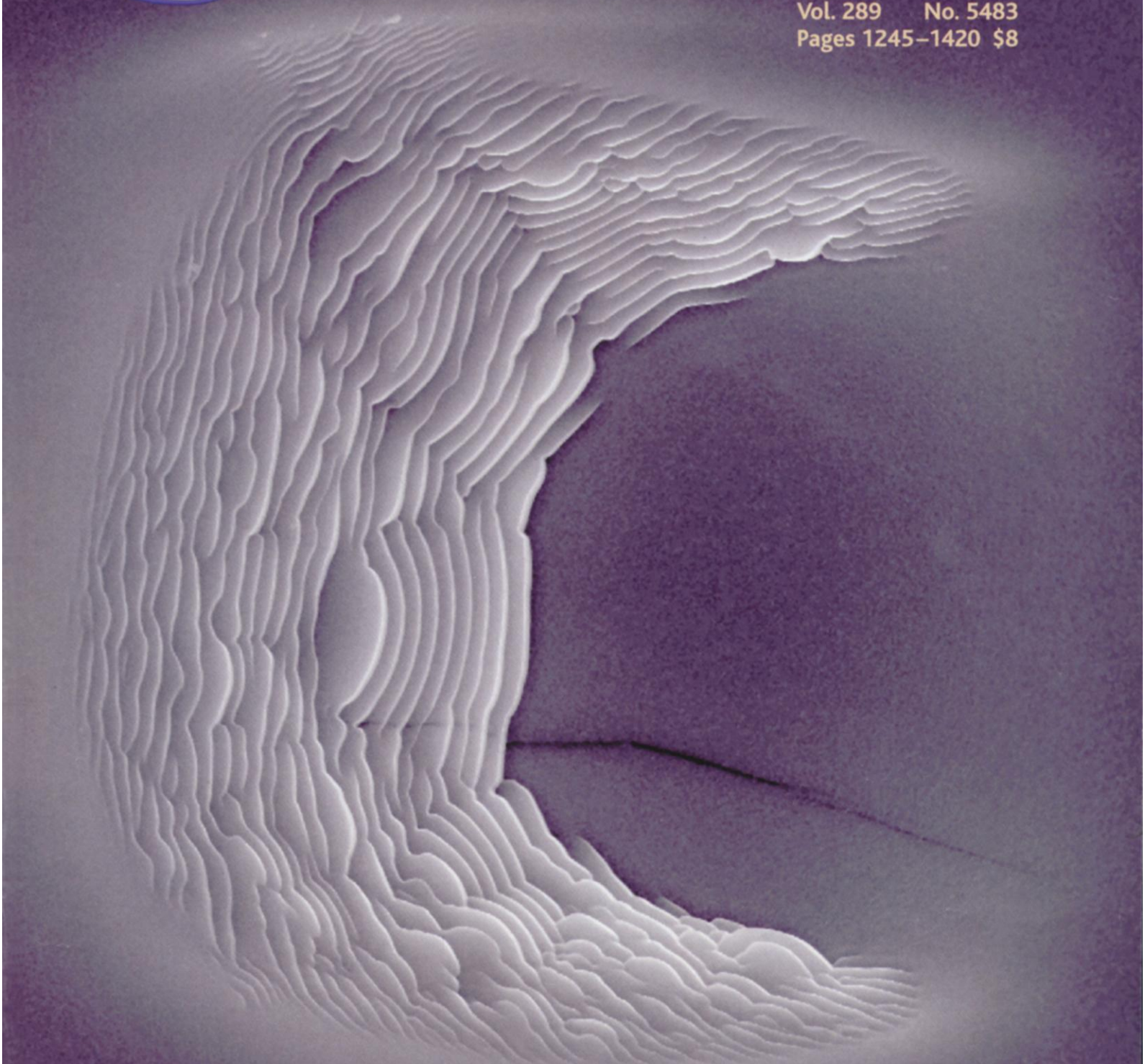
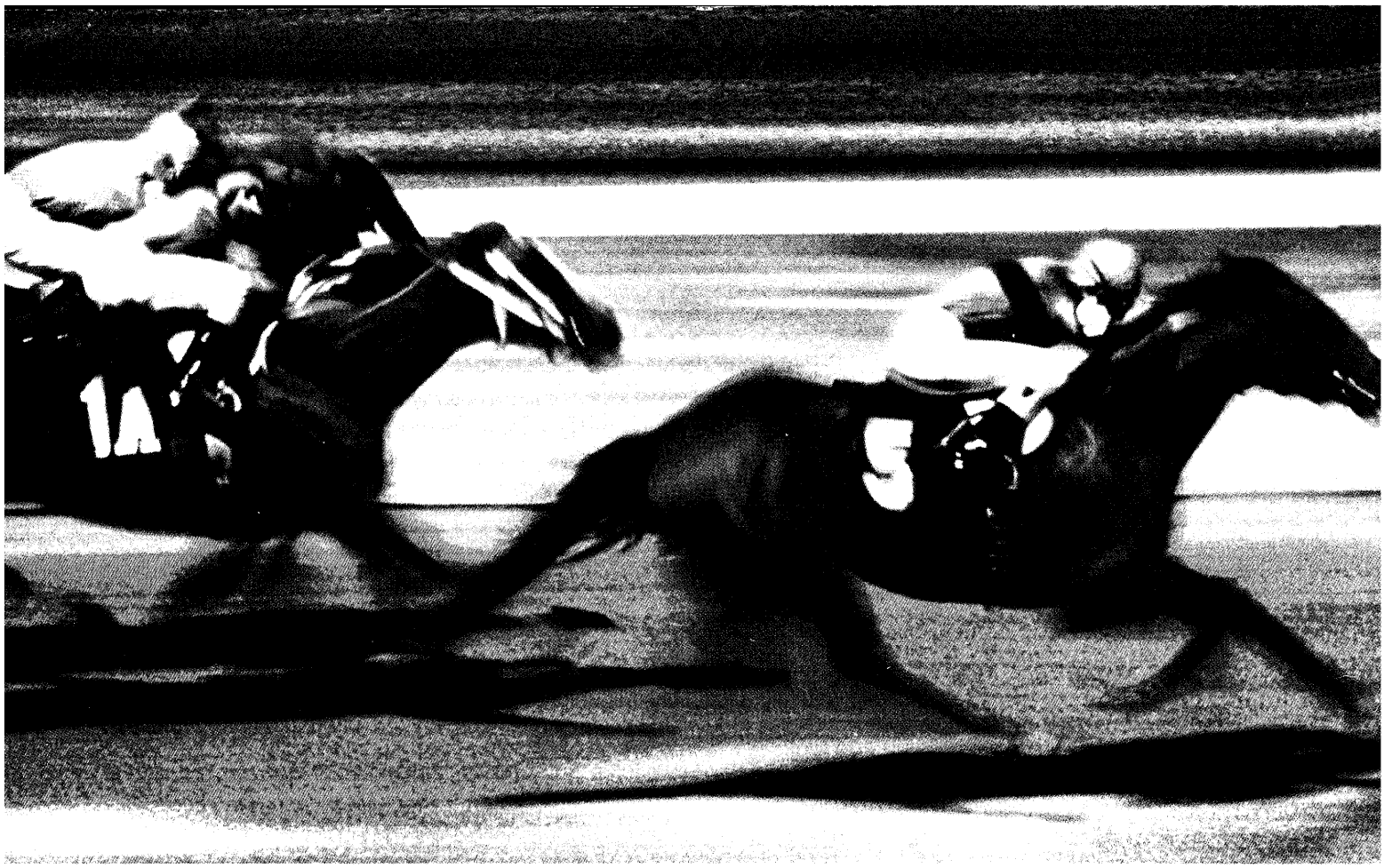
25 August 2000

Science

Vol. 289 No. 5483
Pages 1245–1420 $8



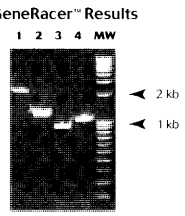
American Association for the Advancement of Science



Accept nothing less than a full-length finish.

Put an end to truncated RACE products with GeneRacer™.

You have some gene sequence but not the 5′ end. Don't bet on conventional RACE methods to find your 5′ end. They often produce mixed results and typically yield the truncated sequence you already have. Only the GeneRacer™ Kit eliminates truncated sequences. You'll get your results faster and obtain the full length you need to get ahead in the race.



Clear, single bands after one round of 30-cycle PCR

Full-length lead. The advanced GeneRacer™ method specifically targets full-length 5′ capped mRNA. Only full-length messages are transcribed and amplified, eliminating truncated sequences from your final results. You'll see a clear single PCR product, saving you time in analysis. *Get the 5′ end and a full-length finish. Call Invitrogen today.*

Invitrogen™
living science

Circle No. 32 on Readers' Service Card

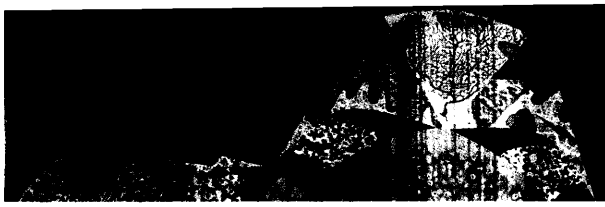
United States Headquarters:
1600 Faraday Avenue
Carlsbad, California 92008
Tel: 1 760 603 7200
Tel (Toll Free): 1 800 955 6288
Fax: 1 760 603 7201
Email: tech_service@invitrogen.com
www.invitrogen.com

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

European Toll Free Numbers:
Order line 00800 5456 5456
Technical support 00800 5345 5345
Fax number 00800 7890 7890

Distributors:
Australia 1 800 882 555
Czech Republic 2 727644 16
Finland 09 584 121
Hungary 01 280 3728
Israel 02 584 1111
Italy 02 38 1951
Japan 03 5684 1622
Korea 02 3471 6500
Poland 058 341 4726
Portugal 021 453 7085
Spain 091 729 0333
Taiwan 080 231 530

All other countries, see our website: www.invitrogen.com



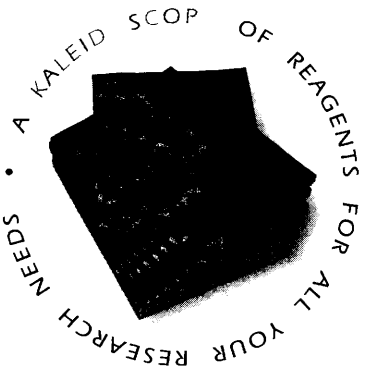
Antibodies

MONOCLONAL • ANTIGEN-PURIFIED POLYCLONAL • BIOTINYLATED • FLUOROCHROME-LABELED

R&D Systems is your source for antibodies to cytokines and related molecules

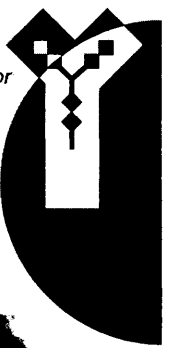
Offering over 1000 antibodies to:

- Cytokines
- Chemokines
- Receptors
- Developmental Factors



- Adhesion Molecules
- Matrix Metalloproteinases
- Neurotrophic Factors
- Apoptosis-related Factors

Look for this symbol in our 2000 Catalog for Antibodies



R&D Systems' Cell and Tissue Staining Kits are now available for detecting goat, mouse and rabbit primary antibodies utilizing three different enzymatic systems, HRP-DAB, HRP-AEC or AP-BCIP/NBT.

Antigen Retrieval Reagents are also available.

For more information about immunohistochemistry, please visit R&D Systems' website at www.rndsystems.com/cyt_cat/ihcprot.html.

Activin A in prostate cancer. *Activin A labeling (red) in paraffin-embedded human prostate cancer tissue was done using R&D Systems' monoclonal anti-Activin A (β_A subunit), Catalog # MAB3381. Detection was done using the anti-mouse HRP-AEC Cell and Tissue Staining Kit, Catalog # CTS003.*

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

North America
R&D Systems, Inc.
McKinley Place NE
Minneapolis, MN 55413, USA
Tel: 612 379-2956
Free: 1-800-343-7475
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 529 449
Free: 0800 37 34 15
Fax: +44 (0)1235 533 420
info@rndsystems.co.uk

Germany
R&D Systems GmbH
Borsigstrasse 7
65205 Wiesbaden, Germany
Tel: +49 (0)6122 90980
Free: 0800 909 4455
Fax: +49 (0)6122 909819
infogmbh@rndsystems.co.uk

Europe Free Phone
Belgique/België: 0800 10 468 614
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

R&D SYSTEMS
1-800-343-7475
www.rndsystems.com

Circle No. 74 on Readers' Service Card

VOLUME 289 25 AUGUST 2000 NUMBER 5483

Science

www.sciencemag.org

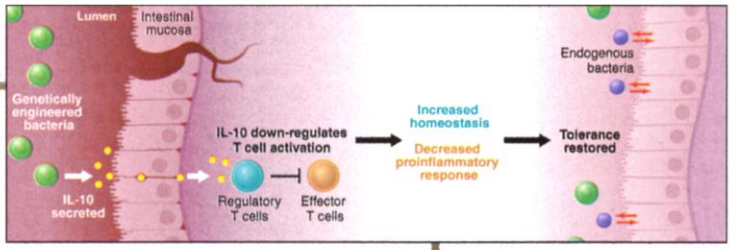
COVER Scanning electron micrograph of a crater that was created during analysis of a melilite crystal from a calcium-aluminum–rich inclusion in the Allende meteorite. This ~40-micrometer-diameter crater was produced by oxygen ion bombardment during secondary ion mass spectrometry. The results indicate that the sample may have contained short-lived radioactive beryllium-10 at the time of its crystallization in the early solar nebula. [Photo: K. D. McKeegan and G. Jarzebinski]

1274
Lighting up the economy?

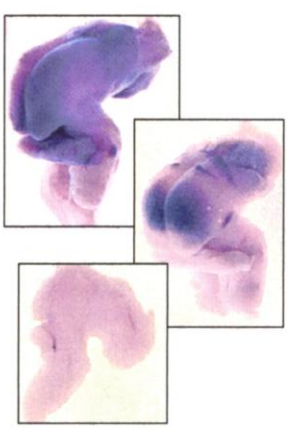
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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): $112 ($62 allocated to subscription). Domestic institutional subscription (51 issues): $340; 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



1311
Blood and guts



1360
Protease control of axon guidance

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 $8.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/83 $8.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

And do it faster and more cost-effectively. Simple, isn't it? We know it is not.

