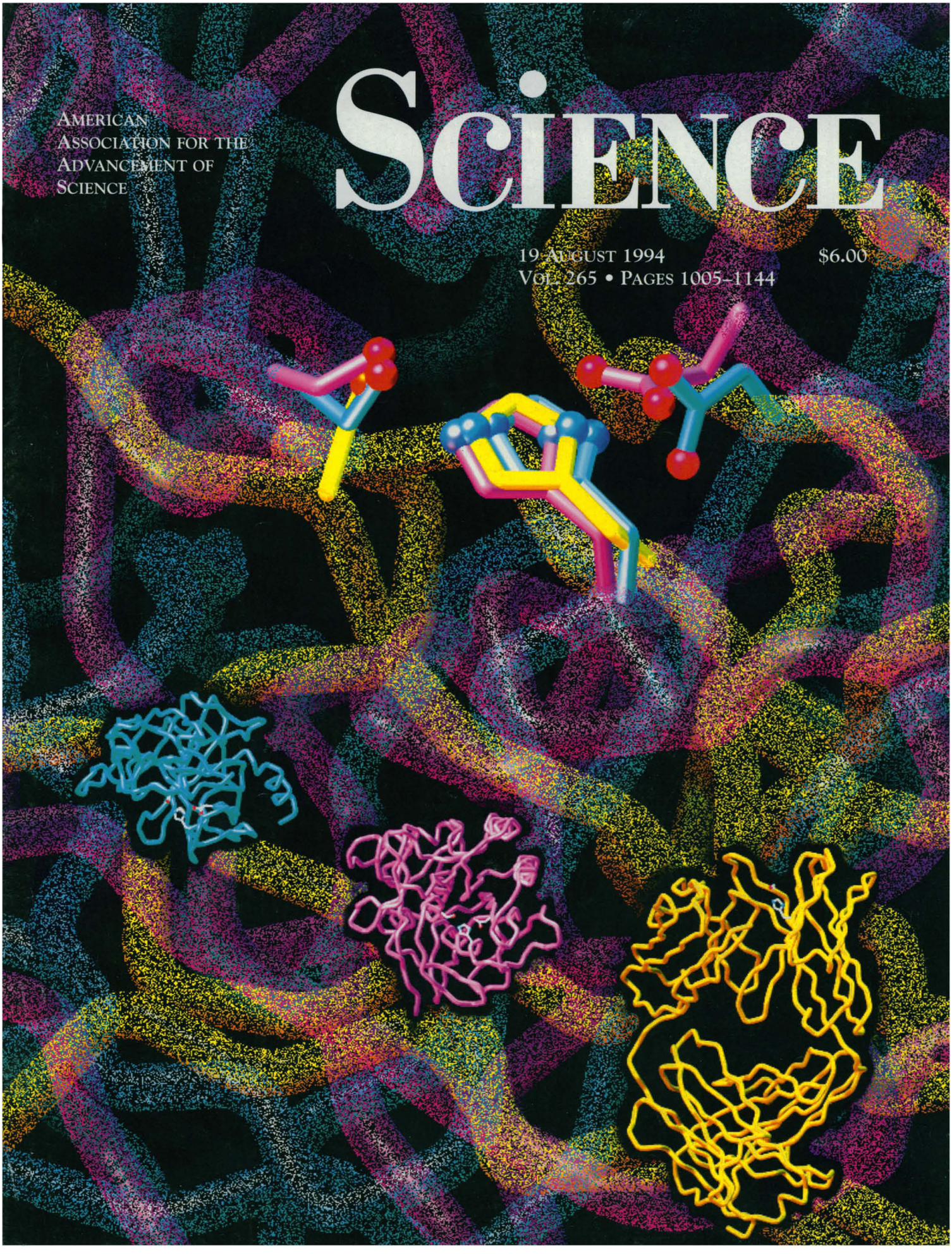

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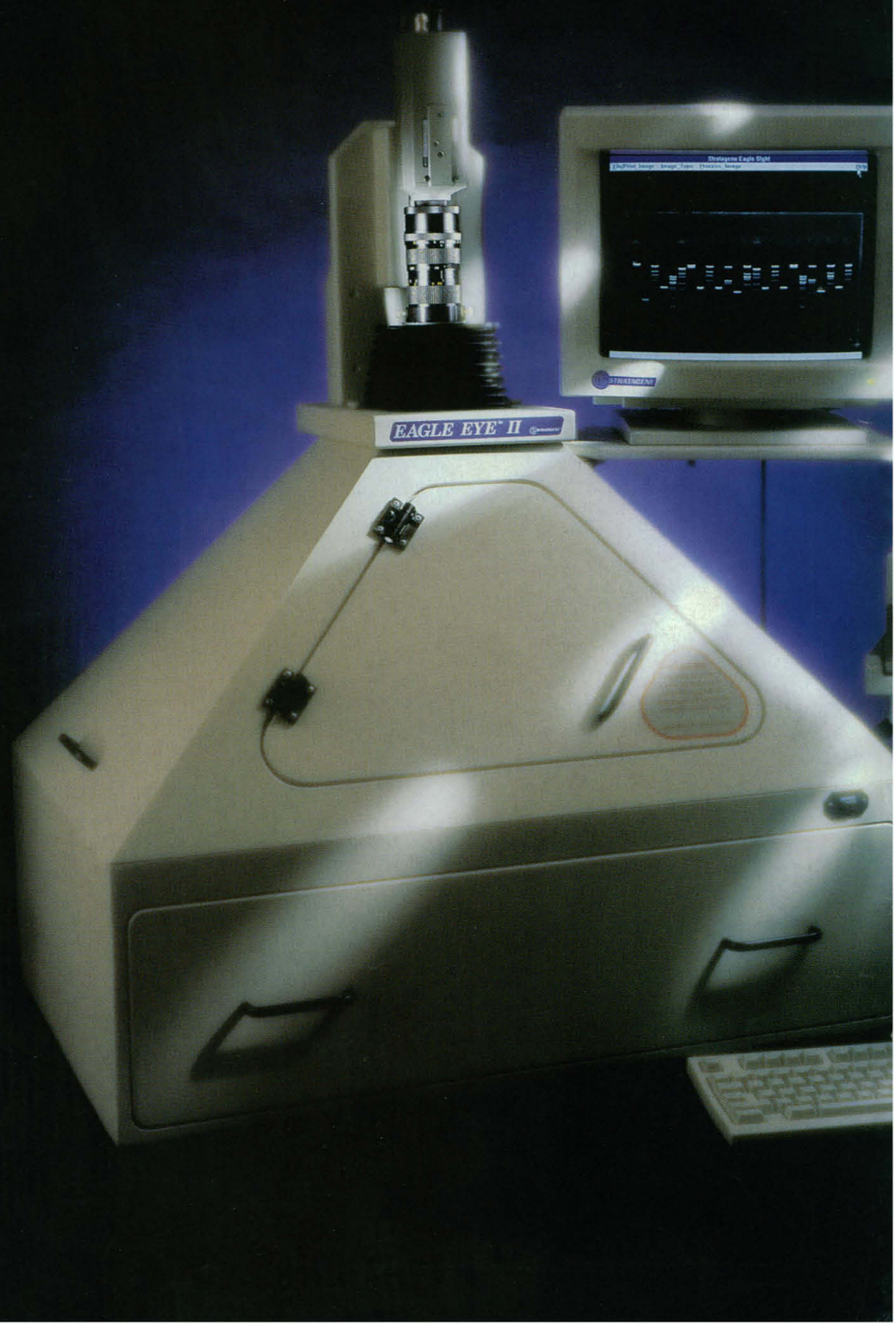

