22 October 1999

Science

Vol. 286 No. 5440
Pages 633–860 $8

Olfaction

American Association for the Advancement of Science

10,000 Scientists.

One Discovery.

InforMax Leads The Industry In Bioinformatics.

A pattern is emerging from the chaos: InforMax is standardizing bioinformatics. Our products are driving research at 60 pharmaceuticals, 250 biotechs and 500 universities worldwide. Securely integrating private research with global databases. Running complex customized search algorithms. Processing DNA and protein sequence analyses at once-impossible speeds. As of now, more than 10,000 researchers rely on our software's exclusive ResearchLogic™ system to accelerate inquiries into the mysteries of genetics... and run the race for rapid drug discovery.

Whether you choose Vector NTI™ Suite for desktop sequence analysis or Software Solution for BioMedicine™ for enterprise bioinformatics, you'll be assured of superior research tools.

Discover us today. Your competition won't be far behind.

Circle No. 56 on Readers' Service Card

InforMax®

Insight Through Bioinformatics

InforMax, Inc.
6010 Executive Blvd., 10th floor
North Bethesda, MD 20852

Phone: 301.984.2206
800.357.3114
Fax: 301.216.0087
Web Site: www.informaxinc.com

InforMax and the InforMax logo are registered trademarks, and ResearchLogic, Software Solution for BioMedicine and Vector NTI are trademarks of InforMax, Inc.

Molecular Biology Reagents

from R&D Systems

Accessory Reagents Also Available

New Expression Arrays

mRNA Expression Profiling

Cytokine Expression Array

R&D Systems' Expression Arrays allow simultaneous monitoring of multiple gene-specific mRNAs on a semi-quantitative basis. Our cytokine array consists of 375 different cloned cDNAs, printed as PCR products onto a charged nylon membrane.

Features

- Includes cytokines, chemokines, interleukins, other immuno-regulatory factors and receptors
- Semiquantitative analysis of mRNAs using one of nine different housekeeping control cDNAs
- All cloned cDNAs are sequenced containing no repetitive elements
- Identify differentially expressed mRNAs by comparing expression profiles from different samples

Expression Arrays are produced in collaboration with Sigma-Genosys

Portion of a Cytokine Expression Array showing analysis of cytokine RNAs expressed in stimulated (1 pg/mL PMA and 10 µg/mL LPS for 4 hours) THP-1 cells. Radiolabeled cDNA was made using poly $(A)^+$ RNA, ^{33}P labeled nucleotide, and oligo $(dT)_{25}$ primer.

Quantikine® mRNA

mRNA Quantitation Kits

Quantikine mRNA is a colorimetric assay that quantitates multiple mRNA targets on the same microplate.

Ask about our RNA Isolation Kit

Kits Available

Human:

- IL-1β
- IL-6
- GAPDH
- IL-2
- IL-10
- IFN-γ

Coming Soon

Human:

- TNF-α
- VEGF

Mouse:

- IFN-γ
- IL-1β
- IL-2
- TNF-α

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 529449
Fax: +44 (0)1235 533420
info@rndsystems.co.uk

Germany
R&D Systems GmbH
Borsigstrasse 7
65205 Wiesbaden, Germany
Tel: +49 (0)6122 90980
Fax: +49 (0)6122 909819
infogmbh@rndsystems.co.uk

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

R&D SYSTEMS

1-800-343-7475

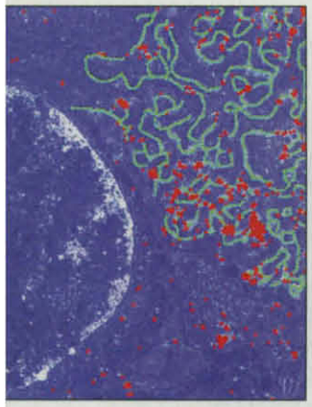
Circle No. 77 on Readers' Service Card

VOLUME 286 22 OCTOBER 1999 NUMBER 5440

Science

www.sciencemag.org

COVER The olfactory bulb of a mouse (image width, 0.5 mm). Axons of olfactory sensory neurons terminate in globose structures, glomeruli, of which there are 1800 per bulb. The vomeronasal nerve carrying pheromone information terminates separately in a diffuse structure, the accessory olfactory bulb (top). Olfactory neurons can be stained blue in this strain of genetically manipulated mice. For recent advances in olfaction, see the special section beginning on p. 703. [Photo: P. Mombaerts]



660
Probing prions

NEWS

NEWS OF THE WEEK

NEWS FOCUS

RESEARCH

RESEARCH ARTICLES

OLFACTION

NEWS

REVIEWS

763
New clues to dinosaur origins

REPORTS

DEPARTMENTS

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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 © 1999 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): $110 ($62 allocated to subscription). Domestic institutional subscription (51 issues): $325; 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. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

SCIENCE'S COMPASS

693 Gamma-ray bursts from supernovae

692
Maps of Earth's mantle

SCIENCE ONLINE
www.scienceonline.org

SCIENCE
THE JOURNAL
www.sciencemag.org

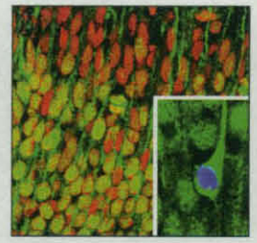
SCIENCENOW
DAILY NEWS SERVICE
www.sciencenow.org

NEXT WAVE
WEEKLY CAREER UPDATES
www.nextwave.org

GRANTSNET
RESEARCH FUNDING DATABASE
www.grantsnet.org

NEUROAIDS
EXPERIMENTAL WEB SITE
www.sciencemag.org/NAIDS

▼NEW
SCIENCE'S STKE
SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT
www.stke.org



741
Notch signaling and neurite growth

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:** $8.00 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.

MMC 10.99

They just out-stripped everybody

Proteomics is upon us in a big way. And when it comes to finding more proteins of interest faster, nothing outstrips the new narrow pH range Immobiline™ DryStrip for 2-D electrophoresis.

Faster target identification with new Immobiline DryStrip

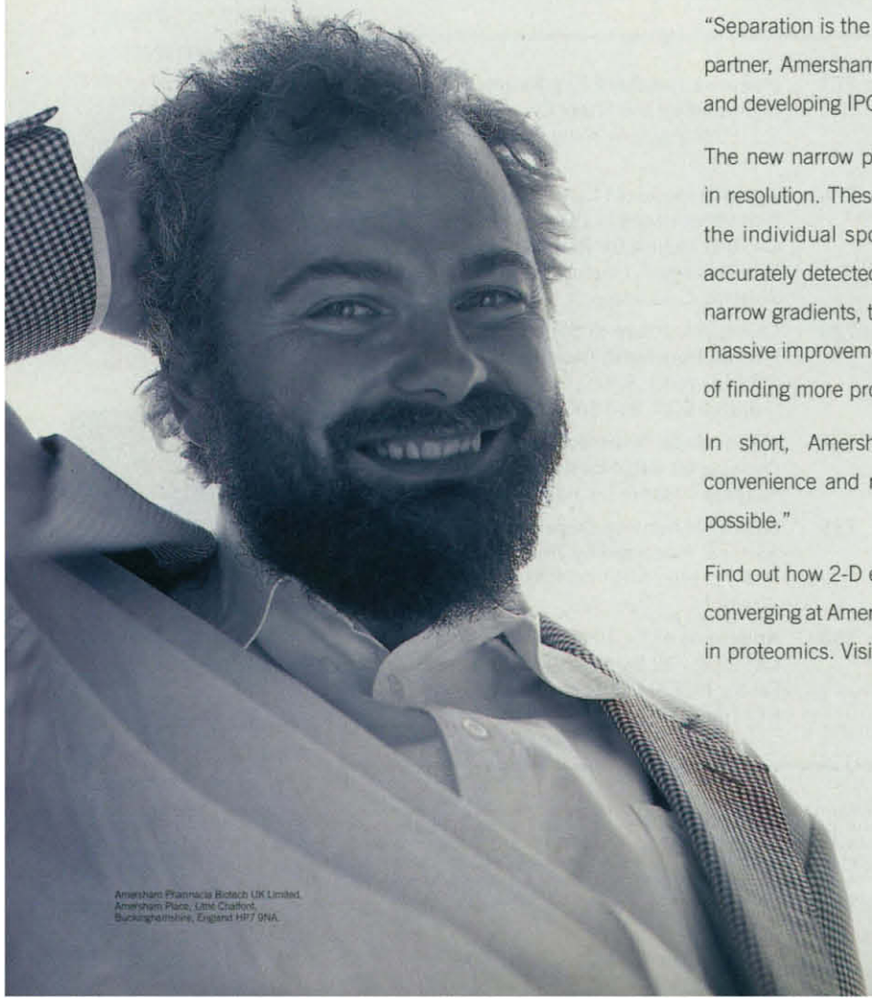
That's the view of Dr. Hanno Langen, head of the proteomics group at Hoffmann-LaRoche genetics department.

"Separation is the key to protein identification. As a serious and innovative partner, Amersham Pharmacia Biotech has been instrumental in pioneering and developing IPG technology.

The new narrow pH range Immobiline DryStrips provide a big step forward in resolution. These one-pH unit gradients greatly improve resolution so that the individual spots are clearly separated from each other and can be accurately detected and quantified by the ImageMaster™ software. With such narrow gradients, the software recognises up to 6000 spots in one sample, a massive improvement over past methods which greatly increases my chances of finding more proteins of interest.

In short, Amersham Pharmacia Biotech's IPG technology offers the convenience and reproducibility that makes serious research in proteomics possible."

Find out how 2-D electrophoresis, mass spectrometry and bioinformatics are converging at Amersham Pharmacia Biotech to provide you with a total solution in proteomics. Visit us at **http://proteomics.apbiotech.com**

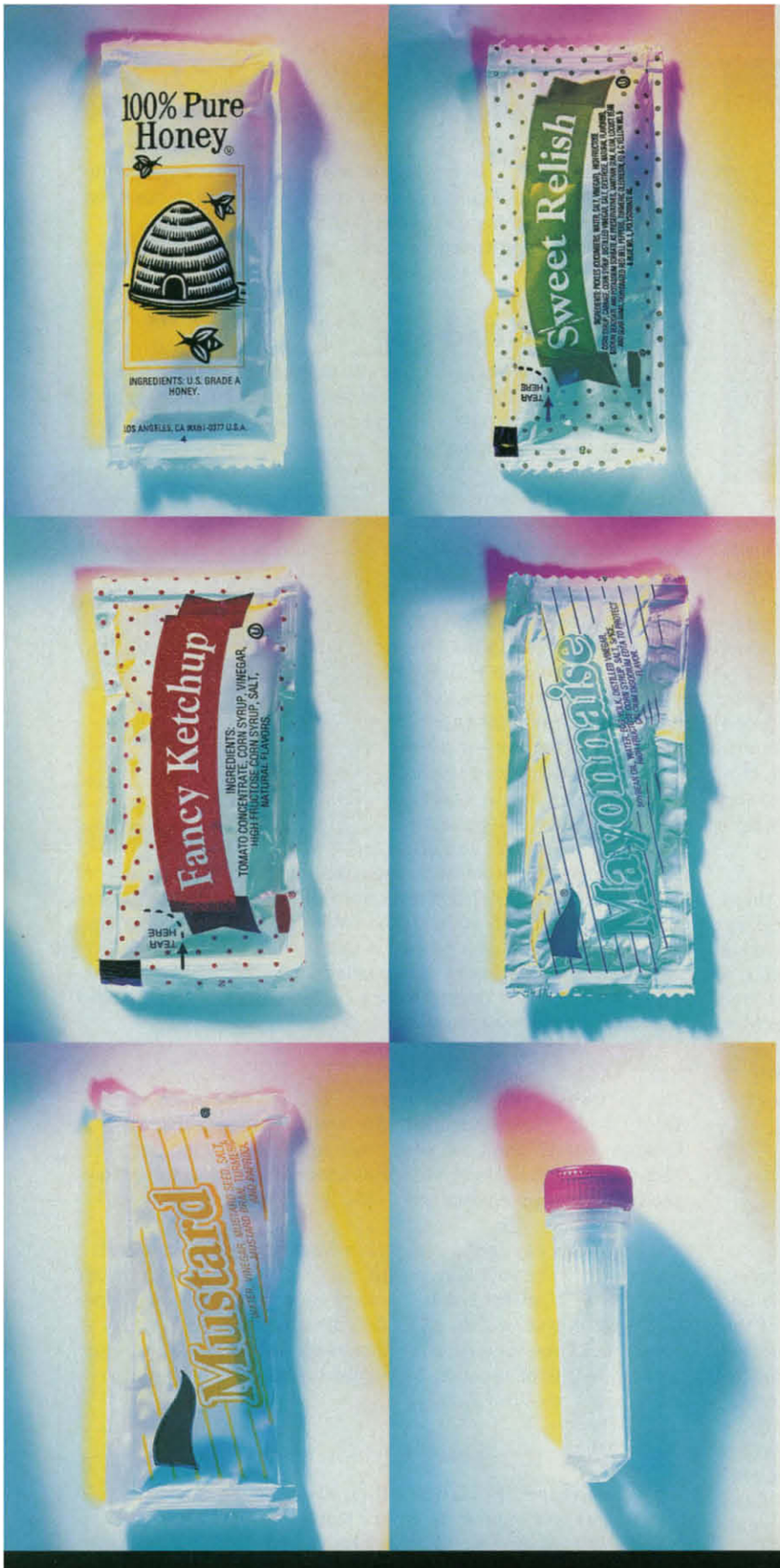


Dr. Hanno Langen, head of the proteomics group at Hoffmann-LaRoche genetics department.

Amersham Pharmacia Biotech UK Limited
Amersham Place, Little Chalfont
Buckinghamshire, England HP7 9NA

amersham pharmacia biotech

Circle No. 81 on Readers' Service Card



Would you put ketchup in your tea?

Different applications call for different *E. coli* strains. Choose the right one and improve your results.

Invitrogen offers seven different *E. coli* strains in the One Shot™ format so you can choose the strain that best fits your transformation needs. In addition to a great selection of strains, One Shot™ Chemically Competent Cells are provided in single-use aliquots for unmatched convenience and efficiency.

Easy-to-Use. One Shot™ Cells are provided in easy-to-use 50 µl aliquots. You can do your transformation right in the tube the cells are provided in. You'll save time because there is no need to thaw and refreeze bulky 200 µl aliquots or transfer cells to a new tube. You'll also save money because you'll never throw away unused cells again.

High-Efficiency. One Shot™ transformation efficiencies are as high as 1 x 10^9 cfu/µg of supercoiled DNA. Plus with single-use aliquots, there's no efficiency-zapping freeze-thaw cycles so you'll always get great results.

	STRAIN	EFFICIENCY	CAT. NO.
	TOP10	1 x 10^9	C4040-03
	TOP10F´	1 x 10^8	C3030-03
	TOP10/P3	1 x 10^8	C5050-03
	INVαF´	1 x 10^8	C2020-03
NEW!	INV110	1 x 10^6	C7171-03
	BL21(DE3)pLysS	1 x 10^8	C6060-03
NEW!	BL21(DE3)pLysE	1 x 10^7	C6565-03

Each One Shot™ Kit includes 20 x 50 µl aliquots of competent cells, βME, SOC medium, and a control plasmid.

Choose the Right Strain. One Shot™ Chemically Competent Cells are the most convenient, efficient way to transform. And with seven strains to choose from, there's sure to be one that's right for your needs. To find out more about One Shot™ Cells, give Invitrogen a call today. Unless, of course, you like honey on your french fries...

Circle No. 53 on Readers' Service Card

European Headquarters:
Invitrogen BV
P.O. Box 2312
9704 CH Groningen
The Netherlands
Tel: +31 (0) 50 5299 299
Fax: +31 (0) 50 5299 281
Email: tech_service@invitrogen.nl
www.invitrogen.com

See us in booth #1232 at AACR

International Toll Free Numbers:
Tel: 00800 5345 5345*
Fax: 00800 7890 7890*
*This number operates in all European countries excluding Finland and Sweden
Finland:
Tel: 990800 5345 5345
Fax: 990800 7890 7890
Sweden:
Tel: 009800 5345 5345
Fax: 009800 7890 7890

Distributors:
Austria 0222 889 18 19
Australia 1 800 882 555
China 010 6255 3477
Hungary 01 280 3728
India 91 80 8391453
Israel 02 584 1111
Italy 02 38 19 51
Japan 03 5684 1622
Malaysia 03 432 1357
Poland 058 341 47 26
Portugal 01 453 7085
Singapore 65 2922130
South Korea 02 569 6902
Spain 03 450 2601
Taiwan 886 2 238 10844
Thailand 246 7243

From all other countries, call our European headquarters at +31 (0) 50 5299 299.

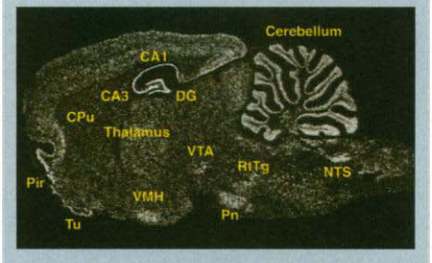
United States Headquarters:
Invitrogen
1600 Faraday Avenue
Carlsbad, California 92008
Tel: 1-800-955-6288
Fax: 760-603-7201
Email: tech_service@invitrogen.com
http://www.invitrogen.com

SEMICONDUCTOR LASERS: TWO IN ONE

Unipolar devices have an advantage over bipolar ones in that they can be operated independent of the polarity of the applied voltage—they are bidirectional. Gmachl *et al.* (p. 749) have now designed quantum cascade lasers that can be operated bidirectionally. Moreover, through careful design of the series of quantum wells that make up the injection region of the laser, they show that a tailored asymmetry can produce lasing at two different wavelengths, depending on the polarity.

AMYLOID SECRET(ASE) REVEALED

Alzheimer's disease is characterized by the progressive formation in the brain of insoluble deposits containing the amyloid β peptide (Aβ). This peptide is generated when the amyloid



precursor protein (APP) is cleaved by two distinct and long-sought proteases, the β- and γ-secretases. Vassar *et al.* (p. 735; see the news story by Pennisi) have identified a transmembrane aspartic protease, beta-site APP cleaving enzyme, or BACE, that has all of the known characteristics of the β-secretase. Future development of BACE-specific inhibitors will allow testing in animal models of Aβ's role in Alzheimer's disease and may lead to new treatments for the disease.

INORGANIC ELECTRONICS FROM SOLUTION

The majority of inorganic electronic devices used today are fabricated in a series of steps that require deposition of inorganic species from the gas phase. These processes are performed at relatively high temperatures and are often rather expensive. Ridley *et al.* (p. 746) introduce an alternative, and potentially cheaper, all-solution route that takes advantage of the reduced melting point of nanocrystals. Cadmium selenide (CdSe) nanoparticles, formed by mixing cadmium iodide and sodium selinide, were suspended in pyridine. The resulting solution was then printed onto a substrate, and a subsequent low-temperature annealing process drives off the pyridine to leave behind a thin film of CdSe. The authors demonstrate the potential of such a process by fabricating thin film transistors with good electrical characteristics.

ICED SEAS

Repeated abrupt climate changes occurred during the long buildup of ice sheets toward the Last Glacial Maximum (LGM). Detailed oceanic records of these events and their effects on sea surface temperatures (SSTs) are scarce, yet important for understanding the mechanisms and extent of abrupt climate change. Sachs and Lehman (p. 756) now provide a high-resolution marine record from the Bermuda Rise of SSTs spanning the period from 30,000 to 60,000 years ago. The record shows several cases where SSTs increased abruptly by 2° to 5°C, which is comparable to the change observed from the LGM to the Holocene. These events parallel those seen in Greenland records. The periods of warming appeared to have been unstable and were followed by either abrupt or continued gradual cooling. Thus, the abrupt climate changes seen in the ice core records affected tropical oceans.

SLOWING GETTING MORE COMPLEX

The issue of complexity in evolution has generated interest in biology, but it has been notoriously difficult to measure the dynamics of complexity in the fossil record. Saunders *et al.* (p. 760) describe the evolution of complexity in the septal sutures of an extinct group of mollusks—ammonoids—in more than 500 genera during the 140 million years from the Devonian to the Triassic, a period that includes three mass extinctions. Although mass extinctions tended to eliminate more complex structures, the large-scale evolutionary trend was toward increased complexity. Thus, they show that two non-random evolutionary trends acted in opposition—a within-lineage–driven bias for increased suture complexity and an among-lineage differential extinction of more complex forms during times of biotic crisis.

OLDEST DINOSAURS?

