10 July 1998

Science

Vol. 281 No. 5374
Pages 133–296 $7

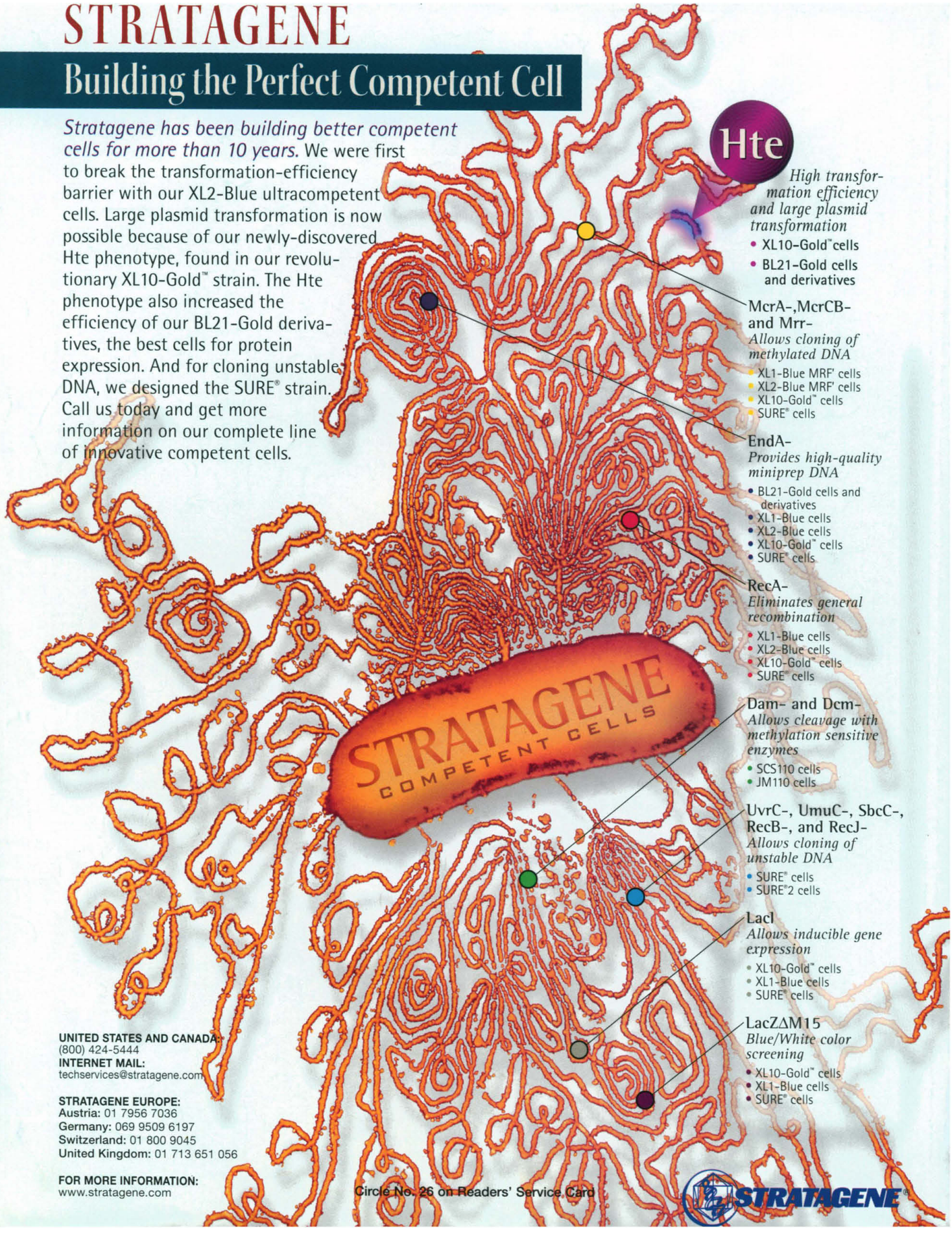
CHEMISTRY AND BIOLOGY OF THE OCEANS

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

STRATAGENE

Building the Perfect Competent Cell

Stratagene has been building better competent cells for more than 10 years. We were first to break the transformation-efficiency barrier with our XL2-Blue ultracompetent cells. Large plasmid transformation is now possible because of our newly-discovered Hte phenotype, found in our revolutionary XL10-Gold™ strain. The Hte phenotype also increased the efficiency of our BL21-Gold derivatives, the best cells for protein expression. And for cloning unstable DNA, we designed the SURE® strain. Call us today and get more information on our complete line of innovative competent cells.



Hte
High transformation efficiency and large plasmid transformation
- XL10-Gold™ cells
- BL21-Gold cells and derivatives

McrA-, McrCB- and Mrr-
Allows cloning of methylated DNA
- XL1-Blue MRF' cells
- XL2-Blue MRF' cells
- XL10-Gold™ cells
- SURE® cells

EndA-
Provides high-quality miniprep DNA
- BL21-Gold cells and derivatives
- XL1-Blue cells
- XL2-Blue cells
- XL10-Gold™ cells
- SURE® cells

RecA-
Eliminates general recombination
- XL1-Blue cells
- XL2-Blue cells
- XL10-Gold™ cells
- SURE® cells

Dam- and Dcm-
Allows cleavage with methylation sensitive enzymes
- SCS110 cells
- JM110 cells

UvrC-, UmuC-, SbcC-, RecB-, and RecJ-
Allows cloning of unstable DNA
- SURE® cells
- SURE®2 cells

LacI
Allows inducible gene expression
- XL10-Gold™ cells
- XL1-Blue cells
- SURE® cells

LacZΔM15
Blue/White color screening
- XL10-Gold™ cells
- XL1-Blue cells
- SURE® cells

UNITED STATES AND CANADA:
(800) 424-5444
INTERNET MAIL:
techservices@stratagene.com

STRATAGENE EUROPE:
Austria: 01 7956 7036
Germany: 069 9509 6197
Switzerland: 01 800 9045
United Kingdom: 01 713 651 056

