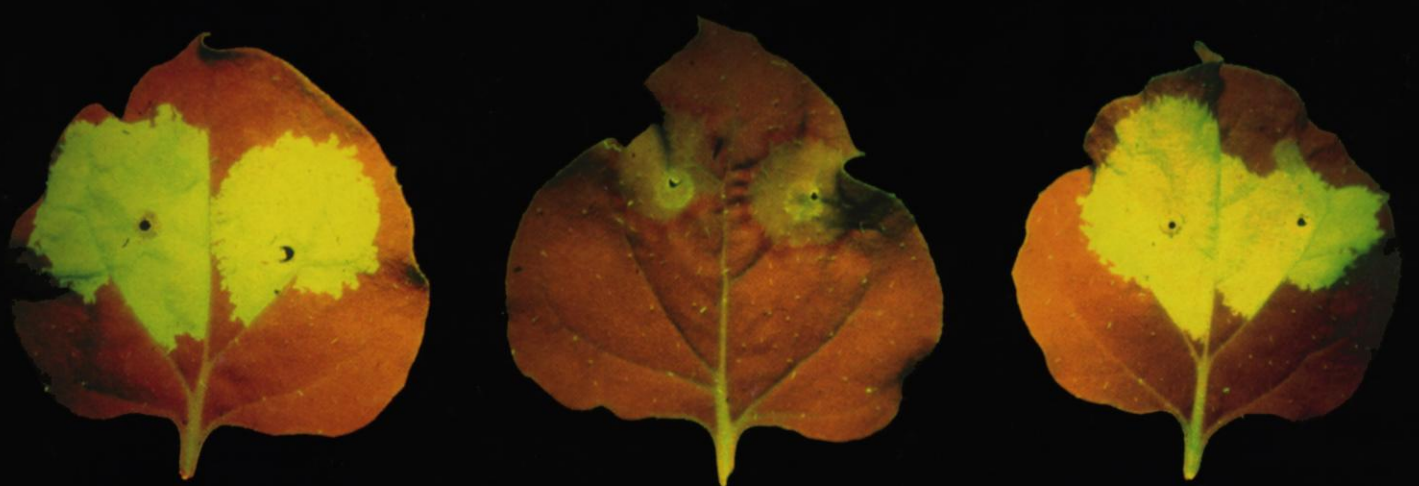
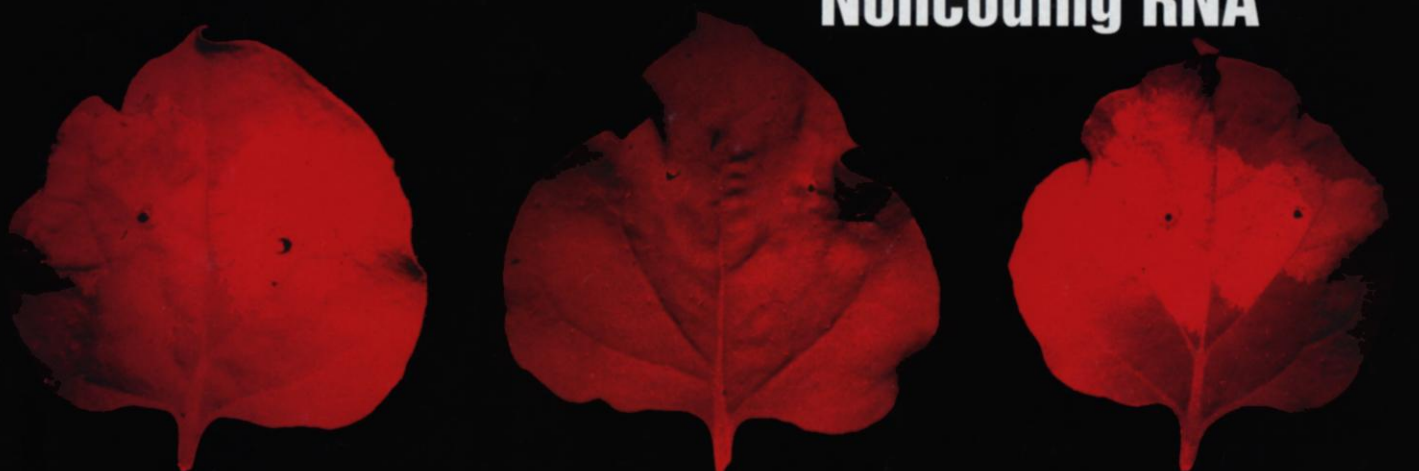
17 May 2002

Science

Vol. 296 · No. 5571
Pages 1189–1352 $9



RNA Silencing and Noncoding RNA



AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

We simply call it the Nikon C1.*

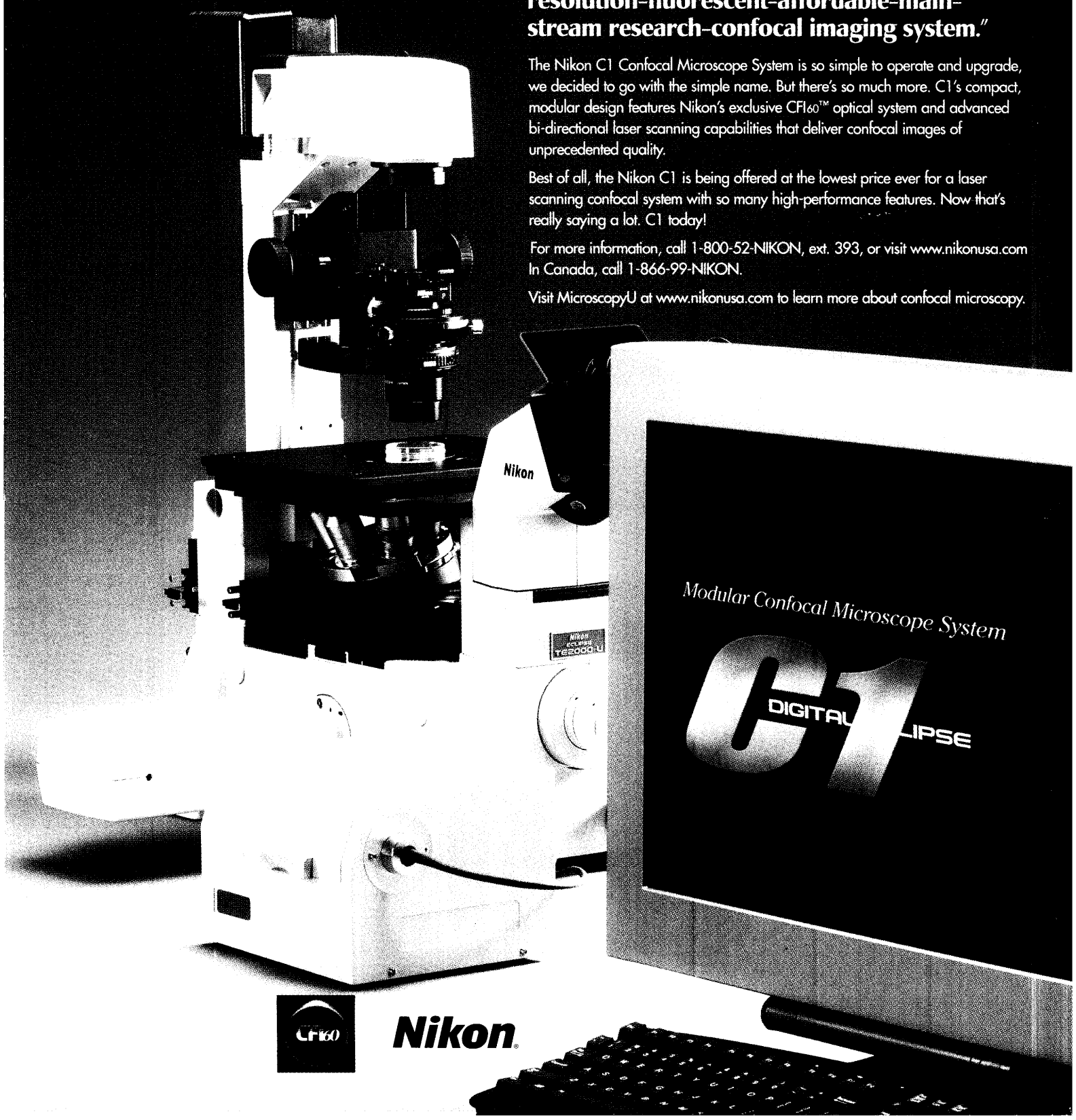
*The alternative was the "Superior 3D-high resolution-fluorescent-affordable-main-stream research-confocal imaging system."

The Nikon C1 Confocal Microscope System is so simple to operate and upgrade, we decided to go with the simple name. But there's so much more. C1's compact, modular design features Nikon's exclusive CFI60™ optical system and advanced bi-directional laser scanning capabilities that deliver confocal images of unprecedented quality.

Best of all, the Nikon C1 is being offered at the lowest price ever for a laser scanning confocal system with so many high-performance features. Now that's really saying a lot. C1 today!

For more information, call 1-800-52-NIKON, ext. 393, or visit www.nikonusa.com
In Canada, call 1-866-99-NIKON.

Visit MicroscopyU at www.nikonusa.com to learn more about confocal microscopy.



High-Fidelity PCR Enzymes

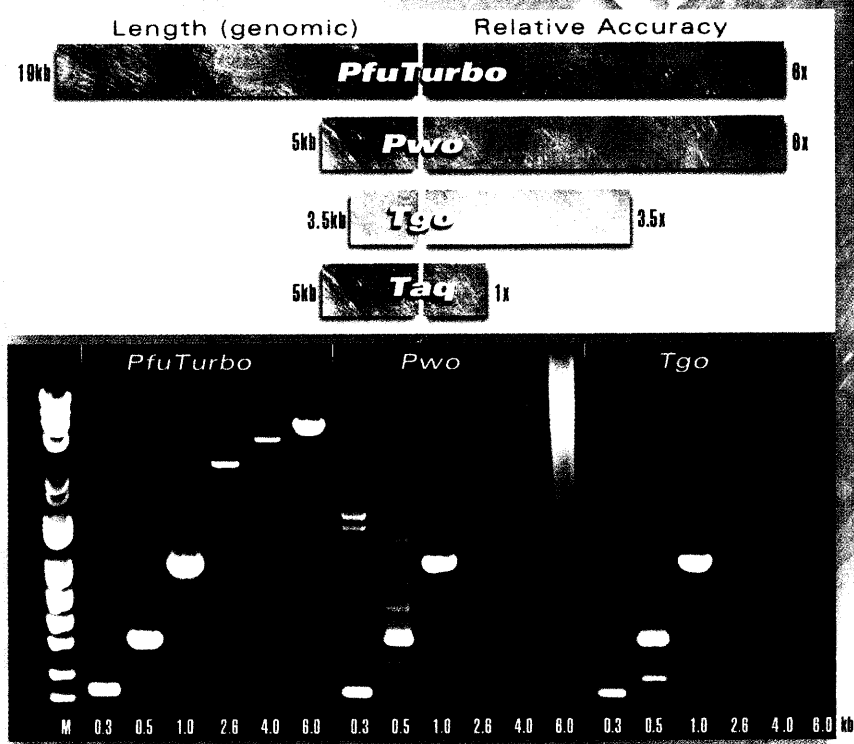
There's more to *PfuTurbo*® than high fidelity.

Robust PCR

PfuTurbo® DNA polymerase* consistently dominates the competition in high fidelity, PCR product yield and length. Competitors have introduced new PCR enzymes claiming high fidelity, but Stratagene's *PfuTurbo* DNA polymerase exhibits the highest fidelity with significantly better overall PCR performance. *PfuTurbo* DNA polymerase is a special formulation of high-fidelity cloned *Pfu* DNA polymerase* plus our patented ArchaeTect™ polymerase enhancing factor*[1], which gives you greater yield over a broader range of target lengths and complexities.

Proven Performance

Pfu DNA polymerase has been helping scientists succeed for years. In fact, over 41% of researchers surveyed use *Pfu* DNA polymerase as their enzyme of choice.‡ Let Stratagene's expertise in high-fidelity PCR work for you. Choose *PfuTurbo* DNA polymerase for your high performance, high-fidelity PCR enzyme.



PfuTurbo® DNA polymerase consistently excels in PCR product yield, length and fidelity in side-by-side comparisons with competitor's DNA polymerases using manufacturer's recommended conditions.

Nothing beats *PfuTurbo*® DNA polymerase

- *Highest fidelity*
- *Greater yields*
- *Longer targets*
- *Hotstart version available*

Stratagene invented high fidelity PCR.

PfuTurbo®
DNA POLYMERASE

PfuTurbo® DNA polymerase	100U	**600250**
PfuTurbo® Hotstart DNA polymerase	100U	**600320**

STRATAGENE USA and CANADA
ORDER: (800) 424-5444 x3
TECHNICAL SERVICES: 800-894-1304

STRATAGENE EUROPE
Belgium, France, Germany, The Netherlands, Switzerland, United Kingdom
European Toll-Free Numbers
ORDER: 00800 7000 7000
TECHNICAL SERVICES: 00800 7400 7400
Austria
0800 312 526

*PfuTurbo DNA polymerase: U.S. Patent Nos. 6,183,997 and 5,948,663 and 5,866,395 and 5,545,552 and patents pending; *Pfu* DNA polymerase: U.S. Patent Nos. 5,948,663, 5,866,395 and 5,545,552 and patents pending; ArchaeTect factor: U.S. Patent Nos. 6,183,997 and patents pending.