The Middle to Late Triassic (about 225 to 230 million years ago) was a crucial period in the early evolution of dinosaurs, yet little has been known about the faunal composition at that time. Flynn *et al.* (p. 763) now report the discovery of a fossil fauna in Madagascar that contains newly identified dinosaur and eucynodont (mammal-like reptiles) taxa. Their discovery represents a major new source of terrestrial vertebrate fossils for a time period that is sampled poorly elsewhere in the world; the dinosaurs may be more ancient than any others worldwide; and the recovery of the eucynodont fills in a 170-million-year gap in the fossil record of the region.

STABILITY WITH MATURITY

Signaling through the transmembrane protein Notch occurs in a variety of tissues in order to determine cell fates during development. Šestan *et al.* (p. 741; see the Perspective by Chenn and Walsh) show that Notch signaling is also important in the already differentiated neurons of the mature cerebral cortex. The various protein components of the signaling pathway are found in dendrites and control dendrite extension.

PROVIDING FEEDBACK

Further clues into the regulation of circadian clocks are the subject of two reports. In plants and insects, cryptochromes (CRYs) are activated by light, and in the fruit fly *Drosophila*, CRY blocks the negative feedback action of the PER-TIM complex. Griffin *et al.* (p. 768) show that CRY1 and CRY2 play a central role in the mammal clock, but in a light-independent fashion—they appear to regulate transcriptional cycling of *Per1* by contacting both the activator and its feedback inhibitors. In *Drosophila*, three of the critical clock genes, *period* (*per*), *timeless* (*tim*), and *Drosophila Clock* (*dClk*), are expressed rhythmically. In their study of the cycling of *dClk*, Glossop *et al.* (p. 766) have found that the molecular clock in *Drosophila* is composed of two interlocked negative feedback loops—the *per-tim* loop, which is activated by the dCLK and CYCLE proteins and repressed by PER-TIM, and the *dClk* loop, in which these proteins exert the opposite effect.

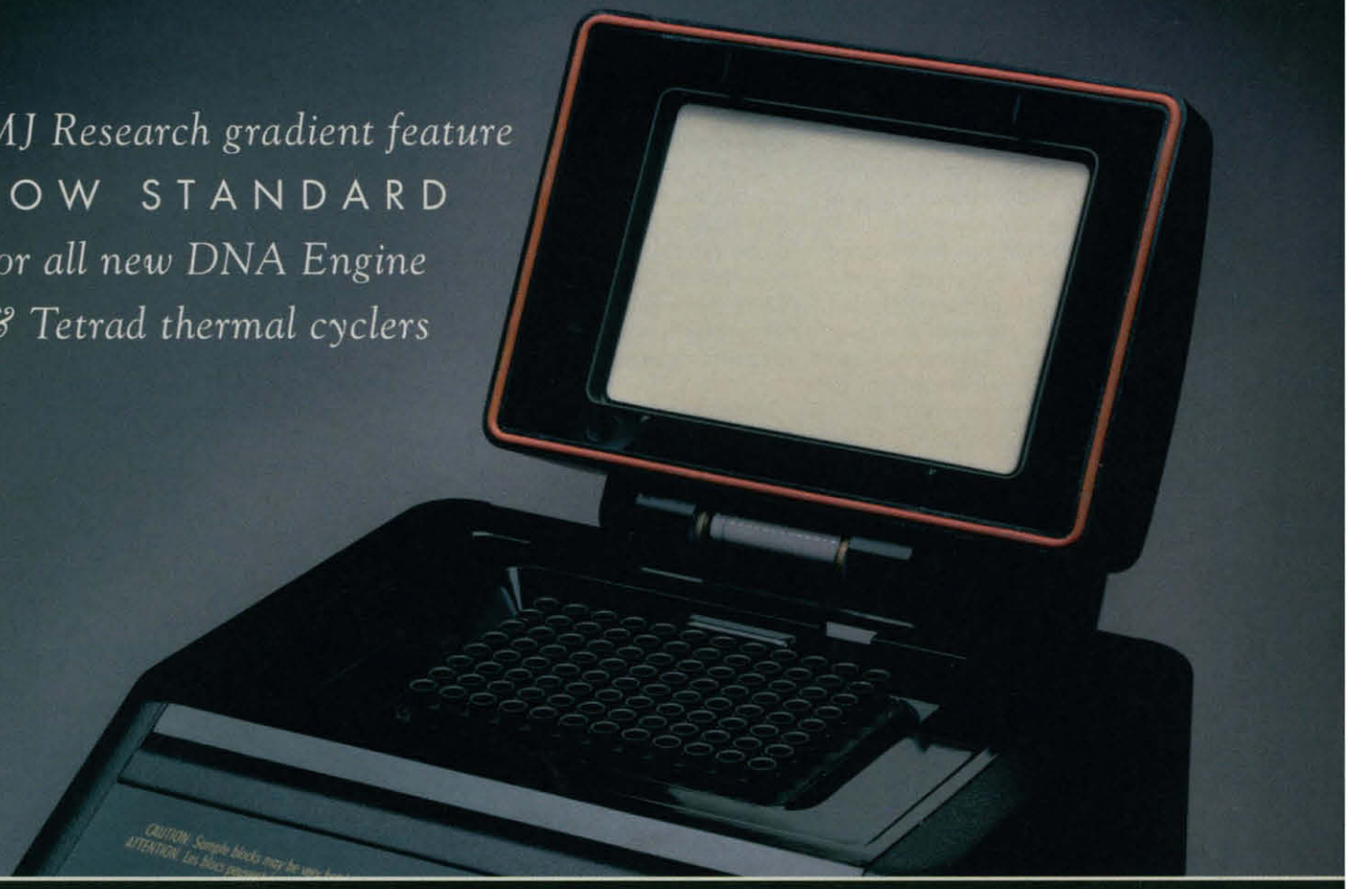
INTERFERING WITH TGF-β

Unregulated cell growth results in tumor production; therefore, it is important to identify developmental factors that regulate cell growth. Transforming growth fac-

CONTINUED ON PAGE 643

THE SMARTEST GRADIENT ON THE BLOCK

The MJ Research gradient feature
NOW STANDARD
for all new DNA Engine
& Tetrad thermal cyclers



The *new MJ Research temperature gradient feature* boasts the capabilities that are crucial for one-step reaction optimization. *Dynamic ramping* brings all wells to the programmed temperature at the same time, allowing uniform incubation times. *Consistent temperature increments* across the block generate the most information per reaction of any Peltier gradient cycler. The *highly accurate gradient calculator* pinpoints the ideal temperature for your thermal cycling reaction in one step. The result is *the highest performing gradient cycler available.*

A natural extension of our *advanced multi-sensor technology*, the gradient software feature is *now standard* on new DNA Engines and Tetrads and a *simple, low-cost upgrade* to older ones.

The MJ Research gradient: *smart design, superior results.*

MJ Research, Inc.

(888) 729-2164 • Fax (617) 923-8080 • Waltham, MA with Distributors Worldwide • info@mjr.com

Call or visit our website at www.mjr.com for more information

NOW SERVICING AND SELLING DIRECT IN CANADA

Circle No. 15 on Readers' Service Card

tor–β (TGF-β) regulates cell growth and differentiation through receptor-mediated phosphorylation of Smad proteins. These Smad proteins in turn form protein complexes and enter the cell's nucleus to activate the transcription of target genes. Stroschein *et al.* (p. 771; see the news story by Vogel) have identified a new player, SnoN, in TGF-β signaling. In the absence of TGF-β, the SnoN oncoprotein binds to a Smad2/Smad4 complex and recruits a transcription co-repressor, thus inhibiting transcription activation. When TGF-β is present, Smad3 triggers the degradation of SnoN and transcription activation resumes. Finally, a negative-feedback mechanism is present in which TGF-β stimulates SnoN production, which then represses the transcription activation function of the Smad complex once again. SnoN is found in various carcinomas. Hence, the transforming activity of SnoN may be explained by its interference with the role of TGF-β in inhibiting cell growth.

TO LIVE OR LET DIE

The release of intracellular calcium (Ca^{2+}) can trigger signals that lead to cell survival or to cell death; two reports illustrate how the same transcription factor, MEF2, which functions in the differentiation of skeletal muscle, can play different roles in the survival of neurons and T cells. During development of the mammalian brain, neurons that make proper synaptic connections and receive signals from other cells experience an increase in the intracellular Ca^{2+}. This Ca^{2+} influx promotes cell survival or resistance to cell death. Mao *et al.* (p. 785) present evidence that MEF2 mediates the pro-survival effects of Ca^{2+} in cultured neuronal cells from the rat cerebral cortex. The increase in Ca^{2+} apparently causes activation of the p38 mitogen-activated protein kinase, which may directly phosphorylate and activate MEF2. Neuronal survival thus appears to be modulated through transcriptional regulation by MEF2, as well as through posttranslational changes in components of the cell death machinery. Activation of mature T cells eventually leads to their demise. It is thought that expression of the Nur77 orphan steroid receptor, whose transcription is dependent on Ca^{2+}, the phosphatase calcineurin, and the transcription factor MEF2, mediates this apoptosis. Youn *et al.* (p. 790) have begun to elucidate the regulation of Nur77 expression and T cell apoptosis. Endogenous MEF2 is bound by Cabin 1, an inhibitor of calcineurin. When intracellular Ca^{2+} increases, calmodulin competes for binding to Cabin 1 at the same site as MEF2 and forces the release of MEF2, which makes it available for assembly into the transcriptional complex.

SOME DISASSEMBLY REQUIRED

The dynamics of the mitotic spindle is regulated in part by katanin, an enzyme that localizes to centrosomes. However, just how this AAA-type adenosine triphosphatase severs microtubules of the spindle has been unclear. Hartman and Vale (p. 782) now reveal the mechanism by which katanin forms a stable multimeric ring. Katanin oligomerization is driven by binding to its substrate, microtubules, and by binding to the nucleotide ATP. Hence, microtubules that comprise the mitotic spindle may assist their own disassembly by serving as a scaffold onto which katanin assembles.

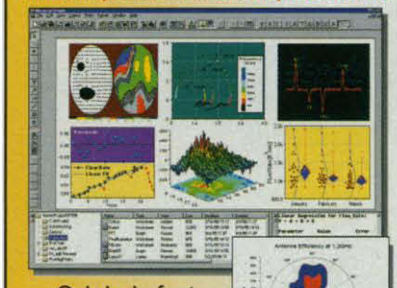
ACCUMULATING DAMAGE WITH AGE

One hypothesis for the cause of aging is that mutations accumulate in mitochondrial DNA (mtDNA). However, previous searches, which have generally studied protein- or RNA-coding regions of mtDNA, have yielded numerous types of age-related mutations, but these occur only at low frequencies (a few percent). Michikawa *et al.* (p. 774; see the news story by Pennisi) have studied the main control region for replication of mtDNA and found frequent point mutations in normal older subjects that were not found in normal young subjects. In particular, a TG transversion was found in up to 50% of the mtDNA molecules from 8 of 14 older subjects that did not appear in mtDNA of 13 younger subjects. Longitudinal studies of three individuals help show that these mutations are not inherited.

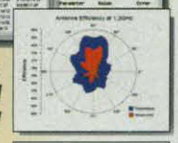
STRUCTURAL PROBE INTO IRON METABOLISM

The transferrin receptor (TfR) delivers transferrin-associated iron into cells for use in a variety of physiological processes, including cell growth. The receptor also binds HFE, the protein that is defective in human hereditary hemochromatosis, an iron storage disease that affects 1 in 300 individuals of northern European origin. Lawrence *et al.* (p. 779) determined the three-dimensional crystal structure of the extracellular domain of TfR. The structure revealed a monomer of three domains, one of which resembles carboxy- and aminopeptidases. This work provides a structural foundation for future studies of how iron uptake and release are controlled in the cell.

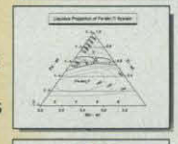
NEW VERSION! 6.0
ORIGIN®
for Windows®
Data Analysis and Technical Graphics Software



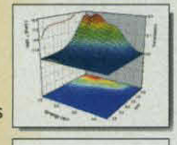
Origin is faster, more flexible, and easier-to-use!



- **New Project Explorer:** a tool that helps navigate through the hundreds of graphs and worksheets in a project file



- **New Data Masking tool:** point and click to exclude data points from curve fitting



- **OLE2 Server,** export graphs in EPS, CGM, JPEG, TIFF, PDF, DXF, and more!
- **Open and run Excel,** drag and drop to create Origin graphs from Excel workbooks and Origin worksheets
- **Toolbar customization:** add your own toolbar buttons that run your own scripts or DLL
- **Faster redraw:** a graphics caching scheme makes it easy to manipulate complex 3D graphs

Visit us at the Society for Neuroscience Show - Booth #254

Download a FREE DEMO at www.origin6.com or call 1-800-969-7720

"Microcal's Origin 6.0 has the most comprehensive graphing engine of this collection; it supports the most graph types, the most data types, and the most customizations."

— Dr. Barry Simon, Ph. D., Desktop Engineering Magazine, April, 1999

Microcal™
Microcal Software, Inc.
One Roundhouse Plaza
Northampton, MA 01060 USA
Tel. US & Canada: 1-800-969-7720 Int'l: 1-413-586-2013
Fax: 1-413-585-0126 Email: info@microcal.com

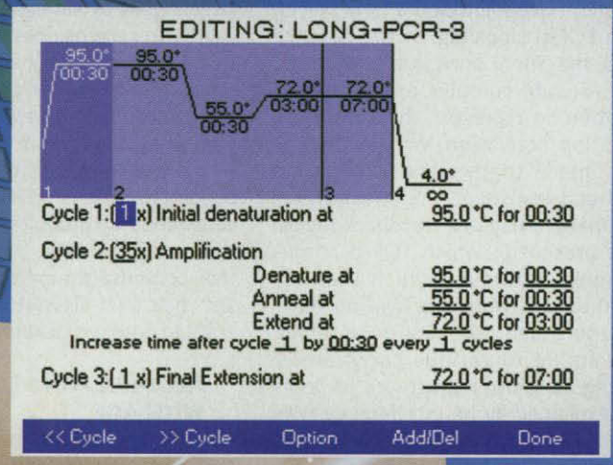
©1999. Origin and LabTalk are trademarks of Microcal Software, Inc. All other brand and product names are trademarks of their respective owners.

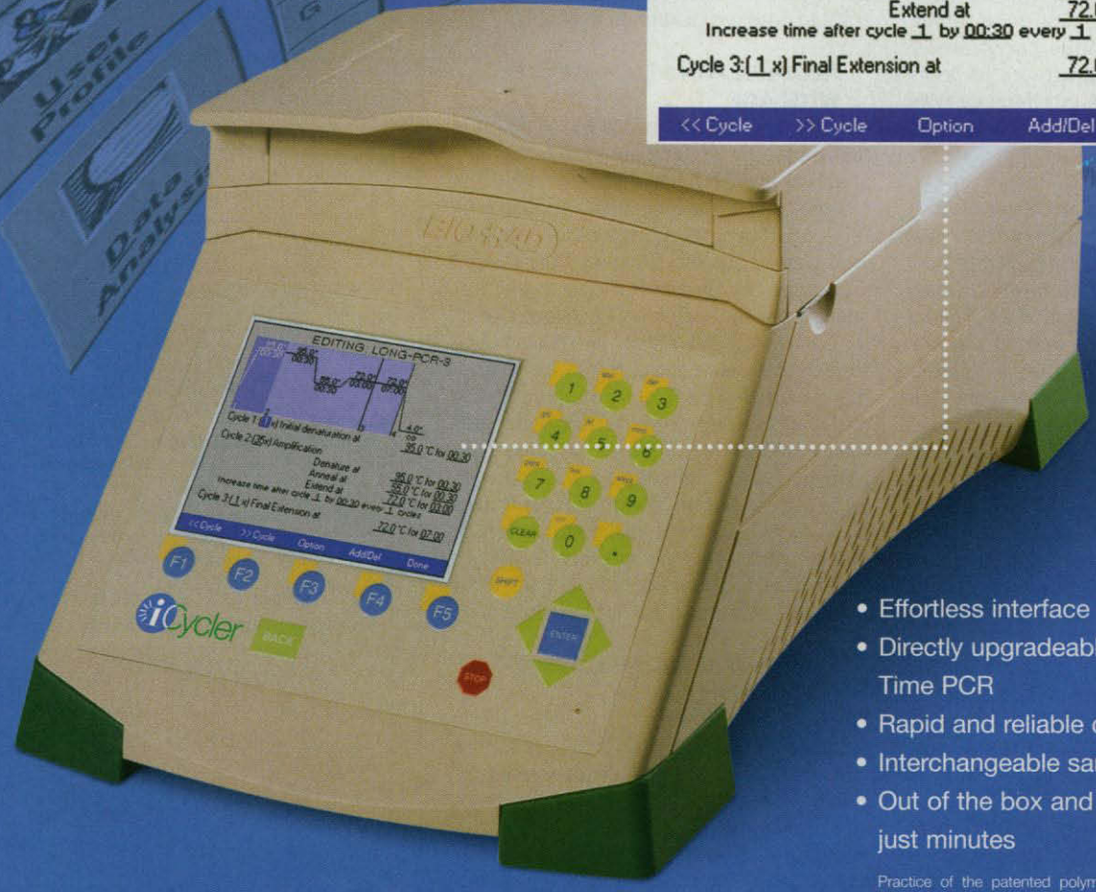
Circle No. 36 on Readers' Service Card

amplify your PCR* expectations

The iCycler™ Thermal Cycler Excels at Performance, Reliability and Ease-of-Use.

The iCycler features the most intuitive interface, including comprehensive informational screens, validation reports and a graphical textual display of a protocol on one screen.





- Effortless interface
- Directly upgradeable for Real Time PCR
- Rapid and reliable cycling
- Interchangeable sample blocks
- Out of the box and running in just minutes

Practice of the patented polymerase chain reaction (PCR) process requires a license. The iCycler includes a licensed thermal cycler and may be used with PCR licenses available from the Perkin-Elmer Corp. Its use with authorized reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents. Some applications may require licenses from other parties.

What Will You Discover Next?

Visit our Life Science web site at discover.bio-rad.com.
Call toll free at 1-800-4BIORAD (1-800-424-6723); outside the U.S., call (510) 741-6996.

