25 June 1999 C1C1CC C25 June 1999

Vol. 284 No. 5423 Pages 2045–2220 \$8

Evolution

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

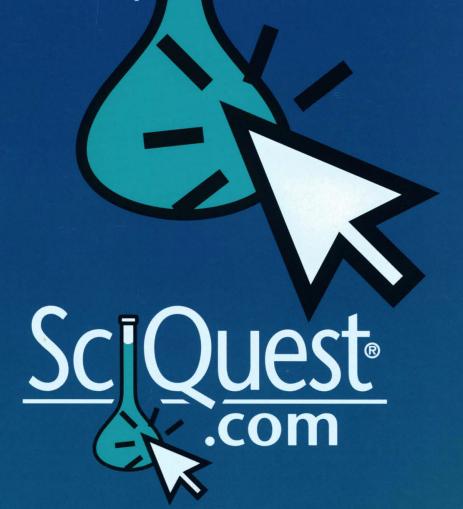
The new order in lab supplies.

Now you can order your lab supplies online from a single website, even if they come from different suppliers.

Reagents. Instruments. Glassware. Whatever. It's fast. It's easy.

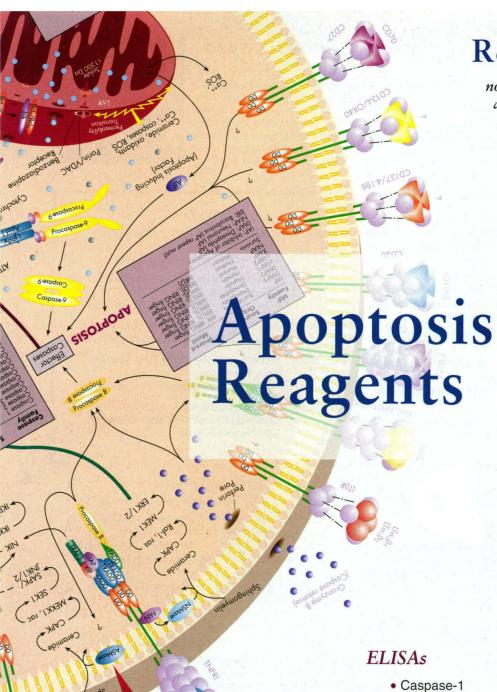
There's one purchase order or credit card, one invoice, and no extra charge.

Visit sciquest.com to order now.



www.sciquest.com / 800-233-1121 / email: questions@sciquest.com

Circle No. 22 on Readers' Service Card



R&D Systems

now offers over 200 products for use in apoptosis research. This extensive range of kits and reagents allows you to customize and optimize apoptosis detection in your specific research model.

Apoptosis detection kits

- Annexin V
- Disruption of mitochondrial membrane potential
- DNA laddering
- TUNEL with in situ, flow cytometry or microplatebased analysis

Activity assays

- Caspases
- Cell Proliferation
- PARP

Recombinant proteins and antibodies

- · Bcl-2 family proteins
- Caspases
- Cytochrome c
- Fas
- · IAP family proteins
- TNF and TNF receptors
- TRAIL and TRAIL receptors
- others
- Fas
- Nitric oxide
- · Reactive oxygen species
- TNF and TNF receptors
- TRAIL and TRAIL receptors

Call for a copy of our new 1999/2000 Apoptosis Catalog

FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC PROCEDURES

Primer pairs and probe cocktails

Bcl-2 family proteins

Survivin

TNF

USA and Canada R&D Systems, Inc. 614 McKinley Place N.E. Minneapolis MN 55413, USA. Tel: 1-800-343-7475 Fax: 612-379-6580 e-mail: info@rndsystems.com UK & Europe
R&D Systems Europe Ltd.
4-10 The Quadrant, Barton Lane
Abingdon, OX14 3YS, UK.
Tel: +44 (0)1235 529 449
Fax: +44 (0)1235 533420
e-mail: info@rndsystems.co.uk

Germany
R&D Systems GmbH
Borsigstraße 7
D-65205 Wiesbaden
Tel: 06122 90980
Fax: 06122 909819
e-mail: infogmbh@rndsystems.co.uk

RED
SYSTEMS

1-800-343-7475

www.rndsystems.com

NEWS OF THE WEEK

SCIENTIFIC PUBLISHING: Varmus Defends

E-biomed Proposal, Prepares to Push

ACADEMIC PUBLISHING: Library-Society

Alliance Puts Bio Journals Online

Implant Disease Risk

Retinoblastoma

Depth of Field

the Latest Big Chill

SCIENCE IN SOCIETY: Panel Discounts

GENE THERAPY: RAC Nixes Plan to Treat

IMAGING: 3D Camera Has No Lens, Great

BIOPATENTS: Legal Fight Over Patents on

CLIMATOLOGY: The Little Ice Age-Only

Science

www.sciencemag.org

COVER Fossils of the large (15 to 30 cm), soft-bodied organism *Pteridinium simplex* are locally abundant in sandstone beds of the terminal Proterozoic (~550-million-year-old) Nama Group in Namibia. New insights from paleontology, geochemistry, and molecular genetics are collectively illuminating the pattern, developmental basis, and environmental context of early animal evolution. These insights are part of the special section on evolution beginning on p. 2105. [Image: A. H. Knoll]





2070 Animal minds

DEPARTMENTS

NETWATCH 2051

THIS WEEK IN SCIENCE 2053

SCIENCESCOPE 2065

RANDOM SAMPLES 2083

CONTACT SCIENCE 2087

AAAS NEWS AND NOTES 2189

NEW PRODUCTS 2193

RESEARCH

Life

NEWS

Ahead

2062

2063

2065

2066

2066

2067

2069

2164

RESEARCH ARTICLE

2148 EIN2, a Bifunctional Transducer of Ethylene and Stress Responses in Arabidopsis J. M. Alonso, T. Hirayama, G. Roman, S. Nourizadeh, J. R. Ecker

REPORTS

2153 Response of Plant-Insect Associations to Paleocene-Eocene Warming P. Wilf and C. C. Labandeira

Warming relations between plants and pests

2156 On the Weakening Relationship Between the Indian Monsoon and ENSO
K. K. Kumar, B. Rajagopalan, M. A. Cane

2159 Gold Solubility in Supercritical
Hydrothermal Brines Measured in
Synthetic Fluid Inclusions R. R. Loucks and
J. A. Mavrogenes

NEWS FOCUS

2070 PRIMATE ABILITIES: Chimps in the Wild Show Stirrings of Culture Life—and Death—in the Forest

2073 PRIMATE ABILITIES: Are Our Primate
Cousins 'Conscious'?
In Labs, Organ Grinders Take Up Tools

2077 INTERNATIONAL COOPERATION: Finding a
New Home for BESSY in the Middle East

2079 PHYSICS: Will the Higgs Particle Make an Early Entrance?

A Tentative Nondiscovery of the Higgs

2081 AMERICAN GENETICS ASSOCIATION: Genomes Reveal Kin Connections for Whales and Pumas

EVOLUTION

2105 The Diversity of Evolution

NEWS

2106 Ecology Returns to Speciation Studies
Size Matters: The Genes Behind
Adaptation

2108 Test Tube Evolution Catches Time in a Bottle

2111 Early Life Thrived Despite Earthly Travails

Going Beyond Appearances to Find Life's History

VIEWPOINTS

2114 The Future of the Fossil Record
D. Jablonski

2116 The Evolution of Species Interactions
J. N. Thompson

REVIEWS

2118 Chemical Etiology of Nucleic Acid Structure A. Eschenmoser

2124 Phylogenetic Classification and the Universal Tree W. F. Doolittle

2129 Early Animal Evolution: Emerging Views from Comparative Biology and Geology A. H. Knoll and S. B. Carroll

2137 The Evolution of Dinosaurs P. C. Sereno

See related Editorial on p. 2087, Perspective on p. 2098, and Report on p. 2153.



SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 1999 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$110 (\$62 allocated to subscription). Domestic institutional subscription (51 issues): \$325; Foreign postage extra: Mexico, Caribbean (surface mail) \$55; other countries (air assist delivery) \$90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. Printed in the U.S.A.

