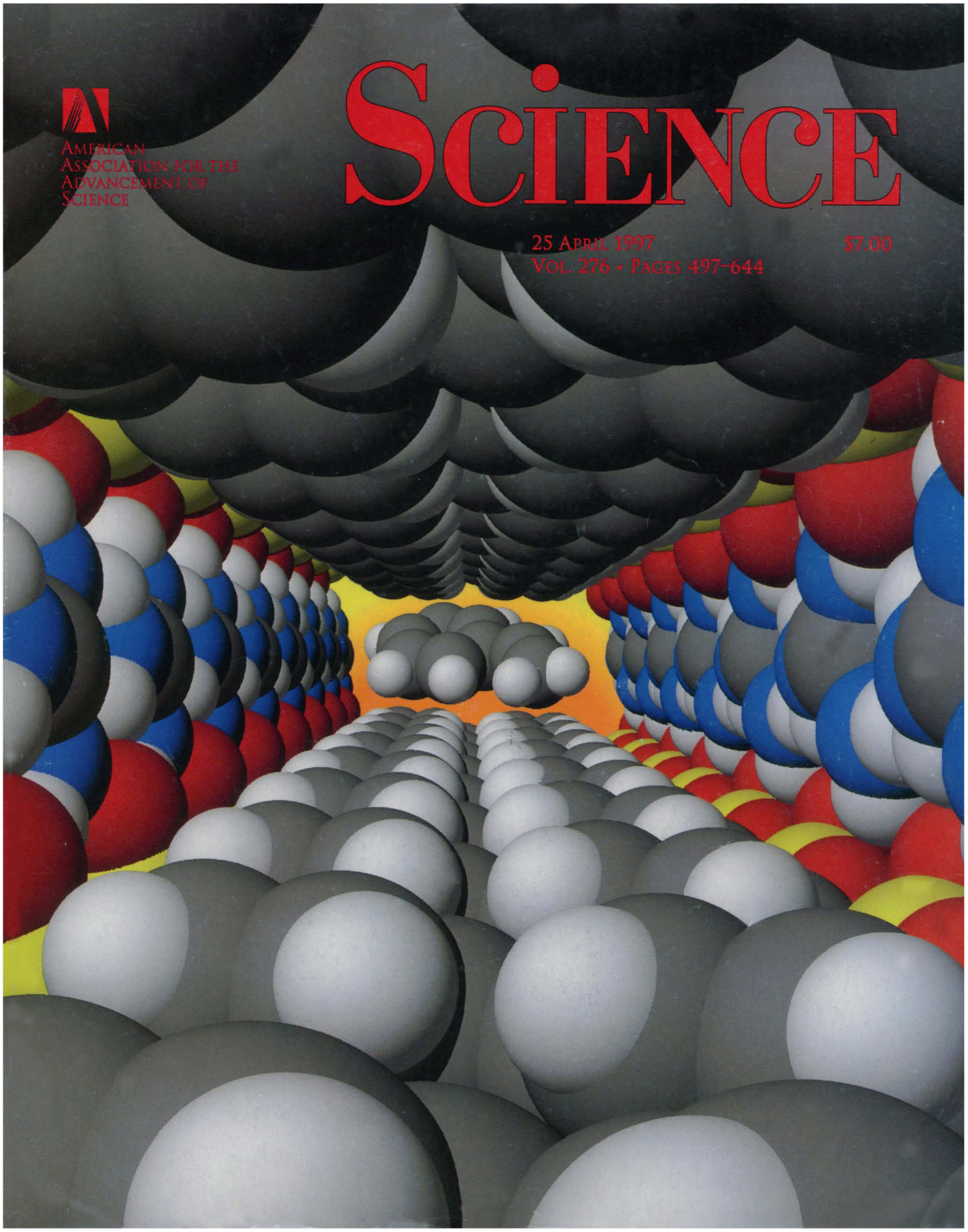
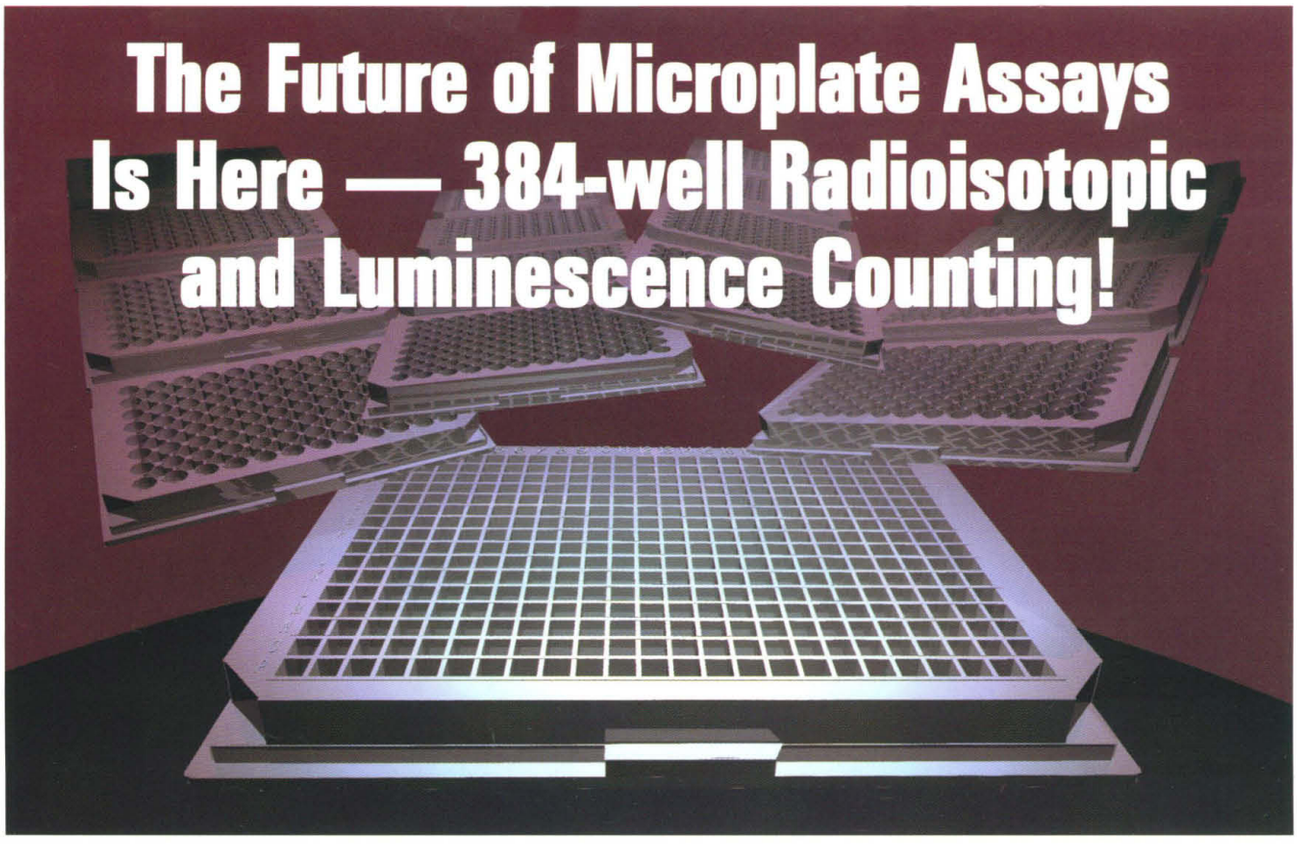


American Association for the Advancement of Science

SCIENCE

25 April 1997 $7.00
Vol. 276 • Pages 497–644

The Future of Microplate Assays Is Here — 384-well Radioisotopic and Luminescence Counting!



TopCount HTS Revolutionizes Microplate Counting — Again

- Measure radioisotopic and luminescence assays in both 96- and 384-well microplates.
- Process 12 luminescence samples simultaneously for throughputs of 10,000 samples per hour, or more.
- Stack up to 40 plates or 15,000 samples for unattended counting.
- Interface with robotic systems for complete automation.

