



AMERICAN
ASSOCIATION FOR THE
ADVANCEMENT OF
SCIENCE

SCIENCE

3 MAY 1996

\$7.00

VOL. 272 • PAGES 617-780



*Cardiovascular
Medicine*

STRATAGENE

QuikChange™

SITE-DIRECTED MUTAGENESIS KIT

Stratagene Times

QuikChange™
Site-Directed
Mutagenesis Kit

Near 100% Efficiency

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

150 Times More Accurate than PCR-based Mutagenesis

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

1-Day Method

Gene in plasmid with target site

1. Mix

Denature plasmid and anneal primers containing the desired mutation

2. Cycle

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

3. Digest

Digest parental DNA template

4. Transform

Transform the resulting annealed double-stranded nicked DNA molecules

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

MUTAGENESIS MADE EASY!

QuikChange™ Site-Directed Mutagenesis Kit catalog #200518

*Patent pending

Circle No. 46 on Readers' Service Card

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

MUTAGENESIS BREAKTHROUGH

150 Times
More Accurate
than PCR-based
Mutagenesis!

REPLICATES ONLY PARENTAL DNA

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

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



STRATAGENE

UNITED STATES:
Stratagene Headquarters
800-424-5444
INTERNET MAIL:
techservices@stratagene.com
AUSTRALIA: 1800-252-204
AUSTRIA: 1 5332666
BRAZIL: 11 530 7833
CANADA: 905 713 1201
DENMARK: 8 6101055
FRANCE: 1 34 60 2424
GERMANY: 0130-840911
HONG KONG: 5785839
ISRAEL: 3 7521687
ITALY: 258013409
JAPAN: (Toyoko) 3 3660 4819
(Funakoshi) 3 5684 1622
KOREA: 2 5560311
MALAYSIA: 37031888
NETHERLANDS: 33 4950094
NEW ZEALAND: 9 443 5867
NORWAY: 22715090
PORTUGAL: 1-4581641
ROC: 2 694 0066 or 2 720 2215
SINGAPORE: 2730898
SPAIN: 1 729 93 33
SWEDEN: 8 680 0845
SWITZERLAND: 3641106
THAILAND: 23080611
UNITED KINGDOM: 0800 585370
OTHER COUNTRIES CALL STRATAGENE U.S.A.

Call Stratagene or your
Stratagene distributor for the complete picture.

The Future of Microplate Assays Is Here — 384-well Radioisotopic and Luminescence Counting!

TopCount HTS Revolutionizes Microplate Counting — Again

- Measure radioisotopic and luminescence assays in both 96- and 384-well microplates.
- Process 12 luminescence samples simultaneously for throughputs of 10,000 samples per hour, or more.
- Stack up to 40 plates or 15,000 samples for unattended counting.
- Interface with robotic systems for complete automation.

Meeting the Demands of Microplate Counting for Today and for the Future

Assays have been scaled down from test tubes to 24-well microplates and the 96-well format. Now, the next step in assay miniaturization is here with the TopCount HTS. Continue today's assays in 96-well plates while converting assays to the higher density 384-well plates — the screening format of the future. With the TopCount HTS you can do both without risk or compromise.

Less Reagents, Less Handling, More Samples

The Packard 384-well plate accommodates assay volumes of up to 80 μ L. This allows practical miniaturization of assays such as scintillation proximity, in-plate binding, liquid scintillation, Cerenkov and luminescence.

TopCount Harnesses the Power of Luminescence

Packard has pioneered the field of high throughput microplate luminescence. Now up to 12 wells can be measured simultaneously in 96- or 384-well plates for throughputs never before possible. Ultra-sensitive photon counting is combined with innovative reagents, such as LucLite with a five hour half-life, for measuring the luciferase reporter gene. Greater capacity, greater throughput.

To complement sample throughput, TopCount now has an extended 40 plate stacker. Load up to 40 plates with the TopCount ZipLoad stacker, carry them safely to the TopCount, load and count. It's that easy.



If your experiments demand accuracy, versatility or high

throughput, TopCount has the answer for your laboratory.

Contact Packard at 800-323-1891 (U.S. only) or 203-238-2351 for more details. Or, visit our Web Site at <http://www.packardinst.com>.



Packard Instrument Company, 800 Research Parkway, Meriden, CT 06450 U.S.A.
Tel: 203-238-2351 Toll Free: 1-800-323-1891 FAX: 203-639-2172
Web Site: <http://www.packardinst.com> Email: webmaster@packardinst.com

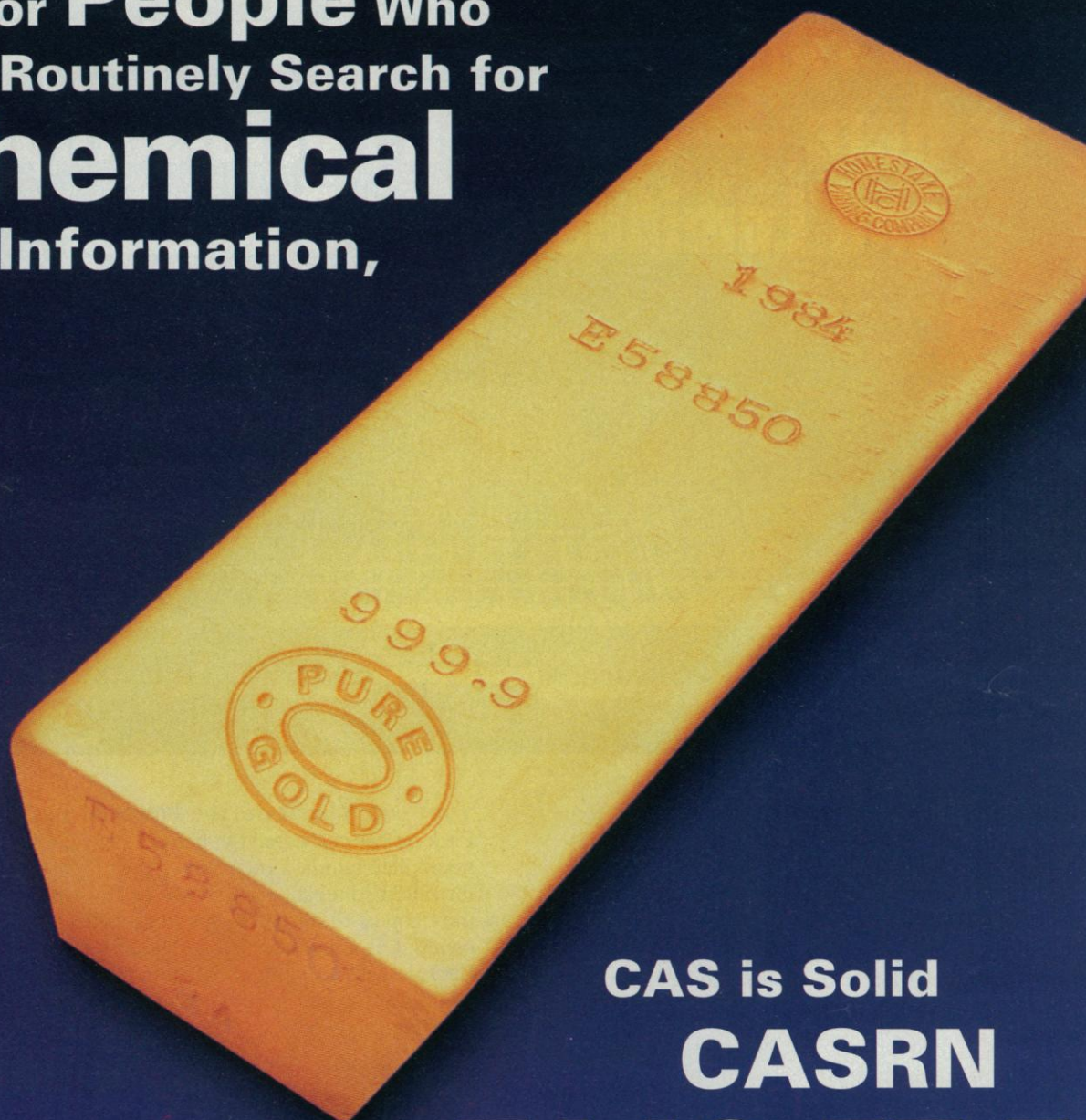


Packard International Offices:

Australia, Mt Waverley 61-3-9543-4266; **Austria**, Vienna 43-1-2702504; **Belgium**, Brussels 32-2-4668210; **Canada**, Ontario 1-800-387-9559; **Central Europe**, Vienna 43-2230-3263; **Denmark**, Greve 45-42909023; **France**, Rungis (33) 1 46.86.27.75; **Germany**, Dreieich 49 6103 385-0; **Italy**, Milano 39-2-33910796/7/8; **Japan**, Tokyo 81-3-3866-5850; **Netherlands**, Groningen 31-50-5413360; Tilburg (013) 5423900; **Russia**, Moscow, 7-095-238-7335; **Switzerland**, Zurich (01) 481 69 44; **United Kingdom**, Pangbourne, Berks (44) 01734 844981.

Circle No. 48 on Readers' Service Card

For **People** who
Routinely Search for
Chemical
Information,



CAS is Solid
CASRN
7440-57-5.

Your Most Valuable Source For Chemical Information.

CAS provides the most comprehensive databases of chemical information in the world, serving research and development in chemicals, pharmaceuticals, and allied fields. In 1995 alone, we added more than 1,000,000 substance records to our CAS Chemical Registry System.

Through CAS Registry Numbers, structure drawings, and a variety of other searching methods, you can easily find the chemistry-

related information you're looking for. And with online, print and CD-ROM convenience, nobody makes searching easier.

With over 14,000,000 substance records, more than 200 databases in our STN online network, and an average of 2,600 new records added to

CHEMICAL ABSTRACTS per day, you might say there's safety in numbers. No matter what your specialization, when you need scientific information, you can feel safe in choosing CAS —The world's leading provider of chemical and related scientific information.