SCIENCE'S COMPASS

EDITORIAL

2087 **Darwin's More Stately Mansion** S. I. Gould

LETTERS

2089 Drug Development in Space? W. G. Laver. Swashbucklers and Brainy Babes? M. Z. Ribalow. Rammal Medal Selection J.-F. Large. Response M. Balter. Mitochondrial Recombination? P. Arctander. Are Centrosomes or Aneuploidy the Key to Cancer? P. Duesberg. Eastern Europe's Research Gamble: The Czech Perspective P. Harmanec, J. Hanzlik, I. Kadlecová

POLICY FORUM

2095 **CARBON AND AGRICULTURE: Carbon** Sequestration in Soils W. H. Schlesinger

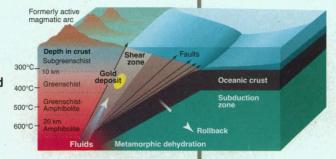
BOOKS ET AL.

2096 BEHAVIOR: Time, Love, Memory A Great Biologist and His Quest for the Origins of Behavior J. Weiner, reviewed by G. S. Stent

2097 PRACTICE OF SCIENCE: Advice for a Young Investigator S. Ramón y Cajal, translated by N. Swanson and L. W. Swanson, reviewed by J. H. Kaas

2101

How Earth makes gold deposits



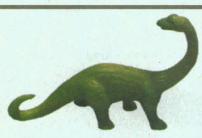
PERSPECTIVES

2098 PALEOECOLOGY: Hungry Herbivores Seek a Warmer World P. D. Coley

2099 MAGNETISM: Shining Soft X-rays on 2166 Magnetic Structures U. Hillebrecht

2101 GEOCHEMISTRY: Nature's Gold Factory 2159 R. Kerrich

▼2102 2177 CIRCADIAN RHYTHMS: A Clock for the Ages R.Y. Moore



2164

2066

2099

2164

Digital imaging

Visible Cone-Beam Tomography With a Lensless Interferometric Camera D. L. Marks, R. A. Stack, D. J. Brady, D. C. Munson Jr., R. B. Brady

_2166 Chiral Magnetic Domain Structures in Ultrathin FePd Films H. A. Dürr, E. Dudzik, S. S. Dhesi, J. B. Goedkoop, G. van der Laan, M. Belakhovsky, C. Mocuta, A. Marty, Y. Samson

2168 **Homeotic Transformation of** Rhombomere Identity After Localized Hoxb1 Misexpression E. Bell, R. J. T. Wingate, A. Lumsden

Odor Response Properties of Rat Olfactory Receptor Neurons P. Duchamp-Viret, M. A. Chaput, A. Duchamp

Regulation of Transcription by a Protein Methyltransferase D. Chen, H. Ma, H. Hong, S. S. Koh, S.-M. Huang, B. T. Schurter, D. W. Aswad, M. R. Stallcup

2177 Stability, Precision, and Near-24-Hour 2102 Period of the Human Circadian Pacemaker C. A. Czeisler, J. F. Duffy, T. L. Shanahan, E. N. Brown, J. F. Mitchell, D. W. Rimmer, J. M. Ronda, E. J. Silva, J. S. Allan, J. S. Emens, D.-J. Dijk, R. E. Kronauer

Arabidopsis Galactolipid Biosynthesis and Lipid Trafficking Mediated by DGD1 P. Dörmann, I. Balbo, C. Benning

Receptor for Motilin Identified in the **Human Gastrointestinal System** S. D. Feighner et al.

TECHNICAL COMMENTS

Culture and Genetic Evolution in Whales S. L. Mesnick, B. L. Taylor, R. Le Duc, S. E. Treviño, G. M. O'Corry-Crowe, A. E. Dizon; C. Schlötterer; R. Tiedemann and M. C. Milinkovitch; W. Amos. Response H. Whitehead

www.sciencemag.org/cgi/content/full/284/5423/2055a

SCIENCE ONLINE

www.scienceonline.org

SCIENCE

THE JOURNAL www.sciencemag.org

SCIENCENOW

DAILY NEWS SERVICE www.sciencenow.org

NEXT WAVE

WEEKLY CAREER UPDATES www.nextwave.org

GRANTSNET

RESEARCH FUNDING DATABASE www.grantsnet.org

NEUROAIDS

EXPERIMENTAL WEB SITE www.sciencemag.org/NAIDS

QUARTERLY AUTHOR INDEX

www.sciencemag.org

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

Annika is part of the team developing the HiTrap range. She has a PhD. in plant physiology and everything's coming up roses.

That's just what you get with our pre-packed HiTrap™ columns. Results. Time after time, giving you peace of mind and time to concentrate on other important aspects of your work.

New HiTrap™ columns for hassle-free purification

HiTrap frees you from the needless details of many purification procedures because we've done all the work. Pre-packed columns and easy-to-follow instructions ensure fast start-up and method optimisation. There are even recommendations for sample handling.

In addition to applications for His-tagged fusion proteins, monoclonal and polyclonal IgG and DNA-binding proteins, the HiTrap range now includes immobilised lectins, immobilised streptavidin and media for purification of IgM and IgY.

Solvent delivery can be as simple as a syringe or as sophisticated as an ÄKTA™design system. No other range offers such a choice of application from affinity to desalting.

Give us a call: in Europe +44 (0)1494 544550; in the US 1-800 526 3593; in Japan +81 3 5331 9336 and from the rest of the world +44 (0)1494 544100.

Or visit our web site: www.apbiotech.com/hitrap

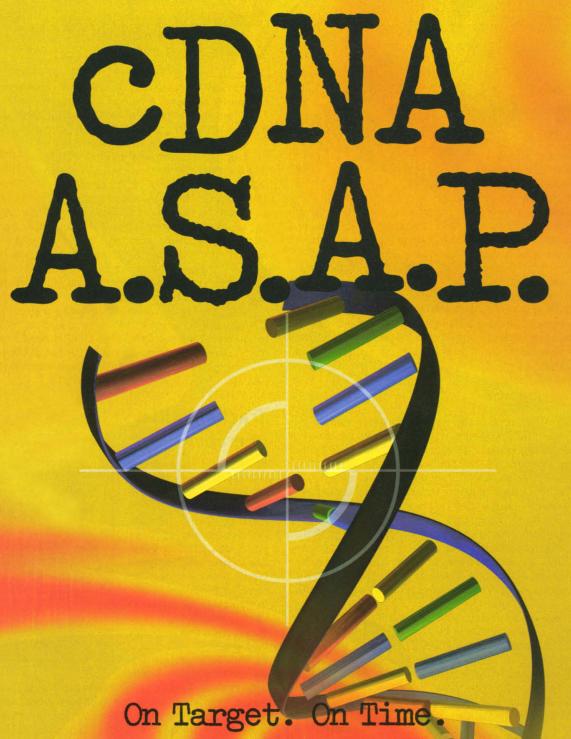
- it'll be an eye-opener.

ith science: dazzle results.

Circle No. 28 on Readers' Service Card

0

amersham pharmacia biotech



When you want the longest target cDNA clone and you want it in a hurry, call Genome Systems. Screen 1 million clones from the library of your choice — or use our SuperPool service to screen 10 million clones from 10 libraries, all at once. With over 30 high-quality oligodT-primed custom libraries available (and more on the way), we offer the fastest high-throughput screening in the business. Choose from Arabidopsis, Drosophila, Human, Mouse, Rabbit, Rat, Xenopus, and Zebrafish tissue-specific libraries.

At Genome Systems, you really do get it faster!

Get it Now. 800-847-7058.

GenomeSystemsInc"

4633 World Parkway Circle, St. Louis, MO, 63134-3115
PHONE: 314.427.3222 FAX:314.427.3324 E-MAIL:info@genomesystems.com WEB: www.genomesystems.com
INTERNATIONAL: Call us free by dialing your country access code + (800 number). Contact your local service provider for details.

A wholly owned subsidiary of Incyte Pharmaceuticals, Inc.

Circle No. 40 on Readers' Service Card

THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

PLANTS UNDER ATTACK

One danger of an increase in global temperature is that it might increase predation of insects on plants. Wilf and Labandeira (p. 2153; see the Perspective by Coley) test this possibility by looking at the fossil record. They examined the predation of insects on plants during the Paleocene and Eocene, about 50 million years ago, a time when Earth's climate warmed considerably. Data from many plant fossils at comparable sites and latitudes in western North America show that predation was significantly greater during the warmer climates of the Eocene.

