AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

# SCIENCE

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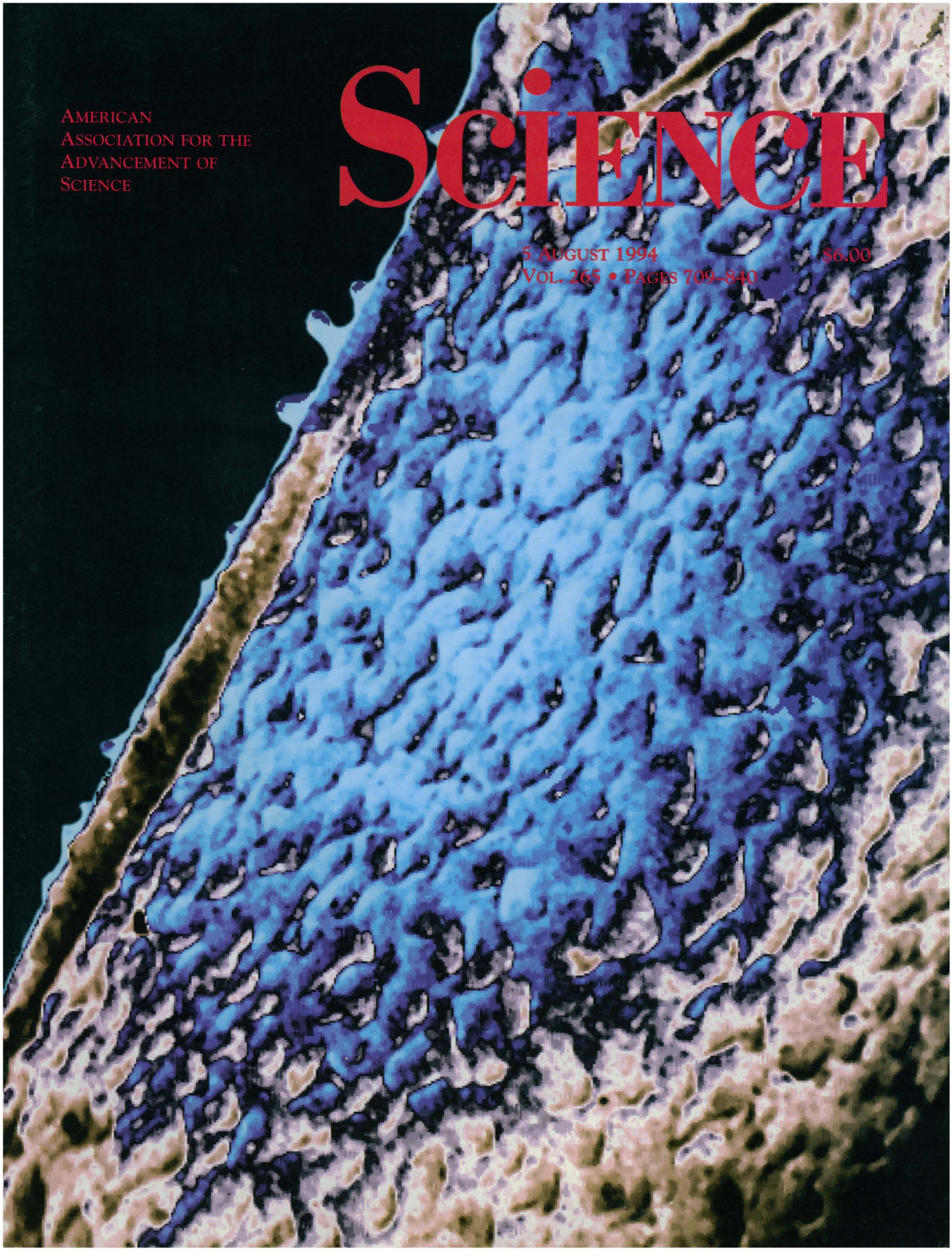