Circle No. 51 on Readers' Service Card

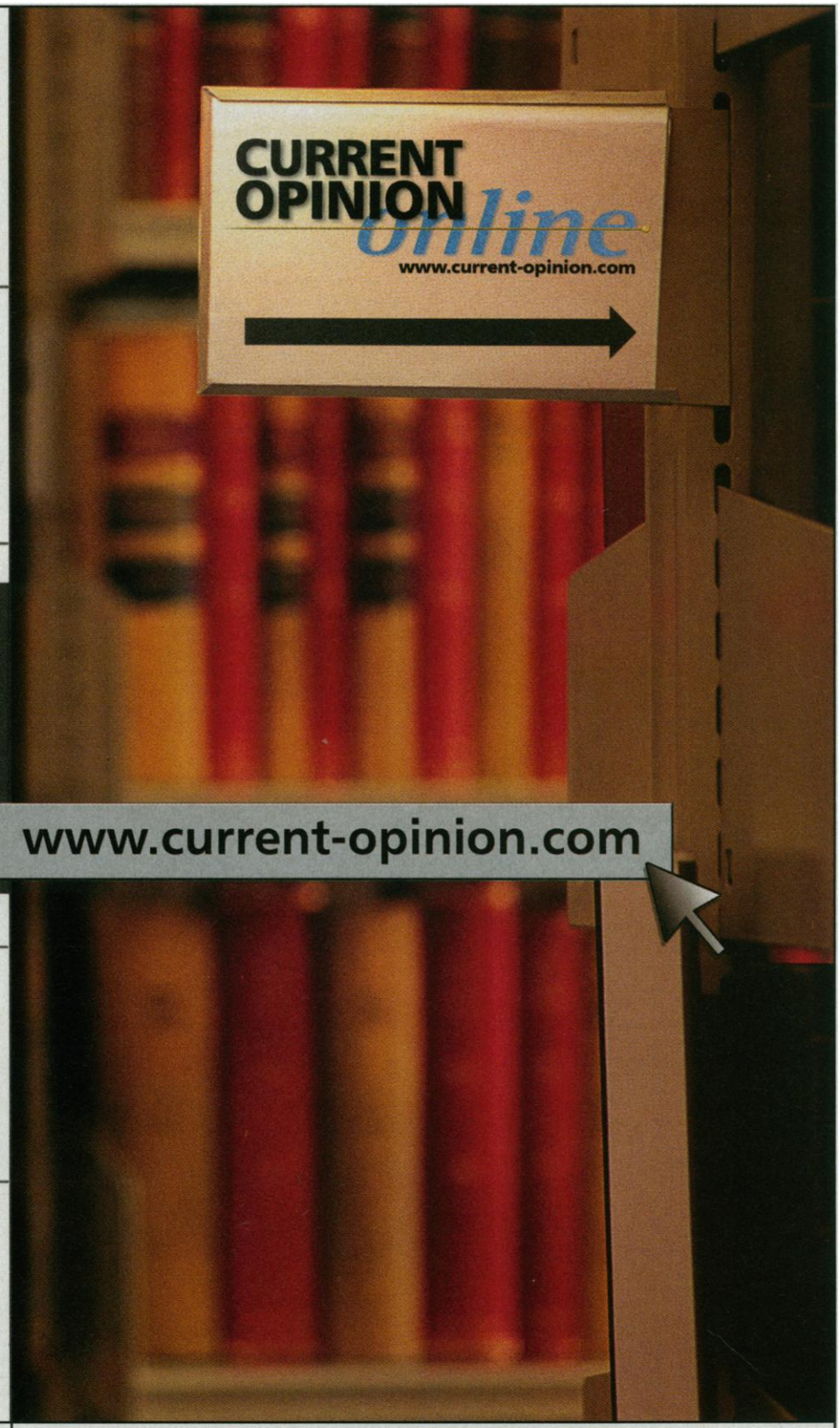
BIO-RAD

Link from reviews to original research – *fast...*

In an intuitive new environment

Search your own life science

- by section
- by year



***FREE** access from Oct. 15th to Dec. 31st 1999*

Institutional online access trial available*

CURRENT OPINION
www.current-opinion.com

Your science signposted – by Current Opinion Journals in:

- *Biotechnology*
- *Cell Biology*
- *Chemical Biology*
- *Genetics & Development*
- *Immunology*
- *Microbiology*
- *Neurobiology*
- *Plant Biology*
- *Structural Biology*

* From December 1st '99. Registration and conditions apply. Full details at www.current-opinion.com

Circle No. 38 on Readers' Service Card

www.sciencemag.org
Science

EDITOR-IN-CHIEF
Floyd E. Bloom

EDITOR
Ellis Rubinstein

MANAGING EDITOR
Monica M. Bradford

EDITORIAL

DEPUTY MANAGING EDITORS: R. Brooks Hanson (Physical Sciences), Katrina L. Kelner (Biological Sciences); SUPERVISORY SENIOR EDITORS Linda J. Miller, Phillip D. Szuromi; SENIOR EDITORS Gilbert J. Chin, Pamela J. Hines, Barbara Jasny, Paula A. Kiberstis (Boston), L. Bryan Ray; ASSOCIATE EDITORS Lisa D. Chong, Beverly A. Purnell, Linda R. Rowan, H. Jesse Smith, Valda Vinson; EDITORIAL SUPPORT Candace Gallery, Carolyn Kyle, Elise Laffman, Patricia M. Moore, Anita Wynn; ADMINISTRATIVE SUPPORT Sylvia Kihara

SCIENCE'S COMPASS

SENIOR EDITOR/POLICY FORUM Barbara Jasny; SENIOR EDITORS/PERSPECTIVES Orla Smith, Julia Uppenbrink; ASSOCIATE BOOK REVIEW EDITOR Sherman J. Suter; CONTRIBUTING EDITORS Kevin Ahern, Richard Peters, Robert Sikorski, David F. Voss; PUBLICATION ASSISTANTS Jeffrey Hearn, Elizabeth Lenox; INFORMATION SPECIALIST Janet Kegg; ASSOCIATE LETTERS EDITOR Christine M. Pearce; PUBLICATION ASSISTANT Charlene King

NEWS

NEWS EDITOR Colin Norman; FEATURES EDITOR Tim Appenzeller; DEPUTY NEWS EDITORS Elizabeth Culotta (contributing editor), Jean Marx, Jeffrey Mervis, Richard Stone; NEWS WRITERS Martin Enserink, Laura Helmuth (intern), Constance Holden, Jocelyn Kaiser, Richard A. Kerr, Andrew Lawler, David Malakoff, Eliot Marshall, Elizabeth Pennisi, Gretchen Vogel BUREAUS: BERKELEY, CA Marcia Barinaga (contributing correspondent); SAN DIEGO, CA Jon Cohen (contributing correspondent); PACIFIC NORTHWEST Robert F. Service; COPY EDITORS Linda B. Felaco, Daniel T. Helgerman; CONTRIBUTING CORRESPONDENTS Barry A. Cipra, Ann Gibbons, Robert Irion, Charles C. Mann, Anne Simon Moffat, Virginia Morell, Evelyn Strauss, Gary Taubes, Ingrid Wickelgren; ADMINISTRATIVE SUPPORT Scherraine Mack, Fannie Groom

EDITING AND PROOFREADING

EDITORIAL MANAGER Cara Tate; SENIOR COPY EDITORS Cay Butler, Harry Jach, Etta Kavanagh, Barbara P. Ordway, COPY EDITORS Jeffrey E. Cook, Jason Llewellyn, Joshua Marcy, Monique Martineau, EDITORIAL COORDINATORS Ellen E. Murphy, Beverly Shields; PUBLICATIONS ASSISTANTS Chris Filiatreau, Joi S. Granger, Gail Murphy; EDITORIAL ASSISTANT Kathy Libal

PRODUCTION

DIRECTOR James Landry; MANAGER Wendy K. Shank; ASSISTANT PRODUCTION MANAGERS, Lizabeth A. Harman (Internet), Rob Masson; ASSOCIATES Patricia Riehn Berg (Internet), Vicki J. Jorgensen, Tara L. Kelly, Jessica K. Moshell, Rebecca Thomas

ART

DESIGN DIRECTOR C. Faber Smith; ART DIRECTOR Alan T. Stonebraker; SCIENTIFIC ILLUSTRATORS Carin Cain, Katharine Sutliff; GRAPHICS ASSOCIATES Holly Bishop, Preston Morrighan, Darcel Pugh; PHOTO RESEARCHER Leslie Blizard

SCIENCE INTERNATIONAL

EUROPE

EDITORIAL: SUPERVISORY SENIOR EDITOR Andrew M. Sugden; ASSOCIATE EDITORS Stella M. Hurtley, Ian S. Osborne, Peter Stern; NEWS: EDITOR Daniel Clery, CORRESPONDENT Michael Hagmann; CONTRIBUTING CORRESPONDENTS Michael Balter (Paris) Robert Koenig (Bern); *SCIENCE*'S NEXT WAVE, UK EDITOR: John MacFarlane; EDITORIAL SUPPORT Jenny Parker, Meleena Thomas; ADMINISTRATIVE SUPPORT Janet Mumford, Liz Ellis

ASIA

JAPAN NEWS BUREAU: Dennis Normile (contributing correspondent); CHINA REPRESENTATIVE Hao Xin; Pallava Bagla (contributing correspondent, India)

*SCIENCE*NOW: www.sciencenow.org

EDITOR Erik Stokstad

SCIENCE'S NEXT WAVE: www.nextwave.org

MANAGING EDITOR Wendy Yee; SENIOR EDITOR Nicole Ruediger WRITER Melissa Mertl; CANADA EDITOR Charles Boulakia; ASSISTANT Suzanne Moore

PUBLISHER
Richard S. Nicholson

ASSOCIATE PUBLISHER
Beth Rosner

MEMBERSHIP/CIRCULATION DIRECTOR
Michael Spinella

MEMBERSHIP/CIRCULATION

SUBSCRIPTION SERVICES: 202-326-6417; 800-731-4939
DEPUTY DIRECTOR Marlene Zendell; MEMBER SERVICES: MANAGER Michael Lung; SUPERVISOR Mary Curry; REPRESENTATIVES Laurie Baker, Pat Butler, Christine Ford, Mari Pope, Jantell Smith; MARKETING: MANAGER Scott Oser; ASSOCIATES Lauri Sirois, Deborah Stromberg; EUROPE MANAGER Jane Pennington; EXECUTIVES Ruth Jackson, Martin Paine; RESEARCH: MANAGER Renuka Chander; BUSINESS AND FINANCE: MANAGER Teressa Stirk; ASSISTANT Susan Maxim; COMPUTER SPECIALIST Charles Munson

FINANCE AND ADVERTISING

BUSINESS AND FINANCE: BUSINESS MANAGER Deborah Rivera-Wienhold; SENIOR ANALYST Randy Yi; FINANCIAL ANALYST Lisa Donovan RIGHTS AND PERMISSIONS: ASSOCIATE Emilie David; ASSISTANT Karen Lentz MARKETING: DIRECTOR John Meyers; ASSOCIATES Catherine Giordano, Allison Pritchard ELECTRONIC MEDIA: MANAGER David Gillikin; COMPUTER SPECIALIST Wendy Green; PRODUCTION ASSOCIATES Mark Croatti, Ellen McGuire, Louis Williams ADMINISTRATIVE SUPPORT Jessica Tierney

PRODUCT ADVERTISING

NATIONAL SALES MANAGER NORTHEAST AND E. CANADA Richard Teeling: 973-694-9173, FAX 973-694-9193 • MIDWEST/ SOUTHEAST Elizabeth Mosko: 773-665-1150, FAX 773-665-2129 • WEST COAST/W. CANADA Neil Boylan: 415-673-9265, FAX 415-673-9267 • MID ATLANTIC AND U.S. INSIDE SALES Christopher Breslin: 410-273-1007, FAX 410-273-1591 NEW MEDIA SALES MANAGER Chris Peterson: 410-560-3960, FAX 410 560-3961 • UK/SCANDINAVIA/FRANCE/ ITALY/BELGIUM/NETHERLANDS Andrew Davies: (44) 7-071-226-216, FAX (44) 7-071-226-233 • GERMANY/SWITZERLAND/AUSTRIA Tracey Peers: (44) 1-260-297-530, FAX (44) 1-260-271-022 JAPAN Mashy Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852 • TRAFFIC MANAGER Carol Maddox; SALES ASSOCIATES Sean Gee, Sheila Myers

RECRUITMENT ADVERTISING

SALES AND PRODUCTION OPERATIONS MANAGER Terri Seiter Azie U.S.: SALES MANAGER Gabrielle Boguslawski: 718-491-1607, FAX 202-289-6742; INTERNET SALES MANAGER Beth Dwyer; SALES SUPERVISOR Daryl Anderson; SALES REPRESENTATIVES Kathleen Clark, Beth Dwyer, Christina Geiger, Bren Peters-Minnis, Kristin Westapher; ASSISTANTS Erika Bryant, Sussy Castilla, Jody Fenty, Shirley Young PRODUCTION: TRAFFIC MANAGER Jennifer Rankin; ASSOCIATE Christine Borkowski U.K./EUROPE: SALES MANAGER Debbie Cummings; SALES EXECUTIVE Sabine Lenud; ASSISTANT Elisabeth Py: (44) 1223-326500, FAX (44) 1223-326532 AUSTRALIA/NEW ZEALAND: Keith Sandell: (61) 02-9922-2977, FAX (61) 02-9922-1100 JAPAN: Mashy Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852

AAAS BOARD OF DIRECTORS

RETIRING PRESIDENT, CHAIR M. R. C. Greenwood
PRESIDENT Stephen Jay Gould
PRESIDENT-ELECT Mary Lowe Good
TREASURER William T. Golden
EXECUTIVE OFFICER Richard S. Nicholson

Lewis M. Branscomb; Robert D. Goldman; Alice S. Huang; Sheila Jasanoff; Sally Gregory Kohlstedt; Marcia C. Linn; Neena B. Schwartz; David E. Shaw

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.

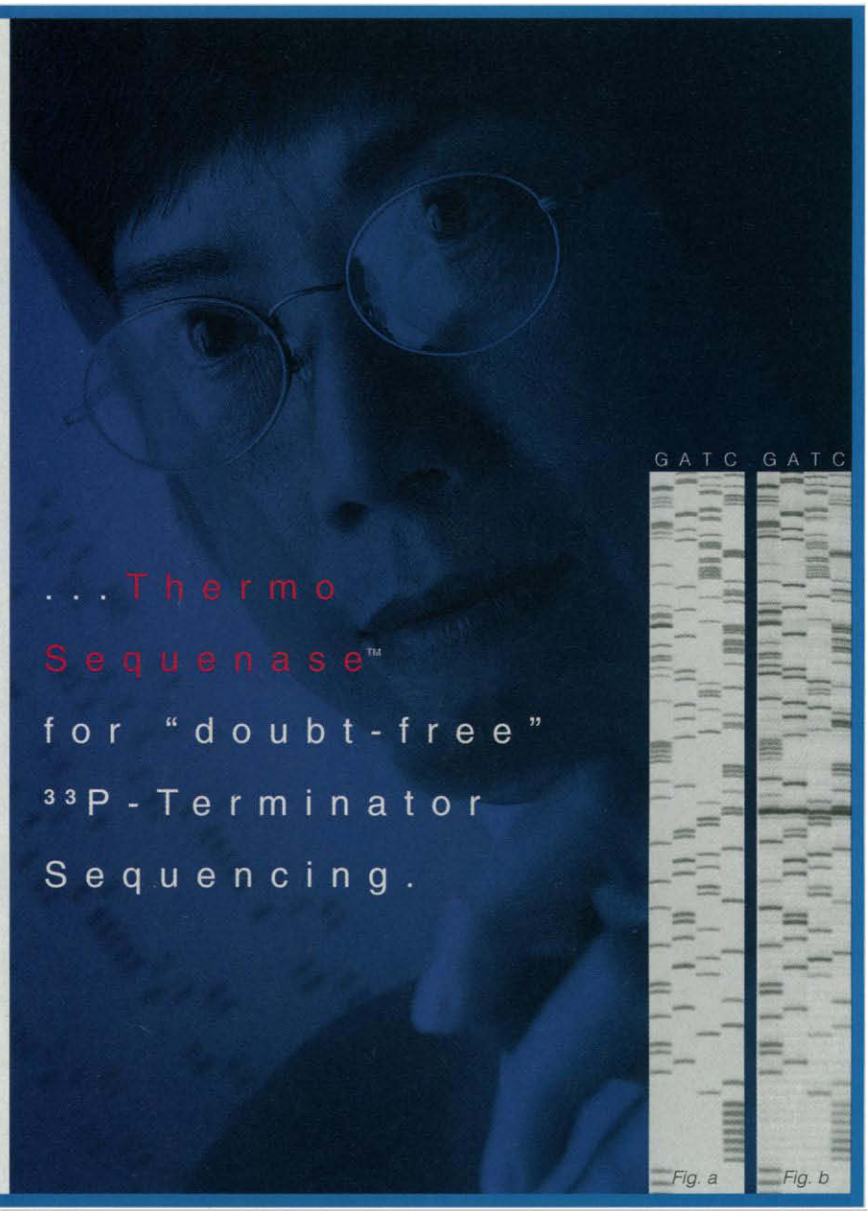
DEPUTY EDITORS

Philip H. Abelson (*Engineering and Applied Sciences*); John I. Brauman (*Physical Sciences*); Thomas R. Cech (*Biological Sciences*)

BOARD OF REVIEWING EDITORS

Frederick W. Alt
Children's Hospital, Boston
Don L. Anderson
California Institute of Technology
Michael Ashburner
University of Cambridge
Frank S. Bates
Univ. of Minnesota, Minneapolis
Stephen J. Benkovic
Pennsylvania State University
Alan Bernstein
Mount Sinai Hospital, Toronto
Michael J. Bevan
University of Washington, Seattle
Seth Blair
University of Wisconsin, Madison
David E. Bloom
Harvard School of Public Health
Piet Borst
The Netherlands Cancer Institute
Henry R. Bourne
Univ. of California, San Francisco
James J. Bull
University of Texas at Austin
Kathryn Calame
Columbia Univ. College of Physicians & Surgeons
Dennis W. Choi
Washington Univ. School of Medicine, St. Louis
Joanne Chory
The Salk Institute
David Clapham
Children's Hospital, Boston
Adrienne E. Clarke
University of Melbourne, Parkville
F. Fleming Crim
University of Wisconsin, Madison
Paul J. Crutzen
Max-Planck-Institut für Chemie
James E. Dahlberg
University of Wisconsin Medical School, Madison
Robert Desimone
National Institute of Mental Health, NIH
Hans Eklund
Swedish Univ. of Agricultural Sciences, Uppsala
Paul T. Englund
Johns Hopkins University School of Medicine
G. Ertl
Max-Planck-Gesellschaft
Richard G. Fairbanks
Lamont-Doherty Earth Observatory
Douglas T. Fearon
University of Cambridge
Harry A. Fozzard
The University of Chicago
Roger I. M. Glass
Centers for Disease Control
Peter N. Goodfellow
SmithKline Beecham, UK
Jack F. Greenblatt
University of Toronto
Peter Gruss
Max Planck Institute of Biophysical Chemistry
Philip C. Hanawalt
Stanford University
Paul Harvey
University of Oxford
M. P. Hassell
Imperial College at Silwood Park
Nobutaka Hirokawa
University of Tokyo
Tasuku Honjo
Kyoto University
Susan D. Iversen
University of Oxford
Eric F. Johnson
The Scripps Research Institute
Hans Kende
Michigan State University
Elliott Kieff
Harvard University
Jeffrey T. Kiehl
National Center for Atmospheric Research, Boulder
Judith Kimble
University of Wisconsin, Madison
Stephen M. Kosslyn
Harvard University
Michael LaBarbera
The University of Chicago
Antonio Lanzavecchia
Basel Institute for Immunology
Nicole Le Douarin
Institut d'Embryologie Cellulaire et Moléculaire du CNRS
Norman L. Letvin
Beth Israel Hospital, Boston
Harvey F. Lodish
Whitehead Institute for Biomedical Research
Richard Losick
Harvard University
Seth Marder
University of Arizona
Diane Mathis
Harvard Medical School
Susan K. McConnell
Stanford University
Anthony R. Means
Duke University Medical Center
Stanley Meizel
University of California, Davis
Douglas A. Melton
Harvard University
Andrew Murray
Univ. of California, San Francisco
Elizabeth G. Nabel
National Heart, Lung, and Blood Institute, NIH
Shigetada Nakanishi
Kyoto University
Roger A. Nicoll
Univ. of California, San Francisco
Staffan Normark
Swedish Institute for Infectious Disease Control
Kiyotaka Okada
Kyoto University
Bert W. O'Malley
Baylor College of Medicine
Stuart L. Pimm
The Univ. of Tennessee, Knoxville
Yeshayau Pocker
Univ. of Washington, Seattle
Martin Raff
University College London
Douglas C. Rees
California Institute of Technology
T. M. Rice
ETH-Hönggerberg, Zürich
David C. Rubie
Universität Bayreuth
Erkki Ruoslahti
The Burnham Institute, CA
Jozef Schell
Max-Planck-Institut für Zuchtungforschung
Ronald H. Schwartz
National Institute of Allergy and Infectious Diseases, NIH
Terrence J. Sejnowski
The Salk Institute
Christopher R. Somerville
Carnegie Institute of Washington, Stanford, CA
Michael P. Stryker
Univ. of California, San Francisco
Cliff Tabin
Harvard Medical School
John Jen Tai
National Taiwan University
Tomoyuki Takahashi
University of Tokyo
Masatoshi Takeichi
Kyoto University
Keiji Tanaka
RIKEN Institute
David Tilman
Univ. of Minnesota, St. Paul
Robert T. N. Tjian
Univ. of California, Berkeley
Yoshinori Tokura
University of Tokyo
Derek van der Kooy
University of Toronto
Geerat J. Vermeij
University of California, Davis
Bert Vogelstein
Johns Hopkins Oncology Center
Gerhard Wegner
Max-Planck-Institut für Polymerforschung
Arthur Weiss
Univ. of California, San Francisco
Zena Werb
Univ. of California, San Francisco
George M. Whitesides
Harvard University
Ian A. Wilson
The Scripps Research Institute
Alan P. Wolffe
National Institute of Child Health and Human Development, NIH
Martin Zatz
National Institute of Mental Health, NIH

The company that brought you Sequenase™ proudly brings you



Thermo Sequenase™ The new standard for manual cycle sequencing.

Are your cycle sequencing results leaving you in doubt? Strong stops, background sequence causing problems?

Thermo Sequenase Radiolabelled Terminator Cycle Sequencing Kit

The combination of USB's Thermo Sequenase Terminator Cycle Sequencing Kit with Amersham Pharmacia Biotech's radiolabelled terminators will give you sequencing results beyond a shadow of a doubt.