Meeting the Demands of Microplate Counting for Today and for the Future

Assays have been scaled down from test tubes to 24-well microplates and the 96-well format. Now, the next step in assay miniaturization is here with the TopCount HTS. Continue today's assays in 96-well plates while converting assays to the higher density 384-well plates — the screening format of the future. With the TopCount HTS you can do both without risk or compromise.

Less Reagents, Less Handling, More Samples

The Packard 384-well plate accommodates assay volumes of up to 80 µL. This allows practical miniaturization of assays such as scintillation proximity, in-plate binding, liquid scintillation, Cerenkov and luminescence.

TopCount Harnesses the Power of Luminescence

Packard has pioneered the field of high throughput microplate luminescence. Now up to 12 wells can be measured simultaneously in 96- or 384-well plates for throughputs never before possible. Ultra-sensitive photon counting is combined with innovative reagents, such as LucLite with a five hour half-life, for measuring the luciferase reporter gene. Greater capacity, greater throughput.

To complement sample throughput, TopCount now has an extended 40 plate stacker. Load up to 40 plates with the TopCount ZipLoad stacker, carry them safely to the TopCount, load and count. It's that easy.

If your experiments demand accuracy, versatility or high throughput, TopCount has the answer for your laboratory.

Contact Packard at 800-323-1891 (U.S. only) or 203-238-2351 for more details. Or, visit our Web Site at http://www.packardinst.com.

PACKARD

Packard Instrument Company, 800 Research Parkway, Meriden, CT 06450 U.S.A.
Tel: 203-238-2351 Toll Free: 1-800-323-1891 FAX: 203-639-2172
Web Site: http://www.packardinst.com Email: webmaster@packardinst.com

Packard Instrument Co. SYSTEM CERTIFIED ISO 9001

Packard International Offices: **Australia**, Mt Waverley 61-3-9543-4266; **Austria**, Vienna 43-1-2702504; **Belgium**, Brussels 32-2-481-85-30; **Canada**, Ontario 1-800-387-9559; **Central Europe,** Schwadorf, Aus. 43 456 2230 015; **Denmark**, Greve 45-42909023; **France**, Rungis (33) 1 46.86.27.75; **Germany**, Dreieich (49) 6103 385-151; **Italy**, Milano 39-2-33910796/7/8; **Japan**, Tokyo 81-3-3866-5850; **Netherlands**, Groningen 31-50-541-33-60; **Russia,** Moscow 7-095-259-9632; **Switzerland**, Zurich (01) 481 69 44; **United Kingdom**, Pangbourne, Berks (44) 01734 844981

Circle No. 18 on Readers' Service Card

Quantikine

ANG	IL-10
CNTF	IL-11
EGF	IL-12
ENA-78*	IL-12 p40*
FGF basic	IL-13
FGF-4	IL-15
G-CSF	LIF
GM-CSF	M-CSF
sgp130	MCP-1
GROα	MIP-1α
HGF	MIP-1β
IFN-γ	OSM
IL-1α	PDGF-AB
IL-1β	RANTES
IL-1ra	SCF
IL-1 sRII	SLPI
IL-2	TGF-β1
IL-2 sRα	TGF-β2
IL-3	TNF-α
IL-4	TNF-β
IL-4 sRα	sTNF RI
IL-5	sTNF RII
IL-6	Tpo*
IL-6 sR	VEGF
IL-8	

Quantikine HS
(high sensitivity)

FGF basic	IL-6
G-CSF	IL-7
GM-CSF	IL-10
IL-1β	IL-12
IL-3	TNF-α
IL-4	

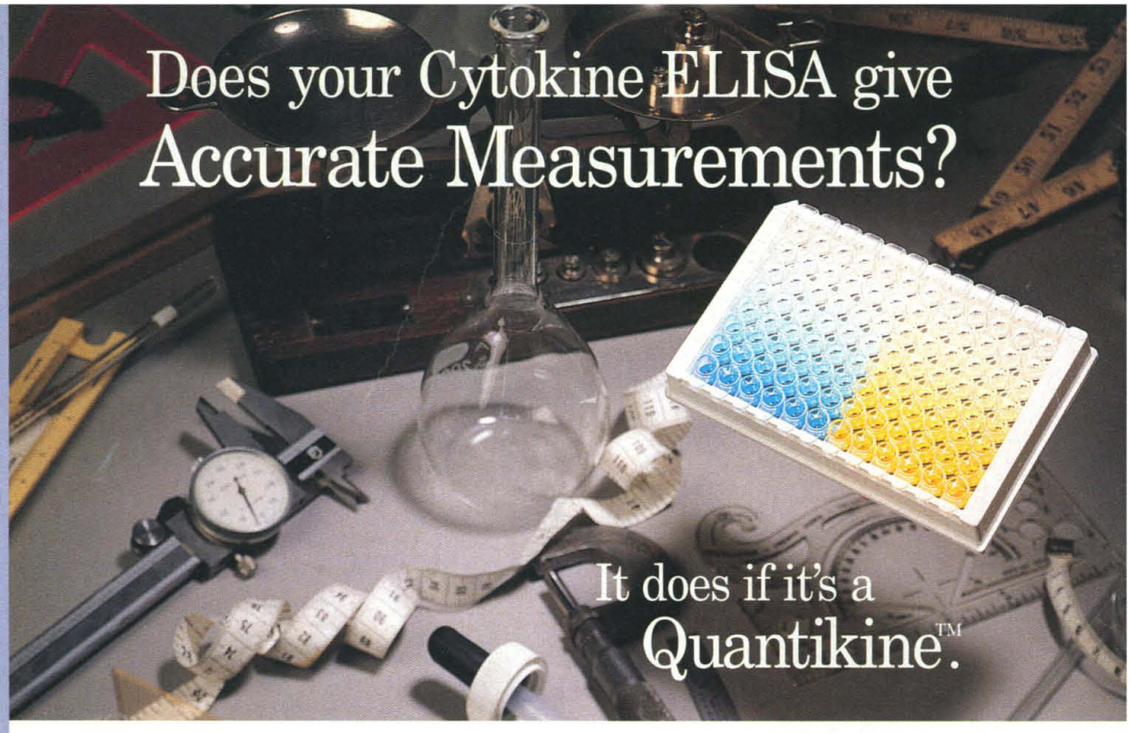
Quantikine M
(mouse)

GM-CSF	IL-13
IFN-γ	KC
IL-1β	MIP-1α*
IL-2	MIP-2
IL-4	TNF-α
IL-6	Tpo*
IL-10	VEGF

** denotes NEW*

R&D SYSTEMS

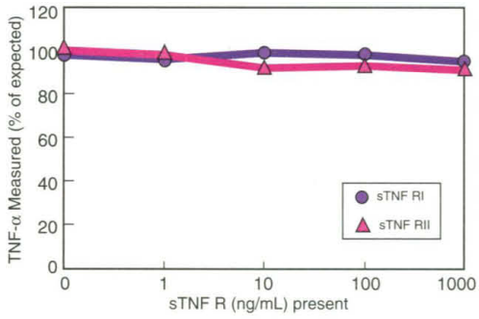
1-800-343-7475



Is your ELISA measuring the cytokine and only the cytokine?

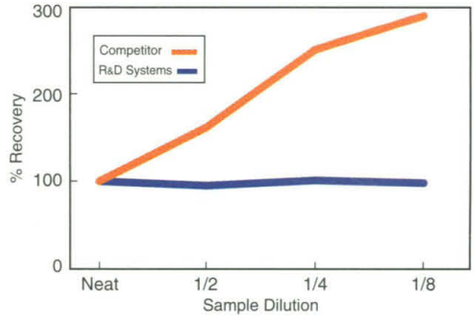
Quantikine Immunoassays are designed to eliminate the effects of cross-reactivity and interference. The lack of cross-reactivity establishes the ability to detect a single cytokine in a complex sample. The lack of interference demonstrates that other substances do not modify the antigen-antibody interaction.

