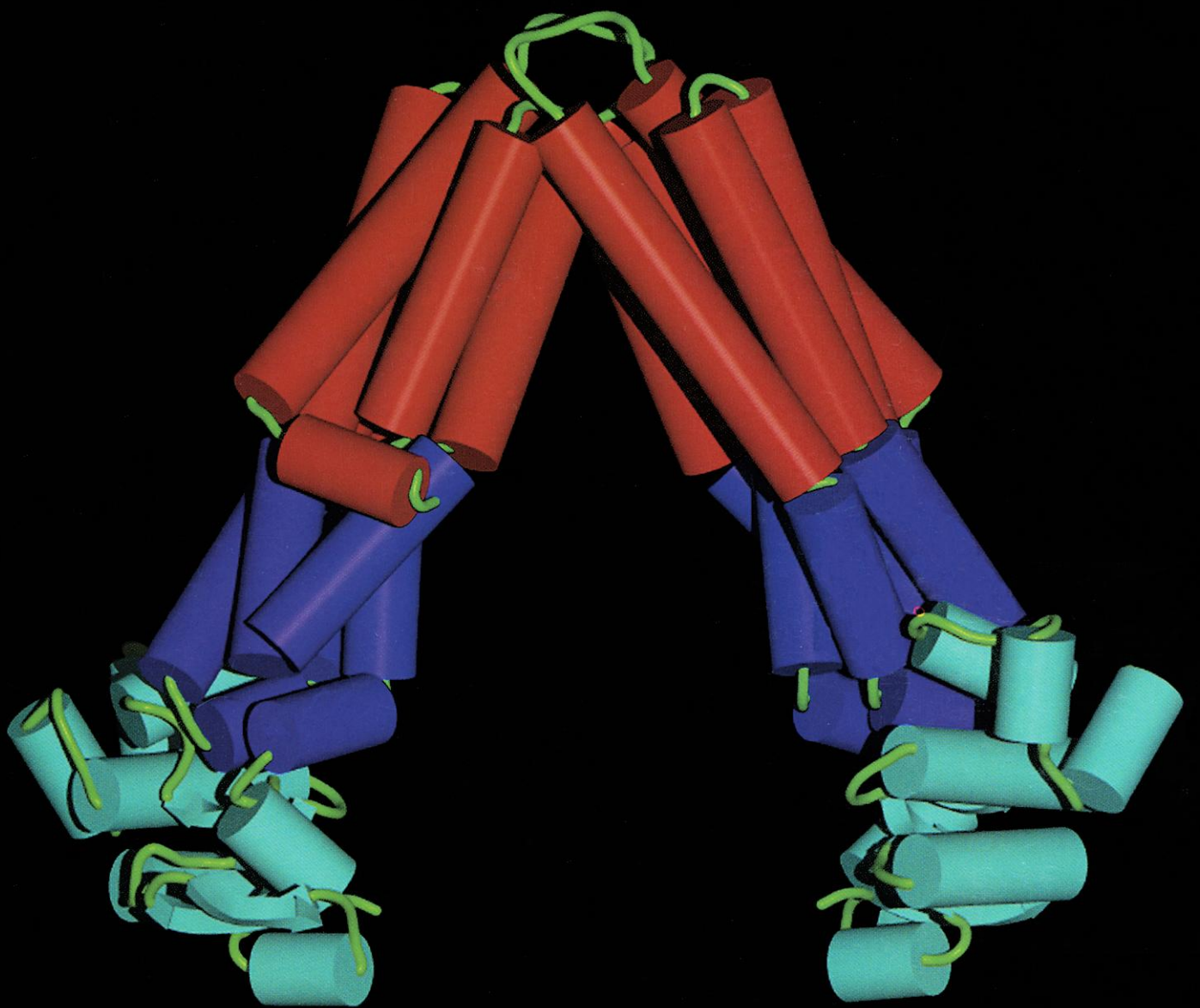
7 September 2001

# Science

Vol. 293 No. 5536
Pages 1717–1940 $9



AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

**Forget the rest—use**

**Save 50% on Sampler Size!**

# GeneJammer™
TRANSFECTION REAGENT

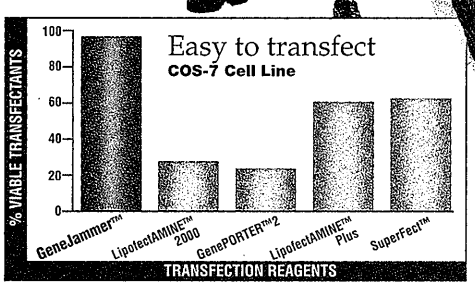
## Stratagene's new polyamine formulation for all your transfections

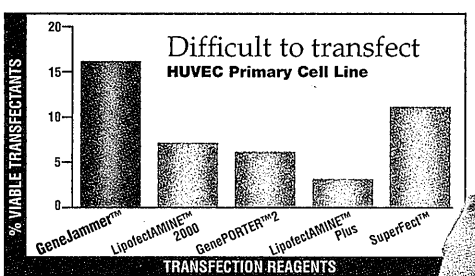
## Really Works

- Ideal for transient or stable transfections
- Successfully transfected in over 100 cell lines*
- Exceptionally low cytotoxicity
- Highest transfection efficiency

## Really Better

Works better in easy- and difficult-to-transfect cells




## Really eliminates the competition!

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

***STRATAGENE EUROPE***
**Belgium, Germany, The Netherlands, Switzerland, United Kingdom**
ORDER: 00800 7000 7000
TECHNICAL SERVICES: 00800 7400 7400
**Austria**
017 956 7036
**France**
00800 7000 7000 or 0800-100391
**INTERNET**
email: techservices@stratagene.com
website: www.stratagene.com

See www.stratagene.com for a current list of successfully transfected cells.

**GeneJammer™ Transfection Reagent**

| | |
|---|---|
| Sampler size | 204132 |
| *(Sampler 50% off while supplies last)* | |
| 1 ml | 204130 |
| 4x 1 ml | 204131 |

STRATAGENE®

Circle No. 30 on Readers' Service Card

# Science

Volume 293 7 September 2001 Number 5536





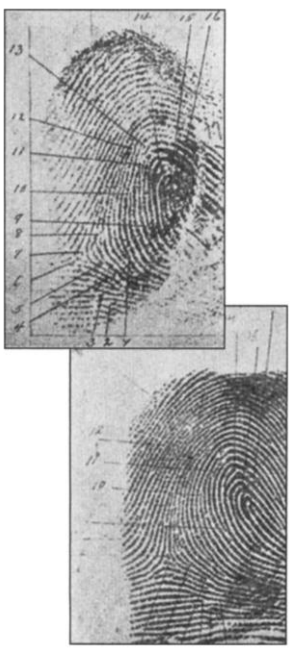

## NEWS





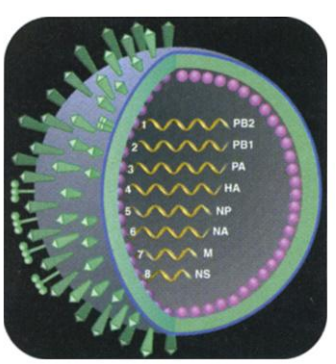


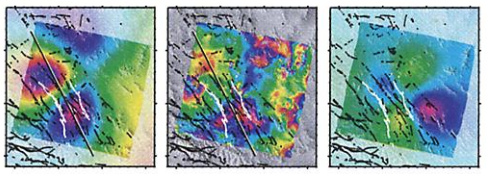
## *SCIENCE*'S COMPASS



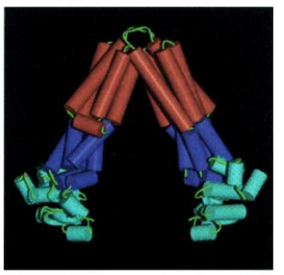








**1814**
Relieving stress by mantle flow



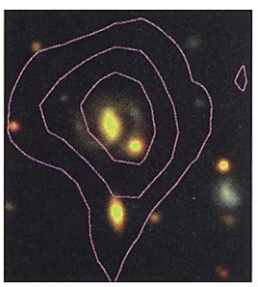
## COVER 1793

Crystal structure of the multidrug resistance ABC transporter homolog MsbA from *Escherichia coli* as viewed from the plane of the lipid bilayer. This class of integral membrane proteins transports hydrophobic molecules such as lipids and drugs across the cell membrane bilayer. The structure of MsbA reveals three domains, which include the transmembrane (red), intracellular (dark blue), and nucleotide-binding (teal) domains. The structure can help elucidate the mechanism underlying multidrug resistance in the treatment of cancer and infectious diseases. [Image: G. Chang and C. B. Roth]

# RESEARCH

### RESEARCH ARTICLE

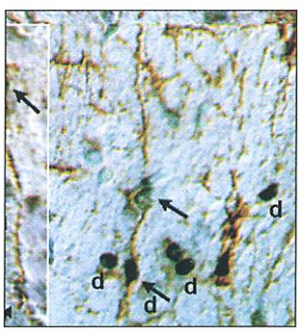




**1800**
Gaseous tracer of cluster formation

### REPORTS






**1820**
Human neural stem cells in the brain

**New on *Science* Express** The MIDAS touch in adhesion


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): $115 ($64 allocated to subscription). Domestic institutional subscription (51 issues): $370; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $87. 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.

# Are you going to fail this test?

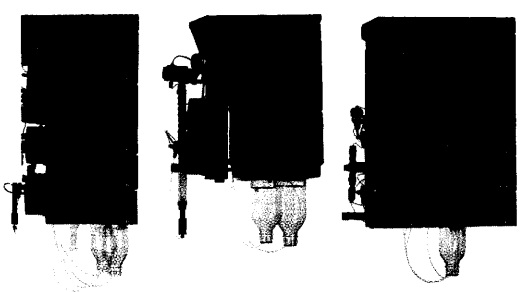
**Ready?**

- Develop a scheme to purify your specific target molecule using the best chromatographic technique
- Make it scaleable to suit all potential steps and stages of research
- To save time and money, identify the optimal column and buffer combination to perform the work today as well as tomorrow
- You have less than 30 seconds to complete the test

Begin

**Want some help? Just rotate this magazine 180°**

amersham pharmacia biotech



We have invested 40 years to make the task of performing separations simpler. Here's how simple it is to perform any separation using any ÄKTA™ system:

- Choose from ready-to-use method templates, available for everything from simple one-step purification to complex column or buffer scouting
- Check running parameters on any ÄKTA using UNICORN™ control software for runs at all stages and scales.
- Inject your sample into one of our pre-packed columns
- Click start

Then walk away, leaving your ÄKTA system to do all of the rest. This gives you the freedom to concentrate on other aspects of your work. You can gain easy access to advice, knowledge and support from the professionals at Amersham Pharmacia Biotech, who have helped make the research activities of countless numbers of scientists simpler. Just go to http://www.apbiotech.com/akta.

Want to simplify your research? Then just remember the letter Ä (as in ÄKTA).

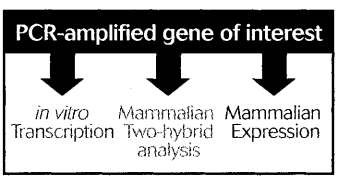
## if you want simpler separations

# Clip, shape, and style the tool of your choice.

## Introducing TOPO® Tools for customized expression.

**To each his own.** Everyone has their own individual style. Now you can express that individuality in your research. TOPO® Tools allows you to create a linear DNA construct that's custom designed for your specific expression needs.

**What'll it be today?** TOPO® Tools uses the combined power of PCR and topoisomerase I to build expression constructs. Simply join the 5′ and 3′ elements of your choice – including promoters and tags – to your amplified gene. Without traditional cloning or transformation, you'll get a functional, linear DNA construct that's ideal for your research. And, you'll save days in the process.




**Style and function.** TOPO® Tools lets you build customized constructs for multiple applications. Mammalian two-hybrid screening, expression analysis in mammalian cells, and production of RNA transcripts are just the beginning. We're designing new 5′ and 3′ elements now. Soon the possibilities will be endless.

Why compromise when you can get what you need with an ideal tool? Call Invitrogen or visit our web site. Express your individuality with TOPO® Tools today.

Invitrogen™
life technologies

Circle No. 17 on Readers' Service Card

**United States Headquarters:**
Invitrogen Corporation
1600 Faraday Avenue
Carlsbad, California 92008
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 (Free Phone Orders): 0800 269 210
Tel (General Enquiries): 0800 5345 5345
Fax: +44 (0) 141 814 6287
Email: eurotech@invitrogen.com

**International Offices:**
Argentina 5411 4556 0844
Australia 1 800 331 627
Austria 0800 20 1087
Belgium 0800 14894
Brazil 0800 11 0575
Canada 800 263 6236
China 10 6849 2578
Denmark 80 30 17 40
France 0800 23 20 79
Germany 0800 083 0902
Hong Kong 2407 8450
India 11 577 3282
Italy 02 98 22 201
Japan 03 3663 7974
The Netherlands 0800 099 3310
New Zealand 0800 600 200
Norway 00800 5456 5456
Spain & Portugal 900 181 461
Sweden 020 26 34 52
Switzerland 0800 848 800
Taiwan 2 2651 6156
UK 0800 838 380
Other countries see our website

# Science online

## www.scienceonline.org

CONTENT HIGHLIGHTS AS OF 7 SEPTEMBER 2001

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

**sciencenow**

www.sciencenow.org

NOW!

## science magazine www.sciencemag.org

### *SCIENCE* EXPRESS www.sciencexpress.org

**Ultrathin Single-Crystalline Silver Nanowire Arrays Formed in an Ambient Solution Phase** B. H. Hong, S. C. Bae, C.-W. Lee, S. Jeong, K. S. Kim

Silver nanowires 4 angstroms in diameter are formed inside the pores of calix[4]hydroquinone nanotubes.

**Prevention of Scrapie Pathogenesis by Transgenic Expression of Anti-Prion Protein Antibodies** F. L. Heppner *et al.*

Immunization with prion proteins in mice induces anti-prion immunity and protects against neuropathological changes associated with scrapie.

▼**Crystal Structure of the Extracellular Segment of Integrin αVβ3** J.-P. Xiong *et al.*
1743 Flexibility and the RGD binding site are hallmarks of integrin structure.

### TECHNICAL COMMENTS

**Interannual Variability in Net Primary Production and Precipitation**

Knapp and Smith (Reports, 19 January 2001, p. 481), drawing on data from 11 Long-Term Ecological Research sites in North America, found that interannual variability in aboveground net primary production (NPP) was not associated with variability in precipitation. Fang *et al.* comment that their own study of trends in China—which compared a normalized difference vegetation index (NDVI) derived from remote-sensing data with historical precipitation data—revealed "a significant positive correlation" between interannual NDVI variability and precipitation variability across the five biome groups studied. In light of that finding, they suggest, "the conclusions of Knapp and Smith need broader investigation." Knapp and Smith, in their response, acknowledge the strengths of remote-sensing data "to robustly test predictions" about ecosystem relationships, but question "a key assumption" of the Fang *et al.* analysis: the notion "that NDVI data can be used to quantify NPP dynamics with equal accuracy and sensitivity across all biomes."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/293/5536/1723a.