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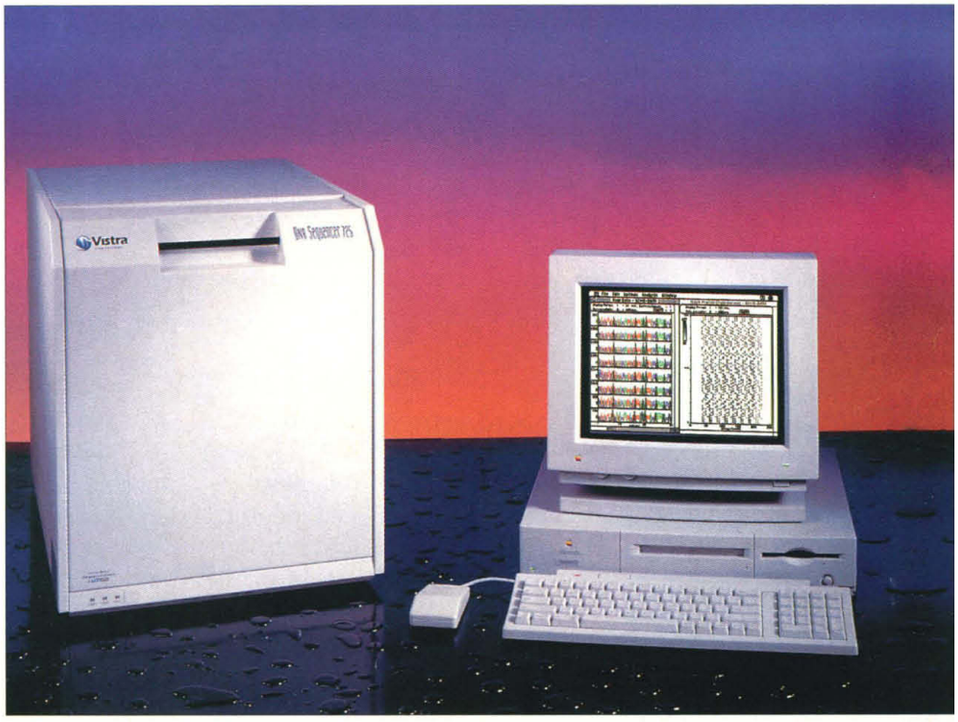


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# Imagine Having The Tools To

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.

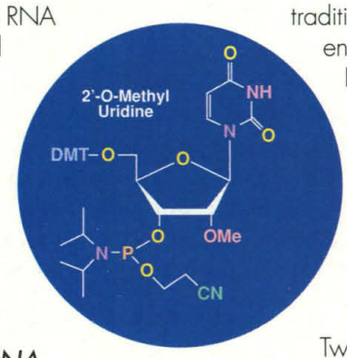
## *RNA*

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.)



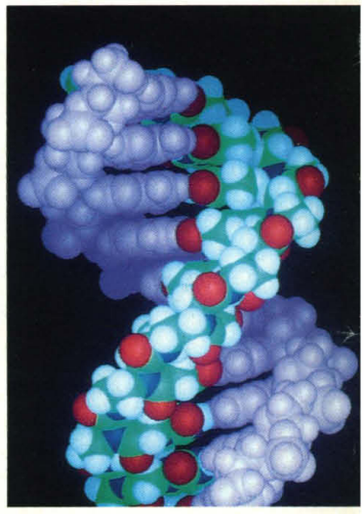

## *Therapeutic and diagnostic grade DNA*

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.

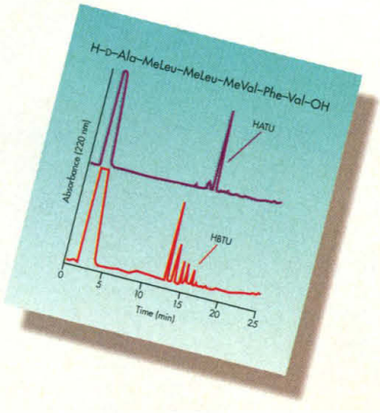
PNAs can be used in many of the same applications as traditional DNA. Their greatest contribution, however, may come from applications that can't be performed using traditional DNA oligonucleotides, such as restriction enzyme blocking, PCR clamping, and DNA mapping.