Cross-reactivity



TNF-α was measured with the Quantikine human TNF-α assay in the presence or absence of sTNF RI or sTNF RII. Concentrations of TNF-α were 125-1000pg/mL. Results demonstrate that neither TNF receptor positively or negatively affects the TNF-α concentration in the Quantikine human TNF-α Immunoassay.

Sample Recovery



A spiked serum sample was serially diluted and run in the Quantikine mouse IL-2 ELISA and a competitor's mouse IL-2 ELISA. Results are based on the percent recovery of the diluted sample.

FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC OR THERAPEUTIC PROCEDURES.

North America
R&D Systems, Inc.
614 McKinley Place NE
Minneapolis, MN 55413, USA.
Tel: 612 379-2956
Fax: 612 379-6580
info@rndsystems.com

Europe
R&D Systems Europe Ltd.
4-10 The Quadrant, Barton Lane
Abingdon, OX14 3YS, UK.
Tel: +44 (0)1235 551100
Fax: +44 (0)1235 533420
info@rndsystems.co.uk

Germany
R&D Systems GmbH
Borsigstrasse 7
65205 Wiesbaden, Germany
Tel: +49 06122 90980
Fax: +49 06122 909819
infogmb@rndsystems.co.uk

Japan
Funakoshi, Co., Ltd.
9-7, 2-Chome
Hongo, Bunkyo-ku
Tokyo 113, Japan
Tel: 81-3 5684-1622
Fax: 81-3 5684-1633

International Distributors – Argentina: (54-1) 942-3654. **Australia:** (61-2) 9521-2177. **Austria:** 01 292 35 27. **Chile:** (56-2) 671-9369. **Greece:** 031 322 525. **Hong Kong:** (852) 2649-9988. **Israel:** (972-9) 764-8787. **Italy:** 39 2 25 75 377. **Korea:** (82-02) 569-0781. **Mexico:** (52-5) 612-0085. **New Zealand:** (64-9) 377-3336. **Spain :** 34 1 535 39 60. **Poland:** 48 22 720 44 54. **Portugal:** 01 352 87 74. **South Africa:** 021 981 1560. **Taiwan:** (866-02) 368-3600. **Venezuela:** (58-2) 239-07-80.

Europe Free Phone – Belgique/België: 0800 10 468. **Danmark:** 80 01 85 92. **France:** 0800 90 72 49. **Nederland:** 060 225607. **Norge:** 800 11033. **Sverige:** 020 79 31 49. **Switzerland:** 0800 55 2482.

www.rndsystems.com

Circle No. 37 on Readers' Service Card

The best choice for a centrifuge today, is one that will improve with age.

Choosing a superspeed centrifuge is a decision you'll live with, you would hope, for many years. So be sure to consider long-term performance. A centrifuge built for reliability, without belts or a vacuum system, will keep its like-new performance longer. And if it's a SORVALL® superspeed, it will even perform better than new.

That's because SORVALL continually develops innovative upgrades for new and installed centrifuges, such as SUPER-LITE™ Aluminum Rotors that allow faster acceleration and deceleration in high-speed runs. Plus, we introduced the versatile SH-3000 rotor with adapters for applications from 132 x 3 mL tubes to 4 x 750 mL bottles, and DRY-SPIN™ Leakproof Bottles in 250 mL and 500 mL sizes – all state-of-the-art advances that were, and are, compatible with SORVALL superspeeds made years ago.

Call us today, and take a close look at SORVALL Superspeed Centrifuges. Discover value that goes beyond performance, with forward thinking that's backward-compatible.

SORVALL®

CENTRIFUGES

Expect more than performance.

USA: (800) 522-7746
France: (01) 69 18 77 77 Germany: 6172/87-2544
Italy: 02/25302372 UK: (01438) 342911
All other Europe, Middle East, Africa: 44 (1438) 342900;
Canada, Asia Pacific, Japan and Latin America:
(203) 270-2080 or contact your local SORVALL representative.
Internet: http://www.sorvall.com

Circle No. 30 on Readers' Service Card

Take aim with the revolutionary **Helios Gene Gun System** A new method of gene delivery •

• **Right on Target**

Target new applications with the Helios Gene Gun System.

The Helios™ Gene Gun creates a whole new way to unlock the mysteries of cell growth and development for *in vivo* applications, especially for advances in gene therapy and genetic immunization (DNA vaccination). The Helios Gene Gun is designed to serve a wide range of research uses, and is the latest addition to the innovative instruments available from Bio-Rad Laboratories, the leader in gene transfer technology. Transfer of genetic material *in vivo* via Biolistic® particle bombardment is now both fast and effective: simply load sample cartridges with DNA- or RNA-coated microcarriers, point the nozzle and fire the device. A low pressure helium pulse reproducibly delivers gold particles coated with the nucleic acids into virtually any target.
Learn more about the Helios Gene Gun system by contacting your local Bio-Rad representative. In the U.S., call 1-800-4BIORAD.

Helios is a trademark of Auragen, Inc. Biolistic is a registered trademark of E.I. DuPont de Nemours and Co. Biolistic technology is exclusively licensed to Bio-Rad Laboratories for commercialization of devices.

BIO-RAD **Bio-Rad Laboratories**

Molecular Bioscience Group

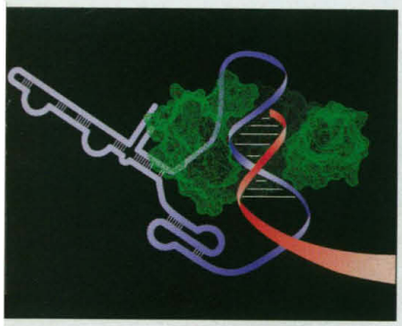
U.S. *(800) 4BIORAD* • ***California*** *(510) 741-1000* • ***Australia*** *02-9914-2800* • ***Austria*** *(1)-877 89 01* • ***Belgium*** *09-385 55 11* • ***Canada*** *(905) 712-2771* • ***China*** *(86-10) 2046622* • ***Denmark*** *39 17 9947* • ***Finland*** *90 804 2200* • ***France*** *(1) 49 60 68 34* • ***Germany*** *089 318 84-0* • ***India*** *91-11-461-0103* • ***Italy*** *02-21609 1* • ***Japan*** *03-5811-6270* • ***Hong Kong*** *7893300* • ***The Netherlands*** *031318-540666* • ***New Zealand*** *09-443 3099* • ***Singapore*** *(65) 272-9877* • ***Spain*** *(91) 661 70 85* • ***Sweden*** *46 (0) 8 627 50 00* • ***Switzerland*** *01-809 55 55* • ***United Kingdom*** *0800 181134*

Circle No. 42 on Readers' Service Card

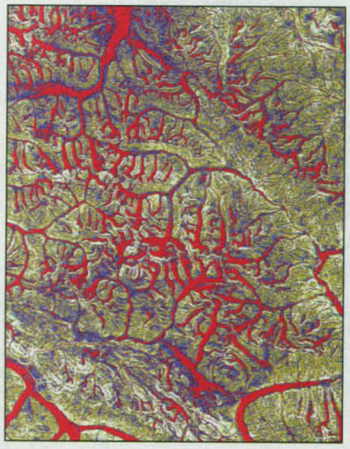
ISSN 0036-8075
25 APRIL 1997
VOLUME 276
NUMBER 5312

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



528 & 561
Telomerase catalytic subunit in hand



571
Glacial tops to topography

NEWS & COMMENT

AIDS Trials Ethics Questioned 520

Publishing Sensitive Data: Who Calls the Shots? 523

Warnings Precede Chinese Temblors 526

Merck Gives Researchers Knockout Deal 527

Report Says ITER Ignition Not Assured 527

RESEARCH NEWS

The Telomerase Picture Fills In 528

Gamma-Ray Bursts: Visible 'Source' Teases Observers 529

Doubts Greet Claim of Cosmic Axis 530

Possible Function Found for Breast Cancer Genes 531

New Test Sizes Up Randomness 532

New Vaccine May Ward Off Urinary Tract Infections 533

Putative Cancer Gene Shows Up in Development Instead 534

Ideas on Human Origins Evolve at Anthropology Gathering 535

PERSPECTIVES

Putting Molecules Behind Bars 543
S. C. Zimmerman

The Rise of Plants and Their Effect on Weathering and Atmospheric CO_2 544
R. A. Berner