FOR MORE INFORMATION:
www.stratagene.com

Circle No. 26 on Readers' Service Card

STRATAGENE®

VOLUME 281 10 JULY 1998 NUMBER 5374

Science

www.sciencemag.org

COVER Photomosaic of a 6-meter-tall submarine hydrothermal deposit. Composed mostly of sulfide minerals, many thousands like it form along the mid-ocean ridge system. Hot, nutrient-rich fluids blend with cold seawater, supporting symbiotic fauna on the surface of the edifice and diverse microbial activity within and beneath it. See Delaney *et al.* and the special section beginning on p. 189. [Mosaic: D. Yoergerk, M. Elend]

159
AIDS rhetoric and realism

DEPARTMENTS

NEWS

NEWS OF THE WEEK

NEWS FOCUS

CHEMISTRY AND BIOLOGY OF THE OCEANS

NEWS

VIEWPOINT

REVIEW

See related News on p. 156, Editorial on p. 173, Perspective on p. 183, and Reports on pages 231, 234, 237, and 240.

RESEARCH

REPORTS

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE
150 YEARS • 1848-1998

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): $108 ($60 allocated to subscription). Domestic institutional subscription (51 issues): $295. 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. IPM #1069624. **Printed in the U.S.A.**

SCIENCE'S COMPASS

ONLINE PRODUCTS AND FEATURES

SCIENCE
THE JOURNAL ONLINE
www.sciencemag.org

***SCIENCE*NOW**
DAILY NEWS SERVICE
www.sciencenow.org

NEXT WAVE
WEEKLY CAREER UPDATES
www.nextwave.org

243
Imaging where the mantle melts

www.sciencemag.org/cgi/content/full/281/5374/143a

253
Building small proteins with β sheets

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $7.00 per issue prepaid includes surface postage; bulk rates on request. **Authorization to photocopy** material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that $4.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for *Science* is 0036-8075/83 $4.00. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

13-98 MMC

It won't take you much more than a minute to read this ad. But it could save you 230. Because that's the amount of time you can look forward to saving every time you use AlkPhos Direct™ for labelling DNA and RNA probes.

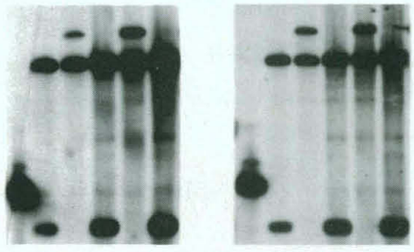
How? Largely because AlkPhos Direct eliminates the need for lengthy post-hybridization antibody incubations associated with conventional hapten-based methods. But there are substantial reductions in time in the pre-hybridization steps as well.

And the results? They're comparable with digoxigenin-quality results as you can see below.

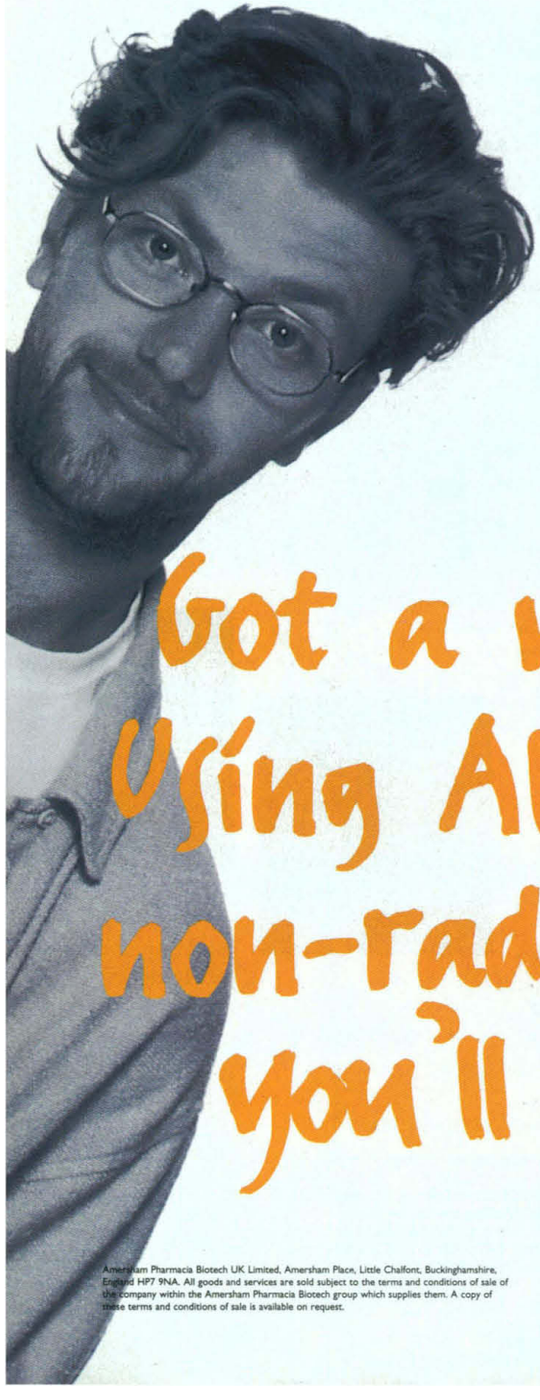
AlkPhos Direct labelling systems are available with CDP-*Star*™ for high sensitivity chemiluminescent applications, or with ECF™ for fluorescence scanning instrumentation.

Time's up. Call us for more information: in Europe +44 (0) 1494 544550; in the US 1-800 526 3593; in Japan +81 3 5331 9336 and from the rest of the world +44 (0) 1494 544100.

Or visit our web site: www.apbiotech.com/alkphos and take advantage of the special AlkPhos Direct introductory offer. There's no time to lose and everything to gain.



Southern blot: Cosmid DNA digested with *Not* I and *Eco*R I, probed with a 1.1 kb probe labelled with AlkPhos Direct (left) and digoxigenin (right).
(Courtesy of Janet Bartels-Carr, Yale University, USA.)