1. Hogrefe, H., et al, (2002) *Proc Natl. Acad. Sci. USA* 99, 596-601

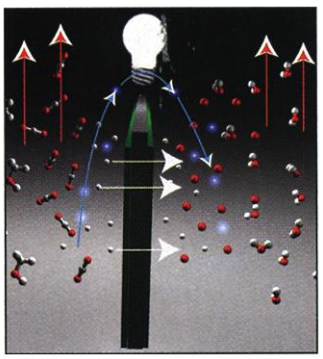
‡ PhorTech International, DNA Amplification, 1999/2000 U.S. MSPPSA Series

www.stratagene.com

STRATAGENE®

Science

Volume 296 17 May 2002 Number 5571

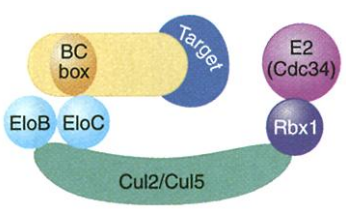


1222
Small fuel cells, big promise

NEWS

1226
Beating the drought

SCIENCE'S COMPASS



1254
E3 ubiquitin ligase complex

1247
The mantle, then and now

RESEARCH

See also **Science's *STKE* on p. 1195 and Report on p. 1319**

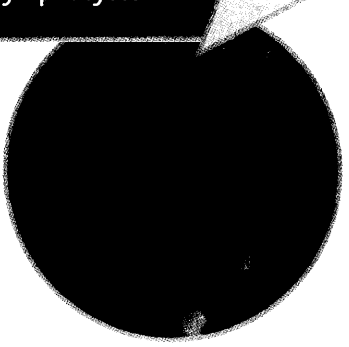
COVER 1259

RNA silencing of green fluorescent protein (GFP) (center) in leaves from *Nicotiana benthamiana* is suppressed by an animal (left; B2 protein of flock house virus) or a plant (right) viral suppressor, leading to enhanced GFP expression (lighter green/yellow areas). The role of RNA silencing in defending both plant and animal genomes from invading foreign nucleic acids, the mechanisms underlying RNA silencing, and noncoding RNAs are considered in this special section. [Image: Shou-Wei Ding]

1305

Tracking the rise of dinosaurs

New on *Science* Express Catching lymphocytes in the act



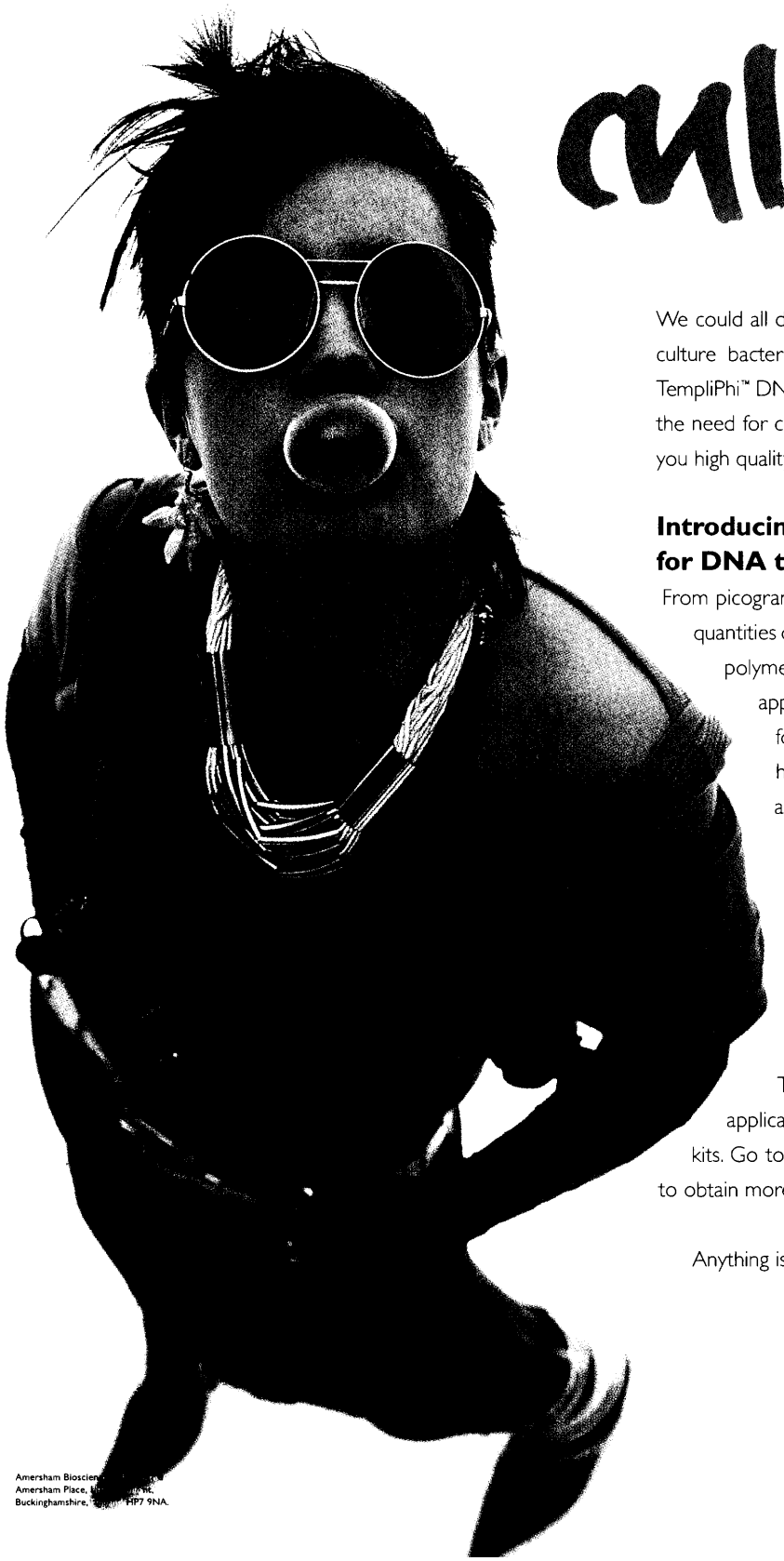
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $120 ($66 allocated to subscription). Domestic institutional subscription (51 issues): $390; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $85. 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.**

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:** $9.00 per issue prepaid includes surface postage; bulk rates on request. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

TEMPLIPHI: THE END OF culture?



We could all do without certain aspects of culture. Like having to culture bacteria and phage for DNA sequencing. Good news: TempliPhi™ DNA Amplification Kits will save you time by eliminating the need for culture growth. They are also simple to use and give you high quality results.

Introducing the easiest solution for DNA template preparation

From picogram starting amounts, TempliPhi generates microgram quantities of template DNA utilizing bacteriophage Phi29 DNA polymerase and rolling circle amplification. This unique approach gives you high quality DNA templates in just four to six hours—with less than 20 minutes of hands-on-time. Uniform quantities of DNA are amplified in all samples, so there's no need to quantify each sample before sequencing—saving you even more time and effort. Amplified DNA can be used directly for sequencing using any chemistry and sequencing platform. Amplified DNA can also be processed by restriction enzymes and stored for future needs. What's more, it makes automation easy.

TempliPhi is easy to use, simple protocols suit all applications and is available in 100, 500 and 10,000 reaction kits. Go to **www.amershambiosciences.com/templiphi** to obtain more information. Put an end to culture.

Anything is possible.

Amersham Biosciences

Amersham Biosciences
Amersham Place,
Buckinghamshire, HP7 9NA.

Scienceonline

www.scienceonline.org

NOW! Daily coverage of science and science policy by *Science*'s news team

sciencenow
www.sciencenow.org

CONTENT HIGHLIGHTS AS OF 17 MAY 2002

science magazine

www.sciencemag.org

SCIENCE EXPRESS

www.sciencexpress.org

A Continuous Source of Bose-Einstein Condensed Atoms
A. P. Chikkatur *et al.*

An optical "scoop" is used to transfer atoms from one condensate to another and thereby provide a continuous reservoir of condensed atoms.

Two-Photon Imaging of Lymphocyte Motility and Antigen Response in Intact Lymph Node M. J. Miller, S. H. Wei, I. Parker, M. D. Cahalan

Two-photon imaging reveals T and B cell behavior in real time within organized lymphoid tissue.

A Heat-Sensitive TRP Channel Expressed in Keratinocytes
A. M. Peier *et al.*

A receptor in the TRP family (TRPV3) that detects warm—but not hot—temperatures is unexpectedly found on skin cells rather than neurons.

TECHNICAL COMMENTS

Spin Polarization of Injected Electrons

LaBella *et al.* (Reports, 25 May 2001, p. 1518) reported that "a large spin-polarized (~92%) current can be injected into GaAs [gallium arsenide] at high temperatures (100 K)," using a "100% spin-polarized" scanning tunneling microscope (STM) tip as the electron source. Egelhoff *et al.* comment that, in relating the measured polarization in the light emitted from the GaAs to the spin polarization of the injected electrons, LaBella *et al.* neglected to corrrect for refraction as the light left the sample; suggest that the group did not measure the spin-relaxation lifetime value of the sample used, which bears on the relationship between the electron spin polarization at recombination and the injected-current polarization; and argue that it is unlikely that the electrons emitted from the STM were indeed 100% spin polarized. Thus, Egelhoff *et al.* conclude, "an electron spin polarization at recombination of 25.2% can be inferred from these experiments," not the 92% cited in the original report. LaBella *et al.*, in their response, agree that their analysis did not adequately account for refraction and acknowledge that they did not measure the spin-relaxation lifetime for the sample studied, although they used a published value for GaAs of a similar hole density and temperature.

The full text of these comments can be seen at
www.sciencemag.org/cgi/content/full/296/5571/1195a

science's next wave

www.nextwave.org

career resources for scientists

CANADA: Medical Science Communication D. Gross

At the end of a grant—and also a job—it was time to go out on a limb and start a medical science communication company.

U.S.: Raising the Visibility of Postdoc Issues J. Marburger

In his keynote address to the Second National Postdoc Network meeting, President Bush's science adviser vigorously affirmed the importance of postdocs to U.S. leadership in S&T.

SINGAPORE: Biocomputing at Singapore's Top R&D Institutes
P. Kolatkar

A U.S.-trained structural biologist and bioinformaticist shares his experiences incorporating biocomputing into the discovery process.

U.K.: Yours Transferredly—Science Guru for a Day P. H. Dee

Taking your science to a class of primary school children can be rewarding—both personally and for your research.

EUROPE: New Cardiovascular Center Puts Heart into Spanish Research S. Bartlett

Aiming to become an international center of excellence, a new research center in Madrid is already planning its Ph.D. and postdoctoral programs.

KNOWLEDGE ENVIRONMENTS

science's sage ke

www.sageke.org

science of aging knowledge environment

Don't Pass the Buck S. Pyne

Institute stakes its claim in age-related research.

Unnerved K. Morgan

Molecule that pumps neurons up also keeps them down.

science's stke

www.stke.org

signal transduction knowledge environment

Perspective: RNA Editing of Neurotransmitter Receptors in the Mammalian Brain C. Schmauss and J. R. Howe

Building diversity from a single transcript.

Perspective: TRAF1—Lord Without a RING J. M. Zapata and J. C. Reed

TRAF1, the only TRAF family member without a RING domain, regulates the signaling capacity of TNFR superfamily members.

ONLINE STAFF

*SCIENCE*NOW EDITORS Martin Enserink, Laura Helmuth, Greg Miller, Erik Stokstad

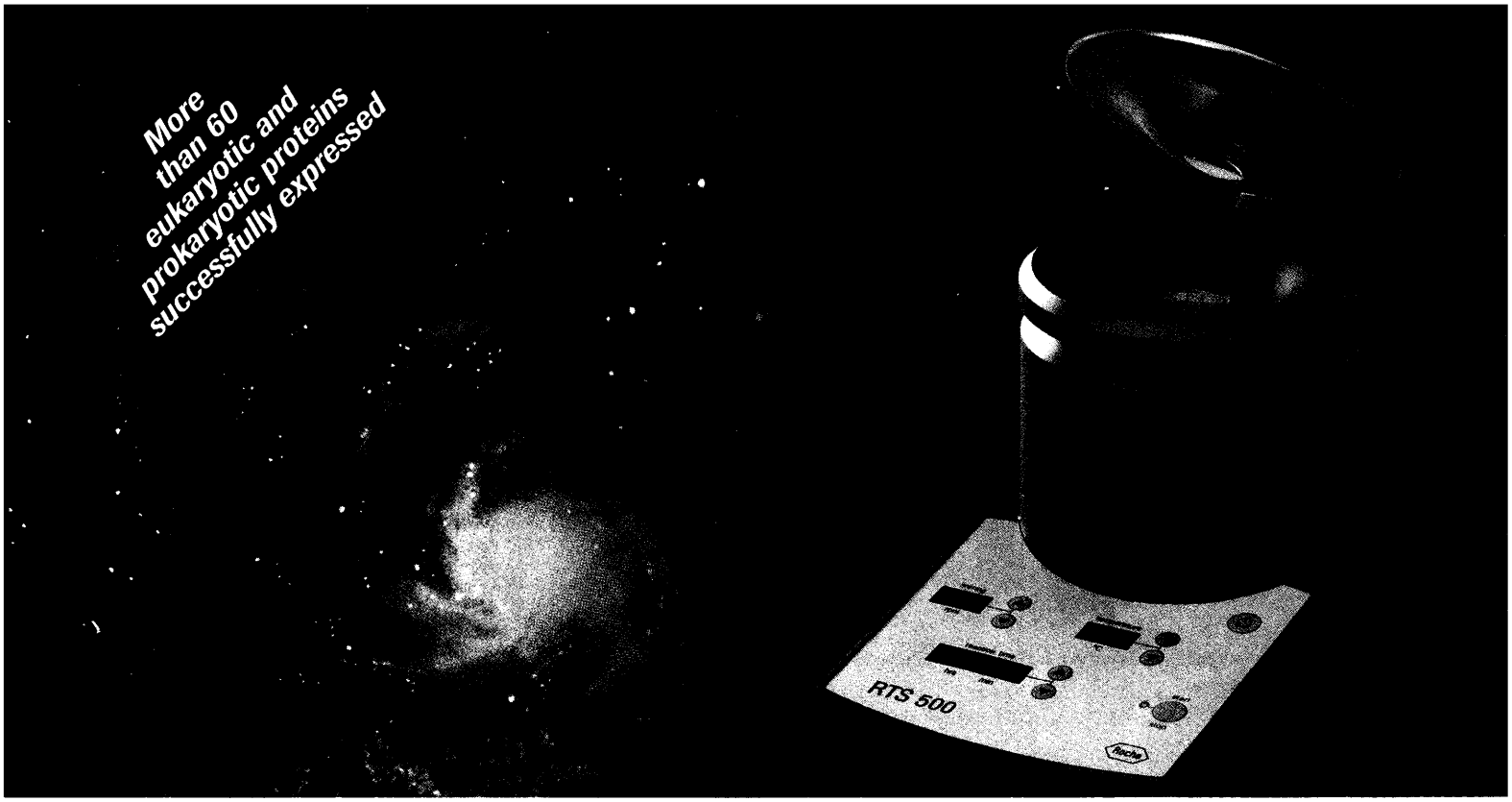
SCIENCE'S NEXT WAVE EDITORIAL: MANAGING EDITOR Crispin Taylor; EDITORS Eick von Ruschkowski (Germany), Kirstie Urquhart (UK), Ric Weibl (US); CONTRIBUTING EDITORS Lesley McKarney (Canada), Robert Metzke (Netherlands), Jennie Wong (Singapore); PROJECT EDITORS Jim Austin, Sibrina Collins, Katie Cottingham, Laure Haak; PRODUCTION ASSOCIATE Lily Han; MARKETING: MARKETING MANAGERS Karen Horting (Global), Hazel Crocker (Europe); PROGRAM DIRECTOR Lisa Kozlowski; MARKETING ASSOCIATE Angela Walker; PROGRAM ASSOCIATES Shajuan Martin, Tammy Minor

AIDSCIENCE SENIOR EDITOR Roberto Fernandez-Larsson; ASSOCIATE EDITOR Paula Werner

SCIENCE'S STKE EDITOR Bryan Ray; MANAGING EDITOR Nancy Gough; ASSOCIATE EDITOR Lisa Chong; PUBLICATIONS ASSISTANT Christopher Kenny

SCIENCE'S SAGE KE EDITORIAL DIRECTOR Kelly LaMarco; SENIOR NEWS EDITOR Evelyn Strauss; ASSOCIATE EDITOR R. John Davenport

ELECTRONIC MEDIA MANAGER Don Hemenway; INTERNET PRODUCTION MANAGER Betsy Harman; ASSISTANT PRODUCTION MANAGER Wendy Stengel; SENIOR PRODUCTION ASSOCIATES Shelia Myers, Lisa Stanford; ASSOCIATES Carla Cathey, Steve Kusek, Louis Williams; LEAD APPLICATIONS DEVELOPER Carl Saffell

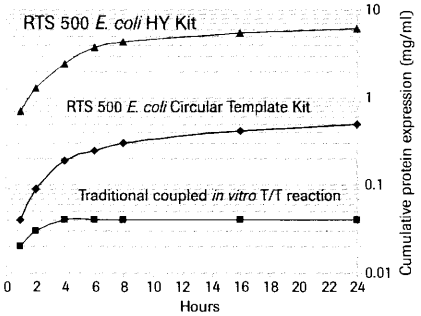


Announcing an End to Limitations in Protein Expression

Express semi-preparative quantities of protein (**500 µg to 5 mg** of protein/ml) using the **Rapid Translation System*** from Roche Applied Science. This advanced *in vitro* transcription/translation technology is exceptionally easy-to-use, and overcomes many limitations of current methods.

