



AMERICAN
ASSOCIATION FOR THE
ADVANCEMENT OF
SCIENCE

SCIENCE

5 JULY 1996

\$7.00

VOL. 273 • PAGES 1-148



**Patterns
of Aging**

STRATAGENE®

QuikChange™

SITE-DIRECTED MUTAGENESIS KIT

Stratagene Times

QuikChange Site-Directed Mutagenesis Kit
~ Mutagenesis made easy! ~

QuikChange™
Site-Directed
Mutagenesis Kit

Near 100% Efficiency

- Eliminates background
- Cuts screening time in half
- Highest efficiency method
- Mutation in virtually all transformants

150 Times More Accurate than PCR-based Mutagenesis

- Extends without PCR
- Uses high fidelity *Pfu* DNA polymerase
- Replicates only parental DNA
- Reduces second-site mutations 150 fold

1-Day Method

Gene in plasmid with target site for mutation

1. Mix

Denature plasmid and anneal primers containing the desired mutation

2. Cycle

Temperature cycle to extend and incorporate mutation primers resulting in nicked circular strands

3. Digest

Digest parental DNA template

4. Transform

Transform the resulting annealed double-stranded nicked DNA molecules

After transformation the XL2-Blue *E. coli* cell repairs the nicks in the plasmid

**MUTAGENESIS
MADE EASY!**

QuikChange™ Site-Directed Mutagenesis Kit catalog #200518

Patent pending

Circle No. 39 on Readers' Service Card

MUTAGENESIS BREAKTHROUGH

*150 Times
More Accurate
than PCR-based
Mutagenesis!*

REPLICATES ONLY PARENTAL DNA

Stratagene has just revolutionized site-directed mutagenesis with the QuikChange site-directed mutagenesis kit. You can now complete your mutagenesis in one day, with a simple 4-step method.

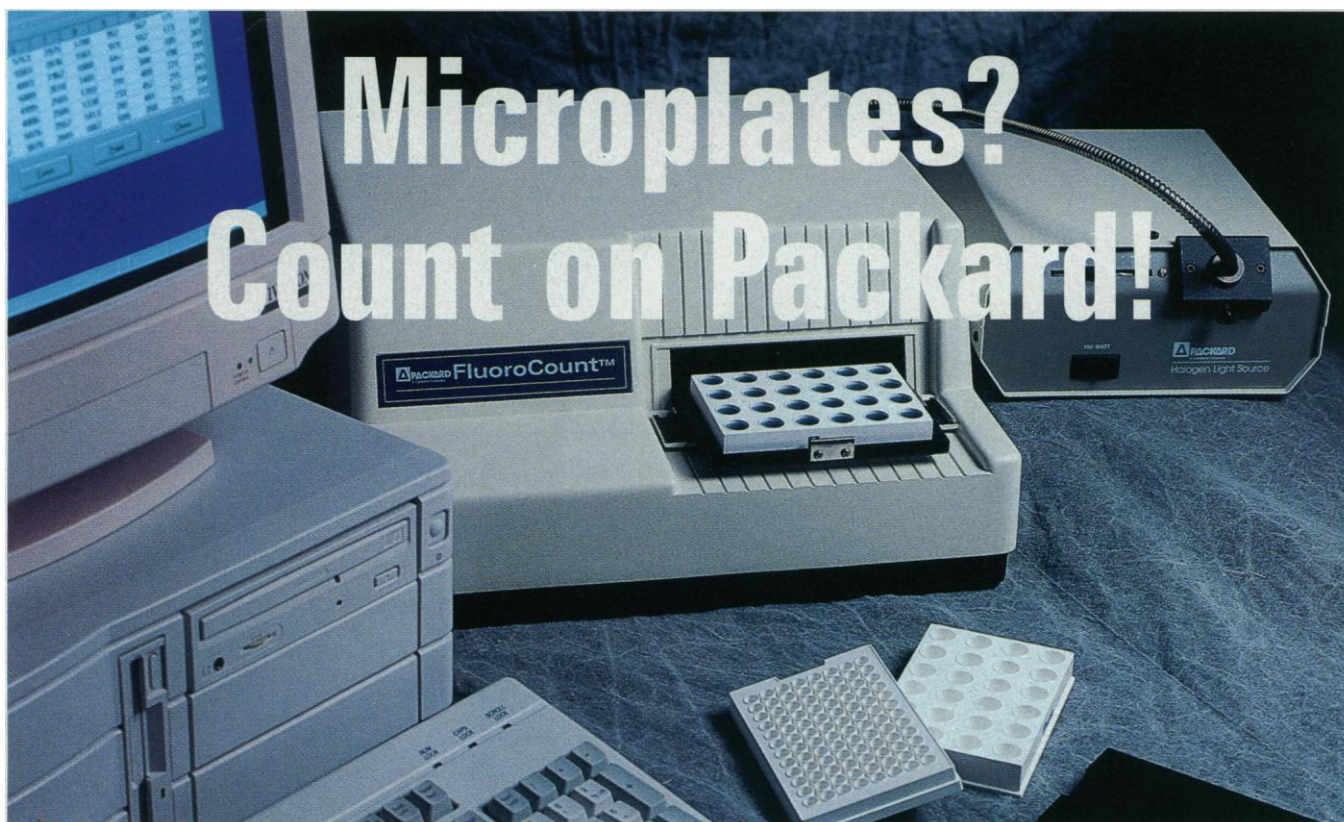
No more single-stranded DNA templates, subcloning into specialized vectors, unique restriction sites, or multiple transformations. And the extreme efficiency of this method cuts your screening time in half!



STRATAGENE®

UNITED STATES:
Stratagene Headquarters
800-424-5444
INTERNET MAIL:
techservices@stratagene.com
AUSTRALIA: 1800-252-204
AUSTRIA: 1 5332666
BRAZIL: 11 530 7833
CANADA: 905 713 1201
DENMARK: 8 6101055
FRANCE: 1 34 60 2424
GERMANY: 0130-840911
HONG KONG: 5785839
ISRAEL: 3 7521687
ITALY: 258013409
JAPAN: (Toyoko) 3 3680 4819
(Punakoshi) 3 5884 1622
KOREA: 2 5580311
MALAYSIA: 37031886
NETHERLANDS: 33 4950094
NEW ZEALAND: 9 443 5867
NORWAY: 22715090
PORTUGAL: 1-4581641
ROC: 2 694 0066 or 2 720 2215
SINGAPORE: 2730893
SPAIN: 1 729 03 33
SWEDEN: 8 680 0845
SWITZERLAND: 3641106
THAILAND: 23080611
UNITED KINGDOM: 0800 585370
OTHER COUNTRIES CALL STRATAGENE U.S.A.

Call Stratagene or your
Stratagene distributor for the complete picture.



Introducing a Complete Line of Microplate Counters for Non-Isotopic Assays

Packard, the company that revolutionized the microplate assay market with its TopCount™ microplate scintillation and luminescence counter, introduces three new non-isotopic microplate instruments.

SpectraCount™

Photometric Microplate Counter features unique single beam detection to extend the linear range of UV/VIS measurements and to handle a greater variety of microplates, including 6, 12, 24, 48 and 96-well plates.

LumiCount™ Microplate Luminometer uses digital photon integration technology to measure glow luminescence assays with high sensitivity. Combined with Packard's enhanced chemiluminescence technology, LumiCount makes it possible to measure a wide variety of assays in both 24 and 96-well plates.