## science's stke www.stke.org

**Perspective: Raf-1 Without MEK?** M. S. Murakami and D. K. Morrison

Does Raf-1 have a role in cell proliferation, in protecting cells from apoptosis, or both?

**Review: Ypt/Rab GTPases—Regulators of Protein Trafficking** N. Segev

Getting from here to there, inside and outside cells.

## science's next wave www.nextwave.org

**Canada: Up and Up—Graduate Tuition Fees in Canada on the Rise, Again** L. McKarney

Average graduate tuition fees in Canada have increased for the fifth year straight. But one university is trying to compensate.

**US: Making the Case for Postdoc Lobbying** R. Bartolo

To improve their working conditions, postdocs need to get more involved in shaping the national agenda for the science lobby.

**UK: CD-ROM Review—Scientists in Business** K. Urquhart

Based on interviews with staff at all levels, this resource gives real insight into working in the commercial sector, and firsthand advice to young scientists applying for industry jobs.

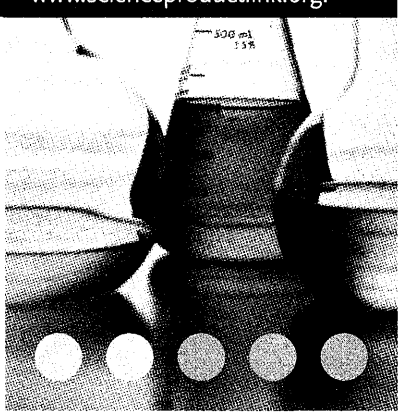
**GrantsNet**
www.grantsnet.org
RESEARCH FUNDING DATABASE

**NEW! AIDScience**
www.aidscience.com
HIV PREVENTION AND VACCINE RESEARCH

**NeuroAIDS**
www.sciencemag.org/NAIDS
EXPERIMENTAL WEB SITE







# THIS WEEK IN Science

edited by Phil Szuromi

## Dealing in Small Volumes

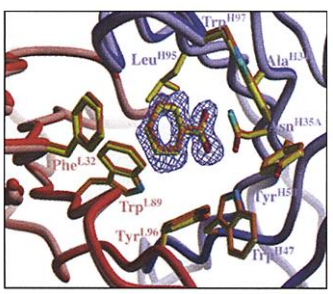
Although pressure-induced solid-state transformations are important in both geology and materials science, they are difficult to understand at a fundamental level because their kinetics can be highly inhomogeneous, and the role of defects can make transition cycles irreproducible. Jacobs *et al.* (p. 1803) tackled this problem by shrinking the sample size to increase homogeneity and eliminate defects. They studied the transition between in CdSe nanoparticles between the low-pressure tetrahedrally bonded phase and the high-pressure, six-coordinate phase. The activation volumes for the forward and reverse transitions are opposite in sign, which indicates the intermediate has a volume in between that of the four- and six-coordinate phases (rather than greater than both). This finding suggests that directionally dependent nucleation occurs that would be consistent with shearing motion along the crystal planes.

## 1800 Galaxies Running Out of Gas

Galaxies that fall into clusters are typically stripped of their cold, neutral hydrogen gas. Zwaan *et al.* (p. 1800) used the recently upgraded Westerbork Synthesis Radio Telescope to search for neutral hydrogen gas of infalling galaxies in older clusters (those at a redshift of about 0.2). They detected hydrogen gas from only one spiral galaxy falling into the Abell 2218 cluster and infer that gas stripping is efficient. This technically challenging detection is consistent with low-density cosmological models.

## Antibodies That Burn Water?

Recently it was shown that antibodies, upon exposure to light, generate hydrogen peroxide through the conversion of photogenerated singlet oxygen. Wentworth *et al.* (p. 1806; see the news story by Service) now show that this process is catalytic, and that the electron source for this reaction is most likely water—not photo-oxidizable residues such as tryptophan, metal ions, nor chloride ions. Water would be oxidized by singlet oxygen to create $H_2O_3$ as an initial intermediate. Crystallographic studies with xenon, a binding-site mimic, suggest that singlet oxygen may be bound near conserved Trp and Tyr residues.




CREDIT: WENTWORTH *ET AL.*

## Firm Numbers

It might be expected that there will be fewer large business firms than smaller ones. However, the specific distribution of businesses as a function of the number of employees is for addressing questions in economics, such as the relation of firm size and capital and the relative importance of small firms. Economists have generally assumed that there should be some cutoff with firm size and that the distribution is lognormal. Axtell (p. 1818) reanalyzed data for the United States' economy and found that the firm sizes have a Zipf distribution, which means that for each 10-fold increase in firm size, the number of firms decreases by 10, and that this distribution has held over time. Thus, there is no cutoff at firm sizes as small as 1 or 2 employees.

## Moving Mantle After the Shock

Large earthquakes deform the continental crust, but it remains unclear whether this deformation is confined to local shearing or more broadly coupled to mantle flow. Pollitz *et al.* (p. 1814) studied 9 months of postseismic geodetic data measured with the global positioning system after the magnitude 7.1 Hector Mine earthquake in California. The observed deformation can be modeled by flow in a relatively low viscosity upper mantle that is coupled to a higher viscosity, stiff lower crust and a more brittle upper crust.

## Pumping Uphill

The ABC transporters, one of the largest classes of membrane proteins engaged in active (energetically uphill) transport, contain a cytoplasmically disposed adenosine triphosphate (ATP)–binding cassette linked to what has been predicted to be a bundle of transmembrane helices (see the Perspective by Higgins and Linton). The subgroup of multidrug resistance (MDR) transporters use the energy from ATP hydrolysis to pump a broad spectrum of hydrophobic drugs out of cells. Chang and Roth (p. 1793; see the cover) have determined the crystal structure at 4.5 angstroms of MsbA, a bacterial ABC transporter that has strong sequence similarity with MDR proteins. Two six-helix bundles form an inverted V shape, intramembrane transport chamber. The authors propose that accessibility to this chamber is regulated cyclically via hydrolysis of ATP at the two globular ABC domains.

## Human Neural Stem Cells

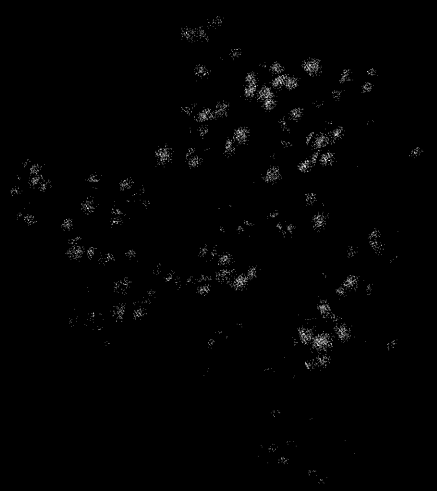
The generative capacity of certain cells found in the adult central nervous system has led to questions of their origin: Are these stem cells set aside during early development, or is their proliferative capacity a result of experimental perturbation? Ourednik *et al.* (p. 1820) addressed this question by transplanting labeled human neuronal stem cells into the developing brain of fetal bonnet monkeys. The transplanted cells both contribute to immediate brain development and also form clusters in the secondary germinal zone.

## Cells Hang On for Dear Life

One explanation for why the development of cancer cells is a relatively rare event is that cells that lose their attachment to a substratum and associated integrin signaling often undergo cell death or apoptosis. Puthalakath *et al.* (p. 1829; see the Perspective by Hunt and Evan) now describe a mechanism by which unattached cells may sense changes in the cytoskeleton and initi-

Published online in *Science* Express

CONTINUED ON PAGE 1727



# NE THIS.

## Or better yet...

**See** it.

**Analyze** it.

**Align** it.

**Dock** it.

***Understand*** **it.**

## Discover BioMedCAChe™

### Finally, software that lets chemists and biologists share discoveries...

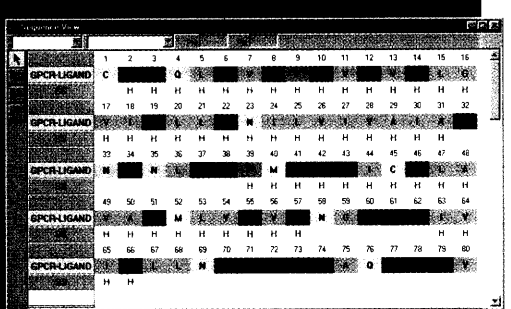
### In One Package – On Your Desktop*

CAChe lets every chemist visualize molecules in 3D, predict conformations, analyze reactivity, predict properties *– before making them in the lab.*

- **Drugs to proteins**
  - Optimize, dock, and model reactions of molecules with tens of thousands of atoms
- **New Sequence Editor**
  - Build, align, edit, mutate, and analyze proteins
- **Model enzyme mechanisms**
  - pKa's, atom charges, binding energies, enzyme kinetics, and more from new quantum chemistry tools
- **Predict any property**
  - Integrated QSAR and QSPR for ADME, LogP, water solubility, Rule-of-5, and more
- **Virtual libraries of compounds**
  - Automate, store, and analyze predicted properties for whole libraries
- **See it all in 3D stereo**
  - –Stereoscopic high-resolution display option

*Windows 95, 98, ME, NT 4.0, and 2000

*Agouti-related protein docked in a homology model of a brain GPCR.*
*(courtesy of Xiang Wang)*




*Protein Sequence Editor*

**Visit our website TODAY: www.CACheSoftware.com/BioMedCAChe**

**Americas**
CAChe Group, Fujitsu
Tel: (1) 503 746 3600
Email: sales@CACheSoftware.com
Web: www.CACheSoftware.com

**Europe**
FQS Poland
Tel: (4812) 429 43 45
Email: ccs@fqspl.com.pl
Web: www.CACheSoftware.com

**Asia**
Fujitsu Ltd
Tel: (81) 43-299-3019
Email: cache@ssd.se.fujitsu.co.jp
Web: www.CACheSoftware.com

FUJITSU



CAChe®

Circle No. 9 on Readers' Service Card

ate the process of apoptosis. A new mammalian Bcl-2 family member called Bmf can promote apoptosis by binding to and inhibiting the pro-survival Bcl-2 proteins. Bmf interacts with dynein light chain 2 and becomes localized to the myosin V motor complex on filamentous actin. In cells in which the actin cytoskeleton was disrupted by treatment with actin-depolymerizing agents or by culture of the cells in suspension (without attachment to a substratum), Bmf was released from its association with the cytoskeleton and freed to interact with Bcl-2. Thus, Bmf appears to function as a sensor that couples alterations in the cytoskeleton to activation of the cell death machinery.

## Pass the Cyanide

Increasingly sophisticated genomic technology has made it feasible to consider transplanting entire metabolic pathways, rather than just single genes encoding single enzymes. Tattersall *et al.* (p. 1826) apply this approach to the plant-pest interaction. By transferring the metabolic pathway for synthesis of a cyanogenic glucoside from *Sorghum* into *Arabidopsis*, the latter plant, the normal host for a flea beetle, is rendered less palatable and even deadly. This type of metabolic engineering may be useful for improving the defense arsenal of other plants as well as for experimental study of plant-pest ecology.

## Distributed Control in a Nervous System

The limited movement of our jointed limbs requires tight control by the central nervous system. Other animals, like the octopus, have flexible arms with much greater degrees of freedom. Sumbre *et al.* (p. 1845) studied movement generation and control in octopus arms in which the connection between the arm's peripheral nervous system and the brain was severed. Arm extension could be elicited by electrically stimulating the arm's nervous system or by touching the arm's skin. The evoked movements were practically identical to natural reaching movements in normal animals. Control of the complex flexible arms of the octopus appears to be distributed between the central nervous system, which gives the overall direction of a planned movement, and the peripheral system that implements the finer details.

CREDIT: SUMBRE *ET AL.*

## Measure Twice, Cut Once

Genes contain both exons, which encode the amino acid sequence, and introns, which do not. The latter must be removed from the pre–messenger RNA (mRNA) transcript with great exactitude—a single base error may result in premature termination of translation as a consequence of a shift in reading frame. In order to guard against synthesizing truncated and potentially deleterious proteins, a multisubunit complex is used to "mark" the place where exons have been joined. If translation terminates upstream of any such mark, then the mRNA is shunted into a degradation pathway called nonsense-mediated decay (NMD). Kim *et al.* (p. 1832) and Lykke-Andersen *et al.* (p. 1836) now provide the first evidence for physical interaction between components of the mark and those of NMD.

## Clues to Lethal Flus

Clues into the molecular basis for the lethality of some outbreaks of influenza A in this century are the subject of two reports (see the Editorial by Layne and the Perspectives by Webster and by Laver and Garman). The1918 influenza pandemic swept through the United States Army and escaped to slaughter more young adults than did World War I. A reanalysis of the gene sequences by Gibbs *et al.* (p. 1842) indicates that a recombination event between swine and human lineages in the hemagglutinin gene of the virus triggered the pandemic. This event would have meant a change in antigenicity, and owing to the previous demography of flu, the immunologically naïve population was apparently precisely the age group that showed the highest mortality from severe lower respiratory tract oedema and hemorrhage. In 1997, a strain of influenza A transmitted from birds killed 6 of 18 infected persons in Hong Kong. Hatta *et al.* (p. 1840) infected mice with human viral isolates and found that a mutation at position 627 of polymerase 1 and cleavabililty of the hemagglutanin glycoprotein had the greatest effects on pathogenecity.

# PolyFect® Transfection Reagent

## Fast and easy transfection, with protocols for:

293

COS-7

HeLa

NIH/3T3

CHO

- Optimized protocols for COS-7, NIH/3T3, HeLa, 293, and CHO cells
- Fast procedure and easy handling
- No removal of complexes required

- Transfection in the presence of serum
- High efficiency
- Economical price

## Transfection has never been so simple — order PolyFect Reagent today!



www.qiagen.com

Circle No. 24 on Readers' Service Card

**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**
Tel. 01293-422-999
Fax 01293-422-922

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

**Distributors:**

**Argentina** Tecnolab S.A. (011) 4555 0010 **Austria/Hungary/Slovenia** R. u. P. MARGARITELLA Austria (01) 889 18 19 **Belgium/Luxemburg** Westburg b.v. 0800-1-9815 **Brazil** 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. (02)4447 1239 **Denmark** Merck Eurolab A/S 43 86 87 88 **Egypt** Clinilab 525 7212 **Finland** Merck Eurolab Oy (09)-804 551 **Greece** BioAnalytica S.A. (01)-640 03 18 **India** Genetix (011)-542 1714 or (011)-515 9346 **Israel** Westburg (Israel) Ltd. 08 66 50 813 or 1-800 20 22 20 **Korea** LRS Laboratories, Inc. (02) 924-86 97 **Malaysia** Research Bialabs Sdn. Bhd. (03)-7312099 **Mexico** Quimica Valaner S.A. de C.V. (5) 525 57 25 **The Netherlands** Westburg b.v. (033)-4950094 **New Zealand** Bialab Scientific Ltd. (09) 980 6700 or 0800 933 966 **Norway** Merck Eurolab 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 (1)-424 73 64 **Singapore** Research Bialabs Pte Ltd 2731066 **Slovak Republic** BIO-CONSULT Slovakia spol. s.r.o. (07) 50221 336 **South Africa** Southern Cross Biotechnology (Pty) Ltd (021) 671 5166 **Spain** IZASA, S.A. (93) 902.20.30.90 **Sweden** Merck Eurolab 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

H05200115WW

# "Sorry officer, I didn't realize I was purifying samples so fast."

The ABI PRISM™ 6100 Nucleic Acid PrepStation. It takes nucleic acid sample prep to the limit.