GLOBAL CLIMATE LINKS

The historic climate record shows that the Indian summer monsoon and the El Niño–Southern Oscillation (ENSO) have been linked: A weak monsoon generally coincided with a warm El Niño event. Another factor influencing the Indian monsoon is Himalayan snow cover, which correlates with Eurasian temperatures. Kumar et al. (p. 2156) have analyzed the historic record and show that the ENSO-monsoon connection has weakened in the last couple of decades. One possible explanation may be recent increases in Eurasian temperatures, which may help sustain monsoon rainfall during warm ENSO events.

THERE'S GOLD IN THOSE ROCKS

The origin of major regional gold deposits has been uncertain; much gold is found in quartz veins in metamorphic rocks, either in a magmatic arc or in oceanic crust accreted to the front of the arc. Knowledge of the solubility of gold with pressure and temperature is critical for inferring how the gold was concentrated in the veinforming fluid and then deposited. Loucks and Mavrogenes (p. 2159; see the Perspective by Kerrich) measured gold solubility by creating gold-rich inclusions in quartz, which served as experimental pressure vessels. The data show that the solubility of gold species in fluids is quite high at high pressure and temperature but drops abruptly with cooling and depressurization. Sudden depressurization of a fluid containing gold could lead to an economically viable deposit.

RECONSTRUCTING THREE-DIMENSIONAL IMAGES

Many fields take advantage of two-dimensional optical imaging to record data, but in many cases it would be more useful to image the object in three dimensions. Most

methods with this capability require a point-by-point scanning of the object or illumination with coherent light (lasers) as in holography. Marks et al. (p. 2164; see the news story by Radov) describe a method that uses ordinary incoherent white light. The cones of light scattered from each point on the object contribute to the total intensity at each pixel, as measured on a two-dimensional sensor array. By analyzing this mutual intensity function using interferometry and algorithms developed for x-ray tomography, the authors were able to reconstruct accurately a three-dimensional image of an illuminated object.

INTEGRATING ETHYLENE RESPONSES

An unusual protein anchors signal transduction for the ethylene hormone in plants and may as well coordinate responses to other volatile chemical signals. Alonso et al. (p. 2148) have now cloned and characterized the EIN2 gene from Arabidopsis.









Analysis of the sequence predicts one domain with 12 transmembrane helices and a second hydrophilic domain that functions in ethylene signaling but shows little similarity to other known signaling proteins. Interactions of EIN2 with the rather distinct ethylene and jasmonate pathways suggest molecular explanations for the coordination of signaling responses.

CLOSURE DOMAINS CLOSED

As electron spins undergo ordering in magnetic materials, energy minimization will cause the material to split into macroscopic regions where all of the individual magnetic moments have the same orientation. Between the domains and near the surface of the films are regions of in-plane magne-

tization called closure domains, which tend to elude imaging by normal magnetic scattering techniques. Dürr et al. (p. 2166; see the Perspective by Hillebrecht) describe a method for imaging based on scattering of circularly polarized x-rays. Magnetization profiles in thin iron-palladium films were obtained in which these in-plane closure domains could be seen.

SMELL AND RESPONSE

Despite the enormous progress made in the molecular biology of olfactory receptors, our understanding of subsequent signal processing in the olfactory system is still rather limited. Duchamp-Viret et al. (p. 2171) examined the odor tuning of rat olfactory receptor neurons assayed by electrophysiological recordings from the nasal mucosa. Their results indicate that the responses of olfactory receptor neurons are only rarely specific to only one odor; the majority of cells respond to a broad range of substances. This finding challenges the hypotheses that one neuron expresses only a single olfactory receptor. Rather, it appears that arrays of neurons are activated in response to a specific odor.

LIKE CLOCKWORK

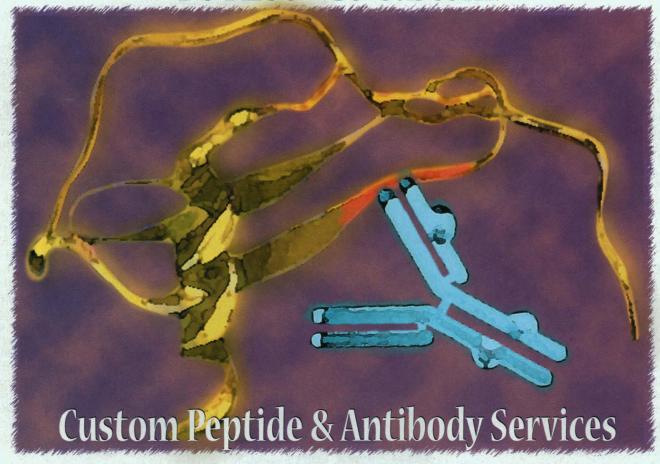
Human circadian clocks have been thought to run with widely variable periods that average near 25 hours, which is considerably longer than that of other animals, and that the period decreases with age, which would account for the wellknown early awakening of elderly people. Czeisler et al. (p. 2177; see the Perspective by Moore) now show that neither of these statements are true. They used an experimental protocol in which young and old subjects were exposed to environmental cues in a rhythm so far from that of the endogenous clock that these cues had no influence on the clock's period. Under these conditions, the free-running period of the human circadian clock was 24 hours and 11 minutes in both young and old subjects, similar to that of other animals.

ACCELERATING TRANSCRIPTION WITH A METHYLTRANSFERASE

The protein-DNA complex of chromatin presents a critical barrier to the transcription process; cells are able to deal with this structural barrier by utilizing chromatin-modifying factors such as histone acetyltransferases, or HATs. Several coactivators have been shown to have HAT activity. Chen *et al.* (p. 2174) now identify a so-called secondary coactivator that in-

CONTINUED ON PAGE 2055

Be First - Go Custom! Be First - Go Custom! Be First - Go Custom!



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

- Thousands of satisfied customers in 30 countries
 - · No hidden costs · Easy order pricing structure
- $\cdot \textit{ In-house expertise in organic chemistry, immunology, biochemistry \& signal transduction}\\$

Peptide Services Include:

BioSource International, Inc.

1-800-242-0607

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

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

Antibody Protocols Include:

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

Options include: Affinity purification and phosphorylation state specific antibody protocols

BOSOURCE



Order on-line at www.qcb.com

For research use only.

Fax: (805) 987-3385 e-mail: peptide@qcb.com

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

AUSTRALIA +61 7 3352 6100 • AUSTRIA +431801 25 256 • CANADA 514 733-1900 • CHILE 56 2 209 6770 • DENMARK +45.86/10.10.55 • EGYPT +202/348.0997
FINLAND +358/3 682 2758 • FRANCE +33.1/42.53,14.53 • CREECE +30 1 52 81 900 • HUNGARY +420/5.745.736 • INDIA +91/80 646 820 • ISRAEL +972/3.934 99 22 • ITALY +39 02 26 28 91
JAPAN +81 3 5645 2751 • MEXICO +525/519 3463 • NEW ZEALAND +64.9/573.0770 • NORWAY +47/22 200 137 • POLAND +48.22/779.8350 • SOUTH AFRICA +27.11/793.6790 • SPAIN +34 3 435 36 01
SWEDEN +46.8/625.1850 • SWITZERLAND +041/420.96.36 • TAIWAN 886 2 2695 9990 • TURKEY +90 (312) 342 4130 • UNITED KINGDOM +44.1/923 241 515

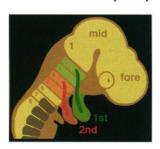
Circle No. 39 on Readers' Service Card

HIS WEEK IN SCIENCE

teracts with a nuclear hormone receptor coactivator to increase transcription activation. This secondary coactivator, CARM1, displays another enzyme activity—that of a methyltransferase. CARM1 may, like HATs, affect chromatin structure through histone modification. Alternatively, CARM1 may affect transcription by modulating the activities of other factors in the transcription complex.

DIRECTING BRAIN DEVELOPMENT

Development of the vertebrate hindbrain and the surrounding branchial arches depends on an intricate interplay between the two types of tissue. By using an ingenious combination of ectopic expression



and orthotopic transplantation, Bell et al. (p. 2168) clarified how Hox genes specify positional identity in these tissues. The results of these studies in chick embryos show that the Hox genes regulate recognition cues that direct the interactions between different tissues.