FluoroCount

FluoroCount™ Microplate Fluorometer is the only fluorescence microplate counter with a user selectable external excitation source. FluoroCount gives unmatched sensitivity for a wide range of assays. Its unique close-

proximity detection design can be configured for either top or bottom reading, for both solution and cell-based assays.

Total System Support for microplate counters is only as dependable as the company that provides it. Packard's unique range of luminescence and fluorescence reagents, its

specialty microplates, and its service and applications support will ensure the performance you need today and tomorrow.

For complete details please call Packard at 1-800-323-1891 (U.S. only), 203-238-2351 or visit our web site.

Count on Packard... we bring you solutions.



LumiCount



SpectraCount



PACKARD
A Canberra Company

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 International Offices:

Australia, Mt Waverley 61-3-9543-4266; **Austria**, Vienna 43-1-2702504; **Belgium**, Brussels 32-2-4668210; **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 385-0; **Italy**, Milano 39-2-33910796/7/8; **Japan**, Tokyo 81-3-3866-5850; **Netherlands**, Groningen 31-50-5413360; Tilburg (013) 5423900; **Russia**, Moscow, 7-095-238-7335; **Switzerland**, Zurich (01) 481 69 44; **United Kingdom**, Pangbourne, Berks (44) 01734 844981.

Circle No. 28 on Readers' Service Card



It's the reason researchers

Introducing new CF® PLAN FLUOR Universal Objectives.

With the introduction of CF® chromatic-aberration-free optics in 1975, Nikon elevated the science of microscopy to a new performance level. Now, to meet the exacting demands of today's advanced techniques, we're raising the level even higher with new CF PLAN FLUOR Universal Objectives.

These highly versatile objectives offer crisp, clear images with any source of illumination and any contrasting method you choose. They provide maximum contrast for observation, photomicrography, and video or digital documentation. And with their center-to-edge field flatness, color corrections and high UV transmission, they are ideal for the latest Epi-Fluorescence techniques.

Nikon is the only microscope manufacturer to formulate and produce 100% of its own glass, and has unparalleled expertise in optical coatings and cements. As a result, we have been able to create these superb objectives. All offer longer working distances with extremely high UV transmission ratios, negligible autofluorescence and large numerical apertures for unsurpassed brightness and contrast.

See for yourself the difference these exciting new objectives can make. Ask for a demonstration. Call **1-800-52-NIKON, ext. 285** today.

Fixed mouse fibroblasts are labeled with MitoTracker™ CMXRos and BODIPY® FL phalloidin, and counterstained with DAPI. Photo courtesy of Jennifer Kramer and Paul Millard, Molecular Probes, Inc. BODIPY is a registered trademark of Molecular Probes, Inc. MitoTracker is a trademark of Molecular Probes, Inc.

©1995 Nikon Inc.

Circle No. 34 on Readers' Service Card

tics

in the life sciences depend on us.

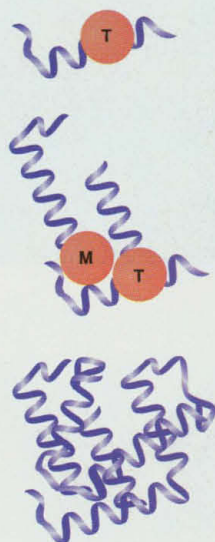


Nikon®



31 & 97

Path of a paleoriver



29

Watching proteins fold

NEWS & COMMENT

- NAE Strives to Re-Engineer Itself 22
Will There Be *Liebowitz v. NAE?* 23

- Black Spots Blot German Coastal Flats 25

- 1997 Budget: Legislators Get Into the Details 25

- Chauvet Study Gets the Go-Ahead 26

- Agencies Scramble to Measure Public Impact of Research 27

- Auguste D. and Alzheimer's Disease 28

RESEARCH NEWS

- Folding Proteins Caught in the Act 29

- Selling the Immune System Short 30

- Long Ago, a River Ran Through It 31

- With Mirrors and Finesse, Labs Domesticate the X-ray Laser 32

- Muscling Transplants Into Mice 33

- Sky-High Findings Drop New Hints of Greenhouse Warming 34

- Chromosomes Yield New Clue to Pairing in Meiosis 35

- Helical Beams Give Particles a Whirl 36



HORIZONS IN AGING

NEWS

- Live Long and Prosper? 42
A 'Big Science' Survey for the Social Sciences 43
Japan: Feeling the Strains of an Aging Population 44
New Populations of Old Add to Poor Nations' Burdens 46
For the Cortex, Neuron Loss May Be Less Than Thought 48
Searching for Drugs That Combat Alzheimer's 50

PERSPECTIVES

- A Search for Earthquake Precursors 77
P. G. Silver and H. Wakita
How T Cells Count 78
E. V. Rothenberg
Mechanisms and Evolution of Aging 80
G. J. Lithgow and T. B. L. Kirkwood

REPORTS

- Colossal Magnetoresistance Without Mn^{3+}/Mn^{4+} Double Exchange in the 81

DEPARTMENTS

- THIS WEEK IN SCIENCE** 9
EDITORIAL 13
Why China Needs Science... and Partners
L. Peng
LETTERS 15
Battling Heart Disease: J. I. Breslow; M. S. Brown and J. L. Goldstein; D. R. Labarthe • Release of RHD Virus in Australia: D. O. Matson; A. W. Smith
SCIENCESCOPE 21

- RANDOM SAMPLES** 37
Chernobyl Power Proposal • The World's Fastest Computer • Calibrating Ozone Damage • Higher-Ups in Charity Scandal Nabbed • New Center to Press Chimp Rights • Depressing Questions
BOOK REVIEWS 75
Species and Specificity, reviewed by J. E. Lesch • Vignettes • Reprints of Books Previously Reviewed • Books Received
PRODUCTS & MATERIALS 128

AAAS Board of Directors

Rita R. Colwell
Retiring President, Chairman
Jane Lubchenco
President
Mildred S. Dresselhaus
President-elect

Sheila Jasanoff
William A. Lester Jr.
Simon A. Levin
Marcia C. Linn
Michael J. Novacek
Anna C. Roosevelt
Jean E. Taylor
Nancy S. Wexler

William T. Golden
Treasurer
Richard S. Nicholson
Executive Officer

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. Copyright © 1996 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$102 (\$55 allocated to subscription). Domestic institutional subscription (51 issues): \$250. 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. Printed in the U.S.A.