A division of the American Chemical Society®

For information: **1-800-753-4227** or **614-447-3731**. Send e-mail to **help@cas.org** or visit our web site at **http://www.cas.org/**.

In the fight against disease, this could be the most powerful weapon yet.



It's not magic. But it may yet work miracles.

This is the trademark of a completely different kind of pharmaceutical venture.

The recently-merged Pharmacia & Upjohn.

It's a partnership that has created a company of quite remarkable depth and scope: over 30,000 people working in 50 countries and serving 200 million people around the world.

And it's for those 200 million people that this announcement should come as very good news.

Because the merger will give two pools of specialised medical talent the opportunity to work together for the first time ever.

Resulting in real, tangible benefits in the fight

against cancer, AIDS, infectious diseases and many other medical conditions.

This merger is not simply a matter of shared resources, however.

It is also about shared ideals.

Our trademark stands as a symbol for humanity, hope and inspiration.

Values that we intend to apply to every single aspect of the way we do business.

You are surprised to hear such sentiments coming from a global pharmaceutical company?

This is not the last time we'll be surprising you.

You can be sure of that.



**Pharmacia
& Upjohn**



646

Getting physical with
proteins



709

Io's core tugs on Galileo

ERIC DEJONG

NEWS & COMMENT

- | | |
|---|-----|
| Relaunching Bell Labs | 638 |
| Partisan Battle Mars Markup of
Joint Authorization Bill | 640 |
| Plan Would Shut Kitt Peak Facilities | 641 |
| Review Threatens Royal Observatories | 641 |
| European Space Science: Cosmologists
Beat Out Mars Explorers | 642 |
| Patent Office Faces 90-Year Backlog | 643 |
| Germany: Staff, Students Protest
University Cuts | 643 |
| Wiley Drops IQ Book After Public Furor | 644 |
| Japan: New Faculty Grants Program
Expands Role of STA Agency | 645 |

RESEARCH NEWS

- | | |
|---|-----|
| Physicists Advance Into Biology | 646 |
| Molecule Promises a Better Buckyball | 648 |
| New Gene Forges Link Between
Fragile Site and Many Cancers | 649 |
| Two Versions of Holography Vie
to Show Atoms in 3D | 650 |

CARDIOVASCULAR MEDICINE



NEWS

- | | |
|---|-----|
| Finding New Drugs to Treat Stroke | 664 |
| Moscow Cardiology Institute Battles
for Its Life | 667 |
| New Devices Are Helping Transform
Coronary Care | 668 |

ARTICLES

- | | |
|---|-----|
| Molecular Pathways Controlling Heart
Development | 671 |
| E. N. Olson and D. Srivastava | |

- | | |
|---|-----|
| Strong Baby Limbs May Kick Image
of Maternal Dinosaurs | 651 |
| "Smart" Genes Use Many Cues
to Set Cell Fate | 652 |
| Sunfish Shows the Way Through the Fog | 653 |
| New Skeleton Gives Path From
Trees to Ground an Odd Turn | 654 |

PERSPECTIVES

- | | |
|--|-----|
| Molecular Electronics Emerges from
Molecular Magnetism | 698 |
| M. Verdaguer | |
| Diabetes Complications: Why Is
Glucose Potentially Toxic? | 699 |
| D. Porte Jr. and M. W. Schwartz | |
| Speciation in Action | 700 |
| J. Coyne | |

DEPARTMENTS

- | | |
|---|-----|
| THIS WEEK IN SCIENCE | 625 |
| EDITORIAL | 629 |
| Heart Attacks: Gone with the Century? | |
| M. S. Brown and J. L. Goldstein | |
| LETTERS | 631 |
| Squid Pro Quo?: J. D. Rummel • Risks from Low Doses
of Radiation: J. S. Puskin and N. S. Nelson; R. H.
Nussbaum; D. A. Pierce and D. L. Preston • Safety of | |



- | | |
|---|-----|
| Hepatitis B Vaccine: H. A. Fields, F. J. Mahoney, H. S.
Margolis • Immunology Taught by Darwin: K. A.
McKean, L. Nunnery, M. Zuk; R. M. Zinkernagel | |
| SCIENCESCOPE | 637 |
| RANDOM SAMPLES | 655 |
| BOOK REVIEWS | 696 |
| PRODUCTS & MATERIALS | 751 |

Board of Reviewing Editors

Frederick W. Alt
Don L. Anderson
Michael Ashburner
Stephen J. Benkovic
Alan Bernstein
David E. Bloom
Piet Borst
Henry R. Bourne
Michael S. Brown
James J. Bull
Kathryn Calame
Dennis W. Choi

David Clapham
Adrienne E. Clarke
John M. Coffin
F. Fleming Crim
Paul J. Crutzen
James E. Dahlberg
Robert Desimone
Paul T. Englund
G. Ertl
Richard G. Fairbanks
Douglas T. Fearon
Harry A. Fozzard

Roger I. M. Glass
Stephen P. Goff
Peter N. Goodfellow
Corey S. Goodman
Peter Gruss
Philip C. Hanawalt
Nobutaka Hirokawa
Tomas Hökfelt
Tasuku Honjo
Susan D. Iversen
Eric F. Johnson
Stephen M. Kosslyn

Michael LaBarbera
Nicole Le Douarin
Charles S. Levings III
Harvey F. Lodish
Richard Losick
Reinhard Lührmann
Ruth Lynden-Bell
Seth Marder
Diane Mathis
Anthony R. Means
Shigetada Nakanishi
Kim Nasmyth

Roger A. Nicoll
Staffan Normark
Stuart L. Pimm
Yeshayau Pocker
Ralph S. Quatrano
Martin Raff
V. Ramanathan
Douglas C. Rees
T. M. Rice
David C. Rubie
Erkki Ruoslahti
Gottfried Schatz

Jozef Schell
Ronald H. Schwartz
Terrence J. Sejnowski
Thomas A. Steitz
Michael P. Stryker
Tomoyuki Takahashi
Masatoshi Takeichi
Keiji Tanaka
Robert T. N. Tjian
Yoshinori Tokura
Emil R. Unanue
Geerat J. Vermeij

Bert Vogelstein
Arthur Weiss
Zena Werb
George M. Whitesides
Owen N. Witte
William A. Wulf

COVER

Dorsal view of a day 15.5 transgenic mouse embryo (1 centimeter long) in which the cardiovascular system was visualized by staining for expression of a transgene controlled by the promotor of the smooth muscle-specific gene *SM22 α* . Staining specifically marks arterial smooth muscle cells throughout the developing

vasculature. The molecules controlling heart development are among the topics highlighted in this special issue on cardiovascular medicine. See page 671 and the special section beginning on page 663. [Image: L. Li, B. Mercer, and E. Olson]



Molecular Genetics of Human Blood Pressure Variation 676
R. P. Lifton

Molecular Genetic Insights into Cardiovascular Disease 681
M. T. Keating and M. C. Sanguinetti

Mouse Models of Atherosclerosis 685
J. L. Breslow

Molecular Therapies for Vascular Diseases 689
G. H. Gibbons and V. J. Dzau

REPORTS

NMR Studies of Single-File Diffusion in Unidimensional Channel Zeolites 702
V. Kukla, J. Kornatowski, D. Demuth, I. Girus, H. Pfeifer, L. V. C. Rees, S. Schunk, K. K. Unger, J. Kärger

Photoinduced Magnetization of a Cobalt-Iron Cyanide 704
O. Sato, T. Iyoda, A. Fujishima, K. Hashimoto

Field-Induced Layering of Colloidal Crystals 706
M. Trau, D. A. Saville, I. A. Aksay

Galileo Gravity Results and the Internal Structure of Io 709
J. D. Anderson, W. L. Sjogren, G. Schubert

Juvenile Skeletal Structure and the Reproductive Habits of Dinosaurs 712
N. R. Geist and T. D. Jones

Concentrations of Tropospheric Ozone from 1979 to 1992 over Tropical Pacific South America from TOMS Data 714
Y. Jiang and Y. L. Yung

Direct Measurement of Coupling Between Dendritic Spines and Shafts 716
K. Svoboda, D. W. Tank, W. Denk

Cell Growth Arrest and Induction of Cyclin-Dependent Kinase 719

Inhibitor p21^{WAF1/CIP1} Mediated by STAT1
Y. E. Chin, M. Kitagawa, W.-C. S. Su, Z.-H. You, Y. Iwamoto, X.-Y. Fu

In Vitro Development of Primitive and Definitive Erythrocytes from Different Precursors 722
T. Nakano, H. Kodama, T. Honjo

Homologous Association of Oppositely Imprinted Chromosomal Domains 725
J. M. LaSalle and M. Lalande

Amelioration of Vascular Dysfunctions in Diabetic Rats by an Oral PKC β Inhibitor 728
H. Ishii, M. R. Jirousek, D. Koya, C. Takagi, P. Xia, A. Clermont, S.-E. Bursell, T. S. Kern, L. M. Ballas, W. F. Heath, L. E. Stramm, E. P. Feener, G. L. King

A Mouse Model of Familial Hypertrophic Cardiomyopathy 731
A. A. T. Geisterfer-Lowrance, M. Christe, D. A. Conner, J. S. Ingwall, F. J. Schoen, C. E. Seidman, J. G. Seidman

The Cytolytic P_{2Z} Receptor for Extracellular ATP Identified as a P_{2X} Receptor (P2X₇) 735
A. Surprenant, F. Rassendren, E. Kawashima, R. A. North, G. Buell

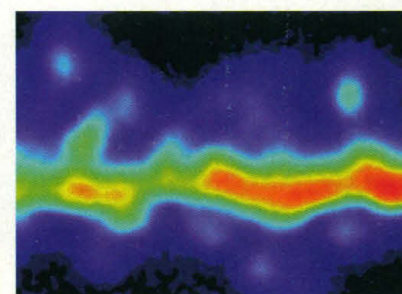
Requirement for BMP Signaling in Interdigital Apoptosis and Scale Formation 738
H. Zou and L. Niswander

Role of Gene Interactions in Hybrid Speciation: Evidence from Ancient and Experimental Hybrids 741
L. H. Rieseberg, B. Sinervo, C. R. Linder, M. C. Ungerer, D. M. Arias

TECHNICAL COMMENTS

Origin of Replication of *Mycoplasma genitalium* 745
J. R. Lobry

Classification of the Arthropod *Fuxianhuia* 746
M. A. Wills; G. D. Edgecombe and L. Ramsköld



716

Dendritic spines revealed

AAAS Board of Directors

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

Marcia C. Linn
Michael J. Novacek
Anna C. Roosevelt
Jean E. Taylor
Nancy S. Wexler

William T. Golden
Treasurer
Richard S. Nicholson
Executive Officer

Sheila Jasanoff
William A. Lester Jr.
Simon A. Levin

■ **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. Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 1996 by the American Association for the Advancement of Science. The title **SCIENCE** is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$102 (\$55 allocated to subscription). Domestic institutional subscription (51 issues): \$250. Foreign postage extra: Mexico, Caribbean (surface mail) \$55; other countries (air assist delivery) \$90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Printed in the U.S.A.