Enjoy the simplicity of the RTS 500

Pipet reconstituted reagents and expression vector into the RTS 500 Reaction Device, place the device into the RTS 500 Instrument, then begin monitoring protein expression.



GFP expression (mg/ml, log scale) using the RTS 500 *E. coli* HY Kit and RTS 500 *E. coli* Circular Template Kit, versus a traditional coupled *in vitro* transcription/translation reaction (T/T).

Perform rapid screening with the RTS 100

- Pre-screen vectors and expression conditions with the RTS 100 *E. coli* HY Kit (3-25 µg protein/50 µl high-yield batch reaction)
- Follow with scale-up using the RTS 500 *E. coli* HY Kit
- Reduce cloning efforts by using PCR generated DNA templates.

Express proteins that defy other methods

- Cytotoxic proteins
- Proteins easily degraded *in vivo*
- Multiple proteins in a single reaction
- Proteins that are insoluble and/or inactive in *E. coli*.

Product	Cat. No.	Pack Size
RTS 500 Instrument†	3 064 169	1 instrument
RTS 500 *E. coli* Circular Template Kit†	3 018 008	5 reactions
RTS 100 *E. coli* HY Kit‡	3 186 148	24 reactions
RTS 500 *E. coli* HY Kit†	3 246 817 3 246 949	2 reactions 5 reactions

Schematic of a RTS 500 Reaction Device containing approximately 5 mg/ml of GFP following a 24-hour reaction.

Visit our Rapid Translation System, web site at
www.proteinexpression.com

For more information, visit us on the web at
www.roche-applied-science.com
- for technical questions, select **Technical Inquiries**
- for a representative near you, select **Local Sales & Support**

Rapid Translation System and RTS are trademarks of a member of the Roche Group.

* The Rapid Translation System currently consists of: RTS 500 Instrument (3.75 kg), the RTS 500 *E. coli* HY Kit, the RTS 500 *E. coli* Circular Template Kit, and the RTS 100 *E. coli* HY Kit (dedicated instrument not required).

† The continuous-exchange cell-free (CECF) technology applied in the RTS 500 products is exclusively licensed by a member of the Roche Group from the Institute of Protein Research at the Russian Academy of Sciences, Pushchino, Russia. The purchase price of this product includes a limited, non-exclusive, non-transferable license under U.S. Patent 5,478,730 or its foreign counterparts, to use only this amount of the product to practice a cell-free expression achieving continuous production of a polypeptide in the presence of a semi-permeable barrier and related processes described in said patents solely for the internal research and development activities of the purchaser.

‡ The purchase price of this product includes a limited, non-exclusive, non-transferable license under a patent pending, exclusively licensed to Roche Diagnostics Corporation ("Roche"), to use only this amount of the product to practice a cell-free expression system achieving continuous production of a polypeptide using a new energy regenerating system described in the patent pending solely for the internal research and development activities of the purchaser.

Roche

Roche Diagnostics GmbH
Roche Applied Science
Mannheim, Germany

THIS WEEK IN Science

edited by Phil Szuromi

Six Contentions on Separation

Social structures are organized such that, for example, one can trace a path through local networks from one individual to another in relatively few steps (the so-called six degrees of separation). Watts *et al.* (p. 1302) have modeled this finding based on six insights into the structure of social networks formed by groups of individuals. This model may prove useful in developing efficient network searches, whether for people or for pages on the World Wide Web.

1305 Triassic-Jurassic Impact?

The cause of the extinction of many species at the Triassic-Jurassic boundary is unknown. Olsen *et al.* (p. 1305; see the news story by Kerr) found an enrichment of iridium at the boundary that may be associated with an extraterrestrial bolide impact. An impact may have wiped out many species and left room for the dinosaurs to grow and dominate in the Jurassic.

And in Brevia ...

Using the power of the Very Large Telescope and a new technique, Della Valle and Gilmozzi. (p. 1275) have found four of the most distant novae, which can be used as "standard candles" to measure the shape and expansion of the universe.

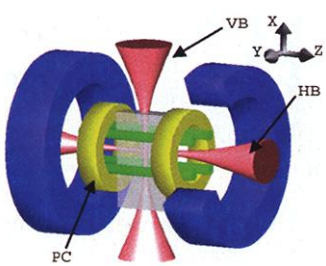
How σ Factor Finds DNA

A major control point of gene expression is the initiation of messenger RNA synthesis. In bacteria, promoter recognition and melting requires a complex that comprises RNA polymerase and the σ factor. Now Murakami *et al.* (p. 1280 and 1285) have determined the crystal structures of *Thermus aquaticus* core RNA polymerase bound to σ and of the holoenzyme complex with a promoter DNA fragment at resolutions of 4.0 and 6.5 angstroms, respectively. The structures give insight into how the holoenzyme recognizes promoters and melts the DNA to give a transcription competent open complex. All of the sequence-specific contacts with the promoter are mediated by the σ subunit, and σ also plays a role in directing the melted DNA template strand into the RNA polymerase active site. The structures provide a basis to design additional experiments that will further improve our understanding of transcription initiation.

Modeling a Heterogeneous Mantle

Seismic velocities increase abruptly at two depths in the mantle, 410 and 660 kilometers (km). These discontinuities are usually attributed to structural transformations of olivine to ringwoodite at 410 km and ringwoodite to perovskite plus magnesiowustite at 660 km. However, not all seismic data are consistent with this interpretation, and two reports detail further studies of mantle structure. Lebedev *et al.* (p. 1300) show that the seismic velocities determined beneath southeast Asia and Australia are definitely correlated with the olivine transformations. In particular, the temperature derivative of the change in pressure of each transformation can be extracted from the seismic data. These results should allow Earth scientists to distinguish anomalous mantle dynamics that may be regional in scale from these global structural transformations. Trampert and van Heijst (p. 1297) have completed a detailed survey of the variations in sound velocities of shear waves that propagate in different directions (called seismic anisotropy) in the transition zone. They find lateral variations in the anisotropy that they relate to heterogeneous structures, such as alignment of grains or alignment of melt pockets.

Shooting Atom Clouds



CREDIT: KHAYKOVICH *ET AL.*

Solitons, waves that propagate without attenuation or broadening, are usually associated with a nonlinear effect that provides the necessary feedback mechanism that maintains the wave disturbance in its original shape. Khaykovich *et al.* (p. 1290) now show that bright solitons can be formed in clouds of atoms in a Bose-Einstein condensate by tuning the interaction between atoms from repulsive to attractive prior to launching the atom bunch into a wave guide. Such a matter-wave packet that does not spread with time should prove useful for atom interferometry and studying atomic collisions.

DNA Damage and Aging

A popular theory postulates that aging is triggered by cellular accumulation of oxidative damage. The causal role of oxidative DNA damage in aging is strongly supported in a study by de Boer *et al.* (p. 1276; see the Perspective by Hasty and Vijg) of mice carrying a mutant version of the DNA helicase gene XPD. This gene causes the rare human disorder trichothiodystrophy (TTD). The XPD mutant mice, which are severely impaired in transcription-coupled repair and mildly impaired in nucleotide-excision repair, exhibited many symptoms of premature aging, including osteoporosis, infertility, early graying, and reduced life-span. Mice doubly mutant for XPD and a second gene required for nucleotide-excision repair, XPA, showed greatly accelerated aging that correlated with an increased cellular sensitivity to oxidative DNA damage. The authors propose that the aging phenotype in the TTD mice is caused by unrepaired DNA damage that compromises transcription, which in turn leads to functional inactivation of critical genes and cell death.

Charged Nanocrystals Light Up in Solution

Semiconductor nanocrystals can accept a charge carrier (an electron or hole). Compound semiconductor nanocrystals such as CdS, when charged in solution at electrodes, tend to be chemically unstable. Ding *et al.* (p. 1293) show that organically capped silicon nanocrystals are stable after electron and hole injection in organic solvents and that oppositely charged nanocrystals can recombine in solution and emit light. Greater light emission was obtained by adding coreactants for the recombination reaction, such as oxalate or persulfate anions.

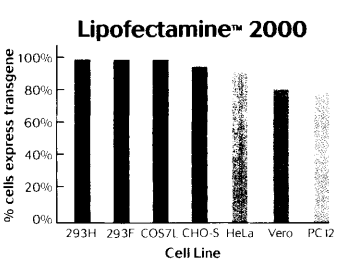
Published online in *Science* Express

CONTINUED ON PAGE 1199

Achieve 99% transfection efficiency in a single stroke.

Take your shot and score to win. With Lipofectamine™ 2000 transfection reagent from Invitrogen, winning transfection is easy.

Transfection power. Lipofectamine™ 2000 gives you the most versatile route to gene delivery and protein expression. Achieve 99% efficiency with common cell lines (see figure). Get the results you want in the cell line you need to work with—even in hard to transfect cells. With Lipofectamine™ 2000 you, not your transfection reagent, choose the best cell line for your experiment.



Rapid, simple protocol. Just mix Lipofectamine™ 2000 with DNA and add to cells. Transfect with or without serum. No washes. No media changes. No delays. It's the ideal reagent for all your experiments, even high-throughput applications. Visit **www.invitrogen.com/lipofectamine2000** for more information and hundreds of cell specific protocols–nothing could be easier.

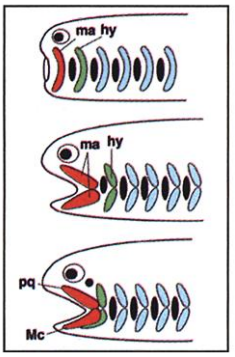
The proven winner. For superior transfection results use Lipofectamine™ 2000, the best Lipofectamine™ available.

Invitrogen
life technologies

Corporate Headquarters:
Invitrogen Corporation
1600 Faraday Avenue
Carlsbad, California 92008 U.S.A.
Tel: 1 760 603 7200
Tel (Toll Free): 1 800 955 6288
Fax: 1 760 603 7229
Email: tech_service@invitrogen.com

European Headquarters:
Invitrogen Ltd
3 Fountain Drive
Inchinnan Business Park
Paisley PA4 9RF UK
Tel: +44 (0) 141 814 6100
Fax: +44 (0) 141 814 6287
Email: eurotech@invitrogen.com

For an office near you go to:
www.invitrogen.com



CREDIT: SHIGETANI *ET AL.*

Narrowing in on Jaw Development

The evolution of vertebrate jaws allowed their diversification into a wide range of feeding niches. Shigetani *et al.* (p. 1316) examined the expression patterns of genes controlling the developing head of the lamprey, a jawless vertebrate. These genes are expressed in regions producing neural crest with a distinct fate from that seen in the developing heads of higher vertebrates such as chicks and mice. Although the correlation between fate and expression correlation has shifted, the relation between genes in the lamprey is the same as in higher vertebrates. A cascade of signals that is present through a broad area of the neural crest and epithelium of the lamprey has been restricted to the mandibular region in vertebrates.

How to Stick Together

Cell-cell adhesion relies upon the direct interaction of integral membrane proteins. One of the primary components is a family of molecules known as cadherins, which contain a string of five highly similar domains disposed on the outside of the cell membrane. Boggon *et al.* (p. 1308) describe the crystal structure of this extracellular portion of C-cadherin and suggest how interactions between C-cadherin molecules on opposing cells and on the same cell serve to create a meshwork that ties the cells together.

Vitamin D Versus Fat

Mechanistic insight into the epidemiologic relation between colon cancer, vitamin D, and a high-fat diet is now offered by Makishima *et al.* (p. 1313), who report that a receptor for vitamin D in the intestine also binds a bile acid called lithocholic acid (LCA). Increased amounts LCA are associated with a high-fat diet, and because it is poorly reabsorbed, it passes into the colon. Binding to the vitamin D receptor stimulates the expression of CYP3A, an enzyme that can catabolize LCA. These results may explain how the enteric system protects itself from the toxic effects of LCA and how vitamin D may guard against colon cancer.

RNA Interference Versus Viruses

Posttranscriptional gene silencing (PTGS) in plants, a form of RNA silencing wherein RNA produced by a gene is destroyed, protects them from invading nucleic acids, mainly viruses and transposons. The biological role of the highly related phenomenon of RNA interference (RNAi) in animals has been less clear. Li *et al.* (p. 1319) now show that RNAi can be induced by viral infection of insect cells and plays a similar protective role. The virus contains a protein that is able to suppress RNAi, indicating that the virus is in an evolutionary "arms race" with its host.

About Faces in the Brain

Babies can discriminate among foreign speech sounds at 4 to 6 months of age, but this ability disappears at about 10 to 12 months and is limited to their native languages. Pascalis *et al.* (p. 1321) report a similar finding in visual processing, in that 6-month-old babies can discriminate individual monkey and human faces. However, 9-month-olds, tested with the same procedure, only discriminate human faces.

Stop-Start Action in NK Cell Activation

The natural killer (NK) cell receptor LY49H was recently identified as being responsible for rendering certain strains of mice resistant to mouse cytomegalovirus (MCMV). Infection with the virus should alter host proteins that interact with LY49H and lead to NK cell activation. Unexpectedly, Arase *et al.* (p. 1323; see the Perspective by Vivier and Biron) found that the ligand for LY49H is a type I–anchored glycoprotein encoded by the virus itself. In mice that are resistant to MCMV, the protein m157 activated LY49H+ NK cells, but m157 bound an inhibitory LY49 NK receptor in a susceptible strain of mice. NK cell inhibition through direct interaction between a viral protein and host receptor may have evolved as a viral evasion strategy, which was followed by the evolution of an activatory protein.

Signal Transduction & Neuroscience | Cytokines | Detection Reagents & Cell Culture | Custom Services

NEW!

BioSource leads the way in MAP Kinase Network Exploration!