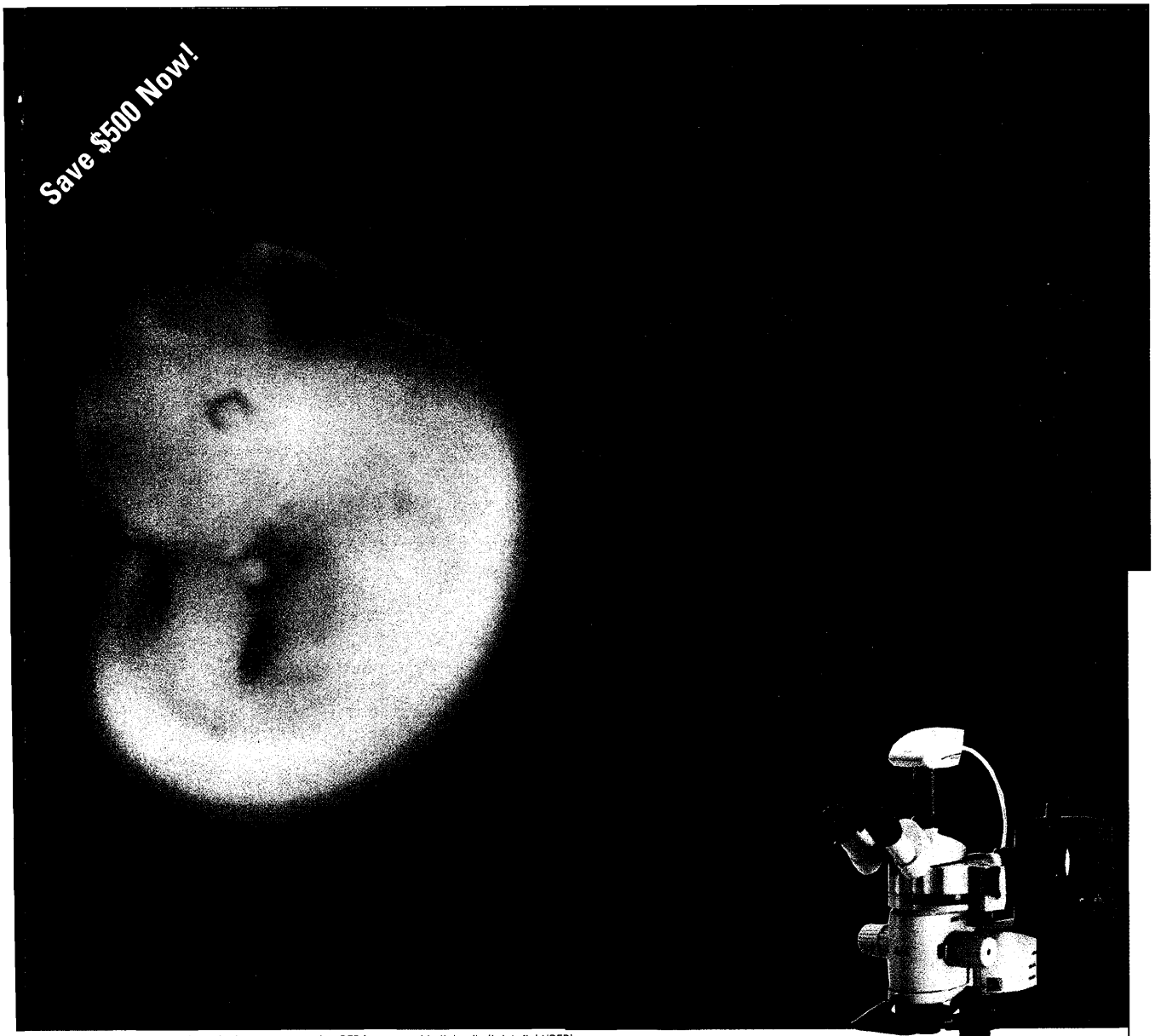
Want faster sample throughput? Take a spin with the ABI PRISM™ 6100 PrepStation. It automates the slowest part of the process—taking the time, error, and tedium out of nucleic acid sample prep. For you, this means higher sample quality. It purifies a range of nucleic acids in a 96-well format, including RNA and gDNA. Moreover, the 6100 PrepStation lets you use the same superior reagents and consumables as the ABI PRISM™ 6700 Automated Nucleic Acid Workstation. Maybe your speed limit's higher than you think. To find out more, visit **www.appliedbiosystems.com/6100**, or talk with an Applied Biosystems sales rep at **1.650.638.5800.**

Applied Biosystems

Data. Decision. Discovery.



Circle No. 14 on Readers' Service Card




Transgenic mouse at embryonic day 11.5 expressing GFP in neuroepithelial cells (brightfield/GFP)
Courtesy of Masahiro Yamaguchi, Department of Physiology, University of Tokyo Faculty of Medicine

# The Freedom to Focus

Leica research microscopes are designed with results in mind. All functions have been carefully engineered to allow you to focus on your experiment, not on your equipment.

No matter what the application, be it vesicle fusion in ***C. elegans***, protein stabilization in **Drosophila**, or protein localization in **Zebrafish**, and whether you are using **GFP+**, **DsRed**, **DAPI**, or all three simultaneously, Leica has the instrument for you!

The Leica MZFLIII fluorescence stereomicroscope is:

- Adaptable – FLUO III™ allows you to change filters in 'the blink of an eye'
- Cutting Edge – Patented TripleBeam™ technology yields high signal-to-noise ratio
- Ergonomic – Comfortable viewing for late night and all day lab sessions

Call 800-248-0123 today for more information on how you can save $500 while making your stereomicroscopes more comfortable to use.

**Fluorescence** **Live Cell Imaging** **Integrated Solutions**

Leica Microsystems Inc.
2345 Waukegan Road
Bannockburn, IL 60015

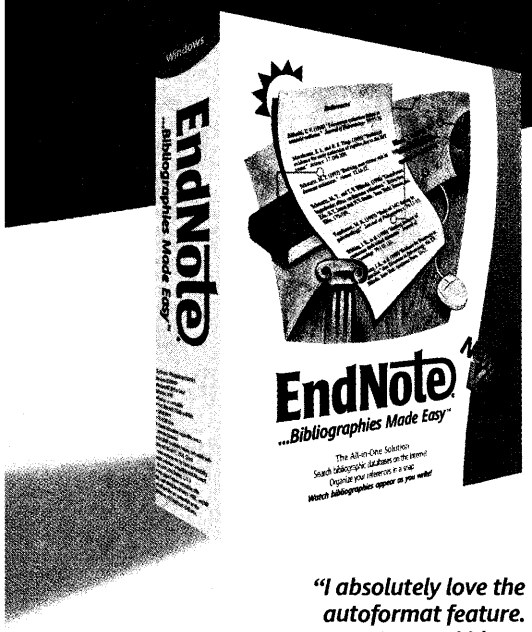
Telephone (847) 405-0123 (800) 248-0123
Fax (847) 405-0164
In Canada Call (800) 205-3422
www.leica-microsystems.com

Leica
MICROSYSTEMS



Circle No. 12 on Readers' Service Card

# The easy bibliography writer




***"I absolutely love the autoformat feature. Very cool idea."***

*—Adam Summers, University of California, Berkeley*

***"Cite While You Write is the crown jewel of EndNote"***

*—Alistair Campbell, Lincoln University, New Zealand*

**Watch bibliographies appear as you write!**

EndNote 5 achieves a new level of integration with Microsoft Word®, making it the easy bibliography writer. With it you can locate and insert citations without leaving Word. EndNote 5's new instant formatting creates your bibliography as you write—no waiting, no guessing, no extra steps. And EndNote knows the bibliographic rules for over 700 styles, so you save time and increase accuracy!

**Publish your papers faster!**

Writing today is a collaborative effort among co-authors, editors and publishers. EndNote 5 helps you collaborate with its new traveling library. Manuscripts contain a hidden traveling library with complete reference data for all citations. When you're ready to send your paper to colleagues, the references travel with it.

When your manuscript is complete, use EndNote 5 to create a publication-ready document in one step!

**Access more content with EndNote 5!**

Most of your research today is done online. Through EndNote 5's easy interface, you can connect to over 280 online sources including subscription resources such as the ISI® *Web of Science*®, Ovid and SilverPlatter, as well as PubMed and hundreds of other public databases. Imagine the time you'll save looking for references to journals, books and other materials with your EndNote 5 personal library. And, you'll never have to re-type a reference!

It's easy to see why over 300,000 researchers, writers and students use EndNote as their easy bibliography writer. Visit **www.endnote.com** and download a **free** demo today for Windows or Macintosh.

***The #1 Bibliographic Program More than 300,000 users worldwide!***

EndNote New V5
...Bibliographies Made Easy™

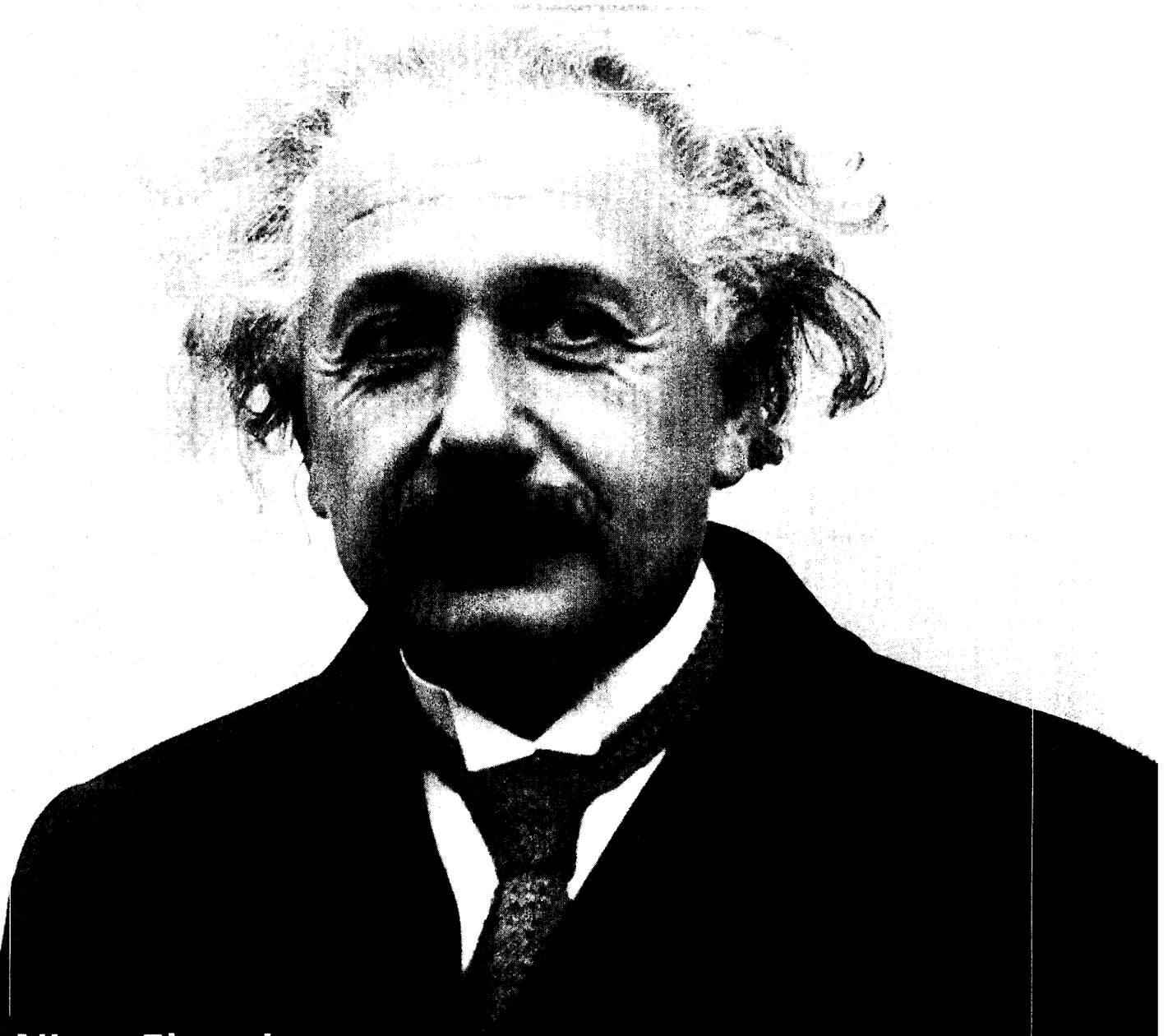
ISI RESEARCHSOFT
THOMSON SCIENTIFIC

Phone: 760-438-5526
Fax: 760-438-5573
E-Mail: info@isiresearchsoft.com
www.endnote.com

ISI Web of KNOWLEDGE



Circle No. 11 on Readers' Service Card



**Albert Einstein** figured out that time and space are relative.
And he knew that nothing could move faster than the speed of light. But when it came to things like money, he **never wasted time thinking** about it. That's where we came in, the people with over 80 years' experience managing portfolios for the world's sharpest minds. Today we could offer Professor Einstein, one of our earliest participants, an even bigger universe to pick from.

**Log on for ideas, advice, and results. TIAA-CREF.org or call 1.800.842.2776**

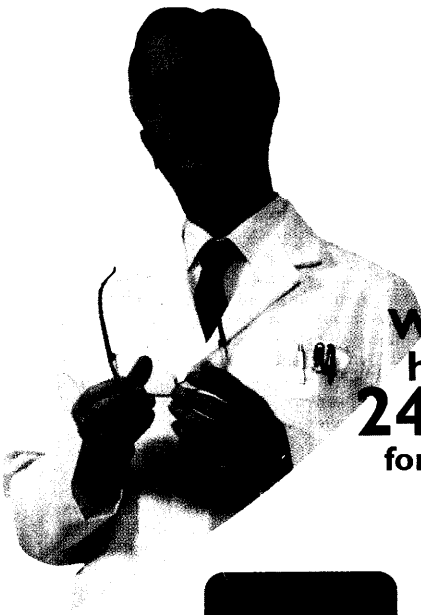
TIAA CREF

*Managing money for people with other things to think about.*

RETIREMENT | INSURANCE | MUTUAL FUNDS | COLLEGE SAVINGS | TRUSTS | INVESTMENT MANAGEMENT

Albert Einstein became a participant in 1933. TIAA-CREF Individual and Institutional Services, Inc., and Teachers Personal Investors Services, Inc., distribute securities products. © 2001 Teachers Insurance and Annuity Association-College Retirement Equities Fund (TIAA-CREF), New York, NY.
Albert Einstein™ licensed by the Hebrew University of Jerusalem, represented by the Roger Richman Agency, Inc., www.albert-einstein.net

Circle No. 23 on Readers' Service Card



# CHARIOT™

## The Vehicle of the Future for Protein Transfection

**Why do I have to wait 24-48 hours for gene expression?**

There is no need to wait 24-48 hours for gene expression from a transfected plasmid. CHARIOT is a revolutionary new transfection reagent which bypasses normal transcription-translation associated with transfected gene expression. CHARIOT allows the researcher to efficiently transfect a variety of cell lines with:

• Peptides • Proteins • Antibodies

CHARIOT is simply mixed with the peptide, protein or antibody of interest and allowed to form a non-covalent complex, which is added to the cells. CHARIOT is serum independent and transfection occurs within 2 hours.