Indicates accompanying feature

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813-1811. **Single copy sales:** \$7.00 per issue prepaid includes surface postage; bulk rates on request. **Authorization to photocopy** material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that \$4.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/93 \$4.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

FastTrack[®] 2.0.

A romp in fresh powder was just the inspiration we needed to isolate the highest yield of pure mRNA.



THIS POWDER is COOL STUFF.

Our latest inspiration is the most economical way to isolate the highest yield of quality mRNA every time. It's the FastTrack[®] 2.0 mRNA Isolation Kit from Invitrogen. The FastTrack[®] 2.0 Kit combines pre-measured oligo(dT) cellulose powder with a gentle, direct mRNA isolation methodology. Tests prove that no bead or magnet produces higher yields of quality mRNA than the oligo(dT) cellulose powder in the FastTrack[®] 2.0 Kit.

DON'T GET STUCK with MAGNETS.

Side-by-side tests (fig. 1) show that FastTrack[®] 2.0 yields 2-3 times more mRNA per isolation than a magnetic bead kit costing more than twice as much. The FastTrack[®] Kit 2.0 includes all of the reagents, tubes, and spin columns you need. All are functionally tested and guaranteed RNase-free. Put the power of powder to work for you. Order the FastTrack[®] 2.0 mRNA Isolation Kit today.

Catalog no. K1593-02 6 reactions
Catalog no. K1593-03 18 reactions

Distributors:

Australia 03 562 6888
Hong Kong 886 2 381 0844
Israel 02 524 447
Italy 02 38 10 31 71
Japan 03 5884 1616
Taiwan 886 2 381 0844
From all other countries, please contact our European headquarters at +31 (0) 5945 15175.

3985 B Sorrento Valley Boulevard
San Diego, California 92121
Fax orders to 619-597-6201

1-800-955-6288

The Gene Expression Folks.

Invitrogen[®]

EUROPEAN HEADQUARTERS:

Invitrogen BV

De Scheip 12, 9351 NV Leek

The Netherlands

Tel: +31 (0) 594 515175

Fax: +31 (0) 594 515312

Email: tech.service@invitrogen.nl

TOLL FREE TELEPHONE NUMBERS:

Austria 0660 8127
Belgium 0800 111 73
Denmark 800 188 67
Finland 990 31 800 5345
France 19 31 800 5345
Germany 0130 8100 43
UK 0800 96 61 93
Switzerland 155 1966
Sweden 020 795 369
Norway 800 113 70
The Netherlands 06 022 8848



Figure 1.

mRNA isolated from 8×10^7 HeLa cells.
Each pellet was resuspended in 50 μ l RNase-free H_2O . 5 μ l was loaded onto a 1% agarose gel.
Lanes 1 and 2: FastTrack[®] 2.0
Lanes 3 and 4: Magnetic Beads

No-passing zone

Traveling down a two-lane road can be slow, but it is even slower when you are not allowed to pass cars ahead of you. Molecules diffusing in channels so confining that they cannot pass each are also expected to be slowed down, but this effect has been difficult to measure. Kukla *et al.* (p. 702) now provide direct nuclear magnetic resonance measurements of molecules diffusing "single file" in zeolite channels. This type of diffusion may also occur in ion channels in cell membranes.

Peaks in pollution

Regional data on long-term trends in tropospheric air pollution for the Southern Hemisphere have been extracted from data from the TOMS satellite. Jiang and Yung (p. 714) compared the TOMS total column ozone values for the high Andes, whose peaks extend through the troposphere, with those of nearby oceanic regions. The derived signals show that tropospheric ozone levels over the tropical Pacific ocean have increased from 1979 to 1992. The likely source of the pollution is biomass burning.

Iron in Io

Io—the odd, sulfur-rich, volcanically active inner satellite of Jupiter—has a metallic core that accounts for as much as 20% of its mass. Anderson *et al.* (p. 709) detected this core using Doppler waves generated by the Galileo orbiter on its closest approach to Io. How this smaller scale version (about the size of the moon) of a differentiated Earth with an iron-rich core evolved and why it is part of the jovian system is still not known.

Heartsick mice

Familial hypertrophic cardiomyopathy (FHC) is a clinically diverse inherited disorder whose effects range from mild shortness of breath to heart failure and sudden death. A subset of FHC is caused by mutations in the β cardiac myosin heavy chain (MHC) gene. Geisterfer-Lowrance *et al.* (p. 731) created a mouse model of FHC by introducing a clinically defined β cardiac MHC mutation into the mouse α cardiac MHC gene. Mice homozygous for the mutation died 7 days after birth. Heterozygotes survived for 1 year and showed age-dependent hemodynamic and histopathologic abnormalities, with males somewhat more affected than females. Preliminary results suggested that exercise capacity was compromised in the heterozygotes. A special section on cardiovascular medicine (pp. 663–693) discusses progress in understanding and treating heart disease.

The layered look

Suspensions of colloidal particles can form ordered crystals, but this process is difficult to control or to confine to two-dimensional layers on a surface. Trau *et al.* (p. 706) have developed an electrohydrodynamic method for growing two- and three-dimensional colloidal crystals on electrode surfaces. The method can be used with particles from the micrometer- to the nanometer-size range and offers a route for assembling nanoparticles into structures.

Imprint by association

Imprinting is a process that distinguishes certain maternal and paternal chromosomal regions that will be differentially expressed during development. LaSalle and Lalande (p. 725) found that the maternal and paternal homologs of human chromosome 15 preferentially associate at a region that has been implicated in imprinting (15q11-q13), and that this association occurs only during the late S phase of the cell cycle. This homologous association was not seen in cells from patients with genetic disorders that result from the lack of a paternal or maternal contribu-

tion to the 15q11-q13 region (Prader-Willi syndrome and Angelman syndrome, respectively). These results suggest that trans-acting elements may be important in imprinting.

Dendritic spine coupling

In order to understand how the dendritic spines are electrically and chemically coupled to the dendritic shaft—a process important in understanding synaptic transmission—Svoboda *et al.* (p. 716) directly measured the diffusion of dextrans with fluorescence imaging techniques. Their findings show that the spines and shafts are chemically but not electrically separate compartments during neuronal transmission.

Broken open

Extracellular adenosine triphosphate (ATP) can cause the lysis of macrophages due to the formation of large membrane pores in the cell's membrane. The identity of the pore—known as the P_{22} receptor—has remained elusive. Surprenant *et al.* (p. 735) describe a bifunctional ATP receptor from rat brain

that, in addition to acting as a traditional ligand-gated ion channel, has the characteristics expected of the P_{22} receptor—the ability to form lytic pores in cells that express the protein.

Both young and old

During evolution, new species can arise from the hybridization of two parental species. Rieseberg *et al.* (p. 741; see the Perspective by Coyne, p. 700) examined the genomic composition of an ancient hybrid sunflower species and three hybrid sunflower lines created in the lab. Although the three experimentally created lines were synthesized by different crossing schemes, they contain similar combinations of genes. Surprisingly, these experimentally created lines resemble very closely the ancient hybrid species.

Chick chick duck

During development of the digits in vertebrates, programmed cell death (apoptosis) causes the loss of interdigital tissue in order to define the digits. Zou and Niswander (p. 738) examined the role of the bone morphoge-



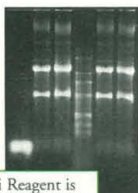
netic protein (BMP) in interdigital apoptosis. The blockage of BMP signal transduction in the developing chick limb by the expression of a dominant negative BMP receptor reduced apoptosis, which resulted in webbed feet as well as a transformation of scales to feathers.



Tri this for size.

Separate RNA, DNA and protein quickly and economically with Tri Reagent™, available only from Sigma in an efficient 25 ml size.

Lab lore has it that the fresher the Tri Reagent™, and the fewer times its container is opened, the better it



Tri Reagent is the method of choice for isolating total RNA.

performs, particularly when working with RNA.

That's why we offer Tri

Reagent in a convenient,

smaller size: a 25 ml bottle

that's ideal for sampling and priced to make sharing unnecessary.

Now you can have your own personal supply of the reagent that isolates RNA, DNA and protein from cells and tissue.

In one hour you'll have pure RNA ready to use in Northern

blots, mRNA isolation, *in vitro* translation, RNase protection assays or PCR.

In two hours, you'll have DNA for PCR, restriction enzyme digestion or Southern blots. And protein for probing in Western blots.

Try Tri Reagent in our exclusive 25 ml size. It's yet another reason why Sigma is the world's leading source of products for RNA and DNA isolation.

To order, call

SIGMA
BIO SCIENCES™

1-800-325-3010 or 314-771-5750, collect. Ask for Tri Reagent, Product Number T-9424.

Tri Reagent™ is a registered trademark of Molecular Research Center, Inc.
The PCR process is covered by patents owned by Hoffmann-La Roche.