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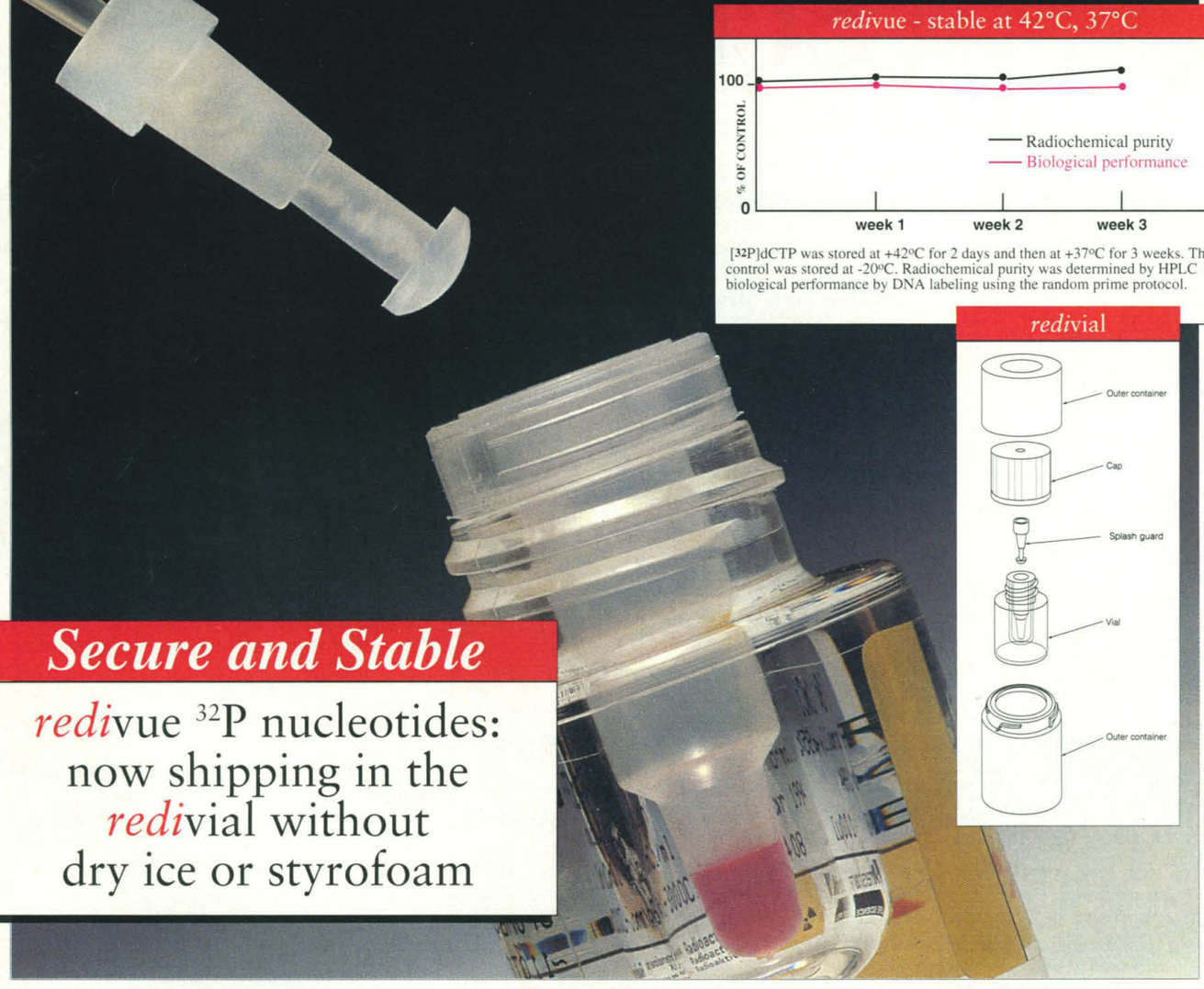

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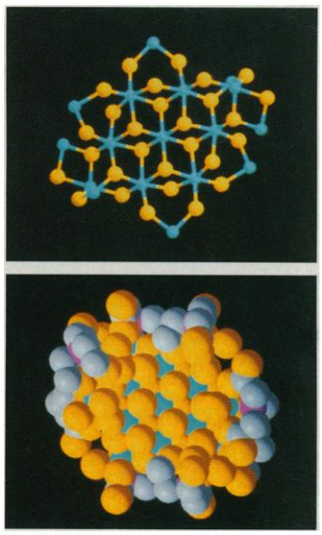
Embryo research guidelines



1054

Magnetism and metal ion clusters

NEWS & COMMENT

RESEARCH NEWS

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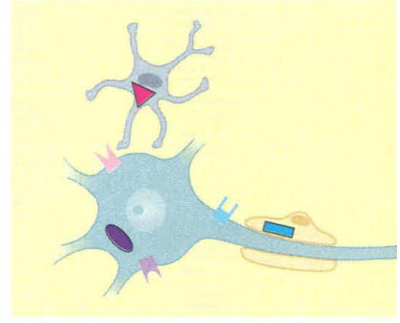
COVER