BioSource phosphoELISA™ Advantages

- Quantitative
- ~10x more sensitive than Western blotting
- Kits contain all reagents needed
- 96-wells, 80 results, 4 hours
- No IP, no gel
- Fully optimized
- Normalize results with Total Protein ELISA

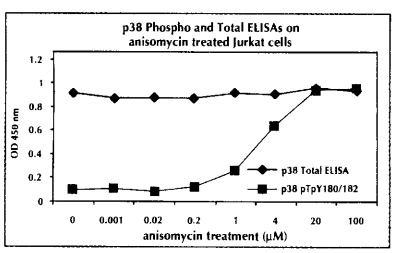
New! phosphoELISA™ kits*: ERK 1/2, p38 MAPK

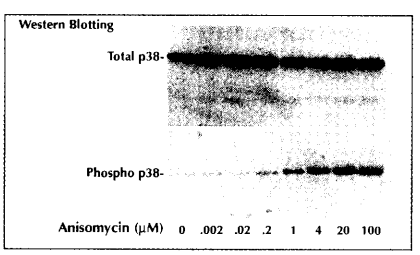
phosphoELISAs™	Total Protein ELISAs
ERK1/2 [pTpY185/187]	ERK1/2
p38 MAPK [pTpY180/182]	p38 MAPK
EGFR [pY1068]	EGFR
EGFR [pY1173]	Rb
Rb [pT821]	Tau
Tau [pS199]	
Tau [pS214]	
Tau [pS396]	

*Patent Pending

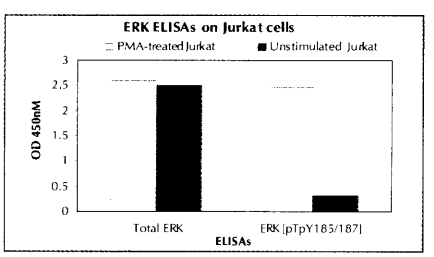
New products available monthly,
visit www.biosource.com for a complete product menu.

Solid Performance. Solid Results.





Cell lysates from Jurkat cells treated with various concentrations of anisomycin were tested with Total p38 MAPK ELISA (Cat.#KHO0061), phospho p38 MAPK ELISA (Cat.#KHO0071) and Western blotting. The data show excellent correlation between ELISA and Western blotting.



Specificity of ERK1/2 [pTpY185/187] phosphoELISA™ (Cat.#KHO0091) and Total ERK1/2 ELISA (Cat.#KHO0081).

SCPS4/02 *For research use only.*

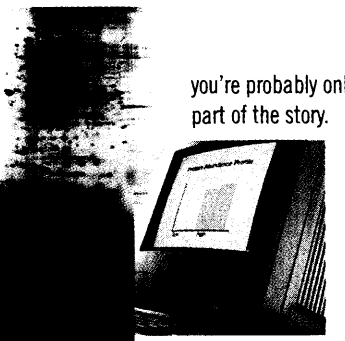
BioSource USA
800.242.0607

BioSource Europe
+32.67.88.99.99

www.biosource.com

BIOSOURCE INTERNATIONAL

> If you identify proteins using 2-D gels,

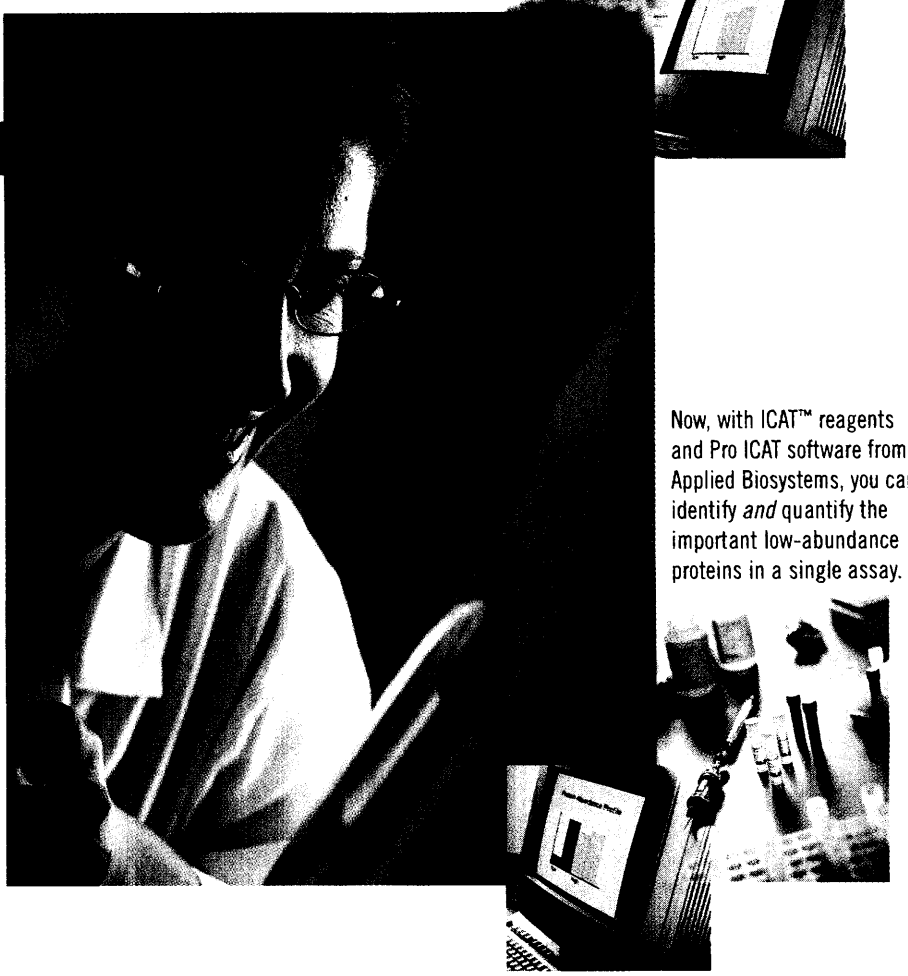


you're probably only seeing part of the story.

The Discovery Moment

January 28, 4:31 PM
Susan Kellerman, Ph.D.

Identifies and quantifies important low-abundance proteins associated with hypertension.



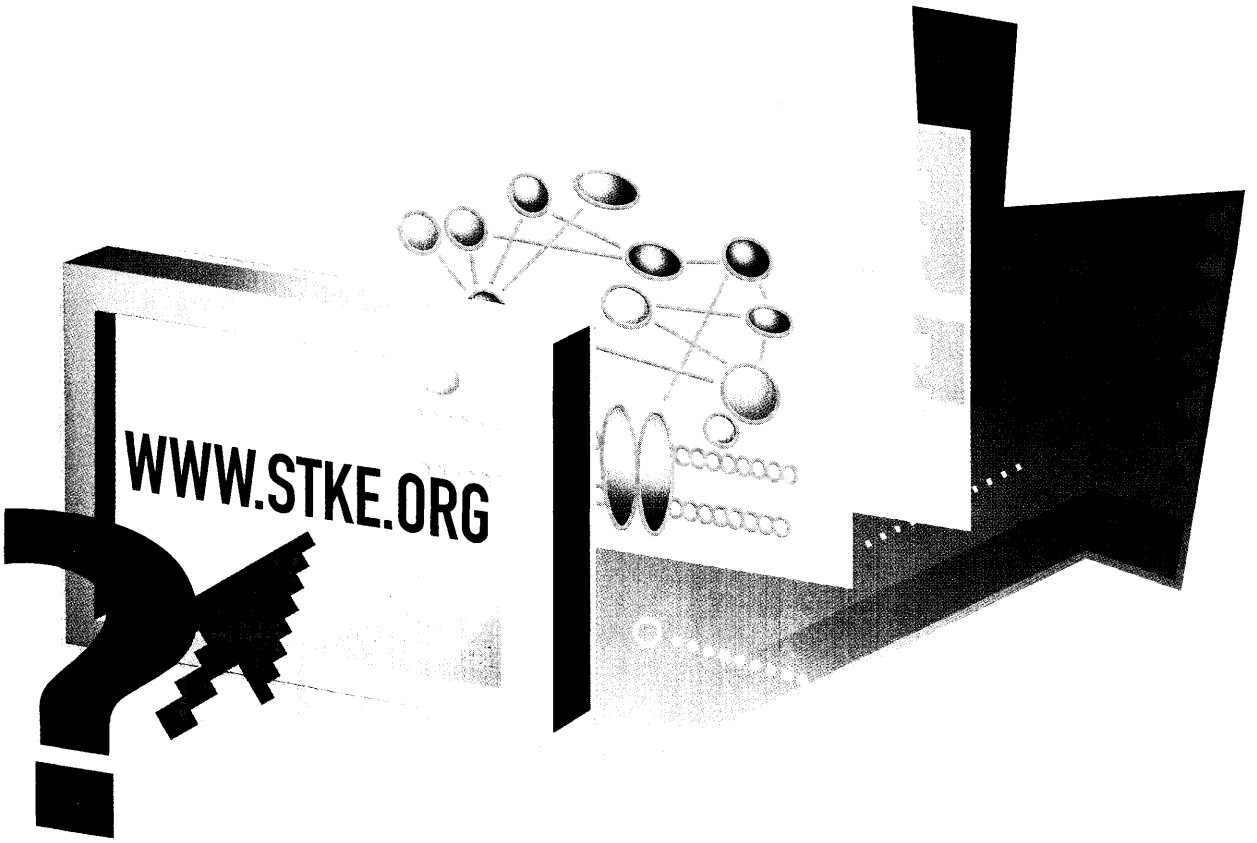
Now, with ICAT™ reagents and Pro ICAT software from Applied Biosystems, you can identify *and* quantify the important low-abundance proteins in a single assay.

After all, shouldn't you spend your time on the proteins that really count?

Find the proteins that matter.

In protein-expression analysis studies, ICAT™ reagent technology provides more complete protein identification and quantification data than is possible today with 2-D gels. Now you can increase proteome coverage, identify and quantify the proteins that matter, and accelerate your discovery efforts. To learn more about ICAT reagents and take advantage of our limited-time promotional offer, call **1.800.345.5224 ext. 2410 or visit www.appliedbiosystems.com/proteomics3f**

Applied Biosystems
Data. Decision. Discovery.



STKE PUTS YOU ON THE RIGHT PATH

Updated weekly, *Science*'s *Signal Transduction Knowledge Environment* (*STKE*) provides the perfect combination of quick summaries and full text access to research papers from over 40 respected scientific journals, plus original *Reviews*, *Protocols*, and *Perspectives*.

You'll also find a Connections Map database of signaling molecules, plus an extended list of helpful e-tools like *personalization options* and *interactive* letters, all at www.stke.org.

To subscribe to *STKE*, or for more information, visit *STKE* at www.stke.org and click *subscriptions*, or contact AAAS at (202) 326-6417 or membership2@aaas.org.

No one can know where new insights in signal transduction might lead you, but *STKE* will help you find the right path.

Science's stke

You're on the right path™

SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

a product of *Science* and Stanford University Libraries

www.stke.org

ABBOTT LABORATORIES

Rapid and efficient profiling of novel kinases

- Novel substrates within a few days
- All annotated human phosphorylation sites
- Small sample volumes
- Benchmarked with leading industry and academic research groups

JERINI
ArrayTechnologies

Further kinase-related applications

- Anti-target screening
- Chemical knockouts
- Transformation of kinase substrate into drug-like inhibitor
- Testing of anti-phosphopeptide antibody specificity

Jerini AG
Invalidenstrasse 130
10115 Berlin, Germany
Phone: +49 - 30 - 9 78 93 - 0
Fax: +49 - 30 - 9 78 93 - 105
e-mail: pepstar@jerini.com
www.jerini.com/array

www.sciencemag.org

Science

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

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

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

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

EDITORIAL/COMPASS SUPERVISORY SENIOR EDITORS Barbara Jasny, Guy Riddihough, Phillip D. Szuromi; SENIOR EDITOR/PERSPECTIVES Orla Smith; SENIOR EDITORS Gilbert J. Chin, Pamela J. Hines, Paula A. Kiberstis (Boston), Beverly A. Purnell, L. Bryan Ray, Linda R. Rowan; ASSOCIATE EDITORS Lisa D. Chong, Marc S. Lavine, H. Jesse Smith, Valda Vinson; EDITOR, *SCIENCE* ONLINE Stewart Wills; ASSOCIATE BOOK REVIEW EDITOR Sherman J. Suter; ASSOCIATE LETTERS EDITOR Etta Kavanagh; INFORMATION SPECIALIST Janet Kegg; CONTRIBUTING EDITOR Kevin Ahern; EDITORIAL MANAGER Cara Tate; SENIOR COPY EDITORS Jeffrey E. Cook, Harry Jach, Barbara P. Ordway; COPY EDITORS Lauren Beben, Monique Martineau, Trista Wagoner; EDITORIAL COORDINATORS Carolyn Kyle, Ellen E. Murphy, Beverly Shields; PUBLICATION ASSISTANTS Chris Filiatreau, Joi S. Granger, Jeffrey Hearn, Elise Laffman, Scott Miller, Gail Murphy, Brian White, Anita Wynn; EDITORIAL ASSISTANTS Lisa Johnson, Yolanda Matthews, Patricia M. Moore, Tunisia L. Riley; EXECUTIVE ASSISTANT Sylvia S. Kihara; ADMINISTRATIVE SUPPORT Patricia F. Fisher

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

NEWS SENIOR CORRESPONDENTS Eliot Marshall, Jean Marx; DEPUTY NEWS EDITORS Robert Coontz, Jeffrey Mervis, Leslie Roberts; ASSOCIATE NEWS EDITOR Laura Helmuth; CONTRIBUTING EDITORS Elizabeth Culotta, Polly Shulman; NEWS WRITERS Jennifer Couzin, Martin Enserink, Constance Holden, Jocelyn Kaiser, Richard A. Kerr, Andrew Lawler (Boston), David Malakoff, Elizabeth Pennisi, Charles Seife, Robert F. Service (Pacific NW), Erik Stokstad, Katie Greene (intern); CONTRIBUTING CORRESPONDENTS Marcia Barinaga (Berkeley, CA), Kathryn Brown, Barry A. Cipra, Jon Cohen (San Diego, CA), Daniel Ferber, Ann Gibbons, Robert Irion, Mitch Leslie (NetWatch), Charles C. Mann, Virginia Morell, Evelyn Strauss, Gary Taubes, David Voss, Ingrid Wickelgren; COPY EDITORS Laura Atwood, Linda B. Felaco, Daniel T. Helgerman; ADMINISTRATIVE SUPPORT Scherraine Mack, Fannie Groom; BUREAUS: Berkeley, CA: 510-652-0302, FAX 510-652-1867, Boston, MA: 617-542-5098, San Diego, CA: 760-942-3252, FAX 760-942-4979, Pacific Northwest: 503-963-1940

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

PREFLIGHT OPERATIONS DIRECTOR David M. Tompkins

ART DESIGN DIRECTOR C. Faber Smith; ART DIRECTOR Alan T. Stonebraker; ASSOCIATE ART DIRECTOR Joshua Moglia; ILLUSTRATORS Cameron Slayden, Katharine Sutliff; ASSOCIATES Holly Bishop, Debra J. Morgenegg, Preston Morrighan; Julie White PHOTO RESEARCHER Leslie Blizard

***SCIENCE* INTERNATIONAL**

EUROPE (science@science-int.co.uk) EDITORIAL SUPERVISORY SENIOR EDITOR Andrew M. Sugden; SENIOR EDITOR/PERSPECTIVES Julia Uppenbrink; SENIOR EDITORS Caroline Ash, Stella M. Hurtley; ASSOCIATE EDITORS Ian S. Osborne, Stephen J. Simpson, Peter Stern; EDITORIAL SUPPORT Jenny Parker; ADMINISTRATIVE SUPPORT Janet Mumford, Lara Crowe, Mark Chadwick; NEWS: EUROPEAN NEWS EDITOR Richard Stone; DEPUTY NEWS EDITOR Daniel Clery; CORRESPONDENTS Michael Balter (Paris: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00), Gretchen Vogel (Berlin: (49) 30-2809-3902, FAX (49) 30-2809-8365) Adam Bostanci (intern)