In our mind's eye, our job is to facilitate the business of bringing new therapies to market faster and more cost-effectively. If that's the business you're in, you'll find us at the very heart of it - discovering, developing and delivering the special technologies and support services – from academic research through to production.

Discover. Develop. Deliver.

Our know-how spans the entire pipeline from gene to medicine. Right now, our MegaBACE™ DNA sequencing platform is accelerating the genome discovery race. The LEADseeker™ homogeneous imaging system can shorten a drug screening cycle five-fold. While STREAMLINE™ delivers pure protein by the tonne. And new discoveries are just in sight.

We understand your requirements because we work closely with our customers to provide the latest systems to accelerate their commercial success. We already have more than 90 such technology collaborations with top drug companies and life science research organizations.

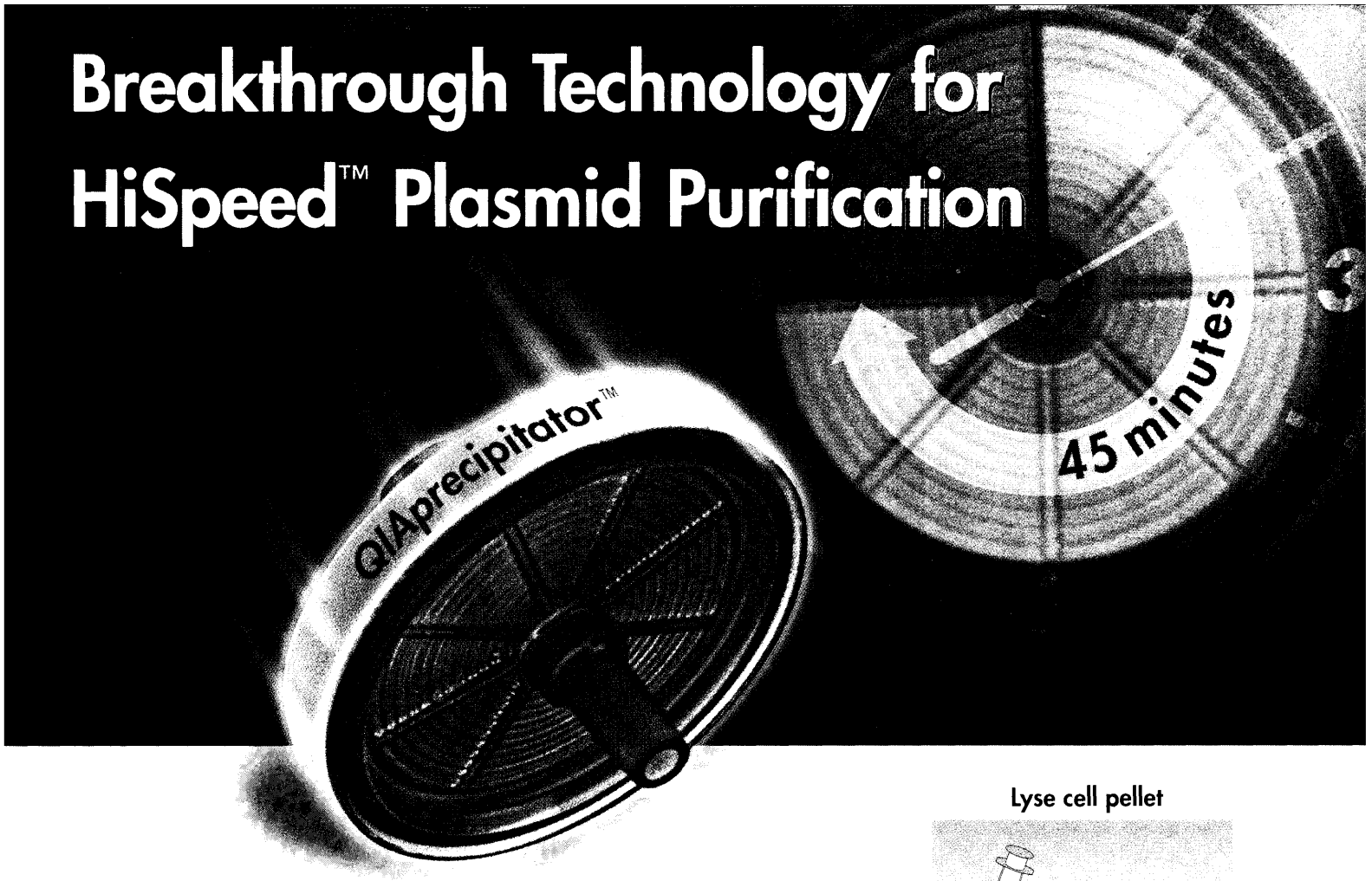
So it doesn't matter where you are in the process or how complex the task. Just ask us. It's that simple.

See for yourself at **www.apbiotech.com**

amersham pharmacia biotech

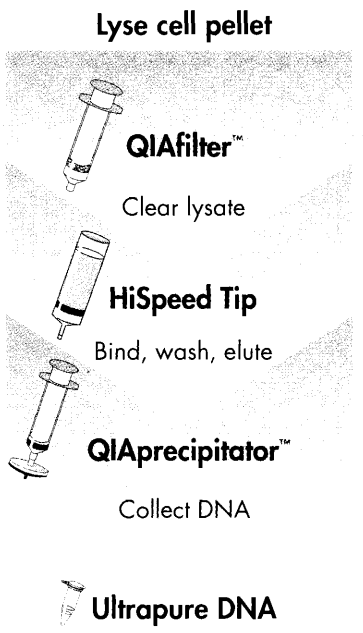
Circle No. 71 on Readers' Service Card

Breakthrough Technology for HiSpeed™ Plasmid Purification



HiSpeed™ Plasmid Midi, the most advanced plasmid purification kit available:

- 45 minutes from cell pellet to DNA sample
- Centrifugation steps eliminated
- No risk of DNA pellet loss during precipitation
- Up to 200 µg yield of high-copy plasmid DNA
- Proven QIAGEN® anion-exchange ultrapurity



Large-scale plasmid purification has never been faster and easier.

Call 1-800-426-8157 to order your kit today!

www.qiagen.com

Circle No. 65 on Readers' Service Card

QIAGEN:

Australia Tel. 03-9489-3666 Fax 03-9489-3888
Canada Tel. 800-572-9613 Fax 905-821-1327
France Tel. 01-60-920-930 Fax 01-60-920-925
Germany Tel. 02103-29-12400 Fax 02103-29-22022
Italy Tel. 02-334-304-11 Fax 02-334-304-26
Japan Tel. 03-5805-7261 Fax 03-5805-7263
Switzerland Tel. 061-319-30-31 Fax 061-319-30-33
UK Tel. 01293-422-999 Fax 01293-422-922
USA Tel. 800-426-8157 Fax 800-718-2056

Distributors:

Argentina Tecnolab S.A. (011) 4555 0010 **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 **Cyprus** Scientronics Ltd (02) 765 416 **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 **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)-424 73 64 **Singapore** Research Biolabs Pte Ltd. 445 7927 **Slovak Republic** BIO-CONSULT Slovakia spol. 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, Germany

QIAGEN

HSP1307000SUS

A HOT BEGINNING

Calcium-aluminum–rich inclusions (CAIs) are found in the most primitive meteorites and are thought to represent some of the first solid particles that formed in the early solar system. McKeegan *et al.* (p. 1334) measured boron isotopes in CAIs to demonstrate that ^{10}Be (which decays to ^{10}B and forms only from nuclear spallation reactions) was present in the early solar system (see the cover). Its presence is consistent with one model for formation of CAIs and other early solar system materials in which the early solar system was bombarded by intense radiation. Possible support for this model also comes from Guan *et al.* (p. 1330), who studied aluminum isotopes (which indicate the presence in the early solar system of ^{26}Mg) and other aspects of the geochemistry of CAIs in enstatite chondrites. These CAIs formed under more oxidizing conditions than their host chondrites, and thus the CAIs likely formed earlier in a different location of the solar system.

IBERIAN ICE

Heinrich events, periodic massive discharges of icebergs from Arctic ice sheets, have showered the sea floor with continental debris many times during the past glacial cycle. Although their impact on the North Atlantic is well documented, it is less clear for areas outside the main ice-rafting belt. E. Bard *et al.* (p. 1321) have combined a variety of geochemical proxies, in a well-dated marine sediment core from the subtropical northeast Atlantic, to demonstrate that cooling and advection of low-salinity water from the Arctic affected the midlatitudes during the three Heinrich events of the past 32,000 years. Their results illuminate the internal complexity of these events and illustrate the utility of combining data from organic and inorganic sediment fractions.

FUNNELING ENERGY

The dynamics of the charge-separated excited states (excitons) in the conjugated polymers that find use in light-emitting diodes is complicated by their rapid quenching and by their movement along and between polymer chains. Yu *et al.* (p. 1327) found that by rigorously excluding O_2, which rapidly quenches excitons, the effects of polymer conformation on exciton dynamics in the solid state could be studied. They dissolved the conjugated polymer MEH-PPV in nonphotoactive polymers, such as polystyrene, in order to avoid interchain effects and then took spectra of single molecules. They found an unexpected sharp, red-shifted emission feature that they attributed to a particular chain conformation, a defect cylinder, which forms through tetrahedral defects. These defects effectively trap and localize the exciton on a chain, and thus act as an "energy funnel" for excitons formed many chain units away.

SQUEEZING OUT PYRUVATE

One model for the origin of life is that the necessary building blocks originated at hydrothermal vents in a series of reaction steps where metal sulfides at elevated pressures and temperatures catalyzed carbon fixation and the formation of more complex organic molecules. Cody *et al.* (p. 1337; see the Perspective by Wächtershäuser) performed experiments that simulate some of the possible conditions of marine hydrothermal systems and show more complex organometallic species forms in this environment that catalyze the formation of pyruvate, a critical biochemical molecule. High pressures appear to compensate for the high temperatures that would normally cause pyruvate to decompose.

EUROPA'S OCEAN STILL AFLOAT

Interpretations of previous data from the Galileo spacecraft have suggested that Europa, the smallest of the Galilean satellites orbiting Jupiter, may have a layer of fluid beneath its icy surface. Kivelson *et al.* (p. 1340; see the Perspective by Stevenson) used magnetometer data collected by Galileo during the 3 January 2000 close flyby of Europa to confirm that changes in Europa's induced magnetic field are driven by a shallow conductive layer. A model of a spherical shell conductor located about 7.5 kilometers below the surface with a conductivity similar to Earth's ocean water fits their new data well.

PRION CONVERSION MECHANISM

The role of protein conformation in the expression and propagation of prion states in yeast is now well established. Serio *et al.* (p. 1317) examined in vitro the mechanism of conformational conversion of one of the yeast prion proteins, Sup35. The soluble protein goes through a series of conformation states in a process, termed nucleated conformational conversion, that leads to assembly into fibrils.

ARCTIC HIDEOUTS

What happened to the flora and fauna of high latitudes during the Pleistocene glaciations? Did they persist in isolated pockets—refugia—where conditions were more benign, and if so, where were these refugia? Abbott *et al.* (p. 1343) present molecular evidence to indicate where one circumpolar arctic plant—the purple saxifrage—initially occurred in the Arctic, the migration routes it followed to achieve a wide distribution, and the refugia it occupied during Pleistocene glaciations. These results provide strong support for the existence of refugia for arctic-alpine plants in the Arctic itself at the time of the last glacial maximum.

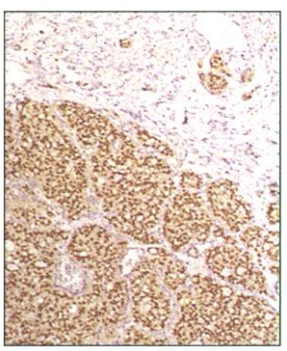
MAKING ALL A'S

One of the signatures of messenger RNAs (mRNAs) is a tail of repeated adenylate bases. Unlike most nucleic acid polymerizations, this reaction does not utilize a template; instead, incoming molecules of adenosine triphosphate are

CONTINUED ON PAGE 1255

FATEFUL FUSION

Chromosomal translocations that produce oncogenic fusion proteins are common in leukemias and soft-tissue tumors but have rarely been observed in solid tumors (carcinomas), which account for 90% of all cancers. In a study of human thyroid follicular carcinomas, Kroll *et al.* (p. 1357) identified a common translocation that fuses the DNA binding region of the PAX8 transcription factor to peroxisome proliferator–activated receptor (PPAR) γ1, a member of the nuclear hormone receptor superfamily. The fusion protein inhibited transcriptional transactivation by PPARγ1 in a dominant-negative manner. Discovery of this fusion event opens up new possibilities for diagnosis and treatment of thyroid cancer.