Got a minute to spare? Using AlkPhos Direct for non-radioactive labelling, you'll have hundreds.

amersham pharmacia biotech

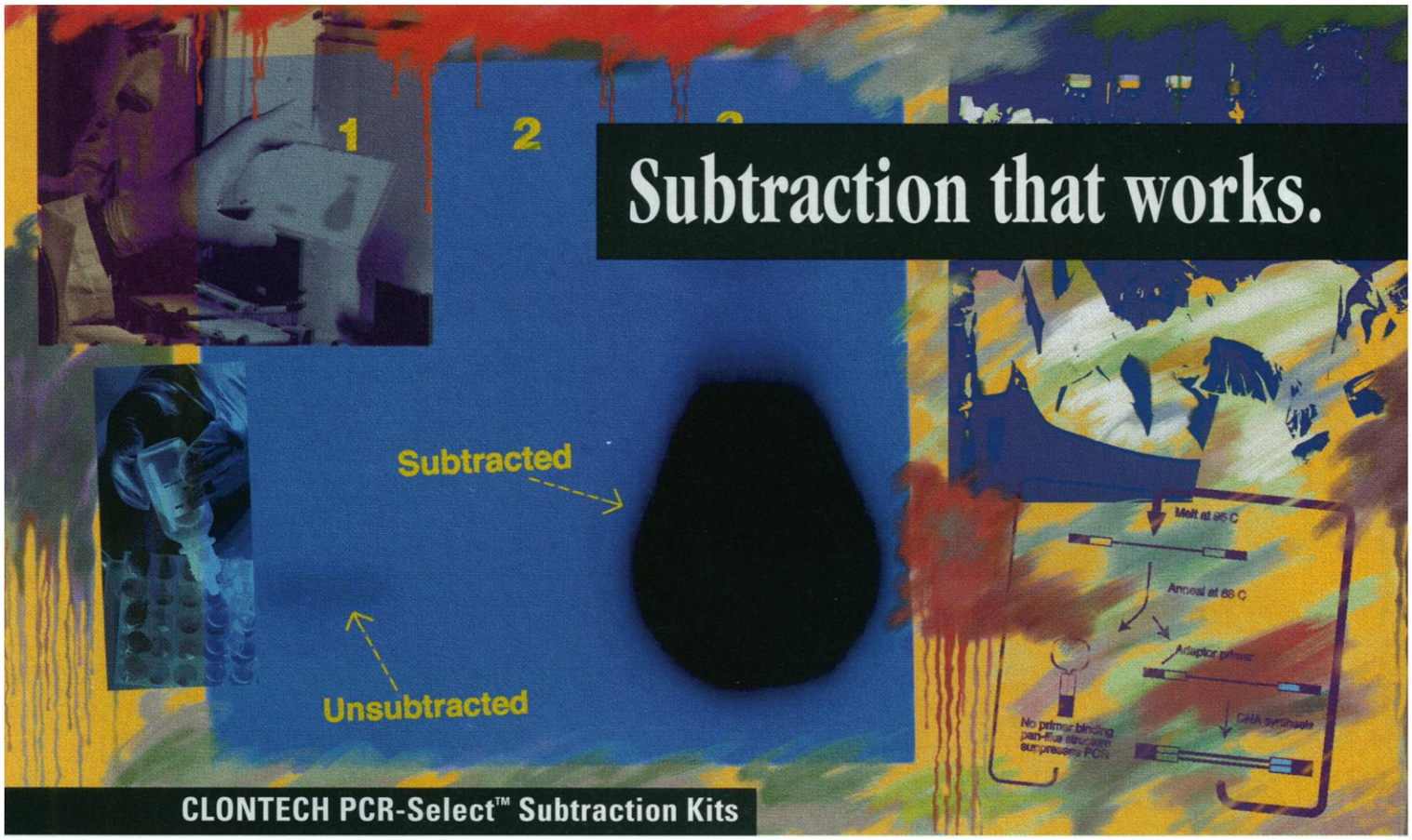
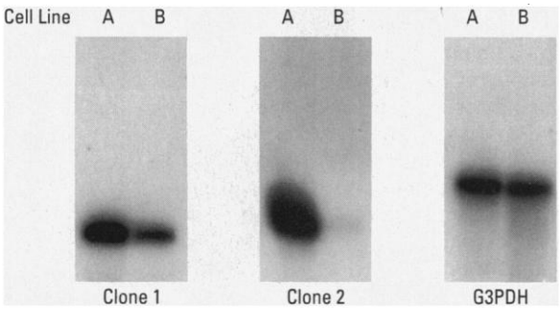


Illustration inspired by the art of Robert Rauschenberg (1925).



PCR-Select is a powerful method for isolating and cloning differentially expressed genes. cDNA amplified from two cell lines (A & B) was blotted and hybridized to labeled cDNA clones isolated using the PCR-Select Differential Screening Kit (#K1808-1). Results confirm differential expression of both clones. Control hybridization with G3PDH, a housekeeping gene, indicates lanes were equally loaded.

Find the latest PCR-Select citations with CLONTECH's Citation Search at www.clontech.com/clontech/Citations.html

CLONTECH's PCR-Select cDNA Subtraction Kit (#K1804-1) uses patented technology* to deliver up to **1,000-fold enrichment of rare cDNA messages**—giving you the best chance for finding novel clones. And by combining PCR-Select with CLONTECH's SMART cDNA technology you can generate a high-quality, subtracted library from as little as 50 ng of total RNA. For fast, highly effective isolation of pathogenicity islands and other genomic differences between bacterial strains, choose the new **PCR-Select Bacterial Genome Subtraction Kit** (#K1809-1). Call **800-662-2566 (CLON)** or contact your local representative.

* U.S. Patent #5,565,340; foreign patents pending.

PCR is covered by patents owned by Hoffmann-La Roche and F. Hoffmann-La Roche, Ltd.