ASIA Japan Office: Asca Corporation, Eiko Ishioka, Fusako Tamura, 1-8-13, Hirano-cho, Chuo-ku, Osaka-shi, Osaka, 541-0046 Japan; (81) 6-6202-6272, FAX (81) 6-6202-6271; asca@os.gulf.or.jp JAPAN NEWS BUREAU: Dennis Normile (contributing correspondent, (81) 3-3335-9925, FAX (81) 3-3335-4898; dnormile@twics.com); CHINA REPRESENTATIVE Hao Xin, (86) 10-6307-4439 or 6307-3676, FAX (86) 10-6307-4358; science@public3.bta.net.cn; INDIA Pallava Bagla (contributing correspondent (91) 11-271-2896; pbagla@ndb.vsnl.net.in)

PUBLISHER **Alan I. Leshner**
ASSOCIATE PUBLISHER **Beth Rosner**
MEMBERSHIP/CIRCULATION DIR. **Michael Spinella**

MEMBERSHIP/CIRCULATION (membership@aaas.org) DEPUTY DIRECTOR Marlene Zendell; MEMBER SERVICES MANAGER Michael Lung; SENIOR SPECIALIST Mary Curry; COORDINATOR Jantell Stone; SPECIALISTS Laurie Baker, Pat Butler, Elizabeth Early, Katrina Smith; MARKETING MANAGER Gregory Urquhart; PRODUCTION MANAGER Lauri Sirois; SENIOR ASSOCIATE Deborah Stromberg; INTERNATIONAL MARKETING MANAGER Ruth Hall; SENIOR EXECUTIVE Martin Paine; RESEARCH MANAGER Renuka Chander; BUSINESS AND FINANCE MANAGER Teressa Ellis; ADMINISTRATIVE SUPPORT Zadia McKinnon; COMPUTER SPECIALIST John Williams

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

REPRINTS Ordering/Billing/Status 800-635-7171; Corrections 202-326-6501

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

FINANCE AND ADVERTISING BUSINESS MANAGER Deborah Rivera-Wienhold; SENIOR ANALYST Randy Yi; FINANCIAL ANALYSTS Lisa Donovan, Jessica Tierney-Rubin; RIGHTS AND PERMISSIONS: ASSOCIATE Emilie David; ASSISTANT Karen Lentz; MARKETING: DIRECTOR John Meyers; RECRUITMENT MARKETING MANAGER Allison Pritchard; ASSOCIATES Mary Ellen Crowley, Amanda Donathen; ELECTRONIC MEDIA: MANAGER Don Hemenway; INTERNET PRODUCTION MANAGER Lizabeth Harman; ASSISTANT PRODUCTION MANAGER Wendy Stengel; SENIOR PRODUCTION ASSOCIATES Sheila Myers, Lisa Stanford; PRODUCTION ASSOCIATES Carla Cathey, Steve Kusek, Louis Williams; LEAD APPLICATIONS DEVELOPER Carl Saffell; ADMINISTRATIVE SUPPORT Joyce Scott

PRODUCT ADVERTISING (science_ advertising@aaas.org) NATIONAL SALES MANAGER Richard Teeling: 973-694-9173, FAX 973-694-9193 • NORTHEAST AND E. CANADA Elizabeth Pointek: 860-612-0306, FAX 413-480-0008• MIDWEST Rick Bongiovanni: 330-405-7080, FAX 330-405-7081 • WEST COAST/W. CANADA B. Neil Boylan: 415-458-1630, FAX 415-458-1631 • MID-ATLANTIC AND SOUTHEAST SALES Christopher Breslin: 443-512-0330, FAX 443-512-0331 • UK/SCANDINAVIA/FRANCE/ITALY/BELGIUM/NETHERLANDS Andrew Davies: 44 (0)1-782-750-111, FAX 44 (0)1-782-751-999 • GERMANY/SWITZERLAND/AUSTRIA Tracey Peers: (44) 1-782-752-530, FAX (44) 1-782-752-531 JAPAN Mashy Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852 ISRAEL Jessica Nachlas 001 972-3-5449123 • TRAFFIC MANAGER Carol Maddox; SALES COORDINATOR Deiandra Underwood

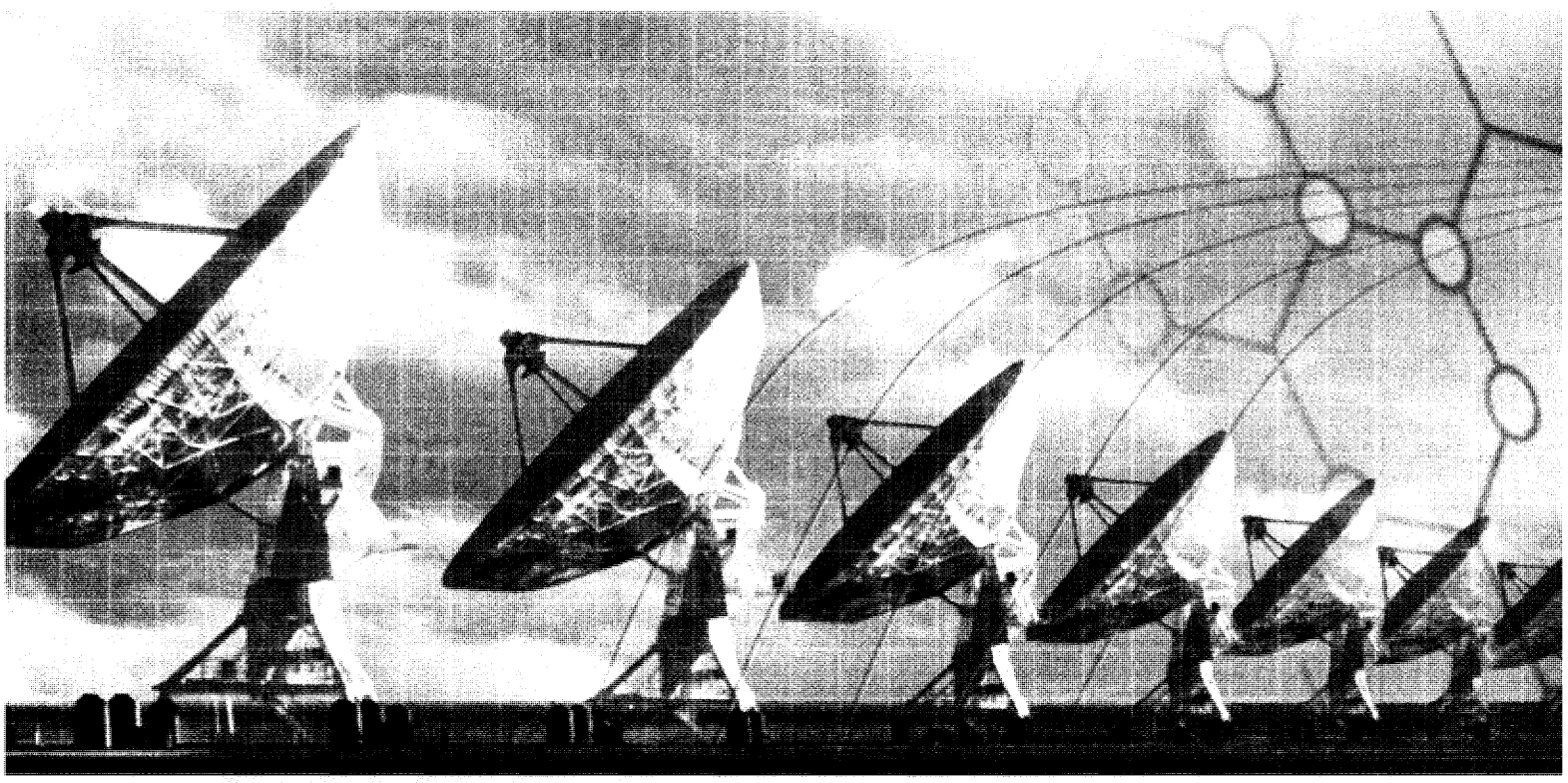
RECRUITMENT ADVERTISING (science_classifieds@aaas.org); PRODUCTION MANAGER Jennifer Rankin; ASSISTANT PRODUCTION MANAGER Deborah Tompkins; U.S.: SALES MANAGER Gabrielle Boguslawski: 718-491-1607, FAX 202-289-6742; WEST COAST SALES MANAGER Kristine von Zedlitz; EAST COAST SALES MANAGER Jill Steinberg; INTERNET SALES MANAGER Beth Dwyer; ASSISTANT SALES MANAGER Daryl Anderson; SENIOR SALES COORDINATOR Erika Bryant; SALES COORDINATORS Rohan Edmonson, Caroline Gallina, Shirley Young; SALES REPRESENTATIVES Kathleen Clark, Sussy Castilla, Christina Geiger, Bren Peters-Minnis; ASSISTANTS Emnet Tesfaye, Timothy Hawk; ASSOCIATES Christine Hall, Dina Freeman, Greta Springett; PUBLICATIONS ASSISTANTS Robert Buck, Jane Vaughn; U.K./EUROPE: SALES MANAGER Debbie Harris; PROMOTIONS COORDINATOR Richard Walters; INTERNET SALES EXECUTIVE Tracy Holmes; AUSTRALIA/NEW ZEALAND: Keith Sandell: (61) 02-9922-2977, FAX (61) 02-9922-1100 JAPAN: Mashy Yoshikawa: (81) 3-3235-5961, FAX (81) 3-3235-5852

AAAS BOARD OF DIRECTORS RETIRING PRESIDENT, CHAIR Peter H. Raven; PRESIDENT Floyd E. Bloom; PRESIDENT-ELECT Mary Ellen Avery; TREASURER David E. Shaw; CHIEF EXECUTIVE OFFICER Alan I. Leshner; BOARD Lewis M. Branscomb; John E. Burris; Nina V. Fedoroff; Karen A. Holbrook; Richard A. Meserve; Norine E. Noonan; Robert C. Richardson; Lydia Villa-Komaroff

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

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

INFORMATION FOR CONTRIBUTORS
See pages 163 and 164 of the 5 April 2002 issue or access www.sciencemag.org/feature/contribinfo/home.shtml



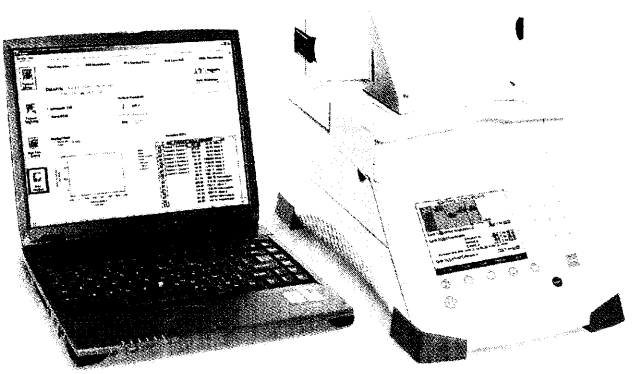
The Search Is Over

New Software
- Automated data analysis
- Intelligent allelic discrimination
- Temperature gradient for assay optimization

New Assay Solutions:
- Real-time PCR certified iQ™ supermix
- Advanced probe and primer design software

Unsurpassed Service:
- On-site, personalized customer support

Find what you're looking for about the iCycler iQ system by visiting our web site at **www.bio-rad.com/iCycler**



Bio-Rad's iCycler iQ System:
Amplify Your Expectations

The polymerase chain reaction (PCR) process is covered by patents owned by Hoffman-LaRoche. Use of the PCR process requires a license.

Visit us on the Web at **discover.bio-rad.com.**
Call toll free at 1-800-4BIORAD (1-800-424-6723);
outside the US, contact your local sales office.

BIO-RAD

READER AND ADVERTISER RESOURCES

Science Careers:

JOB SEARCH

Find exactly the jobs you're looking for quickly and easily at ScienceCareers.org. Job listings are searchable by keyword, discipline, location, and more!

FOCUS ON CAREERS

AD SUPPLEMENT IN THE 24 MAY ISSUE

Careers in Biotechnology & Pharmaceuticals

Biotechnology firms and pharmaceutical companies recruit scientists to oversee such issues as drug development, production, clinical trials, regulatory affairs, and patent protection.

Look for it in the 24 May issue.

Product News:

LAB TECHNOLOGY TRENDS

SPECIAL AD SECTION IN THE 31 MAY ISSUE

Global Biotechnology

World-class biotechnology centers exist in areas throughout the world. This supplement will provide an update on different areas around the world where biotechnology is alive and well including throughout Europe and Sweden in particular.

Look for it in the 31 May issue, which will also be distributed at BIO 2002, 9–13 June, Toronto, Canada.

WWW.SCIENCEPRODUCTLINK.ORG

***Science* Product Link**

Science's online reader service system helps you find information on products advertised in the pages of *Science*. Search by product category, company name, keyword, or page number.

Find it all at www.scienceproductlink.org.

Trade Shows & Conferences

LOOK FOR COPIES OF THE 14 JUNE ISSUE OF *SCIENCE* AT THESE UPCOMING TRADE SHOWS AND CONFERENCES:

SIGNAL TRANSDUCTION BY ENGINEERED EXTRACELLULAR MATRICES
23–28 June, New London, CT (GRC)

NUCLEIC ACID-BASED TECHNOLOGIES
24–26 June, Washington, DC (CHI)

POST-GENOMICS BIOINFORMATICS
24–26 June, San Francisco, CA (IBC)

CHI–Cambridge Healthtech Institute
GRC–Gordon Research Conferences
IBC–IBC Conferences

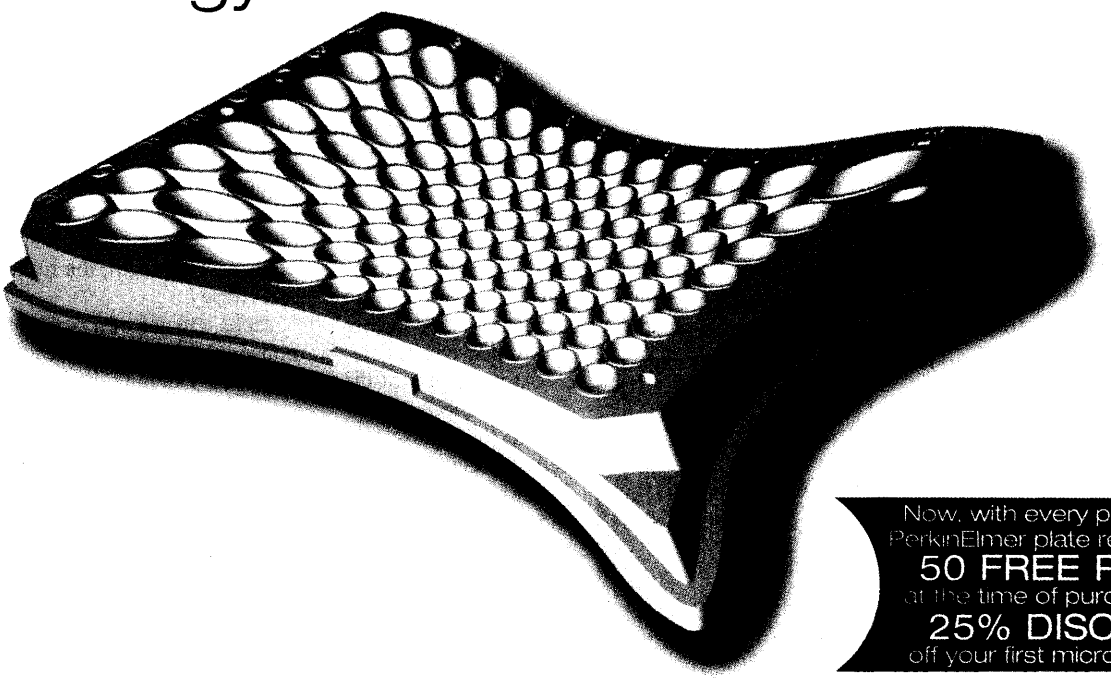
For *Science* sales representatives' contact information, please see the previous page.