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*

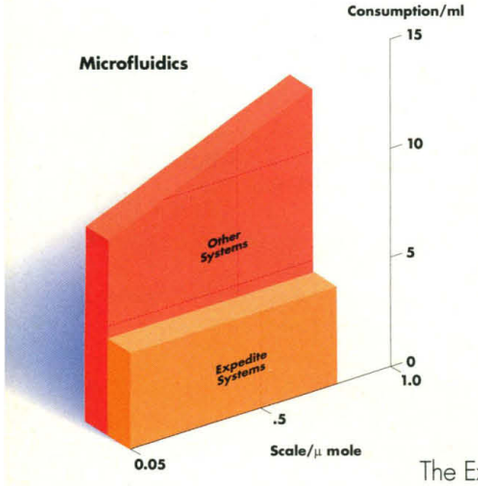
PEG-PS (polyethylene glycol-polystyrene) peptide synthesis supports from Biosearch help you achieve improved peptide purity with shorter cycle times.

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.

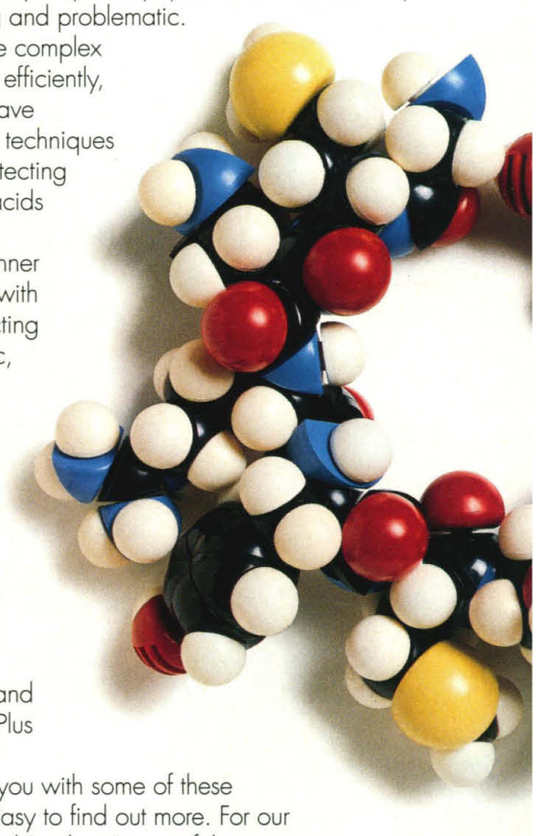
Biosearch membrane supports use a proven PTFE membrane system that directly replaces traditional controlled pore glass (CPG) supports. Membrane devices have standard luer fittings, so they can be plugged into any brand of synthesizer.

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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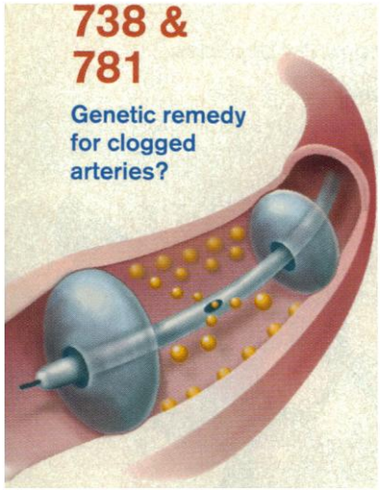
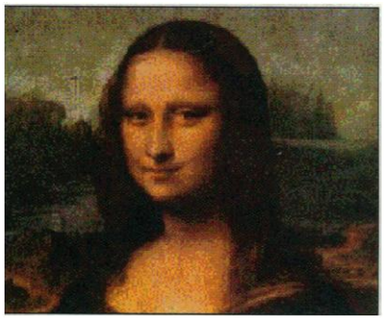


**736 & 749**
**Artful digital storage**

## NEWS & COMMENT



## RESEARCH NEWS



## PERSPECTIVE



## ARTICLE



## RESEARCH ARTICLE



## REPORTS



## DEPARTMENTS

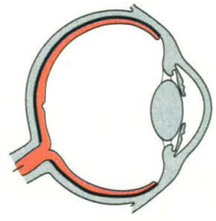
COVER

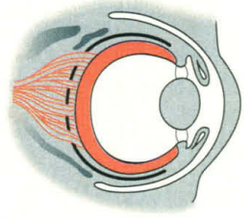
A vapor deposit of ice warmed to 183 kelvin, much as cometary ice is heated during transit through the solar system, in a false-color transmission electron microscope image (×170,000). On warming, initially well-defined crystallites flow into a rolling landscape (blue). Diffraction studies reveal both amorphous and cubic crystalline components. These persist until at a higher temperature all ice transforms into the familiar hexagonal form. See page 753. [Micrograph: P. Jenniskens and D. F. Blake]