Circle No. 51 on Readers' Service Card

1step Bibliographies in Microsoft® Word with the new EndNote® Add-in

Create a bibliography in one step:

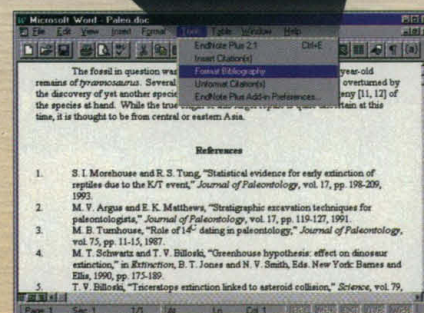
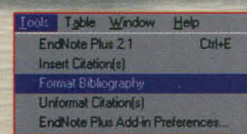
In some bibliographic programs it takes as many as 10 steps to create a bibliography once the in-text citations have been placed in your document. With the new **EndNote Add-in** (included in **EndNote Plus 2.1**), simply choose *Format Bibliography* from Word's **Tools** menu and **EndNote** will create the bibliography instantly!

Keep track of only one document:

When formatting bibliographies in some other bibliographic programs, you have to keep track of up to 3 separate documents. Using the **EndNote Add-in**, you can kiss this confusion goodbye!

Revise the same document as many times as you need:

The **EndNote Add-in** has no problem with last-minute revisions that you've made to your document. You can select another bibliographic style or you can even add or delete citations. Each time you choose *Format Bibliography*, the **EndNote Add-in** will automatically update your citations and bibliography in your document.



To create a bibliography, simply select *Format Bibliography* from Word's **Tools** menu.



Compatible with
Windows 3.1,
Windows NT, Windows 95
and the Mac OS.

All trademarks are property of their respective companies. Mac and the Mac OS logo are trademarks of Apple Computer, Inc. Microsoft Windows and the Windows logo are registered trademarks of Microsoft Corporation.

© Copyright 1996, Niles & Associates, Inc.



Niles & Associates, Inc.

Available for Macintosh and now for Windows!

- Speedy 32-bit processing
- Works under Windows 3.1, Windows 95, Windows NT and Macintosh
- Works with Microsoft Word 6 and 7 (Windows); 5 and 6 (Macintosh)
- A true Word Add-in (not just a collection of Word Basic macros)

There's More ...

- **EndNote** is compatible with WordPerfect and other word processors (no Add-in)
- Includes bibliographic styles for more than 300 journals
- **EndLink** (sold separately) imports from more than 100 online databases and CD-ROMS
- Imports from Reference Manager®, PAPERMAN® and some other bibliographic programs
- If you use any bibliographic program, you qualify for a competitive upgrade price. Call us for details.

"... the most powerful citation manager you can find, short of a personal librarian."
— PC Magazine, December 1995

"Despite its power, EndNote Plus remains surprisingly easy to learn and use."
— Macworld, April 1995

"So the next time you need to prepare a bibliography, don't sweat it—use EndNote Plus 2."
— PC/Computing's Windows 95 Buyer's Guide

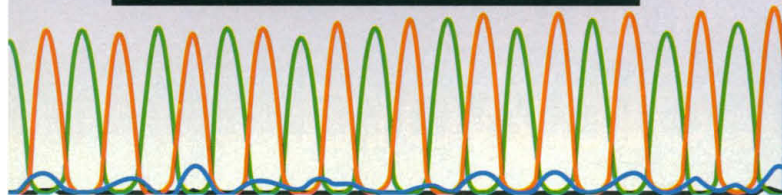
800 Jones Street Berkeley California 94710 USA Phone 800.554.3049 or 510.559.8592 Fax 510.559.8683
E-mail: info@niles.com World Wide Web: <http://www.niles.com>

Australia (+61) 66.58.3674 Germany (+49) (0) 69.970841.11 Japan (+81) 3.3384.8861 Scandinavia (+46) 481.511.23 UK (+44) (0) 1865.784800

Circle No. 23 on Readers' Service Card

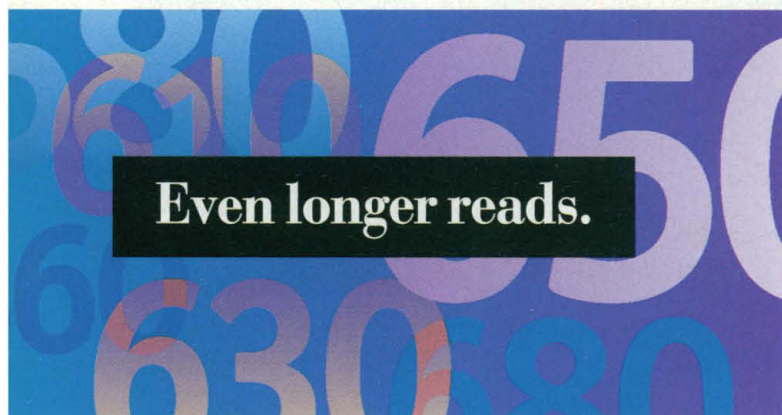
ATATATATATATATATATATATAT

Even stronger.



**The next generation
of ABI PRISM™
dye terminator kits.**

Even longer reads.



New AmpliTaq® FS Enzyme

Even easier.



ABI PRISM™ dye terminator cycle sequencing chemistry revolutionized automated DNA sequencing with unprecedented one-tube convenience and the accuracy of one-lane multicolor detection.

Now, thanks to AmpliTaq® DNA Polymerase, FS—an enzyme engineered specifically for fluorescent sequencing—there's a new generation of dye terminator kits that brings even more to genetic analysis.



Even more robust sequencing. Because the enzyme's low 5'→3' nuclease activity and high dideoxynucleotide incorporation efficiency result in reduced noise and higher signal, even with difficult templates such as AT- and GC-rich DNA.

Even longer reads. Because the nucleotide ratios have been re-optimized for superior performance—often greater than 650 bases with both single- and double-stranded templates.

Even greater convenience. Because smaller amounts of dye-labeled dideoxynucleotides are required, making cleanup of excess dye terminators easier than ever.

Find out how ABI PRISM dye terminator kits can do even more for you. For information on our new generation of cycle sequencing kits with the AmpliTaq FS enzyme, call 1-800-345-5224. Outside the U.S. and Canada, contact your local Perkin-Elmer representative.

PERKIN ELMER

Europe Langen, Germany Tel: 49 6103 708 301 Fax: 49 6103 708 310

Japan Tokyo, Japan Tel: (0473) 80-8381 Fax: (0473) 80-8505

Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223

Australia Melbourne, Australia Tel: (03) 9212-8585 Fax: (03) 9212-8502

Perkin-Elmer PCR reagents are developed and manufactured by Roche Molecular Systems, Inc., Branchburg, New Jersey, U.S.A.



The GeneAmp PCR process is covered by the U.S. patents owned by Hoffmann-La Roche, Inc. and F.Hoffmann-La Roche Ltd. AmpliTaq is a registered trademark of Roche Molecular Systems, Inc. Perkin-Elmer is a registered trademark and ABI PRISM and design are trademarks of The Perkin-Elmer Corporation.

Circle No. 58 on Readers' Service Card

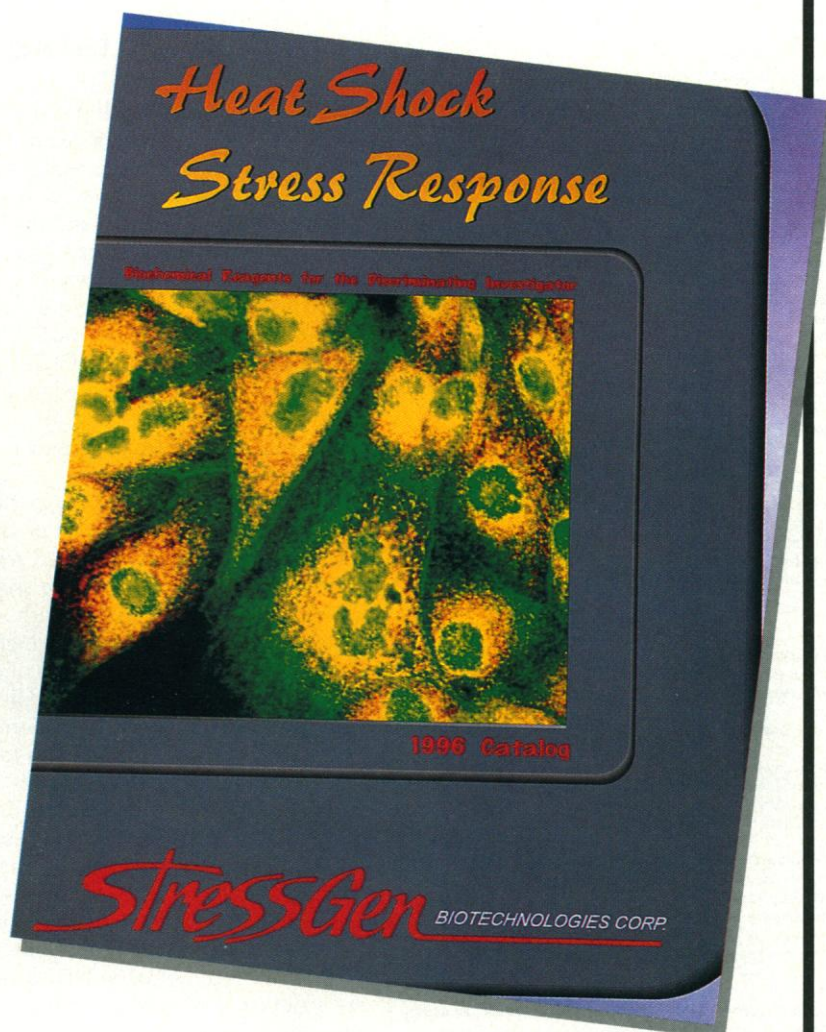
GET STRESSED!

Get your antibodies, proteins, and other research tools from **StressGen** – the stress response experts.

Thyroid Hormone Receptor
Full Length HSP cDNA's
Ubiquitin ■ HSF1
Crystallins
GroES
GrpE ■ DnaJ
TCP-1
Hsp104
Dehydrin
Calreticulin
Grp58(Erp61)
Colligin(Hsp47)
Hsp56(p59)
Synaptotagmin
Heat Shock RNA extracts

NEW
for
1996

We have many other products too! Call the stress response experts for a free catalogue.