In Germany please contact CLONTECH GmbH • Tel: 06221 34170 Fax: 06221 303511
In the UK please contact CLONTECH UK Ltd. • Tel: 01256 476500 Fax: 01256 476499
In Japan please contact CLONTECH Japan Ltd. • Tel: 03 5643 3271 Fax: 03 5643 3252

Australia: 61 2 9417 7866 ■ **Austria and Eastern Europe:** 43 1 889 1819 ■ **Belgium/Luxemburg:** 0 800 1 9815 ■ **Canada:** Now call CLONTECH direct • 800 662 2566 ■ **China:** BEIJING YUANGPING BIOTECH • 86 10 68187551; GENE CO. LTD. • 852 2896 6283; HW SCIENCE & TECHNOLOGY DEVELOPMENT CO., LTD. • 86 22 26647265; SINO-AMERICAN BIOTECH CO. • 86 21 6402 2371; WATSON BIOMEDICALS, INC. • 86 21 65572386 ■ **Czech Republic:** 420 19 65214 ■ **Egypt:** 202 349 8311 ■ **Finland:** 9708 596 19 ■ **France:** 33134 602424 ■ **Germany:** CLONTECH GmbH • 49 6221 34170 ■ **Greece:** 30 1 483 1190 ■ **Hong Kong:** 852 2646 6101 ■ **India:** 091 11 54 21714 ■ **Israel:** 972 4 9960595 ■ **Italy:** 55 5 001871 ■ **Japan:** CLONTECH Japan Ltd. • 81 3 5643 3271 ■ **Korea:** 82 2 556 0311 ■ **Malaysia:** 603 777 2608 ■ **Mexico:** 525 281 4718 ■ **The Netherlands:** 31 33 495 00 94 ■ **Scandinavia:** 46 8 749 5940 ■ **Singapore:** 65 775 7284 ■ **Spain/Portugal:** 34 9 1 630 0379 ■ **Switzerland:** 41 61 272 3924 ■ **Taiwan:** 886 2 27202215 ■ **Thailand:** 662 530 3805 ■ **Turkey:** 90 216 385 8321 ■ **United Kingdom:** CLONTECH UK Ltd. • 44 1256 476500

rev. 6/16/98

CLONTECH
NOW YOU CAN.

1020 East Meadow Circle, Palo Alto, California 94303 USA
Tel: 800-662-2566 (CLON) 650-424-8222 • Fax: 800-424-1350 650-424-1088
E-mail: products@clontech.com orders@clontech.com • Internet: www.clontech.com

(AD82973)

Circle No. 21 on Readers' Service Card

OCEANIC NITROGEN

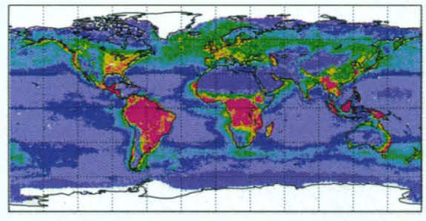
Most reduced nitrogen in the oceans is in the form of dissolved organic nitrogen (DON), a mixture of compounds that has been difficult to characterize. Contamination with living organisms, caused by limitations in filtration methods, has complicated analyses, and thus the sources and cycling mechanisms of this important component of seawater have remained largely unknown. McCarthy *et al.* (p. 231) present data from a range of locations comprising deep water, as well as surface waters, in different oceanic basins and show that the enantiomeric ratios of certain amino acids show similar, distinctive patterns in all of these locations. The observations point toward peptidoglycans, a component of bacterial cell walls, as one of the major sources of DON.

PACIFIC CLIMATE

The climate of the Pacific Ocean appeared to change in the mid-1970s and to have increased the frequency and intensity of El Niño events, which impacted many marine communities in the North Pacific. Guilderson and Schrag (p. 240) examined some of the possible causes and effects of this change using a coral carbon-14 record of upwelling from the Galápagos Islands and suggest that the change coincided with a deepening of the thermocline in the eastern Pacific (less upwelling). In an article, McGowan *et al.* (p. 210) consider the effects of this climate shift on marine ecosystems throughout the North Pacific.

ASSESSING OCEAN PRODUCTIVITY

One way of assessing our understanding of the processes that affect ocean productivity is to evaluate whether sources and sinks of key components are in balance (see the article by Falkowski *et al.*, p. 200). Overall, ocean ecosystems are thought to act as a sink for CO_2, that is, gross production and consumption of CO_2 exceed respiration rates. One concern is that large parts of the ocean are "unproductive," and CO_2 should be released from these ecosystems. Duarte and Agustí (p. 234) compared community respiration and production rates for these unproductive ecosystems. They quantified the carbon budget by using oxygen evolution as a proxy for carbon fluxes. They conclude that most of the ocean ecosystems do release CO_2 but that one-fifth of the ocean is highly productive, which leads to an overall near balance for CO_2 exchange. The net primary productivity of the biosphere as a whole (both oceanic and terrestrial components) affects the fluxes of carbon through the biosphere (see the Perspective by Tans, p.183). Similarities and differences exist between oceans and land, such as for the time scales of turnover and the relative importance of the primary limitations (light, water, and nutrients).



Existing models tend to stress the differences, and few attempts have been made to integrate the two components. Field *et al.* (p. 237) used parallel satellite data sets to devise models that can describe both components and then estimated primary production for both oceanic and terrestrial ecosystems. Such whole-biosphere models are essential for understanding the global carbon cycle and its dynamics.

PUTTING OUT EARLY FIRES

The reported presence of charred bones, ash, charcoal, and colored soil at Zhoukoudian, China, dated to as old as 500,000 years ago, has been widely assumed to be the first solid evidence for the controlled use of fire by early hominids. Weiner *et al.* (p. 251; see the news story by Wuethrich, p. 165, and a related book review by Goudsblom, p. 180) have now reanalyzed the soils and bones. They could not detect ash, charcoal, or fire-related alteration in the soils. Although the bones were indeed burned, they were not burned at the site. Thus, the site does not provide conclusive evidence for the controlled use of fire.