Ribozymes in Wonderland 546
A. D. Ellington, M. P. Robertson, J. Bull

Seeing the Synapse 547
K. L. Kelner

POLICY FORUM

Current Problems and the Future of Antiretroviral Drug Trials 548
J. M. A. Lange

ARTICLE

U-Th Isotopes in Arc Magmas: Implications for Element Transfer from the Subducted Crust 551
C. J. Hawkesworth, S. P. Turner, F. McDermott, D. W. Peate, P. van Calsteren

DEPARTMENTS

THIS WEEK IN *SCIENCE* 505

EDITORIAL 511
Improved Fossil Energy Technology

LETTERS 513
Misplaced Crabs: H. Smith; G. A. Fox; J. K. Pope • Tritium Supply: H. M. Agnew • Rutherford's Contribution: A. Small • Endangered Species "Hot Spots": C. P. Dunn, M. L. Bowles, G. B. Rabb, K. S. Jarantoski; D. Ehrenfeld, R. F. Noss, G. K. Meffe; *Response*: A. Dobson, J. P. Rodriguez, W. M. Roberts, D. S. Wilcove

SCIENCESCOPE 519

RANDOM SAMPLES 537
Early Puberty Getting More Common • Mouse Man Wins Big • Baby, It's Cold Inside • Filling Chinese Botany Gap • Symbiont Society • Flap Over Toilet Tissue

BOOK REVIEWS 541
Amniote Origins, reviewed by J. A. Ruben • *The Neurobiology of an Insect Brain*, S. N. Zill • Browsings

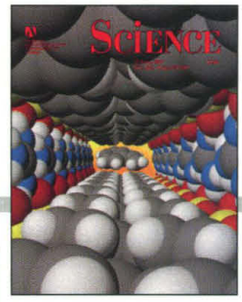
AAAS NEWS & NOTES 618

PRODUCTS & MATERIALS 619

■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005.** Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Domestic individual membership and subscription (51 issues): $105 ($58 allocated to subscription). Domestic institutional subscription (51 issues): $260. Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. IPM #1069624. **Printed in the U.S.A.**

COVER

The synthesis of organic materials with tailored properties requires designs that allow predictable modification of the structure. Host lattices, synthesized from two-dimensional hydrogen-bonded networks (red, white, and blue) linked by molecular pillars (gray and white), trap guest molecules (center) in continuous nanometer-scale channels. The size and chemical nature of the channels can be adjusted systematically by changing the structure of the pillars. See page 575 and the related Perspective on page 543. [Image: J. Sedgewick]



RESEARCH ARTICLES

Antarctic Tectonics: Constraints From an ERS-1 Satellite Marine Gravity Field 556
D. McAdoo and S. Laxon

Reverse Transcriptase Motifs in the Catalytic Subunit of Telomerase 561
J. Lingner, T. R. Hughes, A. Shevchenko, M. Mann, V. Lundblad, T. R. Cech

REPORTS

Vesicle-Specific Noble Gas Analyses of "Popping Rock": Implications for Primordial Noble Gases in Earth 568
P. Burnard, D. Graham, G. Turner

Climatic Limits on Landscape Development in the Northwestern Himalaya 571
N. Brozović, D. W. Burbank, A. J. Meigs

Nanoporous Molecular Sandwiches: Pillared Two-Dimensional Hydrogen-Bonded Networks with Adjustable Porosity 575
V. A. Russell, C. C. Evans, W. Li, M. D. Ward

Scanning Single-Electron Transistor Microscopy: Imaging Individual Charges 579
M. J. Yoo, T. A. Fulton, H. F. Hess, R. L. Willett, L. N. Dunkleberger, R. J. Chichester, L. N. Pfeiffer, K. W. West

Early Forest Soils and Their Role in Devonian Global Change 583
G. J. Retallack

Neurogenesis in Postnatal Rat Spinal Cord: A Study in Primary Culture 586
L. J. Kehl, C. A. Fairbanks, T. M. Laughlin, G. L. Wilcox

Control of Inflammation, Cytokine Expression, and Germinal Center Formation by BCL-6 589
A. L. Dent, A. L. Shaffer, X. Yu, D. Allman, L. M. Staudt

Activation of Auditory Cortex During Silent Lipreading 593
G. A. Calvert, E. T. Bullmore, M. J. Brammer, R. Campbell, S. C. R. Williams, P. K. McGuire, P. W. R. Woodruff, S. D. Iversen, A. S. David

Repression of c-*myc* Transcription by Blimp-1, an Inducer of Terminal B Cell Differentiation 596
Y. Lin, K.-k. Wong, K. Calame

Maintenance of Acetylcholine Receptor Number by Neuregulins at the Neuromuscular Junction in Vivo 599
A. W. Sandrock Jr., S. E. Dryer, K. M. Rosen, S. N. Gozani, R. Kramer, L. E. Theill, G. D. Fischbach

Identification of α-Fodrin as a Candidate Autoantigen in Primary Sjögren's Syndrome 604
N. Haneji, T. Nakamura, K. Takio, K. Yanagi, H. Higashiyama, I. Saito, S. Noji, H. Sugino, Y. Hayashi

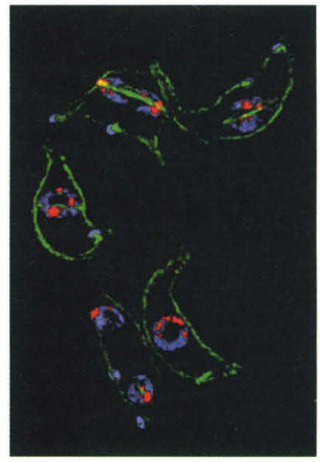
Prevention of Mucosal *Escherichia coli* Infection by FimH-Adhesin–Based Systemic Vaccination 607
S. Langermann, S. Palaszynski, M. Barnhart, G. Auguste, J. S. Pinkner, J. Burlein, P. Barren, S. Koenig, S. Leath, C. H. Jones, S. J. Hultgren

Partitioning of Large and Minichromosomes in *Trypanosoma brucei* 611
K. Ersfeld and K. Gull

Continuous in Vitro Evolution of Catalytic Function 614
M. C. Wright and G. F. Joyce