CONTINUED FROM PAGE 1253

added directly to the 3′ end of the mRNA. J. Bard *et al.* (p. 1346) present the crystal structure of poly(A) polymerase from yeast in complex with two adenine nucleotides, one of which appears to represent the last base attached with the other being the next to be added. In addition to details about the active site mechanism, they describe the structural comparison to other nucleic acid polymerases and the factors contributing to processivity of this enzyme.

WHEN THE ATTRACTION IS GONE

Environmental cues that are attractive or repulsive tell a migrating axon where to go by sending signals through the appropriate cell surface receptors. How is it then that for retraction to occur, a cell surface receptor must first engage with the repulsion factor and then overcome the adhesive force? Hattori *et al.* (p. 1360) and Galko and Tessier-Lavigne (p. 1365) report that these interactions can be broken by metalloprotease enzymes that result in the release of the axon from its captor. In a Perspective, Pasquale discusses how the involvement of cell surface metalloproteases in regulating axon guidance is a compelling solution to this puzzling paradox.

VITAL DRUG DELIVERY

The cytokine interleukin-10 (IL-10) has shown promise in clinical trials for treatment of inflammatory bowel disease (IBD). Because the cytokine is administered systemically, high doses are required that often lead to adverse side effects. Steidler *et al.* (p 1352; see the Perspective by Shanahan) describe a new method of localized IL-10 delivery that allows the therapeutic dose to be reduced substantially. They engineered *Lactococcus lactis*, a bacterium used to produce fermented foods, to secrete high levels of IL-10. Delivery of the live recombinant bacteria by intragastric inoculation prevented the onset of IBD in one mouse model and reversed symptoms of pre-existing IBD in another. In principle, this technology could be used for efficient delivery of any protein therapeutic that is unstable or difficult to produce in large quantities.

WHISTLING IN THE SEA

Dolphins have long been known to communicate by means of a rich repertoire of vocalizations. However, studies have been based mostly on captive individuals, and little has been known about communication in the wild. Janik (p. 1355; see the Perspective by Tyack) has developed a technique that allows the measurement of vocalizations between bottlenose dolphin individuals in the sea without the presence of human observers. Individuals respond to each other using learned, matching whistles over distances of up to half a kilometer. The development of vocal imitation is an important step in the evolution of communication and has implications for the evolution of human language.

TECHNICAL COMMENT SUMMARIES

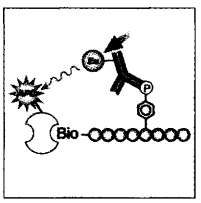
Plant Diversity and Productivity

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/289/5483/1255a

Reporting on a major experiment on plant diversity and productivity in European grasslands, Hector *et al.* (Research Articles, 5 November 1999, p. 1123) found "an overall log-linear reduction of average aboveground biomass with loss of species." Huston *et al.* object to that conclusion, arguing, among other things, that the eight sites studied did not show a consistent positive relationship between diversity and productivity, that the experiments did not properly test for overyielding (i.e., that the productivity of a given polyculture exceeds that of any species from the mixture grown in monoculture), and that some of the observed effects may have stemmed from the "fertilization effect" of the nitrogen-fixing legume *Trifolium pratense*. Huston *et al.* conclude "that species richness per se has no statistically or biologically significant effect on plant productivity across the eight sites."

Hector *et al.* defend their main result, and note that while a small fraction of polycultures were dominated by species that had not been tested in monocultures, excluding those plots from the analysis "does not alter conclusions . . . across all sites." And, although the effects of *T. pratense* on productivity were larger than those of other species, that does not invalidate the broad result, according to Hector *et al.*: "In principle, all effects [of species richness on productivity] can be attributed to the traits of individual species and their interactions." (See the news story by Kaiser.)

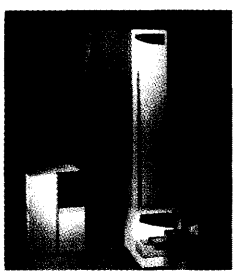
You did your homework. That's why George can still sing lullabies.



LANCE™ Kinase Assay

Unlocking the key to disease is a rewarding vocation with far reaching repercussions.

Maybe you haven't won the Nobel Prize. (Yet.) But your work does make a big difference in someone's life, somewhere. And that's something you can't forget. Neither do we. PerkinElmer Life Sciences (formerly known as EG&G Wallac) believes in



the value of what our customers do. The search for new medicines has always motivated us to provide complete systems solutions for drug discovery — such as our TriLux, ViewLux,™ and VICTOR^2™ systems — and the most supportive service you'll find... always, and as soon as you need it. Because we like helping you make humanity a little healthier.

wallac DRUG DISCOVERY

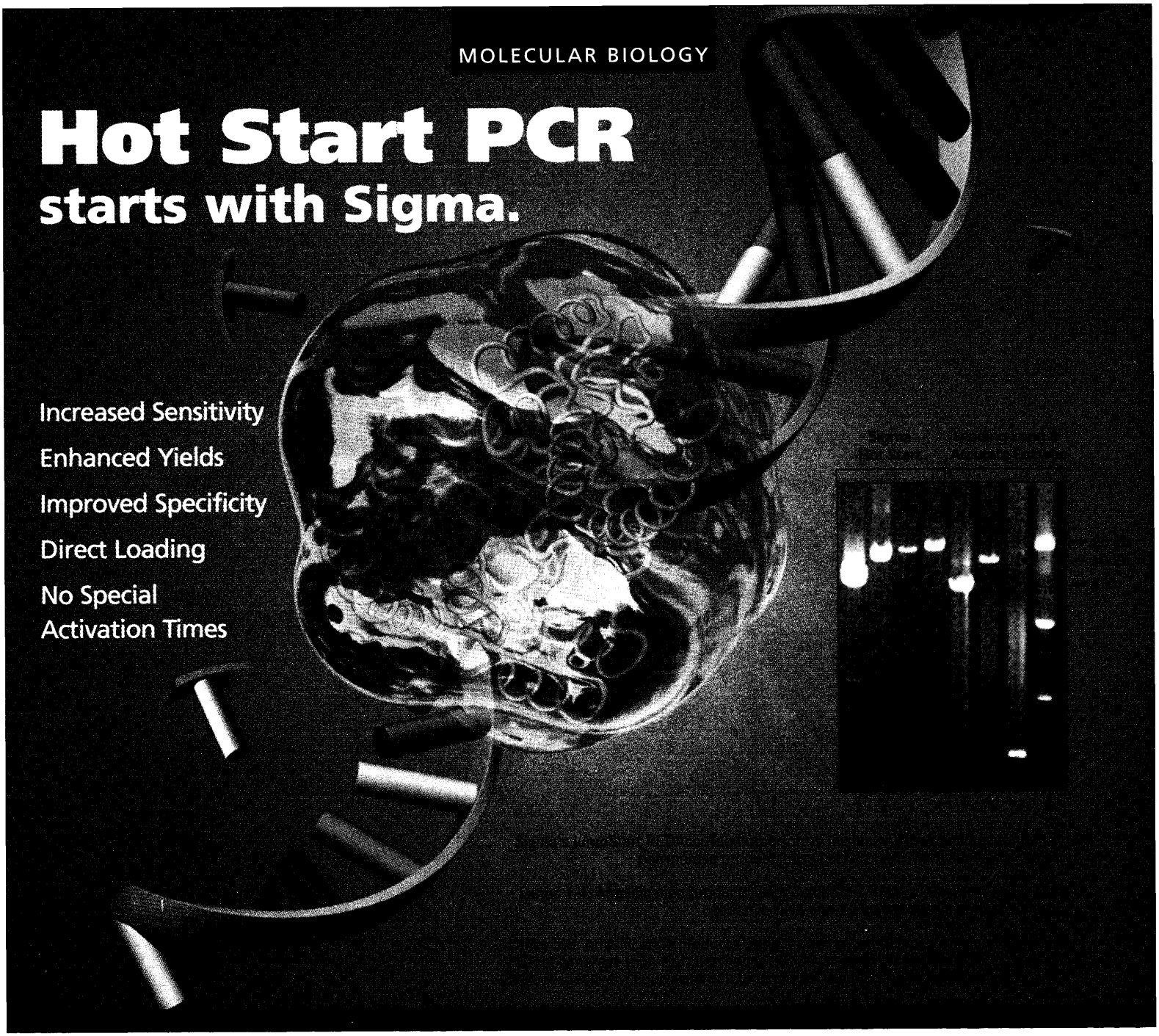
PerkinElmer
life sciences.

9238 Gaither Road, Gaithersburg, MD 20877 USA • P.O. Box 10, FIN-20101, Turku, Finland • 1-800-638-6692 • www.perkinelmer.com

Circle No. 26 on Readers' Service Card

MOLECULAR BIOLOGY

Hot Start PCR
starts with Sigma.



Increased Sensitivity

Enhanced Yields

Improved Specificity

Direct Loading

No Special Activation Times

The commitment to PCR continues through our new optimized Hot Start Reaction Mixes.

Innovative reaction mixes designed with your goals in mind.

JumpStart™ Taq DNA Polymerase
- Optimized Blend for Standard Hot Start PCR
- Improved Specificity and Enhanced Yield

JumpStart™ REDTaq™ ReadyMix PCR Reaction Mix
- 2x mix of REDTaq DNA polymerase, dNTP's and reaction buffer
- Direct Load after PCR

JumpStart™ REDTaq™ DNA Polymerase
- Improved Specificity
- Direct Load after PCR

JumpStart™ REDAccuTaq™ LA
- Significantly increases yields with higher fidelity (up to 6.5x)
- Direct Load after PCR

Purchase of these products is accompanied by a limited license to use in the Polymerase Chain Reaction (PCR) process for research in conjunction with a thermal cycler whose use in automated performances of the PCR process is covered by the up-front license fee, either by payment to Perkin Elmer or as purchased, i.e. an authorized thermal cycler. These products are sold under licensing arrangements with F. Hoffmann-La Roche Ltd., Roche Molecular Systems and The Perkin-Elmer Corporation.

Sigma. Your global source for PCR products.

Visit www.sigma-aldrich.com/hotstart

Circle No. 34 on Readers' Service Card

www.sigma-aldrich.com

ADVANCING LIFE THROUGH SCIENCE

SIGMA-ALDRICH • BOX 14508 • ST. LOUIS • MISSOURI 63178 • USA • 800-325-3010 • 314-771-5765

SIGMA-ALDRICH

Not to spoil the fun, but there are some rather pressing risks at hand. >

> Perhaps you haven't considered all the risks in your intellectual property transaction. Our visionary tools eliminate hazards, and offer remarkable solutions. Log on to the world's safest online marketplace, at www.pl-x.com.

Minimize risk. Maximize opportunity. pl-x

Circle No. 72 on Readers' Service Card

Science

www.sciencemag.org

1200 New York Avenue, NW
Washington, DC 20005
Editorial: 202-326-6550, FAX 202-289-7562
News: 202-326-6500, FAX 202-371-9227
Permissions: 202-326-7074, FAX 202-682-0816
Subscriptions: 800-731-4939 or 202-326-6417, FAX 202-842-1065

Bateman House, 82-88 Hills Road
Cambridge, UK CB2 1LQ
(44) 1223-326500, FAX (44) 1223-326501

EDITOR-IN-CHIEF **Donald Kennedy**
EDITOR **Ellis Rubinstein**
MANAGING EDITOR **Monica M. Bradford**

DEPUTY MANAGING EDITORS R. Brooks Hanson, Katrina L. Kelner
NEWS EDITOR Colin Norman

EDITORIAL/COMPASS SUPERVISORY SENIOR EDITORS Barbara Jasny, Guy Riddihough, Phillip D. Szuromi; SENIOR EDITOR/PERSPECTIVES Orla Smith; SENIOR EDITORS Gilbert J. Chin, Pamela J. Hines, Paula A. Kiberstis (Boston), L. Bryan Ray; ASSOCIATE EDITORS Lisa D. Chong, Beverly A. Purnell, Linda R. Rowan, H. Jesse Smith, Valda Vinson; ASSOCIATE BOOK REVIEW EDITOR Sherman J. Suter; ASSOCIATE LETTERS EDITOR Christine M. Pearce; ASSOCIATE TC/WEB EDITOR Stewart Wills; INFORMATION SPECIALIST Janet Kegg; CONTRIBUTING EDITORS Kevin Ahern, David F. Voss; 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 Carolyn Kyle, Ellen E. Murphy, Beverly Shields; PUBLICATIONS ASSISTANTS Chris Filiatreau, Joi S. Granger, Jeffrey Hearn, Charlene King, Gail Murphy, Anita Wynn; EDITORIAL ASSISTANTS Elise Laffman, Kathy Libal; EDITORIAL SUPPORT ASSISTANTS Osa Atoe, Patricia M. Moore, Brian White, Karen Yuan; EXECUTIVE ASSISTANT Sylvia S. Kihara; ADMINISTRATIVE SUPPORT Patricia F. Fisher

science_editors@aaas.org (for general editorial queries)
science_letters@aaas.org (for letters to the editor)
science_reviews@aaas.org (for returning manuscript reviews)
science_bookrevs@aaas.org (for book review queries)