Thermo Sequenase - gives excellent performance at cycle sequencing temperatures. Helps eliminate secondary structure artifacts.

^{33}P-labelled terminators - yield detection of only truly terminated sequencing fragments. False terminations are not visible because these fragments are not labeled.

- Eliminate stops and BAFLs. (Bands Across all Four Lanes)
- Read the first base after the primer.
- Crisp, clean sequence.
- Detect heterozygotes and mutants more easily.
- Sequencing directly from bacterial colonies is possible.

No other combination for manual cycle sequencing gives more information per gel — long reads, accurate sequence. Doubt-free results.

Above: Elimination of bands across all four lanes (BAFLs) in plasmid template.

Fig. a) Using the Thermo Sequenase Radiolabelled Terminator Cycle Sequencing Kit.

Fig. b) Compared to standard ^{35}S-dATP cycle sequencing where a strong BAFL is observed.

To order within the United States contact USB directly at 1-800-321-9322 or e-mail us at customerserv@usbweb.com. For your authorized USB distributor outside the United States, please contact your local Amersham Pharmacia Biotech office.

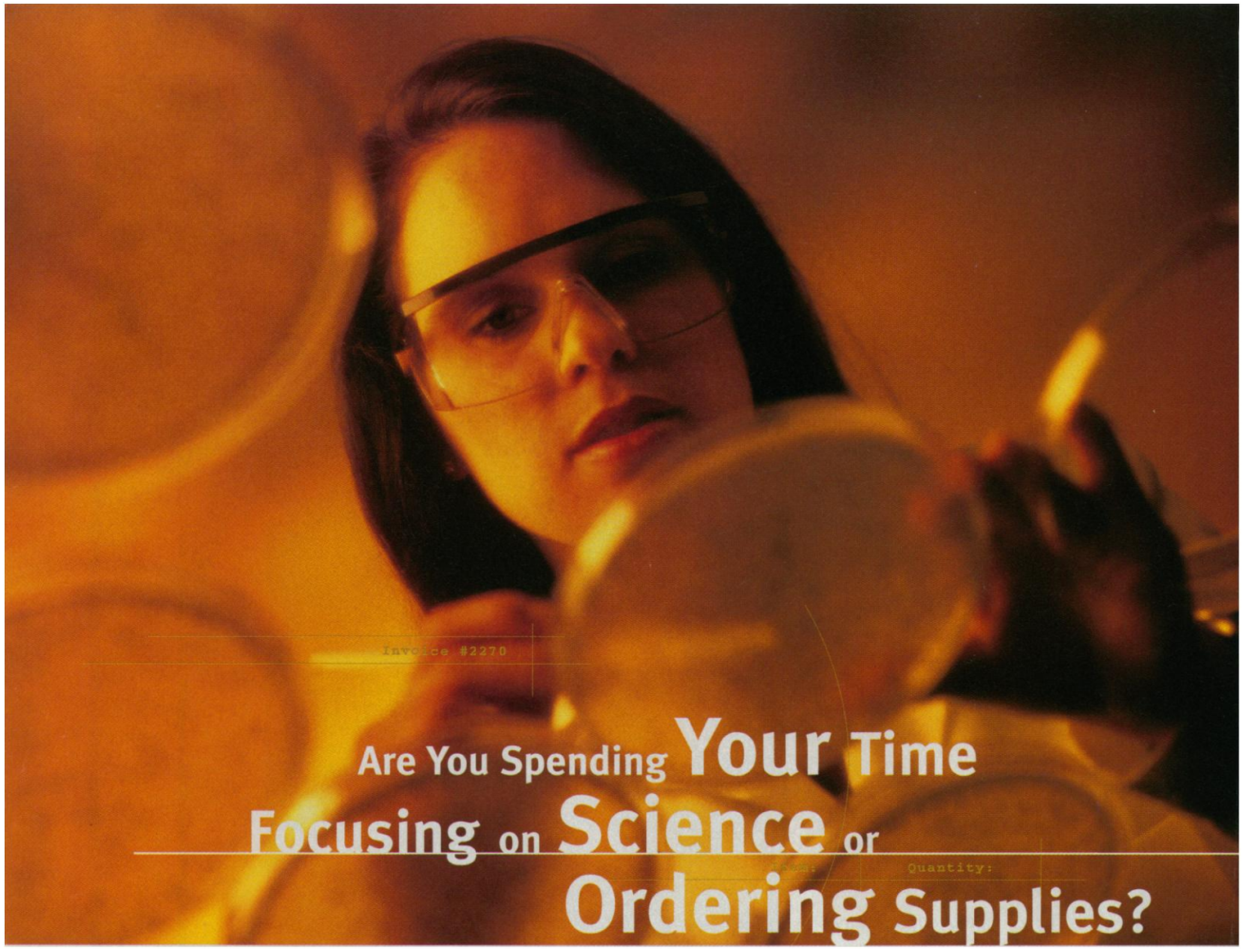
USB Corporation, 26111 Miles Road
Cleveland, OH 4412
800-321-9322
www.usbweb.com

usb™

Rediscover the chemistry

©1999 usb corporation. Sequenase and Thermo Sequenase are trademarks of Amersham Pharmacia Biotech Limited or its subsidiaries.

Circle No. 64 on Readers' Service Card



Chemdex™ —Your One-Stop Shop for Life Science Supplies

The hours you spend ordering lab supplies cut into your day, distracting you from your research. You have more important things to do than search through dozens of catalogs for the product you need or track the status of your order.

Chemdex offers a faster, easier way to order lab supplies with an online marketplace that contains hundreds of thousands of products from the suppliers you know and trust. When you buy through Chemdex, you get:

> An expanding database of reagents, instruments and equipment
> One, simple electronic order form that can be used for multiple suppliers
> A fast, easy-to-use search engine
> A "personal favorites" page for quick and easy re-ordering
> Rapid, real-time order tracking
> World-class customer service and support

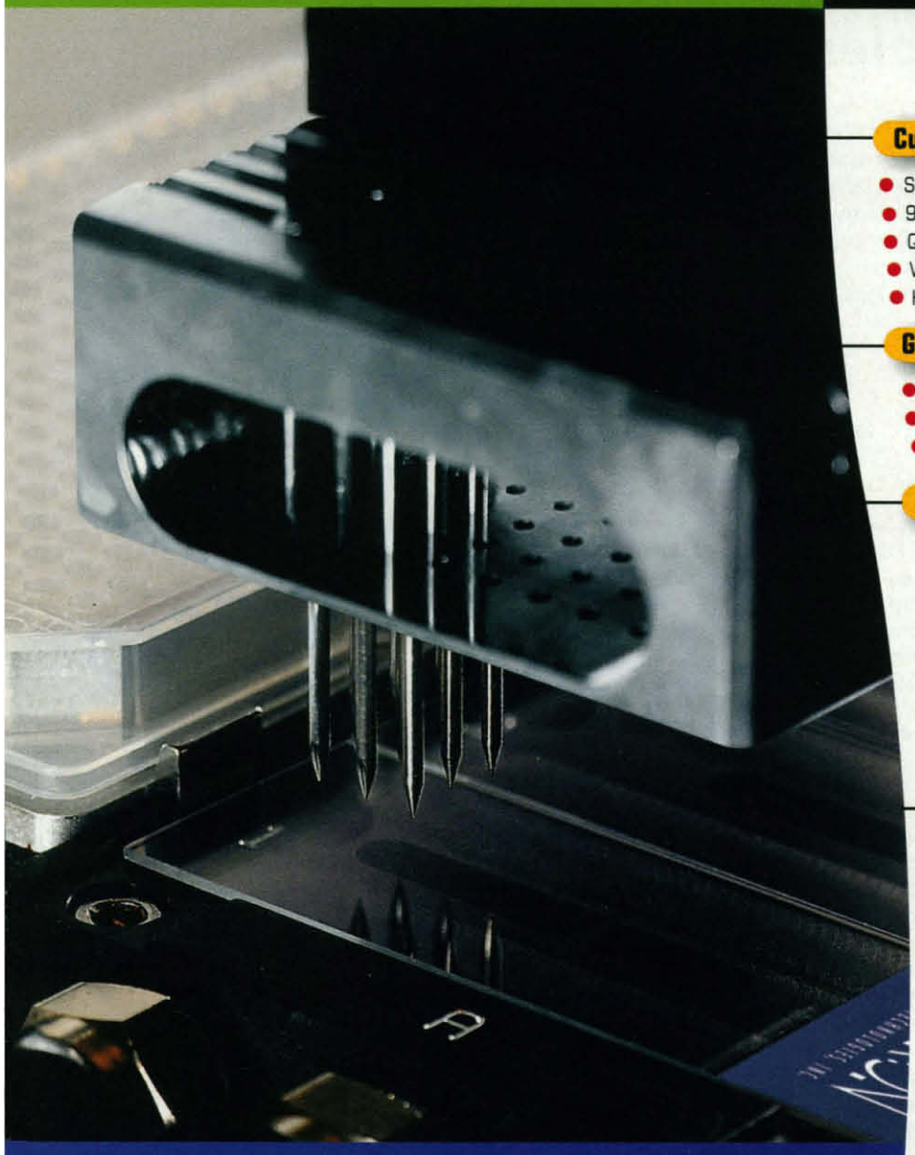
Make Chemdex your one-stop shop for laboratory supplies. Go to www.chemdex.com. You'll spend less time placing orders, and more time focusing on science.

© 1999 Chemdex Corporation. Chemdex is a trademark of Chemdex Corporation.

Circle No. 35 on Readers' Service Card

For the Best DNA

Operon Technologies • The DNA Company



Custom Oligonucleotide Synthesis Service

- Sephadex column purification of every oligo with purchase
- 96-well plate format for your convenience at no extra charge
- Quality large scale synthesis
- Wide variety of modifications
- HPLC and PAGE purification

GeneOp™ Custom Gene Synthesis Service

- Quick turn around
- Low prices
- Sequence accuracy is unconditionally guaranteed

Microarray Products NEW

- **Oligos** - Any desired format or modification for your arraying needs
- **Custom PCR† Service** - High quality, high yield, large scale-up available
- **OPTs™** - Sequenced-optimized, concentration-normalized PCR products
- **OpArray™** - Custom DNA arrays on glass slides

For More Information,

E-mail us at
dna@operon.com for custom synthesis products

E-mail us at
oparray@operon.com for microarray products

1000 Atlantic Avenue, Suite 108
Alameda, California 94501
Tel: 800-688-2248
Fax: 510-865-5255
Customer Service Hours are 7a.m. to 5p.m. PST

† These products are made using the Polymerase Chain Reaction ("PCR") Process which is covered by patents owned by Roche Molecular Systems, Inc. and F. Hoffmann-La Roche LTD. ("Roche"), under license from Roche. No license to use the PCR Process is conveyed expressly or by implication to the purchaser by purchase of these products.

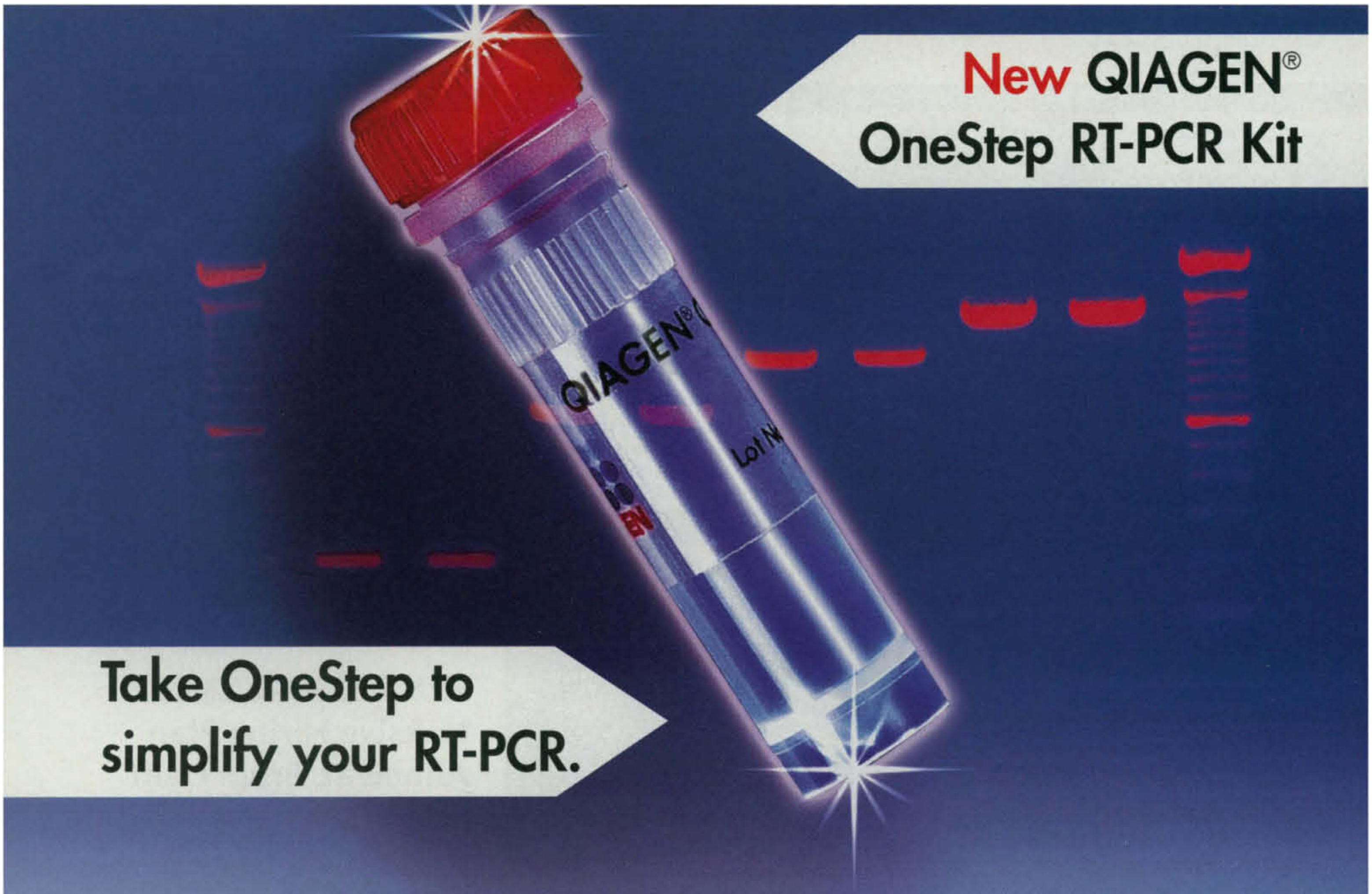
www.operon.com

800.688.2248

Circle No. 50 on Readers' Service Card

OPERON

OPERON TECHNOLOGIES, INC.



The QIAGEN® OneStep RT-PCR Kit is designed for easy and sensitive one-step RT-PCR using any RNA. A unique enzyme combination and specially developed reaction buffer ensure efficient reverse transcription and PCR in one tube.

The QIAGEN OneStep RT-PCR Kit is the one kit that makes your RT-PCR:

- **Simple** — easy one-tube setup
- **Fast** — time-saving procedure
- **Sensitive** — a unique blend of two high-affinity reverse transcriptases and a hot-start PCR enzyme
- **Robust** — optimized buffer for efficient reverse transcription and amplification

QIAGEN OneStep RT-PCR Kit.
One step, one tube — the simplest RT-PCR.

Products containing HotStarTaq DNA Polymerase are sold under licensing arrangements with F. Hoffmann-La Roche Ltd, Roche Molecular Systems, Inc. and The Perkin-Elmer Corporation. 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.
© 1999 QIAGEN, all rights reserved.

www.qiagen.com

QIAGEN: Germany	USA	Australia	Canada	France	Japan	Switzerland	UK
Tel. 02103-892-240	Tel. 800-426-8157	Tel. 03-9489-3666	Tel. 800-572-9613	Tel. 01-60-920-930	Tel. 03-5805-7261	Tel. 061-319-30-31	Tel. 01293-422-999
Fax 02103-892-255	Fax 800-718-2056	Fax 03-9489-3888	Fax 800-713-5951	Fax 01-60-920-925	Fax 03-5805-7263	Fax 061-319-30-33	Fax 01293-422-922

DISTRIBUTORS: Austria/Hungary/Slovenia R. u. P. MARGARITELLA Austria (01) 889 18 19 **Belgium/Luxemburg** Westburg b.v. 0800-1-9815 **Brazil** Labtrade do Brazil (11) 543 1455 or 0800 55 1321 **Central & South America** Labtrade Inc. USA (305) 828-3818 **China** Gene Company Limited (852)2896-6283 **Czech Republic** BIO-CONSULT spol. s.r.o. (02)4447 1239 **Denmark** KEBO Lab A/S 43 86 87 88 **Egypt** Clinilab 525 7212 **Finland** KEBO Lab Oy (09)-804 551 **Greece** BioAnalytica S.A. (01)-640 03 18 **India** Genetix (011)-542 1714 or (011)-515 9346 **Israel** Bio-Lab Ltd. 02. 584 1111 **Italy** GENENCO (M-Medical srl) (055) 500 1871 **Korea** LRS Laboratories, Inc.(02) 924-86 97 **Malaysia** Research Biolabs Sdn. Bhd. (03)-7312099 **Mexico** Quimica Valaner S.A. de C.V. (5) 525 57 25 **The Netherlands** Westburg b.v. (033)-4950094 **New Zealand** Biolab Scientific Ltd.(09) 980 6700 or 0800 933 966 **Norway** KEBO Lab AS 22 90 00 00 **Poland** Syngen Biotech (071) 351 41 06 or 0601 70 60 07 **Portugal** IZASA PORTUGAL, LDA (1)-751 6000 **Singapore** Research Biolabs Pte Ltd. 445 7927 **Slovak Republic** BIO-CONSULT Slovakia s.r.o. (07) 50221 336 **South Africa** Southern Cross Biotechnology (Pty) Ltd (021) 671 5166 **Spain** IZASA, S.A. (93) 902.20.30.90 **Sweden** KEBO Lab (08) 621 34 00 **Taiwan** TAIGEN Bioscience Corporation (02) 2880 2913 **Thailand** Theera Trading Co. Ltd. (02) 412-5672 **In other countries contact:** QIAGEN GmbH, Germany

QIAGEN

Circle No. 80 on Readers' Service Card

Background picture: ABI Model 377 automated fluorescent DNA cycle sequencing of pNoTA/T7™ plasmid DNA prepared by the Perfectprep method.

Perfection comes with Perfectprep®

Imagine, if you can, ultra-pure plasmid DNA which has been rapidly isolated and is now ready for transfection and sequencing: It's almost too perfect to be true! But it is both perfect and true – thanks to Eppendorf's **Perfectprep® Plasmid Kits** for plasmid DNA isolation, which give you:

- Ultra-pure plasmid DNA in next to no time
- Reproducible, high-yield results
- A spin-column format for ease of handling
- Ready-to-use plasmid DNA for manual or automated sequencing, cloning and transfection

Rapid, simple and systematic plasmid purification, adapted to suit sample throughput and the amount of DNA required, whether you want individual purification in one spin column or the simultaneous isolation of 96 plasmid samples. The Perfectprep System offers rapid, reproducible yields of plasmid DNA in a simple-to-use kit system. An extremely efficient binding matrix ensures that yields remain constantly high. The plasmid DNA obtained is ultra-pure, shows no chromosomal DNA or RNA contamination and can be used immediately after isolation for all molecular biological applications, such as automated sequencing, transformation, PCR*, blotting or clonings.

The Perfectprep Plasmid System is available in five different kit versions, including the ultra-rapid Mini-Kit, the economical XL-Kit and the high-throughput 96 Spin-Kit. Without the use of organic substances and fully compatible with Eppendorf centrifuges and rotors, these kits provide plasmid DNA which will make your colleagues green with envy.
Perfectprep from Eppendorf – perfect by name, perfect by nature.

* The Polymerase Chain Reaction (PCR) is protected by patent. The patent is held by Hoffmann-La Roche.