Applications:

- *in vivo* delivery of antibodies, enzymes, regulators
- delivery of inhibitory peptides
- organelle labeling
- protein half-life studies
- transient complementation studies

**FIG. 1** Cells are not fixed

Actin filament labeling of human fibroblast (HS68) cells using anti-actin antibody delivered by CHARIOT. (65% transfection efficiency)

**FIG. 2** Cells are fixed

**FIG. 3** CHARIOT delivery of a 10 kDa protein, labeled with lucifer yellow at the C-terminus, to the nucleus of human fibroblast (HS68) cells. Cells are not fixed. (70% transfection efficiency after 30 min. incubation)

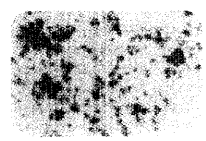
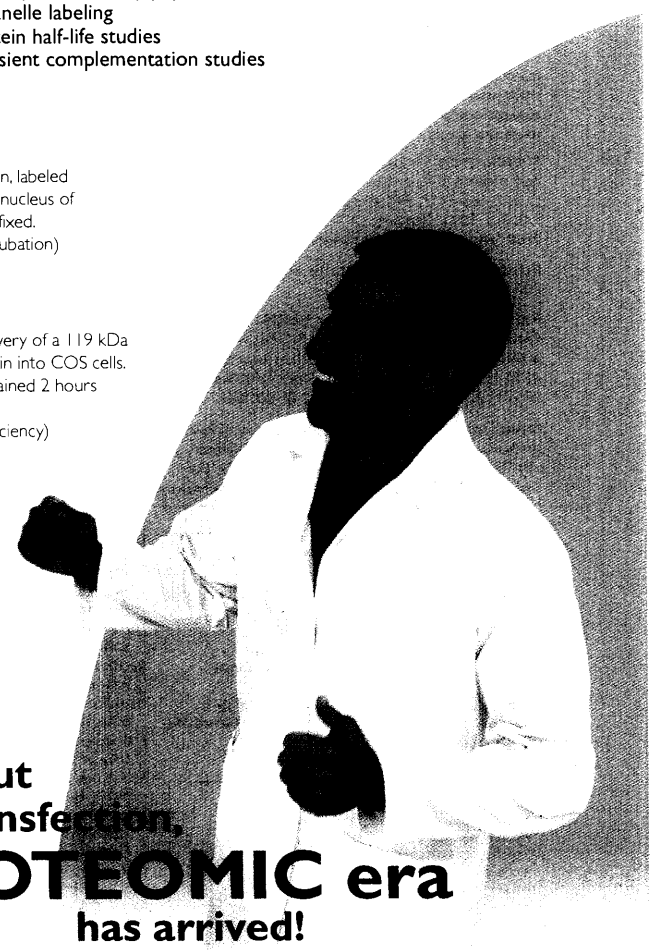


**FIG. 4** CHARIOT delivery of a 119 kDa β-galactosidase protein into COS cells. Cells are fixed and stained 2 hours post-transfection. (60% transfection efficiency)

## CHARIOT Advantages

- Allows for the transfection of peptides, proteins and antibodies
- Can be used to study living cells, no fixing required
- Serum independent
- No need to generate fusion proteins
- Fast and efficient
- Non-cytotoxic
- Non-covalent complex



**Forget about DNA transfection, the PROTEOMIC era has arrived!**

For more information, visit our website:
www.activemotif.com

Or call:
**North America** Toll Free 1.877.222.9543 Direct 760.431.1263
**Europe** Toll Free 00.800.222.95430 Direct 322.653.0001
**Japan** Direct 03.5684.1622

ACTIVE MOTIF

Molecular Biology Tools for Gene Discovery

Circle No. 29 on Readers' Service Card

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), L. Bryan Ray, Linda R. Rowan; ASSOCIATE EDITORS Lisa D. Chong, Marc S. Lavine, Beverly A. Purnell, H. Jesse Smith, Valda Vinson; EDITOR, *SCIENCE* ONLINE Stewart Wills; ASSOCIATE ONLINE EDITOR Chris Grunter; ASSOCIATE BOOK REVIEW EDITOR Sherman J. Suter; ASSOCIATE LETTERS EDITOR Christine M. Pearce; INFORMATION SPECIALIST Janet Kegg; CONTRIBUTING EDITOR Kevin Ahern; EDITORIAL MANAGER Cara Tate; SENIOR COPY EDITORS Jeffrey E. Cook, Harry Jach, Etta Kavanagh, Barbara P. Ordway; COPY EDITORS Joshua Marcy, Monique Martineau; EDITORIAL COORDINATORS Carolyn Kyle, Ellen E. Murphy, Beverly Shields; PUBLICATIONS ASSISTANTS Chris Filiatreau, Joi S. Granger, Jeffrey Hearn, Charlene King, Elise Laffman, Gail Murphy, Anita Wynn; EDITORIAL ASSISTANT Patricia M. Moore; EDITORIAL SUPPORT ASSISTANTS Osa Atoe, Yolanda Matthews, Brian White; EXECUTIVE ASSISTANT Sylvia S. Kihara; ADMINISTRATIVE SUPPORT Patricia F. Fisher

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

**NEWS** SENIOR CORRESPONDENTS Eliot Marshall, Jean Marx; DEPUTY NEWS EDITORS Robert Coontz, Jeffrey Mervis, Leslie Roberts; CONTRIBUTING EDITORS Elizabeth Culotta, Polly Shulman; NEWS WRITERS Martin Enserink, Laura Helmuth, Constance Holden, Jocelyn Kaiser, Richard A. Kerr, Andrew Lawler (Boston), David Malakoff, Elizabeth Pennisi, Charles Seife, Robert F. Service (Pacific NW), Gretchen Vogel, Joshua Gewolb (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 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, Sarah Parker; ADMINISTRATIVE SUPPORT Janet Mumford, Liz Ellis, Viv Hogarth; NEWS: EUROPEAN NEWS EDITOR Richard Stone, CORRESPONDENT Michael Balter (Paris: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00); CONTRIBUTING CORRESPONDENT Robert Koenig (Bern); Ben Shouse (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 **Richard S. Nicholson**
ASSOCIATE PUBLISHER **Beth Rosner**
MEMBERSHIP/CIRCULATION DIR. **Michael Spinella**

**MEMBERSHIP/CIRCULATION** (membership@aaas.org) DEPUTY DIRECTOR Marlene Zendell; MEMBER SERVICES: MANAGER Michael Lung; SENIOR SPECIALIST Mary Curry; COORDINATOR Jantell Stone; SPECIALISTS Laurie Baker, Pat Butler, Elizabeth Early, Katrina Smith; MARKETING: MANAGER Gregory Urquhart; PRODUCTION MANAGER Lauri Sirois; ASSOCIATE Deborah Stromberg; INTERNATIONAL MARKETING MANAGER Ruth Jackson; 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 800-407-9190; Corrections 202-326-6501

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

**FINANCE AND ADVERTISING** BUSINESS MANAGER Deborah Rivera-Wienhold; SENIOR ANALYST Randy Yi; FINANCIAL ANALYSTS Lisa Donovan, Jessica Tierney-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 ASSOCIATE 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: 978-969-1542, FAX 413-480-0008• MIDWEST Rick Bongiovanni: 330-405-7080, FAX 330-405-7081 • WEST COAST/W. CANADA 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 • TRAFFIC MANAGER Carol Maddox; TRAFFIC ASSOCIATE Halimah S. Whitby; SENIOR SALES ASSOCIATE Sheila Myers

**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, Jody Fenty, Christina Geiger, Bren Peters-Minnis; ASSISTANTS Sussy Castilla, Emnet Tesfaye; ASSOCIATES Christine Hall, Dina Freeman; PUBLICATIONS ASSISTANTS Robert Buck, Jane Vaughn; U.K./EUROPE: SALES MANAGER Debbie Cummings; 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 Mary L. Good; PRESIDENT Peter H. Raven; PRESIDENT-ELECT Floyd E. Bloom; TREASURER David E. Shaw; EXECUTIVE OFFICER Richard S. Nicholson; BOARD Lewis M. Branscomb; Nina V. Fedoroff; Karen A. Holbrook; Sally Gregory Kohlstedt; Richard A. Meserve; Robert C. Richardson; Neena B. Schwartz; 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 145 and 146 of the 5 January 2001 issue or access www.sciencemag.org/misc/con-info.shtml

**SENIOR EDITORIAL BOARD**
John I. Brauman, Chair, *Stanford Univ.*
Philip H. Abelson, *AAAS*
Joseph L. Goldstein, *Univ. of Texas Southwestern Med. Ctr.*
Richard Losick, *Harvard Univ.*
Robert May, *Univ. of Oxford*
Marcia McNutt, *Monterey Bay Aquarium Research Inst.*
Vera C. Rubin, *Carnegie Institution of Washington*
Christopher R. Somerville, *Carnegie Institution of Washington, Stanford*
Yoshinori Tokura, *Univ. of Tokyo*
Gerhard Wegner, *Max Planck Inst. of Polymer Research, Mainz*

**BOOK REVIEW BOARD**
David Bloom, *Harvard Univ.*
Michael S. Gazzaniga, *Dartmouth College*
Richard Shweder, *Univ. of Chicago*
Robert Solow, *Massachusetts Inst. of Technology*
David Voss, *Science*
Ed Wasserman, *DuPont*
Lewis Wolpert, *Univ. College, London*

**BOARD OF REVIEWING EDITORS**

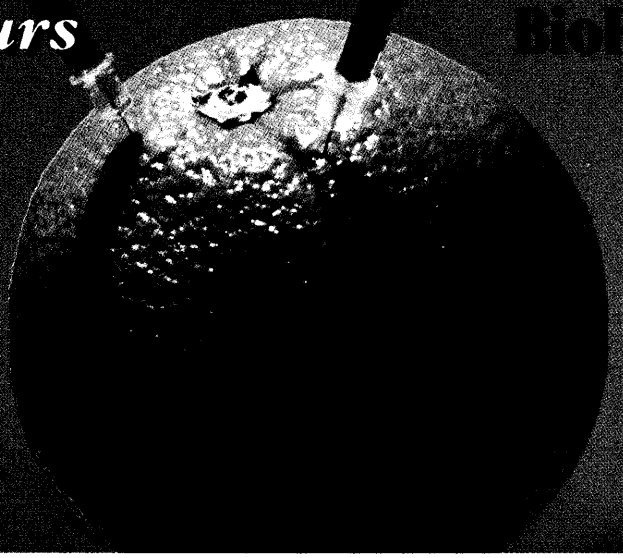
Frederick W. Alt, *Children's Hospital, Boston*
Edouard Bard, *Univ. d'Aix-Marseille III*
Frank S. Bates, *Univ. of Minnesota*
Ray H. Baughman, *Univ. of Texas, Dallas*
Stephen J. Benkovic, *Pennsylvania St. Univ.*
Michael J. Bevan, *Univ. of Washington*
Ton Bisseling, *Wageningen University*
Seth S. Blair, *Univ. of Wisconsin*
Mark Boguski, *NCBI, NIH*
Henry R. Bourne, *Univ. of California, San Francisco*
Lewis M. Branscomb, *Kennedy School, Harvard Univ.*
Joseph A. Burns, *Cornell Univ.*
Dennis W. Choi, *Washington Univ. School of Medicine, St. Louis*
Joanne Chory, *The Salk Institute*
David Clapham, *Children's Hospital, Boston*
Jonathan D. Cohen, *Princeton Univ.*
Daniel G. Colley, *Centers for Disease Control*
F. Fleming Crim, *Univ. of Wisconsin*
Robert Desimone, *NIMH. NIH*
Julian Downward, *Imperial Cancer Research Fund*
Gerhard Ertl, *Fritz-Haber-Institut, Berlin*
Paul G. Falkowski, *Rutgers Univ.*
Douglas T. Fearon, *Univ. of Cambridge*
Jeffrey S. Flier, *Harvard Medical School*
Richard Fortey, *The Natural History Museum, London*
Yves Frégnac, *Unité de Neurosciences Intégratives et Computationnelles, CNRS, Gif-sur-Yvette*
Chris D. Frith, *Univ. College London*
Don Ganem, *Univ. of California, SF*
James Gimzewski, *Univ. of California, LA*
Alex Halliday, *ETH Zentrum, Zürich*
Paul Harvey, *Univ. of Oxford*
Martin Heimann, *Max Planck Institute of Biogeochemistry, Jena*
Tasuku Honjo, *Kyoto Univ.*
Evelyn L. Hu, *Univ. of California, SB*
Herbert Jäckle, *Max Planck Institute for Biophysical Chemistry, Göttingen*
Meyer B. Jackson, *Univ. of Wisconsin Medical School*
Stephen Jackson, *Univ. of Cambridge*
Bernhard Keimer, *Max Planck Inst. for Solid State Research, Stuttgart*
Christian Körner, *Botanisches Institut, Basel*
Alan B. Krueger, *Princeton Univ.*
Michael LaBarbera, *Univ. of Chicago*
Angus I. Lamond, *Univ. of Dundee*
Antonio Lanzavecchia, *Inst. of Res. in Biomedicine, Bellinzona, Switzerland*
Anthony J. Leggett, *Univ. of Illinois, Urbana-Champaign*
Norman L. Letvin, *Beth Israel Deaconess Medical Center, Boston*
Richard Losick, *Harvard Univ.*
Raul Madariaga, *École Normale Supérieure, Paris*
George M. Martin, *Univ. of Washington*
Diane Mathis, *Harvard Medical School*
Andrew Murray, *Harvard Univ.*
Elizabeth G. Nabel, *NHLBI, NIH*
Shigekazu Nagata, *Osaka Univ. Medical School*
James Nelson, *Stanford Univ. School of Medicine*
Roger Nicoll, *Univ. of California, SF*
Roy R. Parker, *Univ. of Arizona*
Michele Parrinello, *Centro Svizzero di Calcolo Scientifico*
Linda Partridge, *Univ. College London*
Suzanne Pfeffer, *Stanford Univ. School of Medicine*
Stuart L. Pimm, *Columbia Univ.*
Danny Reinberg, *Univ. of Medicine and Dentistry-New Jersey*
Janet Rossant, *Univ. of Toronto*
Erkki Ruoslahti, *The Burnham Institute*
David G. Russell, *Cornell Univ.*
Georg Schulz, *Albert-Ludwigs-Universität Freiburg*
Terrence J. Sejnowski, *The Salk Institute*
Kazuo Shinozaki, *RIKEN, Tsukuba Inst.*
Manfred Sigrist, *ETH Hönggerberg, Zürich*
Susan Solomon, *NOAA*
Christopher R. Somerville, *Carnegie Institution of Washington, Stanford*
Will J. Stewart, *Marconi Caswell, Towcester*
Edward I. Stiefel, *ExxonMobil Research and Engineering*
Bruce Stillman, *Cold Spring Harbor Lab.*
Cliff Tabin, *Harvard Medical School*
Tomoyuki Takahashi, *Univ. of Tokyo*
Marc Tessier-Lavigne, *Univ. of California, SF*
Joan S. Valentine, *Univ. of California, Los Angeles*
Michiel van der Klis, *Astronomical Inst. of Amsterdam*
Derek van der Kooy, *Univ. of Toronto*
Bert Vogelstein, *Johns Hopkins*
Arthur Weiss, *Univ. of California, San Francisco*
R. Sanders Willams, *Duke University*
Ian A. Wilson, *The Scripps Res. Inst.*
Richard A. Young, *The Whitehead Inst.*
Martin Zatz, *NIMH, NIH*
Walter Zieglgänsberger, *Max Planck Institute of Psychiatry, Munich*
Maria Zuber, *Massachusetts Inst. of Technology*