COVER

Demographics show that populations are growing older, a situation that is putting a strain on the social and economic resources of countries around the world. The outlook for those gray populations as well as the biological and physiological causes of aging are ex-

plored in News stories (beginning on page 42), a Perspective (page 80), and Articles (beginning on page 54) in this special issue on aging. [Image taken from Gustav Klimt's *Three Ages of Woman* (1905). Scala/Art Resource]



ARTICLES

Longevity, Genes, and Aging 54
S. M. Jazwinski

Oxidative Stress, Caloric Restriction, and Aging 59
R. S. Sohal and R. Weindruch

Replicative Senescence: Implications for in Vivo Aging and Tumor Suppression 63
J. R. Smith and O. M. Pereira-Smith

Menopause: The Aging of Multiple Pacemakers 67
P. M. Wise, K. M. Krajnak, M. L. Kashon

The Aging Immune System: Primer and Prospectus 70
R. A. Miller

Stoichiometric Pyrochlore $Ti_2Mn_2O_7$
M. A. Subramanian, B. H. Toby, A. P. Ramirez, W. J. Marshall, A. W. Sleight, G. H. Kwei

Direct, Nondestructive Observation of a Bose Condensate 84
M. R. Andrews, M.-O. Mewes, N. J. van Druten, D. S. Durfee, D. M. Kurn, W. Ketterle

Homogeneous Linewidths in the Optical Spectrum of a Single Gallium Arsenide Quantum Dot 87
D. Gammon, E. S. Snow, B. V. Shanabrook, D. S. Katzer, D. Park

Two Calorimetrically Distinct States of Liquid Water Below 150 Kelvin 90
G. P. Johari, A. Hallbrucker, E. Mayer

Helium Isotopic Evidence for a Lower Mantle Component in Depleted Archean Komatiite 93
D. Richard, B. Marty, M. Chaussidon, N. Arndt

Transition Element-Like Chemistry for Potassium Under Pressure 95
L. J. Parker, T. Atou, J. V. Badding

Detrital Zircon Link Between Headwaters and Terminus of the Upper Triassic Chinle-Dockum Paleoriver System 97
N. R. Riggs, T. M. Lehman, G. E. Gehrels, W. R. Dickinson

Late Proterozoic and Paleozoic Tides, Retreat of the Moon, and Rotation of the Earth 100
C. P. Sonett, E. P. Kvale, A. Zakharian, M. A. Chan, T. M. Demko

T Cell Activation Determined by T Cell Receptor Number and Tunable Thresholds 104
A. Viola and A. Lanzavecchia

Mapping of Catalytic Residues in the RNA Polymerase Active Center 107
E. Zaychikov, E. Martin, L. Denissova, M. Kozlov, V. Markovtsov, M. Kashlev, H. Heumann, V. Nikiforov, A. Goldfarb, A. Mustaev

Prevention of Islet Allograft Rejection with Engineered Myoblasts Expressing FasL in Mice 109
H. T. Lau, M. Yu, A. Fontana, C. J. Stoeckert Jr.

Evidence for Physical and Functional Association Between EMB-5 and LIN-12 in *Caenorhabditis elegans* 112
E. J. A. Hubbard, Q. Dong, I. Greenwald

Formation of a Transition-State Analog of the Ras GTPase Reaction by Ras-GDP, Tetrafluoroaluminate, and GTPase-Activating Proteins 115
R. Mittal, M. R. Ahmadian, R. S. Goody, A. Wittinghofer

Centric Heterochromatin and the Efficiency of Achiasmatic Disjunction in *Drosophila* Female Meiosis 118
G. H. Karpen, M.-H. Le, H. Le

TECHNICAL COMMENTS

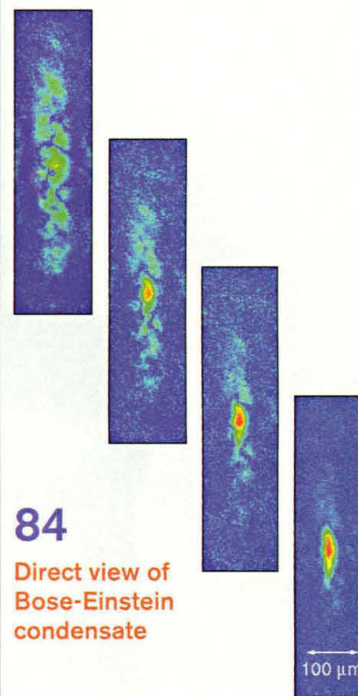
Miocene Deposits in the Amazonian Foreland Basin 122
C. Hoorn, C. G. M. Paxton, W. G. R. Crampton, P. Burgess, L. G. Marshall and J. G. Lundberg; M. E. Räsänen and A. M. Linna

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

Horizons in Aging
<http://www.sciencemag.org/science/content/vol273/issue5271/41a.htm>



84
Direct view of Bose-Einstein condensate



How to Find the Perfect Transfection Tool.

If you're looking for a transfection tool that provides maximum transfection efficiency, look no further. The PerPerfect Lipid™ Transfection Kit allows you to test a panel of eight unique lipids so you can quickly and easily find the one that yields the highest efficiency in your cell line.

Maximize Efficiency

The efficiency of lipid-mediated transfection varies greatly depending on the cell line and lipid used (Figure 1).

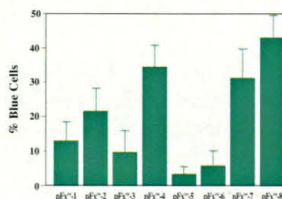


Figure 1: Percent blue cells produced by transfection of CHO cells with a lacZ control vector using PerPerfect Lipids™ (pFx1-8).

That's why we developed the PerPerfect Lipid™ Transfection Kit. Now finding the right lipid for your cell line is easy. Simply transfect the supplied β -galactosidase reporter plasmid with each of the eight PerPerfect Lipids™ (pFx1-8) and assay for the percent of blue cells (Figure 2).

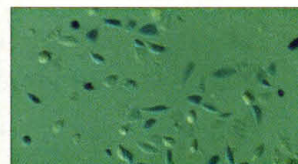


Figure 2: Transfected CHO cells expressing β -galactosidase, stained with X-gal.

Minimize Cost

Once you've found the perfect lipid you can continue to achieve optimum transfection efficiencies. Each PerPerfect Lipid™ is available in individual pack sizes that are convenient and economical to use.

Tested for Results

To make it even easier for you to choose the right lipid, we've tested the PerPerfect Lipids™ in a variety of common cell lines. To see for yourself, check out our web site (<http://www.invitrogen.com>) or call our Technical Services Department.

For perfect transfections with every cell line, there's no better choice than the PerPerfect Lipid™ Transfection Kit and PerPerfect Lipids™. For more information or to place your order, call today.



Telephone (619) 597-6200

Fax (619) 597-6201

<http://www.invitrogen.com>

1-800-955-6288

Circle No. 24 on Readers' Service Card

EUROPEAN HEADQUARTERS:

Invitrogen BV
De Schelp 12, 9351 NV Leek
The Netherlands
Tel: +31 (0) 594 515 175
Fax: +31 (0) 594 515 312
Email: tech_service@invitrogen.nest.nl

Distributors:

Australia 03 9562 6888	Korea 822 569 6902
Hong Kong 86 2 381 0844	Singapore 64 482 3888
Israel 02 524 447	or 29 29 783
Italy 02 33 91 00 72	Spain 03 450 2601
Japan 03 5684 1616	Taiwan 886 2 381 0844

From all other countries, please contact our European headquarters at +31 (0) 594 515 175
PerPerfect Lipids™ are manufactured by Genta, Inc. and licensed to Invitrogen Corporation.

TOLL FREE TELEPHONE NUMBERS:

Belgium 0800 111 73	The Netherlands 06 022 8848
Denmark 800 188 67	Norway 800 113 70
Finland 900 31 800 5345	Sweden 020 795 369
France 19 31 800 5345	Switzerland 155 1966
Germany 0130 8100 43	UK 0800 96 61 93

THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Quantum dot spectra

In a quantum dot, a nanometer-size semiconductor structure, exciting an electron across the band gap produces an exciton (the electron interacting with the hole left in the valence band) that is confined in three dimensions. These excitons can act like atomic states. Gammon *et al.* (p. 87) measured photoluminescence exciton spectra from individual gallium arsenide quantum dots and were able to measure homogeneous (nonbroadened) linewidths of these transitions, which allows exciton lifetimes and dynamics to be explored.