(800) 661-4978 (US ONLY)
(604) 744-2811 (604) 744-2877 (FAX)

info@stressgen.com <http://www.stressgen.com/stressgen>

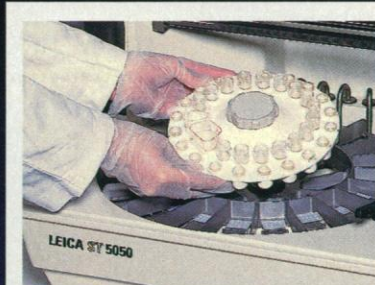
StressGen BIOTECHNOLOGIES CORP.

120 - 4243 Glanford Ave., Victoria, BC, Canada V8Z 4B9

AUSTRALIA BIOCLONE Australia Pty. Ltd +61 (2) 517 1966, AUSTRIA SZABO +43 (1) 489 39 610, BELGIUM SANBIO BV Biological Products +31 (41) 325 1115, CHINA Health Care Products Ltd +852 (0) 2563-5193, COLUMBIA Respresentaciones Biotecnologicas +57 (1) 222-3232, CZECH REPUBLIC Chemos Cz +42 (2) 701-793, DENMARK AMS Biotechnology (Sweden) Ltd +46 (8) 630 02 32, EGYPT Cairo Chemical Company +20 (2) 348-4409, FRANCE TEBU +33 (1) 348462-52, GERMANY BIOMOL Feinchemikalien GmbH +49 (40) 853-2600, GREECE FARMALEX S.A. +30 (001) 6445 612, HONG KONG Onwon Trading +852 (0) 2757-7569, HUNGARY LKB Kereskedelmi Es Szerviz Kft +36 (01) 175-7584, ISRAEL ENCO Scientific Services +972 (3) 934-9922, ITALY SPACE +39 (02) 257 5377, ITALY Diagnostic Brokers Associated +39 (02) 2692 2300, JAPAN FUNAKOSHI Co. Ltd +81 (03) 5684-1622, KOREA KORAM Biotech. Corp. +82 (02) 556-0311, KOREA Essence International Corp. +82 (02) 577-5383, LUXEMBOURG SANBIO BV Biological Products +31 (41) 325 1115, MALAYSIA Kuberan Enterprise +60 (3) 442-6306, NETHERLANDS SANBIO BV Biological Products +31 (41) 325 1115, SPAIN AMS Biotechnology (Spain) Ltd +34 (91) 554-5403, SWEDEN AMS Biotechnology (Sweden) Ltd +46 (8) 630 02 32, SWITZERLAND AMS Biotechnology (Switz.) Ltd +41 (91) 505 522, TAIWAN PROtech Technology Co.Ltd +886 (2) 381 0844, TAIWAN FENG JIH Biomedical & Instruments Co. Lt +886 (2) 647 8855, TAIWAN Cashmere Scientific Co +886 (2) 821 3004, UNITED KINGDOM BIOQUOTE LTD +44 (1904) 431-402

LEICA ST 5050

Excellence in immunostaining



The new automated immunostainer LEICA ST 5050 represents a major advance in immunostaining based on the proven Jung HistoStainer Ig and offers a maximum of quality and flexibility.

Sophisticated software control provides an excellent user interface for the LEICA ST 5050, giving unsurpassed versatility which can even be enhanced by the remote PC option: multiple programs (up to 10) may be run simultaneously in any combination. The temperature can be controlled from ambient and from 25 °C to 45 °C. The temperature can also be preprogrammed to vary during a run, e.g. when the set program enters a critical point. The rinsing parameters of the slides can be programmed, thus adjusting the stringency to the staining method applied. As an "open system" the LEICA ST 5050 accommodates reagents from any supplier. Quality and consistently reproducible results are assumed through design, technology and easy operation.

The new LEICA ST 5050 is the ideal economic, compact unit for routine research and processing – a new standard of excellence in immunostaining.

We shall be glad to provide you with further information if requested.



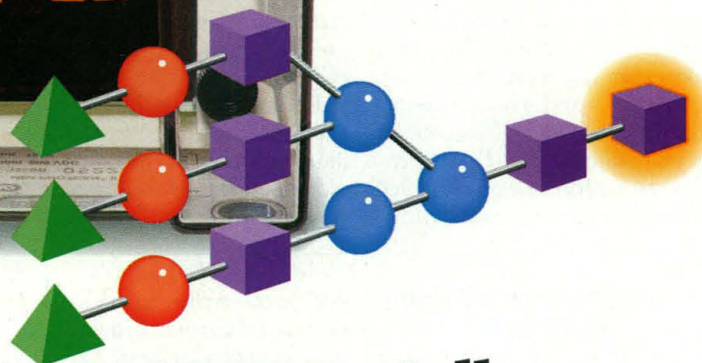
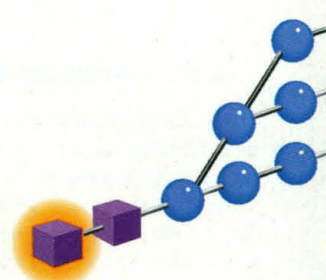
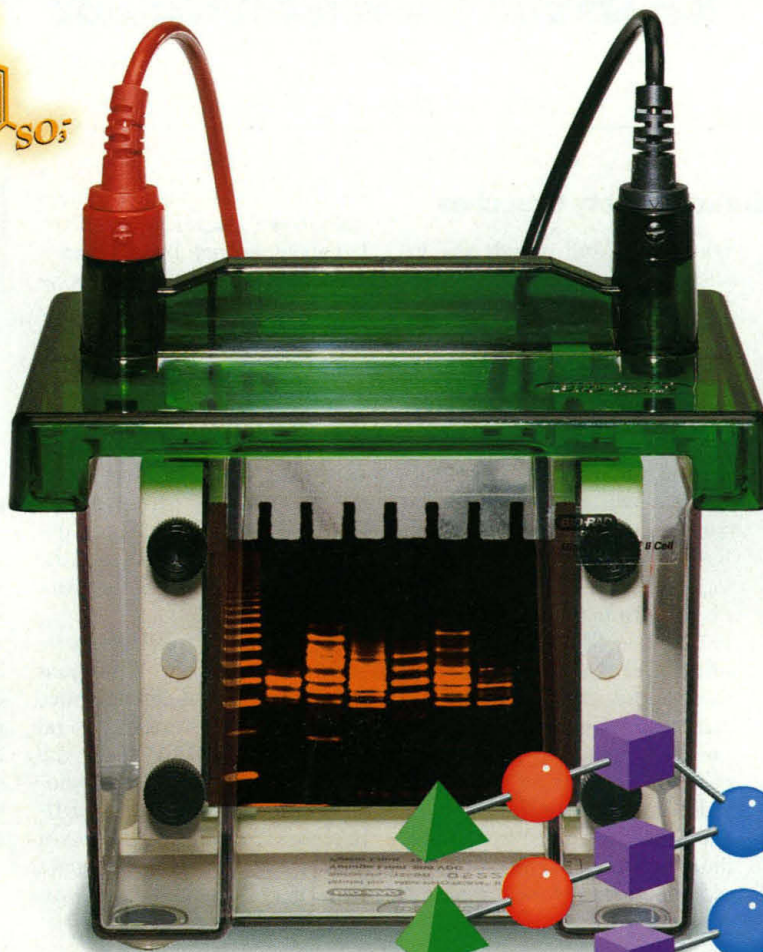
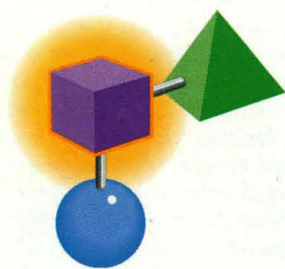
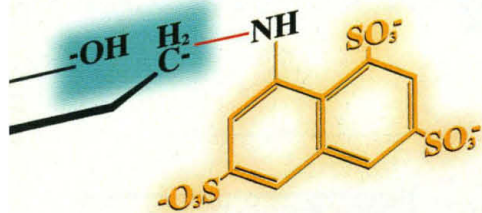
Circle No. 10 on Readers' Service Card

Leica Instruments GmbH
P.O. Box 1120
D- 69226 Nussloch, Germany
0 62 24/143-0 FAX 0 62 24/143 200

Leica Inc.
111 Deer Lake Road
Deerfield, Illinois 60015
800/248-0123 FAX 847/405-0147

Leica Canada Inc.
513 McNicoll Avenue
Willowdale, Ontario M2H 2C9
416/497-2460 FAX 416/497-2053

Leica



Your Mini-PROTEAN® II Cell can separate *more* than just proteins

Answering fundamental questions about the structure of carbohydrates and glycoproteins just got easier. With Bio-Rad's new Glyco Analysis Kits, you can capture important information about glycoproteins using simple and familiar electrophoresis techniques and the Mini-PROTEAN II Cell. *Confirm glycosylation. Separate the oligosaccharides*

**Introducing a simple alternative for
glycoprotein and carbohydrate analysis!**

from the protein for further study. Characterize and sequence. And the new Glyco Doc Imager will assist you in documentation and quantification. To find out more about this simple alternative for glycoprotein analysis, call 1-800-4BIORAD, or contact your local sales representative.