The Perfectprep® System

Kit Size	Bacteria Culture (ml)	Time needed (min)	Yields High Copy Plasmid (µg)	Yields Low Copy Plasmid (µg)
Mini	1–2	25	5–30	1–3
Midi	10–75	120	50–600	10–100
Maxi	100–300	150	250–2,500	50–400
XL	400–800	150	2,000–6,000	200–1,000
96 Minispin	1–1.3	120	2–10	0.05–0.06

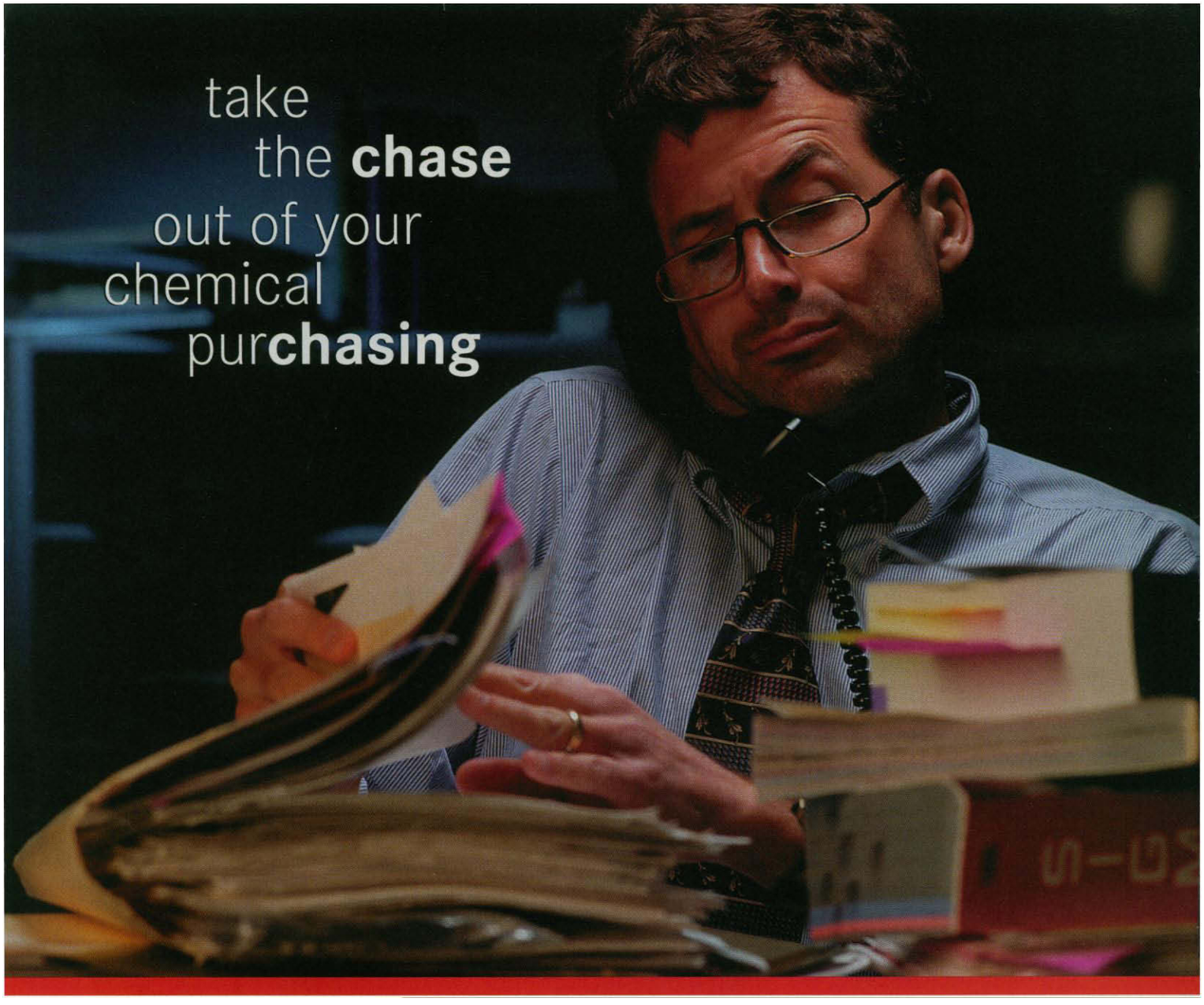
eppendorf® is a registered trademark.

eppendorf

In touch with life

Circle No. 12 on Readers' Service Card

Eppendorf – Netheler – Hinz GmbH · 22331 Hamburg · Germany · Life Science Application-Hotline: +49 180-3666789 · Fax +49 40-538 01-556
e-mail: eppendorf@eppendorf.com · eppendorf home page: http://www.eppendorf.com
Eppendorf Scientific, Inc. · One Cantiague Road · Westbury, NY 11590-0207 · Phone 800-421-9988 or 516-876-6800 · Fax 516-876-8599
e-mail: eppendorf@eppendorfsi.com · website: www.eppendorfsi.com



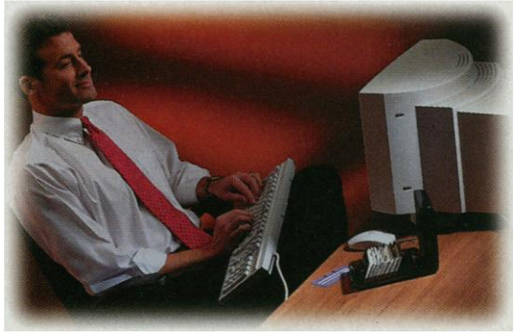
TRY OUR eCOMMERCE SOLUTION @ **www.sigma-aldrich.com**

EASY ON-LINE ORDERING

The Sigma-Aldrich PipeLine™ eCommerce system offers simple, on-line access to over 200,000 products from the Sigma-Aldrich brands: Sigma, Aldrich, Fluka, Supelco and Riedel-de Haën. Now you can place multi-brand orders for biochemicals, chemicals, equipment and laboratory supplies from all of our brands in a single transaction.

FIND WHAT YOU NEED FAST

With eight different ways to search, including product name, product number, CAS number, molecular formula and structure, pinpointing products is a snap.



Stop the chase and log on today.
It will make your job easier.
www.sigma-aldrich.com

A TOTAL INFORMATION RESOURCE

Because we are a manufacturer, we offer not only quality products but the technical knowledge and support to back them up.

- Over 90,000 on-line MSDS's
- Over 2 million on-line Certificates of Analysis
- Thousands of data sheets and technical bulletins

SIGMA-ALDRICH

3050 Spruce Street, St. Louis, MO 63103 • 800-521-8956 or 314-771-5765

Circle No. 54 on Readers' Service Card

DIRECT
From Cells 2 Results

IMPROVED! cAMP kit is now **15-fold** more sensitive with a range of 2000-0.4 fmol/well!

IN LESS THAN 3 HOURS

cAMP and cGMP

Measure **directly** in 0.1M HCl!

- **NON** Radioactive!
- **NO** Neutralization!
- **NO** Extractions!
- **NO** Drying Down and Reconstitution!

NEW PRODUCTS

- **COMPLEMENT C3a & C4a IMMUNOASSAY KITS**
- ***TiterZyme®* & *TiterFluor®* IMMUNOASSAY KITS**
- **PIP & PIP_2 ANTIBODIES**

2000 PRODUCT CATALOG AVAILABLE SOON!

For more info

Assay Designs, Inc.

MORE KITS FROM

Prostaglandins, Cytokines,

Endothelins, Small Peptides,

Steroids, Leptins, Nitric Oxide,

Chemiluminescence Labeling

and COX Activity

Assay Designs, Inc.
1327 Jones Drive
Ann Arbor, MI 48105 USA

phone: (734) 668-6113
toll free: (800) 833-8651 (USA and Canada)
fax: (734) 668-2793
e-mail: info@assaydesigns.com
website: www.assaydesigns.com

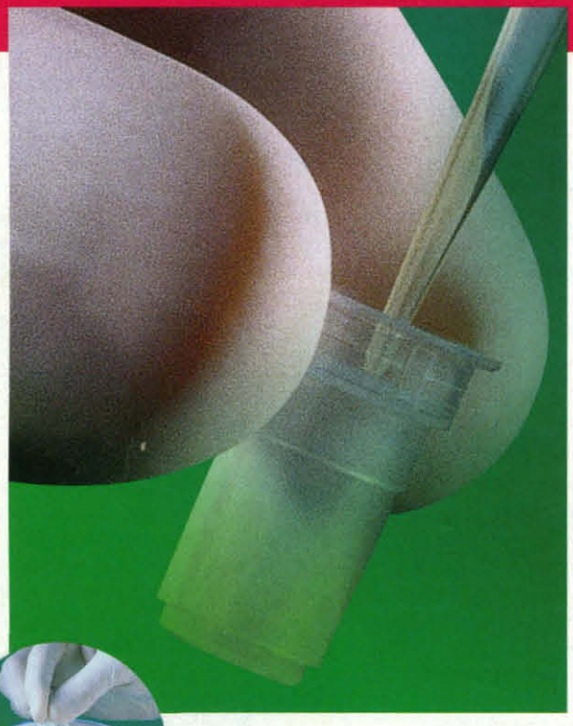
Worldwide distribution!
Contact us for your local distributor.

JOIN US AT NEUROSCIENCE BOOTH #766 & 768

Circle No. 75 on Readers' Service Card

EVERYTHING IS POSSIBLE...WITH THE RIGHT TOOLS.®

High-Performance Dialysis



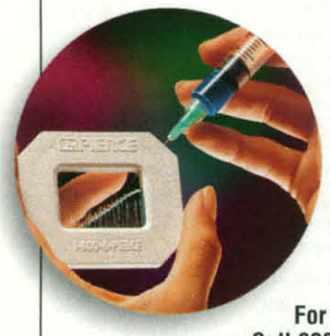
Introducing our smallest breakthrough yet.

Pierce Slide-A-Lyzer® MINI Dialysis Units quickly and efficiently dialyze samples as small as 10 µl.

- **100% Leak Tested:** Soon-to-be patented design prevents wicking around the membrane that can occur in homemade devices.
- **Excellent Sample Recoveries:** Slide-A-Lyzer® MINI Dialysis Units generally recover 9-10 µl after dialysis of a 10 µl sample.
- **Drastically Reduced Dialysis Time:** In less than 10 minutes, 100 µl of pH 2.8 buffer is converted to pH 9.4 dialyzing against a liter of bicarbonate buffer, pH 9.4.
- **Ready to Use:** No membrane treatment or assembly is required. Caps are provided to seal each unit to prevent evaporation and airborne contamination.

Slide-A-Lyzer® MINI Dialysis Units

SnakeSkin™ Dialysis Tubing



Slide-A-Lyzer® Dialysis Cassettes

Trust the entire family of Pierce Dialysis Products.

Slide-A-Lyzer® MINI Dialysis Units
- Very economical and very fast
- Perfect for small (10-100 µl) samples
- Excellent sample recovery (90-100%)

Slide-A-Lyzer® Dialysis Cassettes
- 95%+ sample recovery
- Very high surface area/sample volume ratio for rapid dialysis
- For 100 µl-15 ml sample sizes

SnakeSkin™ Dialysis Tubing
- *Very* easy to fill: The first truly tubular dialysis tubing!
- *Very* easy to use: No preparation or presoaking necessary
- *Very* easy to dispense: Snip what you need
- For 15-100 ml sample sizes

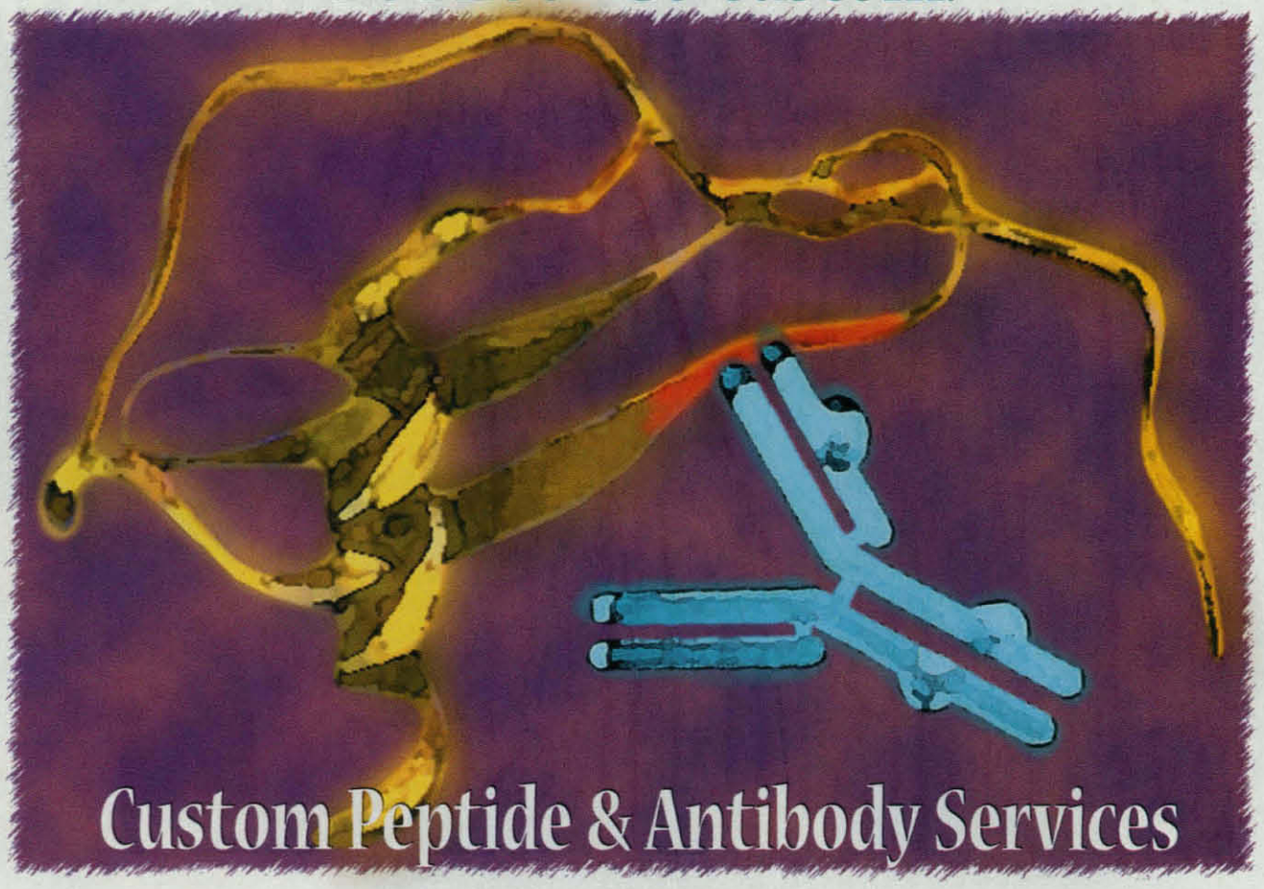
For detailed technical information, visit the Pierce web site at *www.piercenet.com*.
Call 800-874-3723 or, outside the U.S., 815-968-0747 for the name of your local distributor.

Circle No. 34 on Readers' Service Card

PIERCE

3747 N. Meridian Rd. • PO Box 117 • Rockford, IL 61105 U.S.A. • Tel: 815-968-0747 • Fax: 815-968-7316
Technical Assistance E-mail: TA@piercenet.com • Customer Assistance E-mail: CS@piercenet.com • Internet: http://www.piercenet.com
© Pierce Chemical Company, 1999. a Perstorp Life Science Company
Slide-A-Lyzer® and SnakeSkin™ are trademarks of Pierce Chemical Company.

Be First - Go Custom!



Join the many researchers who have successfully published first with novel reagents from QCB

- ***Thousands of satisfied customers in 30 countries***
- ***No hidden costs · Easy order pricing structure***
- ***In-house expertise in organic chemistry, immunology, biochemistry & signal transduction***

Peptide Services *Include*:

Free HPLC and Mass Spec. analysis
Free N-terminal acetylation and C-terminal amidation
Scales from milligrams to >10 grams

Options include: purification to 98+%, phosphopeptides, biotinylation, dyes, fatty acylation, cyclic peptides, etc.

Antibody Protocols *Include*:

Technical assistance in choosing optimal peptide sequences
All peptide work (up to 18 AA's) + 4-8 mg of purified peptide
HPLC purification to >90% and Mass Spec analysis
ELISA titers of >1:15,000

Options include: Affinity purification and phosphorylation state specific antibody protocols

BIOSOURCE INTERNATIONAL QCB

For research use only.

BioSource International, Inc.
1-800-435-2080

Order on-line at www.qcb.com

Fax: (508) 435-2199
e-mail: peptide@qcb.com

BioSource Europe S.A. Tel: +32-67 88 99 00 • BioSource Deutschland GmbH Tel: +49-2102 742 7600 • BioSource Netherlands B.V. Tel: +31-76-501 4824

AUSTRALIA +61 7 3352 6100 • AUSTRIA +431801 25 256 • CANADA 514 733-1900 • CHILE 56 2 209 6770 • DENMARK +45.86/10.10.55 • EGYPT +202/348.0997
FINLAND +358/3 682 2758 • FRANCE +33.1/42.53.14.53 • GREECE +30 1 52 81 900 • HUNGARY +420/5.745.736 • INDIA +91/80 646 820 • ISRAEL +972/3.934 99 22 • ITALY +39 02 26 28 91
JAPAN +81 3 5645 2751 • MEXICO +525/519 3463 • NEW ZEALAND +64.9/573.0770 • NORWAY +47/22 200 137 • POLAND +48.22/779.8350 • SOUTH AFRICA +27.11/793.6790 • SPAIN +34 3 435 36 01
SWEDEN +46.8/625.1850 • SWITZERLAND +041/420.96.36 • TAIWAN 886 2 2695 9990 • TURKEY +90 (312) 342 4130 • UNITED KINGDOM +44.1/923 241 515

Circle No. 40 on Readers' Service Card

Scan Samples as Small as 1µL

Gene Spec I

A Breakthrough in DNA/RNA Measurement

Gene Spec™ I can analyze samples of only 1 to 50 µL accurately and reliably. Absorbance, 260/280 nm ratio, concentration, purity, and protein concentration are all determined instantly.

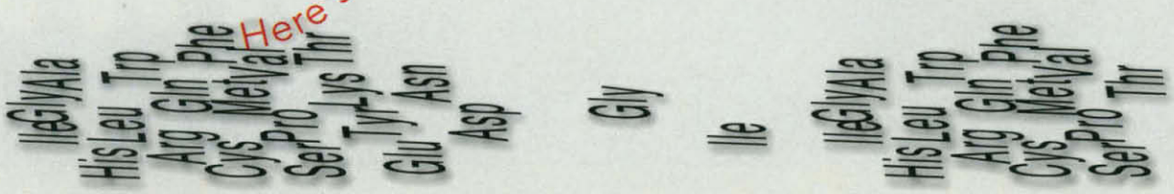
To learn more about the benefits, call 1-800-624-6176 or visit us at www.hitachi-soft.com/gs

HITACHI
Genetic Systems
Hitachi Software Engineering Co., Ltd.

Circle No. 57 on Readers' Service Card

Need Custom PEPTIDES?

Here's An Attractive Offer.



We believe if you try our custom peptide and/or antisera services just once, you'll stick with us. In fact, we'll send you a free amino acid micrograph magnet just for calling and requesting more information!

Peptide Service

We're proactive. Before we put your sequence together, we'll take it apart and thoroughly analyze it to prevent surprises later. Because your project depends on our peptide, we'll offer suggestions for increased success. Of course, you can choose from a variety of purity levels and scales. Since every Sigma-Genosys peptide comes with mass spectral analysis and HPLC documentation, you're bound to be 100% satisfied. Guaranteed.

Antisera Service

We'll take care of it from start to finish. Whether you're a peptide novice or pro, we'll help you design your target sequence, synthesize your peptide and conjugate it to a carrier protein. And yes, we also handle the immunization and sera collection. Hassle-free.

Provide us with your sequence and leave the rest to us.

SPECIAL OFFER!

Free micrograph magnet when you call for more information.

SIGMA GENOSYS

1442 Lake Front Circle • The Woodlands, Texas 77380-3600 • Tel: 1-800-498-2098 or (281) 363-3693 • Fax: (281) 363-5923
Email: ginformation@sial.com • http://www.genosys.com

Micrographs are courtesy of Michael W. Davidson, director of the Optical Microscopy Division of the National High Magnetic Field Laboratory.

Circle No. 62 on Readers' Service Card

Subscribe to *Science Online* today! Simply fax this form to (202) 842-1065, mail it to: AAAS, Membership Services, 1200 New York Avenue, NW, Washington, DC 20005, call (202) 326-6417, or sign up online at http://www.sciencemag.org/subscriptions/howto.shtml#

AAAS Members: ☐ Please begin my access to *Science Online* for just $12 a year.

(Offer good only for AAAS individual members who receive *Science* in print.)