An overlay diagram of the active site catalytic triads of the serine proteases trypsin (solid blue) and subtilisin (solid pink) with the active site catalytic dyad of catalytic antibody 17E8 (solid yellow). The catalytic residues of each protein converge to similar distances and geometries, whereas the polypeptide backbone structures (mottled tubes) are completely different. The inset figures at the bottom are the three-dimensional structures of trypsin (blue), subtilisin (pink), and catalytic antibody 17E8 (yellow). See page 1059. [Figure: Mike Pique, The Scripps Research Institute]

REPORTS

TECHNICAL COMMENTS



1052 & 1107
Stabilizing *wobbler* mice with neurotrophic factors

Indicates accompanying feature

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edited by PHIL SZUROMI

Meteoritic popcorn

Chondrules, millimeter-sized silicate nuggets found in many meteorites, contain within them smaller grains of nickel- and iron-rich material known as "fluffy opaque inclusions," or FOIs. Unlike the bulk of the chondrules in which they reside, FOIs absorb heavily at visible and infrared wavelengths, and their texture suggests episodes of heating in their evolution. Eisenhour *et al.* (p. 1067) investigated this idea in two ways: They irradiated chondrule-like minerals with an optical laser, generating grains much like FOIs seen in meteorites, and they used computer simulations to see under what range of conditions FOIs might be formed. Because chondrules are thought to have originated throughout the early solar nebula, they suggest that electromagnetic events such as nebular "lightning" and flares could have provided the transient heating that produced FOIs.

■

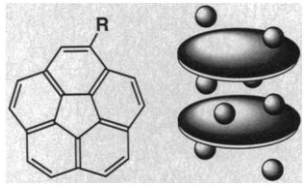
Kept together

Polymer properties can be tailored by blending several polymers together, but such blends are often immiscible and the material separates into distinct phases. Gersappe *et al.* (p. 1072) found that the mechanical properties of blends of two incompatible polymers [in this case, poly (ethyl acrylate) (PEA) and poly (methyl methacrylate) (PMMA)] could be improved by adding graft copolymers of a third immiscible polymer, polystyrene (PS). The graft copolymers have either a PEA or PMMA backbone and have PS side chains. These side chains tend to form interlocking teeth (a "molecular velcro") between regions that, because of phase separation, are predominantly either PEA or PMMA. Binding the regions together in this way led to a threefold improvement in tensile strength.

■

Lithium sandwiches

Large, conjugated hydrocarbons can associate with lithium ions, which can bind to both faces of the hydrocarbon or can even bind to two hydrocarbon molecules to form a "sandwich." Ayalon *et al.* (p. 1065) describe an unusual "triple deck" sandwich that forms in solution. Eight lithium ions coordinate with two corannulene tetraanions, with four lithium ions residing between the hydrocarbons and two lithium ions binding to the exterior face of each corannulene. Nuclear magnetic resonance (NMR) studies show that the exterior and interior lithium ions interchange freely but that the two corannulene molecules do not separate on the NMR time scale. Theoretical studies indicate that the hydrocarbons are not flat but tend to bowl in the same direction and can interconvert through a double inversion.



Carbon microtubes

Fullerenes can be polymerized to form fibers a few micrometers in width and hundreds of micrometers in length. Pekker *et al.* (p. 1077) found that single crystals of the alkali fulleride KC_{60} could be transformed into fibrous bundles when they were partially oxidized in air under toluene. Electron spin resonance and microwave conductivity measurements indicate that these fibers are metallic, even though the fibers are optically transparent.

■

Streams of data

Understanding the long-term deformation areas of high seismic risk where faults are not exposed at the surface such as the New Madrid Seismic zone, have been difficult. Merritts and Hesterberg (p. 1081) show that the change of gradients of streams resulting from uplift related to seismicity on buried faults can be mapped and provide one indication of long-term deformation and strain rates. Analysis of stream gradients in the New Madrid seismic zone suggests that several meters of relative uplift has occurred there during the Holocene.

■

Hosts and parasites

Parasites are a major factor affecting almost every level of organismic evolution. Ebert (p. 1084; see news story by Gibbons, p. 1037) tested current ideas about the evolution of parasite virulence by studying a horizontally transmitted microparasitic disease in zooplankton. Virulence decreased as the geographic distance between parasite and host increased. This finding indicates that there is local adaptation of the parasite, but contradicts the idea that coevolved parasites are less virulent than new parasites. Hafner *et al.* (p. 1087) used sequence analysis of a mitochondrial gene to study molecular evolution in cospeciating gophers and their ectoparasites (chewing lice). Mutation rates were greater in the lice than in the gopher, and the difference was comparable to the difference in generation times of the organisms.

■

Less inflammatory

The classical model for the inflammatory response caused by antibody-antigen complexes—which in autoimmune diseases such as rheumatoid arthritis leads to tissue destruction—is that complexes form that bind to and activate the complement cascade. Sylvestre and Ravetch (p. 1095) show that another component of the immune system—the Fc receptors, which bind antibody-antigen complexes at cell surfaces—is also required to trigger the inflammatory response. A mouse strain deficient in functional Fc receptors shows normal inflammatory responses except to stimulation by immune complexes. This result suggests that certain cells bearing Fc receptors initiate the response that then activates the complement system.

■

Maintaining locality

For embryonic development to proceed normally, the expression of various growth factors must be localized to different regions of the oocyte. Kloc and Etkin (p. 1101) show that the RNA transcripts of the Xlsirts genes, which are repeat sequences that are not translated into proteins, play a role in localizing expression. Injection of antisense molecules to Xlsirt transcripts in stage 4 oocytes released RNA transcripts for Vg1 from their normal localization at the vegetal pole. These transcripts encode for a molecule similar to tumor growth factor–β and is involved in mesoderm formation.