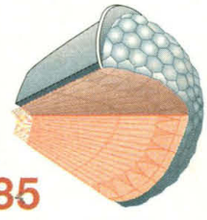



## TECHNICAL COMMENTS










742 & 785
PAX6: Seeing is believing




◩ Indicates accompanying feature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# Increased productivity

Spiraling beneath a school of fish, several humpback whales use their blowholes to create a circular "net" of bubbles. The open-mouthed whales then swim up through the school and engulf the disoriented prey. This communal "bubble-netting" enables the whales to take in more food than normal surface feeding by individuals.

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edited by PHIL SZUROMI

## Holding the bits

Computer users want it all: large data storage capacity, fast transfer rates, and short access time. Optical methods, particularly those based on holography, have long been considered for data storing data, but it has been difficult to achieve all three requirements with current technology. Heanue *et al.* (p. 749; see news story by Glanz, p. 736) report on a holographic storage system that can hold and retrieve digital images and compressed video data in a photorefractive crystal.

■

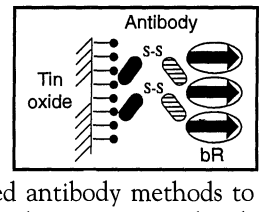
## Examining excitation

Two-electron excited states are usually diradicals, but higher lying zwitterionic excited states, in which the two electrons pair in one orbital, are thought to form in vibrationally excited molecular hydrogen and the twisted state of ethylene. Such states have been difficult to detect spectroscopically. Engebretson *et al.* (p. 759) report spectral evidence for a zwitterionic excited state in a molybdenum dimer compound. Excited-state processes underlie the photodynamics of π-conjugated polymers, which are finding use in nonlinear optics and in light-emitting diodes. Jenekhe and Osaheni (p. 765) show that exciplexes, charge transfer complexes that are stable only in their excited state, have higher quantum yields for luminescence than excimer complexes, which undergo self-quenching.

■

## A unified front

The ability of the protein bacteriorhodopsin (bR) to convert light energy into an electrochemical potential can be put to use in devices such as light sensors but only if the protein adopts a nonrandom orientation. Koyama *et al.* (p. 762) have




used antibody methods to orient the protein at the device surface and improve efficiency.

■

## Even deeper

The origin of earthquakes at depths of 100 to as much as 700 kilometers in subduction zones is uncertain, but the character of the rupture process recorded as seismic energy may provide some clues. Houston and Vidale (p. 771) show that in intermediate depth earthquakes (100 to 350 kilometers), the energy released declines from the beginning of the rupture whereas in deeper earthquakes, energy is released evenly throughout the duration of the rupture. One explanation for this pattern is that faults may become more homogeneous with depth.

## Transforming extraterrestrial water

Surface features on Mars indicate the presence of running water early in its history, but atmospheric conditions that would have allowed liquid water to precipitate do not seem feasible with only carbon dioxide and water vapor. Squyres and Kasting (p. 744) suggest a different history: Water seeped from the interior of the planet and was propelled by convection, not precipitation. The heat necessary to drive convection could be in part geothermal as well as the result of heating by impacts, and only moderate atmospheric temperatures and pressure would have been needed for outflowing water to create the present topography. As comets approach the sun and begin to evaporate, ice is heated from tens of kelvin up to its melting point and undergoes a series of phase transitions. Jenniskens and Blake (p. 753; see cover) used electron diffraction to find a new amorphous form that exists in conjunction with normal cubic ice at temperatures near 150 K. Transformations in the structure of cometary ice alter the diffusion and recombination of certain radicals and can explain the retention and release of gases in space.

## Paired partners

Peptide nucleic acid (PNA) polymers, in which the natural sugar-phosphate moieties have been replaced by polyamide linkages, have been synthesized recently with therapeutic applications in mind. The solution structure of a 1:1 complex between a PNA and an RNA molecule by Brown *et al.* (p. 777) has revealed some details of how these molecules interact with natural nucleic acids. The antiparallel, right-handed conformation of the complex resembles that of an RNA double helix, but the PNA component displays some regions of flexibility in comparison to the relatively well-defined RNA.