CALMING THE GITRACT

Motilin is a peptide hormone long known to stimulate the transport of nutrients (motility) in the gastrointestinal (GI) tract. A human receptor for motilin has now been identified in a mass screening by Feighner et al. (p. 2184). The same receptor also binds to erythromycin and may explain the uncomfortable side effects of this antibiotic. The motilin receptor turns out to be a G protein-coupled receptor that is similar to that for human growth hormone secretagogues. With the motilin receptor now in hand, more effective agonists and antagonists may be designed to treat multiple disorders of GI motility.

DESIGNER LIPIDS

The membranes that make up chloroplasts and house the photosynthetic apparatus have a distinctive lipid composition that is made up largely of galactolipids. Dörmann et al. (p. 2181) have now cloned one of the genes, DGD1, that affects galactolipid assembly in Arabidopsis. Genetic and biochemical studies indicate that the galactolipids are derived from two synthetic pathways, one in the plastid and one in the endoplasmic reticulum. Structure predictions from the cloned gene sequence suggest that the DGD1 protein is associated with the plastid envelope.

TECHNICAL COMMENT SUMMARIES

Culture and Genetic Evolution in Whales

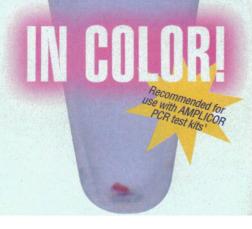
The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5423/2055a

H. Whitehead (Reports, 27 Nov., p. 1708) suggested that, in four species of whale, "the selection of matrilineally transmitted cultural traits, upon which neutral mitochondrial DNA (mtDNA) alleles 'hitchhike,' has the potential to strongly reduce genetic variation. Thus, in contrast to other nonhuman mammals, culture may be an important evolutionary force for the matrilineal whales."

Four comments question whether the data, collected from several different studies, are sufficient to support Whitehead's suggestion. S. L. Mesnick et al. state, "it is difficult to imagine selective sweeps, cultural or otherwise, acting to maintain low interocean diversity." C. Schlötterer states, "low mtDNA diversity could be a result of the effective population size of these species simply being smaller than that of the other species surveyed." R. Tiedemann and M. C. Milinkovitch state, "any stochastic heterogeneity in fecundity through space and time will cause a drastic reduction of mtDNA variability in matrilineal populations." W. Amos states that, in subpopulations where "dispersal from natal group is rare or absent," a hypothesis of "groups as life history units" may account for the data.

In response, Whitehead discusses each comment in turn, providing further details of his analysis and performing some new calculations. He notes that "scientists are currently collecting and analyzing long-term data on the social structure of a number of species of cetaceans" and states, "I presented one possible evolutionary scenario for this phenomenon, but the data are not conclusive, and I strongly support [the] call for an exploration of all feasible explanations."

Precipitate Nucleic Acids.



Pellet Paint™ Co-Precipitant

A highly visible, inert carrier for routine DNA or RNA precipitation.*

EFFICIENT PRECIPITATION OF DNA AND RNA

- · Quantitative recovery of nucleic acids
- · Five minute procedure
- No low temperature incubations
- Suitable for precipitation of dilute samples (<2ng/ml)

NO MORE LOST SAMPLES!

- · Vivid pink pellets are easily located
- Consistent precipitation ends uncertainty
- Precipitation and resuspension steps are easily confirmed

COMPATIBLE WITH MANY APPLICATIONS

- · Pellet Paint contains no DNA, RNA or nucleases
- . No inhibition of downstream reactions
- Qualified for:
- · PCR[†] amplification
- · cDNA synthesis
- · random priming
- · transformation
- ligation
- · restriction digestion · kinase reactions
- · in vitro transcription
- · manual and Cy5** sequencing · in vitro translation
 - gel electrophoresis
 - RNase protection assav
 - · phenol extraction
 - · LiCI precipitation
 - · bacterial
 - electroporation
 - · PEG precipitation



Patent pending

** Cy5 is a trademark of Biological Detection Systems, Inc.

† The PCR process is covered by patents owned by

¹ Taggart, E.W., et al. (1998) J. Clin. Micro. 36, 3408–3409

Novagen, Inc. 601 Science Dr. Madison, WI 53711

800-526-7319

Fax: 608-238-1388 e-mail: novatech@novagen.com

www.novagen.com

Circle No. 31 on Readers' Service Card

Yourelectroporator should not be a variable.



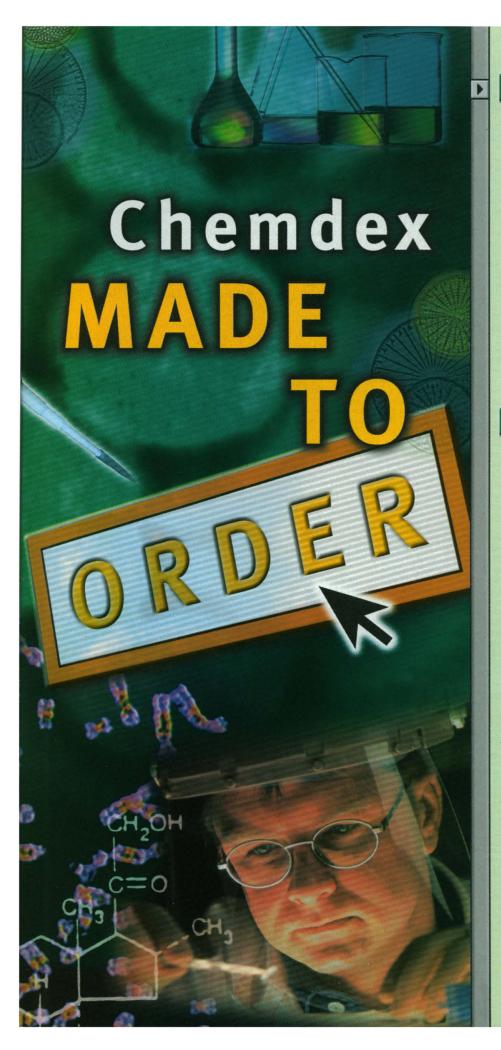
The Gene Pulser II Continues to be the Most Reproducible Electroporator...Period.

For efficient transfection, there are enough variables without your electroporator being one of them. The Gene Pulser II has the unique ability to test and recalibrate its capacitors. This ensures that you get the least amount of variation for reproducible performance today and in years down the road. Sample resistance is tested *before* the pulse, which prevents arcing that could ruin your results. Why repeat experiments? Use your time better with the Gene Pulser II — the only system you can fully trust. For more information, contact your local Bio-Rad representative or visit our website at **discover.bio-rad.com**.

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 86-10-62051850/51 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 03-5811-5270 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



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

Circle No. 46 on Readers' Service Card



EDITOR-IN-CHIEF Floyd E. Bloom

EDITOR Ellis Rubinstein

MANAGING EDITOR Monica M. Bradford

EDITORIAL

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

SCIENCE'S COMPASS

SENIOR EDITORS/PERSPECTIVES Orla Smith, Julia Uppenbrink; Associ-ATE BOOK REVIEW EDITOR Sherman J. Suter; CONTRIBUTING EDITORS

Kevin Ahern, Richard Peters, Robert Sikorski, David F. Voss; PUBLICATION ASSISTANTS Brent Gendleman, Jeffrey Hearn; INFOR-MATION SPECIALIST Janet Kegg; LETTERS AND TECHNICAL COMMENTS: EDI-TOR Christine Gilbert: ASSOCIATE EDITOR Steven S. Lapham: PUBLICA-TION ASSISTANT Charlene King

NFWS

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

LDITING AND PROOFREADING

EDITORIAL MANAGER Cara Tate: SENIOR COPY EDITORS Cay Butler. Harry Jach, Barbara Ordway, Christine M. Pearce; copy EDITORS Jeffrey E. Cook, Etta Kavanagh, Jason Llewellyn, Joshua Marcy; сору DESK Joi S. Granger, Monique Martineau, Ellen E. Murphy, Beverly Shields; Assistant Kathy Libal

PRODUCTION

DIRECTOR James Landry; MANAGER Wendy K. Shank; ASSISTANT PRO-DUCTION MANAGERS, Lizabeth A. Harman (Internet), Rob Masson: ASSOCIATES Vicki J. Jorgensen, Tara L. Kelly, Jessica K. Moshell, Rebecca Thomas

ART

DESIGN DIRECTOR C. Faber Smith; ASSOCIATE ART DIRECTOR Elizabeth Carroll; scientific illustrator Katharine Sutliff; graphics ASSOCIATES Patricia Riehn Berg, Holly Bishop, Preston Morrighan, Darcel Pugh; PHOTO RESEARCHER Leslie Blizard