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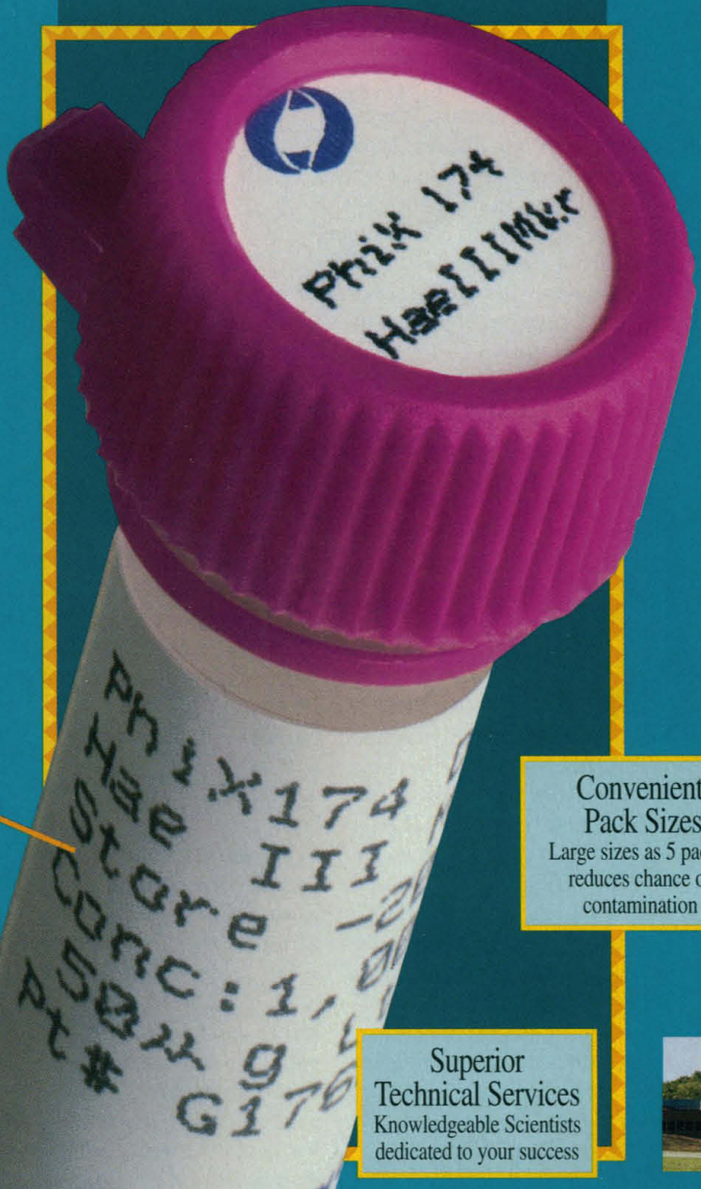

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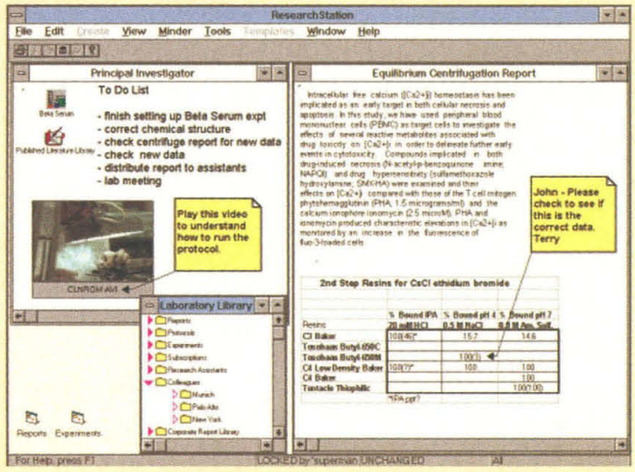

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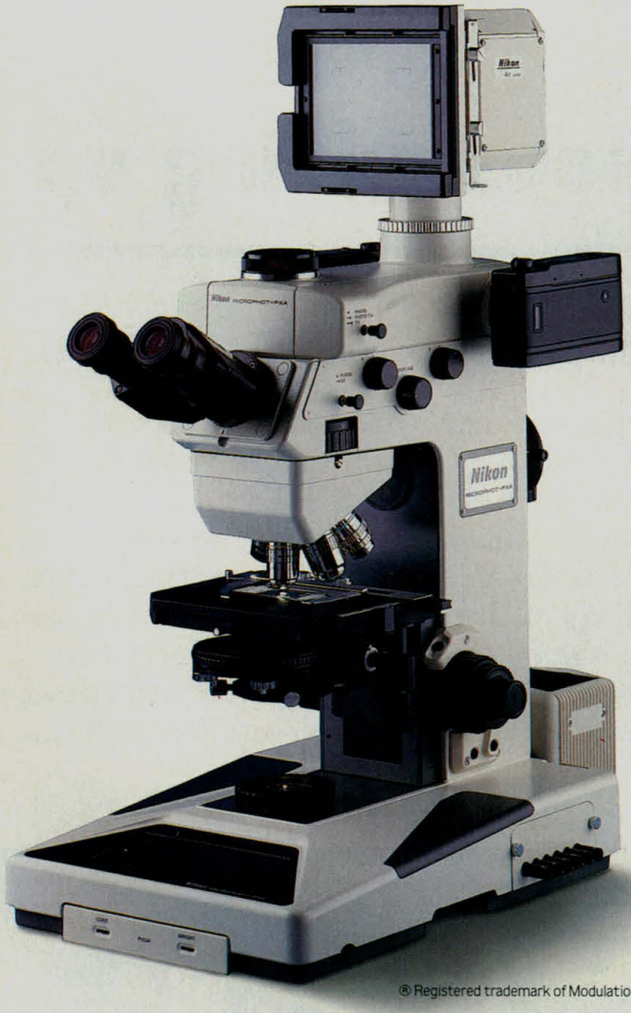

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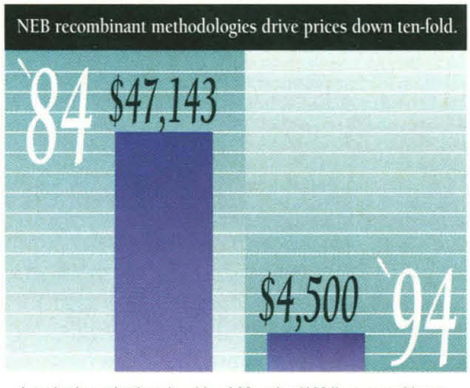