■

## The eyes have it

Vertebrates and insects differ greatly, but their morphogenesis appears to be controlled by a similar gene. Quiring *et al.* (p. 785; see the Perspective by Zuker, p. 742) isolated a gene from *Drosophila* with homology to the vertebrate *Pax-6* gene. Heterozygous mutations in *Pax-6* are responsible for *Aniridia* (loss of the iris and reduction of eye size) in humans and the *Small eye* phenotype in mouse and rats. Homozygous *Pax-6* mutations result in no eyes and lethality. Surprisingly, the *Drosophila Pax-6* homolog maps close to the *eyeless* gene.

■

## Coaxing chromatin

Mammalian genomic DNA is associated with histones and other proteins to form chromatin, and chromatin complexes need to enter an active state for the DNA to be transcribed. Ding *et al.* (p. 796) found that the high mobility group 14 protein, a non-histone protein that has been associated with actively transcribed chromatin, stimulates transcription from chromatin but not from naked DNA templates. This protein increases the rate of elongation by RNA polymerase II but not the rate of initiation.

■

## Lost in translation

The translation of mRNA is strictly regulated during development in a variety of organisms—for example, fertilization results in translation of maternally stored mRNA. Klein and Melton (p. 803) have used one of the rate-limiting components of the translation apparatus, eIF-4E, to study the effect of translational control on differentiation in embryos of the frog, *Xenopus laevis*. An excess of eIF-4E has little effect on total protein synthesis but does cause an induction of mesoderm in tissues normally destined to be ectoderm. This effect may be mediated by releasing restrictions on the synthesis of components of the tumor growth factor–β signaling pathway.

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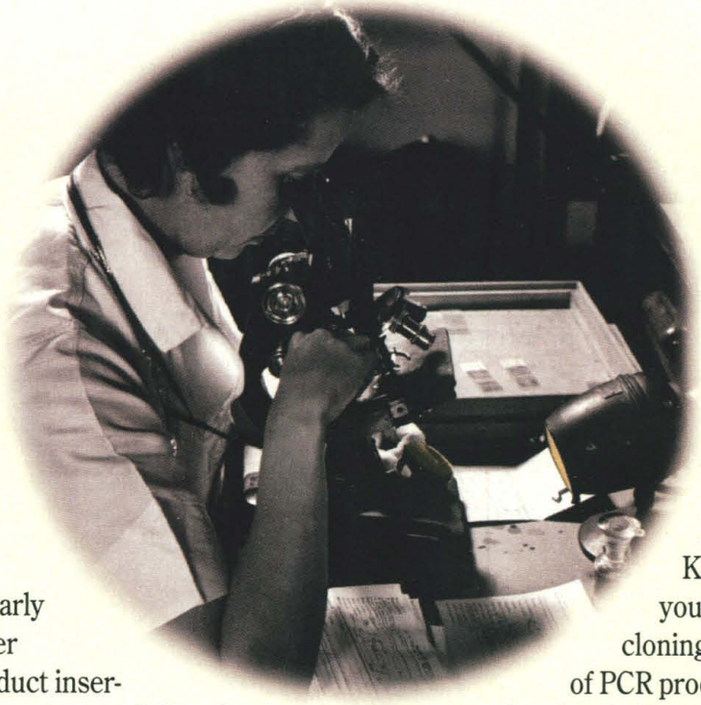