SCIENCE INTERNATIONAL EUROPE

EDITORIAL: OFFICE HEAD Richard B. Gallagher; SENIOR EDITOR Andrew M. Sugden; Associate Editors Stella M. Hurtley, Ian S. Osborne Peter Stern: SCIENCE'S COMPASS: SENIOR EDITOR/PERSPEC-TIVES Julia Uppenbrink; NEWS: EDITOR Daniel Clery; CONTRIBUT-ING CORRESPONDENTS Michael Balter (Paris) Robert Koenig (Bern); science's NEXT WAVE, UK EDITOR: John MacFarlane; AD-MINISTRATIVE SUPPORT Janet Mumford, Liz Ellis

ASIA

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

SCIENCENOW: www.sciencenow.org EDITOR Erik Stokstad

SCIENCE'S NEXT WAVE: www.nextwave.org MANAGING EDITOR Wendy Yee; SENIOR EDITOR Nicole Ruediger WRITER Melissa Mertl; CANADA EDITOR Charles Boulakia; Assis-TANT Suzanne Moore

AAAS BOARD OF DIRECTORS

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

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

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

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

PUBLISHER Richard S. Nicholson

ASSOCIATE PUBLISHER **Beth Rosner**

MEMBERSHIP/CIRCULATION DIRECTOR Michael Spinella

MEMBERSHIP/CIRCULATION

SUBSCRIPTION SERVICES: 202-326-6417; 800-731-4939 DEPUTY DIRECTOR Marlene Zendell; MEMBER SERVICES: MANAGER Michael Lung; supervisor Mary Curry; REPRESENTATIVES Laurie Baker, Pat Butler, Christine Ford, Mari Pope, Jantell Smith; MARKETING: MANAGER Scott Oser; COORDINATOR Lauri Sirois: EUROPE MANAGER lane Pennington: EXECUTIVE Ruth Jackson; RESEARCH: MANAGER Renuka Chander; BUSINESS AND FINANCE: ASSISTANT SUSAN MAXIM; COMPUTER SPECIALIST Charles Munson

FINANCE AND ADVERTISING

BUSINESS AND FINANCE: BUSINESS MANAGER Deborah Rivera-Wienhold; SENIOR ANALYST Randy Yi; FINANCIAL ANALYST Lisa Donovan RIGHTS AND PERMISSIONS: ASSOCIATE Lincoln Richman: ASSISTANT Emilie David MARKETING: DIRECTOR John Meyers; AS-SOCIATE Allison Pritchard ELECTRONIC MEDIA: MANAGER David Gillikin; computer specialist Wendy Green; production associ-ATES Mark Croatti, Ellen McGuire, Louis Williams

David Clapham

Children's Hospital, Boston

Adrienne E. Clarke University of Melbourne, Parkville

PRODUCT ADVERTISING

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

RECRUITMENT ADVERTISING

SALES AND PRODUCTION OPERATIONS MANAGER Terri Seiter Azie u.s.: SALES MANAGER Gabrielle Boguslawski: 718-491-1607, FAX 202-289-6742; SALES SUPERVISOR Daryl Anderson; SALES REPRESENTATIVES Troy Benitez, Kathleen Clark, Beth Dwyer, Bren Peters-Minnis, Kristin Westapher; Assistants Erika Bryant, Christina Geiger PRODUCTION: SENIOR ASSOCIATE Jennifer Rankin; Associates Christine Borkowski, Elizabeth Lenox copy EDITOR/PROOFREADER Chris Filiatreau U.K./EUROPE: SALES MANAGER Debbie Cummings: SALES EXECUTIVE Sabine Lenud: ASSISTANT Elisabeth Py: (44) 1223-326500, FAX (44) 1223-326532 AUSTRALIA/NEW ZEALAND: Keith Sandell; (61) 02-9922-2977, FAX (61) 02-9922-1100 JAPAN: Mashy Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852

DEPUTY EDITORS

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

Frederick W. Alt Children's Hospital, Boston Don L. Anderson

California Institute of Technology Michael Ashburner University of Cambridge Frank S. Bates Univ. of Minnesota, Minneapolis Stephen J. Benkovic Pennsylvania State University Alan Bernstein

Mount Sinai Hospital, Toronto

Michael J. Bevar University of Washington, Seattle Seth Blair University of Wisconsin, Madison David E. Bloom Harvard Institute for

International Development The Netherlands Cancer Institute Henry R. Bourne Univ. of California, San Francisco Iames I. Bull University of Texas at Austin Kathryn Calame Columbia Univ. College of

Physicians & Surgeons Dennis W. Choi Washington Univ. School of Medicine, St. Louis Joanne Chory
The Salk Institute

F. Fleming Crim University of Wisconsin, Madison Paul J. Crutzen Max-Planck-Institut für Chemie James E. Dahlberg University of Wisconsin Medical School, Madison Robert Desimone National Institute of Mental Health, NIH Hans Eklund Swedish Univ. of Agricultural Sciences, Uppsala
Paul T. Englund
Johns Hopkins University School of Medicine G. Ertl Max-Planck-Gesellschaft Richard G. Fairbanks Lamont-Doherty Earth Observatory Douglas T. Fearon
University of Cambridge
Harry A. Fozzard
The University of Chicago Roger I. M. Glass
Centers for Disease Control
Peter N. Goodfellow
SmithKline Beecham, UK
Jack F. Greenblatt University of Toronto

Max Planck Institute of Biophysical Chemistry
Philip C. Hanawalt
Stanford University Paul Harvey
University of Oxford
M. P. Hassell . P. Hassell Imperial College at Silwood Park Nobutaka Hirokawa University of Tokyo Tasuku Honjo Kyoto University Susan D. Iversen University of Oxford Eric F. Johnson The Scripps Research Institute
Hans Kende
Michigan State University
Elliott Kieff Harvard University Jeffrey T. Kiehl National Center for Atmospheric Research, Boulder Judith Kimble

University of Wisconsin, Madison
Stephen M. Kosslyn Harvard University
Michael LaBarbera
The University of Chicago Antonio Lanzavecchia Basel Institute for Immunology Nicole Le Douarin

Institut d'Embryologie Cellu-

Peter Gruss

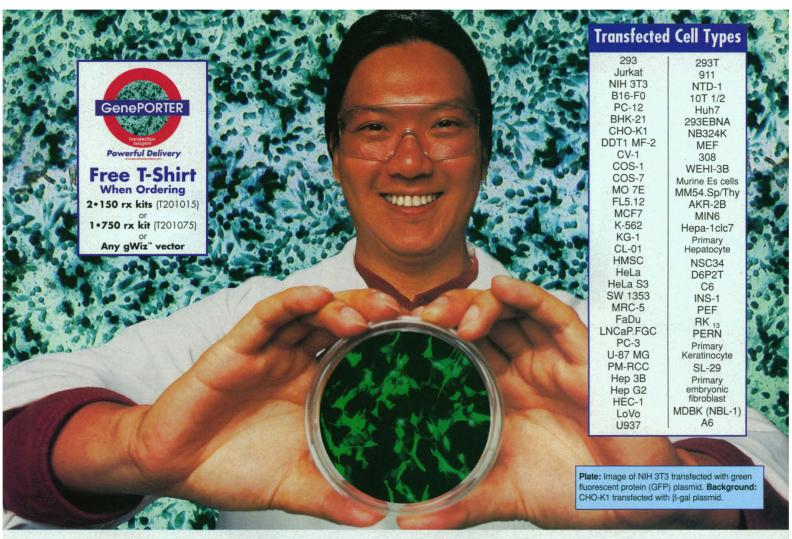
laire et Moléculaire du CNRS Norman L. Letvin Beth Israel Hospital, Boston Harvey F. Lodish
Whitehead Institute for
Biomedical Research Richard Losick Harvard University
Seth Marder
University of Arizona
Diane Mathis Institut de Chimie Biologique, Institut de Chiline Bloosgar, Strasbourg Susan K. McConnell Stanford University Anthony R. Means Duke University Medical Center Stanley Meizel
University of California, Davis
Douglas A. Melton
Harvard University Andrew Murray Univ. of California, San Francisco Elizabeth G. Nabel The Univ. of Michigan Medical Center Shigetada Nakanishi Kyoto University Roger A. Nicoll Iniv. of California, San Francisco Staffan Normark Swedish Institute for Infectious Disease Control Kiyotaka Okada Kyoto University Bert W. O'Malley