Membership # _____

Non-Members: ☐ I want to join AAAS and receive *Science* magazine (51 weekly issues) and access to *Science Online*. I have checked my membership category below:

US RESIDENTS

Professional Member	☐ $122
Postdoctoral/Resident	☐ $99
Full-Time Student	☐ $74

MAIL TO: AAAS, Membership Services, 1200 New York Avenue, NW, Washington, DC 20005
FAX TO: (202) 842-1065
OR CALL: (202) 326-6417

☐ Check enclosed (payable to "AAAS") for: $ _____

☐ Charge $ _____ to my credit card:

☐ Visa ☐ MasterCard ☐ American Express

CARD # _____ EXP.

SIGNATURE _____

NAME (PLEASE PRINT) _____

INSTITUTION _____

STREET ADDRESS _____

CITY _____ STATE _____ ZIP/POSTAL CODE _____

COUNTRY _____

EMAIL ADDRESS _____

Rates valid until 12/31/99. $62 allocated to *Science*. $12 allocated to *Science Online*. Please allow 4 weeks for receipt of first paper issue of *Science*.

S9XSM2

Stay up-to-date on the past, present, and future of science!

24 HOURS A DAY, 7 DAYS A WEEK

past

Access the *Science* archives
Read summaries, abstracts, or full-text articles from back issues of *Science*, as far back as October, 1995.

Search for the specific science news and information you want
Quickly and easily search for past or current articles by keyword, author, article title, or *Science* issue. Instantly hyperlink from articles in *Science* to citations in Medline and the ISI Citation Index, with links to full-text articles in 200 scientific journals.

scienceonline.org

present

Keep up-to-date on new scientific research
From any computer, access the current issue of *Science* on the day of publication. Plus, the online version contains an authors' index, select policy forums, special essays, and supplementary materials (articles, resources, graphics) not found in print.

Daily news briefings
Access *Science*NOW's easy-to-read, daily updates of the hottest scientific, medical, and technological news. Plus, read concise overviews of exciting new research in *Science*'s Compass.

Go shopping
Explore current catalogs, brochures, technical applications sheets and new product information from the world's leading science manufacturers and suppliers.

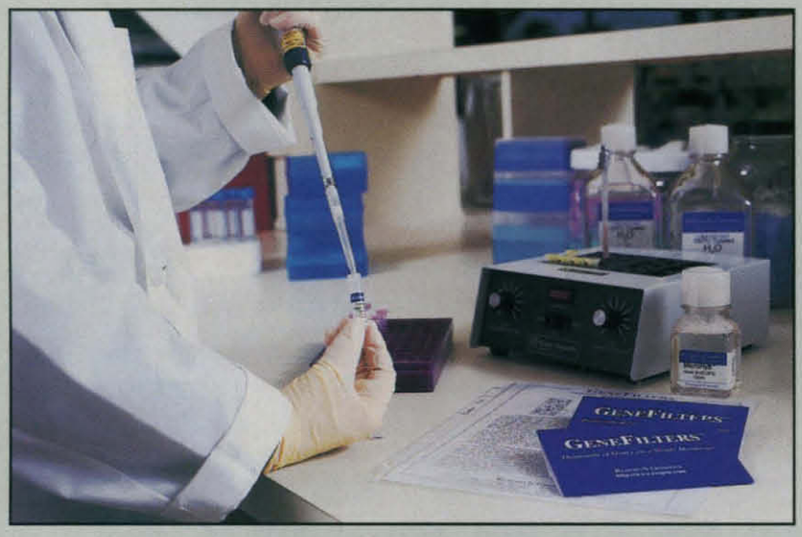
future

Look for a new career
Prepare for your future with *Science*'s NextWave—look for a job, receive career advice, review salary surveys, and more. Plus, sign up for job alerts and we'll notify you via email when jobs open up within criteria you've selected.

Save your valuable time—we'll do the work for you
Don't worry about searching for articles on developing topics in science. We'll let you know when the news comes in. *Science Online* provides personalized email alerting services for online subscribers. Sign up for CiteTrack Personal Alerts, and we'll notify you whenever new content in a participating journal is published that matches criteria based on the topics, authors, and articles you choose.

Total RNA

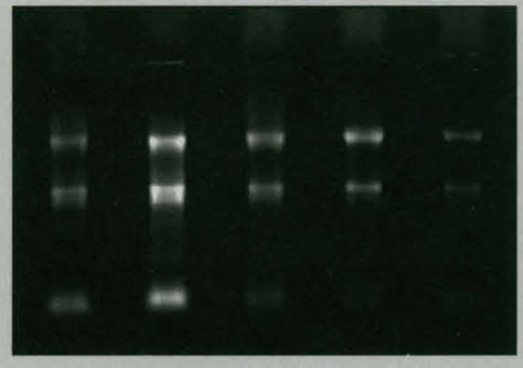
Now Available from Human, Mouse and Rat Tissue



- Preparation of poly-A$^+$ RNA
- cDNA libraries
- Northern analysis
- Differential display
- RT-PCR
- Probe preparation

Tissue specific total RNA extracts are often needed for cDNA synthesis, RT-PCR, Northern electrophoretic or dot blots, or for differential display analysis. Research Genetics now has total RNA from a variety of tissues in stock and ready for shipment. RNA is extracted from fresh tissue using a modified guanidinium thiocyanate method. Extracts are evaluated on denaturing agarose gels for intact 28S and 18S ribosomal RNA. Researchers will receive a total of 250µg of RNA for $250.00. We also offer extracts from paired (tumor and normal) tissues. These are sold as a pair for $500 (250µg of each extract).

Currently, RNA is available from a variety of human, mouse, and rat tissues. Please see our website for a complete list of extracts and to place your order online. Please send e-mail to cnaves@resgen.com if you have questions about this new product.



Samples were run for 1 hr, 20 min at 70 volts on a 1.2% agarose/formaldehyde gel. From left to right, the lanes are human heart, human total brain, fetal liver, fetal thymus and fetal heart.

® Research Genetics and Accelerating Discovery are U.S. registered trademarks/service marks of Research Genetics, Inc. (Huntsville, AL).

Research Genetics®

Accelerating Discovery®

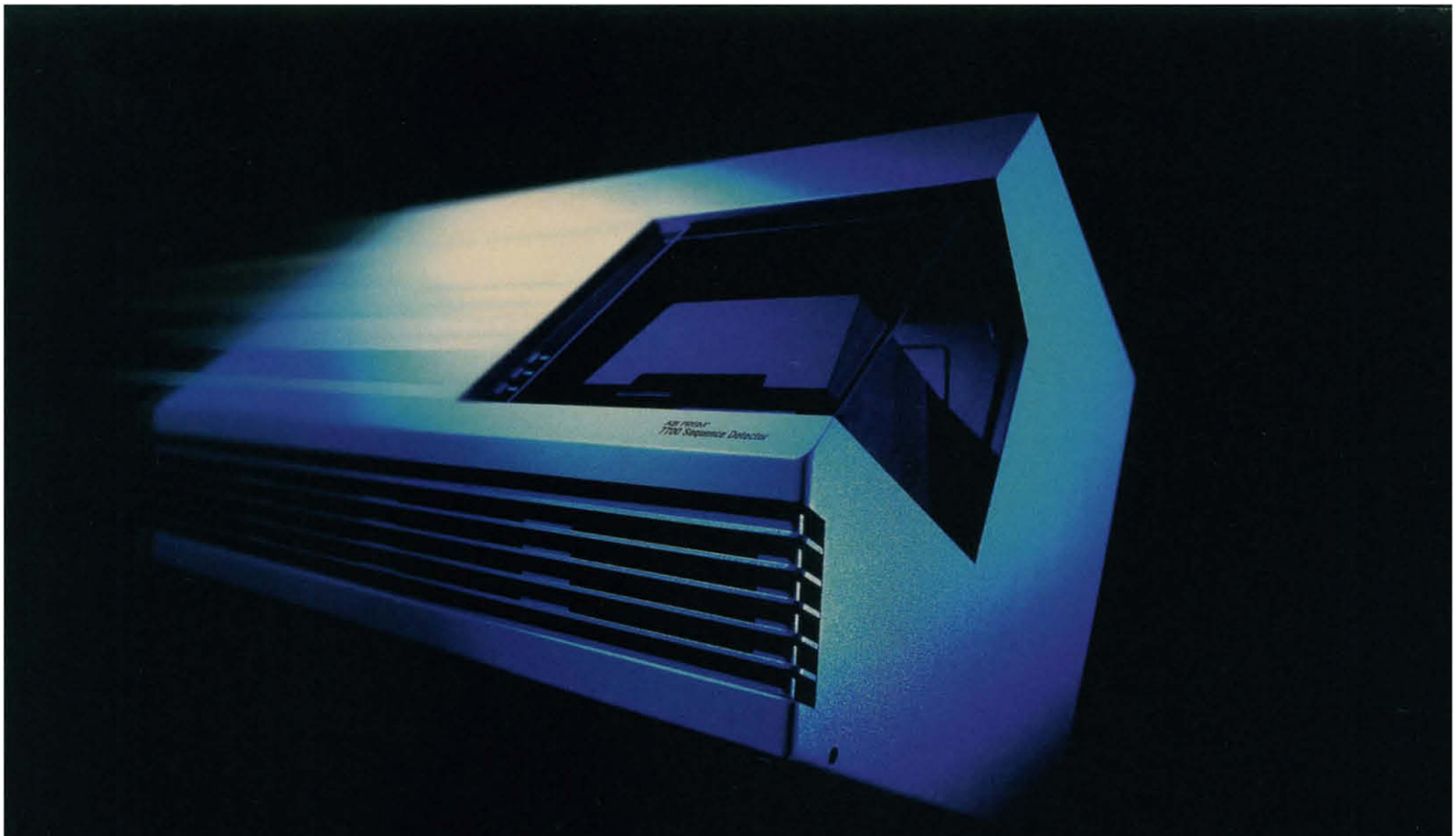
2130 Memorial Pkwy, SW • Huntsville, AL • 35801

U.S. or Canada 800-533-4363 Worldwide 256-533-4363

U.K. 0-800-89-1393 FAX 256-536-9016

http://www.resgen.com

Circle No. 73 on Readers' Service Card



Think of it as a time machine.

The ABI PRISM® 7700 Sequence Detection System compresses weeks of work into hours. Quantitation of nucleic acids is now faster and more automated than ever before due to the breakthrough of real-time quantitative PCR. Not only is the assay development simple and quick using our proven and well-defined assay design guidelines, but all post-PCR processing steps are eliminated by the integration of thermal cycling, detection, and data analysis. No electrophoresis. No radioactivity. This total solution delivers the highest sample throughput available, enabling thousands of reactions per week. Add our world-class service and support, and you've got a whole new way to speed up your research process. For more information, call 1.650.638.5800.

Real-time quantitative PCR. **Work toward discovery, not against time.**

ABI PRISM® 7700 Sequence Detection System

Applied Biosystems

PE Biosystems

Roche

ISO 9000

Tel: 1.800.345.5224 or 1.650.638.5800. Fax: 1.650.638.5884. www.pebiosystems.com

The PCR process is covered by patents owned by Roche Molecular Systems, Inc. and F. Hoffmann La-Roche Ltd. Applied Biosystems, PE, and PE Biosystems are trademarks, and ABI PRISM and its design are registered trademarks, of the Perkin-Elmer Corporation. PE Applied Biosystems develops and manufactures its products in accordance with ISO 9000 quality systems requirements. For Research Use Only. Not for use in diagnostic procedures.

Circle No. 74 on Readers' Service Card

Reliable delivery *at* constant rates.

ALZET® Osmotic Pumps—providing accurate drug delivery for over 20 years.

By ensuring the dependable delivery of biological, chemical or therapeutic agents, either systemically or to a targeted tissue or organ, ALZET osmotic pumps can help ensure the reliability of your data. Using one of ten osmotic pump models which feature a variety of rates and durations, you can continuously deliver diverse compounds to unrestrained animals. You can even use a brain infusion kit for direct delivery to the central nervous system.

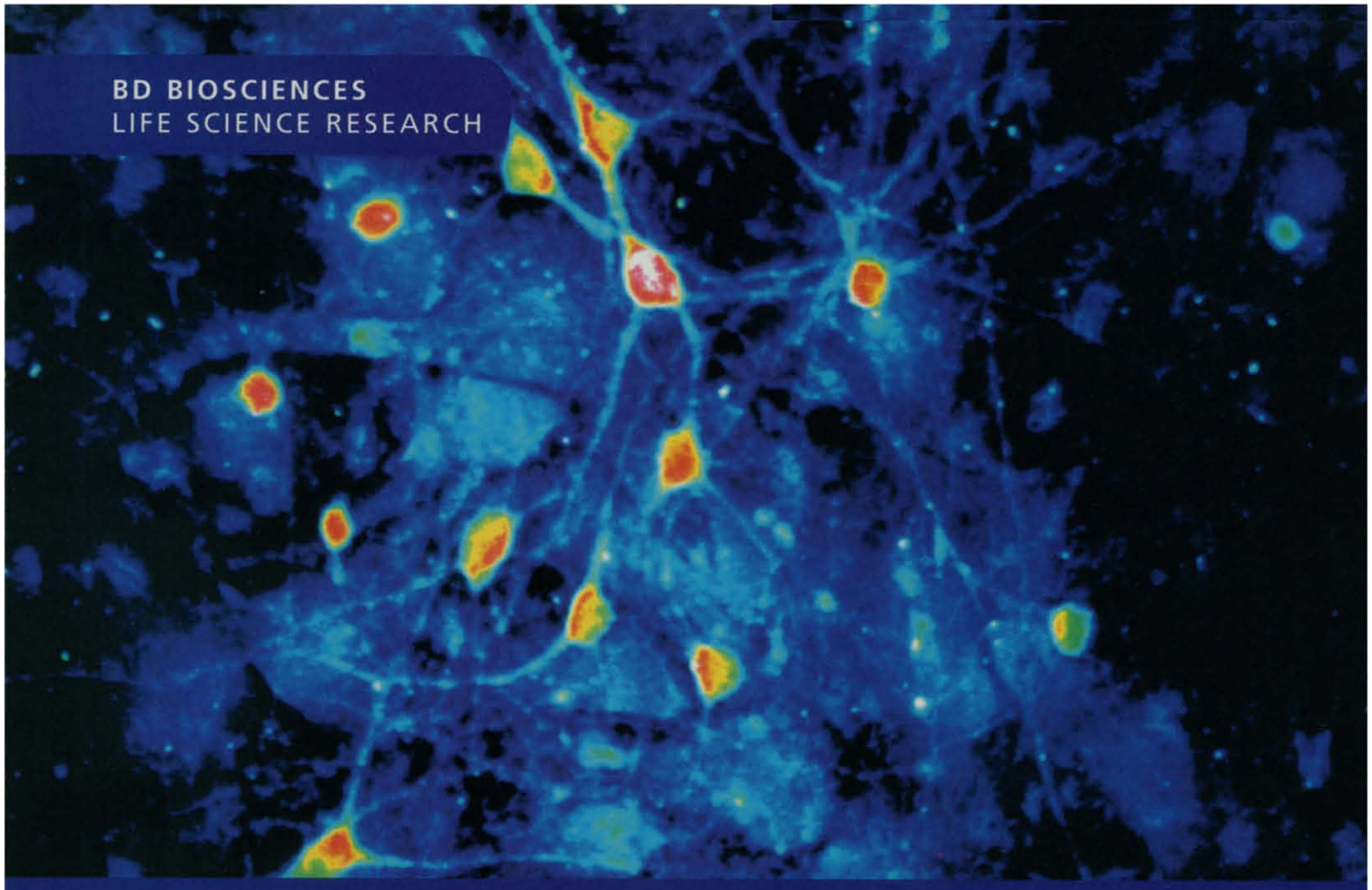
CONTINUOUS DELIVERY CAN SAVE RESEARCHER TIME.

For more than 20 years, ALZET osmotic pumps have helped researchers save critical research time by eliminating the need for frequent, round-the-clock injections. And with zero order delivery, these pumps have proven invaluable in ensuring that predictable compound levels are sustained at therapeutic concentrations, avoiding potentially toxic or misleading side effects.

In fact, more than 5,200 published references attest to the remarkable reliability of these unique self-powered pumps. To learn how you can employ these well proven delivery systems, visit www.alza.com/alzet/rates or call 1-800-692-2990 or 650-962-2251.

alzet®
OSMOTIC PUMPS
www.alza.com/alzet/rates
alzet@alza.com

Circle No. 22 on Readers' Service Card



Connecting You with Solutions for Neuroscience Research

BD Biosciences provides a comprehensive offering of technology, tools, and expertise to accelerate your neuroscience research. We are committed to offering you a complete system of innovative products for cell culture, function, and analysis.

Cell Culture

Our BD BioCoat™ cellware optimizes cell culture performance by promoting attachment, spreading, growth and differentiation of a variety of neuronal cells. We offer various coated vessels, such as glass coverslips, CultureSlides and tissue culture plasticware. Available coatings include Collagen I, Poly-Lysine, Laminin, Poly-D-Lysine/Laminin, Poly-L-Ornithine/Laminin, Laminin/Fibronectin, EHS Natrix.

Cell Function & Analysis

Our BD PharMingen™ and BD Transduction Laboratories™ antibodies enable studies of cell function and analysis, including neurotransmitters and receptors, neurofilaments and other neuronal markers, growth factors, cytokines and receptors, caspases, and the Bcl-2 family. Our BD RiboQuant™ RNase protection assay kit and multi-probe template sets provide a complete system for analyzing mRNA expression.

By bringing together this system of products, BD Biosciences offers a complete solution to the life science research community for neuroscience research.

For research use only. Not for use in diagnostic or therapeutic procedures.

Photo: Neurotransmitter induced calcium waves in astrocytes plated on Laminin/Fibronectin coated coverslips.

BD Biosciences
www.bdbiosciences.com

In the US, please call 1-800-343-2035 for more information on BD BioCoat™ products; for BD PharMingen™ and BD Transduction Laboratories™ products, please call 1-800-848-6227.

Circle No. 72 on Readers' Service Card

BD
Indispensable to human health

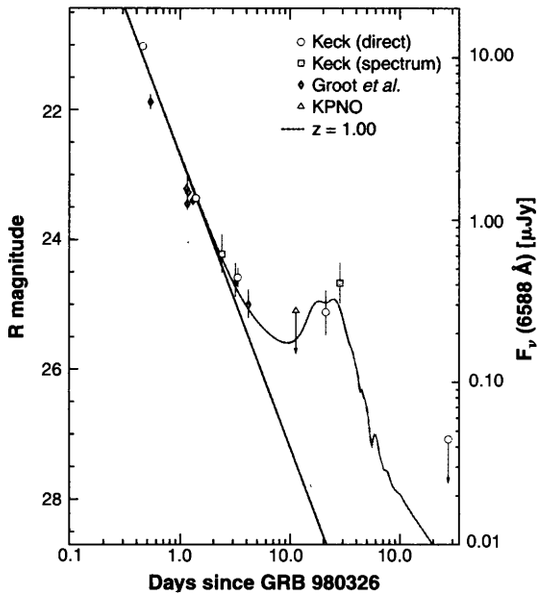
detected simultaneously with the gamma-ray emissions; for a brief moment, this optical emission became as bright as 10 million type Ia supernovae (*7*).

The ability to determine the location of and distance to a GRB and observe its burst and decay in detail at a variety of different wavelengths has allowed astronomers to test GRB models. An early model, developed long before the present observations, proposed that GRBs were caused by a shock wave emerging from the photosphere of a supernova (*3*). However, this model was soon discarded, as the GRB discovery paper already showed that there was no known correlation of GRBs with observed supernovae. Now after detailed studies of several GRBs in the late 1990s have revealed more information, theorists propose a connection between GRBs and supernovae.

There are at present two main models for GRBs. In the first, two compact stars (such as a neutron star and a black hole) coalesce (*8*). In the second, the core of a presumably very massive star collapses, leaving behind a black hole surrounded by a solar mass accretion disk (*9*). In this second, so-called collapsar model, the GRB is produced by a relativistic jet that pierces through the exploding star along its rotational axis. In addition to the fast GRB, a much slower (~10^4 km/s) outflow is produced, giving rise to thermal emission from an expanding photosphere, that is, a supernova. If this model is correct, one would thus expect a (relatively weak) supernova to be apparent in the afterglow light curve of GRBs.