SOLUTION ROUTE TO DIAMONDS

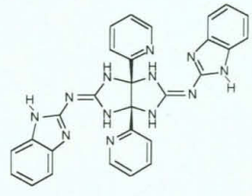
Diamonds are usually synthesized through high-pressure or chemical vapor deposition routes. Li *et al.* (p. 246) report a chemical route that modifies the Wurtz synthesis for coupling alkyl halides by sodium reduction to form alkanes and salts. They instead used carbon tetrachloride as the reactant with the expectation that a similar process would couple the carbon atoms into a tetrahedral network. The reaction proceeds at 700°C and is catalyzed by a nickel-cobalt catalyst. Although the yield of diamond is low (2 percent), the catalytic nature of the reaction suggests that further improvements may be possible.

ALL-β-SHEET PROTEIN DESIGN

Of the two key secondary structure elements of proteins, β sheets and α helices, the former are much less tractable in terms of the rules that govern their formation and stabilization. Studies of small peptides and proteins have provided much insight into α helices, but small β sheets tend not to be stable in aqueous solution without aggregation unless they are stabilized, for example, by disulfide bridges. Kortemme *et al.* (p. 253) used a hierarchical design approach combining modeling and experiment to design a 20 residue protein in which the central 16 residues form a three-strand antiparallel β sheet; the small protein shows a cooperative two-state folding-unfolding transition, a property which is central to natural proteins.

SMALL G-CSF MIMIC

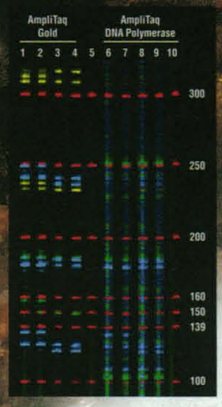
Transmembrane receptors are potential targets for therapeutic drugs, but realization of this potential would require the development of small nonpeptide compounds that mimic activation of such receptors that are normally bound by relatively large protein ligands. Tian *et al.* (p. 257) provide evidence that such molecules can be found. The small molecule called SB 247464 was isolated in a screen for compounds that could mimic transcriptional activation characteristic of the cytokine granulocyte–colony-stimulating factor (G-CSF). SB 247464 appears to bind to the extracellular domain of the G-CSF receptor but at a site distinct from that where G-CSF itself binds. SB 247464 produced effects like those of G-CSF when applied to cells in culture or injected into mice. The compound has considerable specificity: it did not activate other related receptors and activated the mouse G-CSF receptor but not the equivalent human receptor.



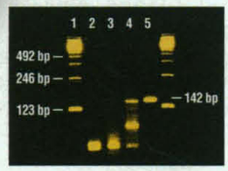
CONTINUED ON PAGE 143

Introducing
AmpliTaq Gold™

Where There's Gold, You'll Find Performance.



Co-amplification of 8 human STR loci. L1, 2: male control DNA; L3, 4: female control DNA; L5: AmpliTaq negative control; L6, 7: male control DNA; L8, 9: female control DNA; L10: negative control.



Amplification of HIV-1 Control DNA. L2: 0 copies, AmpliTaq DNA Polymerase, No Hot Start; L3: 10 copies, AmpliTaq DNA Polymerase, No Hot Start; L4: 10 copies, AmpliTaq DNA Polymerase, manual Hot Start; L5: 10 copies, AmpliTaq Gold.

For PCR performance with higher yield, better specificity and more reliable results, discover AmpliTaq Gold™.

This new version of AmpliTaq® DNA Polymerase provides the specificity of Hot Start PCR, without all the extra steps. In most cases, you can substitute AmpliTaq Gold directly in existing PCR amplification protocols—without re-optimization.

You'll find AmpliTaq Gold saves time and money with dramatically lower drop-out rates, improved specificity, and easier multiplexing.

It also gives you consistently better PCR results. Because AmpliTaq Gold remains inactive until heated, conditions that lead to primer-dimer formation and mispriming are eliminated.

And of course, you have the continued assurance of knowing that AmpliTaq Gold is backed by PE Applied Biosystems' exclusive PCR Performance Guarantee.

So discover AmpliTaq Gold, and discover high performance PCR. To request information, call 1-800-327-3002. Outside the U.S. and Canada, contact your local PE Applied Biosystems representative. On the Internet, visit our home page at http://www. amplitaqgold.com, or e-mail pebio@perkin-elmer.com.

PE *Applied Biosystems*

Europe Langen, Germany Tel: 49 (0)6103 708 301 Fax: 49 (0)6103 708 310
Japan Tokyo, Japan Tel: (047) 380-8500 Fax: (047) 380-8505
Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223
Australia Melbourne, Australia Tel: 1 800 033 747 Fax: 61 3 9212-8502

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

Roche

THIS WEEK IN *SCIENCE*

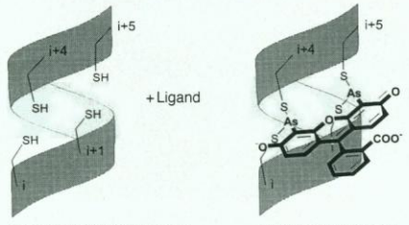
CONTINUED FROM PAGE 141

MALDI AND GENOME ANALYSIS

New technologies for the analysis of large nucleic acids would greatly facilitate the analysis of genomes from humans and model systems. Although matrix-assisted laser desorption/ionization (MALDI) has been considered as a possible alternative to gel electrophoresis, there has not been evidence that it could be applied to fragments of DNA on the order of 2000 nucleotides in length. Berkenkamp *et al.* (p. 260) show that when a suitable liquid matrix is used, the mass of DNA (2200 nucleotides in length) or RNA could be determined to an accuracy of 1 percent.

TAGGING AND DYING PROTEINS

Methods that allow visualization of specific proteins in living cells have numerous applications in cell biology. Griffin *et al.* (p. 269) report a method in which a protein of interest can be labeled with a six–amino acid peptide that binds with high affinity to a small, membrane-permeant fluorescent ligand. They found that a reversible covalent binding reaction occurs between trivalent arsenic compounds and closely spaced pairs of cysteine residues in proteins. They designed a peptide to provide optimal interaction of four cysteines with appropriately spaced trivalent arsenics in an organic molecule. In the presence of a small vicinal dithiol compound to reduce binding to endogenous cellular dithiols, detection of the labeled protein with high specificity was possible. The method is expected to have wide utility for protein labeling in live cells and for affinity tagging to allow rapid protein purification.