Baylor College of Medicine Roy R. Parker University of Arizona, Tucson Stuart L. Pimm The Univ. of Tennessee, Knoxville Yeshayau Poćker Univ. of Washington, Seattle Martin Raff Martin Raff
University College London
Douglas C. Rees
California Institute of
Technology
T. M. Diese T. M. Rice ETH-Hönggerberg, Zürich David C. Rubie Universität Bayreuth Erkki Ruoslahti The Burnham Institute, CA Gottfried Schatz Biozentrum, Basel Jozef Schell Max-Planck-Institut für Zuch Ronald H. Schwartz
National Institute of Allergy
and Infectious Diseases, NIH Terrence J. Sejnowski
The Salk Institute
Christopher R. Somerville
Carnegie Institute of Washington, Stanford, CA

John Jen Tai

Michael P. Stryker
Univ. of California, San Francisco
Cliff Tabin
Harvard Medical School

National Taiwan University Tomoyuki Takahashi University of Tokyo Masatoshi Takeichi Kyoto University Keiji Tanaka RIKEN Institute David Tilman
Univ. of Minnesota, St. Paul
Robert T. N. Tjian
Univ. of California, Berkeley
Yoshinori Tokura Yoshinori Tokura
University of Tokyo
Derek van der Kooy
University of Toronto
Geerat J. Vermei
University of California, Davis
Bert Vogelstein
Johns Hopkins Oncology Center
Gerhard Wegner
Max-Planck-Institut für
Polymerforschung Polymerforschung Arthur Weiss Arthur Weiss
Univ. of California, San Francisco
Zena Werb
Univ. of California, San Francisco
George M. Whitesides
Harvard University lan A. Wilson The Scripps Research Institute Alan P. Wolffe National Institute of Child Health and Human Development, Martin Zatz National Institute of Mental Health, NIH



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

Introducing

GenePORTER™ Transfection Reagent

GenePORTERTM 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.

GenePORTER"

Transfection Reagent

75 reactions (0.75 ml) • T201007 150 reactions (1.5 ml) • T201015 750 reactions (5 x 1.5 ml) • T201075

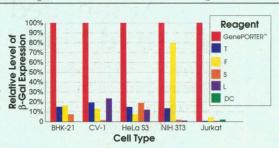


To Order: 888-428-0558

Fax: 619-623-9494

10190 Telesis Court, San Diego, CA 92121, USA
Check out the Gene Therapy Systems web site @
http://www.genetherapysystems.com

Circle No. 38 on Readers' Service Card



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.

New High Expression Vectors

gWiz™ Expression Vectors

Call for a brochure or visit our web page

Patents pend

Gene Therapy Systems International Distributors

Australia • ASTRAL +61-2-9540-2055 Austria • BIO-TRADE +43 1 889 18 18 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 Talwan • PROtech, Ltd. 886-2-23810844 United Kingdom • Lifescreen Ltd. +44 0 1923 241515

TIME MAGHINE

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

The Mini-Prep 24 uses a new method of plasmid purification based on agarose gel 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 with quality DNA while saving you lots of time. **High Purity** - sufficient for automated fluorescent and manual sequencing.

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

Consistent Results - up to 6 µg of plasmid per ml.

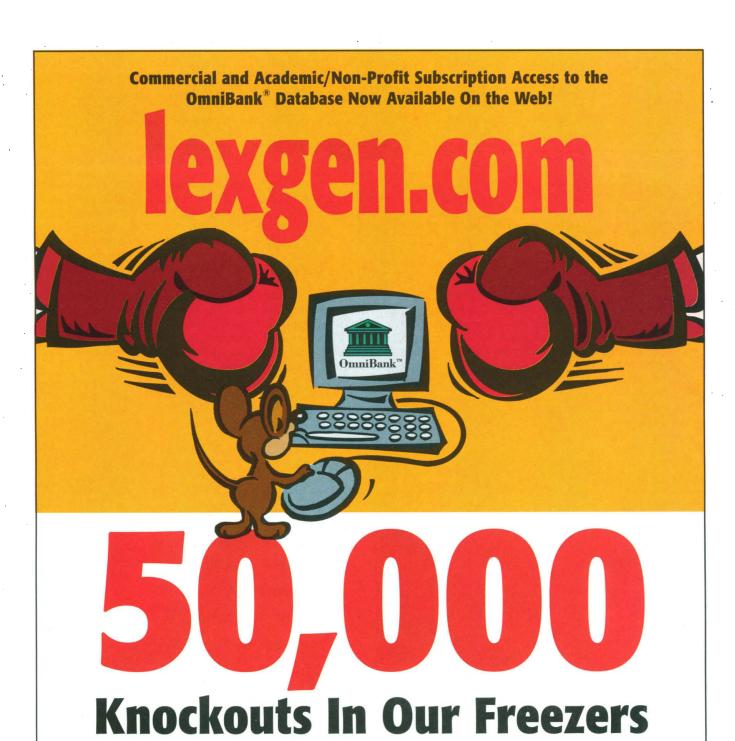
Fast - up to 24 preps per hour, saving you time.

Quality - time and time again.



1-800-466-7949

11339 SorrentoValley Rd • San Diego, CA 92121 Phone: (619) 452-2603 Fax (619) 452-6753 www.macconnell.com



OmniBank® is an Internet database of **over 50,000 cryopreserved ES cell lines**. Each OmniBank® ES cell line contains a single gene trap insertion that is identified by the DNA sequence of each mutated gene. Lexicon uses the OmniBank® ES cell lines to **rapidly generate new mutant mice** for functional genomics research. Also ask about our rapid homologous recombination knockout program using patented and proprietary technologies.

Let Lexicon's novel gene sequences (>40%) and robotic production of mutant mice lead you to discoveries at unprecedented speed.

Non-Profit/Academic Subscriptions www.lexgen.com/omnibank



Commercial Inquiries omnicorp@lexgen.com

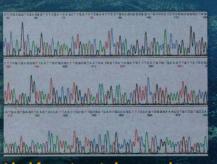
Midiprep with Maxi Capacity

StrataPrep® EF Plasmid Midiprep Kit

- Over 3x greater yields than other kits
- Fast, easy, efficient spin format
- Endotoxin-free DNA (optional step)
- Unique color-indicating protocol
- Application-ready pure DNA

StrataPrep® Technology. The StrataPrep® EF plasmid midiprep kit uses a silica-based fiber matrix technology in a convenient spin column format. Produce high yields (up to 350 µg) of pure DNA in 90 minutes or less.

Endotoxin-Free DNA. The presence of endotoxins will sharply reduce transfection efficiencies in sensitive cell culture lines. The StrataPrep EF plasmid midiprep kit includes a unique step for extracting endotoxins to produce up to a 5-fold increase in transfection efficiency.



Ideal for automated sequencing

StrataPrep, Endotoxin-free

Transfects sensitive mammalian cells

Endotoxin Removal Step (optional) Capture DNA **Pure DNA** StrataPrep EF Plasmid Midiprep method

Pelleted bacteria

Alkaline lysis

UNITED STATES AND CANADA

Circle No. 42 on Readers' Service Card

StrataPrep® EF Plasmid Midiprep Kit Endonuclease A Removal Buffer Pyrogen-free 50-ml Conical Tubes



Call for Papers

A NEW SECTION OF MCB: "MAMMALIAN GENETIC MODELS WITH MINIMAL OR COMPLEX PHENOTYPES"

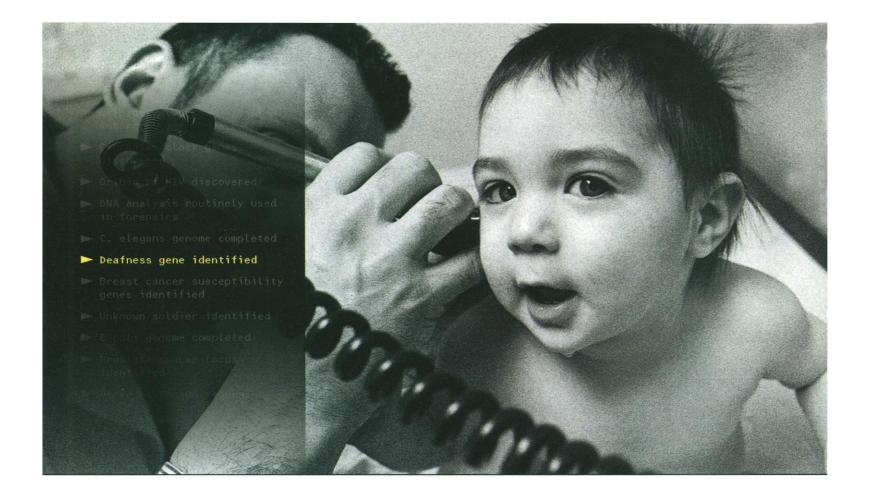
Many mouse knockouts have little or no obvious phenotype, or a very subtle phenotype, making it difficult to publish reports of mutant construction and analysis. Much of the publication problem may be due to a misconception: "no" phenotype is viewed as a "negative result," rather than as one more useful clue to the complex biology of mammals. This is unfortunate: the biomedical community is deprived of essential information, investigators are deprived of essential recognition, and arduous work may be needlessly duplicated in different laboratories. Moreover, as we learn more about redundant pathways, it may become routine to test new mutants in backgrounds containing other targeted deletions. This requires that the single mutants first be characterized, described in the scientific literature, and made available to the research community.