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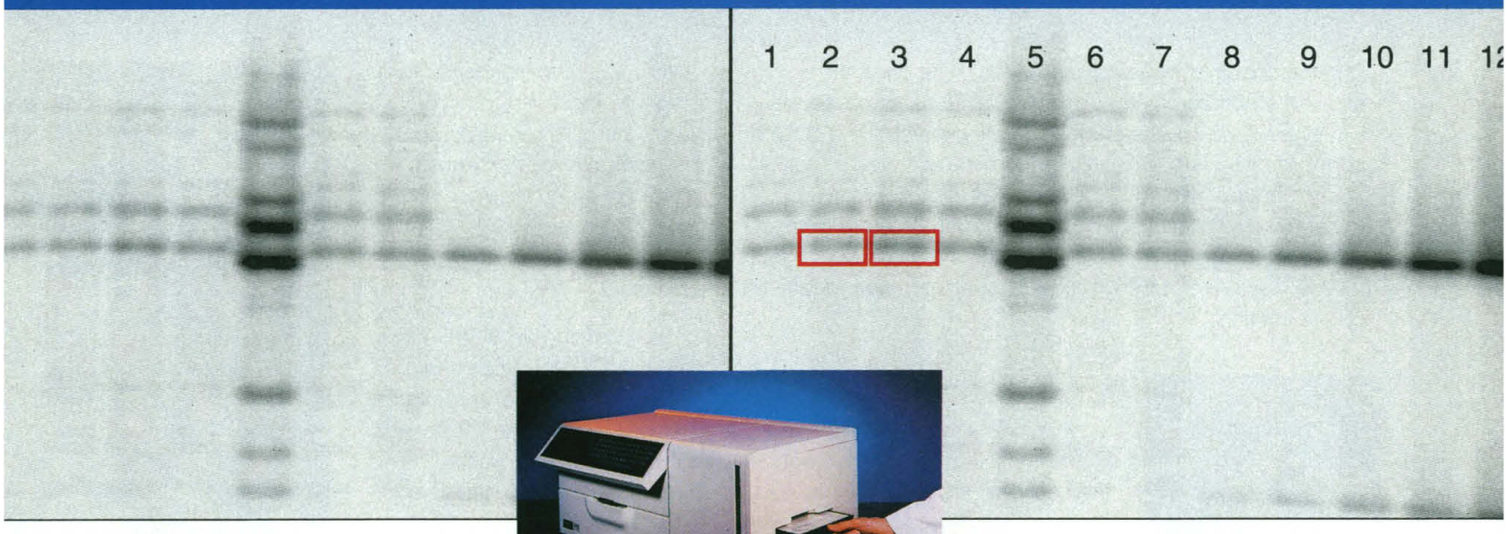
Lane 2 is significantly different from lane 3?



In this analysis, the band in lane 2 really is significantly different from lane 3. (180.5 ± 2.6 cpm vs. 311.4 ± 3.3 cpm)

Prove it.

It's a fact. The peer review journals you want to reach demand consistent, quantitative data. The practice of identifying band presence using "eyeball" assessments for your analysis is simply not acceptable.

That's why, to achieve fast, accurate, quantitative results, you need control of the most sensitive and reliable bench-top imager in the world—right at your fingertips.

The AMBIS 4000.

The world's most trusted imager.
To obtain reliable data quickly and cost-effectively, there's no better way than direct quantitative imaging. The Scanalytics AMBIS 4000 gives you consistent, accurate quantitation with automatic nuclear counting statistics—and it's faster and more reliable than any other method.

With over 500 AMBIS installations around the globe, the AMBIS 4000 has proven to be the logical choice for professionals who can't accept the limitations found with film densitometers and phosphor imagers.

Using the AMBIS 4000 is just like using a liquid scintillation counter. You can even load as many as 10 samples, then easily program the AMBIS 4000 to scan each sample overnight, or over the weekend, unattended. When you return, your samples are ready to be analyzed. And the AMBIS 4000's automatic sample loader makes it ideal for multiple users and high-volume applications.

Powerful Windows™-based software.
You can quickly analyze the data you've collected with Scanalytics software modules. It's easy-to-use and includes high resolution graphics capabilities that let you generate publication-quality images. Plus you can export images and data to desktop publishing programs, spreadsheets, and word processors.

For more information on the AMBIS 4000—the world's most reliable direct quantitative imager— call or write today.

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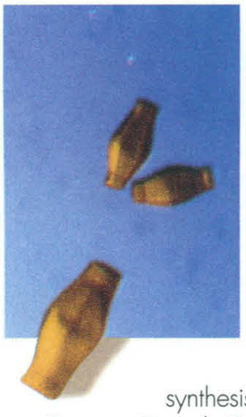
Imagine Having The Tools To

Remember the milestones in your life. The ones that revealed your talent to create, solve, explore, and discover.

Maybe it was a special science fair project. Or a certain insight you had in a college lab. Or maybe it was a tool, like an EM, that let you really delve into what makes things tick. Somehow it all came together into a career in the sciences.

Biosearch specializes in creating tools that fuel your inner drive to discover. Tools that allow your imagination to take on today's frontiers.



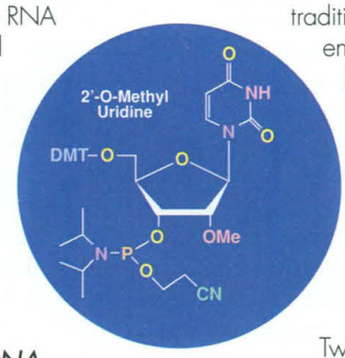
RNA

RNA oligomers have shown promise in therapeutic and diagnostic applications, including inhibition of viral replication, cancer etiology, and gene regulation and expression.

To bring these applications within easy reach, Biosearch was the first to introduce a complete, automated RNA synthesis system with nucleotide monomers, reaction columns, pre-packaged reagents, and optimized synthesis protocols.

Our new Expedite™ RNA chemistry makes your work-up procedures faster, easier, and more efficient. The milder cleavage and deprotection conditions reduce chain degradation and increase yield. The Expedite RNA reagents employ our patented betacyanoethyl phosphoramidite chemistry that's become the method of choice in DNA and RNA synthesis.