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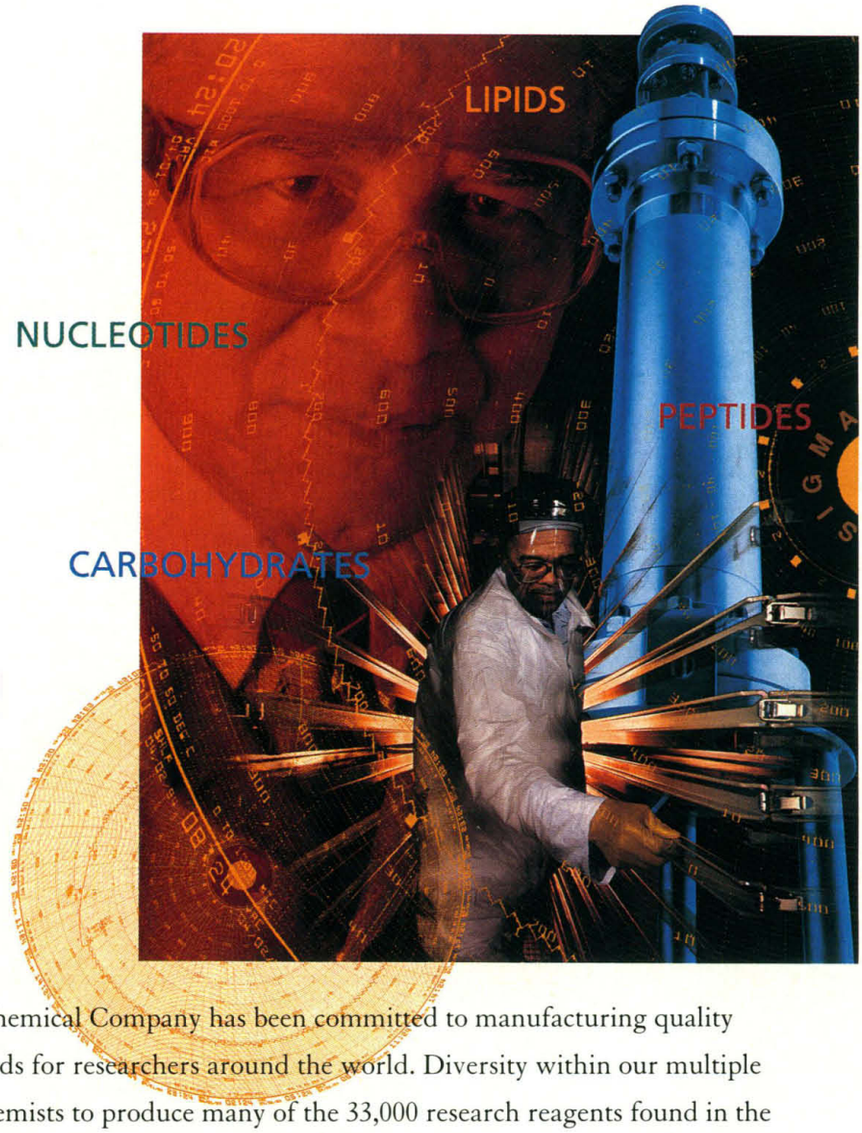


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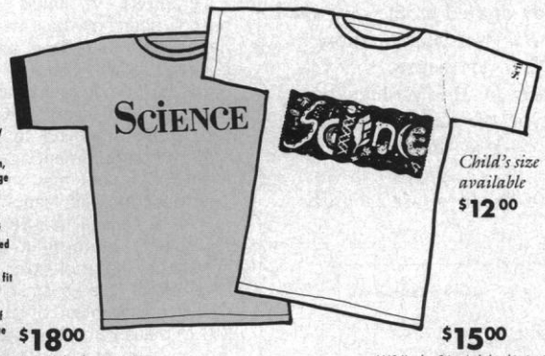


**Science Roll-up Sleeve T-shirt, Style #1501**

*Features:*

- Super heavyweight 100% cotton jersey knit
- Available in medium, large and extra large sizes
- Ash shirt with blue trim roll-up sleeves
- Crew neck & hemmed bottom
- Oversized, relaxed fit
- Made in the USA
- Full front imprint of SCIENCE logo in blue

$18.00

AAAS Member Price. Includes shipping in U.S.
**Non-member price: $20**

*Child's size available*
$12.00

**Science Pictogram T-shirt, Style #1201**

*Features:*

- White Hanes Beefy-T, super heavy-weight 100% cotton jersey knit
- Available in medium, large, extra large sizes; child's size available
- Crew neck & hemmed bottom
- Slightly oversized fit
- Made in the USA
- Full front and left sleeve imprint in blue

$15.00

AAAS Member Price. Includes shipping in U.S.
**Non-member price: $16.50**

## Special Offer: Order two or more T-shirts and receive a 10% discount!

**Its easy to order!**

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SCIENCE

**Yes!** I want to show my support for SCIENCE. Please send me the SCIENCE T-shirts I've checked off below. I have enclosed a check for the amount of the shirts (plus shipping charges for non-US orders). I understand my order is refundable if I am not completely satisfied.