To address these issues, *Molecular and Cellular Biology* (MCB) is initiating a new section of the journal entitled "Mammalian Genetic Models with Minimal or Complex Phenotypes." The new section will be listed separately in the table of contents, and is intended only for knockouts that have no phenotype or unexpected phenotypes that are not easily reconciled with the suspected gene function. Knockouts providing additional information about known gene functions will be published in the section most appropriate for that function.

Manuscripts intended for the new section will be reviewed as are all other reports of original research. The manuscript should describe how the knockout was constructed, and should rigorously document the absence of gene expression. The manuscript should also explain how the phenotype of the mutant animals was characterized, but supporting data should not be shown unless absolutely necessary. Although manuscripts should be formatted as usual, publication will be strictly limited to five printed journal pages and a total of no more than five figures and tables. Manuscript length can be estimated by assuming that 1 printed page equals 5 double-spaced manuscript pages or 53 references; figure and table sizes can be estimated by eye.

Manuscripts for the new section may be submitted immediately. As one purpose of this new section is to make mutants available to the entire biomedical community, authors submitting to this section of the journal must agree to maintain the knockout line for at least 6 months following publication, or to generate cryoembryos.

Three copies of each manuscript should be submitted to: MCB, Journals Department, American Society for Microbiology, 1325 Massachusetts Ave., Washington, DC 20005-4171, U.S.A.



The ABI PRISM® 377 DNA Sequencer. It's a part of discoveries that touch us all.

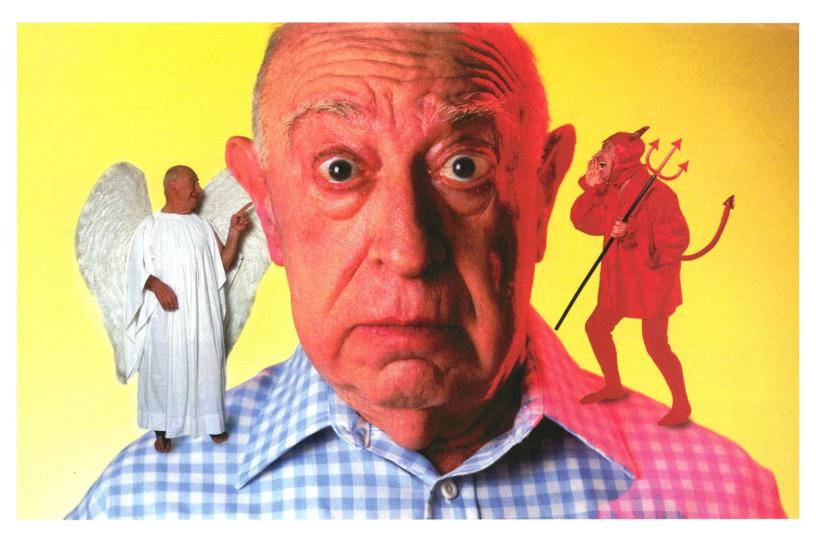
Whether they are identifying the genes that cause deafness or investigating the origin of the HIV virus, thousands of researchers around the world rely on the ABI PRISM® 377 DNA Sequencer to deliver their most important results. With its unparalleled reliability, proven technology, and up to 96-lane capability, the 377 system is the ideal choice to meet the demanding needs of life scientists. Add the world's best DNA reagents, service, and support, and the 377 system emerges as the gold standard. In fact, it's changing life as we know it. For more information, visit our Web site at www.pebiosystems.com/377.

ABI PRISM® 377 DNA Sequencer

Applied Biosystems

PE Biosystems





Resist the Temptation to Screen Libraries.

GeneStorm Expression-Ready Human Genes

CLONES AVAILABLE

404

158

195

198

127

Tempting or not, screening cDNA libraries is a time-consuming but necessary evil. We can help. GeneStorm™ is the only organ-

ized collection of full-length, expression-positive human genes available. Save yourself some time. Spend a few minutes screening the GeneStorm™ database before spending weeks screening a cDNA library.

The GeneStorm™ Difference.

Unlike cDNA libraries and other gene

collections, GeneStorm™ Clones are actually expression- positive clones. This means you don't have to spend time cloning and testing for expression. Simply find your gene of interest in the

GeneStorm™ database and you're ready for downstream functional genomics, gene analysis, and drug discovery applications.

Thousands of Genes. The GeneStorm™ collection now contains thousands of full-length, expression-positive clones. There are many important genes in a variety of categories so you're likely to find the genes you're looking for.

Easy Access. The entire time-saving, expression-positive GeneStorm™ collection

is easily accessible on the GeneStorm™ web site. Make sure you are getting the right advice. Visit the GeneStorm™ web site today (www.invitrogen.com/genestorm) and have the clone you need tomorrow.

Circle No. 34 on Readers' Service Card

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

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

CATEGORY

Cell Receptor Genes

Apoptosis Genes

Signal Transduction and Cell Signaling Genes

Oncogenes, Cancer, and Tumor Suppressor Genes

Adhesion Molecules and Cell Surface Antigen Genes

Cytokines, Chemokines, and Growth Factor Genes

Finland: Tel: 990800 5345 5345 Fax: 990800 7890 7890 Sweden: Tel: 009800 5345 5345 Fax: 009800 7890 7890

Distributors: Austrila 1 800 882 555 China 010 6255 3477 Hungary 01 280 3728 India 91 80 8391453 Israel 02 584 1111 Italy 02 38 19 51 Janan 03 5684 1622

Malaysia 03 736 9198 Poland 058 341 47 26 Portugal 01 453 7085 Singapore 65 2922130 South Korea 02 3471 6500 Spain 03 450 2601 Taiwan 886 2 238 10844

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

United States Headquarters:

Toda Talauay Archide Carlsbad, California 92008 Tel: 1-800-955-6288 Fax: 760-603-7201 Email: tech_service@invitrogen.com http://www.invitrogen.com



The PCR Company

Many things only change a little!

Some things change the world!

1789

L. Galvani Discovery of the electricity

1876

G. Bell

The first telephone, that work efficient

1891

O. Lilienthal

Invention of the first aeroplane

1969

N. Armstrona

The first man on the moon

P 401 999

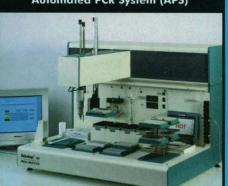
MWG-BIOTECH

Automated cross contamination free PCR

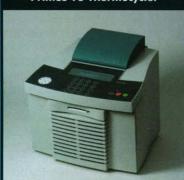
MWGAG BIOTECH

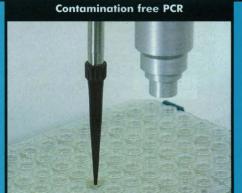
Working for the future!

Automated PCR System (APS)



Primus 96 Thermocycler





www.mwg-biotech.com

GERMANY

ANZINGER STRASSE 7 D-85560 EBERSBERG

TEL.: 0 80 92/82 89-0 FAX: 0 80 92/2 10 84 E-MAIL: info@mwgdna.com

The PCR Company XXXX BIOTECH

The chemically actuated lid, MWG-BIOTECH's newest development, omits one of the last manual steps in automated PCR - to apply the exact pressure for oil free PCR in microtitre plates.