NEWS SENIOR CORRESPONDENTS Eliot Marshall, Jean Marx; DEPUTY NEWS EDITORS Robert Coontz, Jeffrey Mervis, Leslie Roberts; CONTRIBUTING EDITORS Elizabeth Culotta, Polly Shulman; NEWS WRITERS Martin Enserink, Laura Helmuth, Constance Holden, Jocelyn Kaiser, Richard A. Kerr, Andrew Lawler (Boston), David Malakoff, Elizabeth Pennisi, Charles Seife, Robert F. Service (Pacific NW), Gretchen Vogel, John MacNeil (intern); PATHWAYS OF DISCOVERY EDITOR Ivan Amato; CONTRIBUTING CORRESPONDENTS Marcia Barinaga (Berkeley, CA), Barry A. Cipra, Jon Cohen (San Diego, CA), Ann Gibbons, Robert Irion, Charles C. Mann, Anne Simon Moffat, Virginia Morell, Evelyn Strauss, Gary Taubes, Ingrid Wickelgren; COPY EDITORS Linda B. Felaco, Daniel T. Helgerman; ADMINISTRATIVE SUPPORT Scherraine Mack, Fannie Groom; BUREAUS: Berkeley, CA: 510-652-0302, FAX 510-652-1867, Boston, MA: 617-542-5098, San Diego, CA: 760-942-3252, FAX 760-942-4979, Pacific Northwest: 541-342-6290

PRODUCTION DIRECTOR James Landry; MANAGER Wendy K. Shank; ASSISTANT PRODUCTION MANAGER Rob Masson; ASSOCIATES Rebecca Doshi, Vicki J. Jorgensen, Tara L. Kelly, Jessica K. Moshell

ART DESIGN DIRECTOR C. Faber Smith; ART DIRECTOR Alan T. Stonebraker; ASSOCIATE ART DIRECTOR Stephanie D. Halvorson; ILLUSTRATORS Carin Cain, Katharine Sutliff; ASSOCIATES Holly Bishop, Joshua Moglia, Debra J. Morgenegg, Preston Morrighan; PHOTO RESEARCHER Leslie Blizard

***SCIENCE* INTERNATIONAL**

EUROPE (science@science-int.co.uk) EDITORIAL: SUPERVISORY SENIOR EDITOR Andrew M. Sugden; SENIOR EDITOR/PERSPECTIVES Julia Uppenbrink; ASSOCIATE EDITORS Caroline Ash, Stella M. Hurtley, Ian S. Osborne, Stephen J. Simpson, Peter Stern; EDITORIAL SUPPORT Jenny Parker; ADMINISTRATIVE SUPPORT Janet Mumford, Liz Ellis; NEWS: EUROPEAN NEWS EDITOR Richard Stone, CORRESPONDENT Michael Hagmann; CONTRIBUTING CORRESPONDENTS Michael Balter (Paris: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00); Robert Koenig (Bern)

ASIA Japan Office: Asca Corporation, Eiko Ishioka, Fusako Tamura, 1-8-13, Hirano-cho, Chuo-ku, Osaka-shi, Osaka, 541-0046 Japan; (81) 6-6202-6272, FAX (81) 6-6202-6271; asca@os.gulf.or.jp JAPAN NEWS BUREAU: Dennis Normile (contributing correspondent, (81) 3-3335-9925, FAX (81) 3-3335-4898; dnormile@twics.com); CHINA REPRESENTATIVE Hao Xin, (86) 10-6255-9478; science@public3.bta.net.cn; INDIA Pallava Bagla (contributing correspondent (91) 11-271-2896; pbagla@ndb.vsnl.net.in)

***SCIENCE*NOW** (www.sciencenow.org) EDITOR Erik Stokstad

***SCIENCE'S* NEXT WAVE** (www.nextwave.org) EDITORIAL: MANAGING EDITOR Crispin Taylor; EDITORS Robert Metzke (Germany), Kirstie Urquhart (UK); CONTRIBUTING EDITORS Charles Boulakia (Canada), Mark Sincell; WRITER Vid Mohan-Ram; MARKETING: MARKETING MANAGERS Karen Horting (US and Canada), Hazel Crocker (Europe); PROGRAM DIRECTOR Emily Klotz; ASSOCIATE Peter Cherukuri

PUBLISHER **Richard S. Nicholson**
ASSOCIATE PUBLISHER **Beth Rosner**
MEMBERSHIP/CIRCULATION DIR. **Michael Spinella**

MEMBERSHIP/CIRCULATION (membership@aaas.org) DEPUTY DIRECTOR Marlene Zendell; MEMBER SERVICES: MANAGER Michael Lung; SUPERVISOR Mary Curry; COORDINATOR Jantell Stone; SENIOR REPRESENTATIVES Laurie Baker, Pat Butler; REPRESENTATIVES Elizabeth Early, Katrina Smith; MARKETING: MANAGER Scott Oser; ASSOCIATES Lauri Sirois, Deborah Stromberg; EUROPE MANAGER Jane Pennington; SENIOR EXECUTIVE Ruth Jackson; EXECUTIVE Martin Paine; RESEARCH: MANAGER Renuka Chander; BUSINESS AND FINANCE: MANAGER Teressa Ellis; COMPUTER SPECIALIST Charles Munson

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

REPRINTS Ordering/Billing/Status 800-407-9190; Corrections 202-326-6501

MEMBER BENEFITS For Credit Card: MBNA 1-800-847-7378; Car Rentals: Hertz 1-800-654-2200 CDP#343457, Dollar 1-800-800-4000 #AA1115; AAAS Travels: Betchart Expeditions 1-800-252-4910; Life Insurance: Seabury & Smith 1-800-424-9883; Other Benefits: AAAS Member Services 1-202-326-6417.

FINANCE AND ADVERTISING BUSINESS MANAGER Deborah Rivera-Wienhold; SENIOR ANALYST Randy Yi; FINANCIAL ANALYSTS Lisa Donovan, Jessica Tierney; RIGHTS AND PERMISSIONS: ASSOCIATE Emilie David; ASSISTANT Karen Lentz

MARKETING: DIRECTOR John Meyers; ASSOCIATES Mary Ellen Crowley, Amanda Donathen, Allison Pritchard ELECTRONIC MEDIA: MANAGER David Gillikin; ASSISTANT PRODUCTION MANAGER Wendy Green; SENIOR PRODUCTION ASSOCIATE Lisa Stanford; PRODUCTION ASSOCIATES Carla Cathey, Mark Croatti, Robert Owens, Louis Williams ADMINISTRATIVE SUPPORT Joyce Murray

PRODUCT ADVERTISING (science_ advertising@aaas.org) NATIONAL SALES MANAGER NORTHEAST AND E. CANADA Richard Teeling: 973-694-9173, FAX 973-694-9193 • West Coast/W. Canada Neil Boylan: 415-673-9265, FAX 415-673-9267 • MID-ATLANTIC AND U.S. INSIDE SALES Christopher Breslin: 443-512-0330, FAX 443-512-0331 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; TRAFFIC ASSOCIATE Halimah S. Whitby; SENIOR SALES ASSOCIATE Sheila Myers

RECRUITMENT ADVERTISING (science_classifieds@aaas.org); PRODUCTION MANAGER Jennifer Rankin U.S.: SALES MANAGER Gabrielle Boguslawski: 718-491-1607, FAX 202-289-6742; WEST COAST SALES MANAGER Kristine von Zedlitz; EAST COAST SALES MANAGER Jill Steinberg; INTERNET SALES MANAGER Beth Dwyer; ASSISTANT SALES MANAGER Daryl Anderson; SENIOR SALES COORDINATOR Erika Bryant; SALES COORDINATORS Rohan Edmonson, Caroline Gallina, Shirley Young; SALES REPRESENTATIVES Kathleen Clark, Jody Fenty, Christina Geiger, Bren Peters-Minnis; ASSISTANTS Sussy Castilla, Emnet Tesfaye; ASSOCIATES Christine Borkowski, Dawn Bruno, Chris Scarince; PUBLICATIONS ASSISTANTS Robert Buck, Jane Vaughn; U.K./EUROPE SALES MANAGER Debbie Cummings; PROMOTIONS COORDINATOR Richard Walters; 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 Stephen Jay Gould; PRESIDENT Mary Lowe Good; PRESIDENT-ELECT Peter H. Raven; TREASURER William T. Golden; EXECUTIVE OFFICER Richard S. Nicholson; BOARD Lewis M. Branscomb; Nina V. Fedoroff; Robert D. Goldman; Alice S. Huang; Sally Gregory Kohlstedt; Robert C. Richardson; 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.

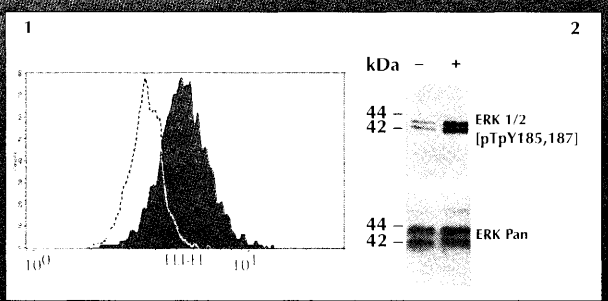
INFORMATION FOR CONTRIBUTORS
See pages 147 and 148 of the 7 January 2000 issue or access www.sciencemag.org/misc/con-info.shtml.

Cutting Edge Products

From BioSource

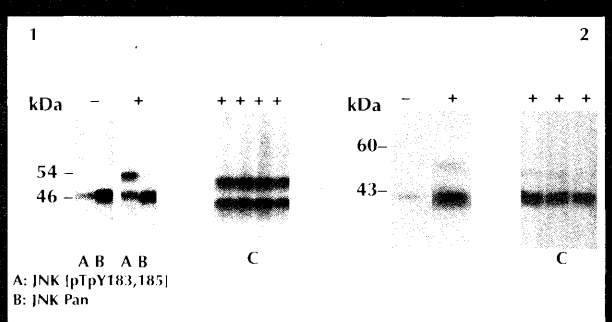
Phosphorylation Site-Specific Antibodies (PSSA)

ERK 1/2 PSSA for use in FACS



Show Me! (1) Flow Cytometry data show treated (red) and un-treated (green) Jurkat cells stained with (anti-ERK 1/2 [pTpY185/187] FITC conjugate (cat.#44-6808). The blue dotted line shows treated cells stained with FITC conjugate pre-incubated with blocking peptide. (2) Activation of MAP Kinase in PC12 cells treated with NGF is demonstrated by comparison to unstimulated control (anti-ERK 1/2 [pTpY185/187] (cat.#44-680).

MAP Kinase Superfamily



Show Me! Activation of MAP Kinase Superfamily proteins in HEK 293 cells treated with UV is demonstrated by comparison to unstimulated controls (anti-JNK 1/2 [pTpY183/185] (cat.#44-682), p38 [pTpY180/182] (cat.#44-684). Evaluation of consecutive lots each of anti-JNK [pTpY183/185] and p38 [pTpY180/182] phosphorylation site-specific antibodies is shown in panel C. The data demonstrate the reproducibility of the antibody production process.

Over 50 PSSA's available, including Src, FAK & Pyk2

Now Available @ biosource.com Signal Transduction Glossary & Methods Booklet

Circle No. 27 on Readers' Service Card

For research use only.

BioSource International, Inc.
1-800-242-0607

BIOSOURCE INTERNATIONAL
biosource.com

Fax: (805)987-3385
e-mail:tech.support@biosource.com

BioSource Europe, S.A. Tel: +32-67 88 99 00 • BioSource Deutschland, GmbH Tel: 0 800 100 85 74
BioSource Netherlands, B.V. Tel: +31-76-501 4824 • BioSource United Kingdom, Ltd. Tel: 0 800 169 1547

Australia +61 7 3352 6100 • Austria +431801 04 250 • 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 +36 1/395 90 48 • India +91/80 634 6520 • 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 228356278 • South Africa +27.11/792.6790 • Spain +34. 93 404 55 02 • Sweden +46.8/625.1850 • Switzerland +041/41-420.96.36 • Taiwan 886 2 2790/ 7902 • Turkey +90 (312) 432 4130

NOW, TIME IS ON YOUR SIDE...

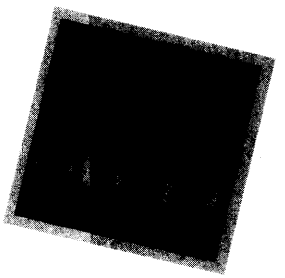
The New **Mini-Prep 24** for Automated Plasmid Mini-Preps

The Mini-Prep 24 uses a new method of plasmid purification based on agarose electrophoresis and subsequent recovery by electroelution.

The Mini-Prep 24 uses premanufactured sample cassettes that come ready for direct loading of up to 2 ml of culture.

Call now to learn how the new Mini-Prep 24 can give you quality DNA while saving you more time than you can imagine.

NO CENTRIFUGATION STEPS



High Purity - sufficient for automated fluorescent and manual sequencing.
Consistent Results - up to 6 µg of plasmid per ml.
Fast - up to 24 preps per hour.
Quality - time and time again.

Easy Operation - begin prep with direct loading of bacteria culture - with no centrifugation step, you save time.

