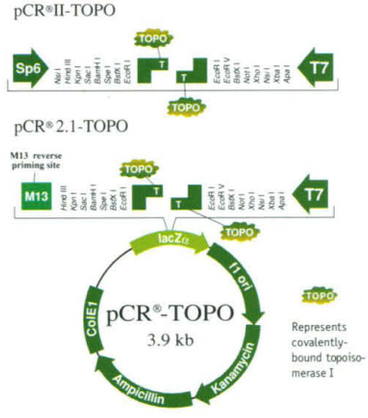

15 January 1999
Science
Vol. 283 No. 5400
Pages 289–448 $8
NEWS FOCUS
Engineering a New Green Revolution
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Lots of things are fast. Jet planes. Bullet trains. Sports cars. With TOPO™ TA Cloning® you can add cloning PCR products to the list.

***Superfast* Cloning.** In just 5 minutes, TOPO™ TA Cloning® lets you ligate *Taq*-amplified PCR products right on your bench top. Simply add 1 µl of your PCR (no clean-up needed!) to the topoisomerase I-activated vector, and 5 minutes later you're ready to transform.

No Extra Steps. TOPO™ TA Cloning® eliminates the need for special primers and vector preparation. There's also no post-PCR modifications. And best of all, there's no waiting. With TOPO™ TA Cloning®, you'll save an entire day.



More Recombinants. TOPO™ TA Cloning® is not just fast–it's efficient. It yields up to 95% recombinants so you'll easily find a positive clone.

Think Fast. If you want to clone your PCR products fast, just call Invitrogen and order a TOPO™ TA Cloning® Kit. It comes with your choice of cloning-ready vector (pCR®2.1-TOPO or pCR®II-TOPO), competent cells, and other reagents to optimize your results. So think fast. Order the TOPO™ TA Cloning® Kit today.

Circle No. 23 on Readers' Service Card

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

International Toll Free Numbers:
Tel: 00800 5345 5345*
Fax: 00800 7890 7890*
*This number operates in all European countries excluding Finland and Sweden
Finland:
Tel: 990800 5345 5345
Fax: 990800 7890 7890
Sweden:
Tel: 009800 5345 5345
Fax: 009800 7890 7890

Distributors:
Austria 0222 889 18 19
Australia 1 800 882 555
China 010 6255 3477
Hungary 01 280 3728
India 91 80 8391453
Israel 02 584 1111
Italy 02 38 19 51
Japan 03 5684 1622
Malaysia 03 432 1357
Poland 058 341 47 26
Portugal 01 453 7085
Singapore 65 2922130
South Korea 02 569 6902
Spain 03 450 2601
Taiwan 886 2 238 10844
Thailand 246 7243

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

United States Headquarters:
Invitrogen
1600 Faraday Avenue
Carlsbad, California 92008
Tel: 1-800-955-6288
Fax: 760-603-7201
Email: tech_service@invitrogen.com
http://www.invitrogen.com

RoboCycler®

TEMPERATURE CYCLER

Uniformity.

Our competitors are turning into pretty good salesmen... for Stratagene!

Compare published temperature uniformity specs:

MJ Research says:
"±0.4°C within 30 sec. of arrival @ 90°."

Perkin Elmer says:
"±0.5°C, 30 seconds after clock start..."

The Stratagene RoboCycler® gives you ±0.1°C at clock start!

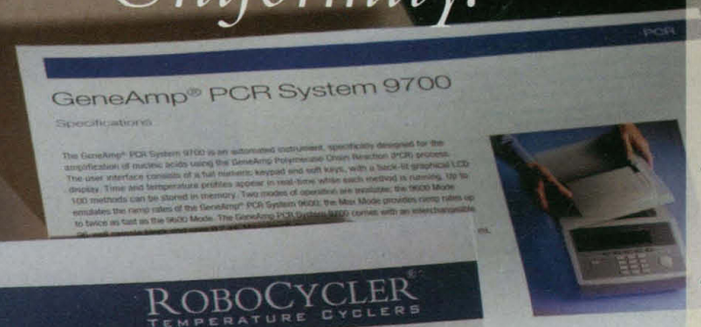
No equilibration time.

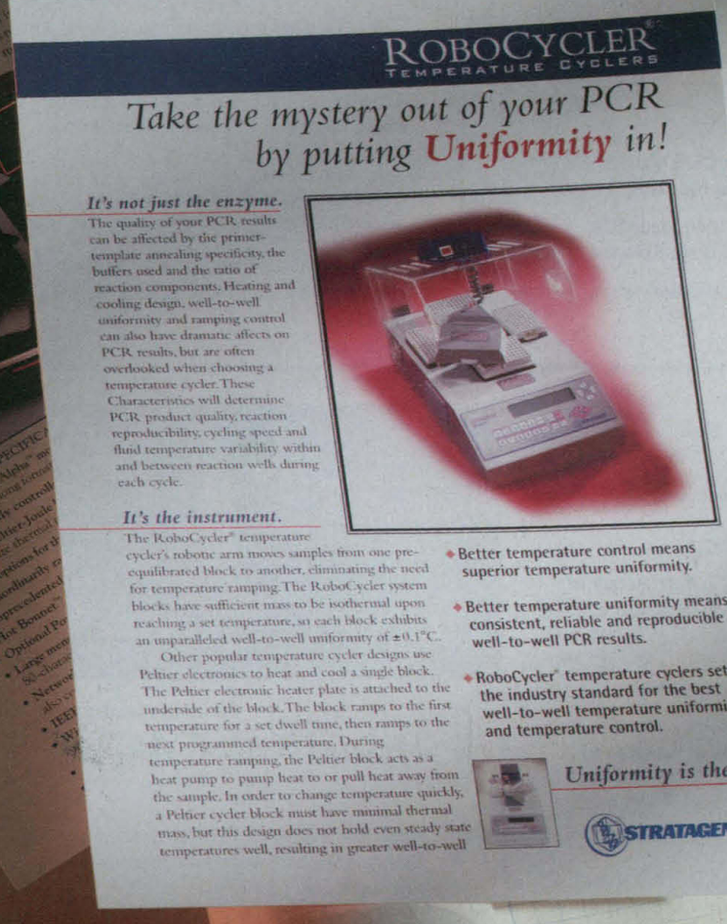
Reliable, predictable, reproducable well-to-well temperature uniformity start-to-finish every time.