579
Imaging changing charges

611
The trypanosomes' chromosomes

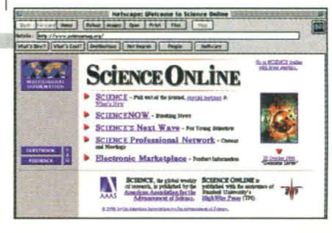


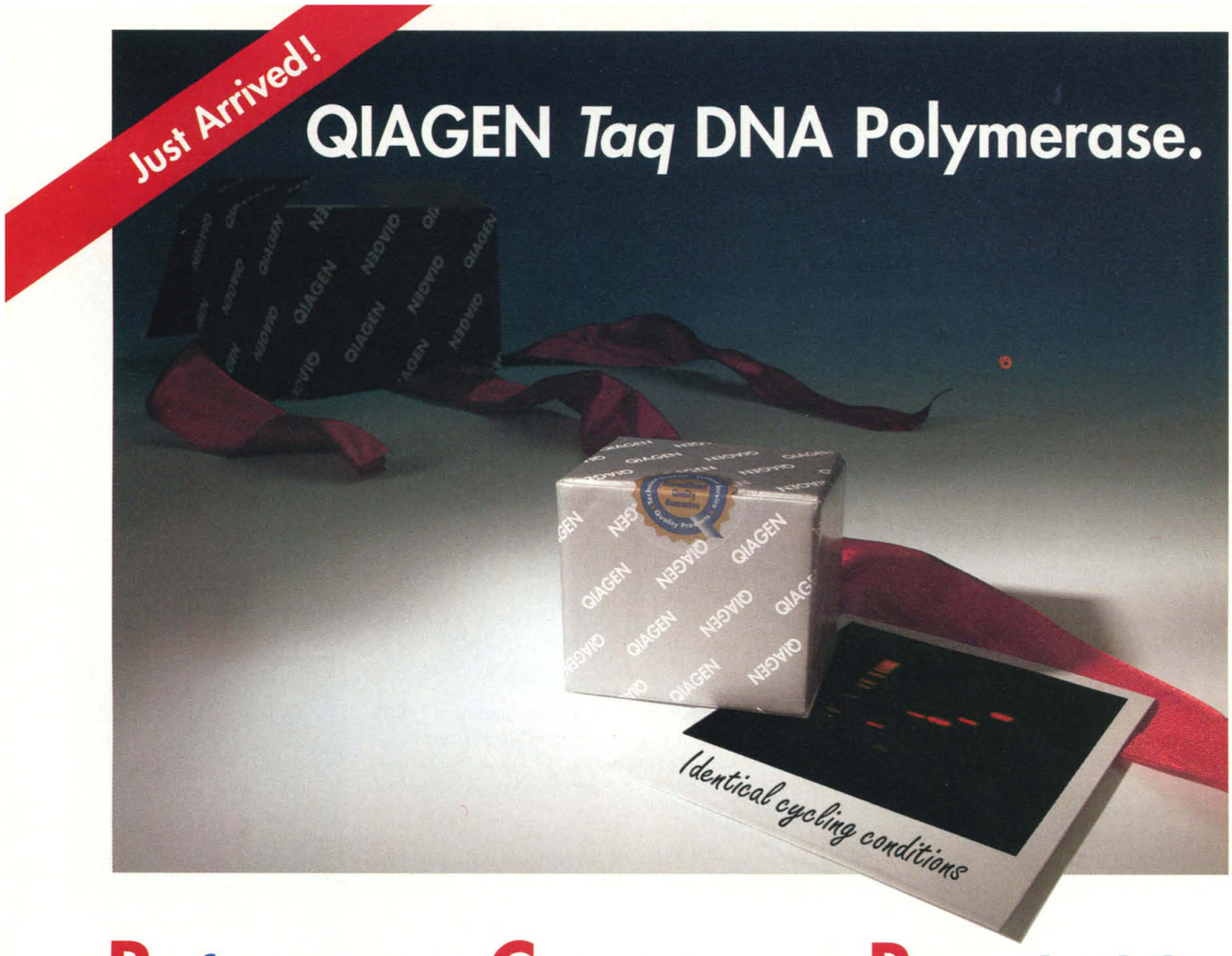
Indicates accompanying feature

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $7.00 per issue prepaid includes surface postage; bulk rates on request. **Authorization to photocopy** material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that $4.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/83 $4.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

On the Web

AIDS Policy Forum
http://www.sciencemag.org/





Performance • Convenience • Reproducibility

The high quality and innovation for which QIAGEN® is renowned are now available for PCR¶. Optimization of individual primer–template systems is no longer necessary when you use our:

- **Robust QIAGEN PCR Buffer**
  developed for optimal amplification of different PCR systems under identical cycling conditions
- **High-quality *Taq* DNA Polymerase**
  lot-to-lot reproducibility guaranteed by our stringent quality control procedure
- **Unique Q-Solution**
  for amplification of difficult templates — supplied with every order of *Taq* DNA Polymerase

QIAGEN *Taq* DNA Polymerase makes high yields of specific PCR product simply routine.

This product is sold under licensing arrangements with F. Hoffmann-La Roche Ltd, Roche Molecular Systems, Inc. and The Perkin-Elmer Corporation.

QIAGEN — Innovation Working for You

Germany: QIAGEN GmbH Tel. 02103-892-0, Fax 02103-892-777
UK: QIAGEN Ltd. Tel. 01293-422-911, Fax 01293-422-922
France: QIAGEN S.A. Tel. 01-60-920-920, Fax 01-60-920-925
USA & Canada: QIAGEN Inc. Tel. 800-426-8157, Fax 800-718-2056
Switzerland: QIAGEN AG Tel. 061-319-30-30, Fax 061-319-30-33
Australia: QIAGEN Pty Ltd Tel. 03-9489-3666, Fax 03-9489-3888

DISTRIBUTORS: AUSTRIA/HUNGARY/SLOVENIA: (1)-889 18 19 **BELGIUM/LUXEMBOURG:** 0800-1-9815 **CHINA/HONG KONG:** (021) 65242386 or (852) 2896-6283 **CZECH/SLOVAK REPUBLIC:** (02) 49 53 77 **DENMARK:** 43 86 87 88 **FINLAND:** (09)-804 551 **GREECE:** (01)-643 6138 **INDIA:** (011)-542 1714 **ISRAEL:** (02)-65244 47 **ITALY:** (055) 500 1871 **JAPAN:** (03)-5684-1620 **KOREA:** (02) 924-8697 **MALAYSIA:** (03)-731 2099 **MEXICO, CENTRAL & SOUTH AMERICA:** (1)-805-294-7940 **THE NETHERLANDS:** (033)-495 00 94 **NEW ZEALAND:** (09) 418 3039 **NORWAY:** 022 90 00 00 **PORTUGAL:** (1)-758 07 40 **SINGAPORE:** (65) 445 7927 **SOUTH AFRICA:** (021) 981 1560 **SPAIN:** (91)-663-05-00 **SWEDEN:** (08) 621 34 00 **TAIWAN:** (02) 880 2913 **THAILAND:** (02) 412 5672 **In other countries contact:** QIAGEN GmbH

QIAGEN

¶The PCR process is covered by U.S. Patents 4,683,195 and 4,683,202 and foreign equivalents owned by Hoffmann-La Roche AG.

Circle No. 38 on Readers' Service Card

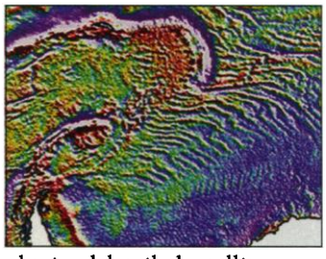
edited by BROOKS HANSON

Landscapes under ice

The relative effects of tectonism and erosion on producing or limiting high elevation and relief have been uncertain. As one test of the importance of these processes, Brozović *et al.* (p. 571) examined the distribution of elevations and hillside slopes in the Himalayas. Hillside slopes reach a minimum near where glaciation has occurred, and elevations evidently do not correlate in detail with tectonic denudation rates. These and other observations suggest that glaciation limits elevation there.

Tectonics under ice

The sea floor around Antarctica is key for reconstructing past plate motions because it connects the Pacific and Atlantic plates, but critical regions of the sea floor are covered with ice. McAdoo and Laxon (p. 556)



obtained detailed satellite gravity data of the ice-covered regions; the data reveal lineations and spreading patterns that describe past plate motions. The data imply that Antarctica comprised two separate plates before about 61 million years ago.

Autoantigen identified

Primary Sjögren's syndrome is a disease in which the immune system attacks and destroys moisture-producing glands, such as tear and salivary glands. The precise target of the attack has not been identified. Now, using a mouse model of Sjögren's syndrome, Haneji *et al.* (p. 604) have come up with a candidate: α-fodrin, a component of the cytoskeleton. They describe T cell and antibody responses to α-fodrin and show that intravenous injection of a recombinant form of the protein protects against development of the disease in mice. Also, patients with primary Sjögren's syndrome show antibody and T cell responses to α-fodrin, while patients with other autoimmune diseases do not.

Telomerase goes retro

Telomerase is a ribonucleoprotein enzyme that replicates the ends of eukaryotic chromosomes or telomeres. Although the RNA components and several telomerase-associated proteins have been isolated, the catalytic protein subunit has remained elusive. Lingner *et al.* (p. 561; see the news story by Barinaga, p. 528) have characterized a 123-kilodalton telomerase protein from the ciliated protozoan *Euplotes* and shown that it contains signature motifs of reverse transcriptases (RTs), enzymes that replicate retroviral genomes and transposable DNA elements through an RNA intermediate. The yeast homolog of p123 was identified as Est2p, a protein known to be required for telomere maintenance. Mutagenesis of the RT motifs in Est2p led to telomere shortening and senescence in yeast, implying that these motifs are critical to telomere elongation and likely constitute the enzyme active site.