MACCONNELL RESEARCH

1-800-466-7949

11339 SorrentoValley Rd • San Diego, CA 92121 *Phone: (619) 452-2603 Fax (619) 452-6753*

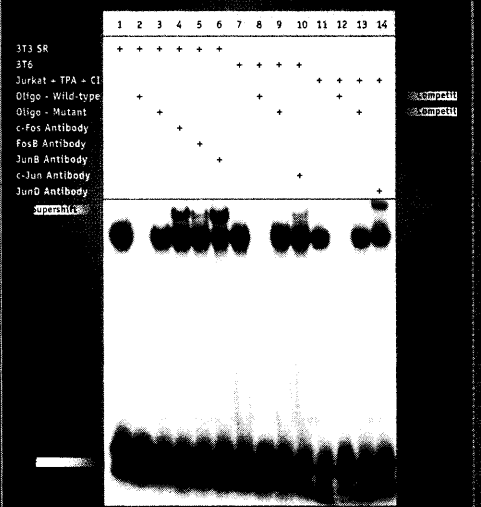
Circle No. 20 on Readers' Service Card *www.macconnell.com*

Kits for Transcription Factors

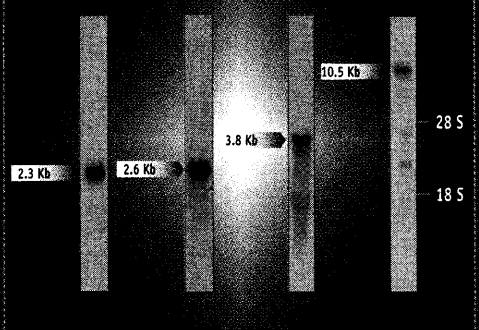
Family Kits

For Screening Transcription Factor Family Members

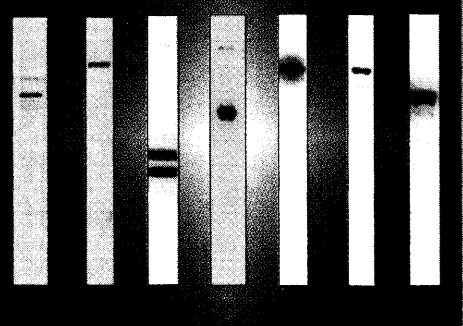
The EMSA
AP-1 Family Nushift™



The Northern
NF-kB/Rel Family Norkit™



The Western
STAT Family Screening Kit



- AP-1 Family
- NF-kB/Rel Family
- C/EBP Family
- STAT Family
- Cell Cycle Regulators
- and many more. . .

Individual Kits

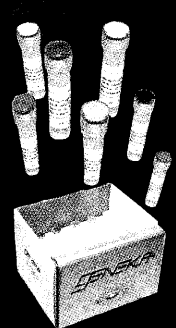
For Studying Individual Transcription Factors

Nushift™/ Nushift™ Plus Gelshift™/Gelshift™ Plus	Norkit™/ Norkit™ Plus	Western TF Antibodies

Over 1,000 Products

See our new 2000 catalog

Three techniques. One supplier.



Flexible
Reliable
Reproducible
Cost & Time Effective

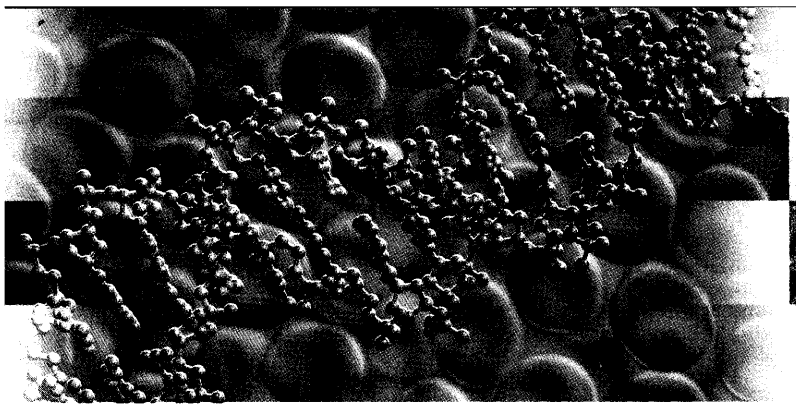
GENEKA BIOTECHNOLOGY INC.

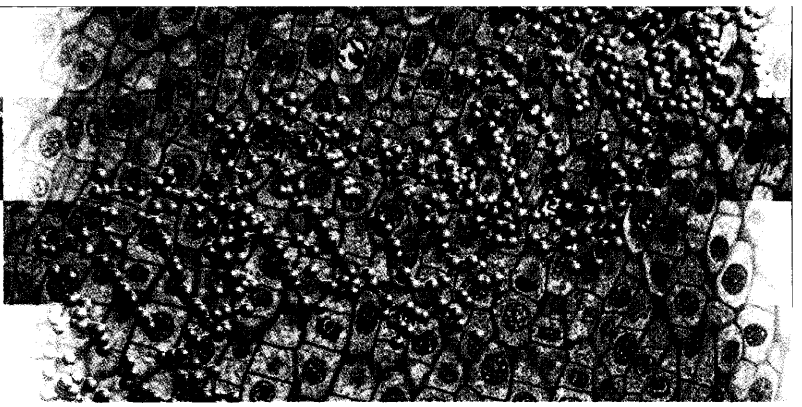
Tel: 1-888-343-6352 Fax: 1-888-528-9225 Web site: www.geneka.com E-mail: info@geneka.com

International Distributors

• Australia 61-2-9521-2177 (toll free in Australia 1800-251-437) • Austria, Germany, Switzerland 49-(0)-40-85-32-600 (toll free in Germany 0800-2466651) • BeNeLux 31-413-251115 • Denmark 45-39-56-20-00 • Finland 358-9-584-121 • France 33-(0)3-88-18-07-22 • Greece 30-1-522-6547 • Italy 39-(0)2-381951 • Japan 81-3-5684-1620 • New Zealand 0800-444-157 • Norway/Iceland 47-22-20-0137 • Spain 34-91-551-54-03 • Sweden 46-8-30-60-10 • Taiwan 886-2-233-18111 • U.K./Ireland 44-(0)-1223-316855

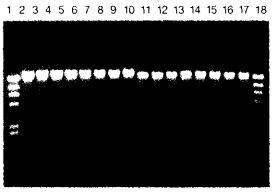
Circle No. 39 on Readers' Service Card





Perfect gDNA from Blood

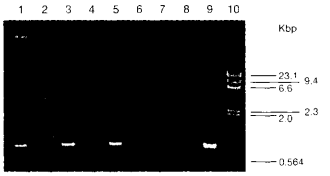
- Ultra-pure genomic DNA
- Extremely high-molecular DNA, with no degradation
- Reproducible high yields
- Rapid, easy handling
- Wide range of applications, also for animal blood



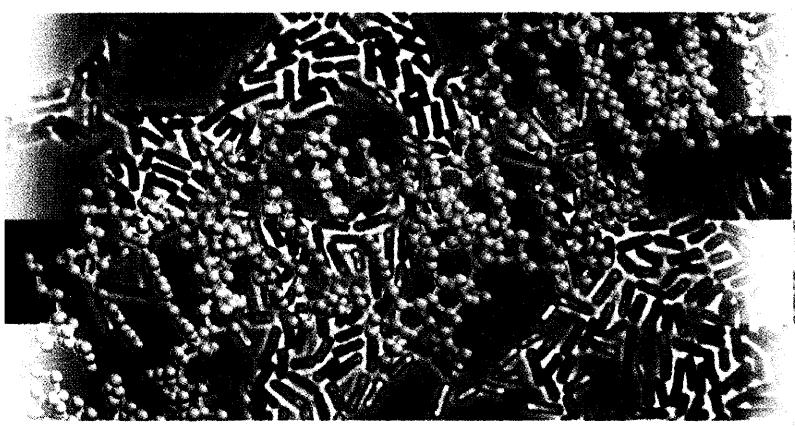
● Yields obtained using the Eppendorf Perfect gDNA Blood Kit and from a competing product. 200 µl fresh human whole blood, 5 µl eluate volume applied.
Lanes 1 and 18: λ *Hind* III Marker
Lanes 2 to 9: Eppendorf gDNA Blood Kit
Lanes 10 to 17: Competing kit

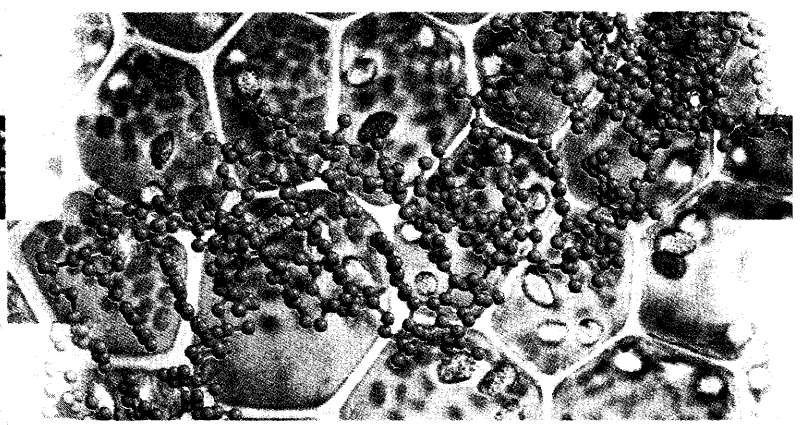
Perfect RNA

- High-quality total RNA
- Extremely high yields
- Outstanding results in sensitive downstream applications (e.g. RT PCR*, Northern Blot, cDNA synthesis)
- Different formats available



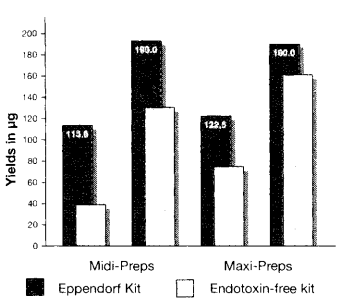
● RT-PCR analysis of total RNA isolated using the Eppendorf Perfect RNA Kits:
Lanes 1 and 2: Perfect RNA Kit (Mini Scale) total RNA
Lanes 3 and 4: Perfect RNA Kit (Midi Scale) total RNA
Lanes 5 and 6: Perfect RNA Kit (Maxi Scale) total RNA
Lane 7: No Reverse Transcriptase control.
Lane 8: Negative PCR control.
Lane 9: Positive control.
Lane 10: λ DNA-Hind III marker.





Perfectprep Plasmid

- Ultra-pure plasmid DNA in next to no time
- High yields
- Outstanding results in sensitive downstream applications (e.g. sequencing, cloning, transfection)
- Easy to handle
- Different formats available



● Yields obtained using the Perfectprep Kit and a competitor's kit from different bacteria strains with high-copy and low-copy plasmids

Phase Lock Gel

- Simplified phenol/chloroform extraction
- Up to 30 % higher nucleic acid yields
- Simple pipetting or decanting of the aqueous DNA solution
- Reduced periods of contact with phenol vapors

eppendorf® is a registered trademark.

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

eppendorf

In touch with life

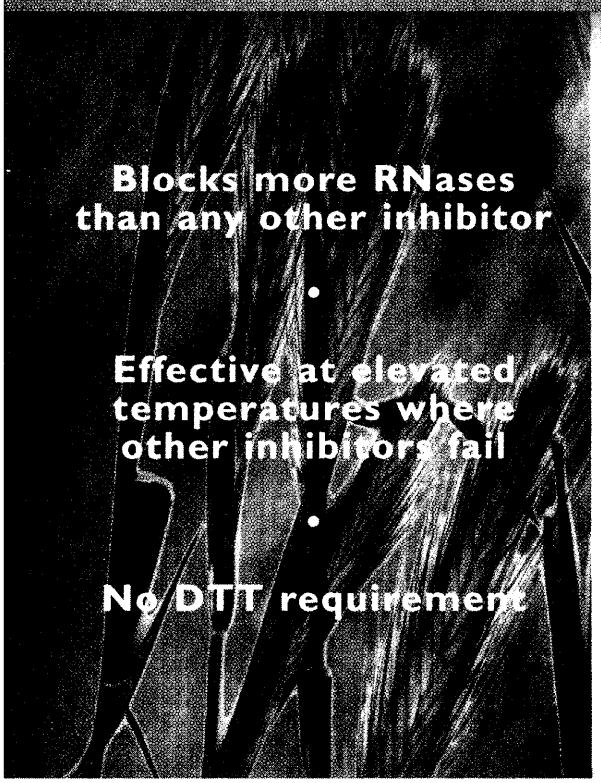
Application Hotline:
+49 180-3 66 67 89

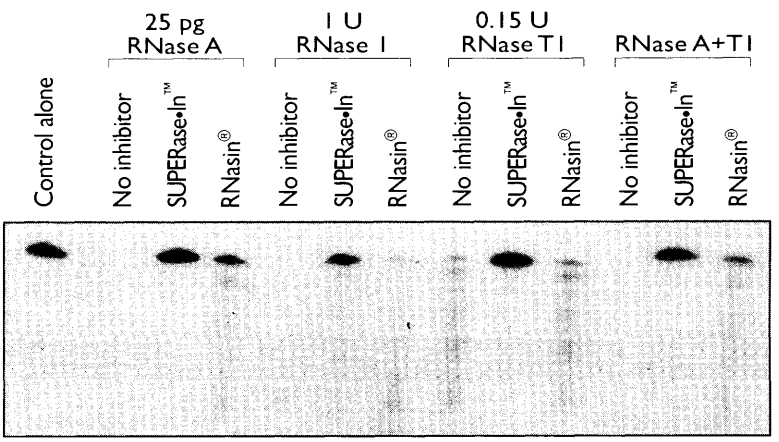
Eppendorf AG · 22331 Hamburg · Germany · Phone +49 40-5 38 01-0 · Fax +49 40-5 38 01-556 · e-mail: eppendorf@eppendorf.com · www.eppendorf.com
Eppendorf Scientific, Inc. · One Cantiague Road · Westbury, NY 11590-0207 · Phone 800-421-9988 or 516-876-6800 · Fax 516-876-8599
e-mail: eppendorf@eppendorfsi.com · www.eppendorfsi.com

Circle No. 21 on Readers' Service Card

SUPERase•In™

The Ultimate RNase Inhibitor





SUPERase•In™ vs. Placental Ribonuclease Inhibitor. A ^{32}P-labeled RNA probe was incubated for 30 minutes at 37°C in the presence of the indicated nucleases and either SUPERase•In or ribonuclease inhibitor protein (RIP). Both the SUPERase•In and the RNasin® were added at a concentration of 1 U/µl.