It's time to change your PCR

Take advantage of the newest technology

The PCR Consumable

The Thermosprint PCR plate, *ultra* fast & ultra thin 96-well PCR consumable for optimum thermal transfer and therefore better results. Ensures absolute airtight sealing of each individual cavity. Frames and hole plates can be autoclaved and re-used. Available as 96-well PCR plates (covered and open) or as 2 x 8 strips. This means it can be matched cost effectively to different sample numbers. The vessels are *compatible* with every 0.2 ml standard thermocycler block.

The PCR Thermocyclers

Multi PCR System including four separate blocks for high throughput PCR. Multi Temperature Gradient block with six different temperature zones for real optimisation. For 96 and 384-well plates with High Temperature Range performance: fastest heating and cooling - extreme block reliability. The High Pressure Lid automatically adjusts to apply the perfect pressure to seal PCR plates (up to 30 kg). Fully automated opening and closing of the lid without manual intervention.

The Automated PCR System (APS)

RoboAmp® & RoboSeq® 4200 the fully integrated PCR robots that automate PCR absolutely cross contamination free (NCC-PCR). The only solution available worldwide that allows automated opening and closing of individual lids. The integrated thermocycler allows automation of PCR protocols, fragment analysis, DNA sequencing and virtually all applications in molecular biology. Optimized for microarray technology.

Amplifies thousands of DNA samples

contamination free.

Circle No. 44 on Readers' Service Card

MWGAG BIOTECH

Your partner for automated PCR

Thermosprint PCR plate

SWITZERLAND

TEL.: +41(0)- 61/4 16 06 16 FAX +41(0)- 61/4 16 06 19 E-MAIL: mwgbiotech@magnet.ch

FRANCE

TEL.: +33-(1) 69 59 20 50 FAX: +33-(1) 69 59 20 55 E-MAIL: info@mwg-biotech.fr

Multi Temperature Gradient block

TEL.: +01-336-812-9995 FAX: +01-336-812-9983 E-MAIL: info@mwgbiotech.com

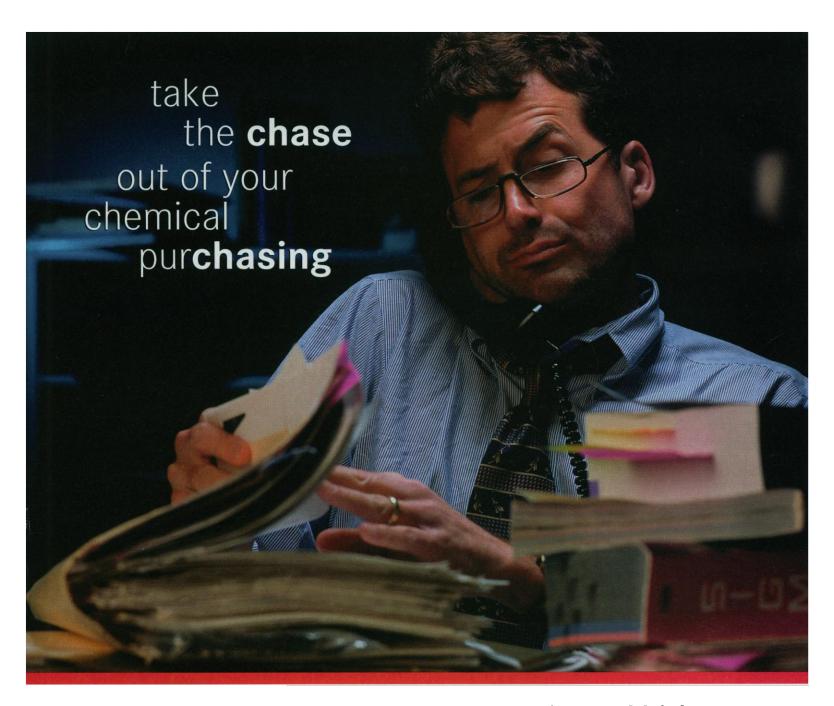
.

TEL.: +44-(0)19 08/24 77 00 FAX : +44-(0)19 08/24 77 24 E-MAIL: info@mwg.co.uk

Applications:

- **PCR**
- ♦ RT-PCR
- Cycle Sequencing
- Genotyping
- Enzymatic Digestions
- Agarose Gel
- Comb Loadin





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

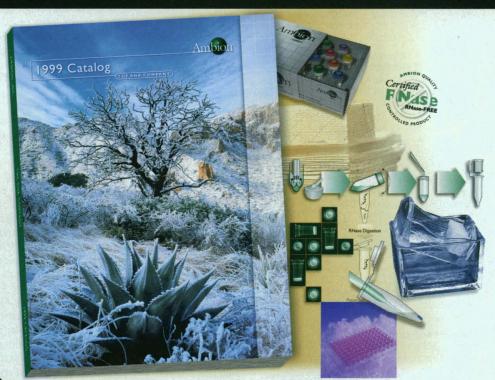
Because we are a manufacturer, we offer not only quality products but the technical knowledge and support to back them up.

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



ABetter, 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

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



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.

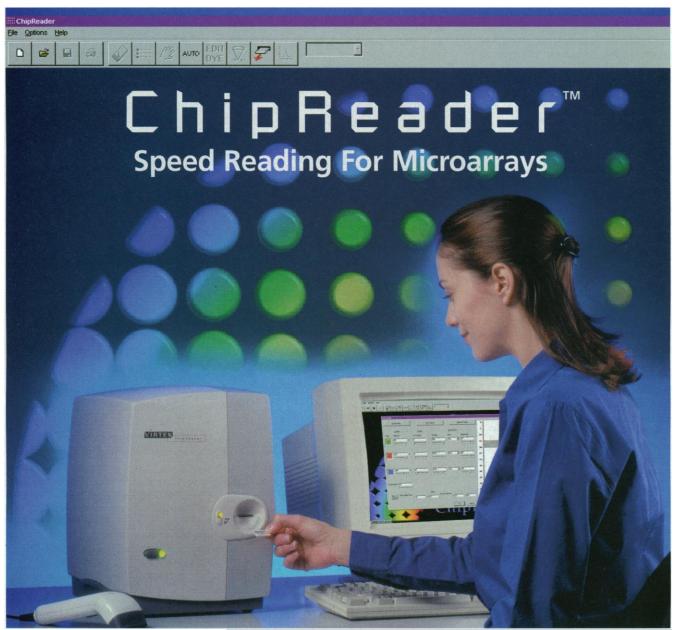
For a complete list of distributors visit our website, http://www.ambion.com



THE RNA COMPANY

AAAS Annual Meeting and Science Innovation Exposition February 17-22, 2 www.aaas.org/meetings Watch the meetings web site for the most CURRENT 2000 MEETING INFORMATION Science Please send me: Name 2000 Meeting Exhibitor Company Information Information Washington, DC Address Student Session AAAS Membership Information Aide Information City . State Zip Call for Contributed Country Poster Papers Phone Fax AMERICAN ASSOCIATION FOR THE

E-Mail Address



ChipReader™ is the first biochip imaging system to offer simultaneous reading of up to 5 different fluorescent dyes.

hipReader is a high-sensitivity laser confocal system for imaging microarray biochips. It offers an array of speed and efficiency benefits.

Highest Sensitivity

Our a-chromatized objective lens provides the highest collection efficiency available.

Highest Throughput

ChipReader works up to 10 times faster than competitive products. The high-speed scanning mechanism reads up to 5 different dyes simultaneously, over a 20 x 20 mm area, in less than one minute.

Greatest Flexibility

ChipReader's modular design accommodates your changing needs. Use standard slides, stainless steel cartridges, or 3" x 4" (76 x 98 mm) glass plates. ChipReader can read glass substrates with the array printed on the top or bottom, wet or dry — with or without a cover glass! It can also read silicon, plastic and nylon substrates.

Smallest Footprint Available

Measuring just II" in length, 9" in width, and I2" in height, there is no greater space-saving imaging option for your microarray biochips!

Circle No. 49 on Readers' Service Card

Easy To Run; User Friendly

To optimize experiment performance, parameters such as speed and number of scans can easily be set using ChipReader's icon driven Windows NT software. It can be integrated with your lab automation systems and is Y2K compliant.

Contact Beverly Giammara, 1-800-933-9011 Visit us at www.virtek.ca