AAAS *Science* is published by The American Association for the Advancement of Science. To subscribe to *Science* and become a member of the AAAS, go to **www.aaas.org**.

Drug Discovery | **Research** | Clinical Screening

Plate Readers

You've never seen plate reading technology this flexible.



Now, with every purchase of a PerkinElmer plate reader, receive
50 FREE PLATES
at the time of purchase AND a
25% DISCOUNT
off your first microplate order!

From Basic Research through Assay Development and High-Throughput Screening, we've got it covered.

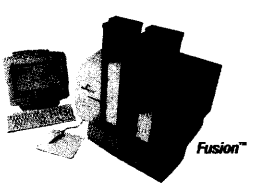
Researchers using plate readers have different needs. Different assays, different budgets, different system requirements. PerkinElmer Life Sciences addresses these needs with the most complete line of multi-detection plate readers available.

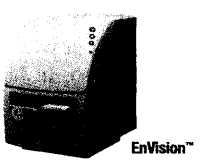
There's the affordable VICTOR²™ – the market leader. With legendary time-resolved fluorescence (TRF) performance and a host of options and accessories such as reagent dispensers and plate stackers, VICTOR²'s capability can expand as your research needs grow.

The *Fusion*™ combines every non-isotopic assay method of detection, including fluorescence polarization and AlphaScreen®, into one affordable, high-performance platform.

And finally, the new, state-of-the-art EnVision™, optimized for high-throughput screening with fast plate reading speeds and applications flexibility.

For help selecting the plate reader most flexible to meet your needs, call us at 1 800 551-2121 today. Or visit us online at www.perkinelmer.com/platereaders.





PerkinElmer™
life sciences.

Worldwide Headquarters: PerkinElmer Life Sciences, Inc., 549 Albany Street, Boston, MA 02118-2512 USA (800) 551-2121
European Headquarters: PerkinElmer Life Sciences, Inc., Imperiastraat 8, BE-1930 Zaventem Belgium

www.perkinelmer.com/lifesciences

New from QIAGEN — BioMag suspensions for fast, flexible, cost-effective cell sorting

Fast, efficient negative selection

BioMag® secondary antibody suspensions allow you to economically purify naive target cells from a heterogeneous cell population using negative selection.

BioMag secondary antibody suspensions are:

- Well suited for negative selection
- Fast and easy — no columns required
- Highly economical

Flexible magnetic cell separation

BioMag suspensions offer a high degree of flexibility in magnetic cell separation. A comprehensive range of secondary antibodies is available, allowing the use of a wide variety of primary antibodies, for sensitivity and specificity.

QIAGEN offers a wide range of BioMag suspensions for many applications:

- BioMag secondary antibody suspensions
- BioMag streptavidin suspensions
- BioMag Protein A and Protein G suspensions

Call QIAGEN today to find out more about this versatile technology and the wide range of applications available.

www.qiagen.com

QIAGEN:

Australia
Tel. 03-9489-3666
Fax 03-9489-3888

Canada
Tel. 800-572-9613
Fax 800-713-5951

France
Tel. 01-60-920-930
Fax 01-60-920-925

Germany
Tel. 02103-29-12400
Fax 02103-29-22022

Italy
Tel. 02-33430411
Fax 02-33430426

Japan
Tel. 03-5547-0811
Fax 03-5547-0818

Switzerland
Tel. 061-319-30-31
Fax 061-319-30-33

UK and Ireland
Tel. 01293-422-999
Fax 01293-422-922

USA
Tel. 800-426-8157
Fax 800-718-2056

Distributors:

Argentina Tecnolab S.A. (011) 4555 0010 **Austria/Slovenia** VWR International GmbH (01) 576 00 0 **Belgium/Luxemburg** Westburg b.v. 0800-1-9815 **Brazil** Uniscience do Brasil 011 3622 2320 **China** Gene Company Limited (852)2896-6283 **Cyprus** Scientronics Ltd (02) 765 416 **Czech Republic** BIO-CONSULT spol. s.r.o. (420) 2 417 29 792 **Denmark** VWR International ApS 43 86 87 88 **Egypt** Clinilab 52 57 212 **Finland** VWR International Oy (09) 804 551 **Greece** BioAnalytica S.A. (10)-640 03 18 **India** Genetix (011)-542 1714 or (011)-515 9346 **Israel** Westburg (Israel) Ltd. 08 6650813/4 or 1-800 20 22 20 **Korea** LRS Laboratories, Inc. (02) 924-86 97 **Malaysia** RESEARCH BIOLABS SDN. BHD. (603)-8070 3101 **Mexico** Quimica Valaner S.A. de C.V. (55) 55 25 57 25 **The Netherlands** Westburg b.v. (033)-4950094 **New Zealand** Biolab Scientific Ltd. (09) 980 6700 or 0800 933 966 **Norway** VWR International AS 22 90 00 00 **Poland** Syngen Biotech Sp.z.o.o. (071) 351 41 06 or 0601 70 60 07 **Portugal** IZASA PORTUGAL, LDA (21) 424 7312 **Singapore** Research Biolabs Pte Ltd 2731066 **Slovak Republic** BIO-CONSULT Slovakia spol. s.r.o. (02) 5022 1336 **South Africa** Southern Cross Biotechnology (Pty) Ltd (021) 671 5166 **Spain** IZASA, S.A. (93) 902.20.30.90 **Sweden** VWR International AB (08) 621 34 00 **Taiwan** TAIGEN Bioscience Corporation (02) 2880 2913 **Thailand** Theera Trading Co. Ltd. (02) 412-5672 **In other countries contact:** QIAGEN, Germany

QIAGEN

CS042002SWW

Less pressure.

Novartis is helping patients reduce their high blood pressure by millions of points...each year.

For Ryan, less pressure means more active living.

"When I was diagnosed, the doctor told me I couldn't do anything strenuous. This year, I climbed the Himalayas and I'm going back for more."

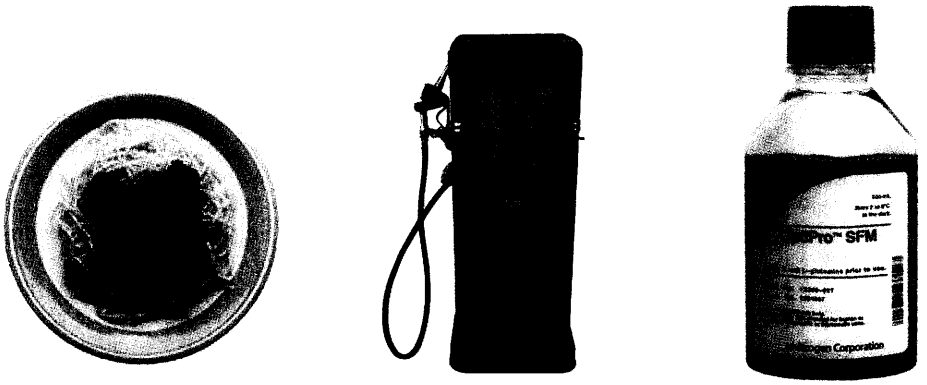
— Ryan Bendixen

When elite Army unit member Ryan Bendixen was diagnosed with severe high blood pressure at age 20, he was devastated. Ryan was suddenly discharged from the Army and faced with the risk of heart attacks, strokes, heart failure and kidney failure. He stopped all athletics, put on weight and became frustrated, angry and depressed. Today, however, because of treatments made possible by Novartis, Ryan is more active than ever. He's married, living in the Rockies, scaling the Himalayas and training to join another elite group – the world's best climbers. Novartis is proud to be the innovative force that's bringing new optimism and hope to patients and their families. Today Ryan is managing his high blood pressure while enjoying a full, active life.

Think what's possible.

NOVARTIS

www.novartis.com



Performance Enhancers

Power your cell culture system with the right nourishment.

Now you can minimize adaptation time, improve control, increase yield and simplify scale-up with the most trusted name in cell culture.

No matter what your cell type.

Hybridomas. CHO cells. HEK (293) cells. Insect cells. Neurons. Blood and bone marrow cells. Keratinocytes. ES cells. Hepatocytes. Endothelial cells. Mammalian cells for virus production.

You name it. We can make a serum-free, protein-free or chemically-defined GIBCO™ medium optimized for its culture.

What's more, we make it in a format to suit your system: dry powder, 1X liquid, concentrates, and new Advanced Granulation Technology™.

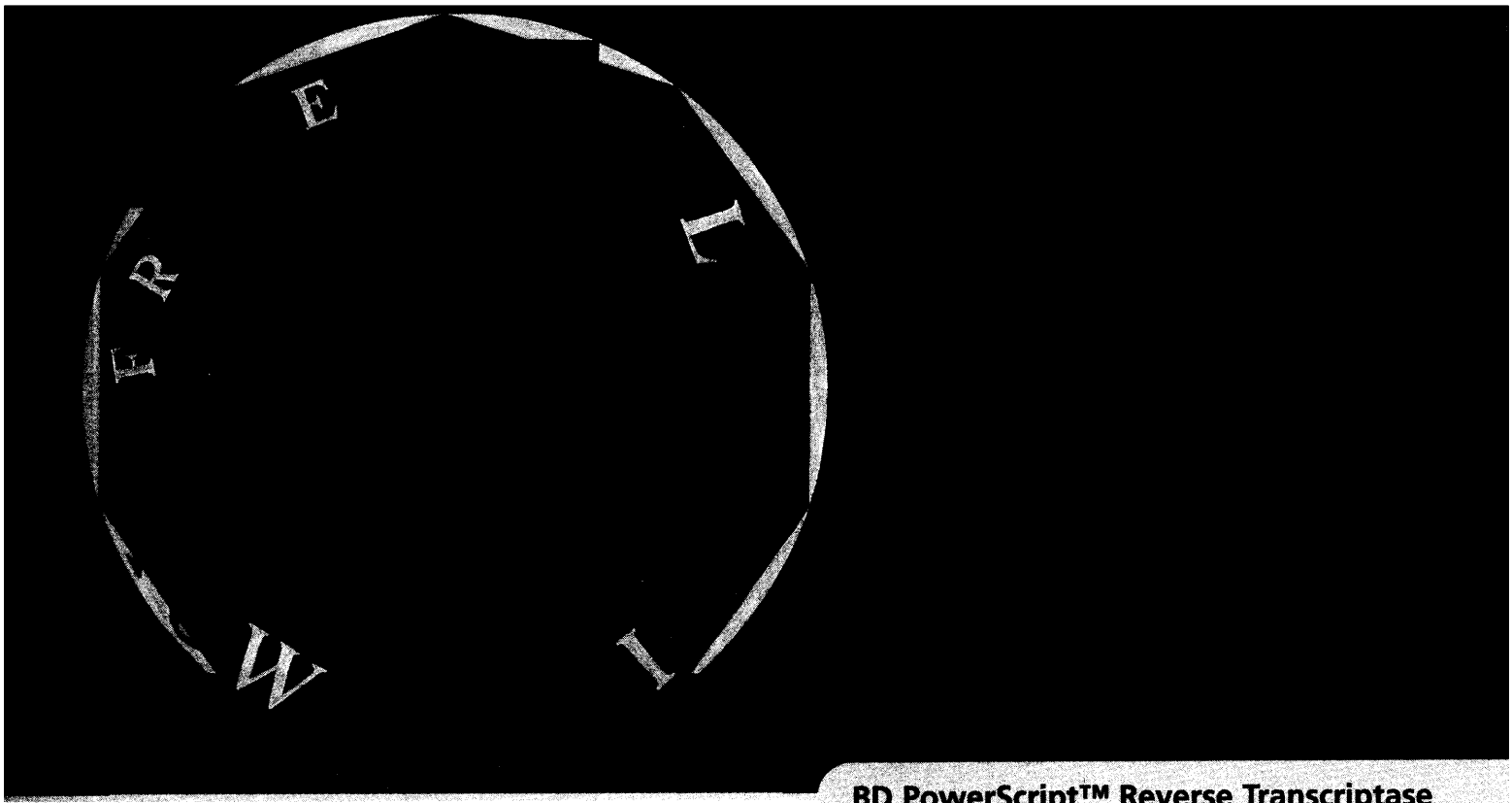
Use GIBCO™ specialty and serum-free nutrient media.

And pump up performance.

www.invitrogen.com

GIBCO™
Invitrogen Corporation

Better Cell Culture Through Innovation



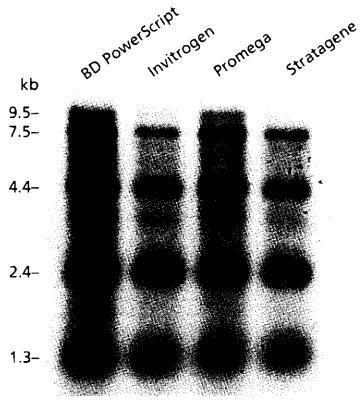
BD PowerScript™ Reverse Transcriptase

Illustration inspired by the art of Robert Indiana.

Power through.

Get the power of longer cDNAs for less money with **BD PowerScript™ Reverse Transcriptase** (RT). BD PowerScript is a superior point mutant of the Moloney murine leukemia virus RT that lacks RNase H activity but retains the wild-type polymerase ability—so you consistently get cDNAs longer than 3 kb. BD PowerScript is cleaner than other commercially available RTs. In fact, we guarantee each preparation to be free of DNase and RNase. And it costs less, making BD PowerScript RT clearly the most economical and best choice for cDNA library construction, RT-PCR, labeling probes, or any application requiring robust reverse transcription.

Call and order today!



Superior first strand cDNA synthesis from BD PowerScript™ RT. A poly A⁺ RNA ladder was incubated with equivalent amounts of different RNase H⁻ RTs using the conditions recommended by each manufacturer. BD PowerScript generated the largest yield of the 9.5 kb fragment.