SUPERase•In™ inhibits MORE RNases under MORE reaction conditions than any other RNase inhibitor available.

Although ribonuclease inhibitor protein (RIP or RNasin®) has been the most commonly used RNase inhibitor, it has limitations. RIP binds only RNase A-type enzymes, functions under a narrow temperature range and requires DTT to prevent the release of active RNases. New SUPERase•In inhibits more RNases - RNase A, B, C, RNase T1 and RNase 1. SUPERase•In remains active up to 65°C and has no DTT requirement. SUPERase•In gives a higher level of protection against RNA degradation than any other product - it's the ultimate RNase inhibitor.

RNasin® is a registered trademark of Promega Corporation.

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

U.S. (800)888-8804

Canada (800)445-1161

iBlink

iBlink™ Info

PRODUCT INFO IN A BLINK!

Why is SUPERase•In™ replacing RIP in commercial kits? An instant iBlink™ email has the answer.

Contact us at iblinksuper@ambion.com.

Ambion®

THE RNA COMPANY™

AMBION, INC. • 2130 WOODWARD ST. • SUITE 200 • AUSTIN, TX 78744-1832

tel(512)651-0200 • fax(512)651-0201 • email: moinfo@ambion.com • www.ambion.com

Circle No. 67 on Readers' Service Card

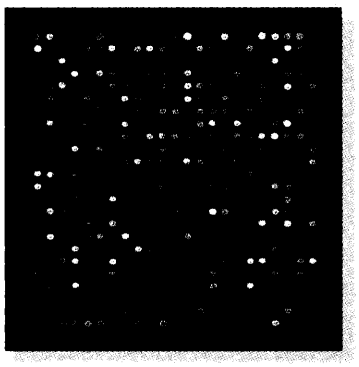
Pick Your Breakthrough!

The first microarray detection kit that:

1. Works consistently
2. Works with <1 microgram of total RNA
3. Works with an 8 hour protocol

Any one of these advances would be a major step forward. But all three at once? Why, this completely changes everything!

3DNA™
Submicro Expression Array Detection Kit



250 nanogram mouse total RNA sample, dual-channel detection using 3DNA Submicro detection kit

It works consistently.
Genisphere's 3DNA Submicro detection kit for expression arrays gives you unprecedented sensitivity without compromise. The kit is utterly reliable and generates more reproducible results than any other detection system. There is also less background noise and a better signal to noise ratio than with any other system. So you can actually trust the data you generate.

It works with submicrogram total RNA samples.
For those of you working with human tumor samples, this advance literally changes the world. Until now submicrogram detection was not possible without sample amplification and all the disadvantages associated with that technique, including bias. With 3DNA Submicro kits, for the first time you are assured faultless consistency with the smallest samples. (Just look at the image above.)

It works with an 8-hour protocol.
The 3DNA Submicro kit's protocol can produce results in 8 hours. It is short, simple and well defined. (In fact, one version of the protocol eliminates all concentration and centrifugation steps.) There is nothing to introduce biases. Without question the utter simplicity of the 3DNA Submicro protocol makes possible its exceptional reliability.

Will you take advantage of all three breakthroughs? Two? One? You get all three at no extra cost. And with it, never before sensitivity, never before reliability with never before speed and simplicity of protocol. The advances are so profound, frankly, you have to use a 3DNA Submicro kit yourself to believe them.

To receive your kit, call us immediately. Before another 8 hours go by.

Genisphere Inc. 14 Philips Parkway Montvale, NJ 07645
Tel #s: 877.888.3DNA 201.651.3100
Fax #s: 877.FAX.3DNA 201.651.3116
www.genisphere.com

Circle No. 44 on Readers' Service Card

Genisphere®
A DATASCOPE COMPANY

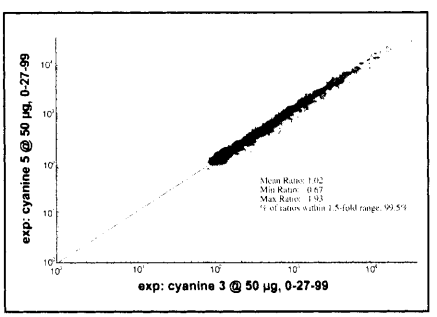
re•al (rē´əl, rēl) *adj.* **1.** Genuine; natural, not artificial or depicted; actually present, not merely apparent. **2.** Having a foundation in fact. **3.** Sincere, straightforward, honest, loyal, true.


everything you need to know about
the biotechnology industry...online
Showcase your company for 12 full months with an online Storefront... compliments of Microsoft and VerticalNet! See site for details!
bioresearchonline.com gives people in the biotechnology industry everything they need:
• Instant buying access to thousands of vendors and suppliers the world over
• Unlimited sales opportunities through customized Storefronts, E-Commerce Centers and other services
• Breaking news—including regulatory info—and the latest technology
www.bioresearchonline.com
• Hot job postings and career opportunities
• Links to the Internet's leading scientific trading community:
All delivered on time, on target, and totally FREE. Become a part of the online community that's 100% focused on the biotechnology industry. And while you're there, check out our sales-building, no-cost Storefront solution.
VerticalNet
Leading Business to E-Business
©2000 VerticalNet, Inc. All rights reserved.
E 36-06043 SCM
Circle No. 17 on Readers' Service Card

NEN® cDNA Labeling Kit for Microarrays: It Doesn't Cost More. It Just Does More.

When does the whole provide greater value than the sum of its parts? When you use an NEN Direct Reagent Kit for cDNA microarray labeling, instead of combining your own reagents from scratch.

NEN's Direct Reagent Kit for cDNA microarray labeling and hybridization gives you the key reagents you need, all in one box.



Precise expression scatter plot with the same RNA population, allowing sensitive detection of differential expression at 2-fold or higher.

You get a fully optimized, QC tested reagent solution for reliable, robust assay performance using any glass microarrays.

Save time and money, generate reproducible results. It's that simple. One kit. One company. No development or validation costs. No hassles. A classic case of the whole delivering more than the sum of its parts.

Learn more about how NEN's Direct Reagent Kits can make accurate, validated cDNA microarray labeling a piece of cake in your lab. Call us at **1-800-551-2121**, or visit our website at **nen.com.**

MICROMAX™
A Family of Microarray Products

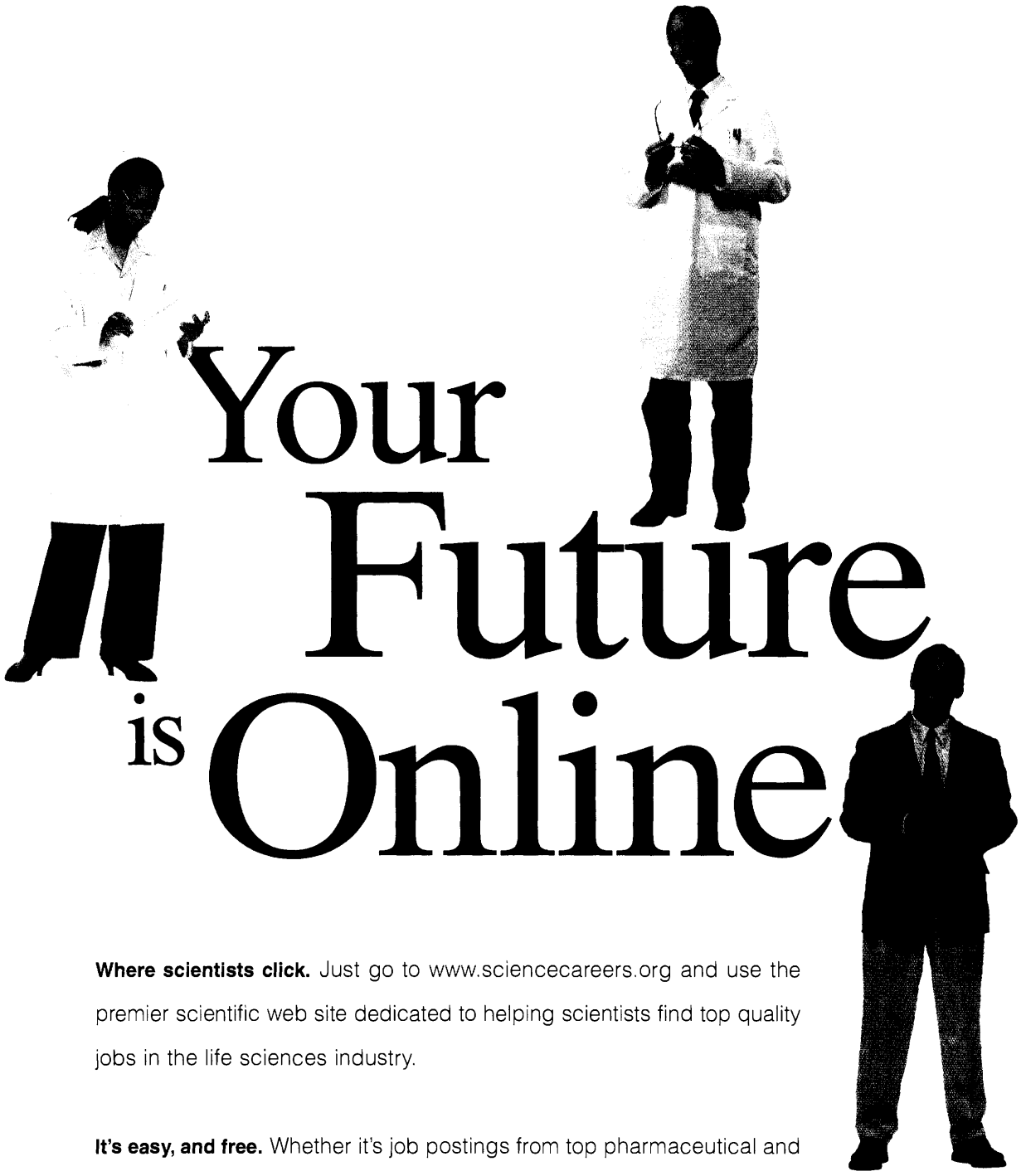
World Headquarters:
NEN® Life Science Products, Inc.
Boston, MA 02118-2512 USA
800-551-2121

European Headquarters:
NEN® Life Science Products
B-1930 Zaventem Belgium
+32 2 717 7924

NEN®
Powering Your Ideas™

nen.com

Circle No. 41 on Readers' Service Card



Your Future is Online

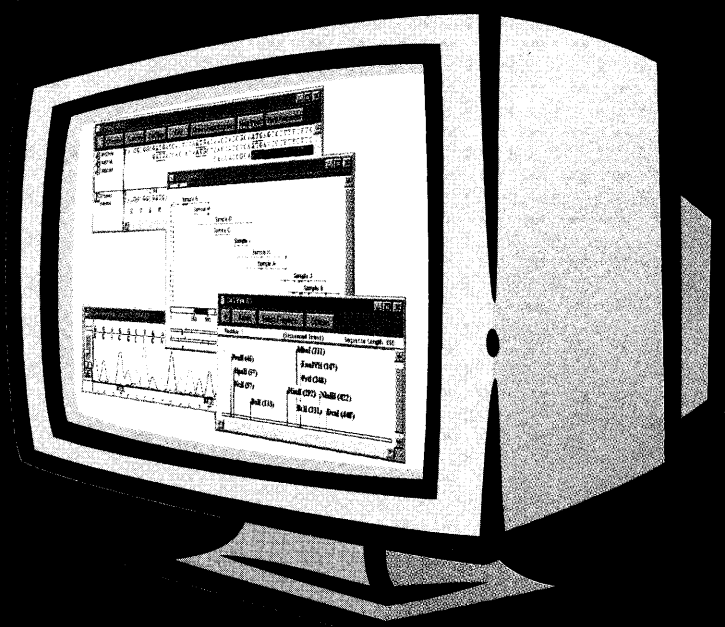
Where scientists click. Just go to www.sciencecareers.org and use the premier scientific web site dedicated to helping scientists find top quality jobs in the life sciences industry.

It's easy, and free. Whether it's job postings from top pharmaceutical and biotechnology organizations, a Resume/CV database, our Job Alerts service, or career advice you need, sciencecareers.org. can help you discover your future.

Science @ CAREERS

www.sciencecareers.org

SEQUENCHER™



Tried the Best DNA Sequencing Software?

Version 4 is Available for Mac & Windows!

Sequencher is the top software tool for DNA sequencing. If you haven't tried version 4, you're going to love the enhancements. Among the new tools are support for mutation detection, mtDNA forensics, quality-based sequence validation and gap optimization . And you get the same high-quality engineering and top-of-the-industry support you expect from Gene Codes Corporation.