Our researchers are currently developing protocols for large-scale synthesis of RNA oligomers. (Photo of RNA crystal, courtesy of Dr. Alex Rich, MIT, was synthesized at a scale of 70 µ mole on Biosearch's 8800 Synthesis System.)



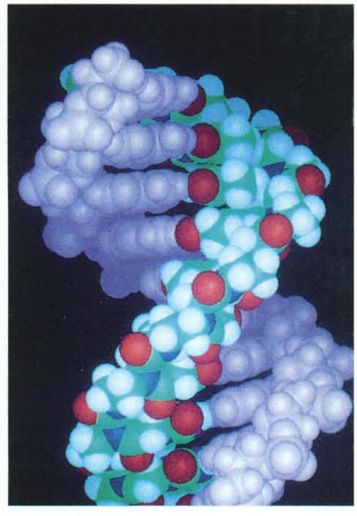
Therapeutic and diagnostic grade DNA

Researchers in the clinical and diagnostic use of DNA are on the verge of creating a new class of pharmaceuticals. Biosearch is proud to pioneer new tools for their work.

Biosearch is the world's leading supplier of systems, chemicals, and reagents for the synthesis, purification, and analysis of therapeutic and diagnostic DNA. We've tightened the specifications on our products to ensure that they can be used for the most demanding applications. A Certificate of Analysis is automatically supplied with all of our DNA synthesis reagents.

We've also substantially expanded our manufacturing capacity to meet the needs for large single-batch production of material, minimizing your need for internal quality control.

In addition to standard reagents, Biosearch can also supply phosphoramidites and bulk quantities of synthesized oligomers on a custom-synthesis basis.



PNA

Peptide Nucleic Acids–PNA oligomers. These molecules are so novel that they're rewriting the very nature of nature. Biosearch is the world leader in the development and synthesis of these exciting new molecules.

Similar to DNA and RNA, PNA carries information in sequences of the four bases: adenine, guanine, cytosine, and thymine. In PNA, however, these code carriers are connected to a completely different backbone–a polyamide backbone similar to that found in peptides. PNA oligomers are more stable than their natural counterparts yet bind more specifically and with higher affinity to natural DNA and RNA.

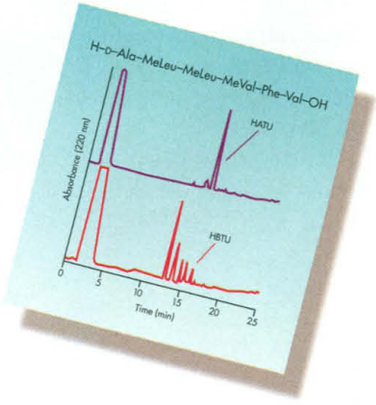
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

Biosearch can provide you with custom PNA oligomers, or the monomers, supports, and reagents to synthesize your own oligomers.

HOAt and HATU peptide coupling reagents

Two new coupling reagents, HOAt and HATU, simplify your peptide synthesis. These new reagents enhance coupling yields and reduce racemization and coupling times. They are particularly effective with difficult couplings and in the synthesis of peptides containing hindered amino acids.

HOAt and HATU have structures similar to the commonly used reagents HOBt and HBTU, and are compatible with all standard activation strategies.



Keep Up With Your Imagination.

PEG-PS™ peptide synthesis supports

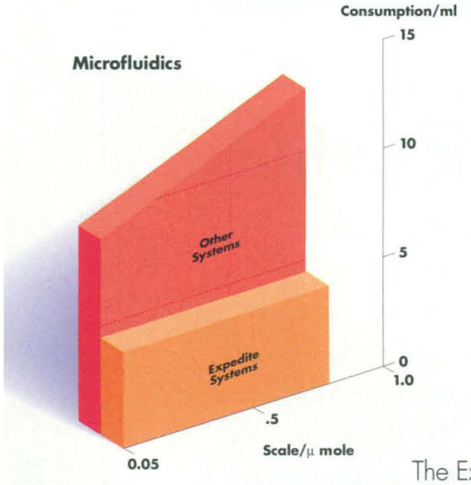
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

Unlike traditional supports, PEG-PS beads more closely resemble the nature of the growing peptide chains. Solvation of the peptide resin is higher, resulting in a higher peptide purity. Synthesis is fast and effective due to high coupling efficiency and minimal side reactions.

PEG-PS supports are easy to handle, compatible with a wide range of solvents, and are especially well suited for the synthesis of long or difficult peptides.

Microfluidics

In the real world, achieving "end product" is not the only concern. There are dozens of production costs as well as the escalating costs of hazardous waste disposal.



Biosearch's Expedite Nucleic Acid Synthesis System, with its patented microfluidics technology, not only enables fast cycle times but also provides the bonus of reduced reagent consumption. The distance between the reagent reservoir and the column is minimized so that a single coupling cycle requires less than 4.5ml of reagents. The Expedite system (with optional trityl monitor) can also separate the chlorinated waste–simplifying disposal tasks and reducing associated costs.

Membrane synthesis

Perform nucleic acid synthesis on a membrane? It's now possible–and practical–thanks to Biosearch Nucleic Acid Membrane Supports, a breakthrough synthesis technology developed by Biosearch.

Biosearch membrane supports use a proven PTFE membrane system that directly replaces traditional controlled pore glass (CPG) supports. Membrane devices have standard luer fittings, so they can be plugged into any brand of synthesizer.

Biosearch membrane supports allow you to synthesize both long and short oligomers on the same type of membrane; no longer do you need to select the size of the CPG according to the length of the oligomer.

With Biosearch membrane supports, not only do you eliminate beads, but there's no centrifuging and no washing. Just remove the membrane from its holder, cleave, and deprotect.

Allyl-based protection for complex peptides

The synthesis of cyclic, branched chain, sulfonated, glycosylated, and phosphorylated peptides have traditionally been time consuming and problematic.