# Easy and Efficient Delivery of DNA or Protein.

## *The choice is yours*

GenePORTER 2

BioPORTER

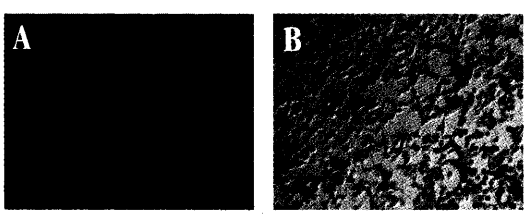


Satisfaction Guarantee
Easy Optimization
Great Results
Higher Efficiencies
Satisfaction Guarantee

Whether you need efficient DNA transfection or direct functional protein transduction, GTS provides the ultimate delivery solution. GenePORTER™ 2 and BioPORTER® reagents are two lipid-based systems designed to satisfy your specific molecular delivery needs.*[1]

## GenePORTER 2 DNA Transfection Reagent:

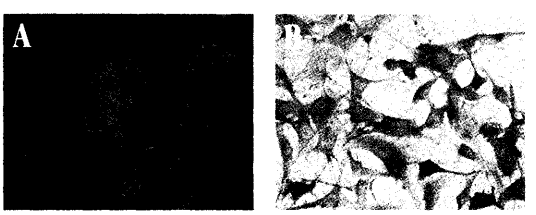
- **High efficiency in hard-to-transfect cell lines**
- **Excellent results with or without serum**
- **Robust performance in diverse cell types**
- **Minimized cytotoxicity**




**Transfection using GenePORTER 2**
A. Rhodamine labeled vector in murine macrophage cells (Courtesy of Dr. Xinsheng Xiong, Scripps Research Inst.)
B. Vector expressing β-gal in HeLa cells

## BioPORTER Protein Delivery Reagent:

- **Direct delivery of proteins into living cells**
- **Intact protein functionality**
- **Great protein uptake efficiency**
- **Fast and easy protocol**




**Protein delivery into mouse fibroblast cells**
A. FITC-labeled antibody/BioPORTER
B. β-galactosidase/BioPORTER

Count on superior efficiency and great functional results. GenePORTER and BioPORTER make molecular delivery effortless no matter what your needs are. Call GTS or your nearest distributor and order today.

GTS
*Advanced Delivery Tools*

| | |
|---|---|
| **GenePORTER™ 2 Transfection Reagent** | |
| QuikEase™ kit (96 single-use vials) | Cat. #T202096 |
| 75 reactions | Cat. #T202007 |
| 150 reactions | Cat. #T202015 |
| 750 reactions. | Cat. #T202075 |
| **BioPORTER® Protein Delivery Reagent** | |
| QuikEase™ kit (24 single-use vials) | Cat. #BP502424 |
| QuikEase™ kit (96 single-use vials) | Cat. #BP509696 |
| 24 reactions | Cat. #BP502401 |
| 96 reactions | Cat. #BP509604 |


**To Order: 888-428-0558**
**Fax: 858-623-9494**
**10190 Telesis Court**
**San Diego, CA 92121, USA**
*For distributors and more information go to:*
**http://www.genetherapysystems.com**


* Patents pending.


1. Zelphati, O *et al.* (2001) Paper in press: *J. Biol Chem.* published on July 10, 2001 as manuscript M104920200

# The W. M. Keck Foundation Is Proud To Announce Its Third Class Of Distinguished Young Scholars In Medical Research

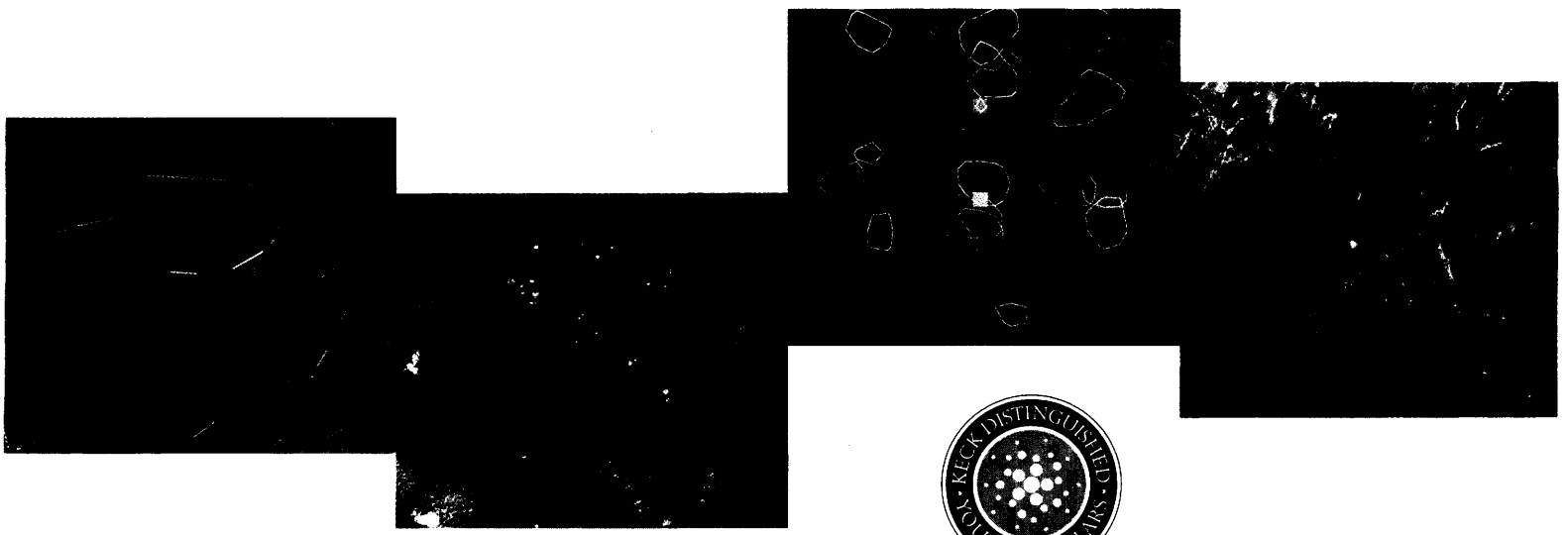
*Dr. Michael Caterina, Johns Hopkins University*
*Dr. Barry Condron, University of Virginia*
*Dr. Katrina Forest, University of Wisconsin, Madison*
*Dr. Xi He, Harvard University*
*Dr. Kelsey Martin, University of California, Los Angeles*

The W. M. Keck Foundation Distinguished Young Scholars in Medical Research Program is a five-year, $25 million initiative designed to give 25 of the nation's best young scientists the financial resources they need to pursue bold ideas now, at the time in their careers when their great creative potential typically exceeds their ability to attract sufficient funding.

Under the program, each institution will receive a grant of up to $1 million to fund these distinguished young scholars' pioneering research into the fundamental mechanisms of human disease.

Selected for their ability to carry forward groundbreaking basic medical research, potential for making a significant impact on the field of biomedicine, and capacity for future leadership, The W. M. Keck Foundation believes these investigators will make profound advancements in critical areas of medical research.

We are proud to offer them our congratulations and ongoing support.



KECK DISTINGUISHED YOUNG SCHOLARS

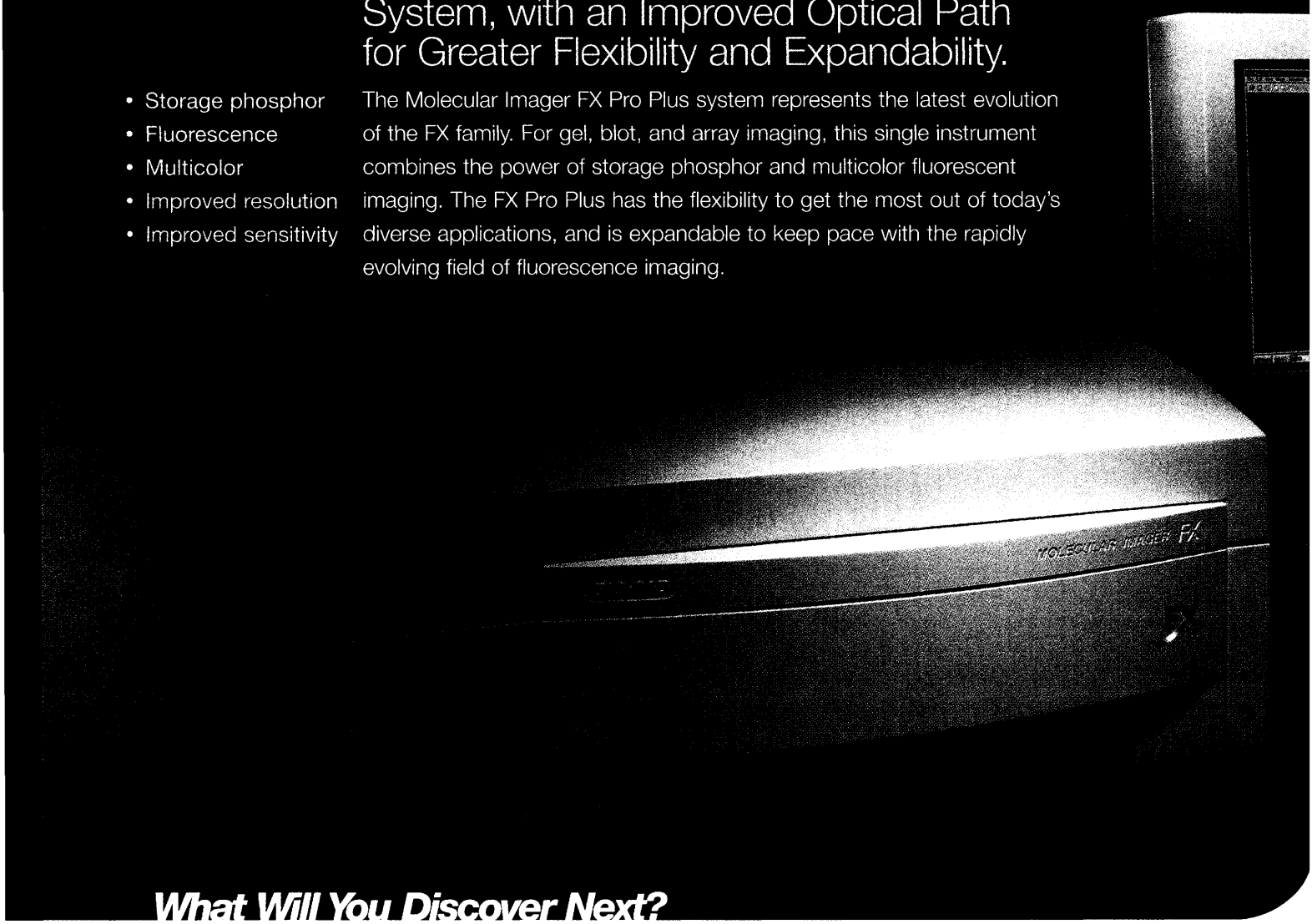
The W. M. Keck Foundation
www.wmkeck.org

# the future of imaging is in the FX Pro Plus

## The New Molecular Imager® FX Pro Plus™ System, with an Improved Optical Path for Greater Flexibility and Expandability.

- Storage phosphor
- Fluorescence
- Multicolor
- Improved resolution
- Improved sensitivity

The Molecular Imager FX Pro Plus system represents the latest evolution of the FX family. For gel, blot, and array imaging, this single instrument combines the power of storage phosphor and multicolor fluorescent imaging. The FX Pro Plus has the flexibility to get the most out of today's diverse applications, and is expandable to keep pace with the rapidly evolving field of fluorescence imaging.