α–helical CCXXCC domain Fluorescent complex

ASSEMBLING RNA POLYMERASE

In *Escherichia coli*, the enzyme responsible for converting the sequence information from DNA into RNA, RNA polymerase, consists of four subunits, two identical α subunits and two related subunits known as β and β′. The latter two subunits catalyze the template-dependent polymerization of ribonucleotides, whereas the pair of α subunits initiate assembly of the complex and interact with other proteins that dictate which genes are transcribed and which remain inactive. Zhang and Darst (p. 262) present a high-resolution structure of the α subunit amino-terminal domain and combine their structural picture with sequence comparisons to identify the likely homologs of these subunits in eukaryotic organisms.

IMMUNE SUPPRESSION BY NON-INFECTIOUS HIV

The Vpr protein encoded by the human immunodeficiency virus (HIV) is packaged into viral particles (virions) and is needed for infection of nondividing cells such as macrophages. Although it was previously known to induce cell-cycle arrest in the G_2 phase, Poon *et al.* (p. 266) have now found that Vpr can do so when it is associated with virions containing noninfectious HIV. Most of the virus particles in an infected individual are noninfectious, and it thus appears that these particles may contribute to immune dysfunction even after treatment with antiretroviral agents.

TECHNICAL COMMENT SUMMARIES

Materials with Negative Compressibilities

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/281/5374/143a

R. H. Baughman *et al.* described (Reports, 6 Mar., p. 1522) "rare crystal phases that expand in one or more dimensions" when compressed and showed them to have "negative Poisson's ratios."

J. A. Kornblatt comments that the "biological literature is just beginning to recognize that this phenomenon might be occurring when proteins and other biologically important species are subjected to pressure." E. B. Sirota and H. E. King Jr. comment that "this phenomenon ... is also exhibited by a rather wide class of common compounds containing alkyl chains."

In response, Baughman *et al.* discuss their "static-lattice" model, as well as the temperature dependence of various crystals. "The importance of this property observation for the rotary phase," they state, "is in the mechanism resulting in the reported negative linear compressibility and the possibility of generalizing this mechanism to identify materials useful for applications."

Total Suspension

Indefinite Storage, Product Protection, Simple Retrieval

It requires great skill and precise handling to suspend living cells while ensuring maximum cell viability and recovery. Forma Scientific's NEW CryoPlus Series Liquid Nitrogen Storage Systems provide easy operation and proven performance.

- Microprocessor liquid level control and alarm system
- 16 preset audible/visual alarm combinations
- Exclusive 24 tri-color LED continuously displays actual LN_2 level and control setpoint
- Four tank sizes with capacities of 6,318, 14,000, 25,000 and 40,300 vials (2.0ml)
- Lockable control panel and lid
- Dual gaskets on lid reduce moisture migration
- Unique non-CFC urethane lid insulation with dedicated vent (patent pending)
- Counterbalanced lid with 100% clearance allows easy retrieval
- Optional Thermal Data Printer available for valuable documentation
- UL, CSA, CE (IEC 1010)

When only basic storage/monitoring is needed, choose Forma's NEW Cryo Series. Forma also offers a complete line of Controlled Rate Freezing Systems, LN_2 Storage Containers, Dry Shippers and a full complement of inventory control systems and accessories.

Forma Scientific, Inc.

Box 649, Marietta, OH 45750
740-373-4763 • Fax: 740-373-6770
USA and Canada 800-848-3080
International Distributors Worldwide
An ISO 9001 Company
http://www.forma.com

Forma Scientific is a subsidiary of ThermoQuest Corporation, a public subsidiary of Thermo Instrument Systems Inc., a Thermo Electron Company.

Circle No. 13 on Readers' Service Card

TSA™ IS THE DIFFERENCE

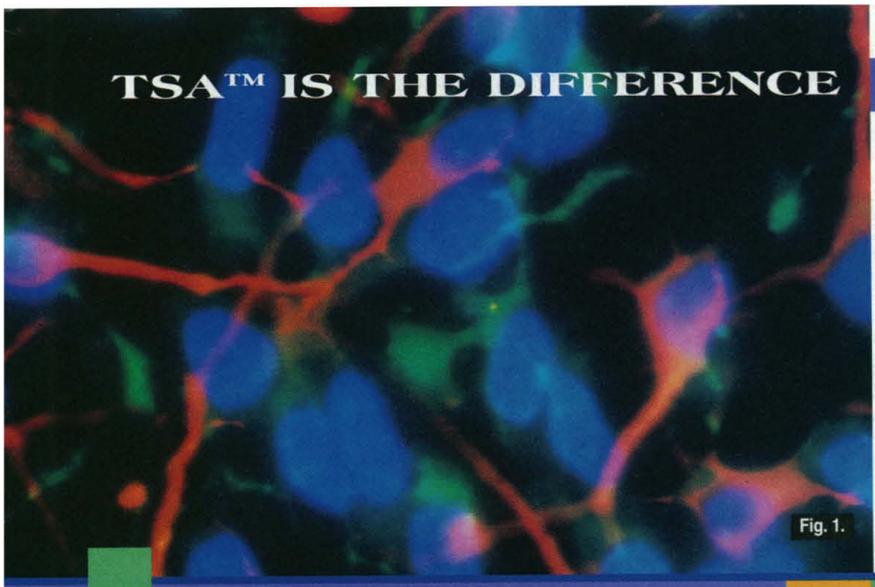


Fig. 1.

See Clearly.

Now you can enhance both chromogenic and fluorescent signals up to 1000 times with Renaissance® Tyramide Signal Amplification (TSA), a powerful new technology from NEN™ Life Science Products. TSA is easily integrated into standard immunohistochemistry (IHC) or in situ hybridization (ISH) protocols, providing Horseradish Peroxidase (HRP) is present in the system.