To synthesize these complex peptides quickly and efficiently, Biosearch scientists have perfected convenient techniques using allyl-based protecting groups. Allyl amino acids can be selectively deprotected in a manner which is compatible with other classical protecting groups (such as Fmoc, Boc, *t*Bu), sensitive amino acids (Met, Trp), and side chain modifications (Tyr(SO_3H)). Biosearch has also developed protocols for the fully automated synthesis of cyclic peptides, branched peptides, and MAPs on our 9050 Plus PepSynthesizer.™

If we've intrigued you with some of these innovative tools, it's easy to find out more. For our "Directory of Chemical Products"–one of the most comprehensive synthesis tool kits in the world–call the Biosearch Group in the US and Canada at 1-800-872-0071, in Germany at (49) 040-853267-36, in Japan at (03) 3471-8191, in France at (33) 1 30127002, and in the UK and the rest of Europe at (44) 0923 211107.

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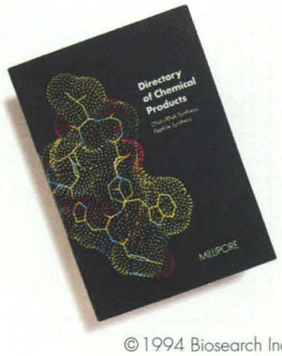

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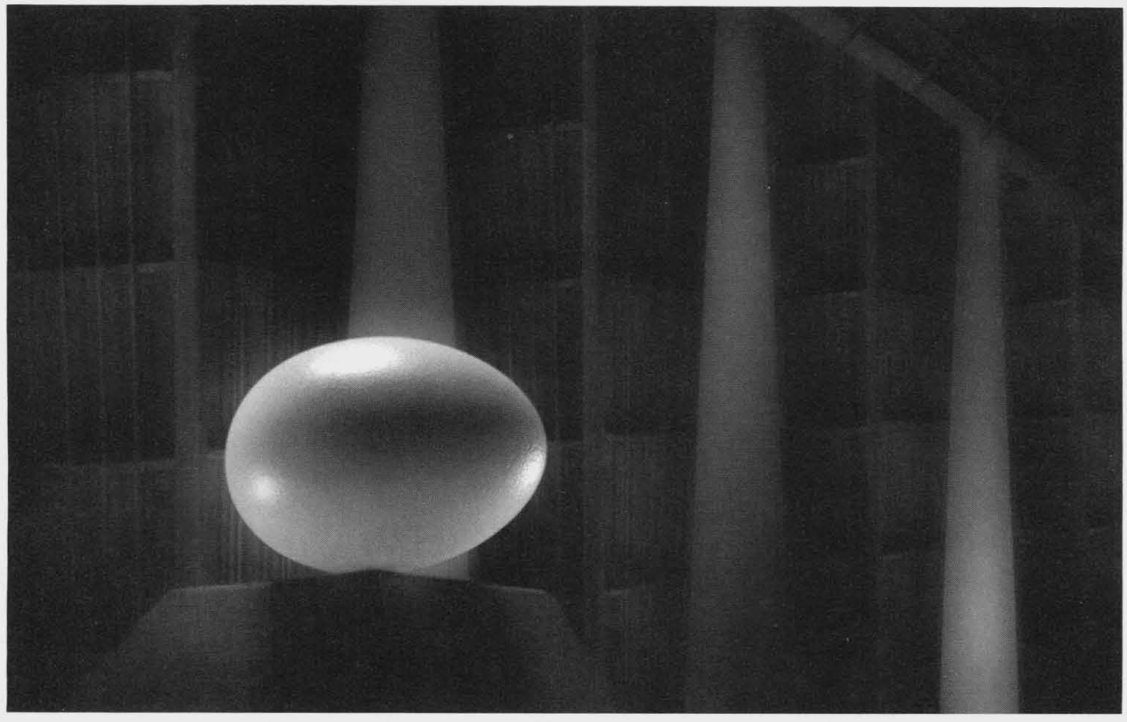

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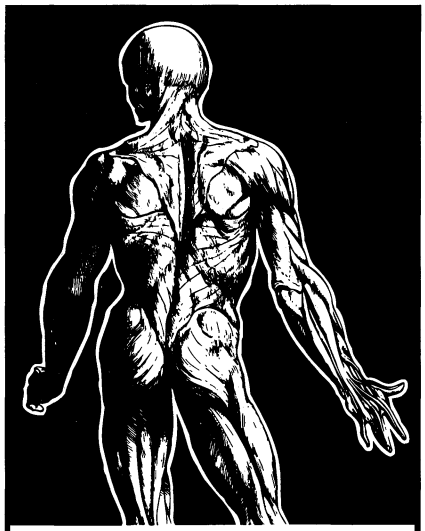

HUMAN GENOME 1994

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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OCTOBER 2-5, 1994 ■ WASHINGTON, D.C.

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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

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

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❑ Monday ❑ Tuesday ❑ Wednesday

