21 May 1999

Science

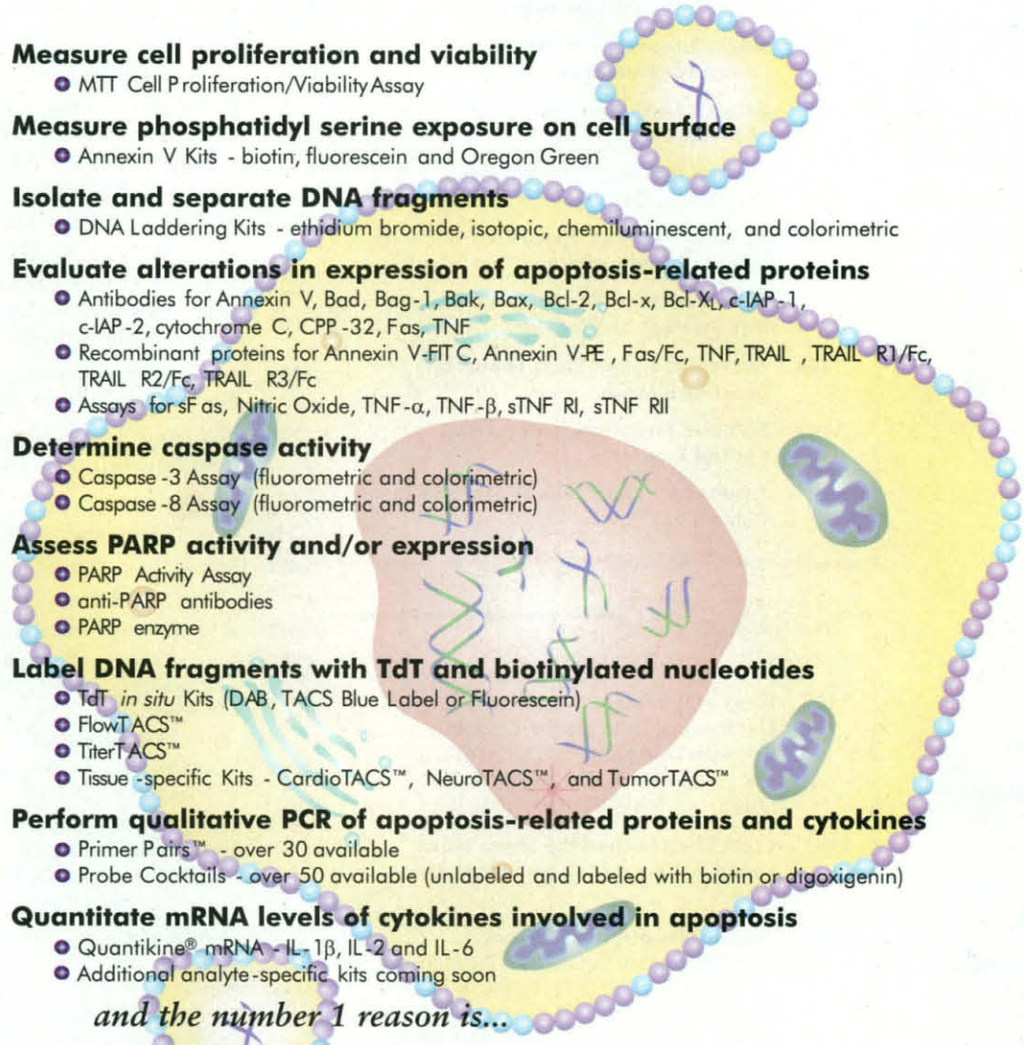
Vol. 284 No. 5418
Pages 1225–1420 $8

Microbes Immunity & Disease

American Association for the Advancement of Science

Top 10 Reasons To Use R&D Systems' Apoptosis Reagents

from the home office in Minneapolis, MN



10. Measure cell proliferation and viability
- MTT Cell Proliferation/Viability Assay

9. Measure phosphatidyl serine exposure on cell surface
- Annexin V Kits - biotin, fluorescein and Oregon Green

8. Isolate and separate DNA fragments
- DNA Laddering Kits - ethidium bromide, isotopic, chemiluminescent, and colorimetric

7. Evaluate alterations in expression of apoptosis-related proteins
- Antibodies for Annexin V, Bad, Bag-1, Bak, Bax, Bcl-2, Bcl-x, Bcl-X_L, c-IAP-1, c-IAP-2, cytochrome C, CPP-32, Fas, TNF
- Recombinant proteins for Annexin V-FITC, Annexin V-PE, Fas/Fc, TNF, TRAIL, TRAIL R1/Fc, TRAIL R2/Fc, TRAIL R3/Fc
- Assays for sFas, Nitric Oxide, TNF-α, TNF-β, sTNF RI, sTNF RII

6. Determine caspase activity
- Caspase-3 Assay (fluorometric and colorimetric)
- Caspase-8 Assay (fluorometric and colorimetric)

5. Assess PARP activity and/or expression
- PARP Activity Assay
- anti-PARP antibodies
- PARP enzyme

4. Label DNA fragments with TdT and biotinylated nucleotides
- TdT *in situ* Kits (DAB, TACS Blue Label or Fluorescein)
- FlowTACS™
- TiterTACS™
- Tissue-specific Kits - CardioTACS™, NeuroTACS™, and TumorTACS™

3. Perform qualitative PCR of apoptosis-related proteins and cytokines
- Primer Pairs™ - over 30 available
- Probe Cocktails - over 50 available (unlabeled and labeled with biotin or digoxigenin)

2. Quantitate mRNA levels of cytokines involved in apoptosis
- Quantikine® mRNA - IL-1β, IL-2 and IL-6
- Additional analyte-specific kits coming soon

and the number 1 reason is...

1. Label DNA Fragments with TdT and BrdU
- apoTACS™ *in situ* Kits - unlabeled (basic), DAB or TACS Blue Label

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

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

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

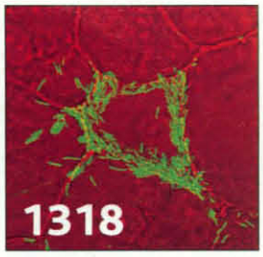
www.rndsystems.com

R&D SYSTEMS
1-800-343-7475

VOLUME 284 21 MAY 1999 NUMBER 5418

Science

www.sciencemag.org



COVER Initial stage of *Pseudomonas aeruginosa* biofilm formation on an explant of human lung tissue. Green shows *P. aeruginosa*, tagged with a fluorescent protein, on the epithelial surface (red-light microscopic image). The bacteria (2 to 3 μm long) form microcolonies in the intercellular junctions around injured cells. A special section on microbes, immunity, and disease begins on p. 1301. [Image: P. Singh, M. Parsek, T. Moninger, E. P. Greenberg, University of Iowa]

1243
The oldest Australian

NEWS

NEWS OF THE WEEK

1242 SPACE: European Ministers Back Commerce Over Space Science

1243 ARCHAEOLOGY: New Date for the Dawn of Dream Time

1246 CLINICAL RESEARCH: Shutdown of Research at Duke Sends a Message

▼1246 1348 PLANETARY SCIENCE: Space Rock Hints at Early Asteroid Furnace

1247 ENVIRONMENTAL POLICY: EPA's Piecemeal Risk Strategy on Way Out?

1248 AUSTRALIA: Budget Backs Report on Boosting Biotech

1249 ECOLOGY: New, Nonchemical Pest Control Proposed

1251 ASTRONOMY: Giant New Telescope Bags Gamma Ray Burst

1251 SOLID-STATE PHYSICS: Picking Up Bits of the Electron's Charge

NEWS FOCUS

1252 SCIENTIFIC COMMUNITY: 'New Physics' Finds a Haven at the Patent Office
A Free Energy Enthusiast Seeks Like-Minded Colleagues

1255 BIOLOGICAL CONTROL: Plan to Import Exotic Beetle Drives Some Scientists Wild

1257 SCIENCE AND RELIGION: Subjecting Belief to the Scientific Method
Searching for Answers to Cosmic Questions

1259 NUCLEAR PROLIFERATION: U.S. Sanctions Block People But Not Goods From India

▼1260 1356 1359 CELL BIOLOGY: Nuclear Transport Protein Does Double Duty in Mitosis

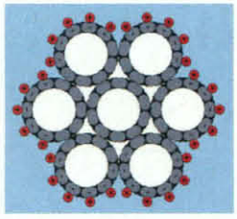
RESEARCH

REPORTS

1335 **Large Magnetoresistance of Electrodeposited Single-Crystal Bismuth Thin Films** F. Y. Yang, K. Liu, K. Hong, D. H. Reich, P. C. Searson, C. L. Chien

1337 **Cracks Faster than the Shear Wave Speed** A. J. Rosakis, O. Samudrala, D. Coker

▼1340 1281 **Carbon Nanotube Actuators** R. H. Baughman, C. Cui, A. A. Zakhidov, Z. Iqbal, J. N. Barisci, G. M. Spinks, G. G. Wallace, A. Mazzoldi, D. De Rossi, A. G. Rinzler, O. Jaschinski, S. Roth, M. Kertesz



1340
The Force be with nanotubes

MICROBES, IMMUNITY, AND DISEASE

1301 Microbe Management

NEWS

1302 A Symphony of Bacterial Voices

1305 Is It Time to Uproot the Tree of Life?
Borrowing—Genes—From Microbial Neighbors

VIEWPOINTS

1308 The Search for Unrecognized Pathogens D. A. Relman

1311 Emerging Infectious Diseases: Public Health Issues for the 21st Century S. Binder, A. M. Levitt, J. J. Sacks, J. M. Hughes

REVIEWS

1313 Phylogenetic Perspectives in Innate Immunity J. A. Hoffmann, F. C. Kafatos, C. A. Janeway Jr., R. A. B. Ezekowitz

1318 Bacterial Biofilms: A Common Cause of Persistent Infections J. W. Costerton, P. S. Stewart, E. P. Greenberg

1322 Type III Secretion Machines: Bacterial Devices for Protein Delivery into Host Cells J. E. Galán and A. Collmer

1328 *Helicobacter pylori* Virulence and Genetic Geography A. Covacci, J. L. Telford, G. Del Giudice, J. Parsonnet, R. Rappuoli

See related Book Review on p. 1279.

DEPARTMENTS

NETWATCH 1231

THIS WEEK IN *SCIENCE* 1233

SCIENCESCOPE 1245

RANDOM SAMPLES 1263

CONTACT *SCIENCE* 1271

NEW PRODUCTS 1377

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. 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

EDITORIAL

1271 **Fault Lines** S. M. Malcom

LETTERS

1273 **Einstein: "All but the Dissertation"** H. I. Brown. **Jaw Origins** G. Koentges. **Asteroid Report** B. J. Peiser. **Y2K: An "Autopsy" of Modern Society?** S. A. Umpleby. **The Web and Conflict of Interest** G. McGee. **Phytohormone-Independent Division of Tobacco Protoplast-Derived Cells: Retractions** J. Schell

POLICY FORUM

1277 DRUG ABUSE: **The Heroin Prescribing Debate: Integrating Science and Politics** G. Bammer, A. Dobler-Mikola, P. M. Fleming, J. Strang, A. Uchtenhagen

BOOKS *ET AL.*

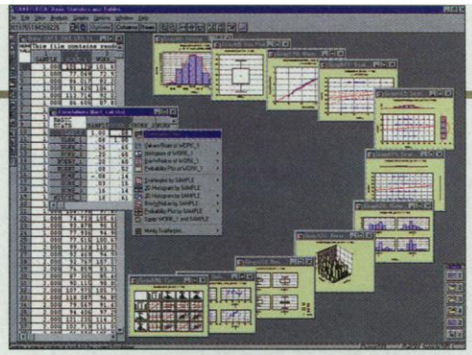
1279 MEDICINE: ***Microbes and Malignancy*** *Infection as a Cause of Human Cancers* J. Parsonnet, Ed., reviewed by D. Ganem

1280 MATERIALS SCIENCE: ***The Structure of Materials*** S. M. Allen and E. L. Thomas, reviewed by P. Wiltzius

PERSPECTIVES

▼1281 1340 MATERIALS SCIENCE: **Carbon Nanotube Muscles** O. Inganäs and I. Lundström

▼1282 1344 CONDENSED MATTER PHYSICS: **The Cuprate Pairing Mechanism** D. J. Scalapino



1291 Sophisticated statistical support

1283 IMMUNOLOGY: **Instruction, Selection, or Tampering with the Odds?** R. L. Coffman and S. L. Reiner

▼1285 1362 1365 BIOCHEMISTRY: **Seeking Ligands for Lonely Orphan Receptors** J.-Å. Gustafsson

TECH.SIGHT

1289 BIOCHEMISTRY: **Biomolecule Mass Spectrometry** F. W. McLafferty, E. K. Fridriksson, D. M. Horn, M. A. Lewis, R. A. Zubarev

1291 SOFTWARE: ***Statistica 5.1 for Windows***, reviewed by B. McCallum

1293 **TechSightings**

▼1344 1282 **The Magnetic Excitation Spectrum and Thermodynamics of High-T_c Superconductors** P. Dai *et al.*

▼1348 1246 **^{26}Al in Eucrite Piplia Kalan: Plausible Heat Source and Formation Chronology** G. Srinivasan, J. N. Goswami, N. Bhandari

1351 **Cloning Genes Encoding MHC Class II–Restricted Antigens: Mutated CDC27 as a Tumor Antigen** R.-F. Wang, X. Wang, A. C. Atwood, S. L. Topalian, S. A. Rosenberg

1354 **BRCA1 Inhibition of Estrogen Receptor Signaling in Transfected Cells** S. Fan *et al.*

▼1356 1260 1359 **Self-Organization of Microtubule Asters Induced in *Xenopus* Egg Extracts by GTP-Bound Ran** T. Ohba, M. Nakamura, H. Nishitani, T. Nishimoto

▼1359 1260 1356 **Stimulation of Microtubule Aster Formation and Spindle Assembly by the Small GTPase Ran** A. Wilde and Y. Zheng

▼1362 1285 1365 **Identification of a Nuclear Receptor for Bile Acids** M. Makishima, A. Y. Okamoto, J. J. Repa, H. Tu, R. M. Learned, A. Luk, M. V. Hull, K. D. Lustig, D. J. Mangelsdorf, B. Shan

▼1365 1285 1362 **Bile Acids: Natural Ligands for an Orphan Nuclear Receptor** D. J. Parks, S. G. Blanchard, R. K. Bledsoe, G. Chandra, T. G. Consler, S. A. Kliewer, J. B. Stimmel, T. M. Willson, A. M. Zavacki, D. D. Moore, J. M. Lehmann

1368 **Modulation of Polyketide Synthase Activity by Accessory Proteins During Lovastatin Biosynthesis** J. Kennedy, K. Auclair, S. G. Kendrew, C. Park, J. C. Vederas, C. R. Hutchinson

1372 **UDP-GlcNAc 2-Epimerase: A Regulator of Cell Surface Sialylation** O. T. Keppler *et al.*

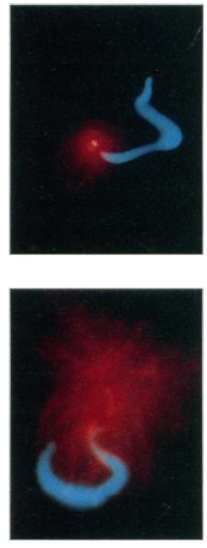
TECHNICAL COMMENTS

Evaluating Evidence of Ancient Animals V. Rai and R. Gautam. ***Response*** A. Seilacher, P. K. Bose, F. Pflüger

www.sciencemag.org/cgi/content/full/284/5418/1235a

Role of Ceruloplasmin in Cellular Iron Uptake: Addendum P. L. Fox, C. K. Mukhopadhyay, Z. K. Attieh

www.sciencemag.org/cgi/content/full/284/5418/1235b



1359
Ran runs spindle formation

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.

The new Amersham Pharmacia Biotech web site is up and running. It's like no other site you've ever visited in Life Science.

Look at the WebCat, our on-line product catalogue, which contains all our latest product information. And, because it gets updated the instant we've got something new for you, you can always be sure it is the very latest.

To help you on your way, we've also incorporated an advanced Search function that speeds you to the information you are most likely to need. A click on the "Related" button on a page will take you directly to technical documentation, application notes, FAQs and any other related subjects.