RoboCycler® TEMPERATURE CYCLER

Uniformity.

PE Applied Biosystems





MJ Research says—
They have Temperature Uniformity, ±0.4°C, within 30 sec. of arrival at Temperature.

Perkin Elmer Says—
±0.5°C 30 sec. After clock start.

Stratagene's RoboCycler® is ±0.1°C AT Clock Start!
—No Equilibration Time—
Uniformity & Predictability from start-to-finish...

RoboCycler's The ONE!

UNITED STATES AND CANADA
(800) 424-5444

INTERNET
techservices@stratagene.com

STRATAGENE EUROPE:
Austria: 017 956 7036
Belgium: 027 13 12 11
Germany: 0699 509 6197
Netherlands: 0800 023 0448
Switzerland: 01 800 9045
United Kingdom: 0171 365 1056

DISTRIBUTORS
For a list of worldwide distributors, please visit the Stratagene Web site at www.stratagene.com

www.stratagene.com

RoboCycler® 40 or 96 Temperature Cycler
RoboCycler® Gradient 40 or 96 Temperature Cycler
RoboCycler® Infinity Temperature Cycler with interchangable 40-,96- and 384-well blocks

STRATAGENE®

Circle No. 37 on Readers' Service Card

VOLUME 283 15 JANUARY 1999 NUMBER 5400

Science

www.sciencemag.org

Cover The cover photograph illustrates a range of rice varieties. Such diversity provided the grist for plant breeders who developed today's high-yielding strains. Now the world needs another boost in grain harvests, and agricultural researchers are pinning their hopes on biotechnology. See the News stories beginning on page 310. [Photo: International Rice Research Institute and Consultative Group on International Agricultural Research]

303
What our early ancestors ate

NEWS

NEWS OF THE WEEK

NEWS FOCUS

DEPARTMENTS

RESEARCH

365 Picking plankton in the Ross Sea

RESEARCH ARTICLES

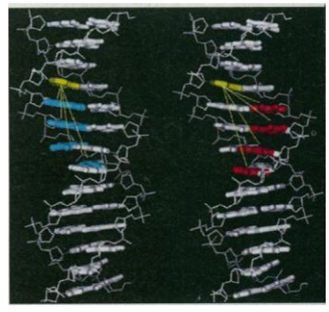
REPORTS

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): $110 ($62 allocated to subscription). Domestic institutional subscription (51 issues): $325; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

SCIENCE'S COMPASS

www.sciencemag.org/cgi/content/full/283/5400/299a



375

Running the bases in DNA electron transfer

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $8.00 per issue prepaid includes surface postage; bulk rates on request. **Authorization to photocopy** material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that $4.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/83 $4.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

Simple isn't it. We know it isn't. Not when you are facing thousands of possible new drug leads and stretched R&D budgets.

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

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

And we continue to develop our contribution with high-performance systems for protein characterisation and exciting new miniaturisation techniques.

We understand your requirements because we work closely with our customers to provide the latest systems to accelerate their commercial success. We already have more than 70 such technology collaborations with top life science companies. The shared experience gives birth to new leading-edge technologies that match actual needs – and the discover, develop, deliver cycle can continue.

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

Discover more at **www.apbiotech.com**

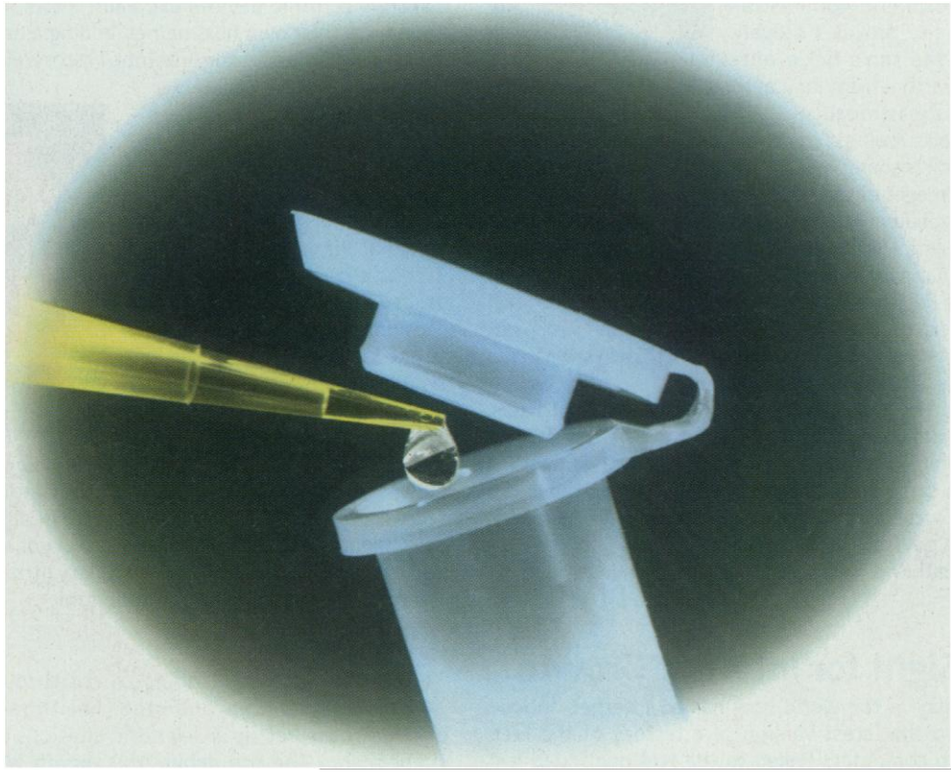
Discover. Develop. Deliver.

amersham pharmacia biotech

Announcing Novagen's New competent cell

singles™

Transformation in a snap.



Thaw. **Add DNA.** **Heat shock.** **Plate.**

(That's it.)

No screw caps. No dispensing. No freeze/thaw. No waste. No foul ß-ME smells!

singles Single aliquot competent cells. Now available for NovaBlue and pET host strains BL21(DE3) and BL21(DE3)pLysS.