Connecting sight and sound

Sensory processing is generally thought of as a one-way pathway in which incoming signals travel to higher processing and integration centers of the brain. It has been suggested that imagining a visual scene causes top-down activation of the primary visual cortex. The primary visual cortex has also been thought to be active during reading of Braille. Calvert *et al.* (p. 593) found that the primary auditory cortex is active not only when listening to speech, as expected, but also when lip-reading silent speech, which suggests that the communication between different modalities can occur quite early in sensory processing and perception.

Sucking up

The early evolution of plants is thought to have had a marked effect on Earth's atmosphere, notably by decreasing atmospheric CO_2 levels. Retallack (p. 583; see Perspective by Berner, p. 544) describes evidence from a fossil soil in Antarctica that well-drained forests had developed by the Middle Devonian, about 380 million years ago. This evolution coincides with predictions and other measurements of a dramatic drop in CO_2 levels.

Stopping cystitis

There is a high incidence of cystitis resulting from *Escherichia coli* infection in women 18 to 40 years old (resulting in millions of hospital visits per year). Langermann *et al.* (p. 607; see the news story by Service, p. 533) found that an adhesin (FimH) at the end of a structure called a pilus on *E. coli* can be used to immunize mice and prevent bacterial colonization of the bladder in an animal model of the infection.

Imaging fractions of a charge

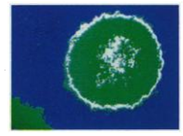
Incorporation of a single electron transistor into a sharp glass scanning probe tip has allowed the detection of extremely small changes in electrical potential. Yoo *et al.* (p. 579) measured the current that tunnels through a small metal island (100 nanometers across); the external field induces oscillations in this current, and by monitoring the periodicity they can detect just 1 percent of an electron charge. They used this device to map electric fields at the surface of a silicon-doped GaAs/$Al_xGa_{1-x}As$ heterostructure.

Reliable transmissions

The synapses that mediate the signal from nerve to muscle are highly reliable, in part because of the high density of receptors on the muscle for acetylcholine, the neurotransmitter that carries the signal across the synapse. Sandrock *et al.* (p. 599) now show that a neuregulin, an extracellular ligand for receptor tyrosine kinases on the muscle, is necessary to maintain the acetylcholine receptors. Knockout mice deficient for only the subtype of neuregulin that contains an immunoglobulin-like domain are myasthenic (their muscles cannot sustain rapid, high-frequency stimulation) and the density of their acetylcholine receptors is reduced.

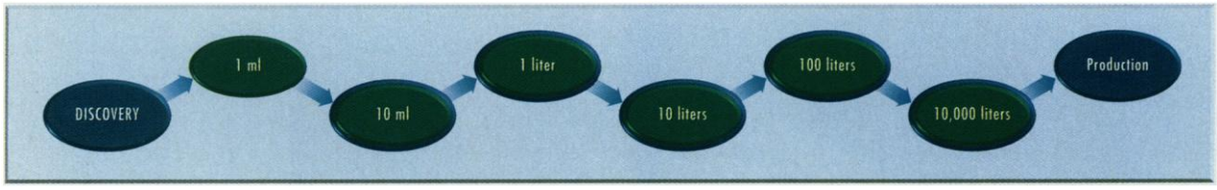
Amicon is now part of Millipore. What does this mean to you? And how will it affect your work? In some ways, amicon BIOSEPARATIONS it won't. The Amicon and Millipore products you use every day will continue to be available. But in other ways, you'll see a big difference.

The biggest difference: choice. Amicon bioseparation products truly complement those of Millipore. So, as a customer, you now have something you didn't have before — more choices in one place. Millipore customers can now call one number (see below) or click on http://www.millipore.com. This may not sound like a breakthrough until you utilize the hundreds of procedural documents for concentration and separation, brought together in one place. Creating what is, arguably, the most experienced and authoritative bioseparation company ever.



HIV in cell culture.

From Discovery to Market, wherever you are, so are we. Whether you are involved in gene therapy, antisense,



Millipore and Amicon offer creative solutions regardless of your operating scale.

choose Amicon advanced bioseparation technology over other physical separation techniques.

If you are a biochemist selecting the filter material and porosity compatible with your product, Millipore probably has what you need. If you are a pharmaceutical process engineer looking for optimal tangential flow rates, pressure and pumping or for chromatographic separation and related plant-wide system controls, the expanded Millipore is the answer. In fact, we can save you precious time on the path to market.

More Information at your fingertips. When you have a question about an Amicon or Millipore product, simply purification of blood fractions, cell culture products or vaccines, consider Millipore your partner. Our membranes, preparative chromatography and filtration systems, process controls and consulting services already have helped dozens of biotechnology and pharmaceutical companies save countless dollars and hours in scale-up and production. We are ready to do the same for you.

Contact us for information about your specific application:

E-mail: protein@millipore.com
Website: www.millipore.com/amicon
North America: 1-800 MILLIPORE
Europe: fax 33-3-88.38.91.95
Japan: (03) 5442-9716
Asia: (852) 2803-9111

Put us to the test. When you want information about Millipore or Amicon products, or need an answer to a specific question regarding your work, we are ready to help. After all, that's what partners are for.

MILLIPORE

Circle No. 28 on Readers' Service Card

Get there first with HP's new LC/MS.

HEWLETT® PACKARD

Because nobody remembers who came in second.

In today's tight research-and-development race, you can get there first with the new benchtop HP 1100 Series LC/MSD.

The first truly chromatographer-friendly system, the new HP LC/MSD gives you immediate access to powerful MS information–the ideal complement to your variable wavelength and diode-array-detector data. You get what you need to speed up R & D cycles: molecular weights, structural information, peak purity analysis and trace-level quantitation–all in one chromatographic run.

The new HP system is the first LC/MS that liquid chromatographers can use from day one:

- Easy-to-use detector–no hardware adjustments, and instrument tuning is automatic.
- Fully integrated LC and MS software–flattens the MS learning curve.
- Powerful software tools for qualitative identification–for tasks like peak purity and protein/peptide analysis.

Get there first, with the new HP LC/MSD. Call **1-800-227-9770,** Ext 2130, or log on to http://www.hp.com/go/chem

The new HP 1100 Series LC/MSD offers a breakthrough in usability.

ISO 9001 REGISTERED

Literature: Circle Reader Service No. 19

Sales Representative: Circle Reader Service No. 35

http://www.sciencemag.org

SCIENCE

■ Published by the **American Association for the Advancement of Science (AAAS)**, *Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

■ The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, to advance education in science, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

INFORMATION RESOURCES

SUBSCRIPTION SERVICES
For change of address, missing issues, new orders and renewals, and payment questions, please contact AAAS at Danbury, CT: 800-731-4939 or Washington, DC: 202-326-6417, FAX 202-842-1065. Mailing addresses: AAAS, P.O. Box 1811, Danbury, CT 06813 or AAAS Member Services, 1200 New York Avenue, NW, Washington, DC 20005 • **Other AAAS Programs:** 202-326-6400

REPRINTS & PERMISSION
Reprints: Ordering/Billing, 800-407-9191; Corrections, 202-326-6501 • **Permissions:** 202-326-7074, FAX 202-682-0816

INTERNET ADDRESSES
science_editors@aaas.org (for general editorial queries); science_news@aaas.org (for news queries); science_letters@aaas.org (for letters to the editor); science_reviews@aaas.org (for returning manuscript reviews); science@science-int.co.uk (for the Europe Office); membership@aaas.org (for member services); science_classifieds@aaas.org (for submitting classified advertisements); science_advertising@aaas.org (for product advertising)

INFORMATION FOR CONTRIBUTORS
See pages 98–99 of the 3 January 1997 issue or access http://www.sciencemag.org/science/home/con-info.shtml.