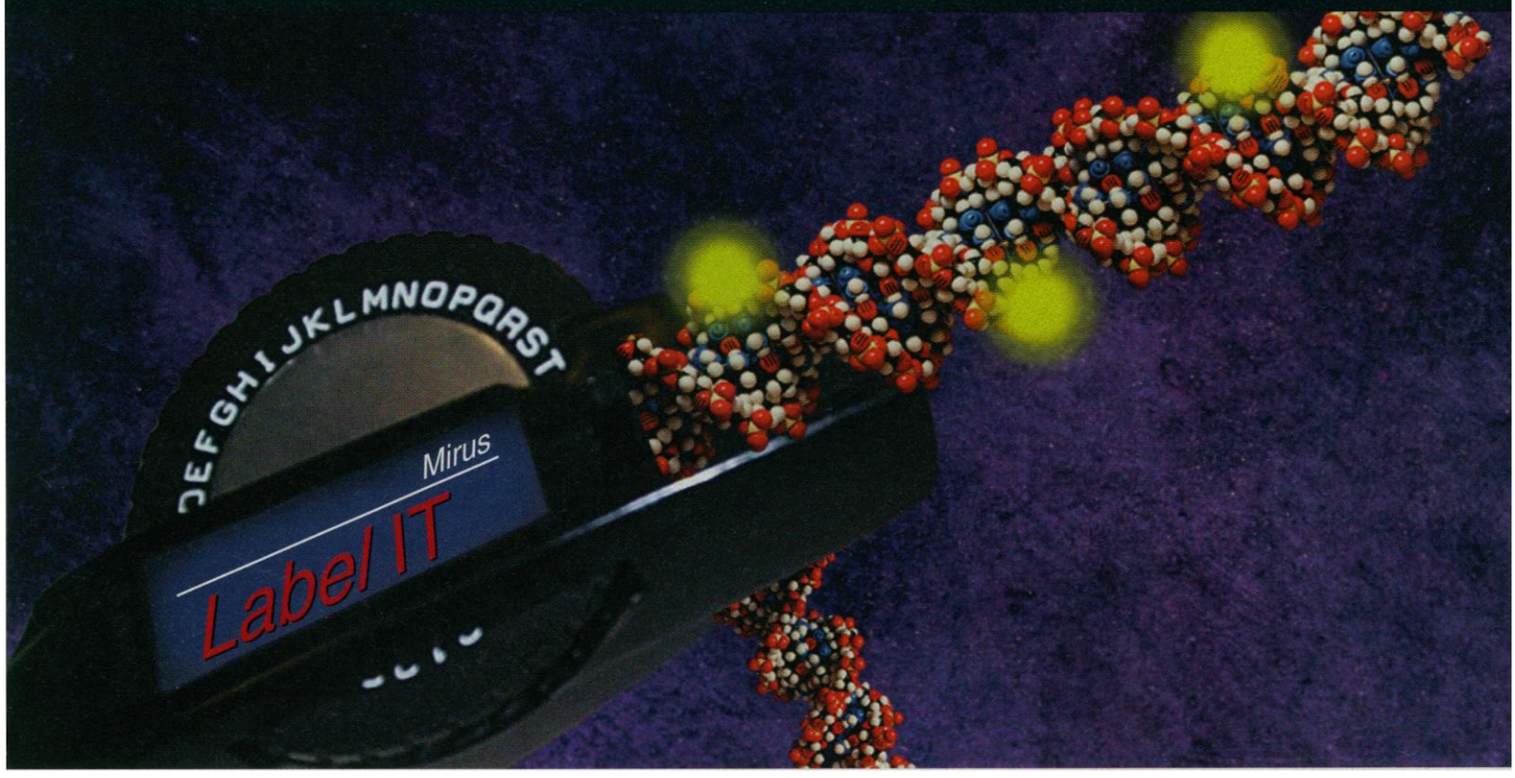
If you don't happen to find the answer you need in any of the above, you can always e-mail your enquiries to our Technical Support help-desk and we'll get back to you with the answer.

These are just some of the features.
Log on now and discover.

www.apbiotech.com

amersham pharmacia biotech

Nucleic Acid Labeling Made Easy



Single-step, nonradioactive labeling just got better!

Mirus

Label IT® Nucleic Acid Labeling Kits are now available with Cy3™ and Cy5™ dyes.

Versatile: Label your nucleic acid with Rhodamine, Fluorescein, Digoxin, Biotin, **AND NOW Cy3 and Cy5 dyes** using just a single reagent.

Fast: Purified, labeled DNA or RNA is obtained in less than 2 hours.

Simple: Just mix the *Label* IT Reagent with your DNA or RNA.

Scalable: Label virtually any concentration of DNA or RNA without destroying your sample, and get quantitative recoveries of labeled product.

Efficient: The *Label* IT Reagents can add at least one label per 10 base pairs of DNA.

From Now On, *Label* IT!

Circle No. 61 on Readers' Service Card

Worldwide distributors:

Austria	genXpress	43-1-789-8106
Belgium:	Sopachem n.v.	32-2-474-50-70
Canada:	Bio/Can Scientific	(905) 828-2455
France	Takara Biomedical Europe S.A.	33-1-41-47-01-14
Germany	MoBiTec GmbH	49-551-371062
Greece	Bega Ltd.	30-1-3300403
India	BioBusiness Development Agency	91-11-559-6820
Israel	Zotal, Ltd.	972-3-5462269
Japan	Takara Shuzo Co., Ltd.	81-775-43-7247
Switzerland	JURO Supply AG	41-41-226-20-60
United Kingdom	Cambridge BioScience	44-1223-316855
United States	Fisher Scientific	800-766-7000

PANVERA

Label IT is a registered trademark of Mirus Corporation.
Cy3 and Cy5 are trademarks of Amersham Pharmacia Biotech.

PanVera Corporation • 545 Science Dr., Madison WI 53711
Phone: 608.233.9450 • Fax: 608.233.3007
E-Mail: info@panvera.com

800.791.1400
In the USA and Canada

www.panvera.com

RAPID PARENT BODY FORMATION

Meteorites are classified either as undifferentiated, which represent the most primitive components of the early solar system, and differentiated, which represent fragments from larger parent bodies that have undergone additional heating and differentiation. All meteorites initially formed from melts, and it was suggested in the 1950s that the heat source for this melting was the decay of radiogenic nuclide aluminum-26 (^{26}Al). Recently, evidence for ^{26}Al was found in undifferentiated meteorites, but not in differentiated ones. Srinivasan *et al.* (p.1348; see the news story by Stokstad) have found evidence for ^{26}Al in a differentiated meteorite, Piplia Kalan, with a measured formation age of about 4.6 billion years that fell in India in 1996. The presence of ^{26}Al in Piplia Kalan suggests that its parent body (inferred to be the asteroid 4 Vesta) accreted, melted, and differentiated within 5 million years after the formation of the solar system. This result would indicate that planetesimal formation was very fast and would reduce the possible time scales that should be considered for at least our solar system.

MAGNETORESISTANCE VIA ELECTROCHEMISTRY

Although much recent attention in magnetic sensing has focused on spin-dependent magnetoresistive (MR) materials (which change resistance in a magnetic fields), bismuth metal does so simply because its electrons can travel faster in an applied field in induced cyclotron orbits. Thin films are needed for applications, however, and good quality films that do not scatter the electrons have proven expensive to fabricate—ultrahigh vacuum processing conditions are needed. Yang *et al.* (p. 1335) now show that electrochemical deposition can create large-grain films that can be annealed into single-crystal films; both exhibit good room-temperature MR properties.

GIVING NANOTUBES THE PUSH

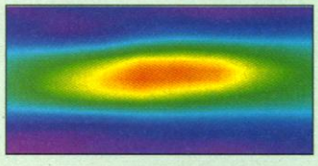
Motors are the common way to convert electricity into mechanical work, but for many microscopic systems, electromechanical actuators, in which an applied voltage creates a mechanical strain in materials such as ferroelectrics or conducting polymers, are a simpler alternative. Baughman *et al.* (p. 1340; see the Perspective by Inganäs and Lundström) show that single-wall carbon nanotubes may be a promising actuator material. Charge injection and depletion into parallel sheets of nanotube "paper," separated by an insulating layer and immersed in salt water, led to large deflections at low voltages (typically 1 volt) as one sheet expanded and the other contracted. Because the nanotubes on the inside of the sheets likely experienced little charging, the work densities produced by even smaller nanotube assemblies may be substantially higher.

FAST CRACKS

When cracks travel through a material, the speed at which they proceed has long been believed to be limited by inherent properties of the material, that is, to be slower than the speed at which shear waves can travel. Rosakis *et al.* (p. 1337) show that crack growth in a brittle polyester resin proceeded at speeds faster by a factor of nearly the square root of two times the material's shear wave speed. Similar processes may be observed in earthquake events.

MAGNETISM AND HIGH-T_c SUPERCONDUCTIVITY

The origin of high-temperature superconductivity is controversial. To help address this problem experimentally, Dai *et al.* (p. 1344; see the Perspective by Scalapino) have made comprehensive neutron scattering and nuclear



magnetic resonance measurements on cuprate superconductors ($YBa_2Cu_3O_{6-x}$) with various amounts of doping. They find good qualitative agreement between the thermodynamics of the magnetic fluctuations and the electronic specific heat. These results provide evidence for magnetism being the driving force behind high-temperature superconductivity.

SETTING UP THE SPINDLE

The small guanosine triphosphatase Ran regulates import and export of RNA and other macromolecules across the nuclear membrane. Two reports provide evidence for a new role of Ran in the regulation of the formation of the mitotic spindle (see the news story by Pennisi). Wilde and Zheng (p. 1359) report that either wild-type Ran in the active, guanosine triphosphate (GTP)–bound form, or a mutant, activated form of Ran stimulated the formation of microtubule asters when added to *Xenopus* egg extract. Formation of asters associated with added sperm centrosomes, as well as independently of the sperm nuclei, were both observed. Ohba *et al.* (p. 1356) altered Ran function by manipulating the RCC1 protein, a nucleotide exchange factor for Ran. Depletion of RCC1 from *Xenopus* egg extracts reduced formation of asters. However, addition of RanGTP to such extracts restored aster formation. Thus, Ran, which is apparently released from the nucleus as mitosis is initiated and the nuclear membrane breaks down, promotes polymerization of microtubules and spindle formation. Consistent with such a role, the Ran-binding protein RanBP1 and the RanGTPase–activating protein RanGAP1 are localized to the centrosome and mitotic spindles, respectively.

IMPROVING SURVEILLANCE

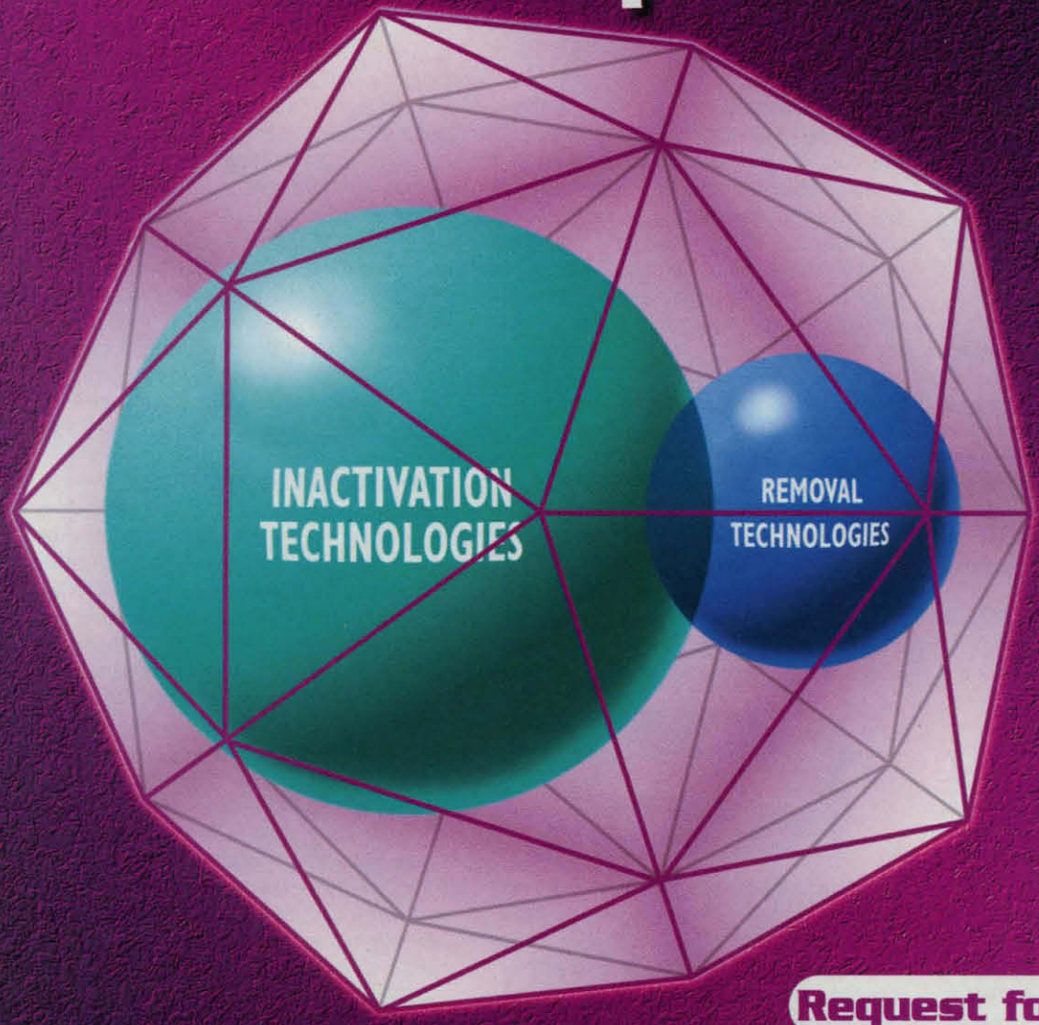
Major efforts are being made to treat or prevent cancer by manipulation of the immune system. "Cancer vaccines" could theoretically boost an individual's immune system by making the immune system highly reactive to any existing tumors. However, to develop a vaccine, antigens generally need to be identified. Methods exist to identify tumor antigens that bind to major histocompatibility complex (MHC) class I. Wang *et al.* (p. 1351) have now devised a method to find antigens that bind to MHC class II proteins. With specific knowledge of which tumor peptides the MHC proteins present to T cells, vaccines, and treatments could be designed to take advantage of the patient's own immune system.

BRCA1 AND ESTROGEN SIGNALING

The protein encoded by the breast cancer susceptibility gene *BRCA1* has been implicated in general cellular processes such as DNA repair and transcription, but its role in tumorigenesis remains unclear. In experiments with transfected cancer cells in culture, Fan *et al.* (p. 1354) show that BRCA1 inhibits estrogen-induced signaling by estrogen receptor–α and blocks the receptor's transcriptional activation function. These observations suggest a hypothesis that can now be tested in animal models—that BRCA1 functions in part to suppress estrogen-dependent transcriptional pathways related to breast epithelial cell growth.

CONTINUED ON PAGE 1235

...Eradicate pathogens in human plasma



Request for Proposals

CONTACT:
Fredrick A. Dombrose, Ph.D.
Executive Director
5925 Carnegie Blvd.,
Suite 500
Charlotte, NC 28209 U.S.A.
Phone: 704.571.4070
Fax: 704.571.4071
E-mail: fdcps@aol.com
Web: www.plasmaconsortium.com

The Consortium for Plasma Science requests proposals for innovative methods that:

- eradicate non-enveloped viruses in whole human plasma
- retain the biofunctionality of the plasma proteins
- are effective, safe and practical.

Proposals may be submitted at any time, and will be evaluated on both technical merit and the business case.

Consortium for Plasma Science, LLC

Circle No. 33 on Readers' Service Card

THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 1233

CLOSING THE LOOP ON CHOLESTEROL

Cholesterol is enzymatically degraded into bile acids to prevent accumulation of fat in the body. These cholesterol by-products not only clear dietary fat from the body, but are also known to somehow regulate cholesterol metabolism and bile acid transport in the digestive system. Parks *et al.* (p. 1365) and Makishima *et al.* (p. 1362) report that bile acids may control these two physiological processes through an orphan nuclear receptor called the farnesoid X receptor (FXR) (see the Perspective by Gustafsson). When bound to bile acids, FXR can interact with another nuclear steroid receptor. This complex can control the transcription of two genes, one that encodes a regulatory enzyme of bile acid synthesis and one that encodes a bile acid transporter protein. Hence, nuclear bile acid signaling may regulate cholesterol homeostasis.

IN SERIES AND IN PARALLEL

Microbial enzyme complexes are responsible for the synthesis of natural products, including important polycyclic antibiotics such as tetracycline. These compounds generally are constructed from simple two- and three-carbon units that are joined in repetitive linkages, modified by hydroxylation or reduction, and then cyclized. The complexes fall into two classes: In one, serially arranged enzyme active sites are highly specific for substrate and different modification reactions are enacted on each unit added, and in another the growing polymer is cycled iteratively around a core of relatively nonspecific active sites. Kennedy *et al.* (p. 1368) find that the cholesterol-lowering drug lovastatin, a fungal natural product, is made using a combination of these serial and iterative modes.

STICKING WITH IT

All eukaryotic cell surfaces display proteins and lipids that are decorated with carbohydrate moieties. This modification is particularly critical for molecules involved in cell adhesion. Keppler *et al.* (p. 1372) show that in hematopoietic cell lines, the addition of sialic acid residues to specific cell surface molecules depends on an epimerase that regulates sialic acid biosynthesis. Epimerase activity was required for the binding of adhesion molecules to leukocytes. Epimerase expression may therefore regulate cell activation and adhesion events in the immune system.

TECHNICAL COMMENT SUMMARIES

Evaluating Evidence of Ancient Animals

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5418/1235a

A. Seilacher *et al.* (Reports, 2 Oct. 1998, p. 80) studied "bedding plane features" in "the Mesoproterozoic Chorhat Sandstone" of central India. They interpreted these trace fossils "as the burrows of wormlike undermat miners," which suggests that "triploblastic animals existed more than a billion years ago."

V. Rai and R. Gautam comment that "these markings are more likely pseudo-trace fossils or casts of some megascopic algae, for several reasons," and note that they have found fossils of *Grypania* species of algae from the same beds, "a little higher up in the succession. ... "

In response, Seilacher *et al.* "agree that pseudofossils are a major problem in Precambrian paleontology," but state that the structures described in their report "do not fall into the morphospace and tapofacies of macroalgae such as *Grypania*, or of shrinkage cracks, or of any other known physical structures." They "look forward to new radiometric ages from ash beds, currently being determined by other groups."