For more information, *phone:* **800.526.7319** *(US & Canada)* • **0800-6931-000** *(Germany call CalBiochem-NovaBiochem GmbH)* • **0800-622935** *(UK call CalBiochem-NovaBiochem)*
visit our web site: www.novagen.com • *send e-mail:* novatech@novagen.com

International Distributors

Australia—Progen Industries Ltd. 7-3375-1888
Austria—Bio-Trade 1-889-1819
Belgium—Euro Biochem scrl 10-43-70-60
Denmark—Bie&Berntsen A-S 44-94-88-22
Finland—Ya-Kemia Oy 9-350-3250
France—TEBU 130-46-3900
India—BioBusiness Development Agency 559-6820
Israel—Megapharm 9-904596
Italy—M-Medical 55-500-1871
Japan—Takara Shuzo Co., Ltd. 77-543-7231
Korea—BOHAN Biomedical 2-577-2002
Netherlands—Omnilabo International BV 76-5795-795
New Zealand—Intermed Scientific Ltd. 9-443-1284
Norway—Bio-Test A/S 22-619-660
Spain—bioNova cientifica, s.l. 91-551-5403
Sweden—Labkemi AB 8-742-4200
Switzerland—Juro Supply AG 41-226-20-60
Taiwan—PROTECH 22-3810844
UK—CalBiochem-NovaBiochem (UK) Ltd.0800-622935 Cambridge Bioscience 1223-316855

Novagen

Circle No. 39 on Readers' Service Card

MASS-INDEPENDENT ISOTOPE FRACTIONATION

Exchange of isotopes as part of a chemical process (reaction or diffusion) almost always reflects the relative masses of the isotopes involved. However, several gases—notably ozone, carbon dioxide, nitrous oxide, and carbon monoxide—and some meteorite grains and minerals seem to preserve a mass-independent relation among the isotopes. As discussed by Thiemens (p. 341) in a review, this effect can be used as a tracer or to provide information on the origins or sources and sinks of the gases, even though the mechanism responsible for the mass-independent fraction may remain obscure. One example of such an effect is the enrichment in the atmosphere of the heavier isotopes (^{17}O and ^{18}O) in ozone relative to the background levels. Asymmetric molecules (such as $^{16}O^{17}O^{18}O$) carry the highest enrichments, whereas symmetric molecules (such as $^{17}O^{17}O^{17}O$) are slightly depleted. Most explanations for this observation invoke kinetic effects induced by molecular symmetry. Mauersberger *et al.* (p. 370) now report rate coefficients for a range of ozone selection channels with different isotopic compositions. The results suggest that the collision process itself, rather than molecular symmetry, determines the enrichment.

NEUTRAL HYDROGEN ON IO

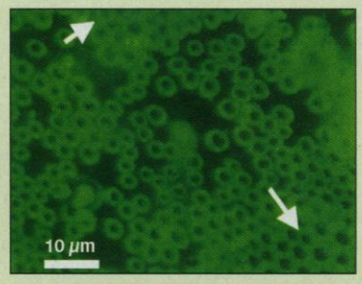
Io, Jupiter's closest large satellite, creates an enigmatic oxygen- and sulfur-rich plasma torus around Jupiter through the satellite's active volcanism and interaction with Jupiter's strong magnetic field. Roesler *et al.* (p. 353) used the Hubble space telescope imaging spectrograph to obtain far-ultraviolet images of neutral oxygen, sulfur, and hydrogen Lyman-α emission of Io's extended atmosphere. The temporal and spatial variations of the oxygen and sulfur suggest that volcanic emissions must be altered or accelerated by the jovian magnetic field, the plasma torus, or both. The hydrogen signal localized near each pole of Io was unexpected and may be produced by hydrogen-rich polar frost, dissociation of hydrogen concentrated at the poles by the jovian magnetic field, or reflection of the solar hydrogen Lyman-α radiation from Io's surface.

STILL WATERS FIX LEAST

One commonly predicted effect of climate change induced by greenhouse gases is an increase in the stratification of the Southern Ocean, a major area of primary production. Arrigo *et al.* (p. 365) show that this change may further hinder the ability of the plankton communities to decrease atmospheric CO_2 by fixation. Their studies of the plankton dynamics in the Ross Sea off Antarctica show that diatoms (which form silicate, not carbonate bodies) dominate in highly stratified waters, whereas *Phaeocystis antarctica* assemblage, which consume a much greater amount of CO_2, dominate in mixed regions.

ORDERED POROUS POLYMERS

Unusual morphologies often result when two different polymer types are joined in one molecule. Rod-coil diblock copolymer, for example, join a rigid polymer based on conjugated monomers (such as polyphenylquinoline, PPQ) with a flexible polymer that forms coils (such as polystyrene, PS).



Jenekhe and Chen (p. 372) show that PPQ-PS diblock copolymers, when placed in solvent (carbon disulfide) that dissolves only the flexible coil, form micelles with diameters of a few micrometers. Solvent evaporation produces a well-ordered porous material that may have several applications, including use as a photonic band gap material.

AN OMNIVOROUS HOMINID?

Early hominids were thought to forage mainly in wooded areas for fruits and C_3 plants (for example, trees, bushes, and herbs). Sponheimer and Lee-Thorp (p. 368; see the Perspective by Kohn and the news story by Vogel) present carbon isotopic evidence from the enamel of teeth from *Australopithecus africanus*, which suggests that this 3-million-year-old ancestor ate more than fruits and leaves. The enamel shows enrichment in ^{13}C consistent with a diet that includes C_4 plants (for example, grasses and sedges) found in more open grasslands, animals that consumed C_4 plants, or both. Thus, *A. africanus* may have had a more diverse diet that included ranging into open grasslands or preying on small, vulnerable mammals without the apparent use of any tools.

INTERBASE ELECTRON TRANSFER IN DNA

Studies of electron transfer through DNA have produced conflicting results, from ultrafast "molecular wire" behavior over many base pairs [characterized by β values of 0.1 per angstrom ($Å^{-1}$) or less] to strongly distance-dependent transport more typical of proteins (β values nearer to 1 $Å^{-1}$). One confounding issue in several previous studies showing ultrafast behavior is that the donors and acceptors have been species intercalated into DNA. Kelley and Barton (p. 375) now study electron transfer in DNA molecules that incorporate fluorescent analogs of adenine (1,N^6-ethenoadenine and 2-aminopurine). Electron transfer rates deduced from fluorescence quenching by guanine or deazaguanine bases yielded β values ranging from 0.1 to 1.0 $Å^{-1}$. They conclude that stacking interactions and reactant energetics strongly influence the distance dependence and that electrons are preferentially transported between bases on the same strand.