ISO 9001 Registered

BIO-RAD

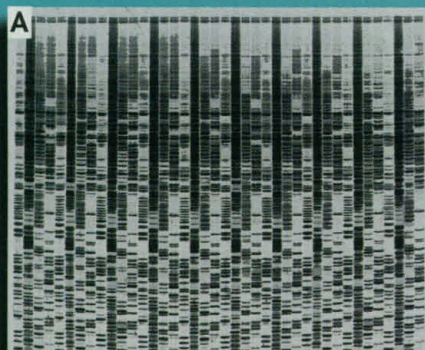
**Bio-Rad
Laboratories**

Life Science Group

U.S. (800) 4BIORAD California (510) 741-1000 Australia 02-9914-2800 Austria (1)-977 89 01 Belgium 09-385 55 11 Canada (905) 712-2771 China (01) 2046622 Denmark 39 17 9947
Finland 90 804 2200 France (1) 49 60 68 34 Germany 089 31884-0 Hong Kong 7893300 India 91-11-461-0103 Italy 02-21609 1 Japan 03-5811-6270 The Netherlands 0318-540666
New Zealand 09-443 3099 Singapore (65) 272-9877 Spain (91) 661 70 85 Sweden 46 (0) 8-735 83 00 Switzerland 01-809 55 55 United Kingdom 0800 181134 SIG 020996

Circle No. 31 on Readers' Service Card

genomylR™ DNA Sequencer for DNA Sequencing & Differential Display

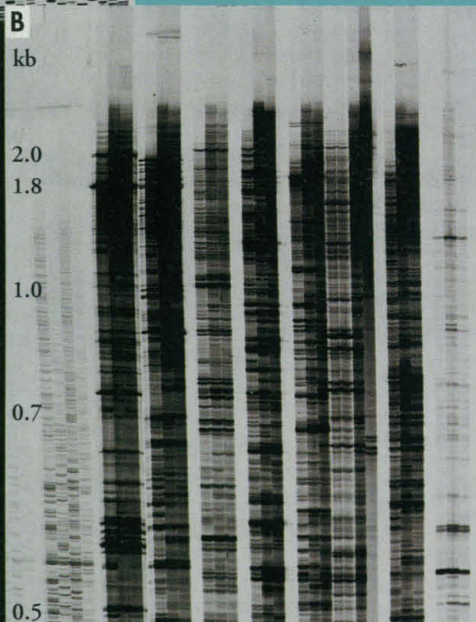


Unsurpassed resolving power and read length

Programmable, microprocessor control provides independent voltage and temperature settings for unrivaled resolving power.

Advanced "air-impingement" temperature control

Proprietary technology maintains a uniform temperature over both sides of a 62 x 33 cm gel for complete temperature control during electrophoresis.



DNA Sequencing

Panel A

Upgrade of conventional manual sequencing

A technically advanced, yet affordable standardized method for minimizing effort and maximizing throughput in dedicated manual sequencing labs.

Adjunct to automated sequencing

Prevents data loss and assures full-length reads by supplementing automated systems when sequencing difficult templates, prescreening clones or closing gaps.

The tool of choice for Molecular Systematics

Achieve dramatically improved throughput and maximum data per gel for rapid completion of phylogenetic projects. Long-read autorads are ideal for archival data storage.

Differential Display

Panel B

Resolution

Dramatically enhanced resolution of all cDNA fragments assures complete spatial separation of all bands for accurate pattern determination.

Read length

The only electrophoresis system capable of resolving cDNA fragments as large as 2-3 kb. Assures maximum coding information for efficient gene identification.

Registration

Completely even cDNA fragment migration across entire gel assures accurate pattern determination across entire width of gel.

Recovery

Improved resolution allows accurate, quantitative recovery of unique cDNA fragments from gel for reamplification and sequencing.

Panel A: pTTQ plasmid template samples run on genomylR DNA Sequencer (2 hr, 100 W, 3000 V, 50°C, 6% HR-1000™ denaturing gel).

Panel B: Large fragment DD-PCR samples run on genomylR DNA Sequencer (18 hr, 100 W, 703 V, 40°C, 6% HR-1000 denaturing gel). Lanes represent total RNA prepared from untreated and treated human cell line cultures. DD-PCR carried out with GenHunter RNAimage™ Kit. Data provided by Dr. Karen Lowe (GenomylR Corporation).

Call today to discuss your research applications with one of our scientists.

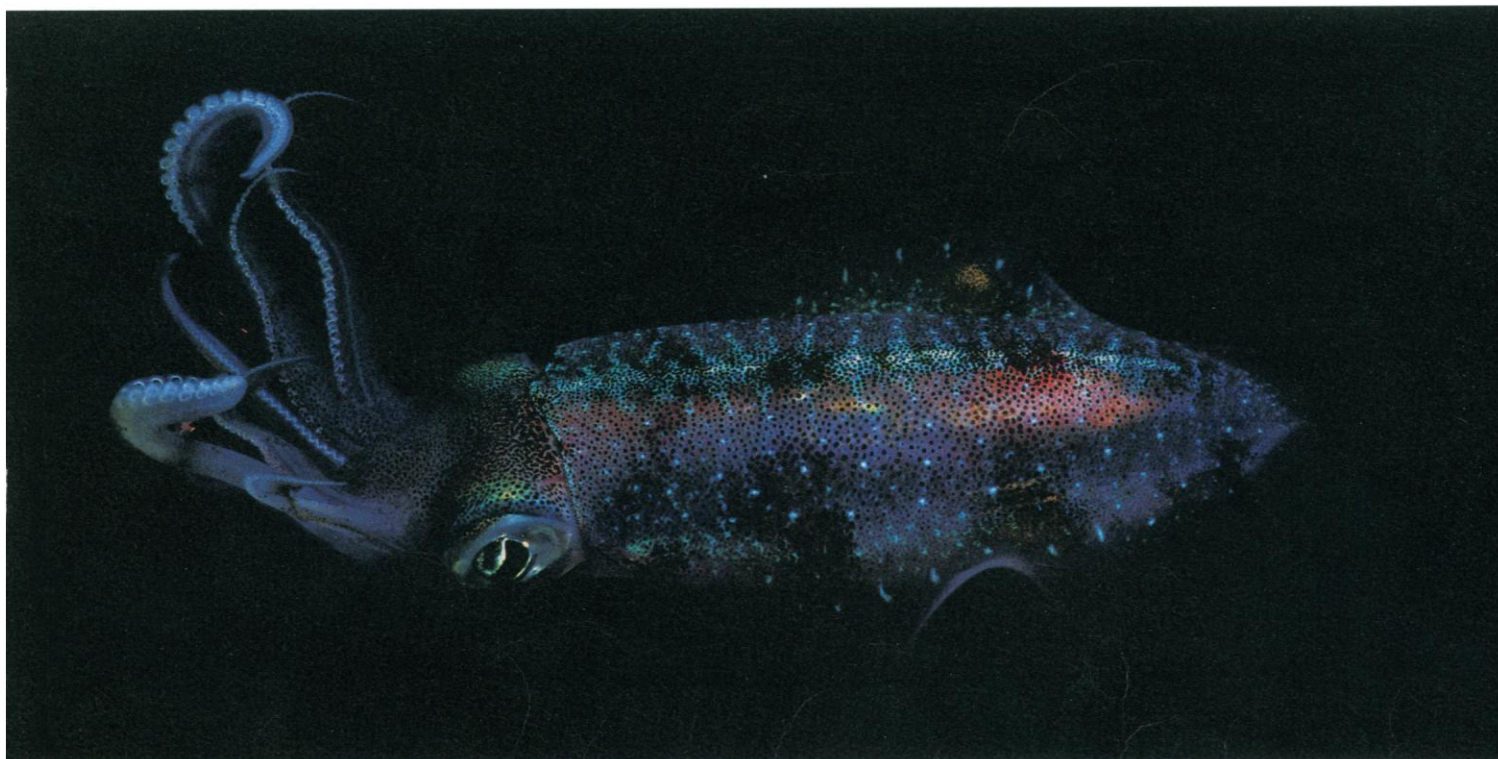


353 Hatch Drive, Foster City, CA 94404

For additional information regarding the genomylR Sequencing System and our complete line of LR-OPTIMIZED products, please call us at **1-800-9GENOME.**

genomylR@aol.com

Circle No. 59 on Readers' Service Card



Flow-through transport.

Flashing an array of brilliant color patterns on its trunk, the Caribbean reef squid propels itself forward by forcing water through its body. When alarmed, it is capable of greatly increasing the flow rate to quickly accelerate away from would-be predators.

POROS® Perfusion Chromatography® columns provide an advancement in high pressure liquid chromatography by greatly accelerating the process of protein and peptide

separation. The unique flow-through particles overcome the limitations of conventional HPLC. So high-resolution separations are performed in just a few minutes, compared to current methods that can take an hour or more.

To learn how to increase the speed and quality of biomolecule separations in your laboratory, please complete and return the attached business reply card. We'll send you a brochure on Boehringer Mannheim POROS Perfusion Chromatography columns.



High-Resolution. In Minutes.



Biochemicals

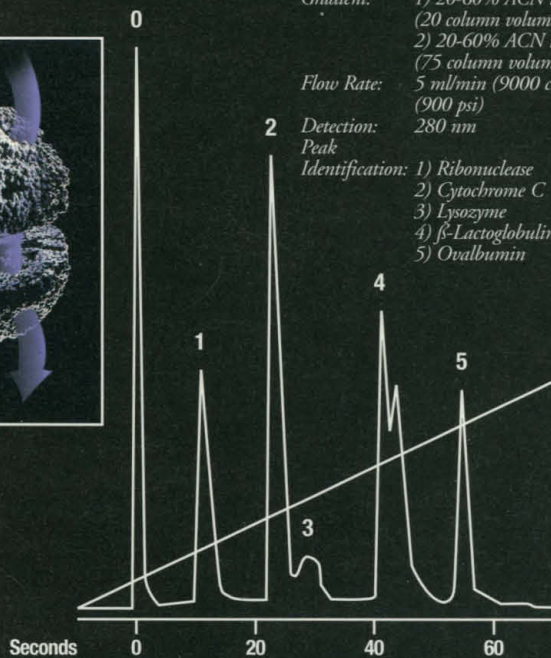
Rapid separation without sacrifice.

POROS® Perfusion Chromatography® provides the first major breakthrough in liquid chromatography in more than 30 years. This revolutionary technology enables biomolecule separation to be performed 10 to 100 times faster than on conventional chromatography media — without sacrificing resolution or capacity!