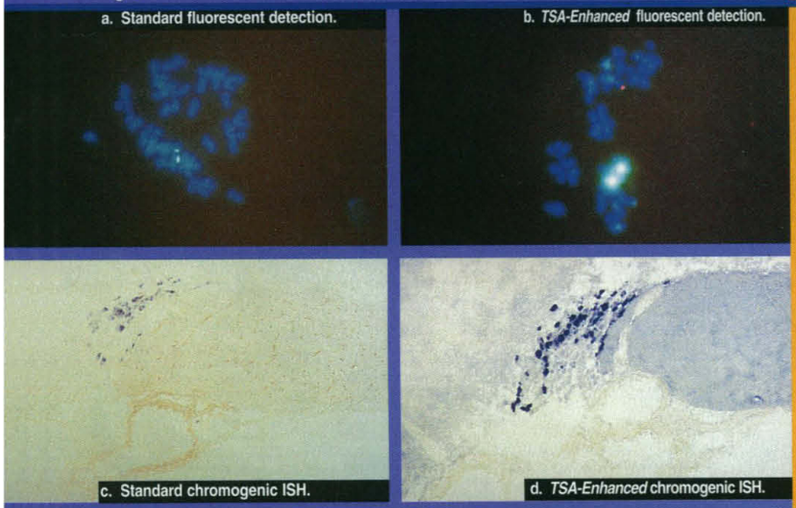
Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University School of Medicine, St. Louis, Missouri.

How does it work?

This technology uses HRP to catalyze the deposition of biotinyl or fluorescent tyramide onto tissue-section or cell-preparation surfaces that were previously blocked with protein. This reaction is quick (less than 10 minutes) and results in the deposition of numerous biotin or fluorochrome labels.

These labels can then be detected directly or indirectly by standard techniques. The deposition occurs right at the enzyme site, resulting in minimal loss of resolution. This easy-to-use signal amplification technique may be applied to both IHC and ISH.

Fig. 2



Enhance signal up to 1000-fold.

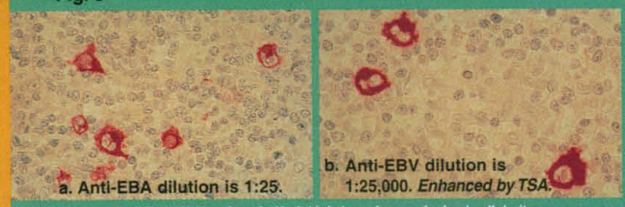
Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads.
Figs. 2 c-d. In situ chromogenic detection of oxytocin in rat brain tissue sections.

Care to Jump?

Call today to learn more about TSA and our complete line of Renaissance labeling and detection products for nucleic acids and proteins. To order call your local NEN office.

Circle No. 30 on Readers' Service Card

Fig. 3



Figs. 3 a-b. IHC of EBV antigen in Hodgkin's Lymphoma of mixed cellularity.
Courtesy of R. Von Wasielewski and S. Gignac, Pathologisches Institut de Medizinischen Hochscule, Hannover, Germany.

Reduce use of valuable reagents.

The use of TSA allows you to conserve your precious antibodies while maintaining the same level of sensitivity.

Fluorescent or chromogenic, it's your choice.

TSA-Direct deposits numerous fluorochromes that can be directly visualized immediately after amplification. TSA-Direct kits are available in a variety of colors: Fluorescein (Green), Tetramethylrhodamine (Red), and Coumarin (Blue).

TSA-Indirect deposits numerous biotins which are then detected by streptavidin conjugated to an enzyme (followed by chromogenic detection) or a fluorochrome (for fluorescent detection).

NEN™ Life Science Products
Boston, MA 02118–2512 USA
1–800–551–2121 • 617–482–9595
Fax: 617–482–1380
Web: http://www.nenlifesci.com

Products available worldwide.
Consult the NEN home page for your local sales office or distributor.
http://www.nenlifesci.com

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.

STATISTICA

STATISTICA (automatically configures itself for *Windows* 95, NT, or 3.1) ■ A complete data analysis system with thousands of on-screen customizable, presentation-quality graphs fully integrated with all procedures ■ Comprehensive *Windows* support, OLE (client and server), DDE, customizable *AutoTask* toolbars, pop-up menus ■ Multiple data-, results-, and graph-windows with *data-graph* links ■ The largest selection of statistics and graphs in a single system; comprehensive implementations of: Exploratory techniques with advanced brushing; multi-way tables with banners (presentation-quality reports); nonparametrics; distribution fitting; multiple regression; general nonlinear estimation; stepwise logit/probit; general ANCOVA/MANCOVA; variance components; stepwise discriminant analysis; log-linear analysis; confirmatory/exploratory factor analysis; cluster analysis; multidimensional scaling; classification tress; canonical correlation; item analysis/reliability; correspondence analysis; survival analysis; a large selection of time series modeling/forecasting techniques; structural equation modeling with *Monte Carlo* simulations; and much more ■ On-line *Electronic Manual* with comprehensive introductions to each procedure and examples ■ Hypertext-based *Stats Advisor* expert system ■ Workbooks with multiple *AutoOpen* documents (e.g., graphs, reports) ■ Extensive data management facilities (fast spreadsheet of unlimited capacity with long formulas, *Drag-and-Drop, AutoFill, Auto-Recalculate,* split-screen/variable-speed scrolling, advanced Clipboard support, DDE links, hot links to graphs, relational merge, data verification/cleaning) ■ Powerful *STATISTICA BASIC* language (professional development environment) with matrix operations, full graphics support, and interface to external programs (*DLLs*) ■ Batch command language and editable macros, flexible "turn-key" and automation options, custom-designed procedures can be added to floating *Auto Task* toolbars ■ All output displayed in Scrollsheets™ (dynamic, customizable, presentation-quality tables with instant 2D, 3D, and multiple graphs) or word processor-style report editor (of unlimited capacity) that combines text and graphs ■ Extremely large analysis designs (e.g., correlation matrices up to 32,000x32,000, virtually unlimited ANOVA designs) ■ Megafile Manager with up to 32,000 variables (8 Mb) per record ■ Unlimited size of files; extended ("quadruple") precision; unmatched speed ■ Exchanges data and graphs with other applications via DDE, OLE, or an extensive selection of file import/export facilities (incl. *ODBC* access to virtually all data bases and mainframe files) ■ Hundreds of types of graphs, incl. categorized multiple 2D and 3D graphs, ternary 2D/3D graphs, matrix plots, icons, and unique multivariate (e.g., 4D) graphs ■ Facilities to custom-design new graph types and add them permanently to menus or toolbars ■ On-screen graph customization with advanced drawing tools (e.g., scrolling and editing of complex objects in 32x real zoom mode), compound (nested) OLE documents, *Multiple-Graph AutoLayout Wizard,* templates, special effects, icons, page layout control for slides and printouts; unmatched speed of graph redraw ■ Interactive rotation, perspective and cross-sections of 3D displays ■ Large selection of tools for graphical exploration of data: extensive brushing tools with animation, fitting, smoothing, overlaying, spectral planes, projections, layered compressions, marked subsets ■ Price **$995.**