FREEZING EPITOPES FOR HIV-1 VACCINES

The initial interactions between the human immunodeficiency virus–type 1 (HIV-1) envelope protein gp120 and the host cell result in a series of conformational changes in the viral envelope that result in cell-virus fusion. LaCasse *et al.* (p. 357; see the Perspective by Montefiori and Moore) used formaldehyde fixation of cells expressing viral envelope protein co-cultured with cells expressing CD4 and the coreceptor CCR5 to capture an intermediate structure. This epitope complex, which has been "frozen" on the expressing cell, was used as an immunogen in a mouse model. Unlike the currently available recombinant gp120 vaccine candidates, the "fusion-intermediate" immunogen stimulated production of antibodies that neutralized a broad array of primary HIV-1 isolates.

PUTTING PATHWAYS TOGETHER

Although the biochemical signaling pathways through which cells respond to various stimuli have generally been elucidated as linear chains of reactions, such pathways interact to form a complex network. Bhalla and Iyengar (p. 381; see the Perspective by

CONTINUED ON PAGE 299

THE LOUIS-JEANTET PRIZE FOR MEDICINE

The 1999 laureates are

Adrian P. BIRD

Institute of Cell and Molecular Biology, University of Edinburgh, United Kingdom
for his work on DNA methylation and gene regulation

Herbert JÄCKLE

Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany
for his work on developmental biology in Drosophila

Jean-Louis MANDEL

Institute of Genetics and Molecular and Cellular Biology, CNRS/INSERM,
Strasbourg, France, for his work on human molecular genetics

The Louis-Jeantet Foundation for medicine awards the three laureates the global sum of CHF 2'100'000, equally divided between them.

The Louis-Jeantet Prize for medicine is not intended to honour past accomplishments but to encourage innovative research. Candidates must be engaged in basic or clinical biomedical research in the European countries members of the Council of Europe. The Prize is awarded each year to one to three researchers or research groups. Since its inception in 1986, the Prize has encouraged forty-four researchers.

Call for nominations

Nominations for the 2000 Louis-Jeantet Prize for medicine will be accepted until February 15, 1999. Candidates must be nominated by scientists, physicians or institutions having detailed knowledge of their research. Self-nominations are not accepted. Selection is made by the Science Committee of the Foundation.

Application forms and further information are obtainable from the Secretary of the Science Committee
The Louis-Jeantet Foundation for medicine, P.O. Box 277, CH - 1211 GENEVA 17, Switzerland
Tel. ++4122 704 36 36; Fax ++4122 704 36 37; Email: info@jeantet.ch; Home page: www.jeantet.ch
Only original signed application forms will be considered.

The name(s) of the laureates of the 2000 Louis-Jeantet Prize for medicine will be announced in January 2000. The Prize Ceremony will take place in Geneva (Switzerland) in April 2000.

FONDATION
LOUIS-JEANTET
DE MÉDECINE

THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 297

Lisman and Fallon) used computation methods to model networks that comprised up to four individual signaling pathways. All of the model parameters were derived from experiment. The results show that such networks can have properties not present in the individual pathways that may be critical for proper cellular regulation. Combinations of common signaling pathways showed, for example, the capacity to remain activated after an initial stimulus was removed and had specific requirements for the amplitude and duration of a signal to reach a threshold for activation. Such coordination may provide a mechanism for storing information.

CHANGE FOR THE BETTER

Mutations, generally deleterious and occasionally advantageous, provide the grist for adaptive evolution. De Visser *et al.* (p. 404) have investigated the complex relation between the rate at which new mutations arise and the course of adaptive evolution in bacterial populations evolving in the laboratory. In small or well-adapted populations, their evolution is limited by the rate at which they can produce new mutations. In large or poorly adapted populations, the rate of new mutations has little effect on the rate of evolution. Thus, a hypermutable phenotype can be advantageous in the right circumstances.

IMMUNE-DEFICIENCY LINK

Mice and humans who lack Bruton's tyrosine kinase (Btk) have an immunodeficiency that primarily affects B cell development and production of serum immunoglobulin. Suzuki *et al.* (p. 390) and Fruman *et al.* (p 393) generated mutant mice, or mice in which only lymphocytes were affected, that were deficient in the p85α regulatory subunit from phosphoinositide-3 kinase (PI3K). These mice had a phenotype similar to that of the Btk deficient mice.

HYPERACTIVITY PARADOX

Psychostimulant drugs have been used for many years to treat children with attention-deficit hyperactivity disorders (ADHD). This therapy was introduced after empirical observations without an understanding of this paradoxical effect. Gainetdinov *et al.* (p. 397; see the news story by Marx) analyzed mice lacking the dopamine transporter gene. These animals showed striking similarities in their behavior to ADHD children and could also be calmed down by psychostimulants. The paradoxical effect depends on normal serotoninergic neurotransmission. These findings may serve as a useful model to develop new therapies to improve these widespread childhood behavioral defects.

CANNABIS, OPIATES, AND REWARD MECHANISMS

Much debate has centered around the linkage between cannabis use and subsequent use of opiates. Ledent *et al.* (p. 401) analyzed mutant mice that were lacking the central cannabinoid receptor CB_1. These animals did not respond to any of the cannabis derivatives, and none of the typical CB_1 receptor–mediated effects could be observed. Although opiates had no unexpected behavioral effect, mutant animals showed less addiction and also less severe withdrawal symptoms. It seems as if CB_1 receptors are involved in the manifestation of physical dependence in opiate addiction. This finding may further our understanding of the processes that lead to drug addiction and may also help to develop new strategies to combat drug addiction.

TECHNICAL COMMENT SUMMARIES

Investigating the Possible Use of Fire at Zhoukoudian, China

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/283/5400/299a

S. Weiner *et al.* (Reports, 10 July, p. 251) reexamined "the oldest reliable evidence for the controlled use of fire by humans" in Layer 10 at Zhoukoudian (the Peking Man site). They found "burned and unburned bones ... present in the same layer with stone tools," but "no ash or charcoal remnants." They concluded that there was only "indirect evidence for burning."