Role of Ceruloplasmin in Cellular Iron Uptake: Addendum

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5418/1235b

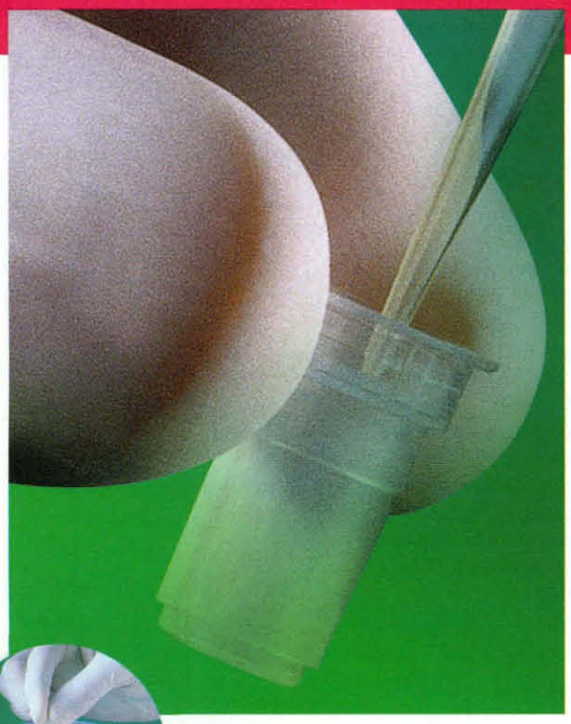
C. K. Mukhopadhyay *et al.* (Reports, 30 Jan. 1998, p. 714) found that ceruloplasmin (Cp) increased "iron uptake by HepG2 cells." Cp synthesis was transcriptionally regulated.

In an addendum, P. L. Fox *et al.* (co-authors of the report) note that the "anti-transferrin receptor monoclonal antibody H68.4 [which was used in the report] is not the preferred reagent for determining the role of the receptor in iron uptake by intact cells," and they thank I. S. Trowbridge for raising the issue. Control experiments with a more effective antibody, 42/6, support the report's original findings. Their complementary studies "provide compelling evidence that Cp-stimulated iron uptake is transferrin- and transferrin receptor–independent."

PIERCE

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

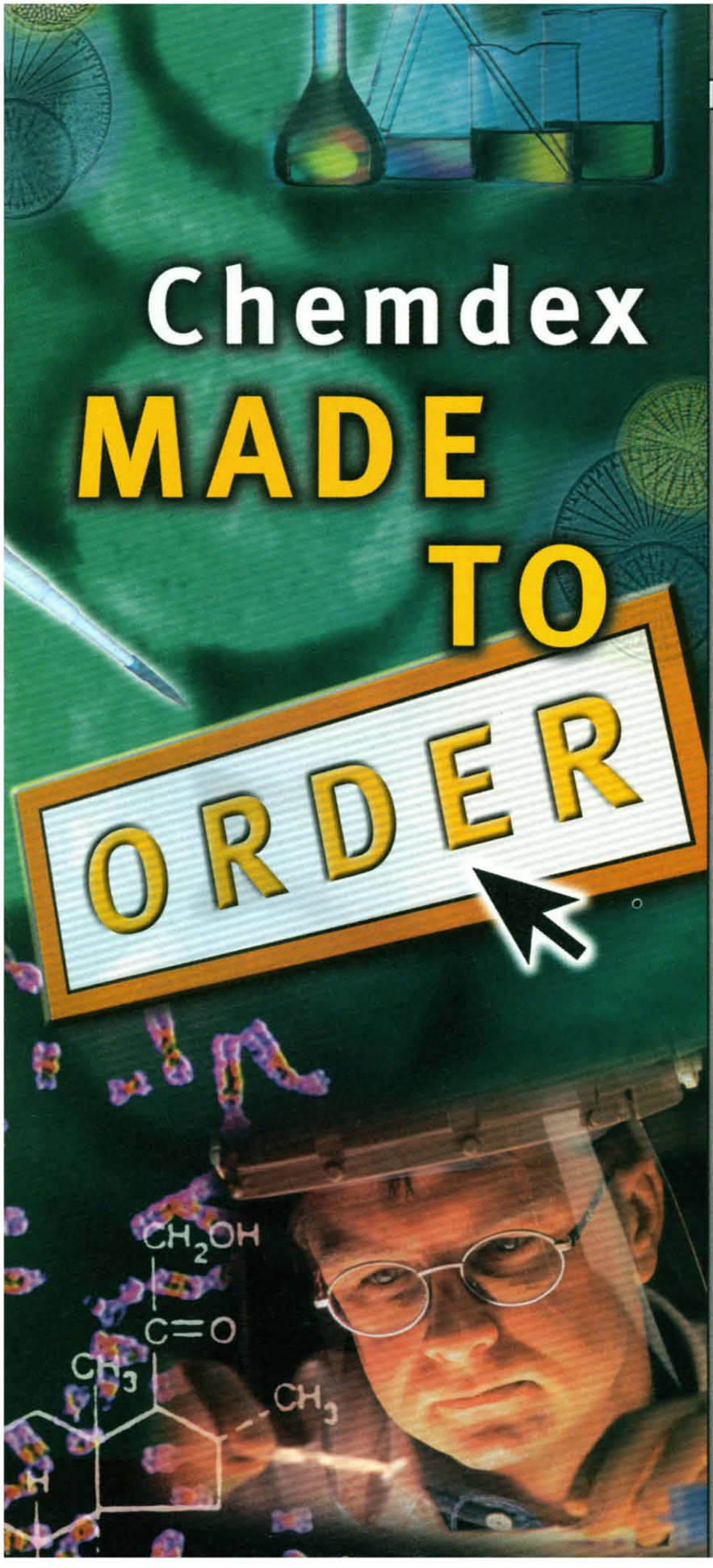
SnakeSkin™ Dialysis Tubing
- *Very* easy to fill: The first truly tubular dialysis tubing!
- *Very* easy to use: No preparation or presoaking necessary
- *Very* easy to dispense: Snip what you need
- For 15-100 ml sample sizes

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. 57 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



Convenient One-Stop Shopping

Buy online at Chemdex.com

The Chemdex Marketplace is the best way to buy biological and chemical reagents online. We are adding lab supplies, instruments, and equipment to create a convenient one-stop source for all your laboratory needs.

When you purchase online with Chemdex, you can:

- Buy from the suppliers you know and trust
- Find what you need quickly with our precision search engine
- Order from multiple suppliers with one electronic order form
- Rely on world-class customer service

Visit the Chemdex Marketplace today at www.chemdex.com.

Custom Procurement Solutions

Streamline your purchasing

Chemdex procurement solutions go far beyond our Web site. Our e-commerce technology can be integrated into your company's current systems and customized to match your existing business rules.

Chemdex procurement solutions feature:

- Custom pricing and catalog views
- Electronic requisition routing and approval
- Summary billing and consolidated reporting

Let Chemdex streamline your organization's purchasing process so you can focus on what's important — research and development.

To learn more about our custom procurement solutions, call 1-888-810-4732 or e-mail enterprise@chemdex.com.

Chemdex
Accelerating Science

Chemdex Corporation
3950 Fabian Way, Palo Alto, CA 94303 • 650-813-0300

Circle No. 42 on Readers' Service Card

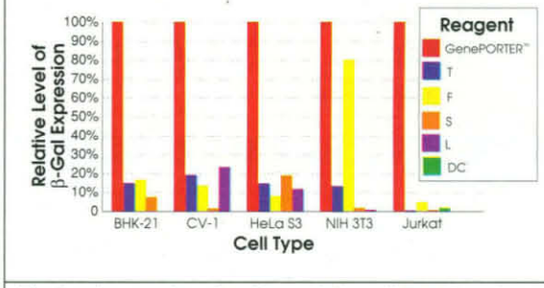
www.sciencemag.org
Science

Finally, a transfection reagent that makes you smile, every time!

Introducing

GenePORTER™ Transfection Reagent*

GenePORTER™ reagent, which incorporates direct hydrophilic conjugation (DHC) technology,* is the latest innovation from the lab of Dr. Philip Felgner, inventor of lipofection. In a variety of cell lines, GenePORTER reagent consistently delivers higher levels of transfection than any other commercially available product. This robust reagent performs in a wide range of conditions, including different ratios of plasmid and reagent. GenePORTER reagent is easy to use and does not require enhancers or special handling of cells, saving time, cost, and reagents. Order GenePORTER reagent today. The results will make you smile.



The β-gal expression plasmid was delivered into cells using GenePORTER or competitor's transfection reagents. Each manufacturers protocol was followed. A colorimetric assay was used to measure β-gal expression 48 hours after transfection.

GenePORTER™
Transfection Reagent
75 reactions (0.75 ml) • T201007
150 reactions (1.5 ml) • T201015
750 reactions (5 x 1.5 ml) • T201075

New High Expression Vectors
gWiz™ Expression Vectors
Call for a brochure or visit our web page
* Patents pending.

GTS
Gene Therapy Systems
"the art of innovation"

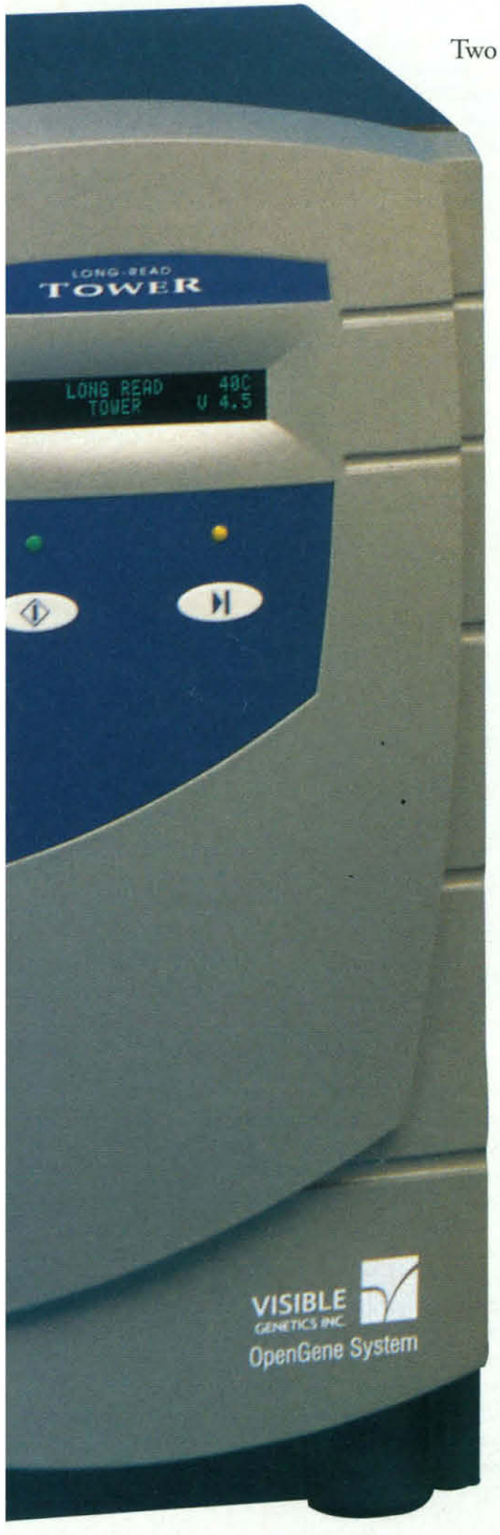
To Order: 888-428-0558
Fax: 619-623-9494
10190 Telesis Court, San Diego, CA 92121, USA
Check out the Gene Therapy Systems web site @
http://www.genetherapysystems.com

Gene Therapy Systems International Distributors

Australia • ASTRAL +61-2-9540-2055 **Austria** • BIO-TRADE +43 1 889 18 19 **Benelux** • BIOzym+31+(0)45 532 77 55 **Denmark, Finland, Norway, Sweden** • KEBO Lab +46 8 621 35 07 **France** • OZYME +1 30 85 92 92 **Germany** • BIOzym GmbH +49 5152-9020 **Italy** • Duotech 39 02 331 066 30 **Japan** • Funakoshi +81-3-5684-1622 **Korea** • Core Bio +82 2 841-7530 **Spain** • BioNova +34 91 551 54 03 **Switzerland** • Axon Lab AG +41 56 484 80 80 **Taiwan** • PROtech, Ltd. 886-2-23810844 **United Kingdom** • Lifescreen Ltd. +44 0 1923 241515

Circle No. 47 on Readers' Service Card

The Long-Read Tower™
Automated DNA Sequencing System.
The smartest way to get results.



Two sequencers in one.... sounds pretty smart, doesn't it? For optimum flexibility, the 2-dye Long-Read Tower is the smartest choice in automated DNA sequencing today.

Flexible and fast

400 bases in just over 30 minutes with the standard MicroCel™ cassette or 1000 bases in under 4 hours with the new Long-Read MicroCel™ cassette.

Disposable MicroCel cassettes are filled and polymerized in under 4 minutes and run at least 3 times faster than comparable competitive systems.

Powerful Analysis Software

A palette of software analysis tools simplifies data interpretation, storage and reporting.

Value

Contact your local VGI representative to discuss one of our very smart purchasing options.

1000 bases in under 4 hours

For research purposes only. Not for use in diagnostic procedures.
Circle No. 19 on Readers' Service Card

How smart is the **OpenGene** system? Very.
For example, GeneObjects software is based on the bright idea that it's a lot more useful if it thinks along with you. For example, you can compare a sample's sequence to databases with thousands of possible matches. In seconds, the software will identify the best fit. What's more, databases are optimized for HLA sequence-based typing, HIV genotyping and HPV applications.
If the **OpenGene** system by Visible Genetics sounds extraordinarily smart, it is. And it comes at an equally attractive, intelligent price. Give us a call and we'd be pleased to arrange a demonstration.

700 Bay St., #1000
Toronto, ON Canada M5G 1Z6

www.visgen.com
info@visgen.com

N. America: Tel. 416-813-3240
Fax 416-813-3262
Toll Free: 1-888-463-6844

Europe: Tel. 33 (0)1 60 87 13 00
Fax 33 (0)1 60 87 13 01

*For research purposes only. Not for use in diagnostic procedures.

VISIBLE GENETICS INC.

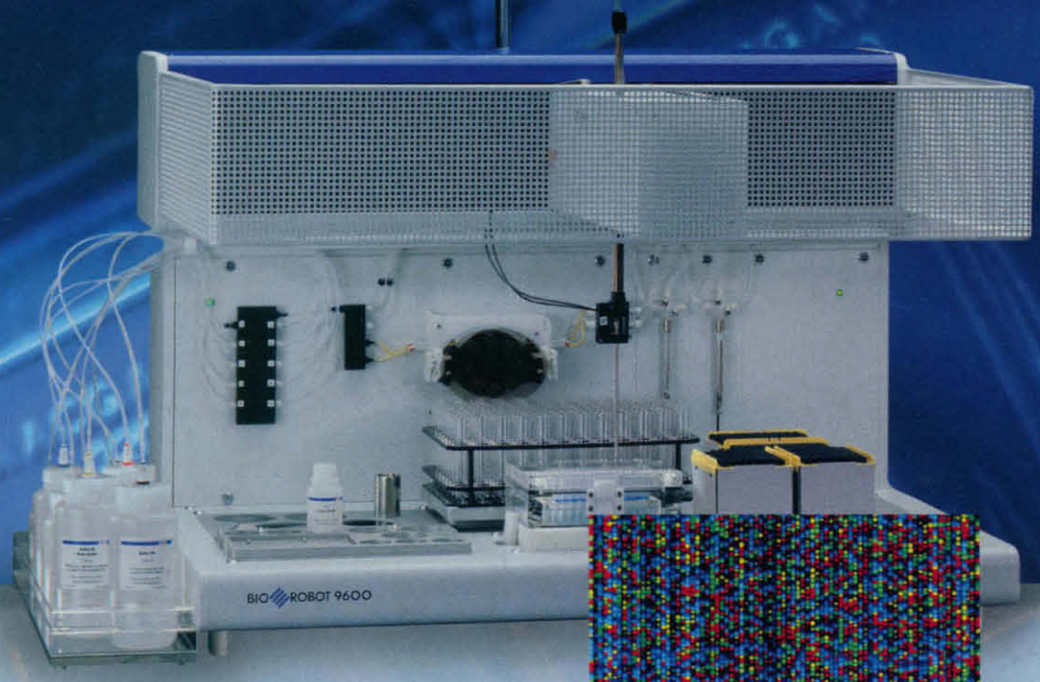
GPS Coordinates: N 43° 39.530, W 079° 23.190.

MORE THAN JUST INSTRUMENTS

Complete systems to automate your sequencing projects

PROJECTS

- Sequencing
- PCR
- Genomic DNA
- RNA
- Liquid handling



QIAGEN® BioRobot™ Systems

Successful automation of demanding sequencing projects requires more than just an instrument for front-end applications. BioRobot™ Systems go further by integrating proven QIAGEN® chemistries, ready-to-run protocols, and innovative instrumentation — for consistent, publication-ready results.

Dependable sequencing preparation — BioRobot Systems bring together our reliable purification technologies and accurate small-volume pipetting to enhance sequencing performance and simplify your projects. Ready-to-run protocols facilitate template purification (plasmid, BAC, PCR products, and M13) and reaction setup. Data are easily exchanged with automated sequencers and other laboratory instruments — for maximum convenience.

Comprehensive system support — The QIAGEN support team is always there to help you with all aspects of the system — chemistry, applications, and instrumentation.

Complete automated systems — from the company that understands molecular biology

Call QIAGEN today at 800-426-8157 ext. 235 for more information.