Sequencher is the "complete software solution" that's become the industry standard - for both major automated sequencing centers and small academic research labs around the world. With Sequencher, your lab will increase productivity, reduce analysis time, and maximize the integrity and quality of your data. And Sequencher is the first and only third party program to be BioLIMS™ certified by PE.

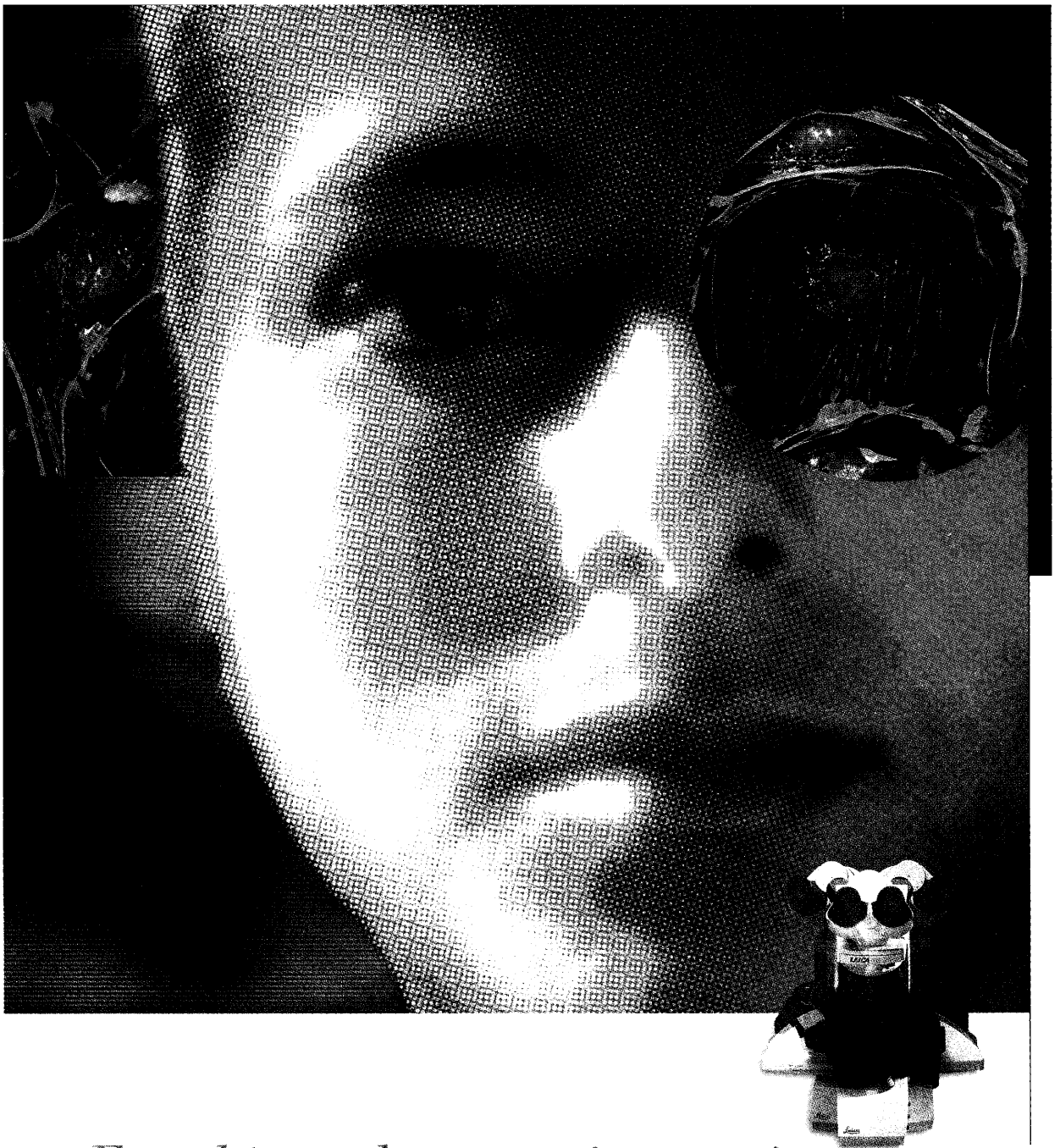
See for yourself. Call for our demo program or visit our website and see what your colleagues have said about Sequencher.

- Assemble contigs with speed, ease and accuracy
- Screen for vector and transposons
- Identify heterozygotes
- Assemble to a wildtype reference sequence to report variants and detect SNPs
- Use Phred and ATQA confidence values and easily edit Phrap projects
- View translations, restriction maps and ORFs
- Use the new Large Gap algorithm for genomic/cDNA comparisons and aligning splice variants
- And enjoy a Scientist-friendly interface that makes it all easy to use!

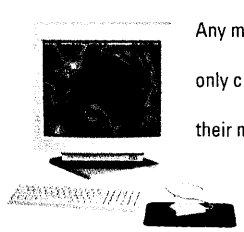
Gene Codes Corp., *640 Avis Dr, Ste 300, Ann Arbor, MI 48108*
phone 734.769.7249 or 800.497.4939 • fax 734.769.7074
info@genecodes.com www.genecodes.com

Gene Codes Corporation
TCA GENE
AGT CODES

Circle No. 77 on Readers' Service Card



Few things show you innovations as accurately as a microscope system.



Any microscope image can only be as precise as the optical system that produced it. That's why we don't only concentrate on improving the technology of our microscope systems, but also pay meticulous attention to their manufacture. The result: the high imaging precision essential today in biology, medicine or industry.

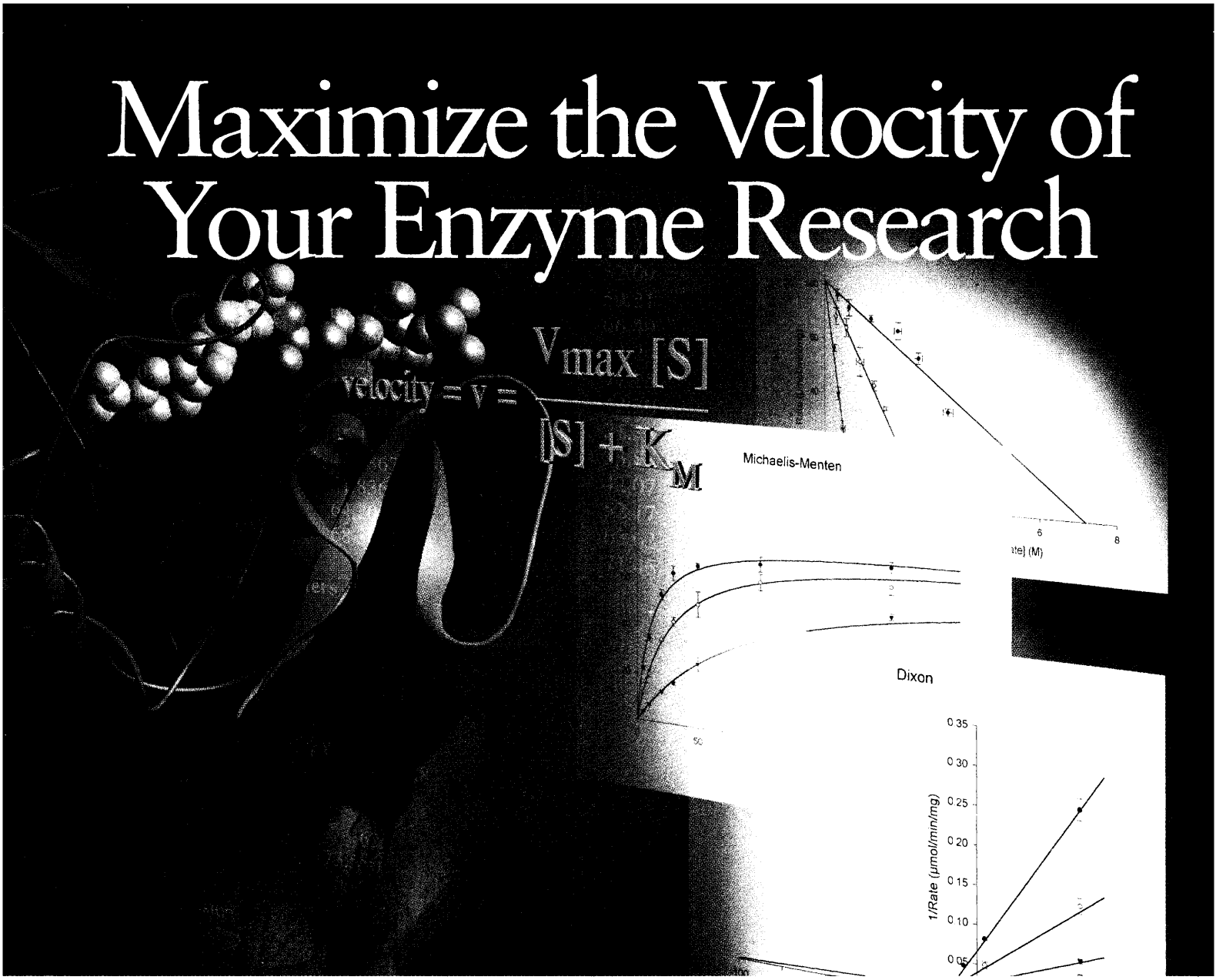
Leica

Leica Microsystems Wetzlar GmbH
Ernst-Leitz-Strasse
D-35578 Wetzlar (Germany)

Tel. +49 (0) 64 41 29-0
Fax +49 (0) 64 41 29-25 99
www.leica-microsystems.com

Circle No. 12 on Readers' Service Card

Maximize the Velocity of Your Enzyme Research



Introducing SigmaPlot 2000's Enzyme Kinetics Module

You spend months gathering data. It's essential that you have the tools to communicate your results clearly and precisely. Scientists worldwide use SigmaPlot® to create and present the exact graphs to best represent scientific data. SigmaPlot provides all the features you need to analyze and convert your data into exact, meaningful graphs that speak volumes with an intuitive and easy-to-use interface. Join the 100,000 researchers worldwide that rely on the technical graphing standard.

And now, we have extended SigmaPlot's capabilities with the new Enzyme Kinetics Module. This SigmaPlot add-on provides the tools to analyze and graph enzyme kinetics data quickly and easily. Directly read data from your instrument or enter data manually, select the type of study and the module does the rest. You get a detailed report of each model you fit and a comparison of the different models to identify the best one for your data, plus interactive graphs enable you to clearly display your results. This timesaving, easy-to-use add-on runs seamlessly within SigmaPlot 2000 so you can find the answers you want in no time!

Order Today, Call Toll-Free (800) 345-4740

SPSS Science			
Americas	Tel: +1.800.621.1393	Fax: +1.800.841.0064	sales@spss.com
Europe	Tel: +49 (0) 2104.9540	Fax: +49 (0) 2104.95410	euroscience@spss.com
U.K.	Tel: 0800.894.982	Fax: +44 (0) 121.471.5169	sales@spss-science.co.uk
France	Tel: 0800.90.37.55	Fax: +49.2104.95410	euroscience@spss.com

Distributors Worldwide: www.spss.com/order/

www.spssscience.com/sigmaplot/ekmodule

Circle No. 38 on Readers' Service Card

SIGMAPLOT
Exact Graphs for Exact Science

YSPEKAD-0800-S A4740

Make ALZET® pumps part of your blueprint for success.

Cutting edge data frequently result from careful experimental planning, which includes consideration of the optimal drug delivery system. ALZET osmotic pumps are the gold standard in continuous infusion studies in animals as small as mice and rats, and allow the effects of agents, even those with short half-lives, to develop fully.

Customize Your Research Plans

ALZET pumps can be used in a variety of ways, from simple subcutaneous or intraperitoneal implantation to targeted tissue or organ infusion using a catheter attachment. Two brain infusion kits broaden your research options by allowing intracerebroventricular or cerebral infusion of brain tissue. These pumps have been used in gene therapy research, exotic animal breeding experiments, and even on the space shuttle.

Draw On Our Experience

Visit the ALZET web site at **www.alzet.com** to learn more about how to incorporate these pumps into your research design. You will find citations on the delivery of hundreds of compounds, as well as references on delivery via a number of different routes. ALZET pumps give you the power to achieve and maintain an effective drug concentration for a sustained period of time, resulting in more accurate data.

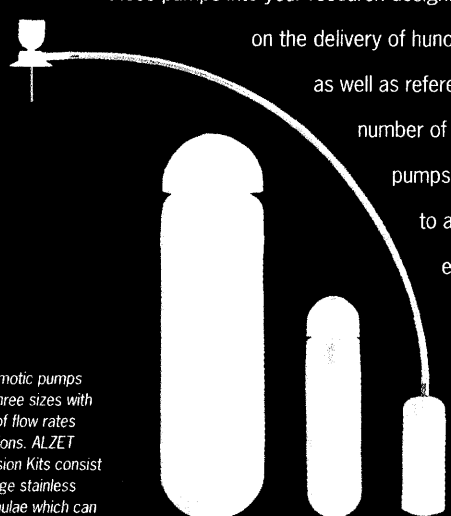


Fig. 2

ALZET osmotic pumps come in three sizes with a variety of flow rates and durations. ALZET Brain Infusion Kits consist of 28 gauge stainless steel cannulae which can penetrate 3-5 mm below the skull surface.