Different waters

Water can form different amorphous solids—for example, condensing water vapor at 100 kelvin (K) produces amorphous solid water (ASW), which if cooled and compressed can form a different phase, a high-density amorphous (HDA) solid. Johari *et al.* (p. 90) show that both ASW and hyperquenched glassy water (formed by rapidly cooling water droplets) form viscous water (water A) at 136 K. Heating HDA water forms a low-density amorphous phase that at 129 K forms another viscous water phase, water B. These two viscous water forms do not thermally interconvert even when they are heated to 148 K. The existence of this barrier between liquids can provide insight into the configuration relaxations that occur in liquid water.

Tide and time

Tides on the Earth, induced by the sun, have resulted in the retreat of the moon from the Earth and an increase in day

Seeing the Bose condensate

Although Bose condensates of alkali metals have been recently observed, this new state of matter has not been directly observed. Such states are distinct in momentum or energy space and thus can coexist spatially with normal state matter. However, application of a potential can force the real-space separation, and Andrews *et al.* (p. 84) now report the observation of light scattering of a Bose condensate of sodium atoms in a magnetic trap.

length. Sonett *et al.* (p. 100) examined several sedimentary rock records that provide an indicator of tidal periods. The day was 18 hours long 900 million years ago, and the moon has retreated at a roughly constant rate since the Precambrian.

River to Nevada

The general paleogeography of a continent can often be determined from the distribution of sediments, but it is much more difficult to reconstruct the origin and course of ancient rivers. Riggs *et al.* (p. 97; see the news story by Wuethrich, p. 31) used the distinct uranium-lead isotope signatures of detrital zircon grains, in conjunction with sedimentologic features, to show that a large river flowed from Texas to Nevada in the Late Triassic (about 200 million years ago) and trace the overall drainage of the region.

Deep and hot

Komatiites are volcanic rocks that are enriched in MgO relative to basalts. Found almost exclusively in the Precambrian deposits, they are considered to represent deep, hot magmas generated at hot spot plumes that erupted early in Earth's history when temperatures were higher. Richard *et al.* (p. 93)

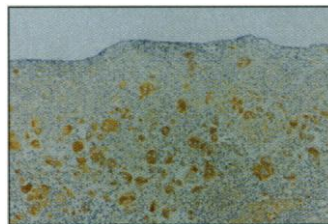
found an enrichment of helium-3 in several fresh olivine crystals in komatiites, indicating that komatiites indeed contain at least a component of a deep mantle plume.

Potassium in the core?

High-pressure, laser-heated diamond anvil studies of the alkali metals by Parker *et al.* (p. 95) show that when potassium is compressed to pressures above 30 gigapascals, it behaves like a transition metal. Compounds of alkali metals and transition metals such as iron and nickel may form at high pressure, and some potassium may be present in Earth's iron-rich core.

Graft protection

Transplanted tissues will normally be rejected unless the T cell response to nonself cells can be avoided. Lau *et al.* (p. 109;



see the news story by Wickelgren, p. 33) show in a mouse model that pancreatic islet transplants can be protected by cotransplanting myoblasts that express the Fas ligand, which

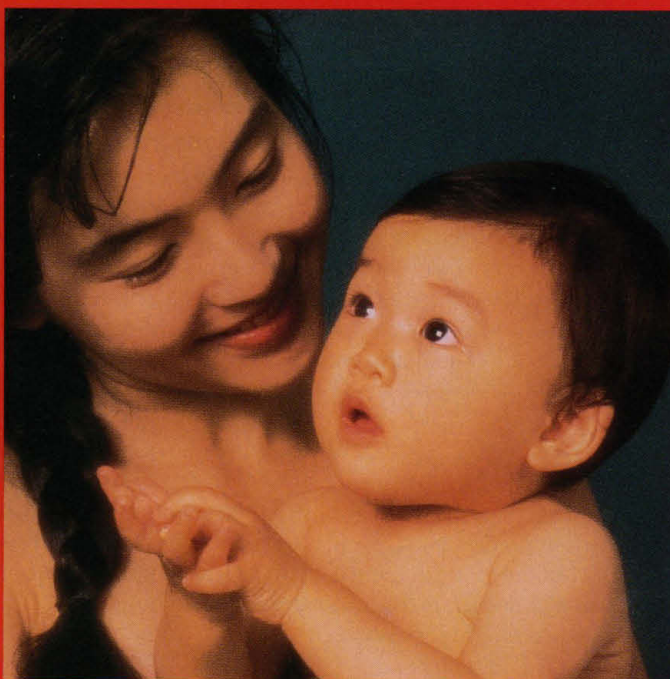
triggers cell death in T cells and is the signal that maintains immunoprivileged sites such as the eye. Graft tolerance was maintained until transgenic expression of Fas ligand ceased.

Cell fate partner

Members of the LIN-12/Notch family of receptors function in cell fate decisions during development. When looking for other components of the LIN-12 signaling pathway in the nematode, Hubbard *et al.* (p. 112) isolated a protein, EMB-5, that interacts with the intracellular signaling domain of LIN-12 and functions in the LIN-12 pathway. Sequencing revealed that EMB-5 is a homolog of a yeast protein SPT6p, that is involved in chromatin structure. Thus, the function of EMB-5 in the signaling cascade could be to alter chromatin structure in order to modify gene activity.

Overlap and disjunction

During meiosis, disjunction ensures that each of the gametes contains the correct number and type of chromosomes. Recombination between homologous chromosomes helps ensure proper disjunction but not all chromosomes undergo recombination. Karpen *et al.* (p. 118; see the news story by Marx, p. 35) examined disjunction of chromosomes that have not undergone recombination by using minichromosomes in *Drosophila*. They find that 1000 kilobases of overlap in the centric heterochromatin was necessary for efficient disjunction. A reduction in heterochromatin increased nondisjunction.



In Perfect Balance

According to the ancient Chinese philosophy of yin and yang, the universe is composed of opposing but interdependent forces. ■ Interestingly, this philosophy resembles the concept of homeostasis, the natural balance that occurs within living organisms, including the harmony between antagonists and agonists that regulate vital functions. Thus, an important factor in the search for new medicines is developing compounds that work together with the body's own restorative and regenerative abilities.

■ To lead healthy lives, we must seek balance with nature, with society, and within ourselves. As a leading pharmaceutical company, Takeda is striving to help people attain this balance.

TAKEDA

Takeda Chemical Industries, Ltd.