QIAGEN BioRobot Systems are not available in all countries; please inquire.
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.

http://www.qiagen.com

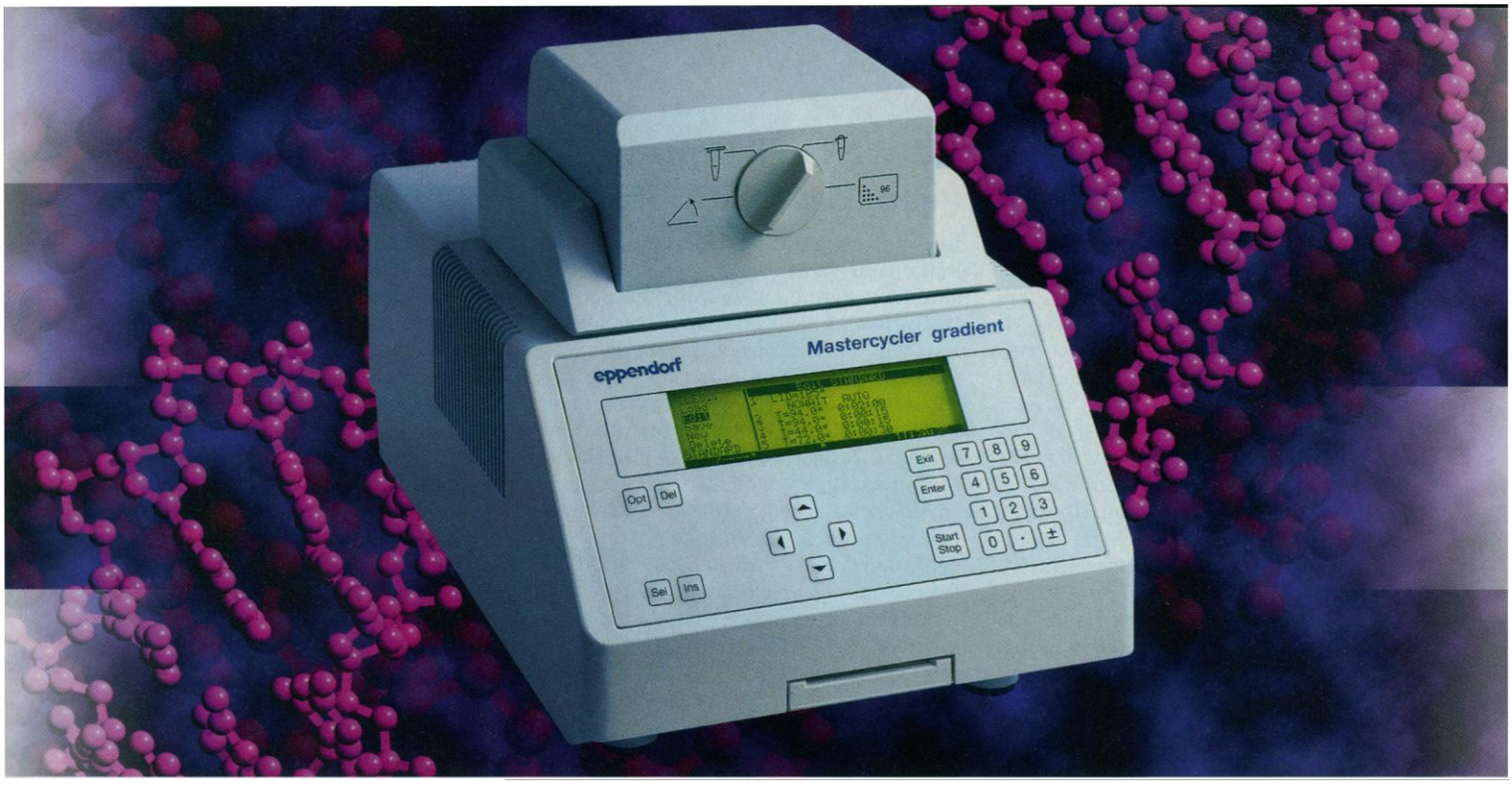
Germany:	USA:	Australia:	Canada:	France:	Japan:	Switzerland:	UK:
QIAGEN GmbH	QIAGEN Inc.	QIAGEN Pty Ltd	QIAGEN Inc.	QIAGEN S. A.	QIAGEN K.K.	QIAGEN AG	QIAGEN Ltd.
Tel. 02103-892-240	Tel. 800-426-8157	Tel. 03-9489-3666	Tel. 800-572-9613	Tel. 01-60-920-930	Tel. 03-5805-7261	Tel. 061-319-30-31	Tel. 01293-422-999
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 Austria (01) 889 18 19 **Belgium/Luxemburg** 0800-1-9815 **Brazil** (11) 543 1455 or 0800 55 1321 **Central & South America** USA (305) 828-3818 **China** (852)2896-6283 **Czech Republic** (02)4447 1239 **Denmark** 43 86 87 88 **Finland** (09)-804 551 **Greece** (01)-643 61 38 **India** (011)-542 1714 **Israel** 02. 584 1111 **Italy** (055) 500 1871 **Korea** (02) 924-86 97 **Malaysia** (03)-7312099 **Mexico** USA (661) 294-7940 **The Netherlands** (033)-4950094 **New Zealand** (09)980 6700 or 0800 933 966 **Norway** 22 90 00 00 **Poland** (071) 351 41 06 or 351 54 20 **Portugal** (1)-751 6000 **Singapore** 445 7927 **Slovak Republic** (07) 54 01 336 **South Africa** (021) 615166 **Spain** (93) 902.20.30.90 **Sweden** (08) 621 34 00 **Taiwan** (02) 2880 2913 **Thailand** (02) 412-5672 **In other countries contact:** QIAGEN GmbH, Germany

QIAGEN

BRXSEQ0499SUS

Circle No. 63 on Readers' Service Card



PCR optimization in one single experiment

licensed and PCR authorized

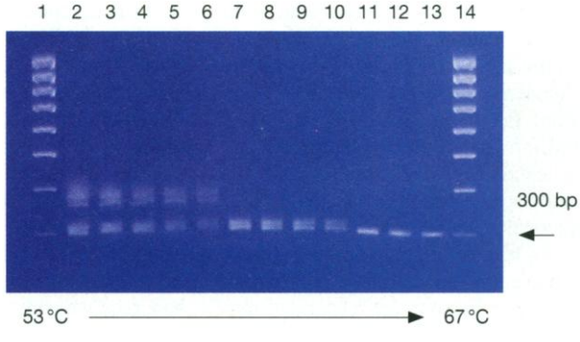
The determination of the right annealing temperature is crucial for establishing a new PCR experiment. The new all-round genius **Mastercycler® gradient** is an innovative, compact thermal cycler for even the most demanding PCR* applications. Its gradient function enables a temperature gradient of up to 20 °C to be generated across the block, thus optimizing the annealing, denaturation, or extension temperature in one single experiment. Its 96-position all-in-one universal block can accommodate 96 x 0.2 ml tubes, 77 x 0.5 ml tubes, or one 96-well plate – without block exchange.

The exact block homogeneity ensures reproducible results. Variable, high incubation speeds as well as time and temperature increments for hot-start, touch-down, and long PCR provide maximum programming flexibility.

The **Mastercycler® personal** is designed to meet personal applications. Its 25-position all-in-one universal block holds 25 x 0.2 ml tubes, 16 x 0.5 ml tubes, or one microplate in a 5 x 5 grid.

Personal memory cards for 10 individually developed protocols allow an easy and comfortable method transfer between both Mastercycler models.

Of course, both Mastercyclers are licensed and authorized for PCR.



● Experimental determination of optimal annealing temperature. The calculated primer annealing temperature was 56.5 °C, the actual annealing temperature is 63.5 °C. The ribosomal spacer region of mycoplasms from H9 cell cultures was amplified.

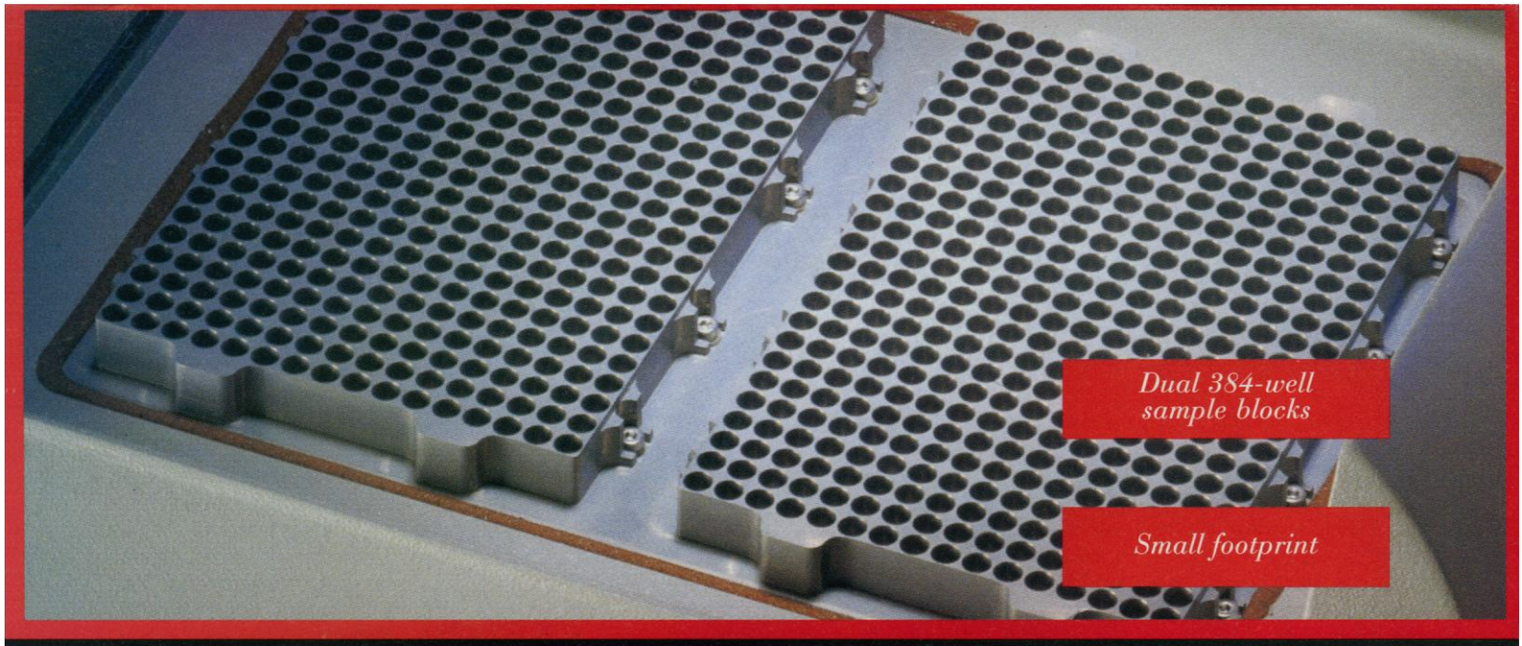
*PCR (Polymerase Chain Reaction) is protected by patent. The patent is held by Hoffmann-La Roche. Practice of the patented Polymerase Chain Reaction (PCR) process requires a license. The Eppendorf Thermal Cyclers are Authorized Thermal Cyclers and may be used with PCR licenses available from the Perkin-Elmer Corporation. Their use with Authorized Reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents.

Circle No. 10 on Readers' Service Card

eppendorf

ISO CERTIFIED 9001

Eppendorf – Netheler – Hinz GmbH · 22331 Hamburg · Germany · Phone (+49) 40-53801-0 · Fax (+49) 40-53801-556
website: www.eppendorf.com · e-mail: eppendorf@eppendorf.com
Eppendorf Scientific, Inc. · One Cantiague Road · Westbury, NY 11590-0207 · USA · Phone 800-421-9988 or 516-876-6800 · Fax 516-876-8599
website: www.eppendorfsi.com · e-mail: eppendorf@eppendorfsi.com



High throughput PCR. Within budget. Without compromise.

Reliable performance

Authorized for PCR

To order, call 1-800-345-5224

The new Dual 384-Well GeneAmp® PCR System 9700.

You don't need more bench space to get higher PCR throughput. With a dual 384-well sample block, the GeneAmp® PCR System 9700 gives you 800% more sample capacity without a bigger base footprint.

That means you can run 768 samples in just 1351 square centimeters. And you can do it with the reliable thermal performance, intuitive programming, and affordability that make the GeneAmp PCR System 9700 the best price-performance value in thermal cycling today.

Interchangeable blocks make it easy to expand the capability of the GeneAmp PCR System 9700

The new Dual 384-Well GeneAmp PCR System 9700 is ideally suited for a wide range of applications and is Authorized for PCR. In addition to the new dual 384-well sample block, the system accommodates standard 96-well sample blocks and other formats as they become available.

So, get more PCR per square centimeter. For information on the Dual 384-Well GeneAmp PCR System 9700, call PE Applied Biosystems at 1-800-345-5224. Outside the U.S., contact your local sales representative, or visit our website at www.perkin-elmer.com.

PE *Applied Biosystems*

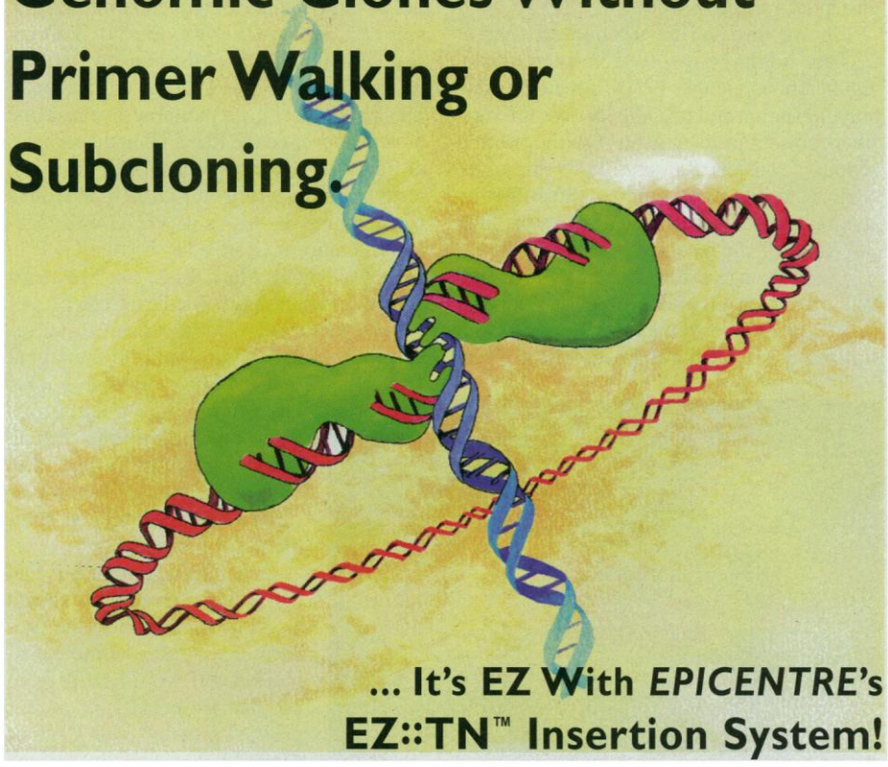
Europe Langen, Germany Tel: 49 (0)6103 708 301 Fax: 49 (0)6103 708 310 **Japan** Tokyo, Japan Tel: (047) 380-8500 Fax: (047) 380-8505 **Latin America** Miami, Florida Tel: (305) 670 4350 Fax: (305) 670-4349 **Australia** Melbourne, Australia Tel: 1 800 033 747 Fax: 61 3 9212-8502

Roche

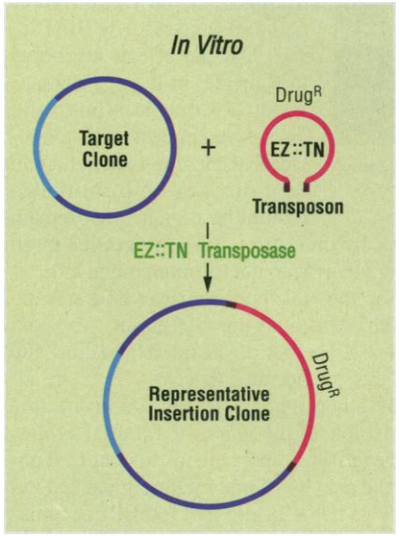
ISO 9000

Circle No. 34 on Readers' Service Card

Now, Accelerate Complete Sequencing of cDNA and Genomic Clones Without Primer Walking or Subcloning.



... It's EZ With *EPICENTRE*'s EZ::TN™ Insertion System!



Here's How It Works.

Simply incubate your target DNA in any vector with an EZ::TN Transposon and the EZ::TN Transposase provided in the kit for 1-2 h. Then stop the reaction, transform competent *E. coli* cells with an aliquot of the reaction mixture, and plate on media that select for the vector containing the target DNA and for the antibiotic resistance encoded by the EZ::TN Transposon used. A single reaction will generate a population of up to millions of DNA sequencing template clones, each with a randomly-inserted EZ::TN Transposon. Then, rapidly determine the complete sequence of the target by using the primers in the kit to sequence bidirectionally from the primer-binding sites on the EZ::TN Transposon.

The EZ::TN Insertion System:

– Yields More Insertions Than Any Other System - About 10^6 Per μg With A 6-Kb Plasmid Target. A single standard reaction generates more than enough insertion clones for complete sequencing, even with large target sizes or limited quantities of target DNA. No CsCl purification of target DNA is needed.

– Generates Insertions That Are More Random Than Other Systems. This permits you to close all sequencing gaps.

– Uses The Simple Cloned Single-Polypeptide EZ::TN Transposase and Simple EZ::TN Transposons. The only requirement for EZ::TN Transposon DNA is that it be flanked by specific 19-basepair sequences recognized by the EZ::TN Transposase. Other systems require a complicated transposase enzyme consisting of multiple polypeptides and transposons with larger recognition sequences. A simple system means better results and fewer problems. You can use an EZ::TN Transposon provided in the kit, design a custom transposon, or choose from a growing variety of EZ::TN Transposons with different drug-resistance markers and other features available from Epicentre.

– Has Many Uses Besides Sequencing. The unique properties of the EZ::TN Insertion System enable experiments using artificial transposons with different selectable or screenable markers, priming sites, promoter regions, or a variety of structural genes, control elements, or other sequences. You can also use artificial transposons to generate mutations or gene "knockouts".