BD Biosciences

Clontech
Discovery Labware
Immunocytometry Systems
Pharmingen

BD

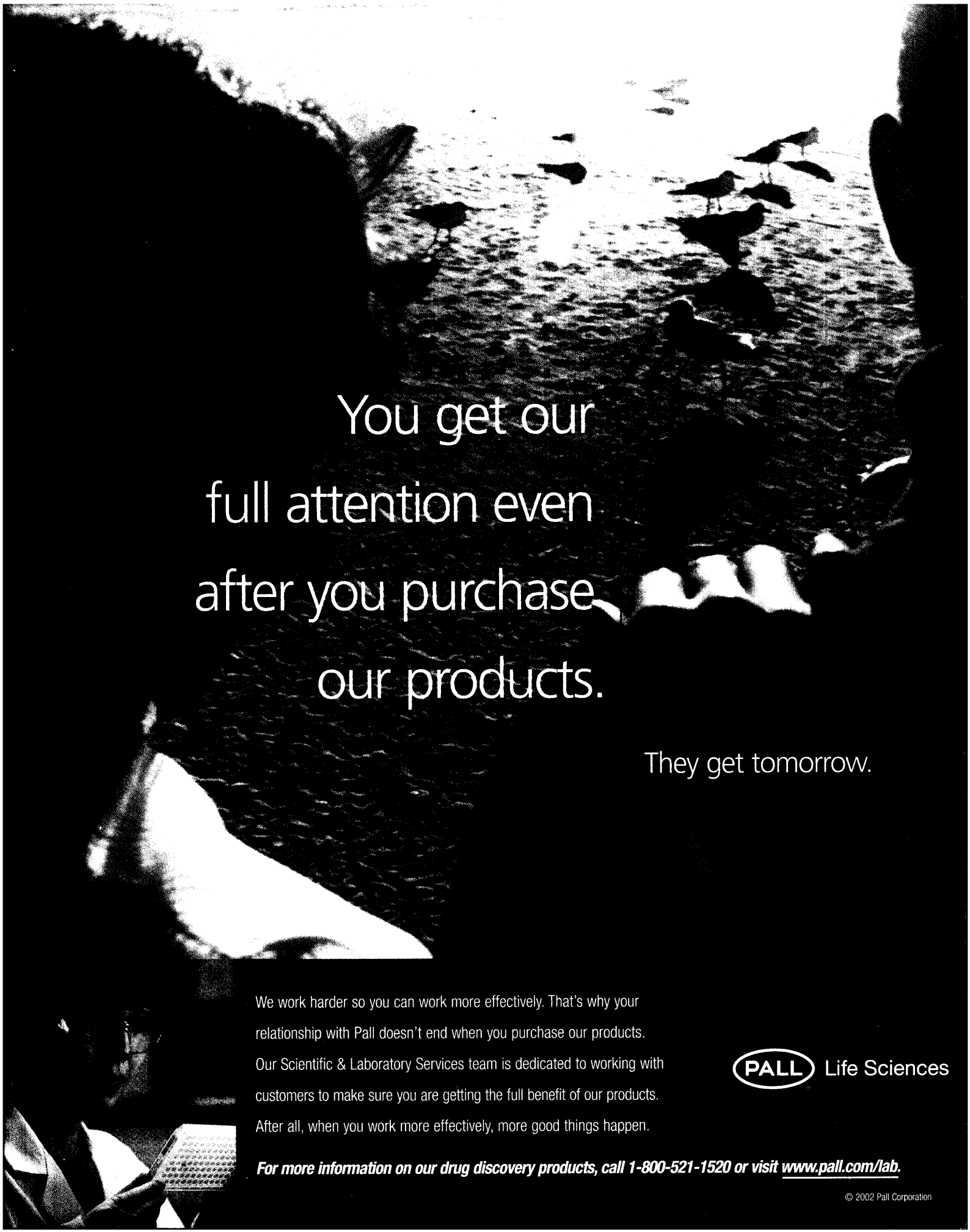
BD Biosciences Clontech

www.bdbiosciences.com

United States	Canada	Europe	Japan	Asia Pacific	Latin America/Caribbean
877.232.8995	888.259.0187	32.53.720.211	81.24.593.5405	65.6861.0633	55.11.5185.9995

For country-specific contact information, visit **www.bdbiosciences.com/how_to_order/**

AD23109



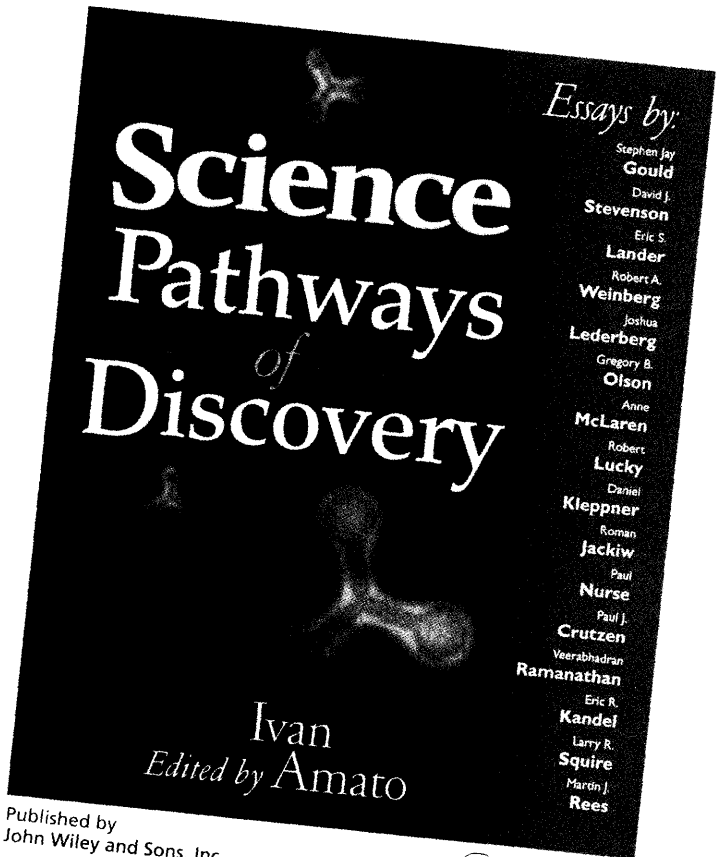
We work harder so you can work more effectively. That's why your relationship with Pall doesn't end when you purchase our products. Our Scientific & Laboratory Services team is dedicated to working with customers to make sure you are getting the full benefit of our products. After all, when you work more effectively, more good things happen.

PALL Life Sciences

For more information on our drug discovery products, call 1-800-521-1520 or visit www.pall.com/lab.

Just published!

A Definitive History from the World's Leading Scientists



Published by
John Wiley and Sons, Inc.

WILEY
Independent Thinkers
wiley.com

In *Science Pathways of Discovery,* some of the sharpest scientific minds of our time reveal what science has in store by examining the histories of a dozen crucial areas of scientific inquiry. Originally published as a year-long series in *Science*, this awe-inspiring compendium features brilliant and provocative contributions from:

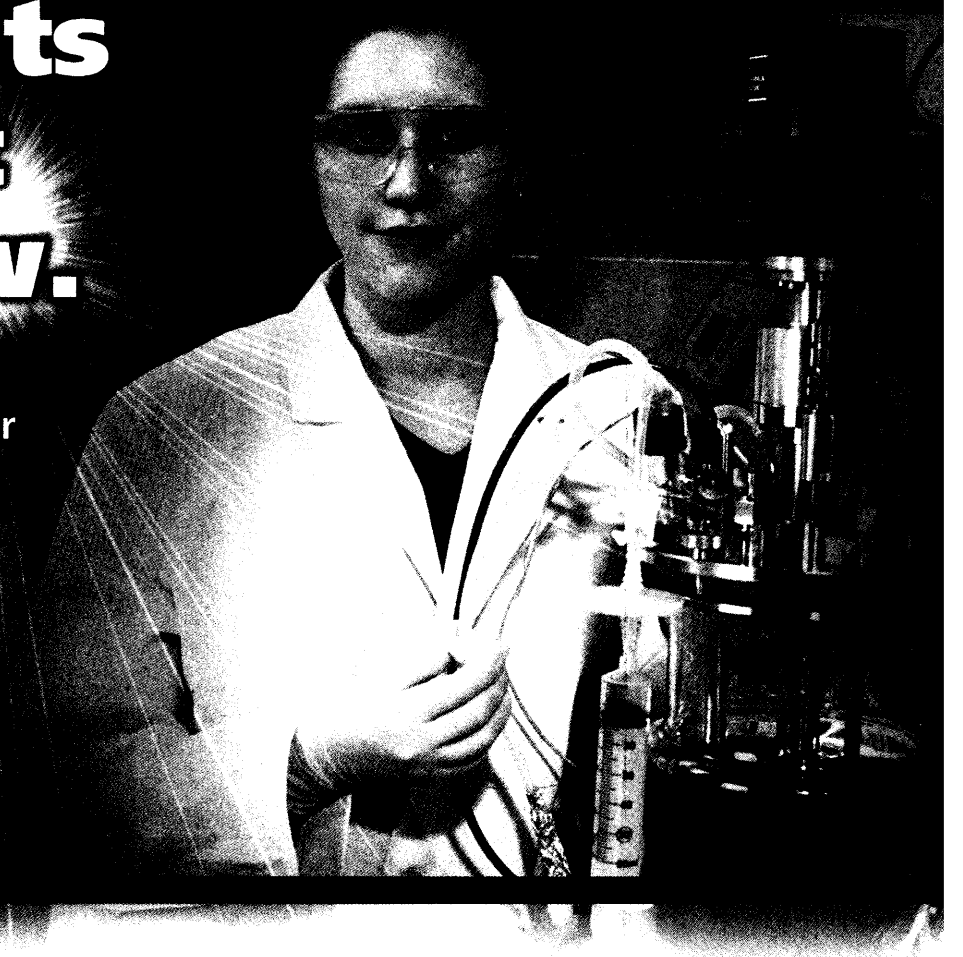
- **Stephen Jay Gould** on the "science wars"
- **David J. Stevenson** on planetary science
- **Eric S. Lander** and **Robert A. Weinberg** on genomics
- **Joshua Lederberg** on the history of infectious disease
- **Gregory B. Olson** on materials science
- **Anne McLaren** on cloning
- **Robert Lucky** on science communication
- **Daniel Kleppner** and **Roman Jackiw** on quantum physics
- **Paul Nurse** on biological cell theory
- **Paul J. Crutzen** and **Veerabhadran Ramanathan** on atmospheric sciences
- **Eric R. Kandel** and **Larry R. Squire** on neuroscience
- **Martin J. Rees** on the biography of the universe

Order online at the AAAS Bookstore, www1.fatbrain.com/aaas, and receive a 25% discount

THE CELL CULTURE COMMITMENT

The products you need today.

The results you want tomorrow.



- Quality media available for shipment today
- Exceptional performance and consistent results
- Expert advice from R & D specialists – customizable formulations

We're committed to the highest standard of cell culture support. Now and into the future.

Why settle for inconsistent quality and service or back-ordered product? We're here for your long-term needs, providing the high quality media you need – when you need it. Because when your research starts with the strongest possible foundation, your results are solid – ***every single time.***

Call 1-800-718-4328 for a Competitive Quote on cell culture products, today.
Visit our Web site at sigma-aldrich.com/commitment_sci.

The new $55 million R & D Center keeps Sigma-Aldrich on the leading edge of cell culture.

availability, ordering & tracking
sigma-aldrich.com
scientific tools, products & information

LEADERSHIP IN LIFE SCIENCE, HIGH TECHNOLOGY AND SERVICE
SIGMA-ALDRICH CORPORATION • BOX 14508 • ST. LOUIS • MISSOURI 63178 • USA

SIGMA-ALDRICH

www.NovartisCarePlan.com

OSTEOPOROSIS | **HIGH BLOOD PRESSURE** | GLAUCOMA | SCHIZOPHRENIA | CANCER | DIABETES | ALZHEIMER'S

Medicine for your Medicare patients? Novartis has an offer to make them feel better.

In November 2001, Novartis was one of the first pharmaceutical companies to launch a prescription discount card offering valuable savings to Medicare enrolled patients lacking prescription drug coverage. Today, Novartis is a founding partner of the Together Rx, L.L.C., a new alliance of seven major pharmaceutical companies offering patients valuable savings on more than 160 medicines through one easy-to-use, completely free Rx savings card – the Together Rx™ card.

Novartis is proud to offer meaningful savings to a broad range of patients in need through its comprehensive and flexible prescription savings plan. In addition, Novartis continues to offer free medicines on a short-term basis to qualifying patients through its physician based Patient Assistance Program.

Enhanced Savings on Novartis Prescription Drugs

SINGLES up to $18,000/yr*	COUPLES up to $24,000/yr*	$12/prescription
$18,001 - $28,000/yr*	$24,001 - $38,000/yr*	25-40% off**

*Alaska: $35,000 singles/$48,000 couples; Hawaii: $33,000 singles/$44,000 couples.

**Consumer savings may vary on select Novartis products. Savings and product listing are subject to change. Consumers can anticipate obtaining savings of approximately 25 to 40 percent, depending on the pharmacy's customary pricing for the specific medication.

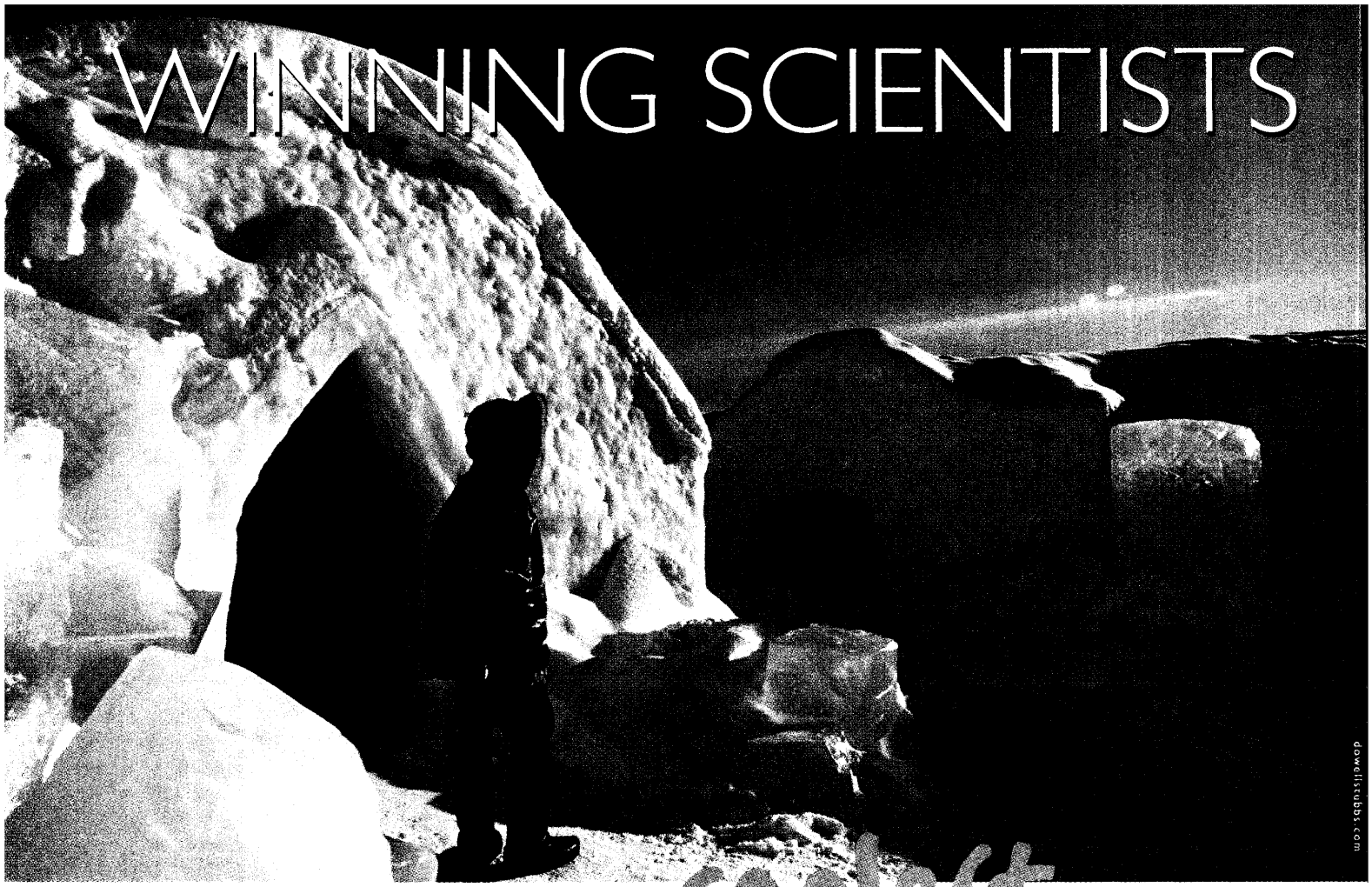
Patients Can Enroll Now

Together Rx™ Card
available JUNE 2002
www.Together-Rx.com
1-800-865-7211

Novartis Patient Assistance Program
available through
physicians' offices

NOVARTIS

Think what's possible.