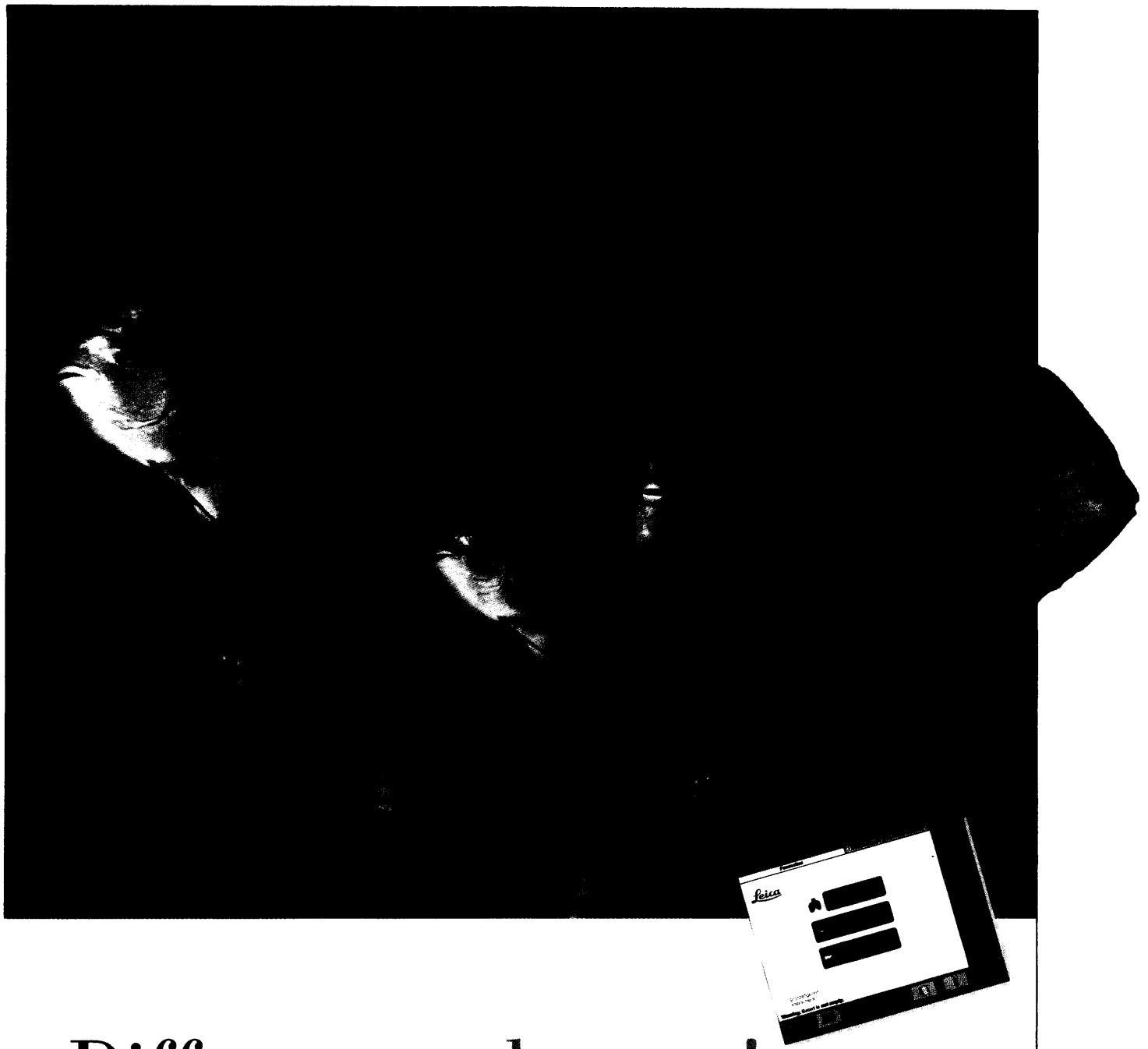



***What Will You Discover Next?***

*Visit our Life Science web site at discover.bio-rad.com. Call toll free at 1-800-4BIORAD (1-800-424-6723); outside the US, contact your local sales office.*

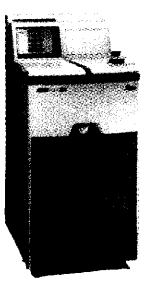
BIO-RAD

Circle No. 15 on Readers' Service Card



# Different to the rest !

## The NEW Leica ASP300 Tissue Processor



ASP300/HBU/E

On the surface, all tissue processors may seem the same. But now Leica Microsystems offers you something different: a uniquely simplified instrument using the latest user-friendly, colour touch screen system. Smart design and proven technology are combined to create a new standard in automated tissue processing. Allow us to show you in your laboratory why the Leica ASP300 is different.

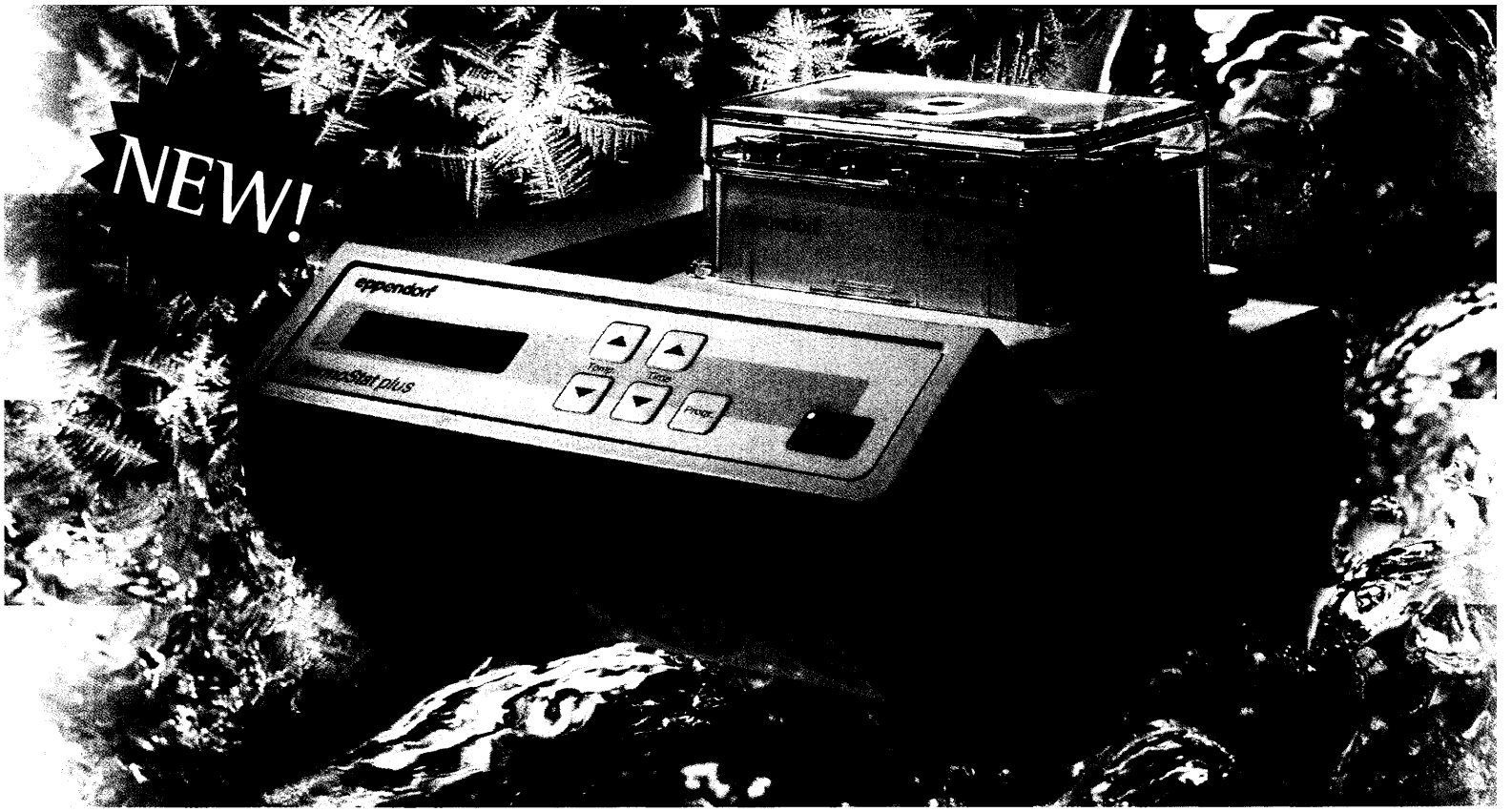

Leica Microsystems Nussloch GmbH
Heidelberger Strasse 17-19
D-69226 Nussloch

Phone +49 6224 143 0
Fax +49 6224 143 200
www.leica-microsystems.com


Leica

MICROSYSTEMS

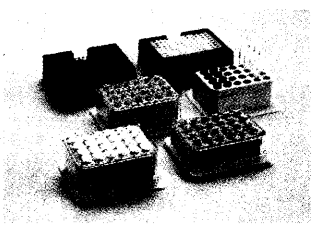
Circle No. 6 on Readers' Service Card

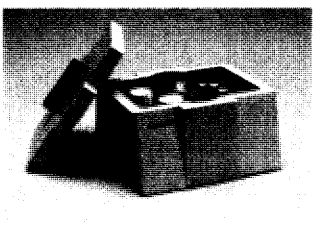



# Red-hot features and ice-cool reactions

Samples and reagents often have to be temperature-controlled constantly and with the utmost precision on the lab bench. Eppendorf has given this requirement top priority and developed the **ThermoStat plus**, a compact bench-top device for a wide spectrum of applications in a temperature-control range from –5 °C to 99 °C! In addition to single temperature-control and no time limit, both the temperature and the run time are individually programmable, which means that you can automatically run up to four temperature levels and four time phases in succession. The integrated RS 232 interface can be used to control your ThermoStat plus and to record its results in accordance with GLP.

The perfect insulation of the thermoblocks guarantees precise temperature control. What is more, there is no risk of burns to users' hands as the tubes can be removed easily at all times, even during the temperature-control process. Of the six exchangeable thermoblocks which can be used with the ThermoStat plus, five have the same design as those for the Eppendorf Thermomixer comfort. Another compatible partner is the IsoTherm-System® with its tailor-made racks and cool packs. And the universal CombiBox thermoblock transforms the ThermoStat plus into a temperature-stable reagent depot, with space for individual tubes with a height of up to 60 mm.
Eppendorf ThermoStat plus: A red-hot tip for every lab!





- Exact temperature control of all commonly used lab tubes
- Temperature-control range from –5 °C to 99 °C
- Autoclavable, non-freeze racks with 24 numbered positions facilitate rapid handling of all samples

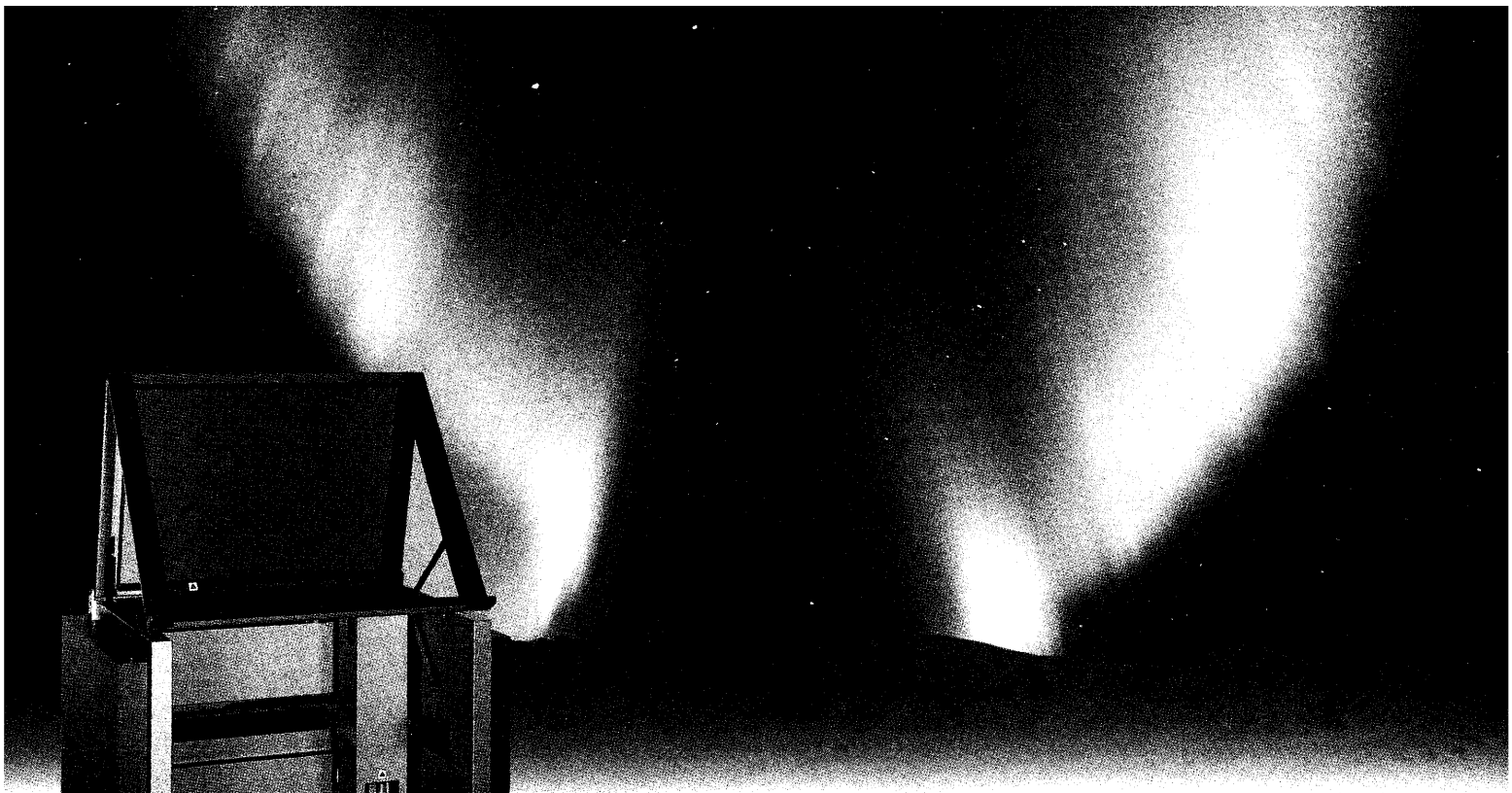
- Exchangeable thermoblocks:
  - for 24 x 0.5 ml, 1.5 ml or 2.0 ml micro test tubes
  - for microtiter plates with all well forms, incl. deepwell plates
  - for headspace tubes and other lab tubes (Ø 11–12 mm, height 30–76 mm)
  - CombiBox for tubes of various shapes and a height of up to 60 mm

**eppendorf**

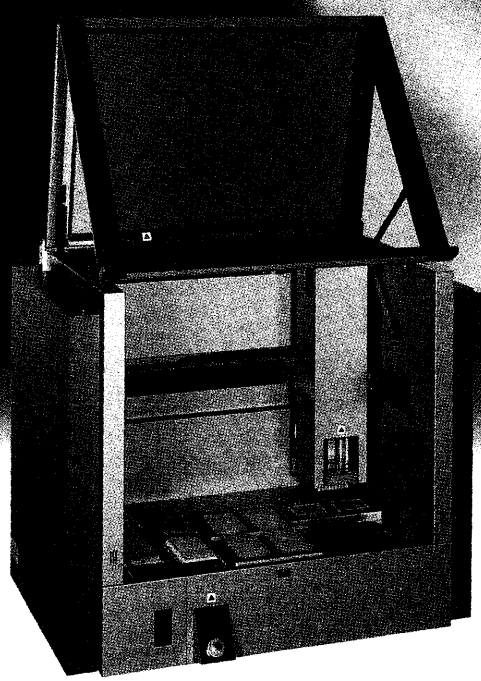
***In touch with life***

Eppendorf AG · 22331 Hamburg · Germany · Phone +49 40-53801-0 · Fax +49 40-53801-556 · e-mail: eppendorf@eppendorf.com · Internet: www.eppendorf.com
Brinkmann Instruments, Inc. · One Cantiague Rd. · Westbury, NY 11590-0207 · Phone 800-645-3050 or 516-334-7500 · Fax 516-334-7506
e-mail: info@brinkmann.com · Internet: www.brinkmann.com

Circle No. 3 on Readers' Service Card



Northern lights (aurora borealis)



Instrument Dimensions:
40 in. x 26 in. x 35 in.

*Isolate bacterial and fungal DNA from difficult-to-process research samples*

# MagNA Pure LC

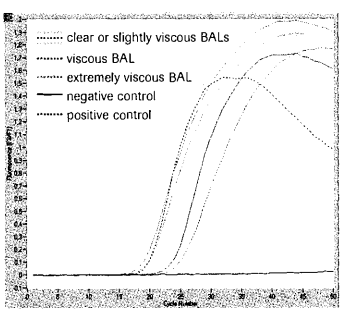
## Fully Automate Nucleic Acid Isolation and PCR Setup

with a single instrument – the MagNA Pure LC from Roche Molecular Biochemicals.