Circle No. 40 on Readers' Service Card

Head Office: 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 541, Japan Tokyo Head Office: 12-10, Nihonbashi 2-chome, Chuo-ku, Tokyo 103, Japan

MEMBERSHIP/CIRCULATION

Director: Michael Spinella
Deputy Director: Marlene Zendell
Member Services: Donald Crowl, *Manager*; Mary Curry, *Supervisor*; Pat Butler, Helen Williams, Laurie Baker, *Representatives*
Marketing: Dee Valencia, *Manager*; Jane Pennington, *Europe Manager*; Hilary Baar, *Assistant Manager*
Research: Renuka Chander, *Manager*
Business and Finance: Robert Smariga, *Manager*; Nina Araujo de Kobes, *Coordinator*

ADVERTISING AND FINANCE

Associate Publisher: Beth Rosner
Advertising Sales Manager: Susan A. Meredith
Recruitment Advertising Manager: Janis Crowley
Business Manager: Deborah Rivera-Wienhold
Finance: Randy Yi, *Senior Analyst*; Shawn Williams, *Analyst*
Marketing: John Meyers, *Manager*; Allison Pritchard, *Associate*
Electronic Media: David Gillikin, *Manager*; Pamela Sams, *Production Associate*
Product Advertising: Carol Maddox, *Traffic Manager*; Amber Haslacker, *Sales Associate*
Product Advertising Sales: East Coast/E. Canada: Richard Teeling, 201-904-9774, FAX 201-904-9701 • **Midwest/Southeast:** Elizabeth Mosko, 312-665-1150, FAX 312-665-2129 • **West Coast/W. Canada:** Neil Boylan, 415-673-9265, FAX 415-673-9267 • **UK, Scandinavia, France, Italy, Belgium, Netherlands:** Andrew Davies, (44) 1-457-838-519, FAX (44) 1-457-838-898 • **Germany/Switzerland/Austria:** Tracey Peers, (44) 1-260-297-530, FAX (44) 1-260-271-022 • **Japan:** Mashy Yoshikawa, (3) 3235-5961, FAX (3) 3235-5852
Recruitment Advertising: Terri Seiter Azie, *Sales and Production Operations Manager*; Eric Banks, Nancy Hicks, Celeste Miller, Bethany Ritchey, *Sales*; Debbie Cummings, *European Sales Manager*; Wendy Green, *Production Associate*; Nichole Robinson, *Advertising Assistant*
Recruitment Advertising Sales: US: Janis Crowley, 202-326-6532, FAX 202-289-6742 • **Europe:** Debbie Cummings, +44 (0) 1223-302067, FAX +44 (0) 1223-576208 • **Australia/New Zealand:** Keith Sandell, (61) 02-922-2977, FAX (61) 02-922-1100 • **Japan:** Mashy Yoshikawa, (3) 3235-5961, FAX (3) 3235-5852
Permissions: Lincoln Richman
Exhibits Coordinator: Arlene Ennis
 Send materials to *Science* Advertising, 1200 New York Avenue NW, Washington, DC 20005.

SCIENCE EDITORIAL BOARD

Charles J. Arntzen
 David Baltimore
 J. Michael Bishop
 William F. Brinkman
 E. Margaret Burbidge
 Pierre-Gilles de Gennes
 Joseph L. Goldstein
 Mary L. Good
 Harry B. Gray
 John J. Hopfield

F. Clark Howell
 Paul A. Marks
 Yasutomi Nishizuka
 Helen M. Ranney
 Bengt Samuelsson
 Robert M. Solow
 Edward C. Stone
 James D. Watson
 Richard N. Zare

■ 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, payment questions, and other membership services, please contact AAAS at Danbury, CT: 1-800-731-4939 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_letters@aaas.org (for letters to the editor); science_reviews@aaas.org (for returning manuscript reviews); science@science_intl.co.uk (for the Europe Office); membership@aaas.org (for membership services); science_classifieds@aaas.org (for submitting classified advertisements); science_advertising@aaas.org (for product advertising)

INFORMATION FOR CONTRIBUTORS

See pages 93–94 of the 5 January 1996 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; TDD: 202-408-7770

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 Bureau: 33 1 49 29 09 01, FAX 33 1 49 29 0900

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; haoxin@sun.ihep.ac.cn

BOARD OF REVIEWING EDITORS

Frederick W. Alt
Children's Hospital, Boston
 Don L. Anderson
California Institute of Technology
 Michael Ashburner
Univ. of Cambridge
 Stephen J. Benkovic
Pennsylvania State Univ.
 Alan Bernstein
Mount Sinai Hospital, Toronto
 David E. Bloom
Harvard Institute for International Development
 Piet Borst
The Netherlands Cancer Institute
 Henry R. Bourne
Univ. of California, San Francisco
 Michael S. Brown
Univ. of Texas Southwestern Medical Center
 James J. Bull
Univ. of Texas at Austin
 Kathryn Calame
Columbia Univ. College of Physicians & Surgeons
 Dennis W. Choi
Washington Univ. School of Medicine, St. Louis
 David Clapham
Mayo Foundation
 Adrienne E. Clarke
Univ. of Melbourne, Parkville
 John M. Coffin
Tufts Univ. School of Medicine
 F. Fleming Crim
Univ. of Wisconsin, Madison
 Paul J. Crutzen
Max-Planck-Institut für Chemie
 James E. Dahlberg
Univ. of Wisconsin Medical School, Madison
 Robert Desimone
National Institute of Mental Health, NIH
 Paul T. Englund
Johns Hopkins Univ. School of Medicine

G. Ertl
Max-Planck-Gesellschaft
 Richard G. Fairbanks
Lamont-Doherty Earth Observatory
 Robert E. Fay
U.S. Bureau of the Census
 Douglas T. Fearon
Univ. of Cambridge
 Harry A. Fozzard
The Univ. of Chicago
 Roger I. M. Glass
Centers for Disease Control
 Stephen P. Goff
Columbia Univ. College of Physicians & Surgeons
 Peter N. Goodfellow
SmithKline Beecham
 Peter Gruss
Max Planck Institute of Biophysical Chemistry
 Philip C. Hanawalt
Stanford Univ.
 Paul Harvey
Univ. of Oxford
 M. P. Hassell
Imperial College at Silwood Park
 Nobutaka Hirokawa
Univ. of Tokyo
 Tomas Hökfelt
Karolinska Institutet
 Tasuku Honjo
Kyoto Univ.
 Susan D. Iversen
Univ. of Oxford
 Eric F. Johnson
The Scripps Research Institute
 Elliott Kieff
Harvard Univ.
 Stephen M. Kosslyn
Harvard Univ.
 Michael LaBarbera
The Univ. of Chicago
 Nicole Le Douarin
Institut d'Embryologie Cellulaire et Moléculaire du CNRS
 Charles S. Levings III
North Carolina State Univ., Raleigh
 Harvey F. Lodish
Whitehead Institute for Biomedical Research

Richard Losick
Harvard Univ.
 Reinhard Lührmann
Institut für Molekularbiologie und Tumorforschung der Philipps-Universität
 Ruth Lynden-Bell
Queen's Univ., Belfast
 Seth Marder
California Institute of Technology
 Diane Mathis
Institut de Chimie Biologique, Strasbourg
 Anthony R. Means
Duke Univ. Medical Center
 Shigetada Nakanishi
Kyoto Univ.
 Kim Nasmyth
Research Institute of Molecular Pathology, Vienna
 Roger A. Nicoll
Univ. of California, San Francisco
 Staffan Normark
Swedish Institute for Infectious Disease Control
 Stuart L. Pimm
The Univ. of Tennessee, Knoxville
 Yeshayau Pocker
Univ. of Washington, Seattle
 Ralph S. Quatrano
Univ. of North Carolina, Chapel Hill
 Martin Raff
Univ. College London
 V. Ramanathan
Scripps Institute of Oceanography
 Douglas C. Rees
California Institute of Technology
 T. M. Rice
ETH-Hönggerberg, Zürich
 David C. Rubie
Universität Bayreuth
 Erkki Ruoslahti
The Burnham Institute, CA
 Gottfried Schatz
Biozentrum, Basel
 Jozsef Schell
Max-Planck-Institut für Züchtungsforschung