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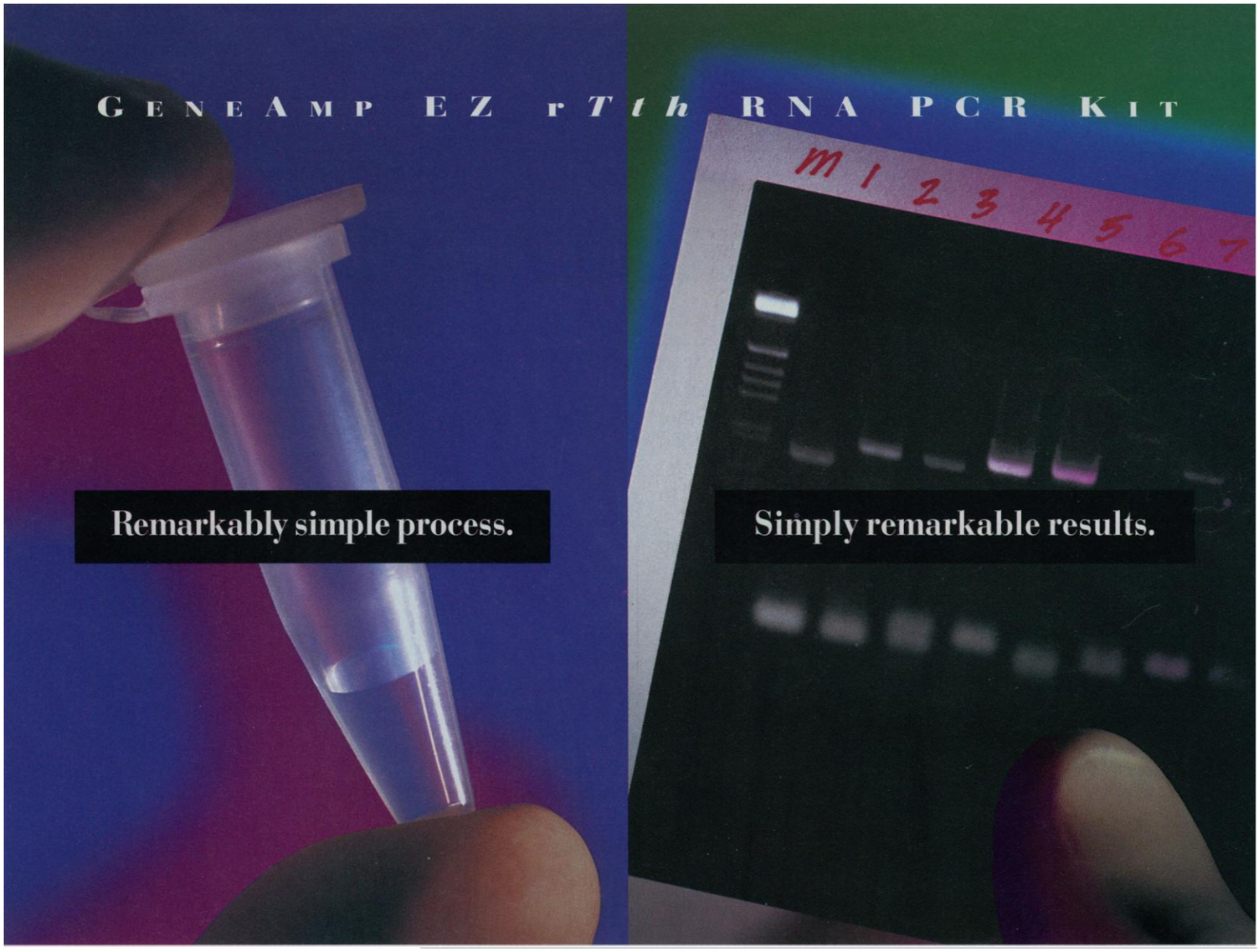

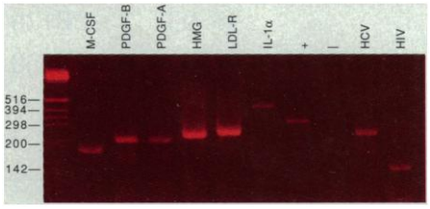

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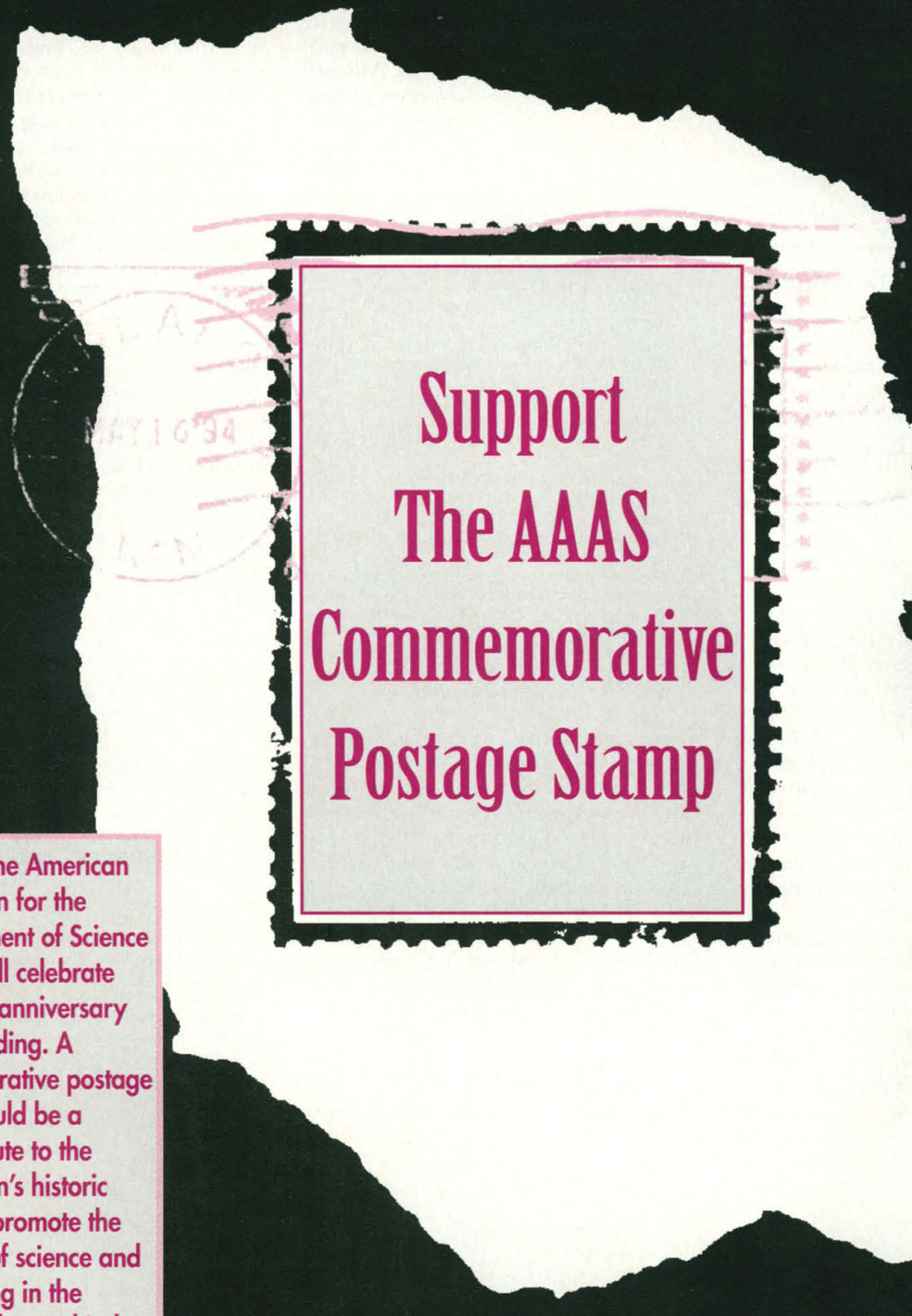

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