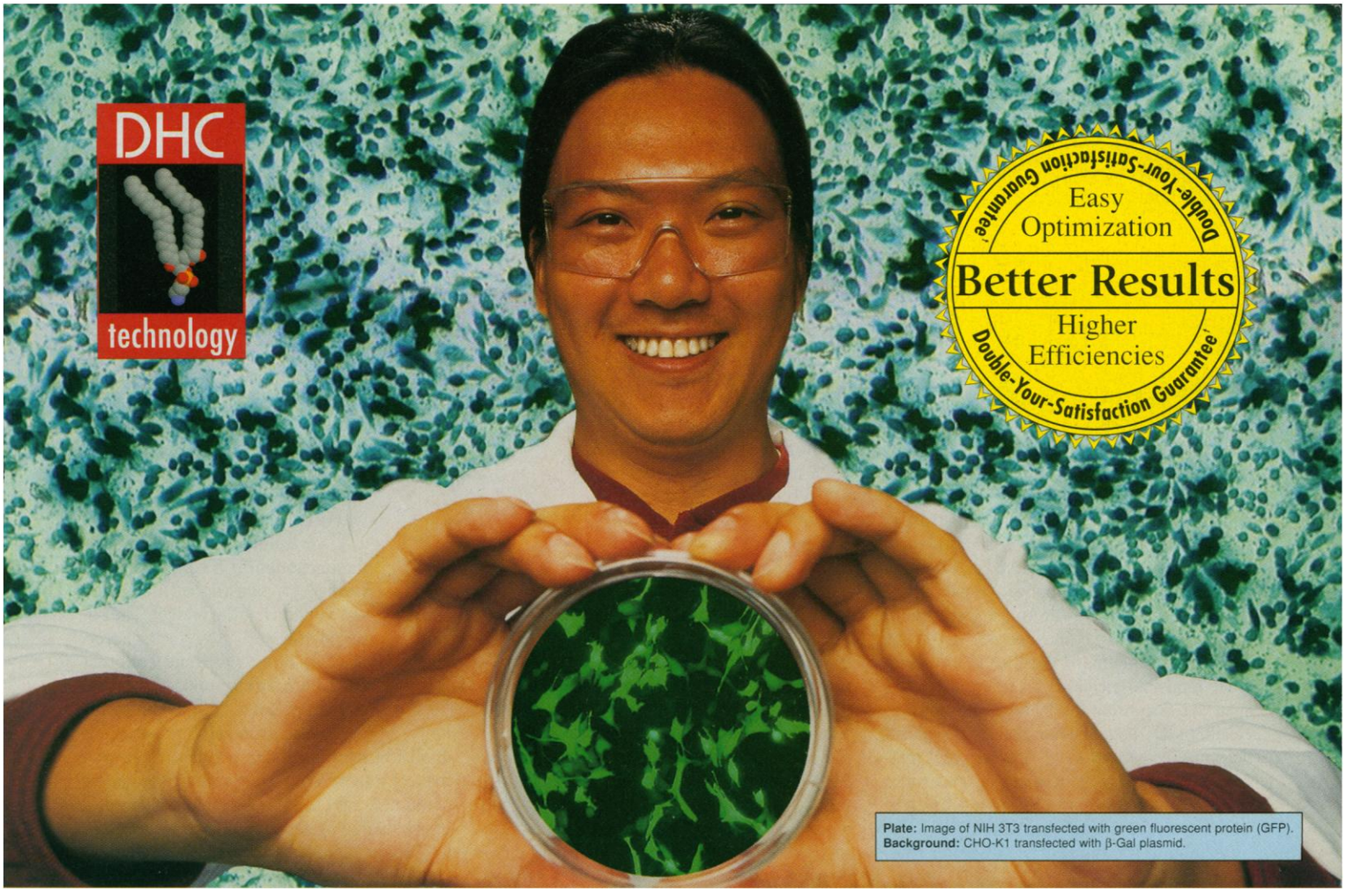
X. Wu comments that Weiner *et al.* "do not fully address the wealth of data collected at the entire site since the 1930s, and they do not adequately account for problems of material transport by water that apply to the particular sample they studied." He states that other studies do "show that fire was used in this site."

In response, S. Weiner *et al.* state that the "demonstration of free carbon" in earlier studies "does not necessarily imply that the organic matter was burned." They agree with Wu that there is "evidence in support of fire use" and that "many open questions" remain, but state that there is not "conclusive, direct evidence for the use of fire by *Homo erectus*."

www.sciencemag.org
Science

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.



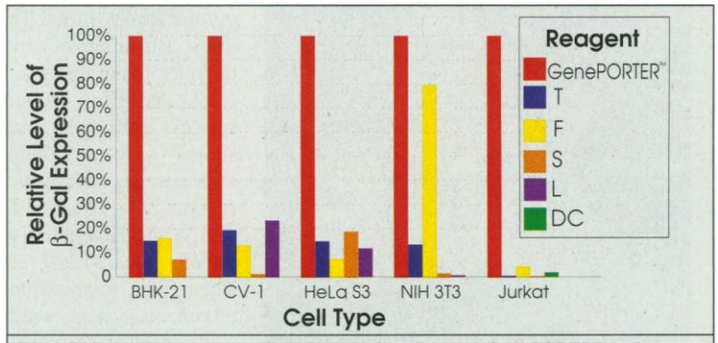
Finally, a transfection reagent that makes you smile, every time!

Introducing

GenePORTER™ Transfection Reagent*

GenePORTER™ reagent, which incorporates direct hydrophilic conjugation (DHC) technology*, is the latest innovation from the lab of Dr. Philip Felgner, inventor of lipofection. We at Gene Therapy Systems are so confident as to the performance of our product, we stand behind it with a double-your-satisfaction guarantee† on cell types listed. In a variety of cell lines, GenePORTER reagent consistently delivers higher levels of transfection than any other commercially available product. Without compromising transfection efficiency, this robust reagent performs in a wide range of conditions, including different ratios of plasmid and reagent. GenePORTER reagent is easy to use and does not require enhancers or special handling of cells, saving time, cost, and reagents. Order GenePORTER reagent today. The results will make you smile.

GenePORTER™ Transfection Reagent	75 reactions • T201007 150 reactions • T201015 750 reactions • T201075



The β-Gal encoding plasmid was delivered into cells using GenePORTER and competitor's transfection reagents. Each manufacturers protocol was followed. β-Gal expression was measured 48 hours after transfection by a colorimetric assay.

Transfected Cell Types†	
HeLa S3	BHK-21
293	CHO-K1
Jurkat	CV-1
NIH 3T3	COS-1
B16-F0	COS-7
PC-12	

* Patents pending.

† If you do not get better transfection results following our protocol, kit purchase price will be refunded or double-the-kit price will be applied to your GTS, Inc. account toward future purchases. Offer valid in USA only and ends 1/31/99. Guarantee is limited to cell types in this ad. The purchased GenePORTER reagent must be returned using the GTS, Inc. return policy. This offer is limited to one T201007 or T201015 kit per customer.