Ronald H. Schwartz
National Institute of Allergy and Infectious Diseases, NIH
 Terrence J. Sejnowski
Salk Institute
 Thomas A. Steitz
Yale Univ.
 Michael P. Stryker
Univ. of California, San Francisco
 Tomoyuki Takahashiz
Univ. of Tokyo
 Masatoshi Takeichi
Kyoto Univ.
 Keiji Tanaka
RIKEN Institute
 David Tilman
Univ. of Minnesota, St. Paul
 Robert T. N. Tjian
Univ. of California, Berkeley
 Yoshinori Tokura
Univ. of Tokyo
 Emil R. Unanue
Washington Univ. School of Medicine, St. Louis
 Geerat J. Vermeij
Univ. of California, Davis
 Bert Vogelstein
Johns Hopkins Oncology Center
 Arthur Weiss
Univ. of California, San Francisco
 Zena Werb
Univ. of California, San Francisco
 George M. Whitesides
Harvard Univ.
 Owen N. Witte
Univ. of California, Los Angeles
 William A. Wulf
Univ. of Virginia

Purified Recombinant Human PROTEINS

Drug Metabolizing Enzymes:

Cytochrome P450
3A4, 2E1
3A4, 2D6 (BaV Microsomes)
Oxidoreductase
Cytochrome b₅
Glutathione Transferases
A1-1, M1-1, P1-1

Signal Transduction:

PKC Isozymes α , β II, γ , ϵ , ζ
Estrogen Receptor
Vitamin D₃ Receptor
H-Ras
Rab 3A
Apolipoprotein E2, E3, E4

All of PanVera's purified, recombinant human proteins offer high physical purity and excellent biological activity. PanVera proteins are expressed either in baculovirus-infected insect cells or from recombinant *Escherichia coli*.

PanVera also offers Custom Services in large scale protein expression and purification, as well as assay development for drug screening and quality control applications.

800-791-1400

(In the USA and Canada)

PanVera Corporation

545 Science Drive • Madison, WI USA
Phone: 608-233-5050 • Fax: 608-233-3007
Email: info@panvera.com



Internet Homepage: <http://www.panvera.com/>

In Japan contact TaKaRa Shuzo Co., Ltd., Otsu, Shiga, Japan Phone: +81 775-43-7247 Fax: +81-447-43-9254
In the UK contact Cambridge Bioscience, Cambridge, UK Phone: +44 1223-316855 Fax: +44 1223-360732 E-mail: cbio@clx.compulink.co.uk

STATISTICA

and Windows 3.1
and Windows 95

STATISTICA (automatically configures itself for Windows 95 or 3.1) ■ A complete data analysis system with thousands of on-screen customizable, presentation-quality graphs fully integrated with all procedures ■ Comprehensive Windows support, OLE (client and server), DDE, customizable *Auto Task* toolbars, pop-up menus ■ Multiple data-, results-, and graph-windows with *data-graph* links ■ The largest selection of statistics and graphs in a single system; comprehensive implementations of: Exploratory techniques with advanced brushing; multi-way tables with banners (presentation-quality reports); nonparametrics; distribution fitting; multiple regression; general nonlinear estimation; stepwise logit/probit; general ANCOVA/MANCOVA; stepwise discriminant analysis; log-linear analysis; confirmatory/exploratory factor analysis; cluster analysis; multidimensional scaling; canonical correlation; item analysis/reliability; correspondence analysis; survival analysis; a large selection of time series modeling/forecasting techniques; structural equation modeling with *Monte Carlo* simulations; and much more ■ On-line *Electronic Manual* with comprehensive introductions to each procedure and examples ■ Hypertext-based *Stats Advisor* expert system ■ Workbooks with multiple *AutoOpen* documents (e.g., graphs, reports) ■ Extensive data management facilities (fast spreadsheet of unlimited capacity with long formulas, *Drag-and-Drop*, *AutoFill*, *Auto-Recalculate*, split-screen/variable-speed scrolling, advanced Clipboard support, DDE links, hot links to graphs, relational merge, data verification/cleaning) ■ Powerful *STATISTICA BASIC* language (professional development environment) with matrix operations, full graphics support, and interface to external programs (DLLs) ■ Batch command language and editable macros, flexible "turn-key" and automation options, custom-designed procedures can be added to floating *Auto Task* toolbars ■ All output displayed in *Scrollsheets*™ (dynamic, customizable, presentation-quality tables with instant 2D, 3D, and multiple graphs) or word processor-style report editor (of unlimited capacity) that combines text and graphs ■ Extremely large analysis designs (e.g., correlation matrices up to 32,000x32,000, unlimited ANOVA designs) ■ Megabyte Manager with up to 32,000 variables (8 Mb) per record ■ Unlimited size of files; extended ("quadruple") precision; unmatched speed ■ Exchanges data and graphs with other applications via DDE, OLE, or an extensive selection of file import/export facilities (incl. ODBC access to virtually all data bases and mainframe files) ■ Hundreds of types of graphs, incl. categorized multiple 2D and 3D graphs, ternary 2D/3D graphs, matrix plots, icons, and unique multivariate (e.g., 4D) graphs ■ Facilities to custom-design new graph types and add them permanently to menus or toolbars ■ On-screen graph customization with advanced drawing tools (e.g., scrolling and editing of complex objects in 32x real zoom mode), compound (nested) OLE documents, *Multiple-Graph AutoLayout Wizard*, templates, special effects, icons, page layout control for slides and printouts; unmatched speed of graph redraw ■ Interactive rotation, perspective and cross-sections of 3D displays ■ Large selection of tools for graphical exploration of data: extensive brushing tools with animation, fitting, smoothing, overlaying, spectral planes, projections, layered compressions, marked subsets ■ Price \$995.

Quick STATISTICA (for Windows) ■ A subset of *STATISTICA*; comprehensive selection of basic statistics and the full analytic and presentation-quality graphics capabilities of *STATISTICA* ■ Price \$495.

STATISTICA/QC - Industrial statistics add-on package (requires *STATISTICA* or Quick *STATISTICA* for Windows) ■ The largest selection of industrial statistics in a single package; quality control charts (compatible with real-time data acquisition systems), process capability analysis, R&R, sampling plans, and an extremely comprehensive selection of experimental design (DOE) methods ■ Flexible tools to customize and automate all analyses and reports (incl. "turn-key" system options, and tools to add custom procedures) ■ Price \$495.

STATISTICA/Mac (for Macintosh) ■ Price \$695 (Quick - \$395).

Domestic sh/h \$12 per product; 30-day money back guarantee.

STATISTICA has received the highest rating in EVERY comparative review of statistics software in which it was featured, since its first release.