Constructed from submicron-sized particle clusters, POROS column packing beads contain two types of pores that enhance biomolecule transport into and out of the particles. Large pores (through pores) allow liquid flow throughout the particle. Smaller pores (diffusive pores) create binding sites with short diffusion pathlengths. In contrast to conventional HPLC column packing beads, this unique combination of pores unlocks the interior of the POROS particle to contribute to the high speed separation process — without the trade-offs of lowered resolution and capacity.



60 second/75 column volume gradient



Data courtesy of PerSeptive Biosystems, Inc.

Column: POROS R2/M
(2.1 mmID/30 mmL)
(0.1 ml column volume)
Eluent: 0.1% TFA/ACN
Gradient: 1) 20-60% ACN in 0.4 min
(20 column volumes)
2) 20-60% ACN in 1.5 min
(75 column volumes)
Flow Rate: 5 ml/min (9000 cm/hr)
(900 psi)
Detection: 280 nm
Peak Identification: 1) Ribonuclease
2) Cytochrome C
3) Lysozyme
4) β -Lactoglobulin
5) Ovalbumin

Attain high purity preparations in minutes with POROS columns and media. And because your biomolecules spend less time on the column, you can enhance the recovery of biological activity.

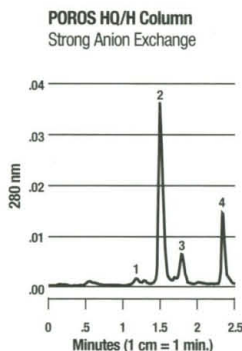
POROS columns and media from Boehringer Mannheim are available in a broad range of selectivities applicable to most major modes of liquid chromatography. So regardless of the technique you are using, POROS

columns provide a fast solution for preparative and analytical separations. And because POROS columns operate on all conventional HPLC, FPLC®, and low-pressure systems, you can accelerate your separations today without upgrading your existing equipment.

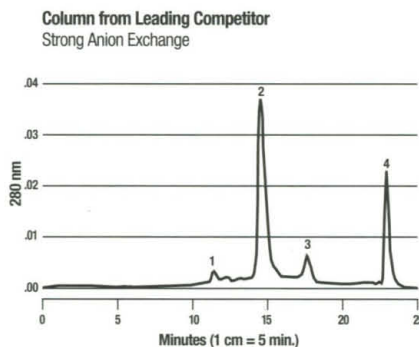
POROS MEDIA SELECTIVITY

- ION EXCHANGE
 - Strong and Weak Anion
 - Strong and Weak Cation
- AFFINITY
 - Heparin, Protein A, Protein G
 - Activated Affinity Matrices
- HYDROPHOBIC INTERACTION (HIC)
- REVERSED-PHASE

To receive more information on Boehringer Mannheim POROS Perfusion Chromatography columns, please complete and return the attached business reply card. For faster response, contact your local Boehringer Mannheim representative or visit us on the Internet at <http://biochem.boehringer.com>. Because in the laboratory, few commodities are as valuable as time.



Column: POROS HQ/H column
4.6 x 50 mm
Sample Volume: 100 μ l
Flow Rate: 3060 cm/hr (8.5 ml/min)
Buffer A: 20 mM Tris/bis-Tris propane, pH 7.0
Buffer B: 20 mM Tris/bis-Tris propane, 500 mM NaCl, pH 7.0
Gradient: 0-40% B in 11 column volumes, 40-100% B in 4 column volumes
Peak Identification: 1) Transferrin
2) Anti-TSH
3) Anti-IgE
4) β -Galactosidase



Column: Competitor 5 mm x 50 mm
Sample Volume: 100 μ l
Flow Rate: 306 cm/hr (1 ml/min)
Buffer A: 20 mM Tris/bis-Tris propane, pH 7.0
Buffer B: 20 mM Tris/bis-Tris propane, 500 mM NaCl, pH 7.0
Gradient: 0-40% B in 11 column volumes, 40-100% B in 4 column volumes
Peak Identification: 1) Transferrin
2) Anti-TSH
3) Anti-IgE
4) β -Galactosidase

Data generated by Boehringer Mannheim.

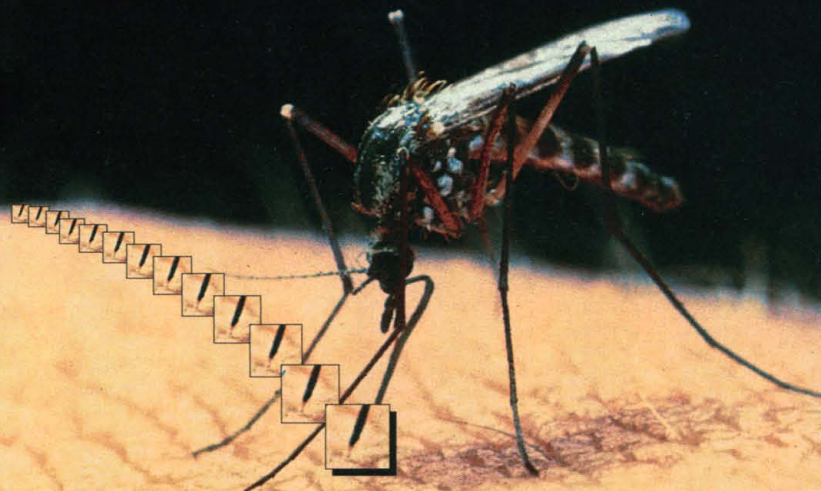
High-Resolution. In Minutes.

FPLC is a registered trademark of Pharmacia Biotech AB. POROS and Perfusion Chromatography are registered trademarks of PerSeptive Biosystems, Inc. ©1996 Boehringer Mannheim



Biochemicals

Whatever your target...



Be sure to get the native DNA!

Proteinase K–DNA grade

... ready-to-use solution of the highest purity available ... free of contaminating nucleic acids ... packed under laminar flow in an aerosol free environment ... the next generation of quality!

For further information, please contact us:

Merck KGaA, Darmstadt/Germany
Phone (+49) 61 51-72 75 93
Fax: (+49) 61 51-72 68 59

Circle No. 32 on Readers' Service Card

Buy Hours. By Ours.

Intracellular cytokine detection in hours, not days.

Introducing the FASTIMMUNE™ Cytokine System from Becton Dickinson.

The FASTIMMUNE Cytokine* System is a powerful new tool for studying the interrelationships of the human cytokine network. Unlike bulk ELISA assays, this easy-to-use reagent system provides comprehensive cell-by-cell flow cytometric results from whole blood in only a few hours. High sensitivity and low background are ensured by stringent antibody selection, proprietary permeabilization chemistry, and proven conjugation technology. For more information, please contact Becton Dickinson Immunocytometry Systems today at (800) 223-8226.

Circle No. 41 on Readers' Service Card

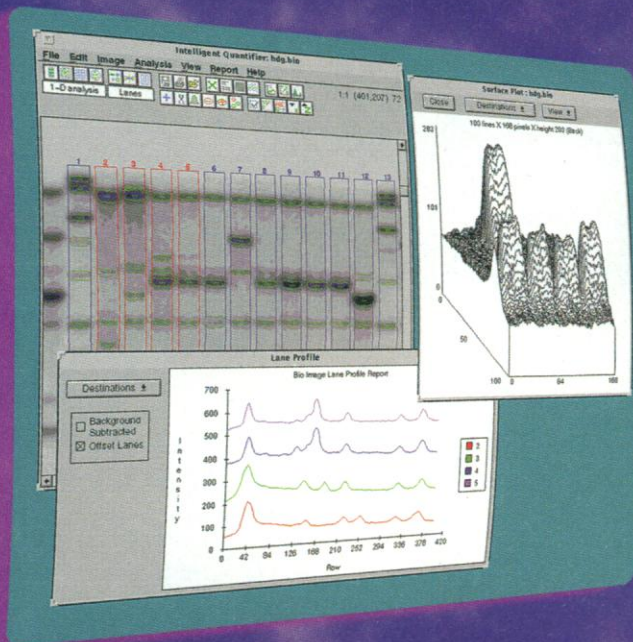
**For research use only. Not for use in diagnostic procedures.*

**BECTON
DICKINSON**

FASTIMMUNE is a trademark of Becton Dickinson and Company.
©1996 Becton Dickinson and Company.



Electrophorealfast



**Redefining how you think
about electrophoresis image analysis**

Fast is a relative term. Take image analysis. Some people are happy to get their sample analyzed in a day.

Doing it in minutes is unthinkable.

Unless you're working with Bio Image®.

Bio Image has been the leader in electrophoresis image analysis since 1983. If you analyze 1-D or 2-D samples, DNA sequences, high-density grids, or colonies, we can help you do it faster.

How? By accepting images from virtually any imaging device—including our own. By letting you identify, quantify and size samples in seconds. And by providing software on PCs, Power Macs and Suns—with direct links to spreadsheet and database programs.

Image analysis doesn't get any faster than Bio Image. But don't take our word for it. Find out for yourself.

Call us to qualify for a free demo disk or sample analysis.

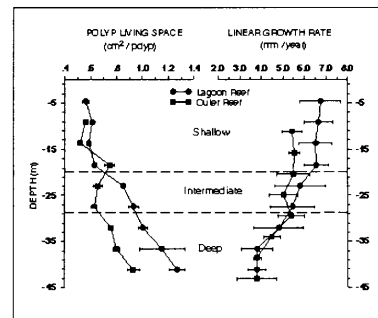
Call 1-800-BIO-IMAGE (1-313-930-9900 outside the U.S.) or e-mail info@bioimage.com

Bio Image is a registered trademark of B.I. Systems Corporation



Bio Image®

How To Improve Your Image.



Improve your image by illustrating your scientific data with publication-quality graphs. Whether for journals, grants, or to demonstrate the results of your analysis, you'll find the easy-to-use SigmaPlot® scientific software the tool for you.

Powerful graphing flexibility

This powerful, award-winning program gives you stunning customized graphs that will show off your work in ways that plain text and graphs from spreadsheets simply cannot touch. With SigmaPlot, you have the flexibility to create graphs that communicate your scientific studies clearly and concisely. And with amazing ease.