Circle No. 41 on Readers' Service Card

GTS Gene Therapy Systems "the art of innovation"

To Order: 888-428-0558

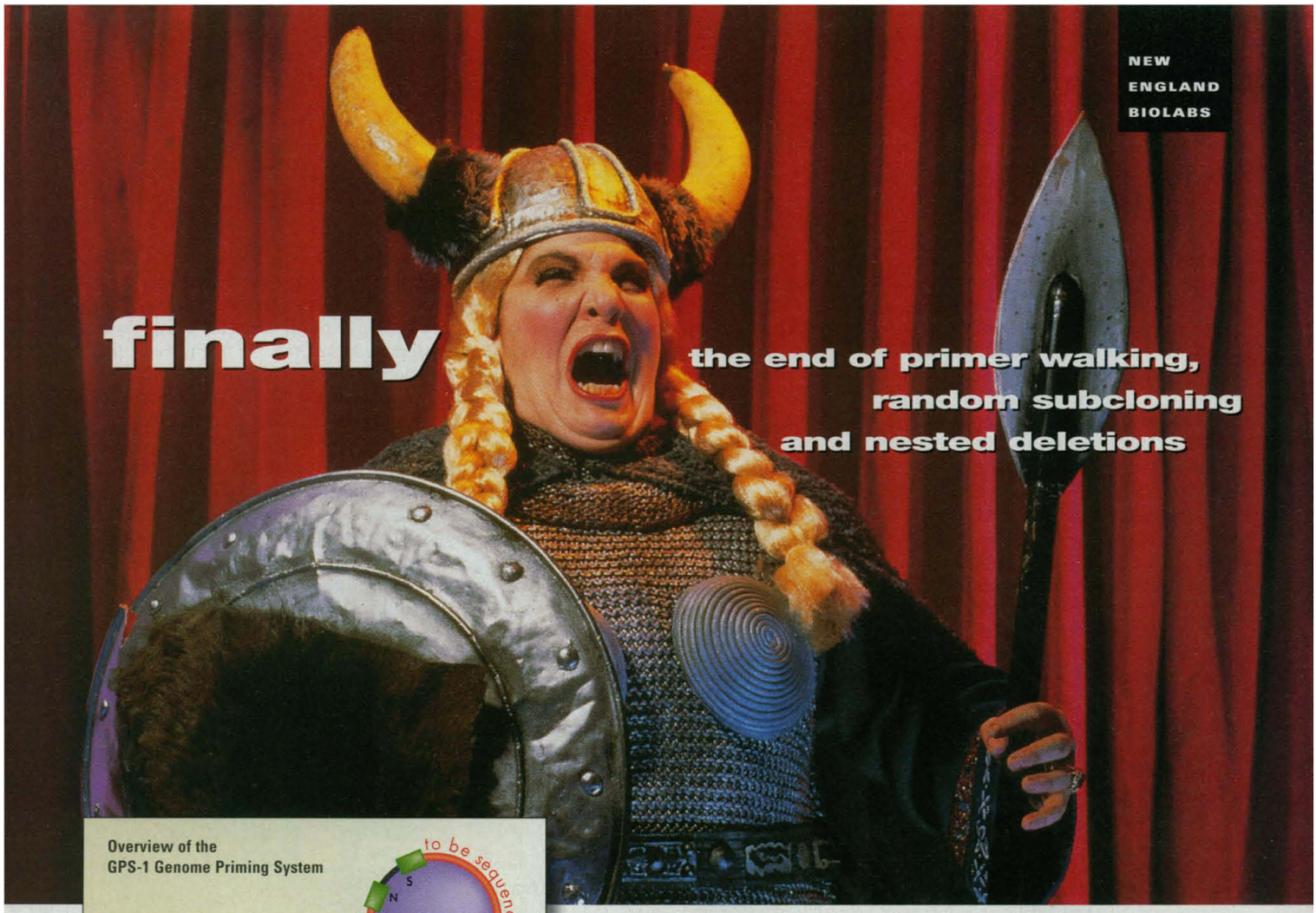
Fax: 619-587-1499

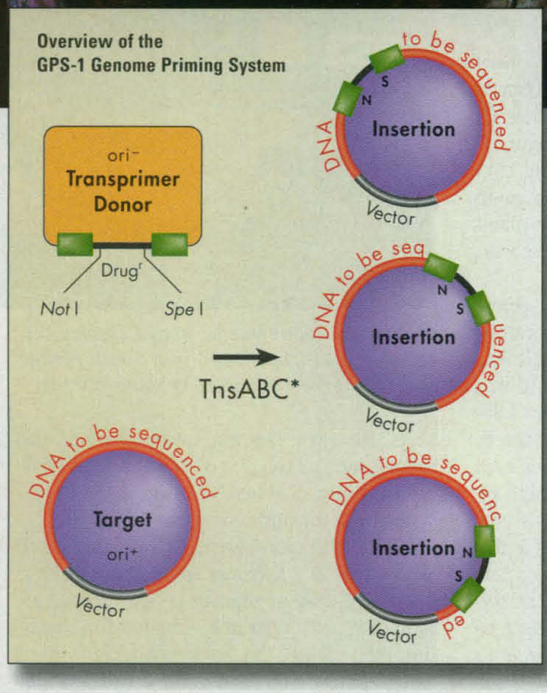
10190 Telesis Court
San Diego, CA 92121, USA

For the complete product list check out the GTS Website @
http://www.genetherapysystems.com

GTS International Distributors

Australia • ASTRAL +61-2-9540-2055 **Austria** • BIO-TRADE +43 1 889 18 19 **Denmark, Finland, Norway, Sweden** • KEBO Lab +46 8 621 35 07 **France** • OZYME +1 30 85 92 92 **Germany** • Biozym Diagnostik GmbH +49 5152-9020 **Japan, Rep. of China, Korea** • Takara +81-77-543-7231 **Switzerland** • Axon Lab AG +41 56 484 80 80 **Taiwan** • PROtech, Ltd. 886-2-23810844 Takara +81-77-543-7231 **United Kingdom** • Lifescreen LTD. +44 0 1923 241515





Transprimer is inserted randomly into the target DNA, generating a set of insertion products with only one Transprimer per molecule.

choose GPS™-1 Genome Priming System and complete your sequencing project in no time.