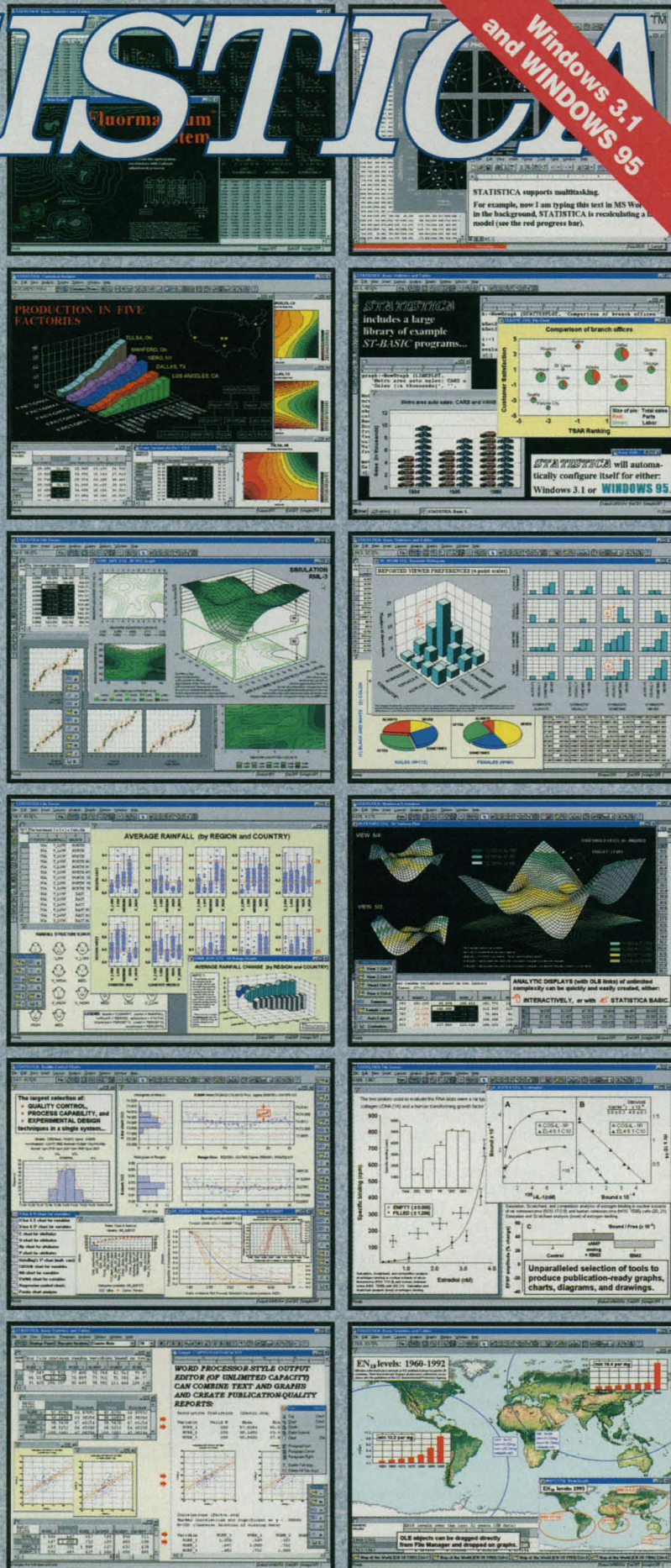


StatSoft®

2300 E. 14th St. • Tulsa, OK 74104 • (918) 749-1119
Fax: (918) 749-2217 • WEB: <http://www.statsoftinc.com>
e-mail: info@statsoftinc.com

Circle No. 11 on Readers' Service Card

Overseas Offices: StatSoft of Europe (Hamburg, FRG), ph: 040/ 4200347, fax: 040/4911310; StatSoft UK (London), ph: 01462/482822, fax: 01462/482855; StatSoft France, ph: (1) 34 52 39 22, fax: (1) 34 52 28 48; StatSoft Polska, ph: 12-391120, fax: 12-391121; StatSoft Italia, ph: 49-893-3227, fax: 49-893-2897; Available from other Authorized Representatives worldwide: Australia: Hearne, ph: (03) 9602 5088, fax: (03) 9602 5050; Sweden: AkademiData Scientific, ph: 018-210035, fax: 018-210039; Finland: Statsoft Oy, ph: 24-7334678, fax: 24-7333867; Belgium: Texma NewTech, ph: 010 616 628, fax 010 616 957; South Africa: Osiris, ph: 12-660-2884, fax 12-660-2886; Japan (Macintosh): Three's Company, Inc., ph: 03-3770-7600, fax 03-3770-7784; Japan (Windows): StatSoft Design Technologies, Inc., ph: 03-3667-1110, fax: 03-3668-3110; Taiwan: Intelligent Integration Corp., ph: 2-698-2060, fax: 2-698-2061; The Netherlands: Exstat, ph: (0) 50.5267310, fax: (0) 50.5277665; Russia: SoftLine Corp., ph: (095) 126-9065, fax: (095) 232-0023; Hungary: CheMicro, ph: 1 131-3847, fax: 1 132-9330. StatSoft, the StatSoft logo, STATISTICA, and Scrollsheet are trademarks of StatSoft, Inc.



Filtration Problems?



The Solution Is Clear — Millipore® Filters From Techware



When it comes to filtration problems, there's no clearer solution than Millipore® Filtration Products from Sigma-Aldrich Techware.

One phone call is all it takes to gain immediate access to Millipore's comprehensive family of ready-to-use, disposable filter devices...as well as over 10,000 other brand-name laboratory equipment and supply products.

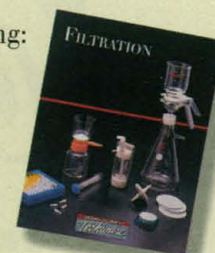
In addition to this wide selection of top quality products, Sigma-Aldrich Techware backs each purchase with

unequaled service and support, including:

- Same day shipping
- Comprehensive technical support
- Competitive pricing

So for solutions that are perfectly clear, rely on Millipore filtration products from Sigma-Aldrich Techware — your single, most convenient source for brand name laboratory supplies and equipment.

Circle the number below for your free Filtration Product Guide.



SIGMA-ALDRICH
Techware
FROM BENCHTOP TO BOOKSHELF

SIGMA® 
Call collect: 314-771-5750, 800-325-3010,
or contact your local Sigma office.

AUSTRALIA AUSTRIA BELGIUM BRAZIL CZECH REPUBLIC FRANCE GERMANY HUNGARY INDIA ITALY JAPAN
KOREA MEXICO NETHERLANDS POLAND SPAIN SWEDEN SWITZERLAND UNITED KINGDOM UNITED STATES

Millipore is a registered trademark of Millipore Corporation.

A Sigma-Aldrich Company

Circle No. 3 on Readers' Service Card



AAAS with Pride!

In 1998 AAAS will celebrate its 150th anniversary. Get an early start by ordering your AAAS products now! Each attractive, high-quality item features the new AAAS logo. What's more, a portion of each sale goes to support 150th anniversary activities.



AMERICAN ASSOCIATION FOR THE
ADVANCEMENT OF SCIENCE

Buy 2 or
more of the
same item =
10%
Discount

Qty	Size		Non-Mem.	Member	Discount	Total
		Natural T* (M, L, XL)	\$13.50 \$10.00	\$10.00 \$8.00		
		Navy T* w/color (M, L, XL)	\$17.00 \$12.00	\$12.00 \$9.60		
		Science Cards (12)	\$13.50 \$10.00	\$10.00 \$8.00		
		Blue and White Mug†	\$12.50 \$10.00	\$10.00 \$8.00		
		Navy & Natural Cap	\$19.50 \$10.50	\$10.50 \$8.40		
		Gold-toned Lapel pin	\$4.75 \$3.00	\$3.80 \$2.40		
Subtotal						
Shipping and handling			\$4.00			
DC and California add applicable sales tax						
For shipments to Canada, add 7% GST tax						
For foreign air mail, add 25% of subtotal						
						(1) Total

(1) All payments must be in U.S. dollars.
* all tees are 100% cotton
† Laser-etched porcelain

Name and Address (please print)

Name _____

Address _____

City, State, Zip Code _____

Province, Country, Postal Code _____

Payment information ☐ Check/Money Order enclosed ☐ MC/Visa

Credit card number _____ Exp. date _____

Signature _____

Mail To: AAAS Distribution Center, P.O. Box 521, Annapolis Junction, MD 20701 or
FAX (301) 206-9789, **Credit Card orders** by Phone 1-800-222-7809



EurekaAlert!