To learn more about the **EZ::TN INSERTION SYSTEM,** contact **EPICENTRE** or visit our **WEBSITE** at: **www.epicentre.com/transposomics.htm**

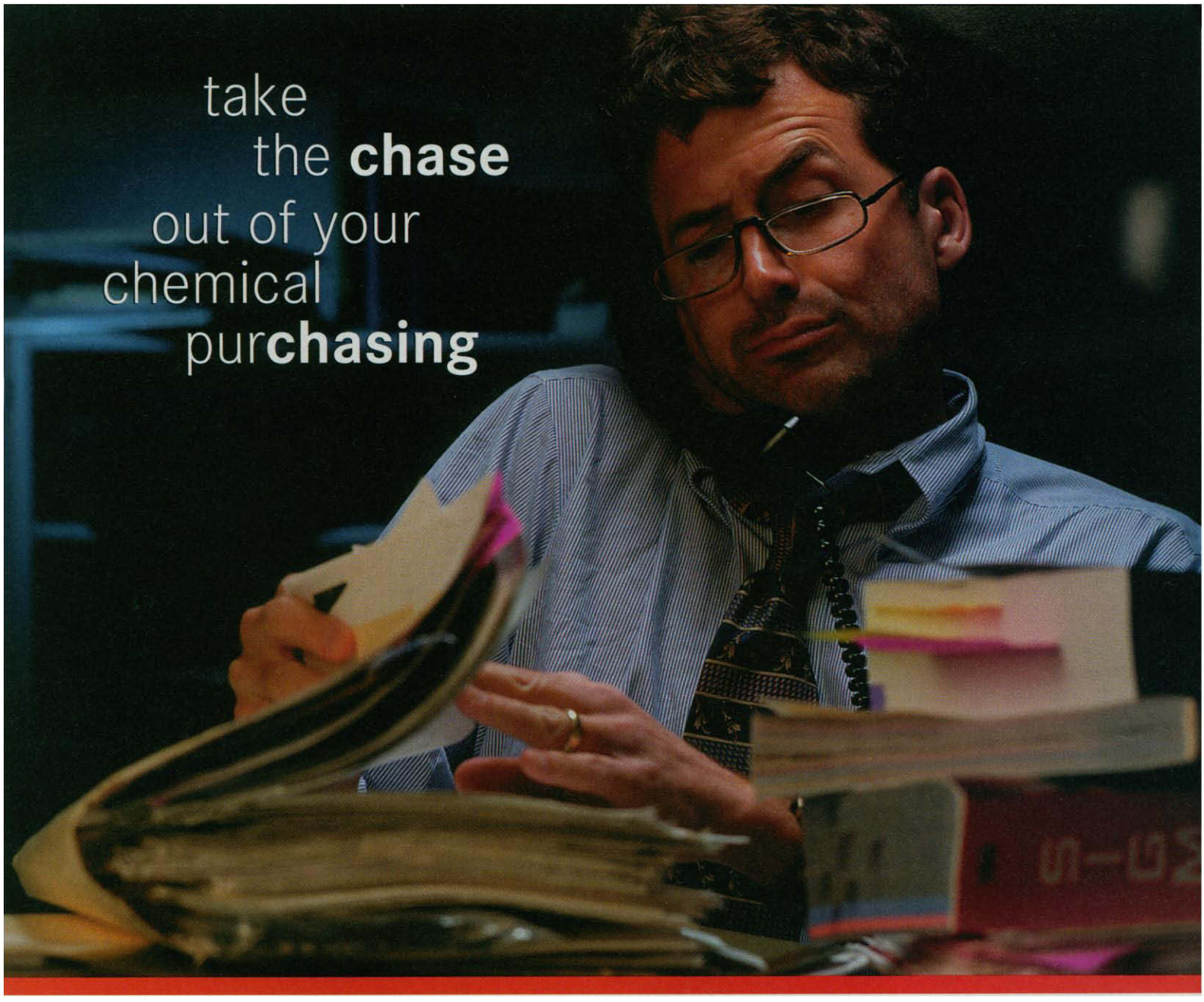
CALL ABOUT A LIMITED-TIME INTRODUCTORY PRICE!

EPICENTRE®
...when you need to be sure of the quality

800-284-8474 (USA only)
tel:608-258-3080
fax:608-258-3088
www.epicentre.com
techhelp@epicentre.com

Outside of the U.S. contact the distributor in your country, or call 608-258-3080 or fax 608-258-3088. **Argentina/Uruguay:** 54-1-822-6164, **Australia:** (02)9540-2055, **Austria:** 0222-74040-190, **Benelux:** 045-532-7755, **Brazil:** 021-592-6642, **Canada:** 800-661-6431, **Finland:** 3-6822-758, **France:** 1-30-46-39-00, **Germany:** 5152-9020, **Hong Kong/China:** 852-2-896-6283, **India:** 0091-11-463-6224 or 91-11-686-8795, **Israel:** 02-5335599, **Italy:** 02-891391, **Japan:** 03-3545-5720 or 06-441-5103, **Korea:** 82-2-924-8697, **Mexico:** 8-371-60-50, **New Zealand:** 9-443-1284, **Poland:** 48-58-3457646, **Singapore:** 779-3388, **South Africa:** 011-792-3428, **Spain:** 34-3-4502601, **Sweden:** 46-8-625-18-50, **Switzerland:** 056-624-0100, **Taiwan:** 886-2-932-1528, **Turkey:** 312-435-0775, **United Kingdom:** 1223-366500

Circle No. 60 on Readers' Service Card



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

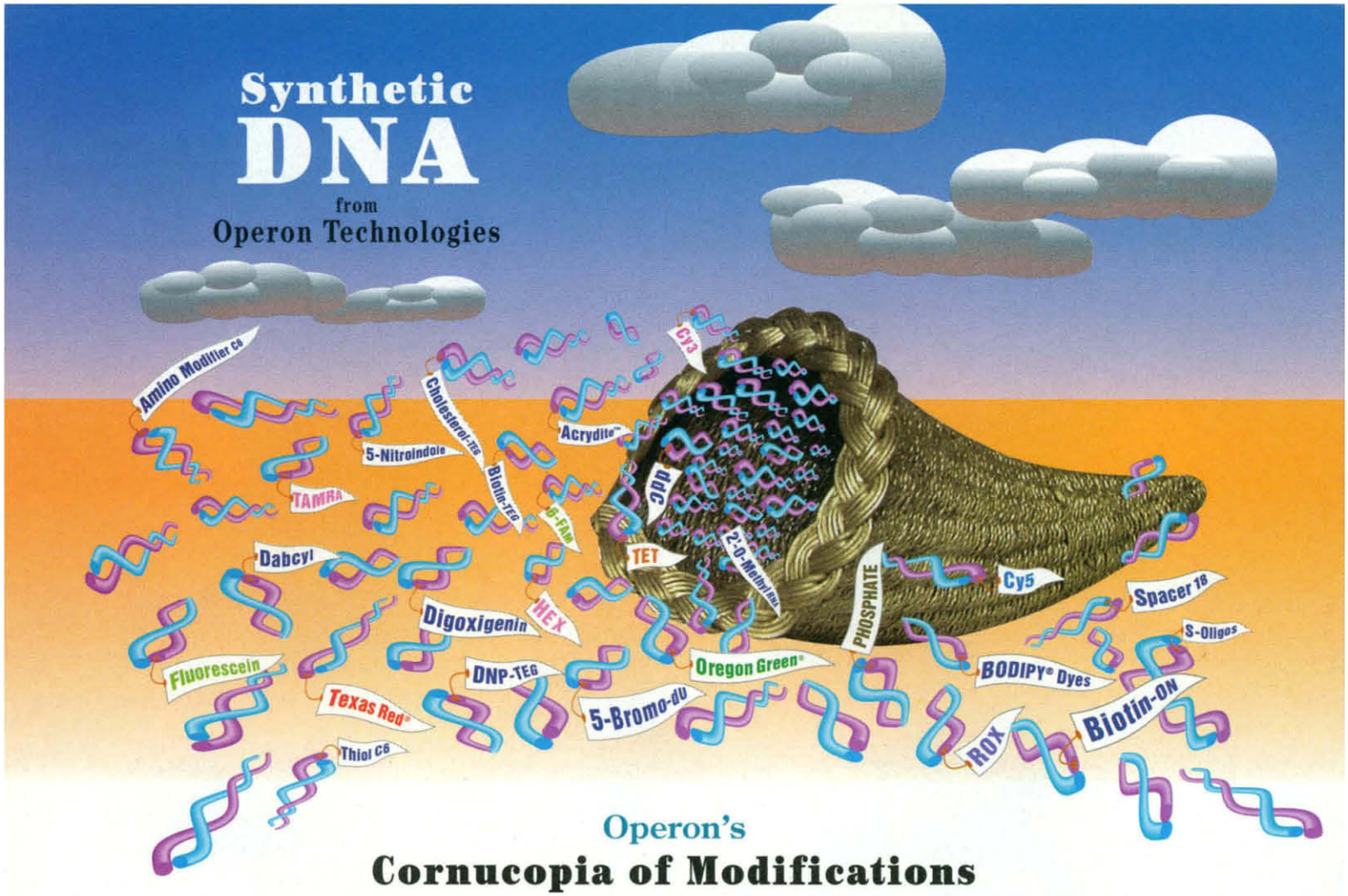
Because we are a manufacturer, we offer not only quality products but the technical knowledge and support to back them up.

- 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. 56 on Readers' Service Card



Operon's
Cornucopia of Modifications

Operon Technologies is pleased to offer a cornucopia of modifications available with our custom oligonucleotides. For applications that require fluorescent labels, we offer many dyes, including HEX, TET, 6-FAM, TAMRA, ROX, Cy3, Cy5, Oregon Green®, and Texas Red®. We offer phosphorothioates, propyne derivatives, and 2'-O-Methyl RNA residues which can be used to modify oligos for antisense studies. All commonly modified bases such as deoxyinosine, deoxyuridine, and deoxynebularine, as well as many halogenated bases including 5-bromo-deoxyuridine and 5-iododeoxycytidine are available. We also offer a wide variety of modifications with aminolinkers, biotin labels, and special attachments such as digoxigenin. For a more complete list of possible modifications, please call our customer service department at 800-688-2248 and ask for our catalog.

List Prices for Custom DNA Services

Custom DNA Synthesis Prices

Scale	Price/base	Set-up
0.05 µmole	$0.60	$5.00
0.2 µmole	$1.20	$10.00
1.0 µmole	$2.40	$20.00

(Larger scales available)

Purification Options

Method	Price
Sephadex	free
HPLC	from $30
PAGE	from $45

(Many scales available)

Sequence Modifications

Modification	Price	Modification	Price
Amino Modifier	$25	HEX, TET, 6-FAM	$70
Biotin	$50	Phosphate	$25
Cy3	$70	Oregon Green®	$125
Cy5	$70	ROX	$125
Digoxigenin	$125	TAMRA	$125
Fluorescein	$50	Texas Red®	$125

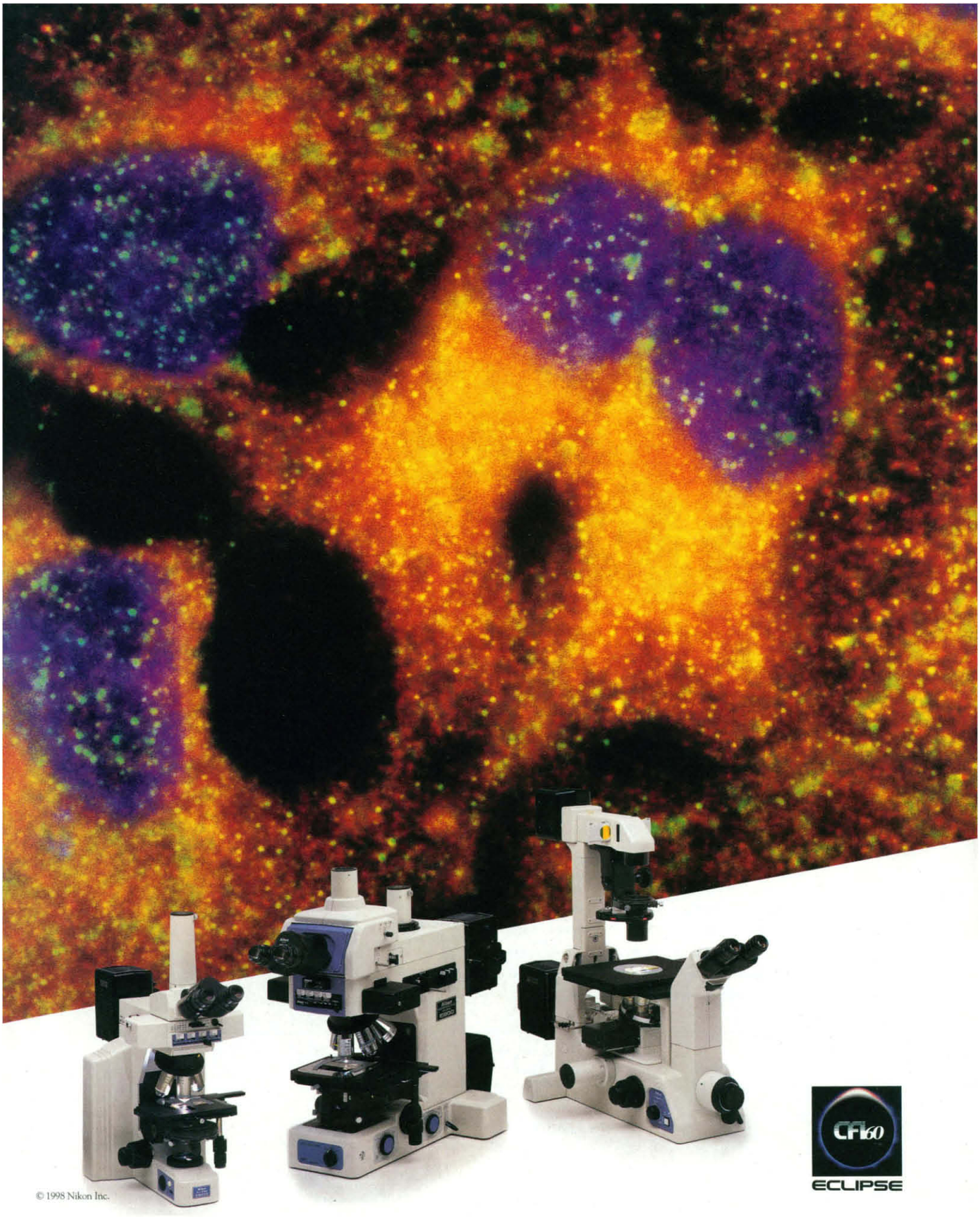
(Many other modifications available)

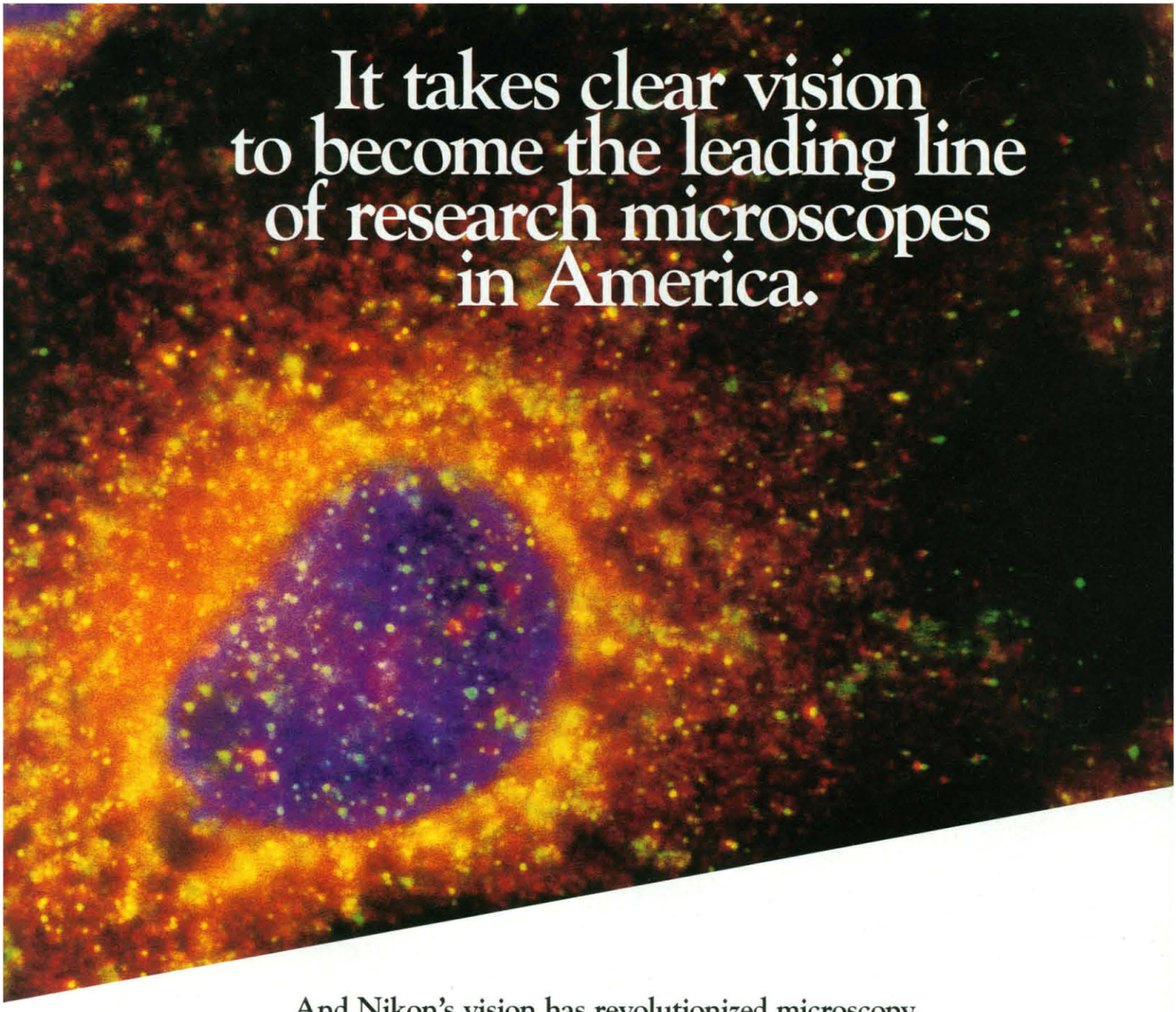
OPERON
OPERON TECHNOLOGIES, INC.