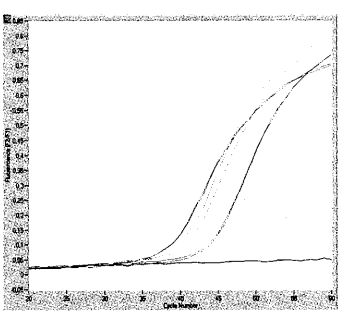
- Use reliable magnetic bead technology to purify DNA, RNA, or mRNA from an assortment of sample types.
- Apply MagNA Pure LC's pipetting flexibility to prepare reaction mixes that are ready for use in the LightCycler Instrument or 96-well format thermocyclers.

For more information, contact your local representative, or visit us at ***http://biochem.roche.com/magnapure***

- Use the new MagNA Pure LC DNA Isolation Kit III to obtain high-quality DNA from your most difficult research samples – bronchoalveolar lavage (BAL), cerebrospinal fluid (CSF), urine, sputum, swabs, and stool.
- Isolate DNA from gram-positive and gram-negative bacteria, such as *S. aureus*, *C. pneumoniae*, *H. pylori*, and *B. pertussis*, as well as fungi, like *C. albicans* and *A. fumigatus*.
- Analyze purified DNA with the LightCycler Instrument's real-time PCR, or with other PCR platforms – from sample to results in less than three hours.




DNA from six different *S. aureus*-positive BAL research samples, analyzed by LightCycler PCR.



DNA from three different *H. pylori*-positive stool research samples, analyzed by LightCycler PCR.

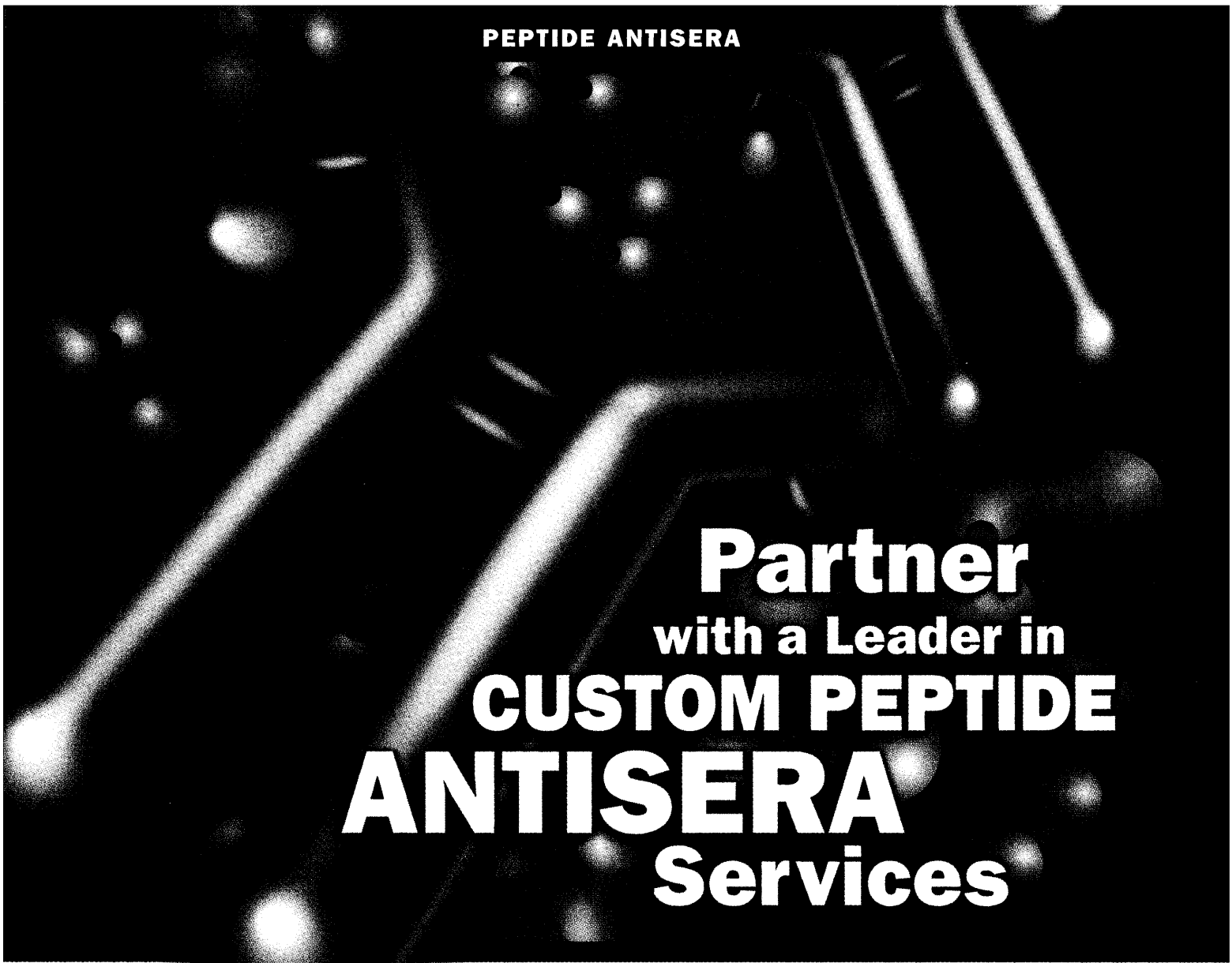
**Argentina** +54-11 4954 5555; **Australia** +61-2 9899 7999; **Austria** +43-1 277 870; **Belgium** +32-2 247 4930; **Brazil** +55 -11 3666 3565; **Canada** +1-450 686 7050; (800) 361 2070; **Chile** +56-2 3752000; **China** +86 21 5240 2211; **Columbia** +57-1-417 8860; **Czech Republic** +420 2 20 382 550; **Denmark** +45 36 39 99 99 (Information); +45 49 12 66 66 (Orders); **Egypt** 202-361 90 47; **Finland** +358-9 525 33-1; **France** +33-4 76 76 46 85; **Germany** +49-621 759 8568; **Greece** +30-1 6166100; **Hong Kong** +852-2485 7596; **India** (22) 431 2312; **Indonesia** +62-21 525-7738; **Iran** 00 98 212 08 2266; + 00 98 218 78 5656; **Israel** 972 6 6380569; **Italy** 039-2817 530; **Japan** +81-3 5443 5284; **Kenya** 00254-2-74 46 77; **Kuwait** 00965-483 26 00; **Luxembourg** 00352-4824821; **Malaysia** +60-3 755 50 39; **Mexico** +52-50-81-5827; **Netherlands** +31-36 5394 911; **New Zealand** +64-9 276 4157; **Nigeria** 00234-1-96 09 84; **Norway** +47-23 373 300; **Philippines** +63-2 893 45 67; **Poland** +48-22 667 91 68; **Portugal** +351-21-4171717/ 4164400; **Republic of Ireland** 1 800 40 90 41; **Russia** (49) 621 759 8636; **Saudi Arabia** +966 1 4010333; **Singapore** +65-371 66 32; **South Africa** +27-11 886 24 00; **South Eastern Europe** (01) 277 87; **South Korea** +82-2 550 3356; **Spain** +34-93 201 44 11; **Sweden** +46-8 404 88 00; **Switzerland** +41 -41 799 61 61; **Taiwan** +886-2 2505 25 33; **Thailand** +66-2 937 04 44; **Turkey** +90-212 213 32 80; **United Kingdom** +44-1273 480 444; **USA** +1-800 262 1640



Roche

Roche Diagnostics GmbH
Roche Molecular Biochemicals
Mannheim, Germany

Circle No. 25 on Readers' Service Card




No one is better equipped than Sigma-Genosys to be your partner in custom peptide antisera production. We produce antisera for some of the world's leading pharmaceutical companies and academic institutions. Just send us your peptide sequence and leave the rest to us.*

- Custom Peptide Design & Synthesis
- Conjugation to Carrier Protein
- Immunization into Two Animals
- Sera Collection

Save yourself the time and hassles involved in antisera production. Call Sigma-Genosys at 877-710-1502.

**Sigma-Genosys also offers a partial antisera service, in which you supply the antigen and we perform the immunization and sera collection. Optional services such as protocol extensions, ELISA and affinity purification are also available. Contact our in-house representatives for details.*

*Have questions? Call us. Whether you're a novice or pro, you can count on our technical support for answers.*

**www.genosys.com**

LEADERSHIP IN LIFE SCIENCE AND HIGH TECHNOLOGY

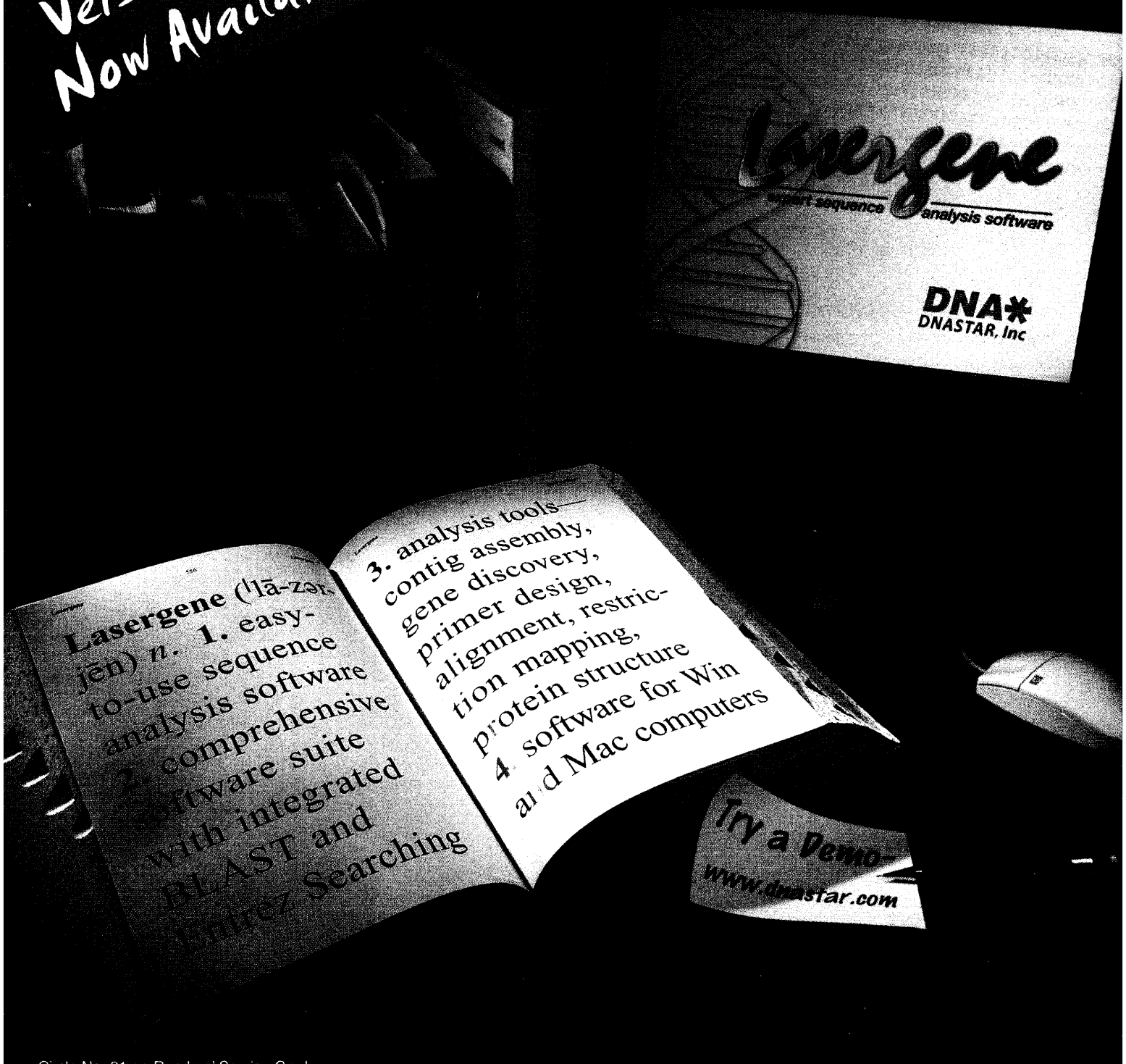
1442 LAKE FRONT CIRCLE • THE WOODLANDS, TX 77380-3600
877-710-1502 • FAX: 281-363-2212 • EMAIL: GINFORMATION@SIAL.COM • A Member of the Sigma-Aldrich Family

SIGMA GENOSYS

Circle No. 28 on Readers' Service Card

# Defining Sequence Analysis

## Version 5.0 Now Available!

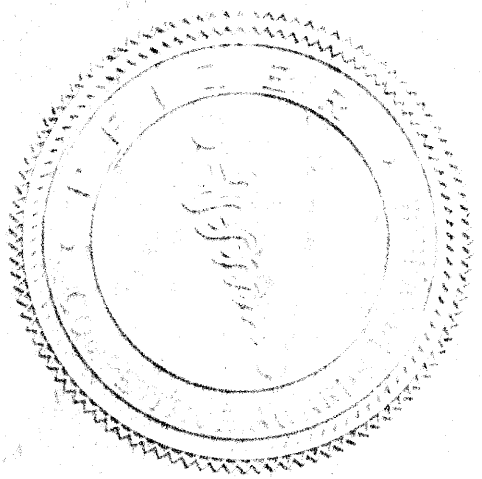



Circle No. 31 on Readers' Service Card


**DNASTAR, Inc. 1228 S. Park St., Madison, WI 53715 USA www.dnastar.com**
**Tel: 608•258•7420 Fax: 608•258•7439 e-mail: info@dnastar.com**

**GATC Biotech AG, Jakob-Stadler-Platz 7, 78467 Konstanz, Germany www.gatc-biotech.com**
**Tel: +49 (0) 7531 81 60 0 Fax: +49 (0) 7531 81 60 81 e-mail: bioinformatics@gatc-biotech.com**


**DNA* DNASTAR, Inc**



# Dedicated to Achievement in Medical Research

## Pfizer is proud to announce the 2002 Competitive Awards Program for scientific research related to doxazosin

The Pfizer Competitive Awards Program provides grants to members of the medical community to be used for the study of doxazosin. In past years the program has involved internationally respected researchers and has yielded exciting scientific information.

Proposals for the 2002 Competitive Awards Program must be received by October 31, 2001.

Submission of a proposal under the 2002 Competitive Awards Program is not made in confidence, and shall not create or be conditioned on any obligation or restriction on the part of Pfizer with regard to its use.

For more information contact the local Pfizer Medical Director at 212-573-2638 or e-mail doxazosinawards@pfizer.com.