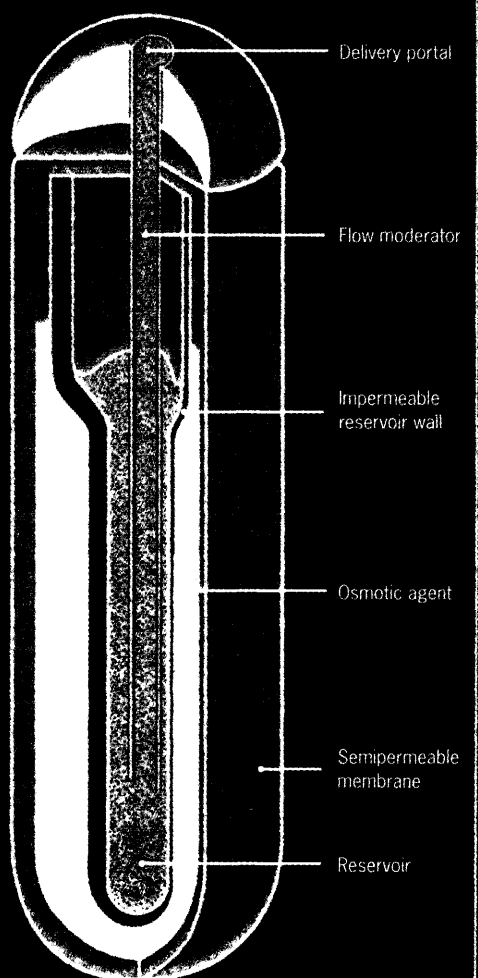
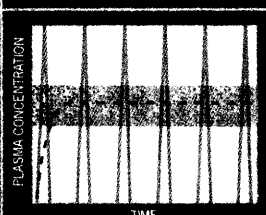


Fig. 1

The ALZET pump operates as interstitial fluid is attracted into the pump by the osmotic layer at a rate limited by the outer, semi-permeable membrane. As the osmotic layer hydrates, it compresses the flexible reservoir, which expels drug from the delivery portal of the pump.

Circle No. 15 on Readers' Service Card

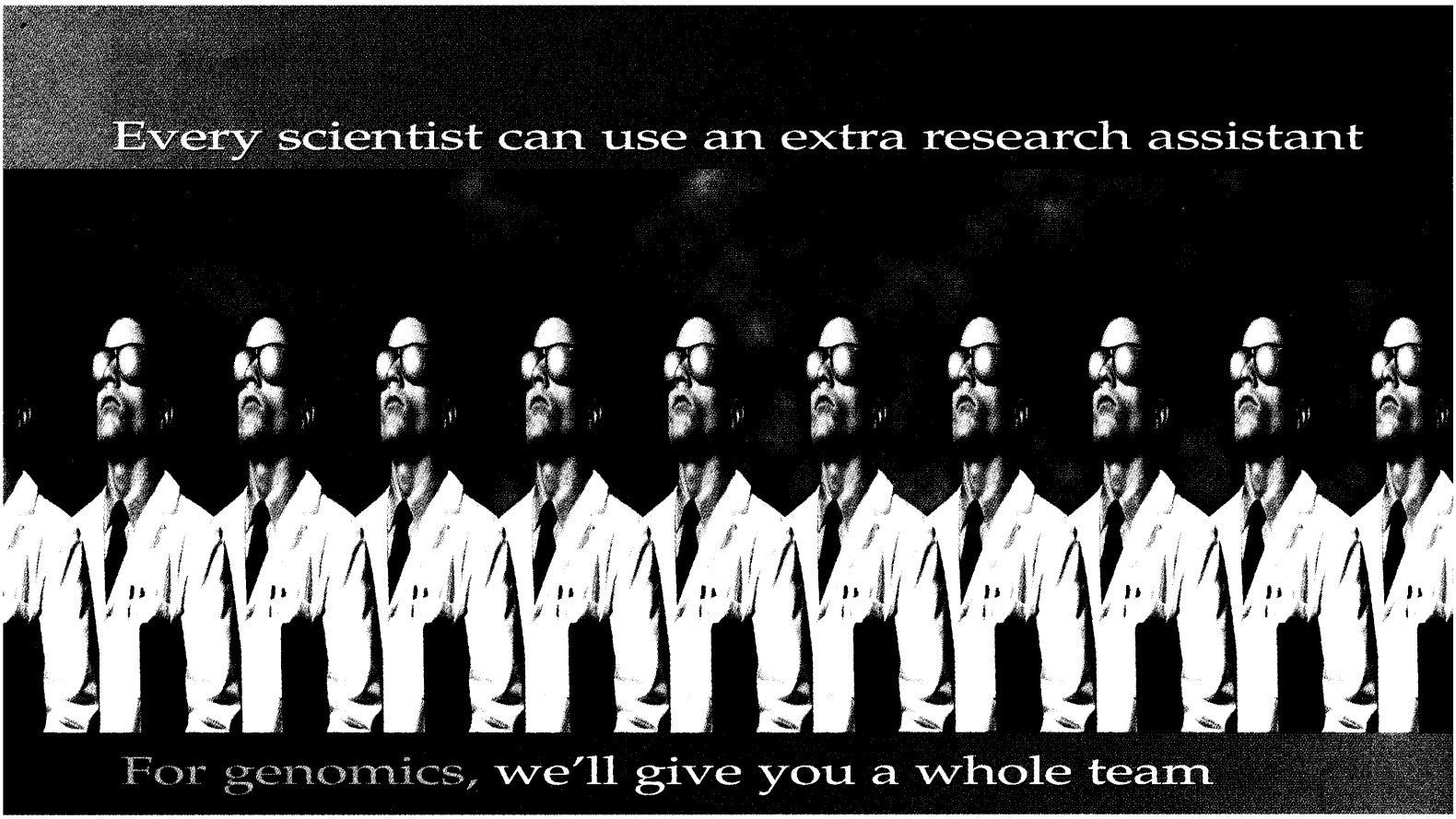


Eliminate Fluctuations in Plasma Drug Concentration

Fig. 3

Prolonging exposure to recombinant proteins by multiple daily injections results in repeated fluctuations in the level of protein in plasma and tissues, and corresponding variations in protein effects over time. Because the protein concentration is constantly changing during the course of the experiment, the resulting data can be misleading as to the nature of the protein's effects and the dose required to elicit them. ALZET pumps provide continuous drug infusion to maintain a constant plasma level (dashed line) within the effective concentration range (shaded bar).

alzet®
OSMOTIC PUMPS
www.alzet.com



DoubleTwist.com Agents

- Perform Comprehensive Sequence Analysis
- Retrieve Assembled ESTs
- Identify Protein Domains
- Retrieve and Analyze Human Genome
- Monitor for Identical ESTs
- Monitor for Identical cDNAs
- Monitor for Similar cDNAs
- Monitor for Similar Proteins, Search EST Database
- Monitor for Similar Proteins
- Monitor DoubleTwist Human Genome Database
- Monitor for Identical Genomic DNA
- Monitor for DNA Patents
- Monitor for Protein Patents
- **... and more on the way.**

A special breed of research inquiry
At your command

- Automated agents that search and monitor public and proprietary databases
- Continuous updates per your specifications
- A reporter of news and studies relevant to your research
- A purchasing agent to move your experiment forward

DoubleTwist.com
Portal to the Code™

Circle No. 29 on Readers' Service Card

Take a More Productive Path

for DNA Sequencing and Fragment Analysis

Flexibility

Short or long runs from the sample plate

Automatic switching between sequencing and genotyping

Performance

- Longer read length
- Faster cycle times

Results

- Sequence up to 80,000 bases per day
- Manage difficult and complicated sequences

Make the Right Move

- Trade up your sequencer to a CEQ™ 2000XL
- See our web site for details

Take a more productive path by visiting our web site at

www.beckmancoulter.com/CEQ2000

BECKMAN COULTER™

Innovate SIMPLIFY Automate

Worldwide Bioresearch Division Offices:

Australia (61) 2 9841-6000 **Canada** (905) 819-1234 **China** (86) 10 6515 6028 **Eastern Europe, Middle East, Africa** (41) 22 994 07 07 **France** 01 49 90 90 00 **Germany** (89) 358700 **Hong Kong** (852) 2814 1431/2814 0481 **Italy** 02 95 36 921 **Japan** 03 5404 8359 **Mexico** 525-559-1635 **Netherlands** 0297-230630 **Singapore** (65) 339 3633 **South Africa** (27) 11-805-2014/5 **Spain** 91 728 7900 **Sweden** 08-98 53 20 **Switzerland** 0800 850 810 **Taiwan** (886) 2 2378 3456 **U.K.** 01494 441181 **U.S.A.** 1-800-742-2345.

Circle No. 69 on Readers' Service Card

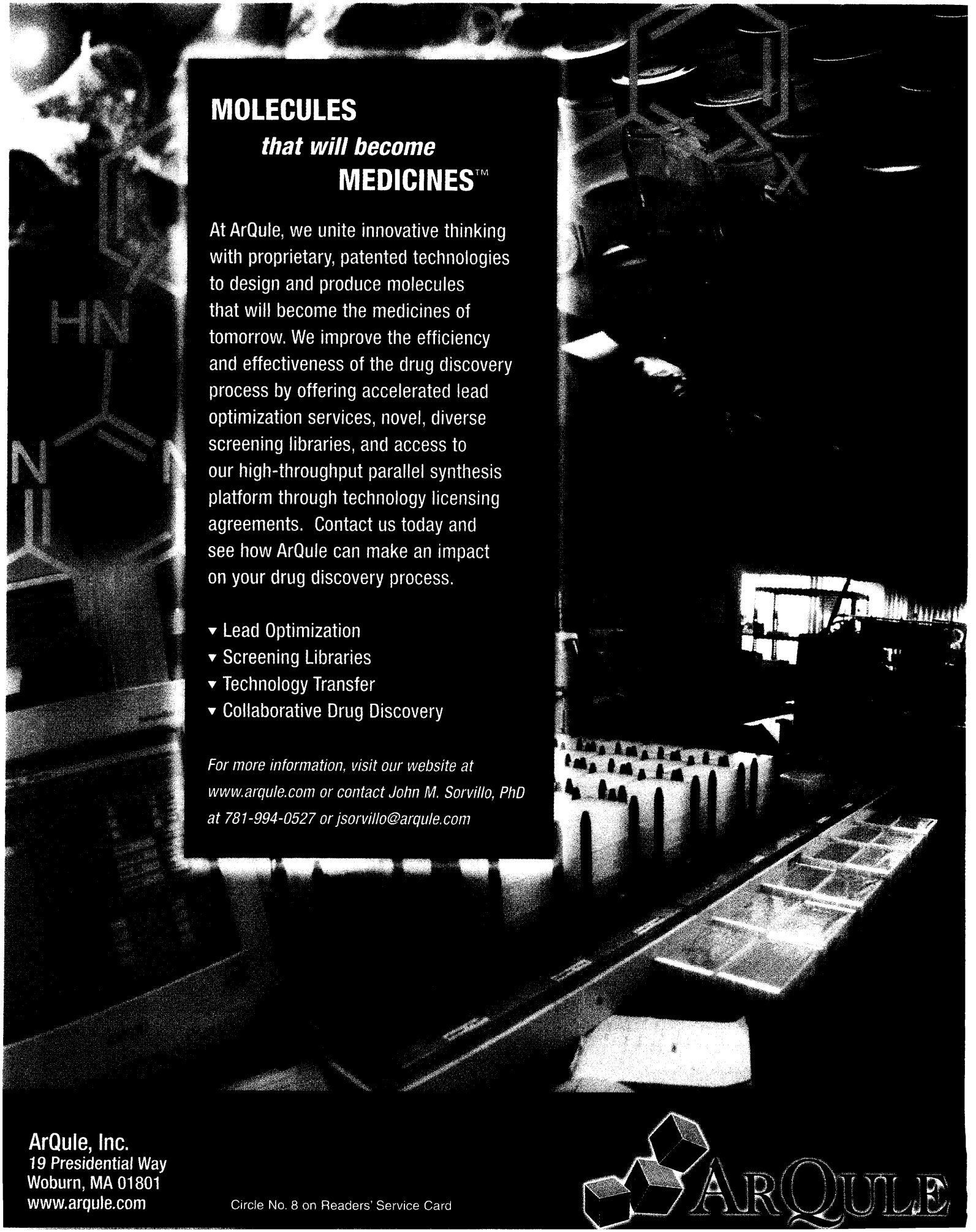
biotechnology europe

LEVELING THE PLAYING FIELD

The following organizations have placed ads in this Product Advertising Supplement which begins on page 1373.

Turn to Page 1373

Science
www.scienceonline.org



MOLECULES
that will become MEDICINES™

At ArQule, we unite innovative thinking with proprietary, patented technologies to design and produce molecules that will become the medicines of tomorrow. We improve the efficiency and effectiveness of the drug discovery process by offering accelerated lead optimization services, novel, diverse screening libraries, and access to our high-throughput parallel synthesis platform through technology licensing agreements. Contact us today and see how ArQule can make an impact on your drug discovery process.

- Lead Optimization
- Screening Libraries
- Technology Transfer
- Collaborative Drug Discovery

For more information, visit our website at www.arqule.com or contact John M. Sorvillo, PhD at 781-994-0527 or jsorvillo@arqule.com

ArQule, Inc.
19 Presidential Way
Woburn, MA 01801
www.arqule.com

Circle No. 8 on Readers' Service Card

ARQULE