The first direct evidence for a connection between GRBs and supernovae came from observations of GRB980425, which occurred on 25 April 1998 (see figure on previous page). The BeppoSAX satellite determines an area called the error box, in which a GRB must have occurred. The error box for GRB980425 also contained a supernova, SN1998bw, located in a spiral arm of galaxy ESO 184-G82 (*10*). This galaxy lies at a distance of ~40 megaparsecs from Earth, cosmologically speaking just around the corner from the Milky Way. GRB980425's energy budget was quite small, a factor of ~10^5 smaller than that of normal GRBs. The probability of finding a supernova as bright as SN1998bw that would explode within a day of the burst inside the error box of GRB980425 is on the order of 10^{-4}, and thus a physical association between the two seemed likely (*10*). Some researchers have rejected the association, because of the presence of a faint x-ray source in the GRB error box (which does not coincide with the supernova) that could be the GRB afterglow. But a recent analysis of this x-ray source by Pian *et al.* (*11*) shows that it is unlikely to be a GRB afterglow.

Independent of its association with the GRB, SN1998bw was a remarkable event.



Afterglow. R-band light emission of GRB980326 as measured by various sources superimposed on a relatively faint supernova light curve (red) at a redshift of about 1, which fits the data well.

It is by far the most luminous supernova observed to date at radio wavelengths, and its properties indicated the presence of a mildly relativistic outflow at about 90% the speed of light (*12*). It has been classified as a type Ic supernovae; that is, hydrogen and helium are absent in its spectra. Such supernovae are believed to have lost their hydrogen- and helium-rich envelope in a strong stellar wind or as a result of mass transfer in a binary star. The optical light curve and spectra of SN1998bw indicate that the exploding star was a CO star of about 10 solar masses, whose core collapse probably left a black hole. The amount of radioactive ^{56}Ni produced in the event has been estimated to be ~0.75 solar masses, an order of magnitude higher than that of typical type Ic supernovae, with a total explosion energy of several 10^{52} ergs (*13*).

A recent study (*14*) has been able to fit the decay properties of GRB980425 and SN1998bw with a model similar to the collapsar model.

Recently, evidence for a second GRB coinciding with a supernova was found in the case of GRB980326 (*14*). Several weeks after the burst, the afterglow brightened by a factor of 60, compared with the extrapolation of the early power law decay (see figure on this page). Afterward, the flux decay continued, showing that the flattening of the light curve does not reflect the steady light of a host galaxy. Bloom *et al.* (*14*) successfully modeled the light curve of GRB980326 with a combination of a power law afterglow and the light curve of SN1998bw, redshifted to about 1. The very steep afterglow decay of GRB980326 can be explained by a blast wave propagating in the wind of a massive star.

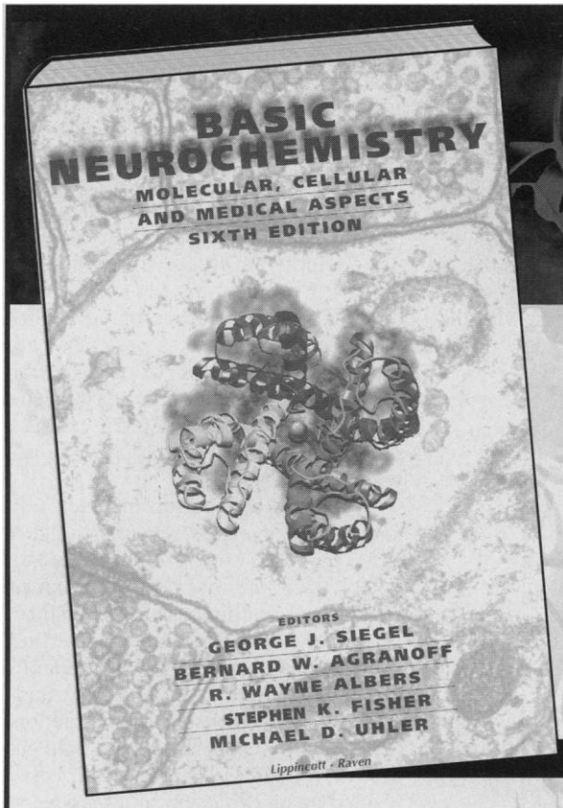
A similar connection between GRBs and supernovae was recently suggested (*15*) for the optical light curve of GRB970228, the first GRB to be optically identified. In this case, the redshift is known, and the only free parameter in the fit to the light curve is the exponent of the power law component. Chevalier and Li (*16*) have shown that after subtraction of the supernova contribution, the light curve of GRB970228 is also steep and best explained by an explosion in a massive stellar wind, lending further support to the association between GRBs and supernovae.

The exciting consequence of these recent studies is that at least some GRBs, and perhaps all of them, originate from the core collapse of very massive stars. The supernova connection provides a direct link between GRBs and crucial events in the evolution of massive stars and galaxies. This framework for describing GRBs promises a rapid increase in our understanding of this violent phenomenon.

CREDIT: J. BLOOM

References and Notes

1. See G. J. Fishman and C. A. Meegan, *Annu. Rev. Astron. Astrophys.* **35**, 415 (1995) for a review on GRB theory; see also T. Piran, *Phys. Rep.* **314**, 575 (1999).
2. C. Meegan *et al.*, *Nature* **355**, 143 (1992).
3. S. A. Colgate, *Can. J. Phys.* **46**, 5476 (1968); *Astrophys. J.* **187**, 333 (1974).
4. G. Schilling, *Science* **286**, 395 (1999).
5. E. Costa *et al.*, *Nature* **387**, 783 (1997); J. Van Paradijs *et al.*, *ibid.* **386**, 686 (1997); D. Frail *et al.*, *ibid.* **389**, 261 (1997).
6. M. Metzger *et al.*, *ibid.* **387**, 878 (1997).
7. C. A. Akerlof *et al.*, *ibid.* **398**, 400 (1999).
8. J. M. Lattimer and D. N. Schramm, *Astrophys. J.* **192**, L145 (1974); D. Eichler *et al.*, *Nature* **340**, 126 (1989); R. Mochkovitch *et al.*, *ibid.* **361**, 236 (1993).
9. S. E. Woosley, *Astrophys. J.* **405**, 273 (1993); B. Paczynski, *ibid.* **454**, L45 (1998).
10. T. J. Galama *et al.*, *Nature* **395**, 670 (1998); E. Baron, *ibid.*, p. 635.
11. E. Pian *et al.*, private communication.
12. S. R. Kulkarni *et al.*, *Nature* **395**, 663 (1998).
13. K. Iwamoto *et al.*, *ibid.*, p. 672; S. E. Woosley *et al.*, *Astrophys. J.* **516**, 788 (1999).
14. J. S. Bloom *et al.*, preprint available at http://xxx.lanl.gov/abs/astro-ph/9905301.
15. D. Reichart, *Astrophys. J.* **521**, L111 (1999); T. J. Galama *et al.*, preprint available at http://xxx.lanl.gov/abs/astro-ph/9907264.
16. R. Chevalier and Z. Li, *Astrophys. J.* **520**, 271 (1999), preprint available at http://xxx.lanl.gov/abs/astro-ph/9908272.



Basic Neurochemistry

Molecular, Cellular and Medical Aspects, Sixth Edition

Editor-in-Chief:
George J. Siegel, MD

Editors:
Bernard W. Agranoff, MD
R. Wayne Albers, PhD
Stephen K. Fisher, PhD and
Michael D. Uhler, PhD

Illustrations by Lorie M. Gavulic, MFA

Sponsored by the American Society for Neurochemistry

Basic Neurochemistry provides a clear introduction to the chemistry underlying brain structure and function. The standard text for the field, it's your key to understanding the fundamental processes involved in nervous system functions as well as in neurological and psychiatric disorders.

The Sixth Edition features extensive revision of all chapters for current content. In addition, new chapters by new contributors cover these topics:

- ✓ cell-cell interactions
- ✓ intracellular trafficking
- ✓ nerve growth and regeneration
- ✓ apoptosis
- ✓ and prion disease.
- ✓ adhesion molecules and extracellular matrix
- ✓ cytosol-nuclear communication
- ✓ excitotoxicity
- ✓ drug addiction

Your colleagues praised the previous edition of **Basic Neurochemistry**, saying...

"Excellent.... Basic Neurochemistry falls into that rare category of the only book that's needed [for] an excellent grounding in our subject." —*Journal of Neurochemistry*

"A real winner.... It has broad appeal as a text, a reference, or simply to broaden your view of the neurosciences." —*Journal of Neuroscience Research*

1999 • 1,183 pages • 557 illustrations • 95 tables

Basic Neurochemistry 6e (TEXT) 0-397-51820-X
Basic Neurochemistry 6e(CD-ROM) 0-7817-1745-0
SAVE! Basic Neurochemistry 6e (TEXT & CD-ROM SET) 0-7817-1746-9
Basic Neurochemistry 6e (SLIDE SET) 0-7817-1742-2

LIPPINCOTT WILLIAMS & WILKINS
A Wolters Kluwer Company

It's Easy to Order!

CALL: In the U.S. 800-638-3030; Outside the U.S. 301-714-2334
FAX: In the U.S. 301-824-7390; Outside the U.S. 301-714-2365
WORLD WIDE WEB: LWW.COM • E-MAIL: ORDERS@LWW.COM
Or order directly from you local medical bookstore or publisher representative

L9NEB672 D9B672

Circle No. 25 on Readers' Service Card

Q: PEPTIDES?
A: PEN LABS

Q: GMP?
A: PEN LABS

You've got questions? We've got answers.

As a leading supplier of synthetic peptides for over 25 years, we know what it takes to provide GMP products on time and on budget. And we know that when qualifying a cGMP manufacturing partner for your pharmaceutical-grade peptide, it's critical that you ask the right questions. We suggest you start with these:

1. Are the manufacturing facilities under strict environmental control, FDA- licensed and inspected?
2. Are cGMP procedures and processes validated?
3. Will your DMF (drug master file) be developed and maintained to FDA standards?
4. Will purity, identity, and integrity be evaluated by validated QC methods?
5. Are all cGMP personnel qualified, fully trained and cGMP certified?

At Peninsula Laboratories, the answer to each of these questions is an emphatic YES! Your peptide will be produced in full compliance with cGMP requirements. And our facilities stand up to the closest scrutiny.

So, bring all your cGMP questions to Peninsula Laboratories. We make it our business to provide you with answers.

Any questions? Contact Peninsula Laboratories today. We'll give you the answers along with a free copy of our comprehensive 100-page guide, *GMP Manufacturing of Synthetic Peptides*. Phone: (800) 922-1516, ext.174. Fax:(650) 595-4071. E-mail: GMP@penlabs.com.

Visit us on the Web at
www.penlabs.com

PENINSULA LABORATORIES

601 Taylor Way, San Carlos, CA 94070

Circle No. 24 on Readers' Service Card

GIBCO BRL® Products and Services for Cell Culture.

LIFE TECHNOLOGIES®

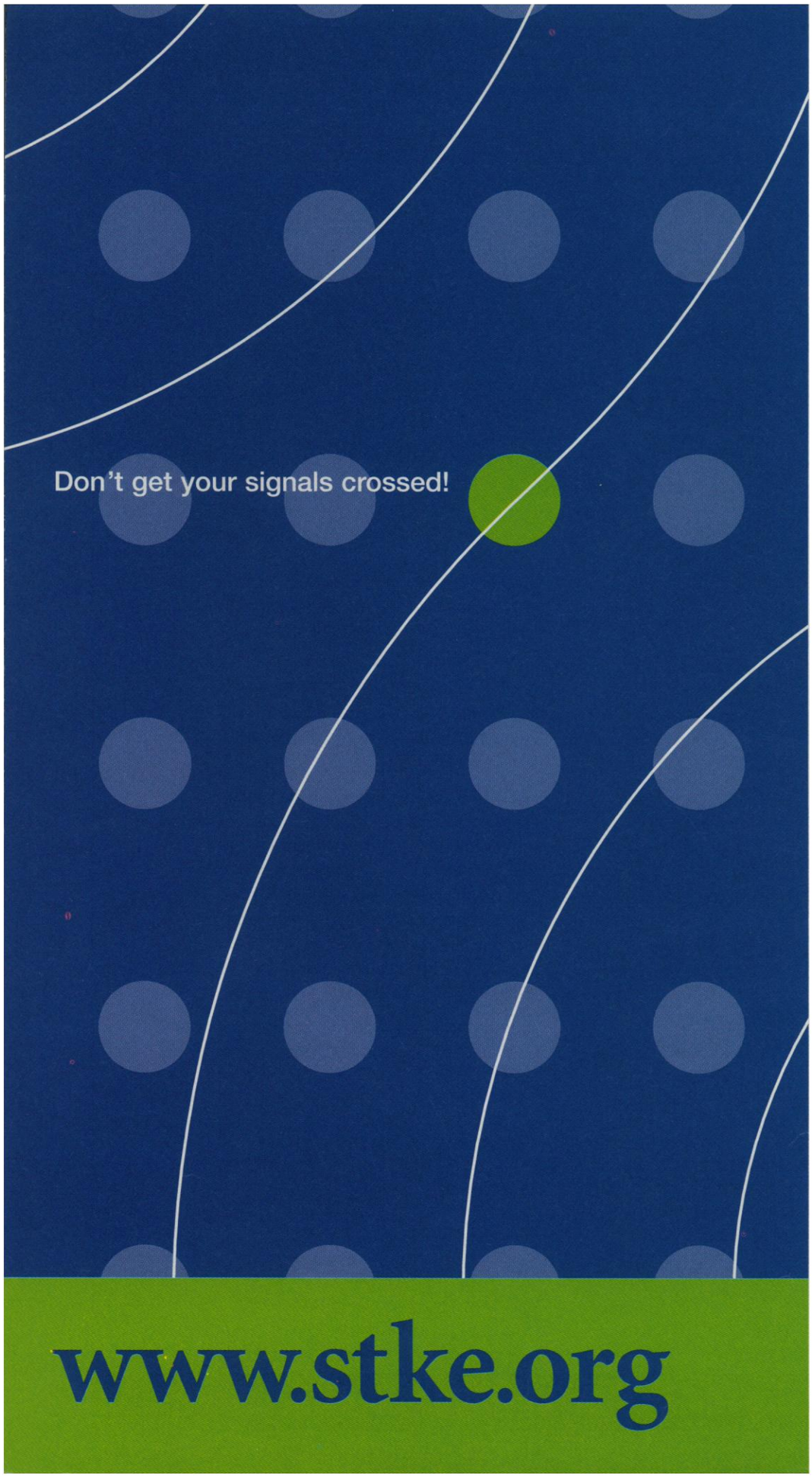
Essential Technologies for the Science of Life™

Internet Ordering and Information: **www.lifetech.com**

U.S. Academic Orders/TECH-LINE℠: (800) 828-6686
U.S. Government Orders/TECH-LINE: (888) 584-8929
U.S. Industrial Orders/TECH-LINE: (800) 874-4226
Latin America Orders/TECH-LINE: (301) 610-8709 **Canada Orders:** (800) 263-6236

These products are for laboratory research use only and are not intended for human or animal diagnostic, therapeutic, or clinical uses, unless otherwise stated. ©1999 Life Technologies, Inc. 98-09CRE

Circle No. 59 on Readers' Service Card



Feeling overwhelmed by all of the information that is constantly being published on signal transduction?

The editors of *Science* and the technical staff of Stanford University's HighWire Press have your solution—*Science*'s Signal Transduction Knowledge Environment (STKE).

Benefits Include:

VIRTUAL JOURNAL

Say goodbye to scanning dozens of tables of contents every week.

THE CONNECTIONS MAP

Having trouble keeping track of a thousand and one protein kinases? Not anymore.

CONTINUOUSLY UPDATED REVIEWS

Original content that is updated as frequently, as extensively, as developments in the field warrant.

Come to **www.stke.org** to improve your signal-to-noise ratio.

Science's stke

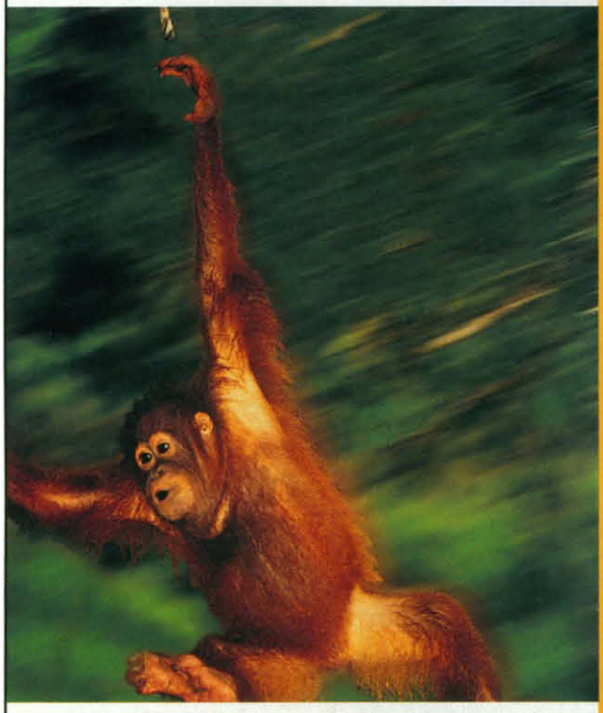
Signal Transduction Knowledge Environment

a product of *Science* & Stanford University Libraries

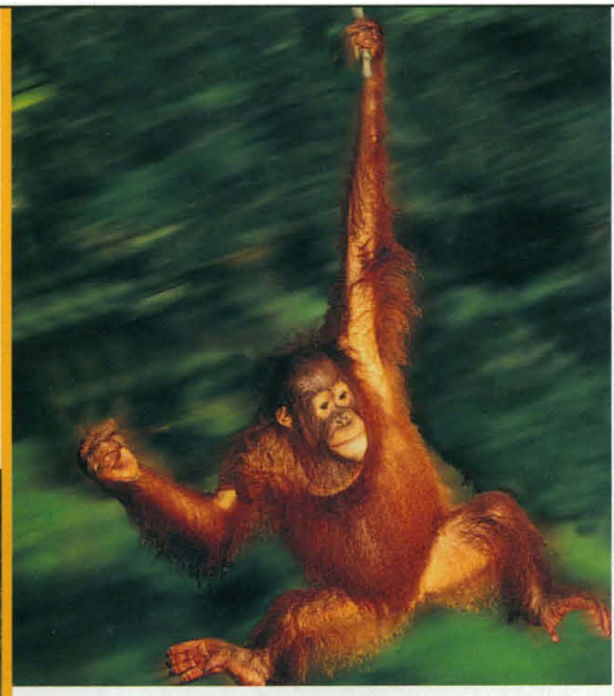
Science

AAAS HHMI

What a Difference



Accuracy Makes.



If you haven't been using our DNA sequencing services, you've been missing something. We provide exceptionally accurate DNA sequencing – over 99.995% accurate for genome sequencing. Our sequencing reads for plasmid inserts are typically over 900-1000 bases at greater than 99% accuracy.

At MWG-Biotech, Inc. we offer a variety of DNA sequencing services to fit most needs, from hundreds of base pairs to megabase pairs. Whether it's a cloning project or gap closures in your genome sequencing, we have it covered. Long read sequencing is our specialty, for fast performance at low cost. Accuracy, satisfaction and confidentiality are assured.

After all, DNA sequencing shouldn't be a hit-or-miss affair. And with MWG it isn't.

MWG Inc BIOTECH

4170 Mendenhall Oaks
Parkway, Suite 160
High Point, NC 27265

TEL: 336.812.9995
FAX: 336.812.9983
info@mwgbiotech.com

ONLINE ORDERING AND TRACKING

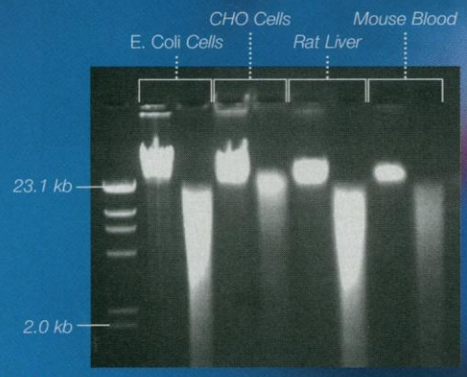
www.mwgbiotech.com

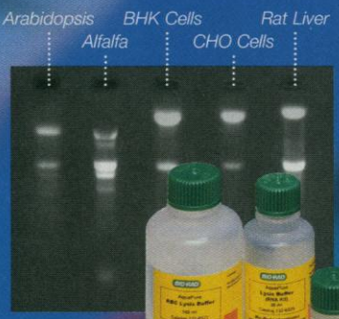
Circle No. 70 on Readers' Service Card

DNA and RNA of the highest purity and yield.