Experience from the experienced

Thousands of your colleagues have already seen how SigmaPlot can help them create compelling graphs—like the one shown here. Researchers. Technicians. Professors. Scientists. Engineers. Over 100,000 of them! They've all come to rely on SigmaPlot for their publication-quality graphs.

To find out how you, too, can improve your image and illustrate your research data using SigmaPlot, call Jandel Scientific Software today. Ask for your copy of our FREE full-color brochure.

**90-DAY
MONEY-BACK
GUARANTEE!**

1-800-452-6335

(International calls: 415-453-6700)

New versions for Macintosh® and Windows® 3.1, NT, and 95

Jandel
SCIENTIFIC SOFTWARE

ASCSP056

Circle No. 33 on Readers' Service Card

Circle No. 55 on Readers' Service Card

Save 25%
on BioMax MS
film + screen pack



©ALLSPORT/Mike Powell

For a winning combination, put yourself in the picture

Getting the right image is crucial to achieving the best results. In the field of autoradiography, Amersham™ has long been committed to scientists in this area through the Hyperfilm™ range of films and accessories, backed by comprehensive technical support. Now there is an added dimension - Kodak® autoradiography films supplied by Amersham.

Kodak is recognised as a world leader in film development - from the popular X-Omat® AR general

purpose film to the new high performance BioMax® MR and BioMax MS films that offer unparalleled resolution and sensitivity respectively.

Scientists demand and expect the best from their chosen supplier. Amersham recognises this and is committed to not only satisfying autoradiography needs, but also providing expert support. To get ahead, contact us now to find out about Kodak products from Amersham.



Amersham International plc
Amersham Place, Little Chalfont,
Buckinghamshire, HP7 9NA England.
Tel: 01494 544000
Fax: 01494 542929

For further information
contact your local office.

Australia
Sydney (02) 894-5188

Belgium
Gent (092) 41-52-70

Canada
Oakville (416) 847-1166

Denmark
Birkerød (45) 82-02-22

Far East
Hong Kong (852) 2802-1288

France
Les Ulis (1) 69-1828-00

Germany
Braunschweig (05307) 930-0

Iberica
Madrid (91) 304-42-00

Italy
Milan (02) 508 8220

Japan
Tokyo (03) 38-16-1091

Nederland
's-Hertogenbosch (0736) 41-83-35

Norway
Gjettem (67) 54-63-18

Sweden
Solna (08) 444-71-80

Switzerland
Zürich (01) 3157050

UK Sales
Little Chalfont (0800) 515313

USA Arlington Heights
IL (800) 323-9750

Export Office
Little Chalfont (0) 1494 544100

All goods and services are sold subject to the terms and conditions of sale of the company within the Amersham Group which supplies them. A copy of these terms and conditions is available on request.
™Hyperfilm and Amersham are trademarks of Amersham International plc.
© Kodak, X-Omat and BioMax are trademarks of Eastman Kodak company.
© Amersham International plc 1996. All rights reserved.

Circle No. 30 on Readers' Service Card

MKDK

Amersham LIFE SCIENCE



In Perfect Balance

According to the ancient Chinese philosophy of yin and yang, the universe is composed of opposing but interdependent forces. ■ Interestingly, this philosophy resembles the concept of homeostasis, the natural balance that occurs within living organisms, including the harmony between antagonists and agonists that regulate vital functions. Thus, an important factor in the search for new medicines is the development of compounds that work together with the body's own restorative and regenerative abilities. ■ To lead healthy lives, we must seek balance with nature, with society, and within ourselves. Through pharmaceutical research, we are striving to help people attain this balance.

TAKEDA
Takeda Chemical Industries, Ltd.

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

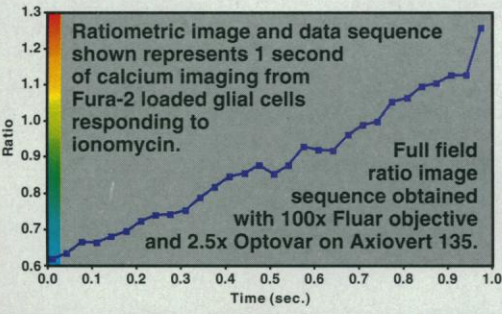
Circle No. 9 on Readers' Service Card

0 sec.

ATTOFLUOR[®] RATIOVISION[®]
 Digital Fluorescence Microscopy

New High-Speed RatioArc[®] Excitor
 For Imaging at 30 Ratios / Second!

SPECIAL OFFER
 For a Limited Time Only!



See What You're Missing in 1 Second.
See What You'll Miss If You Don't Act Soon.

LIMITED TIME OFFER:
 (U.S. and Canada only)

When you order our state-of-the-art fluorescence workstation before June 30, 1996, you'll receive FREE:

- RatioArc system for ultra-high speed imaging and photometry (\$14,000 value) AND our
- HBO 100W lamp assembly (\$4,000 value)

ATTOFLUOR RATIOVISION provides effortless image acquisition, processing, archiving and data file manipulation in an integrated turnkey system.

- Patented vibration-free, solid-state RatioArc excitor changes excitation wavelengths at video rate for full field ratio imaging with high efficiency optical throughput. RatioArc can switch wavelengths to achieve up to 1000 ratios / second!
- Zeiss AXIOVERT or AXIOSKOP with Fluor objectives for exceptional fluorescence transmission.
- RatioVision software in Windows[®]. Duration of high-speed experiments limited only by disk space.
- Highly sensitive, compact intensified CCD camera with digital sensitivity control.
- Ideally suited for kinetic measurements of calcium, pH, cyclic AMP and other ions with simultaneous analysis of multiple dyes.
- New versatility with integrated imaging and photometry.

For immediate information, contact your Zeiss representative, Or call (800) 233-2343; fax (914) 681-7446.

ZEISS

Carl Zeiss, Inc.
 Microscope Division
 One Zeiss Drive
 Thornwood, NY 10594
 E-mail: micro@zeiss.com

SEE WHAT YOU'RE MISSING

1 sec.

Circle No. 38 for literature only.
 Circle No. 39 for literature and demo.

Discover New Effective Drugs For Human Cancer

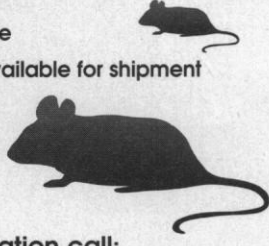
METAMOUSETM



- Evaluates all anti-tumor and anti-metastatic therapeutics
- Replicates human clinical responses including metastasis
- More clinically relevant than subcutaneous or transgenic models
- Same-organ tumor transplantation: fresh patient tumors or established lines
- All major cancer types available
- Contract research or models available for shipment

Wang, X. et al. Matrix metalloproteinase inhibitor BB-94 inhibits human colon tumor growth and spread in a patient like orthotopic model in nude mice. Cancer Res. 54, 4726-28 1994.

Hoffman, R. Orthotopic is orthodox: why orthotopic transplant metastatic models are different from all other models? J. Cellular Biochem. 56, 1-4, 1994.



For more information call:

Tel-(800) 511-2555 • Tel-(619) 654-2555 • Fax-(619) 268-4175

USA/Canada

7917 Ostrow Street **ANTICANCER INCORPORATED** San Diego, CA 92111, USA

Circle No. 21 on Readers' Service Card

MICROMANIPULATORS

STABILITY

MP-185 MICROMANIPULATOR



ULTRASTABLE MOTORIZED MICROMANIPULATION

PRECISION MOVEMENT WITH 25NM STEP SIZE

LOCAL HAND-HELD OR COMPUTER CONTROL

CONTINUOUS OR STEPPED MOTION

SERIAL INTERFACE FOR ROBOTIC APPLICATIONS

SUTTER INSTRUMENT COMPANY

40 LEVERONI COURT, NOVATO, CA 94949

PHONE: 415.883.0128 FAX: 415.883.0572

INFO@SUTTER.COM HTTP://WWW.SUTTER.COM

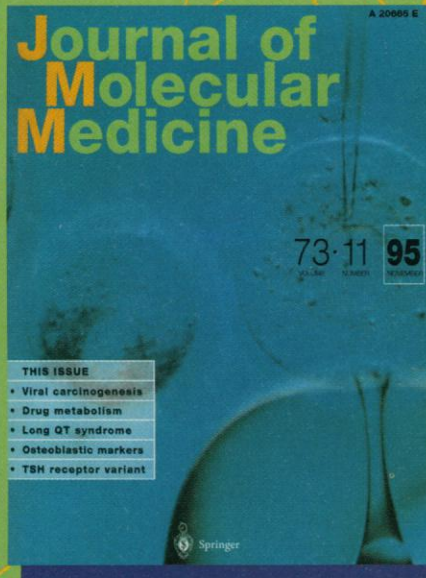
MICROPIPETTE/NEEDLE PULLERS

MICROELECTRODE BEVELERS

OPTICAL FILTERWHEELS

Circle No. 11 on Readers' Service Card

A WORLD OF SCIENCE



Subscription in 1996:
vol. 74, 12 issues; DM 528,-
plus carriage charges



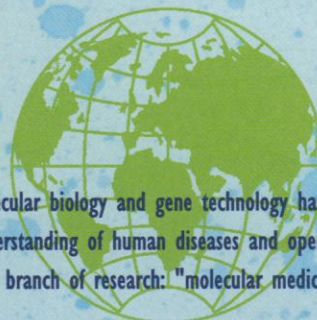
To order:
Springer-Verlag
P.O. Box 31 13 40,
D-10643 Berlin,
Germany

FAX

+49 30 8207 448

email

subscriptions@springer.de



Molecular biology and gene technology have enhanced the understanding of human diseases and opened the door to a new branch of research: "molecular medicine".

The **Journal of Molecular Medicine** provides an international forum for clinical and basic researchers, covering the issues of biology and pathophysiology across all major fields of medicine.

Now in its second year of publication, the **Journal of Molecular Medicine** has already made an impact, proving itself a **MUST** for every scientist engaged in biomedical research.

- Can you afford not to subscribe to the only journal covering all important aspects of molecular medicine?
- Request your **free** sample copy NOW.



Springer

IMCA.3182/MNTZ/SF