EDITORIAL & NEWS CONTACTS

North America
Address: 1200 New York Avenue, NW, Washington, DC 20005
Editorial: 202-326-6501, FAX 202-289-7562
News: 202-326-6500, FAX 202-371-9227 • **Bureaus: Berkeley, CA:** 510-841-1154, FAX 510-841-6339, **San Diego, CA:** 619-942-3252, FAX 619-942-4979, **Chicago, IL:** 312-360-1227, FAX 312-360-0537, **Boston, MA:** 617-566-7137, FAX 617-734-8088

Europe
Headquarters: 14 George IV Street, Cambridge, UK CB2 1HH; (44) 1223-302067, FAX (44) 1223-302068
Paris Correspondent: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00

Asia
Japan Office: Carl Kay, Esaka-cho 5-chome 11-10, Suita-shi, Osaka 564 Japan; (81) 6-368-1925, FAX (81) 6-368-6905; science@magical.egg.or.jp • **News Bureau:** (81) 3-3335-9925, FAX (81) 3-3335-4898 • **China Office:** Hao Xin, (86)10-6255-9478; science@public3.bta.net.cn

SIGMA FBS. SOURCED ONLY IN THE U.S.A.

You can't be too certain of your sources. That's why we collect and process our fetal bovine serum exclusively in the US. We offer complete traceability and documentation – assuring researchers control over their serum sources and minimizing the risk from possible contamination with exotic viral agents such as BSE.

Our Complete Control Program focuses on all aspects of the serum process to assure complete customer confidence with Sigma FBS. All material sold by Sigma in the US is collected at USDA-inspected abattoirs.

WHEN IT COMES TO FBS SOURCES,

WE KNOW OUR BOUNDARIES.

Our raw FBS is sourced only from qualified vendors, passing stringent on-site audits by our sourcing audit team.

We require certificates of origin from vendors from which fetal blood is sourced, as well as lot traceability to the original USDA-inspected plant where the blood was collected. Additionally, all samples are evaluated in our own facilities before processing as a final Sigma product.

It all results in a fetal bovine serum you can use with full confidence – proving we not only know our boundaries, we stay well within them. For ordering or information, call 1-800-325-3010 or 314-771-5750.

SIGMA®
Biochemicals and Reagents for Life Science Research

Circle No. 17 on Readers' Service Card

One of these had room for improvement...

so we reinvented *Taq*!

Taq2000™

DNA POLYMERASE FROM STRATAGENE

First there was *Taq* DNA polymerase for thermostable amplification of DNA Now there's *Taq2000*™ DNA polymerase, the future of PCR†.

Taq2000 is a highly purified, recombinant DNA polymerase providing the highest yield and specificity for all types of PCR.

† Purchase of these enzymes is accompanied by a license to use them in the Polymerase Chain Reaction (PCR) process in conjunction with an Authorized Thermal Cycler. Stratagene's PCR products are sold under licensing arrangements with Roche Molecular Systems, Inc., F. Hoffmann-La Roche Ltd. and The Perkin-Elmer Corporation.

PCR amplifications were performed using Stratagene's *Taq2000* DNA polymerase or competitor's cloned *Taq* DNA polymerase. The PCR extension times were 4 minutes, 8 minutes and 12 minutes for a 1.9kb amplicon of transgenic mouse genomic target DNA.

- ***Optimized to reduce smearing and increase yield***
- ***Most highly purified DNA polymerase available***
- ***Best* Taq *for extreme PCR conditions***
- ***Minimizes smearing in long PCR***
- ***Licensed for PCR***

Taq2000™ DNA polymerase... —*it's a whole new* Taq

Circle No. 36 on Readers' Service Card

INTERNET MAIL
techservices@stratagene.com

USA
Corporate Headquarters
(800) 424-5444
(619) 535-5400
Fax: (619) 535-0045

GERMANY
Stratagene GmbH
Telephone: (06221) 400634
Telefax: (06221) 400639

UNITED KINGDOM
Stratagene Ltd.
Telephone: (01223) 420955
Telefax: (01223) 420234

SWITZERLAND
Stratagene GmbH
Telephone: (01) 3641106
Telefax: (01) 3657707

STRATAGENE

icies for conservation and environmental protection, the distribution of endangered species is only one element among many that should be considered. Others include the distribution of endangered habitat types, the need for accessible natural areas and wilderness in all parts of the country, and the ecological services provided by natural habitats. Also, in recent years there has been a major shift in environmental thinking to include ecosystem-based information as a critical element in strategic planning. Although this concept is not yet fully codified into law, there is general recognition that endangered species occur in a much larger ecological context than their county-level distributions would indicate. The analysis of Dobson *et al.* does not take these factors into account.

The analysis by Dobson *et al.* underscores the plight of certain parts of the country that have an especially high number of species at risk; the results say little about the conservation status and needs of the rest of the country. Nor do the results inform us about the pressing need for proactive conservation policies to help keep new "hot spots" from developing and to preserve and enhance the wilderness and important natural and seminatural areas that remain elsewhere in the United States. Wood turtles in the northeast, granite outcrop wildflowers in Arkansas, grizzly bears and wolves in the Rocky Mountains, and Michigan peat bogs would be further endangered were conservation laws to be based on a simplistic reading of this report.

David Ehrenfeld
Founding Editor, Conservation Biology,
Cook College, Rutgers University,
New Brunswick, NJ 08903, USA
Reed F. Noss
Editor, Conservation Biology,
Oregon State University,
Corvallis, OR 97331, USA
Gary K. Meffe
Incoming Editor, Conservation Biology,
Savannah River Ecology Laboratory,
Aiken, SC 29802, USA

Response: We did not argue in our report that analyses of "hot spots" on a national scale should be the only criteria in determining conservation priorities. Nevertheless, identifying national "hot spots" and protecting them strikes us as an essential step, which does not preclude state, county, and community initiatives, nor those undertaken by private individuals and organizations. Dunn *et al.* regret the loss of biodiversity on private lands, as do we. Recent studies indicate that over half of the species on the federal endangered species list have more than 80% of their habitat on nonfederal land (*1*). Modifying the ESA to reward private landowners whose land harbors such species (for example, with tax incentives, including estate tax breaks) would promote good stewardship and thus advance the recovery of imperiled species. Most of the endangered species that inhabit federal lands in the wilder regions of the West require protection through careful habitat management that is less exploitative than that currently practiced. In many cases, such protection could become self-financing if the present subsidies for extractice industries and recreational activities were replaced by realistic pricing mechanisms that acknowledged both the value of the resources extracted and the species placed in jeopardy through these activities (*2*).

We agree with Ehrenfeld *et al.* that the protection of natural communities and locally uncommon (but nationally unendangered) species should be a crucial component of the nation's biodiversity policy. But that was not the point of our report, which was to gain a better understanding of the distribution of nationally endangered species in the hope that this might

Photo courtesy of the Wisconsin Dept. of Tourism.

Argentina/Uruguay: 1-822-6164 • Australia: 02-9540-2055
Austria: 0222-74040-190 • Benelux: 045-532-7755
Brazil: 021-592-6642 • Canada: 800-268-5038
Finland: 3-6822-758 • France: 1-30-46-39-00 Germany: 5152-2075
Greece: 1-6005977 • Hong Kong/China: 852-2-896-6283
Israel: 02-5335599 • Italy: 02-891391
Japan: 03-3545-5720 or 06-441-5103 • Korea: 82-2-924-8697
Mexico: 8-371-60-50 • New Zealand: 9-443-1284
Norway, Denmark, Finland, Iceland, Sweden: 22-20-0137
Singapore: 779-3388 • South Africa: 011-792-3428
Spain: 34-3-450-2601 • Sweden: 46-8-625-1850
Switzerland: 056-624-0100 • Turkey: 312-435-0775
United Kingdom: 1-223-366500

Eureka!!

New!

My PCR works at last!

Now amplify even the most difficult template with the new MasterAmp™ Technology.

Epicentre's unique new PCR products* incorporate MasterAmp™ PCR Enhancement Technology** to dramatically improve PCR performance. Even DNA that is very difficult to amplify, such as templates with high GC content or extensive secondary structure, is amplified using *MasterAmp* PCR Kits and PCR-Qualified Thermostable Enzymes.