World's Leading Supplier of Synthetic DNA

1000 Atlantic Avenue, Suite 108 • Alameda, CA 94501
Phone: 800-688-2248 • Fax: 510-865-5255 • E-mail: dna@operon.com • Web: http://www.operon.com

Circle No. 48 on Readers' Service Card





And Nikon's vision has revolutionized microscopy.

The vision is Eclipse. The technology is groundbreaking. Eclipse microscopes, with their CFI60™ optical system, redefine infinity with the longest working distances, highest numerical apertures, and widest magnification range and documentation field sizes ever. Eclipse microscopes have proven themselves in research facilities across the country.

In fact, the Eclipse E800™ and TE300/200™ are America's number one selling research microscopes in their class.*

And you can rely on all the Eclipse microscopes to meet the most diverse observation and imaging requirements, with better clarity than ever before. Experience the clear vision of Eclipse for yourself. To schedule a demonstration of either the E800, E600, or the inverted TE300/200, call us at: **1-800-52-NIKON, ext. 330.**

The vision continues...

New high-tech advancements continue to be developed including our new physiology workstation, the Eclipse E600FN™ with its unique, easy-to-position, focusing nosepiece. Or, check out the ultimate in digital microscope automation, the new Eclipse E1000™.

www.nikonusa.com

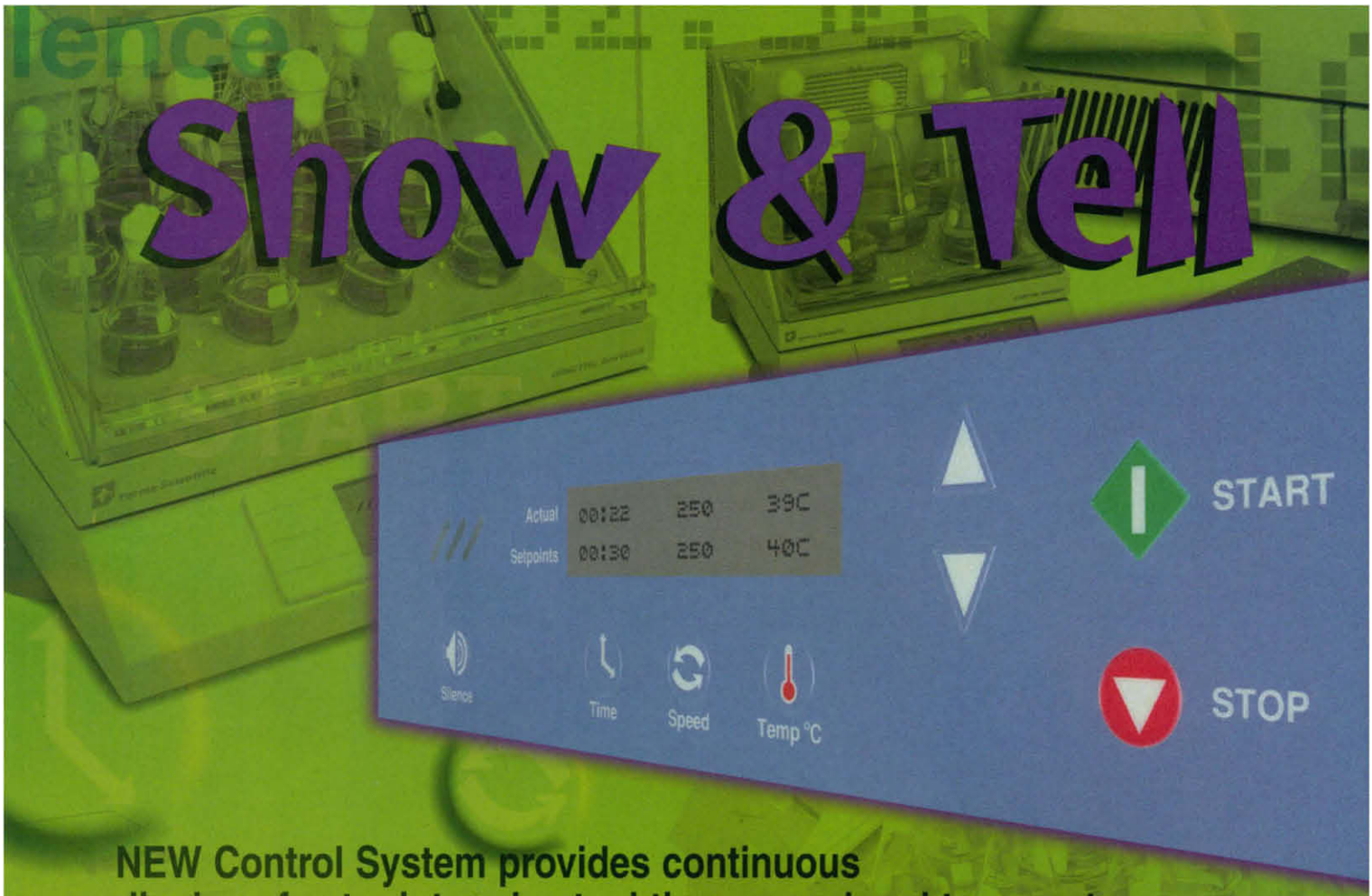
Nikon

Redefining Infinity

*Based on the Opto-Precision Instruments Association's (OPIA) Fourth Qtr. 1997, U.S.A. Microscope Survey

Circle No. 51 on Readers' Service Card

Show & Tell



NEW Control System provides continuous display of setpoint and actual time, speed and temperature.

- *Simultaneous display* of run and setpoints for "at-a-glance" monitoring, an exclusive feature found only on Forma's NEW 400 Series Orbital Shakers.
- Microprocessor Control/Monitoring System provides precise control with easy, three button programming using colorful icons.
- Available in tabletop and console models. Consoles feature unique HEPA filtration (U.S. Patent #5,577,837).
- Triple counterbalanced mechanism provides optimum handling of full or unbalanced loads and completely eliminates "walking" (U.S. Patent #5,558,437).
- Units are UL Listed, CSA Certified and bear the CE Mark, an industry exclusive.
- Best warranty in the industry: 2 year or 12,000 hour warranty, whichever comes later, on entire unit, including parts and labor. Unit Production Lifetime warranty on shaker mechanism, parts only.

Forma Scientific, Inc.

Box 649, Marietta, OH 45750
740-373-4763 • Fax 740-373-6770
USA and Canada 800-848-3080
International Distributors Worldwide
An ISO 9001 Company
http://www.forma.com

Forma Scientific is a subsidiary of ThermoQuest Corporation, a public subsidiary of Thermo Instrument Systems Inc., a Thermo Electron Company

Circle No. 36 on Readers' Service Card

MORE THAN 97 NEW WAYS TO STUDY

RNA Better, Faster, Easier.

Choose from the best selection of leading edge products and kits optimized for solving the unique challenges of RNA analysis. In the new 1999 Catalog, you will discover more than 97 new products to help you optimize isolation for higher yields, increase the sensitivity of detection assays and quantitate RNA better, faster and easier.

ISOLATE, DETECT, QUANTITATE

Do you isolate, detect or quantitate RNA? Then you need the innovative products from Ambion, The RNA Company.

New in the 1999 Catalog

- NEW ADVANCES IN RNA ISOLATION THAT OPTIMIZE YIELDS
- TOOLS TO IMPROVE RT-PCR QUANTITATION AND USE RELATIVE RT-PCR IN A NEW WAY
- A REVOLUTIONARY METHOD TO PERFORM IN SITU HYBRIDIZATIONS
- NEW WAYS TO IMPROVE YIELDS IN TRANSCRIPTION:TRANSLATION REACTIONS

GET INFORMATION NOW VIA EMAIL ON THE BEST NEW PRODUCTS OF 1999:

To immediately receive descriptions, catalog numbers and prices on the hottest new products and to request your 1999 Catalog, email your postal mailing address to 99cataloginfo@ambion.com

Catalogs may also be requested by phone, fax or the reader service number below.

For a complete list of distributors visit our website, http://www.ambion.com

U.S. (800)888-8804
Canada (800)445-1161

Ambion®
THE RNA COMPANY™

Circle No. 44 on Readers' Service Card

Ambion, Inc. • 2130 Woodward St. • Austin, TX 78744-1832 • tel(512)651-0200 • fax(512)651-0201 • email: moinfo@ambion.com • www.ambion.com

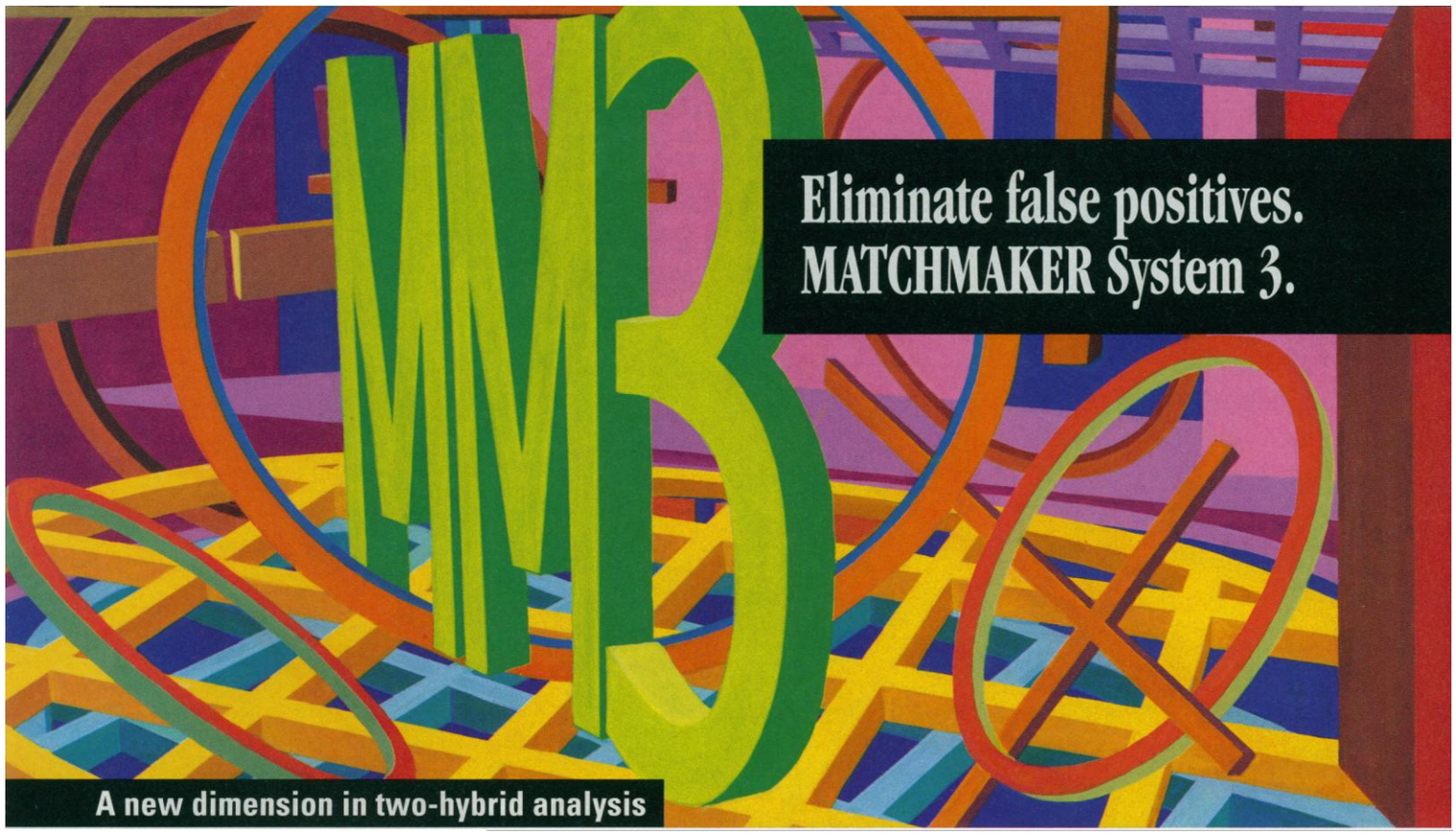


Illustration inspired by the art of Al Held.

MATCHMAKER System 3 (#K1612-1) breaks through the barrier of false positives that has encumbered two-hybrid analysis. System 3 eliminates false positives, increases sensitivity, and facilitates independent confirmation of protein interactions. Three reporters with distinct control regions yield strong and specific responses to activation. Inserts can be expressed *in vitro* immediately from a T7 promoter and are tagged with c-Myc or hemagglutinin (HA) for easy analysis. Streamline your analysis even further by using **MATCHMAKER Pretransformed Libraries.** Call and order today!

Use our high-quality yeast media and convenient nutritional dropout supplements!

Try YEASTMAKER™ Kits for high efficiency yeast transformation and reliable plasmid isolation.

Also available: GAL4 and LexA Monoclonal Antibodies

In Germany please contact CLONTECH GmbH • Tel: 06221 34170 Fax: 06221 303511
In the UK please contact CLONTECH UK Ltd. • Tel: 01256 476500 Fax: 01256 476499
In Japan please contact CLONTECH Japan Ltd. • Tel: 03 3523 9777 Fax: 03 3523 9781
In Switzerland please contact CLONTECH AG • Tel: 061 68354 50 Fax: 061 68354 52

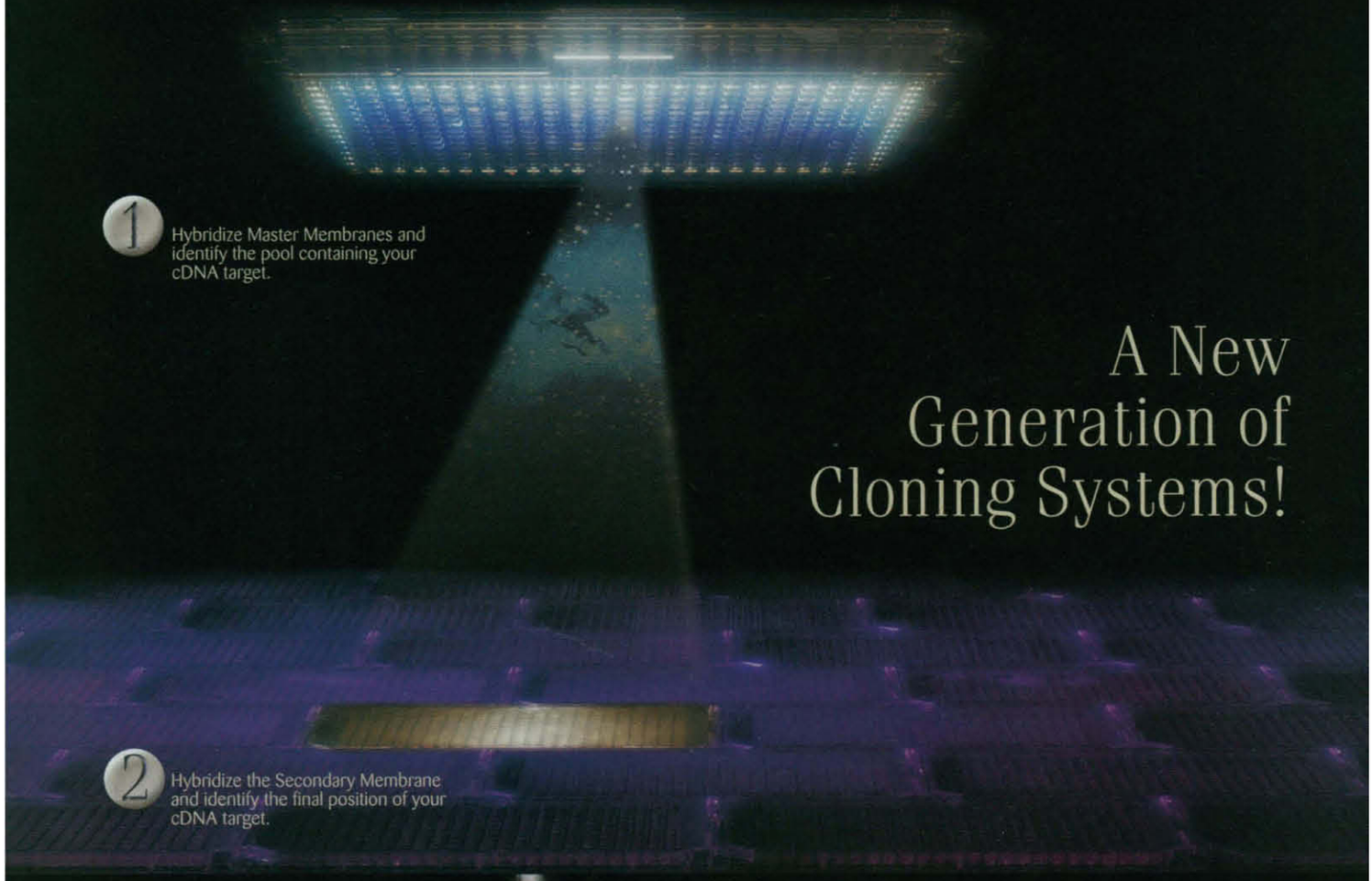
Distributors: Australia: 61 7 3273 9100 ■ **Austria and Eastern Europe:** 43 1 3106688 ■ **Belgium/Luxembourg:** 0 800 1 9815 ■ **Brazil:** 55 11 66940539 ■ **Canada:** Now call CLONTECH direct • 800 662 2566 ■ **China:** BEIJING YUANGPING BIOTECH • 86 10 68187551; GENE CO. LTD. • 021 6428 7163; SINO-AMERICAN BIOTECH CO. • 86 21 6402 2371 ■ **Czech Republic:** 420 19 7265214 ■ **Egypt:** 202 349 8311 ■ **Finland:** 358 9708 596 19 ■ **France:** 33134 602424 ■ **Greece:** 301 51 53882 ■ **Hong Kong:** 852 2646 6101 ■ **Hungary:** 36 1 280 3728 ■ **India:** 91 11 54 21714 ■ **Israel:** 972 4 9960595 ■ **Italy:** 39 55 5 001871 ■ **Korea:** 82 2 556 0311 ■ **Malaysia:** 603 777 2611 ■ **Mexico:** 525 281 4718 ■ **The Netherlands:** 31 33 495 00 94 ■ **Norway:** 47 22 421 520 ■ **Poland:** 49 06221 34170 ■ **Portugal:** 351 361 36 20 ■ **Scandinavia:** 46 8 728 00 65 ■ **Singapore:** 65 775 7284 ■ **South Africa:** 27 21 615166 ■ **Spain:** 34 9 1 630 0379 ■ **Taiwan:** 886 2 27202215 ■ **Thailand:** 662 530 3804 4 ■ **Turkey:** 90 216 385 8321 rev.4/7/99

CLONTECH
NOW YOU CAN.