COME FROM THE coolest PLACES

Raised north of the Arctic circle, near Sweden's famous Icehotel, Åsa Apelqvist was the regional winner of the 2001 Amersham Biosciences & *Science* Prize for Europe.

No matter where you come from, a journey of a thousand miles begins with a single step. So if you are embarking on the journey that is the study of science, here's your chance to gain international acclaim for yourself and your school. If you completed your Ph.D. in molecular biology* during 2001, describe your work in a 1,000 word essay. Then enter it into the 2002 Amersham Biosciences & *Science* Prize for young scientists.

Your essay will be reviewed by a panel of distinguished scientists, who'll select one grand prize winner and up to seven other winners. The grand prize winner will get his or her essay published in *Science*, receive US$25,000, and win a trip to the awards ceremony. Your essay may be submitted in English, French, German, Spanish, Japanese or Chinese (Mandarin). The closing date for entries is July 15, 2002.

Go to **www.amershamscienceprize.org** to obtain the mandatory entry form. And take your step. Jamie H. Cate did and won the regional prize for North America in 1998. What's more, he recently won a prize for the best paper published in *Science*—"Crystal Structure of the Ribosome at 5.5 Å Resolution" *Science*, **292:** 883-896 (2001).

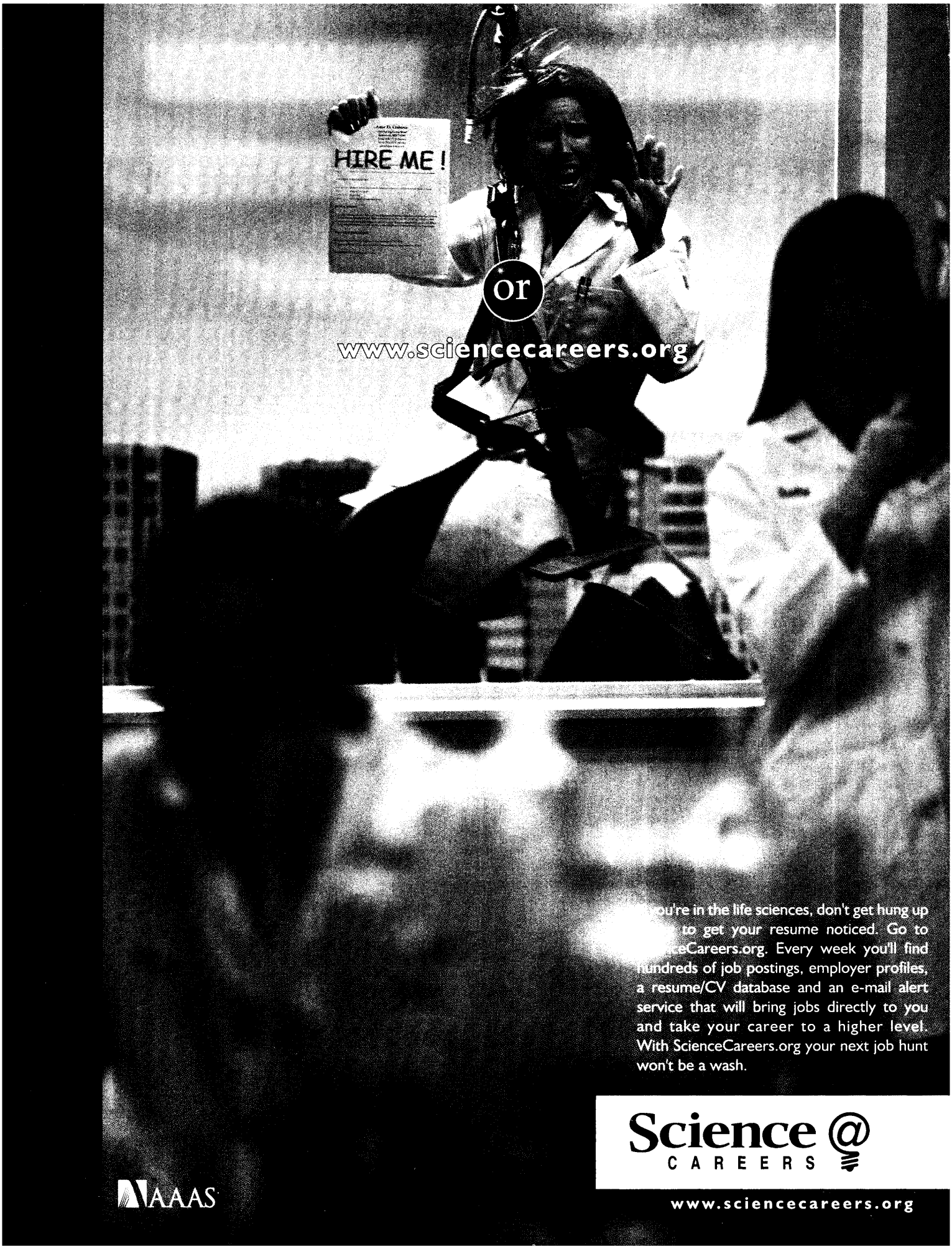
* For the purpose of this prize, molecular biology is defined as "that part of biology which attempts to interpret biological events in terms of the physico-chemical properties of molecules in a cell" (McGraw-Hill Dictionary of Scientific and Technical Terms, 4th Edition).

AMERSHAM BIOSCIENCES & SCIENCE

prize FOR YOUNG SCIENTISTS

Science

Amersham Biosciences



...ou're in the life sciences, don't get hung up ... to get your resume noticed. Go to ...ceCareers.org. Every week you'll find hundreds of job postings, employer profiles, a resume/CV database and an e-mail alert service that will bring jobs directly to you and take your career to a higher level. With ScienceCareers.org your next job hunt won't be a wash.

Science @ CAREERS

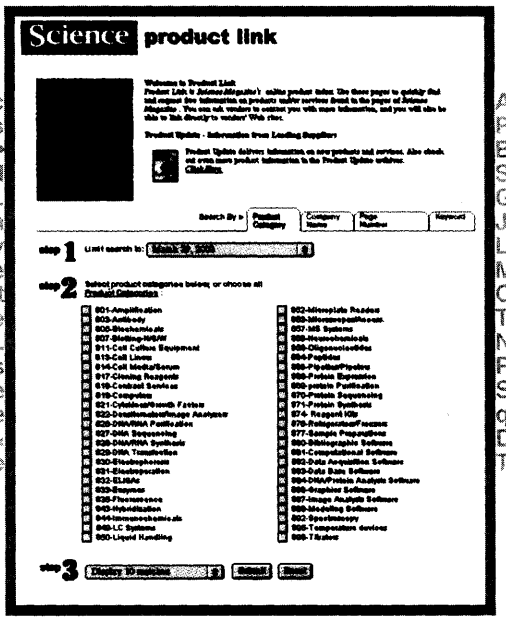
AAAS

www.sciencecareers.org

Looking for great products? Look here.

www.scienceproductlink.org

Affymetrix • Alpha Diagnostic
Applied Biosystems • Aventis
Bio Search Technologies •
Epoch Biosciences • Genemed
Genosys Bio technologies, Inc.
DNA Technologies Invitrogen
Kodak Scientific Imaging Sy
Connell Research • Messe
Midland Certified Reagent
GmbH • MJ Research • Nature
Century Pharmaceuticals, Inc.
England Peptides • Novartis
Peptron • PerkinElmer Life
Chemical Company • Pyrose
Qiagen • Quatar Research &
Sequenom, Inc. • Stratagene



Ambion • Amersham Bioscience
Pharma AG • Bi0-Synthesis, Inc.
Biostat • Brinkmann Instru
Synthesis, Inc. • Genomics One
Genotech InoGenex • Inte grated
Jerini Peptide Technologea
Leica Mycrosystems • Mac
Muchen GmbH • Microarrays,
Company, Inc. • Mittenyi Biotec
Technology Corporation • New
New England Biolabs • New
Pharmaceutical/Rudder Finn
Sciences • Pharmagene • Pierce
quencing AB • Qbiogene, Inc.
Development • R&D Systems,
Thermo Haake • TIAA-CREF

Science's Online Reader Service System

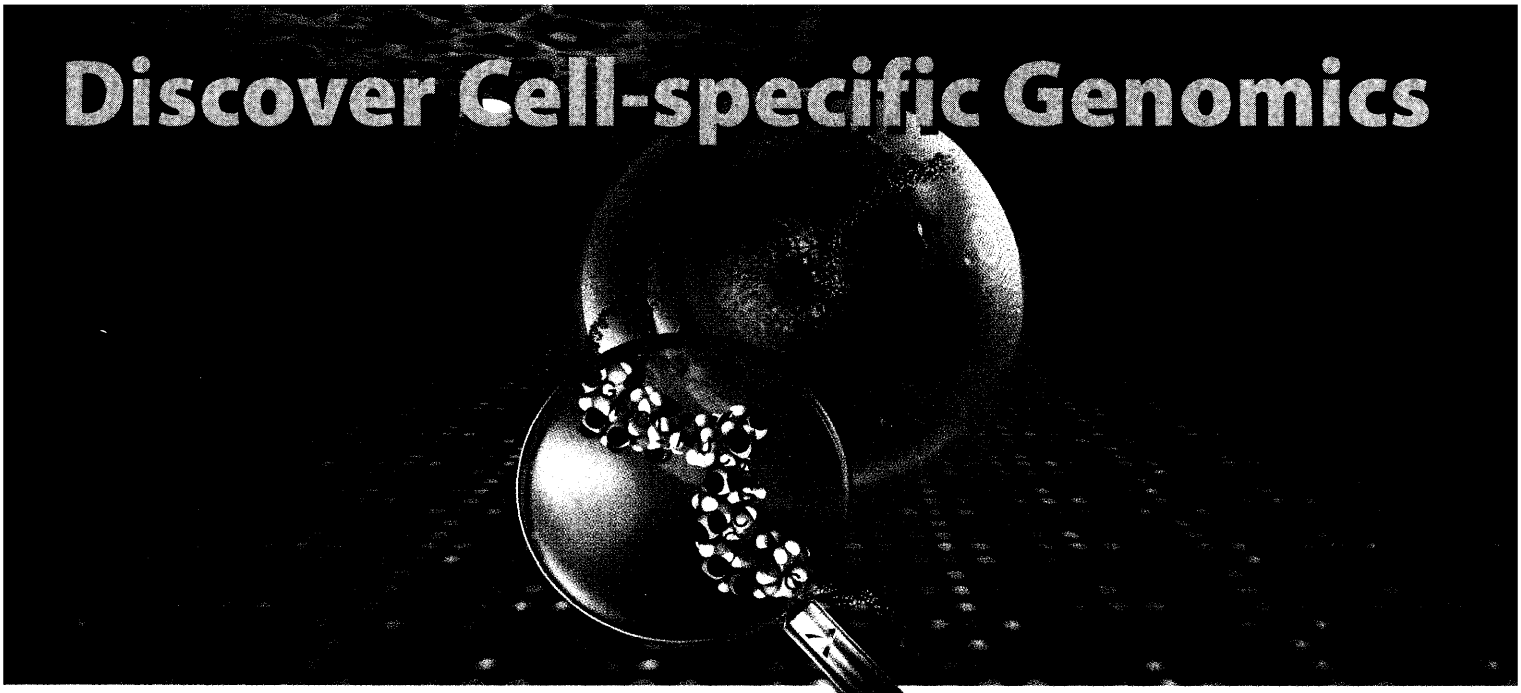
Find out about products advertised in *Science* — *instantly.*

Science's Product Link is a great way to find out about new products advertised or featured in *Science* — *instantly*. Search for products advertised in *Science* by:

product category • company name • page number • keyword

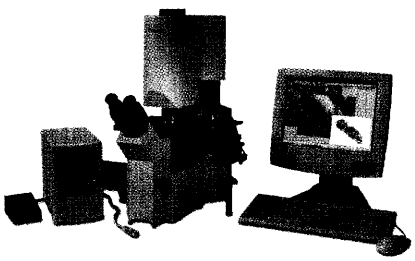
You can look for product information in current and back issues. And you can link to advertisers' websites for more information.

Science



Start with cells instead of tissues. See what you've been missing.

PixCell® II Laser Capture Microdissection System

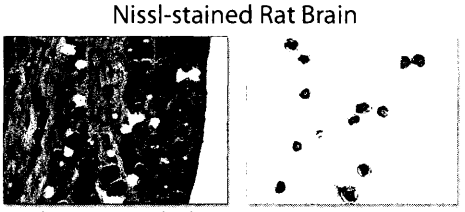


- **Study molecular differences on a cell-specific level**
- **Capture cells with speed and precision using an established method**
- **Visually confirm the identity and quality of captured cells**

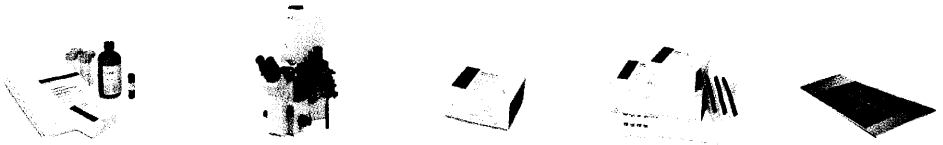
Are you still working with tissues? Focus on the biology of specific cells with the PixCell II Laser Capture Microdissection (LCM) System. Rapidly collect individual cells from heterogeneous tissue sections and cell smears. Nucleic acids and proteins prepared from these small homogeneous populations of cells provide highly specific material for downstream molecular analysis.

Over 200 published articles have made the PixCell II LCM System the new standard in sample preparation. Learn more at www.arctur.com.

Nissl-stained Rat Brain



After capture of cells | Captured neurons



HistoGene™ Tissue Preparation Kits | PixCell® II Laser Capture Microdissection System | PicoPure™ RNA Isolation Kit | RiboAmp™ RNA Amplification Kit | Microarray Processing

ARCTURUS
SYSTEMS FOR MICROGENOMICS

650.962.3020 tel 888.446.7911 toll-free contact@arctur.com **www.arctur.com**