Fig. 1. PCR of the human ApoE gene (75% GC). Lane 1, standard PCR (Taq); lanes A-L, PCR with each of the 12 *MasterAmp* 2X PCR PreMixes using *AmpliTherm* DNA Polymerase.

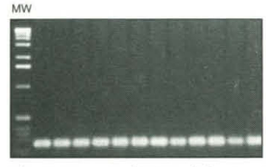


Fig. 2. Repeated PCR of the ApoE gene using *MasterAmp* PCR PreMix K (lane K, Fig. 1) and *AmpliTherm* DNA Polymerase.

Quickly optimize amplification conditions using the *MasterAmp* PCR Optimization Kit.

- It's easy! Just add a mixture of template, primers, and PCR-Qualified enzyme to each ready-to-use PCR PreMix, and cycle. (Fig. 1)
- Once the optimal PCR PreMix is identified, it can be conveniently purchased separately for consistently high yields. (Fig. 2)

Other *MasterAmp* products include:

- ***MasterAmp* PCR Core Kits with Taq or AmpliTherm™ DNA Polymerase.**
- **PCR-Qualified Enzymes with *MasterAmp* PCR Enhancer:** Taq, Tfl, Tth, and the new *AmpliTherm* DNA Polymerase for reliable amplification of particularly difficult templates. Enzymes are available separately or in the *MasterAmp* PCR Enzyme Sample Kit.

Licensed for PCR

Free! - Limited time offer
Receive 100 units each of *AmpliTherm* & Taq DNA Polymerases free with purchase of a 20-template size *MasterAmp* PCR Optimization Kit.
This offer is limited to 1 per customer.

MasterAmp

EPICENTRE® TECHNOLOGIES
1202 Ann Street Madison, WI 53713
800-284-8474
...when you need to be sure of the quality

Money Back 100% Guarantee

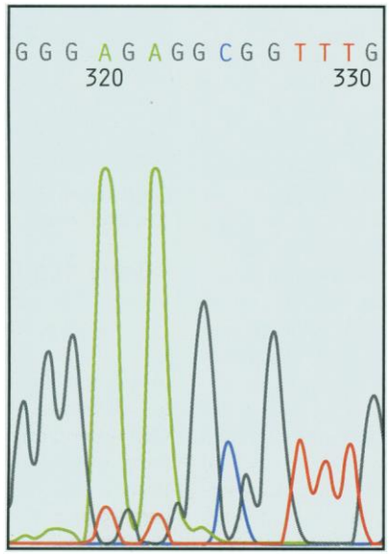
Outside of the U.S. contact the distributor in your country or call 608-258-3080 or fax 608-258-3088.
E-mail: techhelp@epicentre.com ❖ World Wide Web: http://www.epicentre.com

** These products are sold under licensing arrangements with F. Hoffmann-La Roche Ltd., Roche Molecular Systems, Inc. and The Perkin-Elmer Corporation.*
*** Patents pending.*

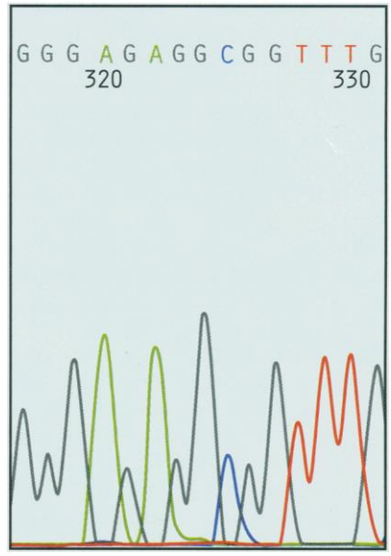
Circle No. 39 on Readers' Service Card

New dRhodamine dye terminators

Our best DNA sequencing chemistry just got better.



Conventional dye terminators



New ABI PRISM dRhodamine dye terminators

Compared to conventional dye terminators, the new ABI PRISM™ dRhodamine terminators provide cleaner signal and more uniform peak patterns. As a result, you get greater basecalling accuracy for every sequencing application, including heterozygote determination.

A set of terminators based on four new dichlororhodamine dyes makes the difference. Combined with AmpliTaq® FS enzyme, they give you less background noise, with even peaks and a significant improvement in the "weak G after A" pattern characteristic of conventional rhodamine dye terminators.

Of course, some things are exactly the same. You still get the one-tube convenience of our previous dye terminator kits. And the new dyes were developed specifically for ABI PRISM 377, 377XL and 310 systems, so performance is guaranteed on all those platforms.

For 377, 377XL and 310 systems.

See what a difference the accuracy of ABI PRISM dRhodamine dye terminators can make in your sequencing. To order in the U.S., call 1-800-345-5224. Outside the U.S., contact your local sales representative. On the Internet, visit www.perkin-elmer.com/ab.

PE Applied Biosystems

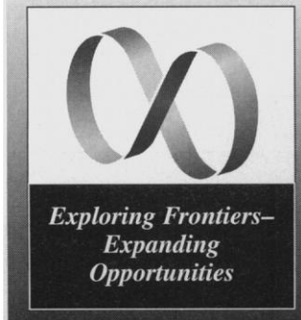
Europe Langen, Germany Tel: 49 (0)6103 708 301 Fax: 49 (0)6103 708 310
Japan Tokyo, Japan Tel: (0473) 80-8500 Fax: (0473) 80-8505
Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223
Australia Melbourne, Australia Tel: 61 3 9212-8585 Fax: 61 3 9212-8502

PE Applied Biosystems PCR reagents are developed and manufactured by Roche Molecular Systems, Inc., Branchburg, New Jersey, U.S.A.

Roche

ISO 9000

Circle No. 29 on Readers' Service Card



Mark Your Calendar for the 1998 AAAS Meeting

1998 AAAS Annual Meeting and Science Innovation Exposition

February 12-17, 1998

Pennsylvania Convention Center

Philadelphia, Pennsylvania

The 1998 AAAS Meeting—the premier event for science and technical professionals—where you can...

✔find out about the latest issues and emerging research from all areas of science
✔learn of fertile synergies between disciplines
✔exchange and publicize new developments
✔debate critical issues in science policy and education
✔meet leaders in your field and network with your colleagues

Proposed Theme Tracks:

•Emerging Science: Transforming the Next Generation
•Communication: Technology, Policy, and Society
•Energy: What Does the Future Hold?
•The Changing Environment of Science
•The Changing Science of Environment
•Discovering Biological Diversity: From Conservatories to Molecular Prospecting
•Education into the Next Century

General Tracks:

•Communicating Science
•Environment, Food, and Natural Resources
•From Molecules to Cells
•Global Change/Earth Systems Science
•Human Development, Language, and Society
•Life Science and the Science of Life
•Neurobiology, Brain, and Behavior
•Physical Sciences
•Public Health and Medicine
•Science, Engineering, and Public Policy
•Science and Society

Science Innovation:

A series of about 15 sessions, addressing leading edge research and applications in molecular biology, medicine, physiology, instrumentation, and computer science.

The 1998 Preliminary Program will be available in September.
Complete this coupon to reserve your copy.

1998 AAAS MEETING

Please send me the following information:

☐ Preliminary Program and Registration Forms
☐ Career Development Program
☐ Call for Poster Papers Forms
☐ Student Session Aide Application
☐ Exhibitor Prospectus and Contract

Please type or print clearly

NAME _____

COMPANY _____

MAILING ADDRESS _____

CITY _____ STATE _____ ZIP _____

TELEPHONE _____ FAX _____ COUNTRY _____

E-MAIL ADDRESS _____

Mail: AAAS, Meetings Dept., 1200 New York Avenue, NW, Washington, DC 20005
Phone: (202) 326-6450 FAX: (202) 289-4021 Email: confinfo@aaas.org
Meetings Home Page:
http://www.aaas.org/meetings/meetings.htm
Scope Online: http://www.aaas.org/meetings/scope

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

INQA1

Circle No. 34 on Readers' Service Card