The world's first
centralized on-line service
for research news.

Check it out on the World Wide Web at
<http://www.eurekaalert.org>

For more information, call the AAAS News &
Information Office at 202-326-6440. Or send a
message to webmaster@eurekaalert.org.



AMERICAN ASSOCIATION FOR THE
ADVANCEMENT OF SCIENCE



Get Clones Quick

With Genome Systems

Library Screening Services

Get an 85-100kb, 120+kb, or 1,000kb Genomic Clone In a Matter of Days

Our services include; P1 (85kb) genomic library screening service (human, ES mouse for knockouts, rat and drosophila).

- New!** Human PAC/BAC™ (120kb+ insert) genomic library screening service.
- New!** Human PAC/BAC™ high density filters.
- New!** Human PAC/BAC™ "Down to the Well"™ PCR*able DNA pools.
- New!** Fluorescent in-situ hybridization (FISH).
- New!** YAC library screening service (human, mouse).
- New!** Go Germlinesm ES and MEF cells for making mouse knockouts.
- New!** Custom robotic colony picking and spotting services.

Other P1 or PAC/BAC™ services include:

- DNA Preparation
- DNA Insert End Sequencing
- DNA Insert Orientation
- DNA Subcloning

GenomeSystemsInc™

8620 Pennell Drive
St. Louis, Missouri 63114, USA

(800) 430-0030 or, (314) 692-0033
Facsimile: (314) 692-0044

France: Appel gratuit, 0590-2104

Germany: Rufen sie uns an zum ortstarif, 0130-81-9081

UK: Call us free on, 0800-89-3733

email address: Genome@MO.net

World Wide Web: <http://www.genomesystems.com>

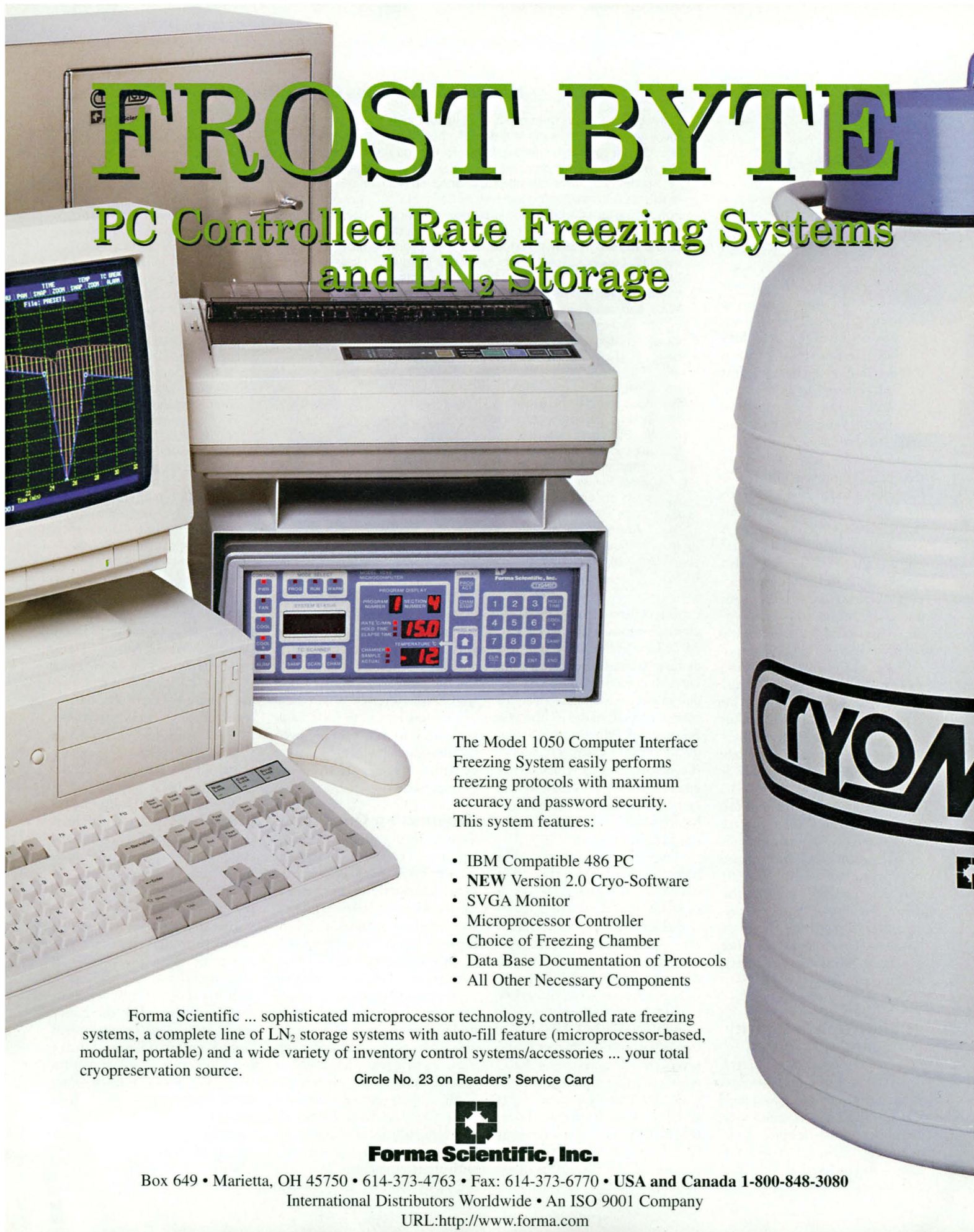
Circle No. 13 on Readers' Service Card

*The PCR process is covered by patents owned by Hoffman-LaRoche



FROST BYTE

PC Controlled Rate Freezing Systems and LN₂ Storage



The Model 1050 Computer Interface Freezing System easily performs freezing protocols with maximum accuracy and password security. This system features:

- IBM Compatible 486 PC
- **NEW** Version 2.0 Cryo-Software
- SVGA Monitor
- Microprocessor Controller
- Choice of Freezing Chamber
- Data Base Documentation of Protocols
- All Other Necessary Components

Forma Scientific ... sophisticated microprocessor technology, controlled rate freezing systems, a complete line of LN₂ storage systems with auto-fill feature (microprocessor-based, modular, portable) and a wide variety of inventory control systems/accessories ... your total cryopreservation source.

Circle No. 23 on Readers' Service Card



Forma Scientific, Inc.

Box 649 • Marietta, OH 45750 • 614-373-4763 • Fax: 614-373-6770 • **USA and Canada 1-800-848-3080**

International Distributors Worldwide • An ISO 9001 Company

URL: <http://www.forma.com>