## The winners of last year's Pfizer Competitive Awards Program

### Cardiovascular

Ronald E. Law
Los Angeles, CA, USA

Martin E. Matsumura
Charlottesville, VA, USA

Thomas Pickering
New York, NY, USA

Antonio Lopez-Farré
Madrid, Spain

Manuel Labiós Gómez
Valencia, Spain

J.M. Galceran
Barcelona, Spain

José Ramón González-Juanatey
Santiago de Compostela, Spain

Giuseppe Schillaci
Perugia, Italy

Jesús Egido
Madrid, Spain

Joan M. Mauri
Girona, Spain

Josep Galceran
Palamós, Spain

Joan Llibre
Barcelona, Spain

Francesco Portaluppi
Ferrara, Italy

**Judges**
Stevo Julius
Lewis Landsberg
Hans Lithell

### Urology

Kazem M. Azadzoi
Boston, MA, USA

Donna Peehl
Stanford, MA, USA

Gary J. Miller
Denver, CO, USA

Tufan Tarcan
Istanbul, Turkey

Toby C. Chai
Baltimore, MD, USA

Anthony Heaney
Los Angeles, CA, USA

Mónica López-Barahona
Madrid, Spain

Ada Elgavish
Birmingham, AL, USA

**Judges**
Georg Bartsch
Claus Roehrborn
William Steers


Special *in vivo* packagings

# *From the* **PEI** *people :*
# *The* **jetPEI**™ *transfection reagents*

*For genes and oligos*

- **jetPEI** the robust cell culture reagent with broad spectrum
- **jetPEI-Gal** for hepatocytes
- **jetPEI-Man** for macrophages and dendritic cells
- **jetPEI-RGD** for ephithelial and endothelial cells
- **jetPEI-Fluo** track gene delivery with fluorescent tags

Attractive price • easy protocol • +/- serum


Circle No. 8 on Readers' Service Card

www.polyplus-transfection.com

PolyPlus transfection SAS BP 21, 67401 Illkirch cedex France

Phone : +33 390 244 328 - Fax : +33 390 244 329

Poly transfection™

The transfection-dedicated company

# IDTONTV

DISCOVER WHAT SO MANY PEOPLE ALREADY HAVE.

## The Next Wave™

with LEONARD NIMOY

*Be sure not to miss The Next Wave, a groundbreaking half-hour television series about new technologies and their impact on the way we work. The Next Wave, which airs on CNBC as paid programming, will highlight IDT as a prominent and dedicated player in advancing biotechnology research on their September 16th show at 12:30PM central time.*

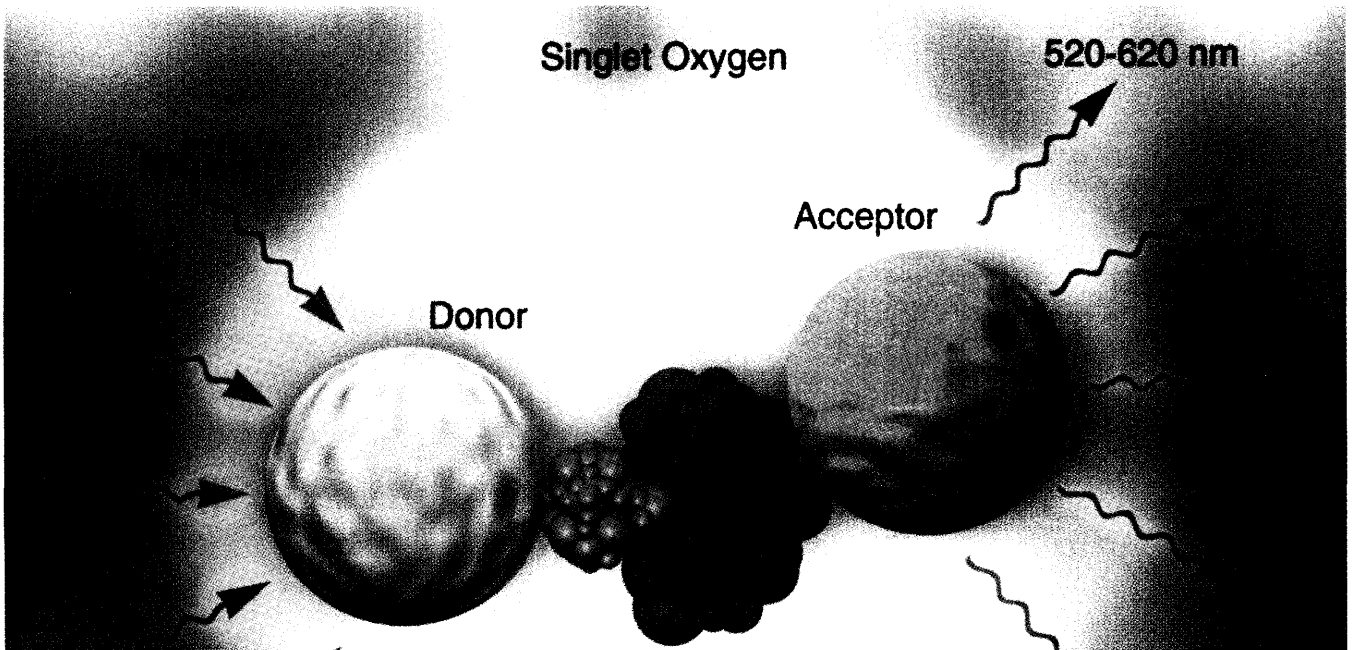
IDT

INTEGRATED DNA TECHNOLOGIES, INC.

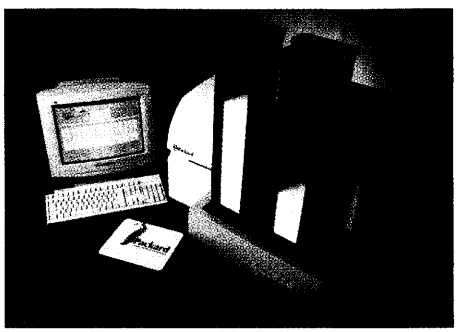
www.nextwavetv.com

www.idtdna.com

**FP BRET²™ Absorbance Fluorescence Intensity Luminescence TRF HTRF® FRET AlphaScreen™**




# Any Assay, Any Format, Any Method of Detection, One Instrument



## Fusion™

## Packard's New Universal Microplate Analyzer Optimized for BRET²™ and AlphaScreen™ Technology...

If your research takes you from solution to cell based assays, in 6- to 1536-well formats, using virtually any non-isotopic method of detection, the Fusion™ universal microplate analyzer is the only instrument that can meet your ever changing needs.

From basic research to assay development, to high throughput screening, Fusion is the first multi-detection platform that you configure to suit both your research requirements and budget.

Fusion is the only multi-detection plate reader optimized to take advantage of versatile new BRET²™ and AlphaScreen™ assay technologies from BioSignal Packard.

Call, write, fax, or visit our Web site today to learn how one instrument can do so much in so many ways.

**www.packardinstrument.com/fusion.htm**

Packard BioScience

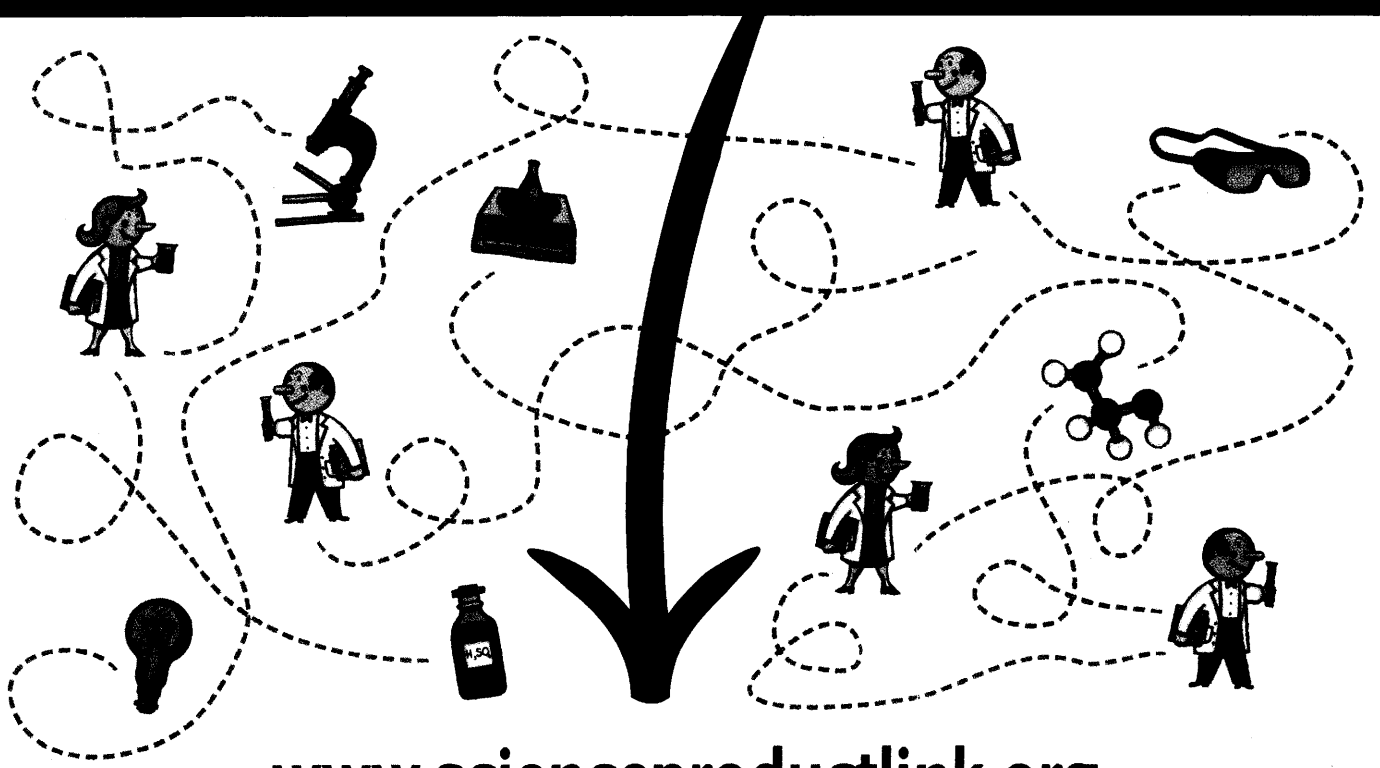
**Packard BioScience Company**
800 Research Parkway
Meriden, CT 06450 U.S.A.
Tel: 203-639-2598 Toll Free: 1-800-323-1891
Fax: 203-639-2172

For international offices visit our Web site or contact the Packard BioScience U.S.A. office.

M5933 (M3704-09)

Circle No. 19 on Readers' Service Card

# What's the shortest distance between two points?



## www.scienceproductlink.org

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

*Science* announces a great way to find out about new products advertised or featured in *Science* — instantly. *Science's* Product Link is a new online reader service program and online product information service that allows readers to search for products advertised or featured in *Science* by

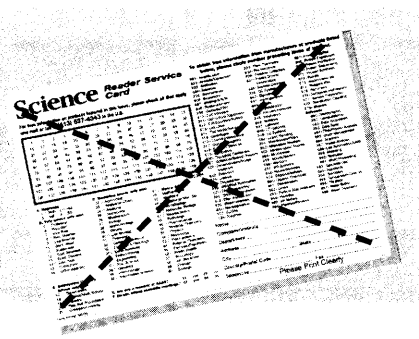
- product category,
- company name,
- keyword, and
- page number.

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

If you prefer, you can request to have product information delivered via

- e-mail,
- regular mail,
- telephone, and
- fax.

**Science**
*Discover the Future*




**_Science_ Reader Service**

With the publication of the 5 October issue, *Science* is eliminating the print reader service card. Starting with that issue, all product information can be requested online at **www.scienceproductlink.org**

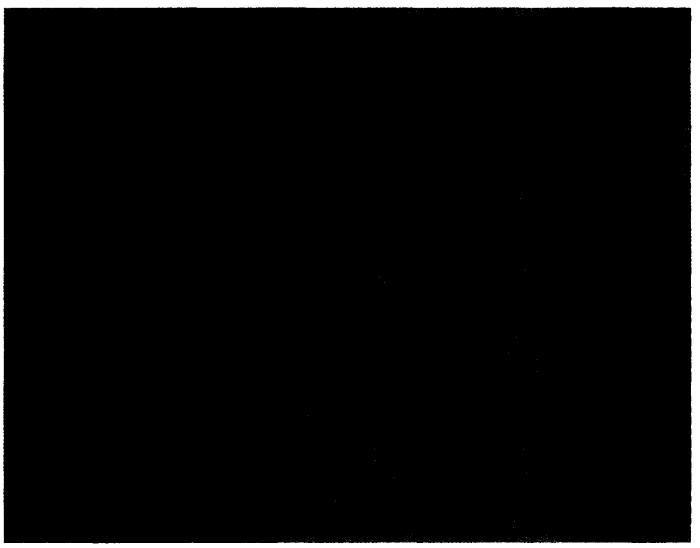
Drug Discovery | Research | Clinical Screening

▼

Proteomics

# ProXPRESS and Progenesis -

## one proteomic imaging system that does it all. precisely.



Accelerate your proteomic research with the new ProXPRESS™ Proteomic Imaging System from PerkinElmer Life Sciences, Inc. No other imaging system gives you better resolution and the flexibility to use any dye in either the VIS and UV spectrum range, for the most accurate, reproducible detection and quantitation of low-abundance proteins on large 2D gels. The ProXPRESS delivers all this and more.

*Superior detection over a wide dynamic range:*
The ProXPRESS offers infinite wavelength selection without sacrificing performance for unlimited detection capabilities.

*One system for all applications:*
The ProXPRESS does it all – fluorescence, luminescence, absorbance and reflection – and the ability to detect up to four different colors at once, providing maximum application flexibility and value, for proteomic and non-proteomic needs.

**Get It Done. 10 times faster.**

**Progenesis™ "hands-free" 2D analysis software from PerkinElmer Life Sciences**

*High sensitivity and superb reliability:* The ProXPRESS virtually eliminates the chance of missing critical data. A specially designed detector unit delivers excellent quantitation and high resolution over the entire sample area for more precise, accurate data.

*Tomorrow's technology, today:* With the Progenesis bioinformatics tool, 2D gel image analysis is no longer the major limiting process in high throughput Proteomics. Progenesis and ProXPRESS together improve the accuracy and sensitivity of 2D gel imaging and help to smash the bottleneck by automating and accelerating 2D gel image analysis.

**Take Advantage Of Our Limited Introductory Offer.**

For a limited time only, the new ProXPRESS Proteomic Imager is available at just $59,900 – a substantial savings.

For more information or for a demonstration, contact PerkinElmer Life Sciences at (800) 551-2121.

Or visit our website at www.perkinelmer.com/lifesciences

**Products You Trust**

NEN

wallac

GENOMIC SOLUTIONS IN PARTNERSHIP

PerkinElmer™
life sciences.

**Worldwide Headquarters:** PerkinElmer Life Sciences, 549 Albany Street, Boston, MA 02118-2512 USA (800) 551-2121
**European Headquarters:** PerkinElmer Life Sciences, Imperiastraat 8, B-1930 Zaventem Belgium +32 2 717 7911
Technical Support: in Europe: techsupport.europe@perkinelmer.com
in US and Rest of World: techsupport@perkinelmer.com



**www.perkinelmer.com/proteomics**

Circle No. 59 on Readers' Service Card