New England Biolabs introduces GPS-1, a fast, *in vitro* Tn7 transposon-based method for generating a population of DNA sequencing templates containing primer-binding sites (Transprimer element) at randomly interspersed positions. Simply supply your DNA of interest (0.08 µg per 20 µl reaction mix), follow a short protocol, transform into *E. coli*, miniprep colonies and then sequence.

- Transprimer is inserted randomly into the target DNA: no "hot spots" for insertion
- High efficiency: 10^3-10^5 insertion products recovered per reaction; entire protocol takes less than 90 minutes
- Unique rare-cutting restriction enzyme sites within Transprimer facilitate insert mapping
- DNA sequence can be obtained from both strands of target DNA using supplied primers
- Faster than primer walking, random subcloning and nested deletion methods

GPS-1 Genome Priming System

#7100 10 reactions ***Special Introductory Price until 3/1/99***

Includes: pGPS1 (Kan^r) and pGPS2 (Cam^r) Transprimer donor plasmids, TnsABC* Transposase, control target plasmid, sequencing primers for the two ends of the Transprimer, buffers and instruction manual.

For further information on GPS-1, visit **www.neb.com** or call 1-800-NEB-LABS

- **New England Biolabs Inc.** 32 Tozer Road, Beverly, MA 01915 USA 1-800-NEB-LABS Tel. (978) 927-5054 Fax (978) 921-1350 email: info@neb.com
- **New England Biolabs Ltd., Canada** Tel. (800) 387-1095 (905) 672-3370 Fax (905) 672-3414 email: info@ca.neb.com
- **New England Biolabs GmbH, Federal Republic of Germany** Tel. 0800/BIOLABS (06196) 3031 Fax (06196) 83639 email: info@de.neb.com
- **New England Biolabs (UK) Ltd.** Tel. (0800) 31 84 86 (01462) 420616 Fax (01462) 421057 email: info@uk.neb.com

NEW ENGLAND BioLabs® Inc.

DISTRIBUTORS: Australia (07) 5594-0299; Belgium (0800)1 9815; Brazil (011) 366-3565; Denmark (39) 56 20 00; Finland (9) 584-121; France (1) 34 60 24 24; Greece (01) 5226547; Hong Kong 2649-9988; India (542) 311473; Israel (03) 9229013; Italy (02) 381951; Japan (03) 5820-9408; Korea (02) 556-0311; Mexico (5) 280-5691; Netherlands (033) 495 00 94; New Zealand 0800 807809; Norway 22 09 15 00; Singapore 4457927; Spain (03) 902 20 30 90; Sweden (08) 30 60 10; Switzerland (061) 486 80 80; Taiwan (02) 28802913

Circle No. 38 on Readers' Service Card

• Neural Progenitor Cells • Serum-Free and Low Serum Media • Custom Cell Isolations •

BIOWHITTAKER
A CAMBREX Company

Clonetics®

Normal Human Cell Systems
Your Partner In Cell Culture...

the WORLD Center for Cell Culture Excellence™

...Call Us For All Your Human Cell Culture Needs

Innovative Cell Systems, Since 1986 for Research in:

- Cell Therapy
  - Tissue Replacement
  - Degenerative Disease
- High Throughput Screening
- Toxicology
- Cell Biology

Providing the Best In-Vitro Models

- Relevant Non Transformed Human Cells
- Optimized Culture Systems Matching Cells and Medium
- Low Serum and Serum-Free Media
- Standardized/Quality Controlled Products GMP Manufacturing Available
- The Leading Research Team in Human Cell System Development

BioWhittaker is a certified ISO-9001 Quality Management System Company

UK: 011 8 979 5324 • **Europe:** 32 87 32 16 11 • **USA, Canada and all other:** 301 898 7025

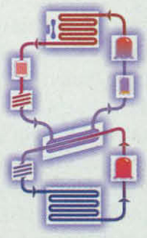
• Western Blots of Clonetics Cells • Custom Cell Isolations • Ancyte™ Animal Cell Systems •

Muscle Cell Systems • Skin Cell Systems • Lung Cell Systems • Prostate Cell Systems • Mammary Cell Systems • Renal Cell Systems

Endothelial Cell Systems • Primary Human Hepatocytes • Dendritic Cell Systems • Human Astrocytes • Osteoblasts

Circle No. 28 on Readers' Service Card

If it's worth saving, it's worth saving in a Revco, now with Legaci™, our time-tested combination of custom built Copeland compressors and DuPont Suva® refrigerants.



Legaci™ represents years of research, life testing and quality assurance.

For ultra-low storage of high value materials, you need reliability, stability and dependability, no compromise. That's why Revco has developed *Legaci*™, a refrigeration system created exclusively for life science, pharmaceutical and laboratory applications.

Legaci™ represents a collaborative effort between Revco and the world's leading compressor and refrigerant manufacturers, Copeland and DuPont. Together, we've life tested new compressor hardware and refrigerant chemistry which, combined, deliver the highest reliability coefficients ever offered. Before you buy an ultra-low freezer, learn more about *Legaci*™.

When it comes to your work and our freezers, it's what's inside that counts.

Chest and upright models to -86°C

800-252-7100
www.revco-sci.com/legaci

REVCO
the future, inside

275 Aiken Road, Asheville, NC 28804 www.revco-sci.com
USA 800-252-7100 Canada 800-447-3826 International 828-658-2711 Fax 828-645-3368

Legaci™ Refrigeration System Powered by Copeland DuPont Suva®Refrigerants

Circle No. 35 on Readers' Service Card

HELPING YOU BUILD A SECURE FINANCIAL FUTURE IS AN IMPORTANT JOB.

FORTUNATELY, TIAA-CREF HAS THE PERFECT RESUME.

With 80 years of leadership experience in our field, TIAA-CREF is eminently qualified to help you build a comfortable, worry-free retirement.

Our references are equally impeccable—today, two million of the best minds in America trust us with their retirement plans, turn to us for mutual funds and their insurance needs.

Allow us to review our qualifications.

Superior strength

With $200 billion in assets, TIAA-CREF is the world's largest retirement organization—and among the most solid. TIAA is one of only a handful of companies to have earned top ratings for financial strength, and CREF is one of Wall Street's largest investors.[1]

Solid, long-term performance

We seek out long-term opportunities that other companies, in pursuit of quick gains, often miss. Though past performance can't guarantee future results, this patient philosophy has proven extremely rewarding.