Dedicated Quantum Prep® Kits for:

- non-toxic genomic DNA and total RNA isolation
- transfection quality DNA
- efficient gel extraction
- high yield maxipreps
- rapid minipreps





New

Quantum Prep AquaPure Genomic DNA Isolation Kits. Scalable, phenol-free protocols eliminate spin columns and membranes to allow processing of a wide range of sample sizes. Samples of purified DNA (left) were digested with *Eco* R1 (right).

New

Quantum Prep AquaPure RNA Isolation Kits. Non-toxic aqueous reagent protocols eliminate the need for phenol and chloroform extractions for the isolation of highly purified RNA from cells, animal and plant tissue, and whole blood.

Nucleic Acid Purification Products. Over forty years, Bio-Rad has been the leader in separation, purification and analysis of proteins and nucleic acids. Our nucleic acid purification products help molecular biologists obtain DNA and RNA of the highest purity and yield. So when it comes to your laboratory needs, trust Bio-Rad — the company that knows about separations. For more information, contact your Bio-Rad representative, or visit our web site.

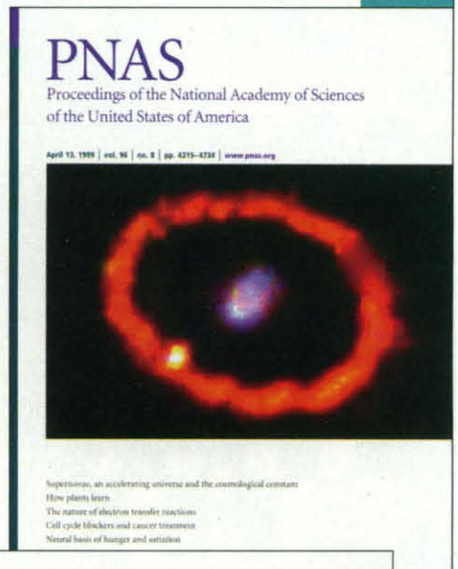
What Will You Discover Next?

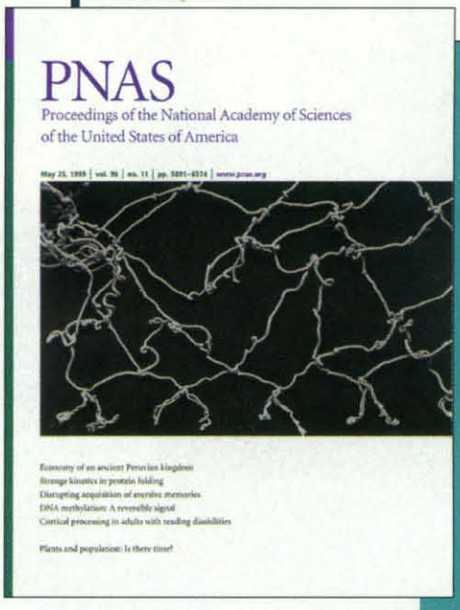
Visit our Life Science web site at discover.bio-rad.com.
Call toll free at 1-800-4BIORAD (1-800-424-6723); outside the U.S., call (510) 741-6996.

BIO-RAD

Circle No. 52 on Readers' Service Card

Call for Papers in the Physical Sciences, Social Sciences, and Mathematics





The National Academy of Sciences is targeting the physical sciences, social sciences, and mathematics as areas to promote through its official journal, the *Proceedings of the National Academy of Sciences*. Among the many advantages of publishing in PNAS are:

- **Rapid publication**
- **Broad, interdisciplinary worldwide audience**
- **Fast, thorough peer review**
- **Publication costs are waived for those with insufficient funds**
- **Second most-cited scientific journal in the world**
- **PNAS Online is robust with free interjournal links, free back issues, free collections of papers, and extensive links to other databases (www.pnas.org)**

Many institutions already have campus-wide site licenses for PNAS Online. PNAS also encourages the distribution of preprints. PNAS articles receive broad media coverage, and exceptionally noteworthy papers are highlighted by commentaries or featured on the journal cover.

Direct Submission

Papers may be submitted directly to the PNAS Editorial Office, which will identify an Academy Member expert in your field to edit your paper. Alternatively, you may contact an expert Academy Member yourself to conduct the review.

For further information about publication of research in the physical sciences, social sciences, and mathematics, please contact:

Guy Riddihough
Associate Recruiting Editor
PNAS
2101 Constitution Ave NW FO2013
Washington, DC 20418 USA

Phone: 1-202-334-1370
Fax: 1-202-334-2738
Email: griddiho@nas.edu

PNAS

Circle No. 44 on Readers' Service Card

Now available:

Enough titles to trigger some effector functions.

ISBN: 0122270754

List price $250.00/ Our price $175.00
You save $75.00

List price $95.00 / Our price $66.50
You save $28.50

ISBN: 0124005608

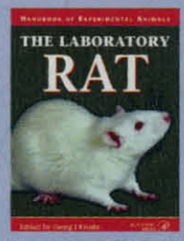
ISBN: 0122886607

List price $69.95 / Our price $48.96
You save $20.99

ISBN: 012643140X

List price $99.95 / Our price $69.97
You save $29.98

ISBN: 012426400X



List price $189.95 / Our price $132.96
You save $56.99

ISBN:0126392900

List price $49.95 / Our price $34.96
You save $14.99

ANNOUNCING THE NEW PROFESSIONAL & TECHNICAL STORE AT AMAZON.COM

What does Amazon.com know about science? Enough to know that you need the latest science books, and you need them fast. And at our new Professional & Technical store, that's exactly what you'll get. Thousands of scientific titles, plus expert and peer book reviews. Not to mention everyday savings of up to 30%. It's something we call synthesis. And it's something you'll find at www.amazon.com/professional.

EARTH'S BIGGEST SELECTION JUST GOT BIGGER.
books video dvd music auctions e-cards toys electronics

©1999 Amazon.com, Inc. All rights reserved. Amazon.com is the registered trademark of Amazon.com, Inc.

Tomorrow's Science Today...

...at your convenience

Subscribe to Science and ScienceONLINE
www.scienceonline.org

All US orders or enquiries:
TEL: 202 326 6417 FAX: 202 842 1065
EMAIL: membership@aaas.org

All International orders or enquiries:
TEL: +44 (0)1223 326 500 FAX: +44 (0)1223 326 501
EMAIL: subscriptions@science-int.co.uk


The hungry old Wolf will huff, puff and blow your house down!
What is your cloning system made of: straw, wood or idle promises?
Fear not.
Remember,
every new gene
or therapeutic
discovered will
begin with a cloning experiment.
Our purpose is humble,
but our Technology is not.
TrueBlue® Technology
is simply superior!
...now make your
life's work immortal.
GENOMICS ONE™
Tel: (450) 688-4499 • Fax: (450) 688-9100
Info@GenomicsOne.com • www.GenomicsOne.com
© 1999 Genomics One Corporation.
Circle No. 63 on Readers' Service Card

TOTAL IMAGING SOLUTIONS

for Macintosh and Windows

www.scanalytics.com

NEW

Free PC with every order of IPLab for Windows!

- IPLab software provides fully-integrated image acquisition, enhancement and analysis
- Finally, a conflict-free workstation pre-configured for your imaging needs

Call 703-208-2230 for details

from Scanalytics, Inc.

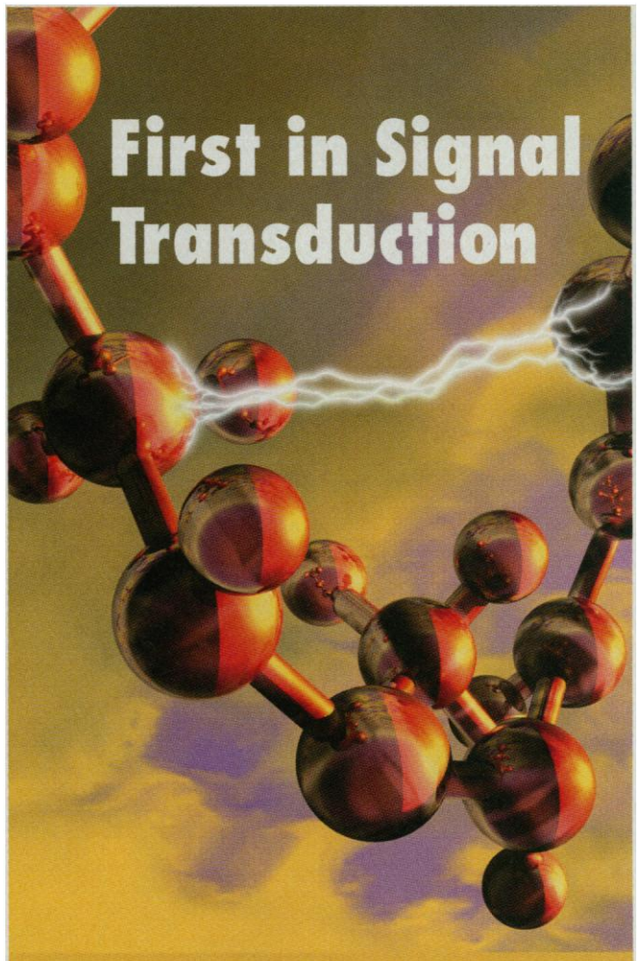
The Innovations Leader in Scientific Imaging

Visit us at the 1999 Neuroscience Meeting
October 24-27, Miami Beach, FL, Booth 1614

Scanalytics, Inc.

8550 Lee Highway
Suite 400
Fairfax, VA 22031
Phone: (703) 208-2230
Fax: (703) 208-1960
Email: info@scanalytics.com

Circle No. 76 on Readers' Service Card



First in Signal Transduction

Products for:

- *Apoptosis*
- *Lipid signaling*
- *Protein kinases/phosphatases*
- *Gene regulation*
- *Proteasome and proteases*

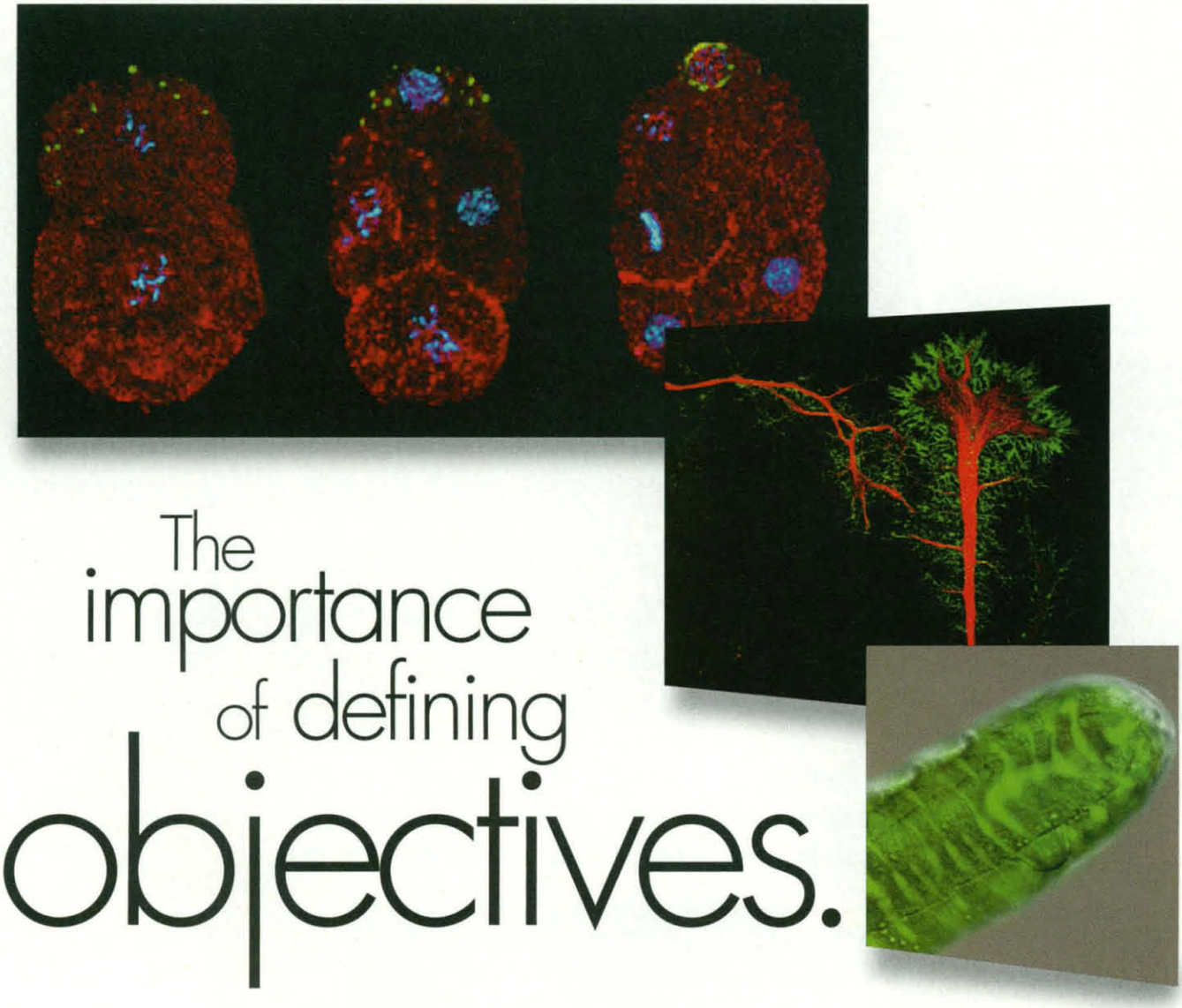
Call: 800-942-0430
Visit: www.biomol.com

BIOMOL®

Capture the Power

BIOMOL Research Laboratories, Inc.
5100 Campus Drive Plymouth Meeting, PA 19462-1123 USA
phone: 610-941-0430 fax: 610-941-9252
e-mail: info@biomol.com

Circle No. 8 on Readers' Service Card



The importance of defining objectives.

Whatever your advanced imaging objectives, advanced CFI60™ optics can handle them.

When your requirements involve spectral wavelength imaging from the IR to the UV, the secret to great images is the improved signal-to-noise performance designed into Nikon's CFI60 objectives.

You'll find over 80 CFI60 objectives including those needed for techniques such as multi-photon/confocal, detection of GFP expression, DIC, phase contrast, fluorescence and deconvolusion-restoration microscopy.

For a demonstration of how important it is to define your research objectives with CFI60, call **1-800-52-NIKON, ext. 362.** Or visit us at **www.nikonusa.com**

CFI60
ECLIPSE

Fig. 1 - C. elegans specimen; 3-photon excitation technique on Nikon Diaphot with 60X Plan Apo Oil objective. Provided by J. White, Univ. of Madison, WI and Bio-Rad.

Fig. 2 - Manduca sexta thoracic pupil neurons specimen; immunocytochemical technique on Nikon PCM2000 Confocal with 20X Plan Apo objective. Provided by R. Luedeman and P. Jansma, Univ. of Arizona.

Fig. 3 - Drosophila embryos; time lapse GFP technique on Nikon TE300 with 10X Plan Fluor objective and simple PCI software. Provided by B. Burnip, Compix Inc. and B. Sanson, Univ. of Cambridge, UK.

Circle No. 60 on Readers' Service Card

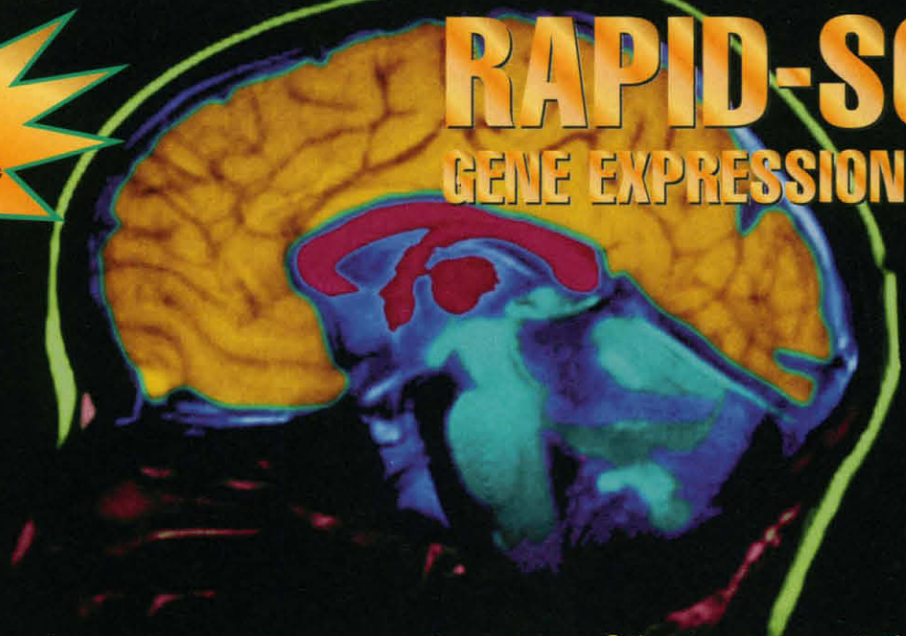
Nikon

Redefining Infinity

© 1999 Nikon Inc.

24 Major Tissue Human and Mouse Panels Also Available

RAPID-SCAN™
GENE EXPRESSION PANELS

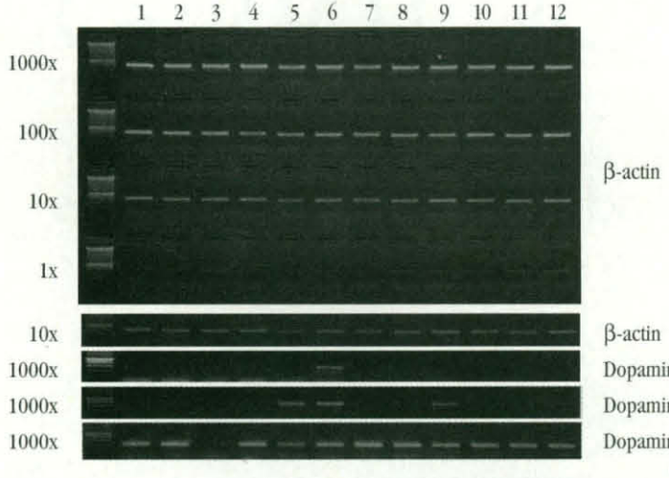


Comprehensive Gene Expression Profile in Just *Three* Hours!

Semi-Quantitative, PCR-Based Analysis of High-Quality,
First Strand cDNAs from 12 Distinct Regions of Human Brain.
(Arrayed on a 48-well Plate / Normalized Against β-actin mRNA / Covering a 4-log Dilution of Each cDNA)

No Radiolabeing of Probe / No Blot Hybridization /
No Filter Washing / No Phosphoimaging or Autoradiogram Exposure
Just do a PCR reaction and run an agarose gel!

1. Frontal Lobe
2. Temporal Lobe
3. Cerebellum
4. Hippocampus
5. Substantia Nigra
6. Caudate Nucleus
7. Amygdala
8. Thalamus
9. Hypothalamus
10. Pons
11. Medulla
12. Spinal Cord



Rapid Scan™ Panels	Catalog #
24 Tissue Human Panel	HSCA-101
24 Tissue Mouse Panel	MSCB-101
12 Tissue/Stage Drosophila Panel	DSCC-101
12 Tissue/Region Human Brain Panel	BSCD-101

Additional panels coming soon.
Call OriGene for more information.

INTERNATIONAL DISTRIBUTORS

Austria and Eastern Europe: RuP Margaritella GmbH
(tel) +43 1 889 18 19 (fax) +43 1 889 18 19 20
France: Clinisciences
(tel) +33-1 42 53 14 53 (fax) +33-1 46 56 97 33
Germany and Benelux Countries: Eurogentec
(tel) +32 4 366 0150 (fax) +32 4 365 5103
Italy
(tel) +39 02-5801 34 50 (fax) +39 02-5801 34 38
Sweden (tel) +46-8-3060 10
Switzerland (tel) +41 061-795 9610
United Kingdom: Cambridge Bioscience
(tel) +44 (01223) 316855 (fax) +44 (01223) 360732

For all other countries, visit the OriGene website or call 301 340 3188

ORIGENE TECHNOLOGIES, INC.

Circle No. 68 on Readers' Service Card

6 Taft Court, Suite 300
Rockville, Maryland 20850
To Order Call 1-888-267-4436
Phone: 301-340-3188
Fax: 301-340-9254
e-mail: custsupport@origene.com
Internet: http://www.origene.com

PCR is covered by patents owned and licensed by Hoffmann-La Roche, Inc. *© 1999 OriGene Technologies, Inc.*