**Shipping Address** *(please print)*

Name

Address

City, State/Province, Country, Postal Code

Telephone and Fax

Please allow 4 weeks for delivery inside the US. Outside the US please allow 6 weeks for delivery. Prices and shipping charges subject to change without notice. Shirts returned must be in salable condition. Wash., D.C. residents please add sales tax.

**Payment Information**

☐ US dollar check ☐ Visa ☐ MasterCard

Important: All payments must be made in US dollars. $25 minimum order for all credit card orders. Make check payable to AAAS Science Publications, Inc.

Credit card number Expiration date

Signature

AAAS Membership No.

QTY SIZE STYLE NO. DESCRIPTION PRICE

Discount: Less 10% for two or more t-shirts. . . . . .

Subtotal . . . . . .

Outside the US: Add $3.50 per shirt/air delivery. . . . . .

**Total Enclosed** . . . . . .

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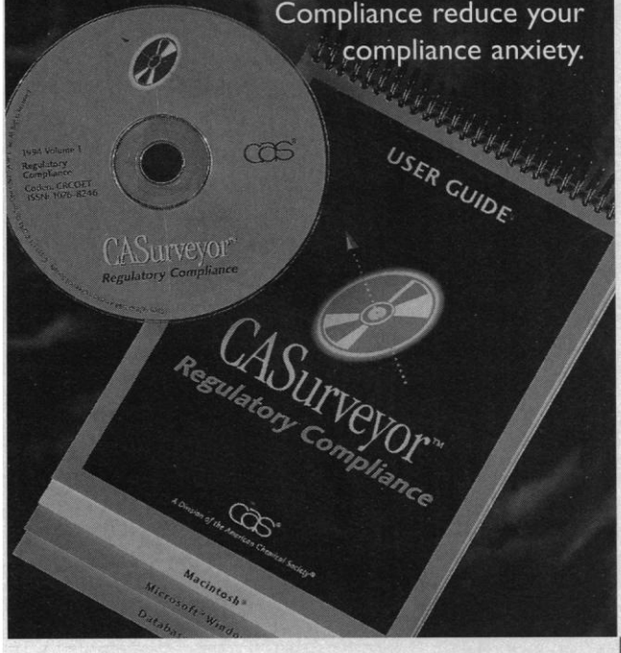


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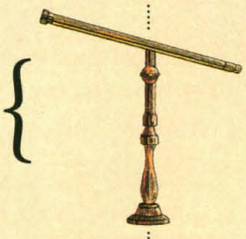
Circle No. 22 on Readers' Service Card

# Behind Every Great Discovery Lies a Significant Research Tool

*1608 - Hans Lippershey, a Dutch optician, invents the telescope*

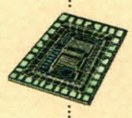


*1609 - Galileo discovers the Milky Way*

*1828 - English inventor William Sturgeon devises the electromagnet*

*1831 - Physicist Joseph Henry revolutionizes communication with the electromagnetic telegraph*

*1970's - U.S. scientists develop the microchip*



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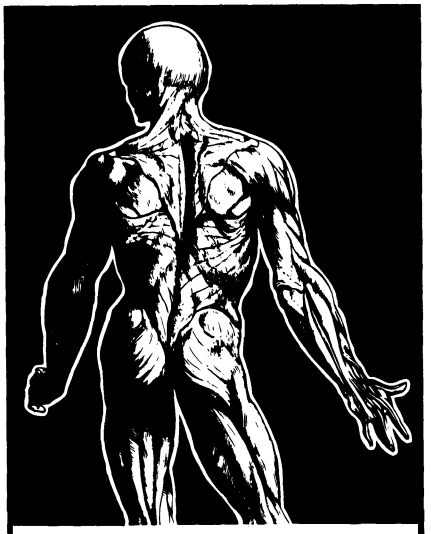
# SCIENCE and HUGO Present



# 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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