Surprisingly low expenses

TIAA-CREF's operating costs are among the lowest in the insurance and mutual fund industries.[2] Therefore, more of your money goes where it should—towards ensuring your future.

Easy diversification

We offer a wide variety of expertly managed investment options to help build your assets. With stock, bond, money market, and real estate accounts to choose from—as well as a guaranteed annuity—TIAA-CREF makes diversification easy.

Unrivaled service

We believe that our service distinguishes us from every other retirement company. In a recent nationwide survey of retirement plans, TIAA-CREF was voted number one in participant satisfaction.[3]

If you work in education, research, or related fields, why not put TIAA-CREF's experience to work for you? To find out more, visit our Web site at **www.tiaa-cref.org or call us at 1 800 842-2776.**

TIAA CREF

Ensuring the future for those who shape it.℠

[1]A++ (Superior). A.M. Best Co.; AAA. Duff & Phelps; Aaa. Moody's Investors Services; AAA. Standard and Poor's for stability, sound investments, claims-paying ability, and overall financial strength. These ratings of TIAA as an insurance company do not apply to CREF or the TIAA Real Estate Account. [2]*Standard & Poor's Insurance Rating Analysis*, 1998; Lipper Analytical Services, Inc., *Lipper-Directors' Analytical Data*, 1998 (Quarterly). [3]DALBAR, Inc., *1997 Defined Contribution Excellence Ratings*. For more complete information, including charges and expenses, call 1 800 842-2733, extension 5509, for CREF and TIAA Real Estate Account prospectuses. Read them carefully before you invest or send money. TIAA-CREF Individual and Institutional Services, Inc., distributes CREF certificates and interests in the TIAA Real Estate Account. 12/98

Make the Move To 384-Well Non-Isotopic Assays!

Make the move to Packard's FluoroCount® and LumiCount® for your fluorescent and luminescent applications. Now capable of 384-well measurements!

FluoroCount Fluorescence Detection

- Now even more flexible with 6-, 12-, 24-, 48-, 96- and 384-well measurements
- Top and bottom reading capabilities
- External excitation source provides ultra sensitivity
- UV excitation down to 260 nm!

LumiCount Luminescence Detection

- Glow applications in 96- and now, 384-well formats
- Excellent sensitivity with unique Digital Photon Integration (DPI)
- Internal temperature control from ambient +5 °C to 45 °C for cell cultures

The best value in microplate counters just got better!

Packard
A Packard BioScience Company

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

Packard International Offices:
Australia 03-9543-4266 or 1 800 335 638; **Austria** 43-1-2702504;
Belgium 32(0)2/481.85.30; **Canada** 1-800-387-9559;
Central Europe 43 456 2230 015; **Denmark** 45-43909023 or 45-43907151;
France (33) 1 46.86.27.75; **Germany** (49) 6103 385-151;
Italy 39-2-33910796; **Japan** 81-3-3866-5850; **Netherlands** 31-50-549 1296;
Russia 7-095-259-9632; **Switzerland** (01) 481 69 44;
United Kingdom 44 (0)118 9844981

Circle No. 42 on Readers' Service Card

Detection Technology Begins and Ends With KPL

PROTEIN
RNA
DNA

KPL introduces our new line of Detector™ Kits that provide you with fast, sensitive detection without radioactivity!

COOL ASSAYS

RNADetector™ Northern
Non-isotopic Northern blot that rivals ^{32}P

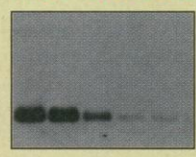
DNADetector™ Southern
Chemiluminescent detection of Southern blots and colony lifts

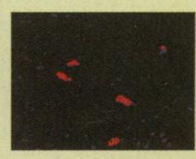
DNADetector™ *In Situ*
Fluorescent and chromagenic *in situ* hybridization systems

ExpressDetector™ Nickel-HRP
Direct detection of recombinant his-tagged proteins

Protein Detector™
Chromagenic and chemiluminescent Western blot and ELISA systems

HOT RESULTS





- Sensitivity equivalent to radioactivity in a fraction of the time
- Complete kits reduce preparation and optimization time

SPECIAL OFFER:

Celebrate our 20th anniversary and receive 20% off when you purchase any of the Detector™ kits listed here. First time orders only. Call 1-800-638-3167 (U.S.) or 301-948-7755 for more information and a free catalog.

Kirkegaard & Perry Laboratories
KPL

20 Years of Detection Expertise

2 Cessna Ct., Gaithersburg, MD 20879-4174, U.S.A.
800-638-3167 (U.S.) or 301-948-7755
Fax: 301-948-0169
www.kpl.com

Circle No. 22 on Readers' Service Card

Request for Proposals

High-throughput Screening and Combinatorial Chemistry Approaches for Cystic Fibrosis Drug Discovery

Application Receipt Date: Open

Developments in the understanding of the cystic fibrosis (CF) basic defect and the role of the CF gene product, CFTR, have enabled scientists to develop strategies for new therapies.The Cystic Fibrosis Foundation (CFF) is soliciting proposals to utilize the growing body of knowledge about CF to develop systems that rapidly discover chemical compounds which correct the function of CF cells. This will be achieved by using the technologies of high-throughput screening (HTS) and combinatorial chemistry (CC).

The CFF will consider proposals for review that address the following issues, but are not limited to:

- developing miniaturization technologies, indicator dyes, marker proteins, cell systems, and related technologies to facilitate the development of HTS technologies related to CF drug development;
- furnishing potential therapeutic agents to evaluate as potential lead compounds for CF drug development;
- creating HTS facilities that serve as resources for evaluating prospective chemical agents resulting from combinatorial chemistry or other entities for evaluation and;
- developing chemical derivatives of existing lead compounds for consideration as candidate drugs.

The application of HTS and CC to develop new anti-*Pseudomonas aeruginosa* drugs will be considered.

Review and Award: The maximum amount awarded will be $1.5 million over two years. Each application must contain "milestone achievement objectives" and the appropriate timetable for completion of each. Continued funding for the project will be, in part, based upon milestone attainment.

Submission: An original, plus 20 copies, must be sent to the CFF, Attn: Office of Grants Management,
6931 Arlington Road
Bethesda, MD 20814
(301) 951-4422.

Cystic Fibrosis Foundation

Circle No. 20 on Readers' Service Card