1020 East Meadow Circle, Palo Alto, California 94303 USA
Tel: 800-662-2566 (CLON) 650-424-8222 • Fax: 800-424-1350 650-424-1088
E-mail: products@clontech.com orders@clontech.com • Internet: www.clontech.com
 (AD91807)

Circle No. 40 on Readers' Service Card

Human Universal cDNA Library
ARRAY I



1 Hybridize Master Membranes and identify the pool containing your cDNA target.

A New Generation of Cloning Systems!

2 Hybridize the Secondary Membrane and identify the final position of your cDNA target.

3 Receive isolated clone containing your gene of interest.

STRATAGENE brings you the HUCL Array I on nylon membranes. The Master Membranes represent 1,536 pools of 96 clones, and for each pool there is a corresponding Secondary Membrane arrayed with the individual clones. This unique format allows you to clone your gene of interest in two simple hybridization steps, saving you months of tedious lab work. A truly exceptional cDNA library!

- **Universal library with 29 different tissues represented**
- **Extensively normalized to reduce the representation of abundant gene transcripts**
- **Over 145,000 primary clones arrayed**
- **Average insert size of ~1.7kb**

HUCL Array I Master Membranes CATALOG # 937811
HUCL Secondary Membranes CATALOG # 937820*
HUCL Clones CATALOG # 937830*

*In addition to the catalog number, identification coordinates are required to order the Secondary Membranes and Clones.

www.stratagene.com

UNITED STATES AND CANADA
(800) 424-5444

INTERNET
techservices@stratagene.com

STRATAGENE EUROPE:
Austria: 017 956 7036
Belgium: 027 13 12 11
Germany: 0699 509 6197
Netherlands: 0800 023 0448
Switzerland: 01 800 9045
United Kingdom: 0171 365 1056

DISTRIBUTORS
For a list of worldwide distributors, please visit the Stratagene Web site at www.stratagene.com

STRATAGENE

Circle No. 64 on Readers' Service Card

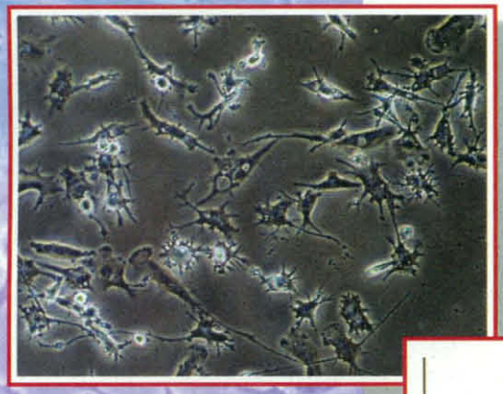
BIOWHITTAKER
A CAMBREX Company

the WORLD Center for Cell Culture Excellence.

Announcing

POIETICS™ Primary Human Hematopoietic Progenitor Cells...

...and Cells of the Immune System

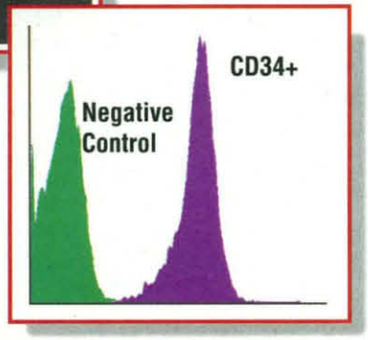


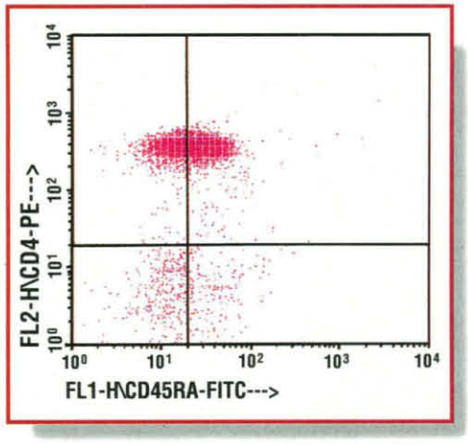
Applications:

- Drug Discovery
- Toxicology Research
- Myelotoxicity Assay
- Cell Maturation Pathway Research
- Immune Response Research
- T Cell Activation: Th1; Th2

Features:

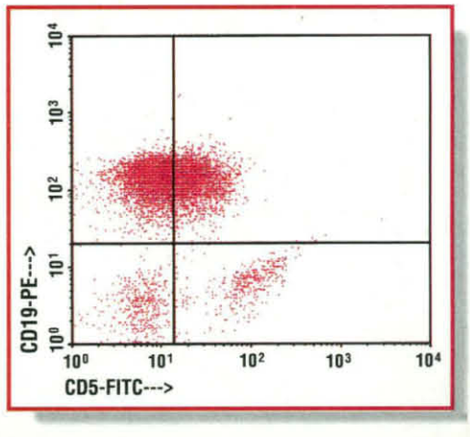
- Selection of Bone Marrow Cell Types Offered as Fresh or Cryopreserved
- Consistent, Reliable Supply for Standing Orders
- Standardized, Approved and Monitored Collection Process
- Multiple Donors Available
- Cell Culture Media Systems Available





Cell Types Available:

- Bone Marrow Mononuclear Cells
- CD34⁺, AC133⁺ Cells from Bone Marrow, Cord Blood, Fetal Liver
- CD4⁺ Cord Blood T Cells, "naive", Expressing CD45RA
- Dendritic Cell Precursors
- Committed Erythroid Progenitors CD36⁺, >85% Pure
- CD19⁺ Cord Blood B Cells
- Irradiated Stromal Cells



Custom Services

- Quadratox Panel- Drug Toxicity Across 4 Species
- Clonogenic Assays
- Quantitative LTC-IC
- CD34⁺ Proliferative Assays
- Lineage Marker ELISA

Standardize Your Research! Call Your Clonetics® Technical Specialist Today.

For Technical Information:
US & Canada (800) 852-5663
All other locations:
(301) 898-7025 ext. 7505

"Ask About Our New User Discount"

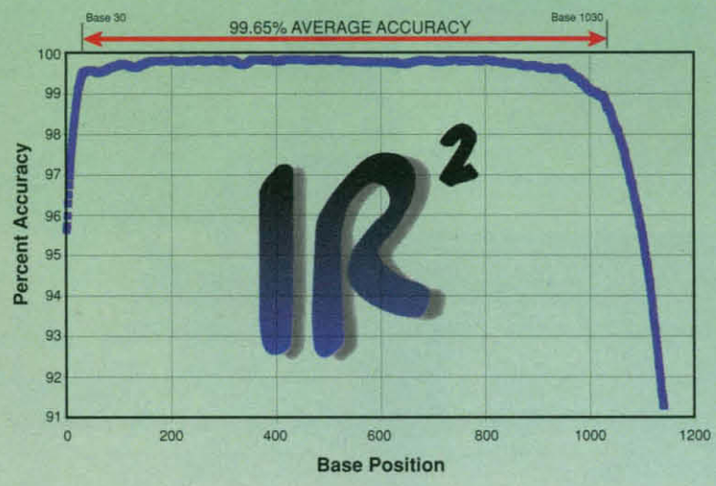
TO PLACE AN ORDER CALL:
(800) 344-6618
FAX: (301) 845-1008
E-MAIL: cs@biowhittaker.com
Internet: www.poietic.com, or www.clonetics.com

CERTIFIED ISO 9001

Circle No. 46 on Readers' Service Card

Your Options and Output Keep Getting Better.

- 2200 samples from a > 2.2 million bp project
- Average reads > 1000 bp
- Average Accuracy: 99.65%



Data courtesy of Drs. P. Brottier, H. Crespeau & P. Wincker, GENOSCOPE National Sequencing Center, EVRY Cedex, France.

Real World Results

LI-COR IR^2 Systems are making a measurable difference in labs worldwide by consistently delivering very long read lengths with very high accuracy. New Base ImagIR 4.1 software features a further advancement in base calling accuracy and a new curve file format. PHRED quality values are now included in LI-COR curve files, allowing them to be imported directly into PHRAP. The new curve file format also promotes high base calling accuracy from PHRED sequencing software.

CALL TODAY to learn about other new ways your options keep getting better with LI-COR.

LI-COR®

Biotechnology Division

800•645•4267

www.licor.com

Circle No. 41 on Readers' Service Card

the search for meaning

"There is no higher or lower knowledge, but one only, flowing out of experimentation".

Leonardo da Vinci (1452 - 1519).
Scientist, artist, engineer.

The lifeblood of science is experimentation. Discovery.

Not targets. Not budgets. And definitely not deadlines.

So anything that helps you achieve more, faster, and more effectively has to be good news.

Bio-Rad offers premium quality convenience products for electrophoresis and blotting-Ready Gel™ pre-cast gels, sample loading buffers, protein and nucleic acid electrophoresis running buffers and western, Southern and northern blotting buffers.

Ready Gel™ precast gels
Pre-mixed buffers and reagents

Pre-mixed, pre-cast and pre-measured buffers and gels from Bio-Rad are the obvious answer where speed and reliability are key, giving you more time to focus on what really matters. Your achievements.

"What is it that breathes fire into the equations and makes a universe for them to describe?" asks Stephen Hawking. "Why does the universe go to the bother of existing?"

Well, somebody's got to find out.

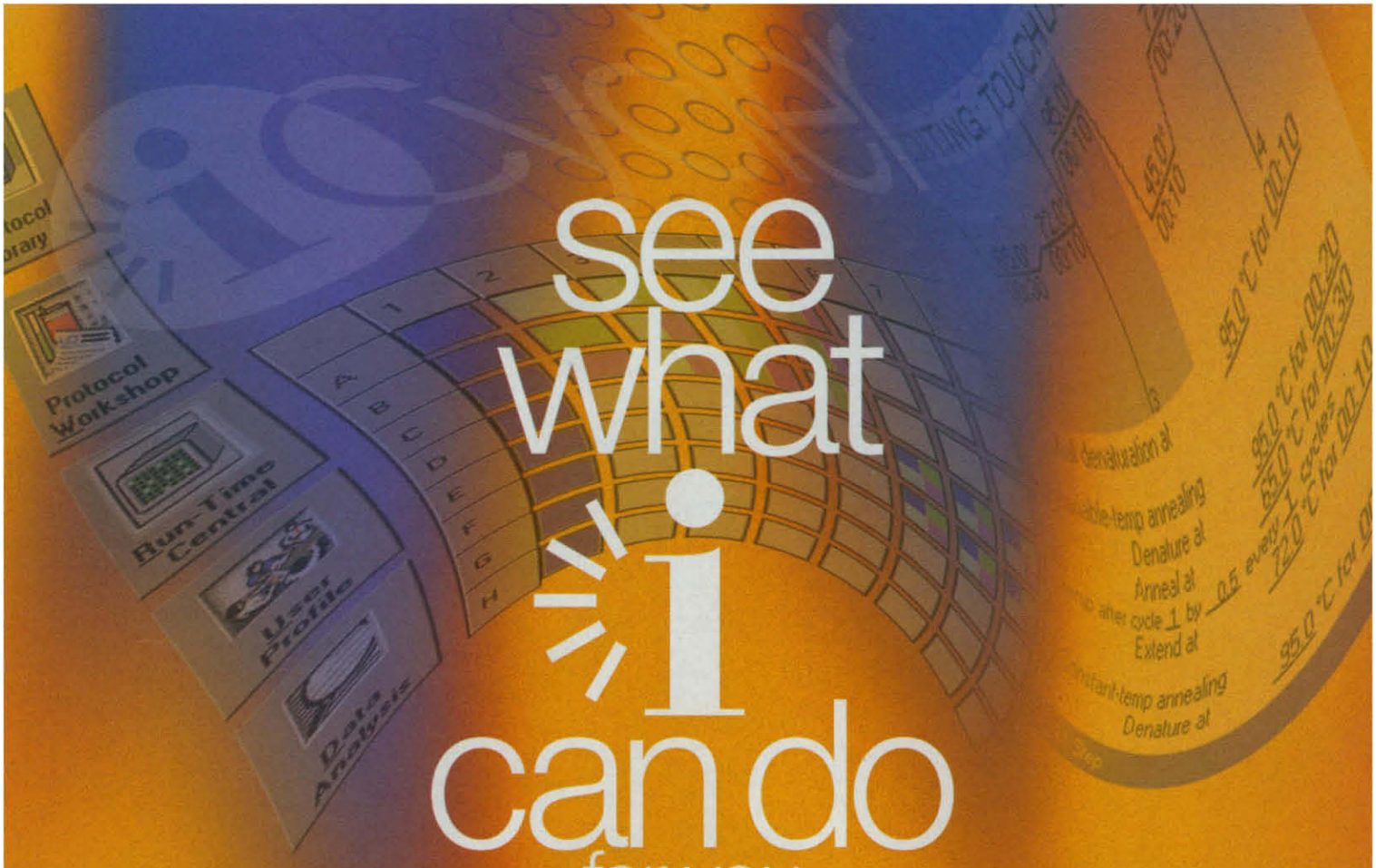
We'll be there to support your search - wherever your mind and all our tomorrows take us.

make a difference

BIO-RAD

www.discover.bio-rad.com

Circle No. 39 on Readers' Service Card

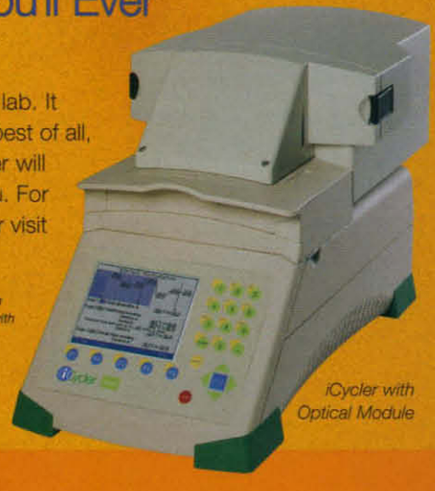


see what i can do for you

The New iCycler™ is All You've Ever Wanted From a Thermal Cycler and All You'll Ever Need for Real Time PCR*.

- **AFFORDABLE, QUANTITATIVE PCR**
- **INTUITIVE, ANALYTICAL SOFTWARE**
- **EFFORTLESS SAMPLE MULTIPLEXING**

The iCycler maximizes what a thermal cycler can do for your lab. It features multiple sample formats, easy graphic interface and, best of all, direct upgradability to Real Time Quantitative PCR. The iCycler will raise your expectation of what a thermal cycler can do for you. For more information, contact your local Bio-Rad representative, or visit our website at **discover.bio-rad.com**.



iCycler with Optical Module

* *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.*

BIO-RAD **Bio-Rad Laboratories**

Life Science Group

Website www.bio-rad.com **U.S.** (800) 4BIORAD **Australia** 02 9914 2800 **Austria** (01) 877 89 01 **Belgium** 09-385 55 11 **Canada** (905) 712-2771
China 86-10-62051650/51 **Denmark** 45 39 17 99 47 **Finland** 358 (0)9 804 2200 **France** 01 43 90 46 90 **Germany** 089 318 84-0
Hong Kong 852-2789-3300 **India** (91-11) 461-0103 **Israel** 03 951 4127 **Italy** 39-02-216091 **Japan** 03-5811-6270 **Korea** 82-2-3473-4460
Latin America 305-894-5950 **Mexico** 514-2210 **The Netherlands** 0318-540666 **New Zealand** 64-9-4152280 **Norway** 22-74-18-70
Russia 7 095 979 98 00 **Singapore** 65-2729877 **Spain** 34-91-661-7085 **Sweden** 46 (0)8-55 51 27 00 **Switzerland** 01-809 55 55
United Kingdom 0800-181134

Sig 031799

Circle No. 38 on Readers' Service Card

Luminescence with the highest standard

... and most value for your budget.

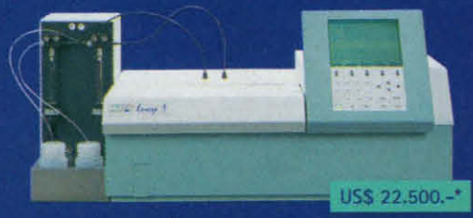
Luminometer

Photometer

Automation

Software

For research and routine labs

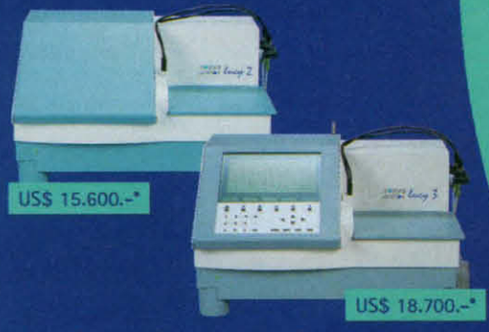


US$ 22.500.-*

anthos Lucy1

- high sensitivity
- temperature control
- syringe dispensers
- suited for all applications

Instruments for routine tasks



US$ 15.600.-*

US$ 18.700.-*

anthos Lucy2, Lucy3

- compact design
- easy to use
- evaluation onboard (Lucy3)
- suited for all applications

anthos is worldwide leading in measurement technology and microplate instrumentation. **Unsurpassed in performance and price.** More than 50 distributors worldwide guarantee best support. anthos luminometers feature additional photometry capability and dispensers providing a maximum of flexibility for new applications and for changing labels.

rosys anthos

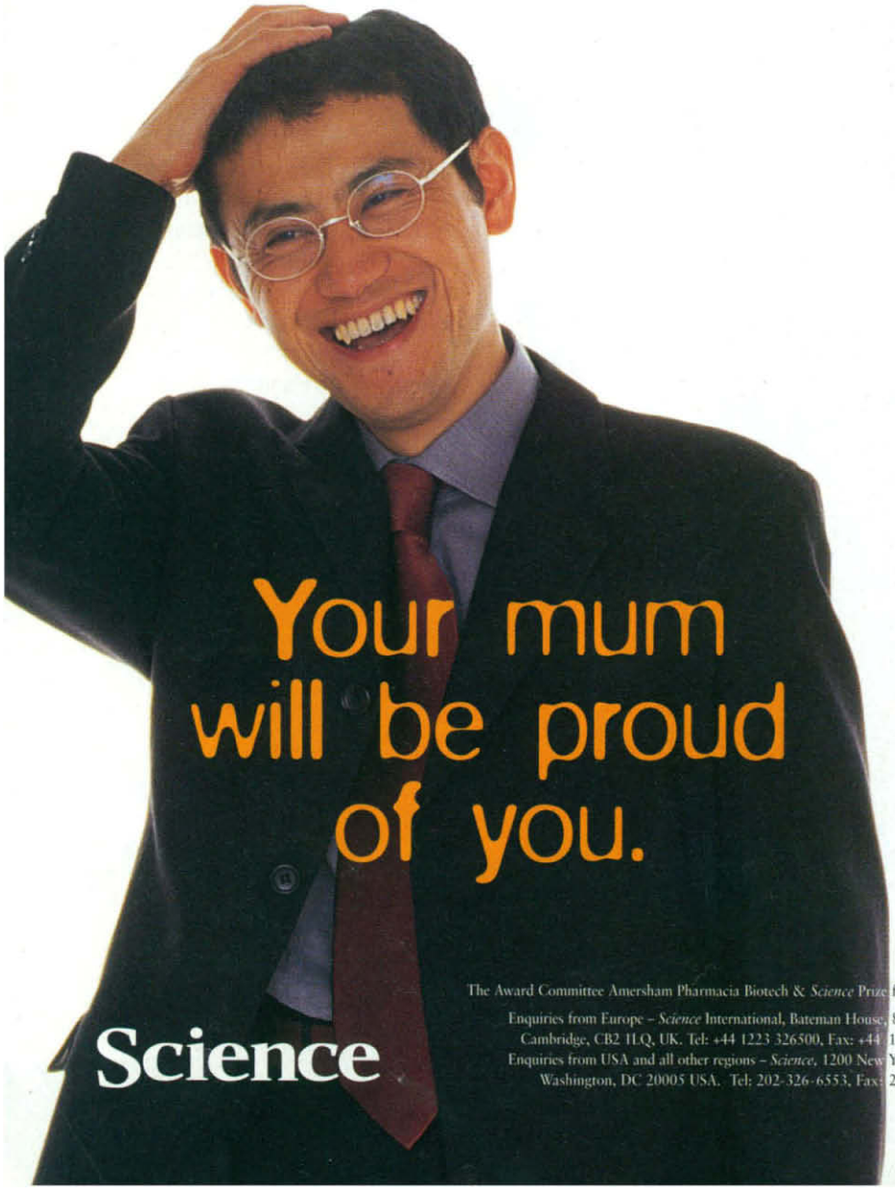
Contact us

for detailed product information and personal consulting:

anthos labtec instruments, Lagerhausstrasse 507, A-5071 Wals/Salzburg, Austria,
Tel: (+43) 662 857 220, Fax: (+43) 662 857 223, homepage: www.anthos-labtec.com,
e-mail: anthos@anthos-labtec.com

(*recommended enduser price)

Forget the international acclaim, the career advancement, the money.



AMERSHAM PHARMACIA BIOTECH & SCIENCE

Prize FOR YOUNG SCIENTISTS

Will it be your parents' turn this year?

The annual Amersham Pharmacia Biotech & *Science* Prize is one of the most prestigious international awards of its kind for young scientists. It can help achieve quite a lot for those who enter, putting bright, new scientific talent in the spotlight; bringing international acclaim to them and their universities; advancing their careers and earning winners and runners-up a handy cash prize (the first prize amount has been increased to $25,000, with up to seven additional prizes of $5,000).

Call for entries

You must be a recent Ph.D. graduate (awarded between 1 January and 31 December 1998) working in molecular biology. Submissions must be in the form of a 1000-word essay, in English, French, German, Spanish, Japanese or Mandarin Chinese, on your thesis, highlighting the significance of its contribution and overall implications in the field. The winning essay will be published in *Science*.

Closing date for entries is 15 June 1999. Prizes will be presented at an award ceremony in December 1999.

Full details and the required entry form can be requested from the administrator at the address below, or via these Web sites:

http://www.aaas.org/science/prize.htm

http://www.apbiotech.com

Hiroyuki Noji
(Ph.D. awarded by Tokyo Institute of Technology), winner of the 1998 Amersham Pharmacia Biotech & *Science* Prize for Young Scientists.

Science

The Award Committee Amersham Pharmacia Biotech & *Science* Prize for Young Scientists

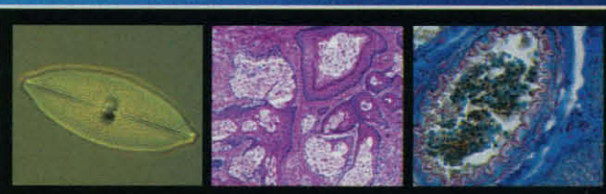
Enquiries from Europe – *Science* International, Bateman House, 82-88 Hills Road, Cambridge, CB2 1LQ, UK. Tel: +44 1223 326500, Fax: +44 1223 326501.
Enquiries from USA and all other regions – *Science*, 1200 New York Avenue, NW, Washington, DC 20005 USA. Tel: 202-326-6553, Fax: 202-789-8172.

amersham pharmacia biotech

Circle No. 31 on Readers' Service Card

Color Filter and IR Filter removed for 8 bit or 12 bit monochrome image acquisition

Color Filter and IR Filter in the light path for 24 bit or 36 bit color image acquisition



Color Digital and 12 Bit High Sensitivity Monochrome... Still Made Easy!

Introducing...

SPOT 2

The new SPOT-2 cooled CCD digital camera combines the spectacular color imaging capabilities of the original SPOT camera with the ability to slide a dual position color filter out of the light path for monochrome image acquisition. This greatly reduces the exposure times and ease of focusing for low light level images.

SPOT & SPOT-2 Software Features

- Easily switch from 8 or 12 bit monochrome to 24 or 36 bit color image acquisition
- Derive true, non-interpolated colors from the 1.4 million pixel array using 3-shot digital technology
- Includes auto and manual image acquisition, post picture editing, image merging, database archiving, measurement module and Twain driver
- Windows 95/98, Windows NT and MAC compatible

Our digital cameras deliver much more at an affordable price!

SPOT™

DIAGNOSTIC instruments, inc.

SPOT... The first cooled CCD color digital camera designed specifically for microscopes

To inquire about our family of SPOT cameras, please contact us or visit our website at www.diaginc.com

Phone: 810-731-6000 Fax: 810-731-6469 E-mail: info@diaginc.com

Circle No. 27 on Readers' Service Card

The State of the Art, Revolutionary

Lynx™ el Tissue Processor

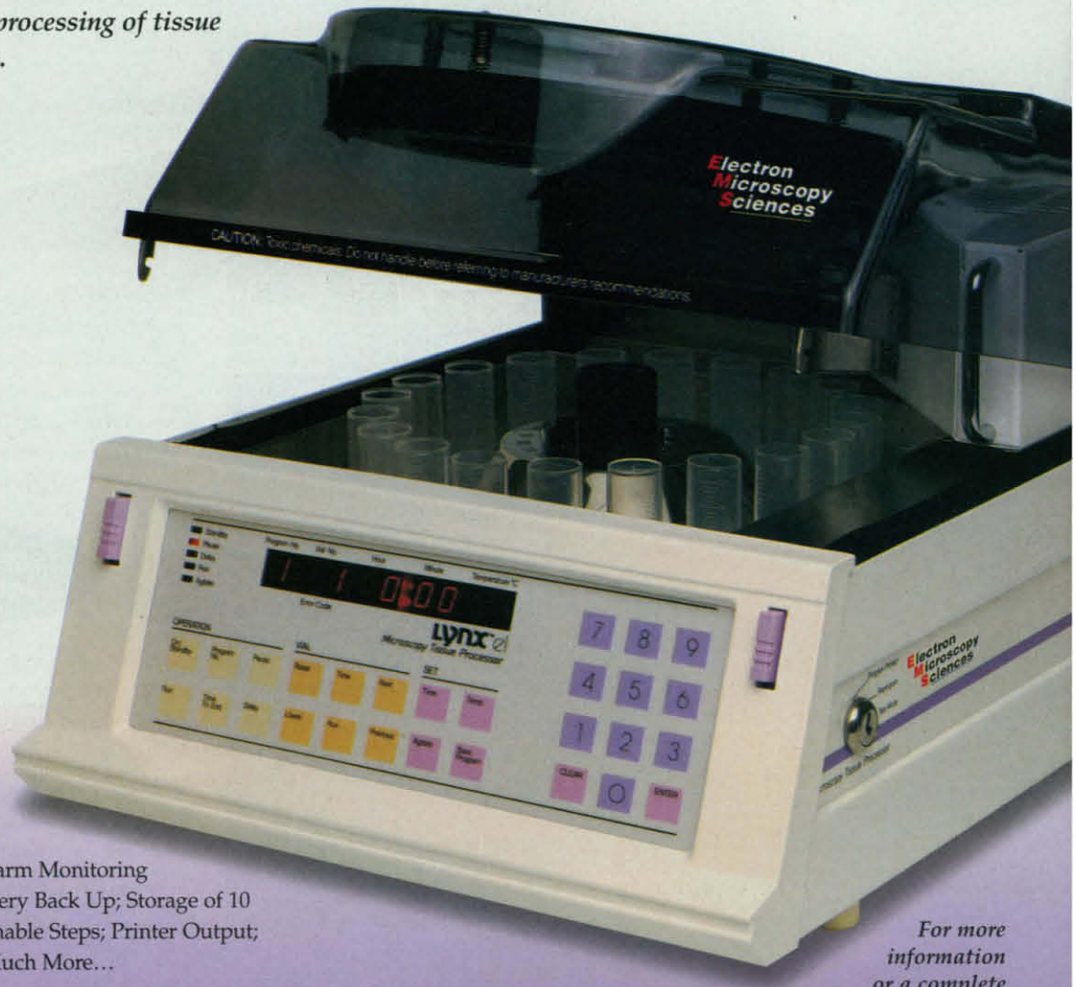
Electron Microscopy Sciences and the manufacturers of the "LYNX" Automated Tissue Processor have formed an alliance committed to bringing you only the best...

The EMS LYNX Automated Tissue Processor now made even better... for Electron Microscopy and Light Microscopy.

Dramatically reduce your sample preparation cost and time with improved reproducible results!!

The EMS LYNX allows for the processing of tissue all the way through 100% resin.

"LYNX" Available Exclusively at Electron Microscopy Sciences.



Primary uses:

- Ultrastructural Studies
- Extremely Hard Tissues - Undecalcified Bone
- High Resolution Light Microscopy
- Immunohistochemistry
- Dehydration for SEM
- Deparaffinization
- "En-bloc" Staining
- And Much More

This state of the art Automated Tissue Processor has many unique features making the unit the most versatile and reliable unit on the market at a very competitive price.

Features:

Stainless Steel Working Surfaces; Enclosed Benchtop Unit; Reagent Turntable, Max of 56 Specimens; 20 Reagent Vials/Cycle; Temp Range of 4ºC - 60ºC; Built in Exhaust Fan; Alarm Monitoring System; Multiple Safety Features; Battery Back Up; Storage of 10 Programs Each with 20 Pre-programmable Steps; Printer Output; Delay Start of Programs; and Much Much More…

For more information or a complete brochure on the "LYNX" Automated Tissue Processor, please call or write us today.

Electron Microscopy Sciences

Opening the Doors to New Techniques in the Laboratory

321 Morris Road • P.O. Box 251 • Ft. Washington, PA 19034
(215) 646-1566 • FAX (215) 646-8931
Email: sgkcck@aol.com • www.emsdiasum.com

Circle No. 58 on Readers' Service Card

Order Online!
www•promega.com

Death Assays by Design

APOPTOSIS

Cell SIGNALING

Promega Delivers...
Clarity to Cell Signaling Research!

Promega offers **non-radioactive** assay systems for assessing cell death and apoptosis, including the detection of caspase-1 and caspase-3-like activity in cells and tissues.

- NEW • Anti-PARP p85 Fragment pAb Cat.# G7341
  Novel Marker for Apoptosis
- NEW • CaspACE™ Assay System, Colorimetric Cat.# G7220, G7351
  Includes Z-VAD-FMK Inhibitor
- CaspACE™ Assay System, Fluorometric Cat.# G3540
- DeadEnd™ Colorimetric Apoptosis Detection System Cat.# G7130
- Apoptosis Detection System, Fluorescein Cat.# G3250
- CellTiter 96® AQueous One Solution Cell Proliferation Assays* Cat.# G3580
- CellTiter 96® AQueous Non-Radioactive Cell Proliferation Assays* Cat.# G5421
- CellTiter 96® Non-Radioactive Cell Proliferation Assays Cat.# G4000
- CytoTox 96® Non-Radioactive Cytotoxicity Assay Cat.# G1780

Anti-PARP p85 Fragment pAb

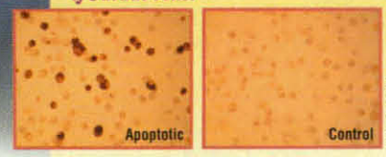
Caspase Assays

Tunel DNA Fragmentation Assays

Cell Proliferation Assays

Cytotoxicity Assay

Anti-PARP p85 Fragment pAb Immunocytochemical Staining of Jurkat cells.



2561GA02/9A

For further information on Promega's Apoptosis Products request literature packet LF077 or visit our website.
Learn what else Promega has to offer for cell signaling research by requesting our Cell Signaling Applications Guide (BR071) and Neuroscience RESOURCE (AP006).

www•promega.com

Promega

NORTH AMERICA
Promega Corporate Headquarters
2800 Woods Hollow Rd., Madison, Wisconsin
Toll Free in USA (800) 356-9526
Toll Free FAX in USA (800) 356-1970
Phone (608) 274-4330
FAX (608) 277-2516

Fisher Scientific Canada
Toll Free in Canada (800) 234-7437

EUROPE
▲ Austria +800-77663422
▲ Belgium 0800-18098
Czech Republic 02 206 10151
Denmark 44 94 88 22
Finland 358 9 7552550
▲ France 0800 48 79 99
▲ Germany +800-77663422
Greece 1 6436138
Hungary 1 251 0344
Ireland 018224222
▲ Italy 800 69 1818
▲ Luxembourg (+31)(0)71 532 4244
▲ The Netherlands 0800-0221910
Norway 22715090
Poland 58 3414726
Portugal 1 3613620
Russia 095 135 4205
Slovak Republic 95 632 4729
Slovenia 0 64 351 510
Spain 93 404 52 14
Sweden and Iceland 0346 83050
▲ Switzerland 01 830 70 37
▲ United Kingdom 0800 3789941

LATIN AMERICA
Argentina and Uruguay 1 4383 3000
Brazil
bioBRAS (*Belo Horizonte*) 31 2919877
Promicro (*Sao Paolo*) 118690699
Chile 22472976
Colombia 1 271 5319
Ecuador 3258483
Mexico 5 281 4718
Venezuela 2 265 0891

MIDDLE EAST/AFRICA
Egypt 2 245 1785
Israel 8 9477077
Lebanon 1 249836
South Africa 21 981 1560
Turkey 216 385 8321

PACIFIC ASIA
▲ Australia 1 800 225 123
China, People's Republic
▲ *Representative Office*
Promega Beijing 10 68498287
Joint Venture
(SP) 21 6483 5136
(SABC) 379 432 2510
Hong Kong 2646 6101
India 11 684 5685
Indonesia 21 489 1718
▲ Japan 03 3669 7981
Korea (02) 478 5911
Malaysia 3 7048600
New Zealand 93664784
Pakistan 92 51 518 469
Singapore 775 7284
Taiwan 022382578
Thailand 2 295 2532

▲ **Indicates Promega Branch Office or Representative Office.**

030899.eps
AD8025CR

Circle No. 50 on Readers' Service Card