Quick STATISTICA (for Windows) ■ A subset of *STATISTICA*; comprehensive selection of basic statistics and the full analytic and presentation-quality graphics capabilities of *STATISTICA* ■ Price **$495.**

STATISTICA Industrial System (requires *STATISTICA* or Quick *STATISTICA*) ■ The largest selection of industrial statistics in a single package; quality control charts (real-time data acquisition options), process capability analysis, R&R, Weibull Analysis, sampling plans, and an extremely comprehensive selection of experimental design (DOE) methods ■ Flexible tools to customize and automate all analyses and reports (incl. "turn-key" system options, and tools to add custom procedures) ■ Price **$995.**

NEW **STATISTICA Neural Networks** (interfaces with, but does not require *STATISTICA*) ■ The most comprehensive, universal, and user-friendly NN application available on the market, featuring unique, automatic (AI) algorithms to find the best NN architecture and best subsets of variables; supports multiple networks and designs of practically unlimited sizes ■ Price **$795.**

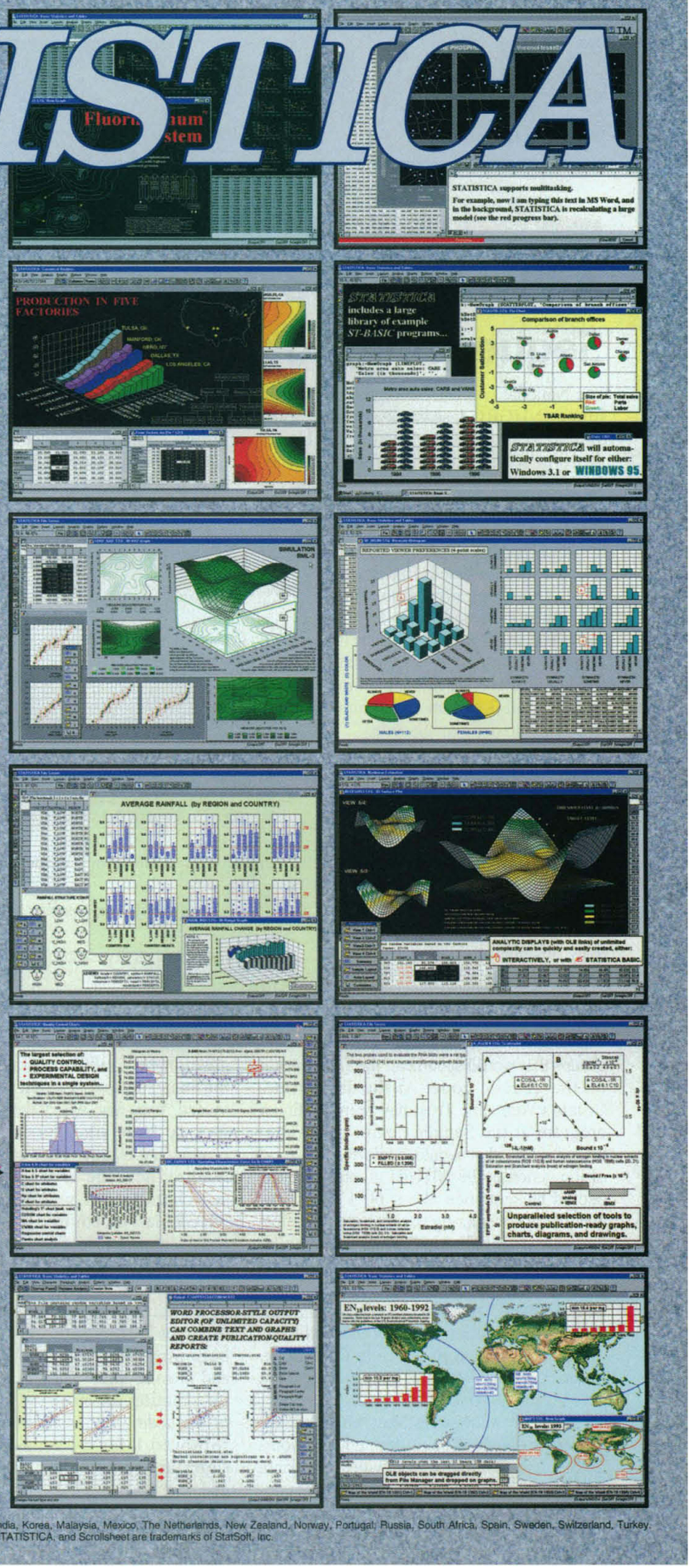
STATISTICA/Mac (for Macintosh) ■ Price **$695** (Quick - **$395**).

Overseas prices vary. Domestic sh/h $12; 30-day money back guarantee.

STATISTICA has received the highest rating in EVERY comparative review of statistics software in which it was featured, since its first release.

Circle No. 2 on Readers' Service Card

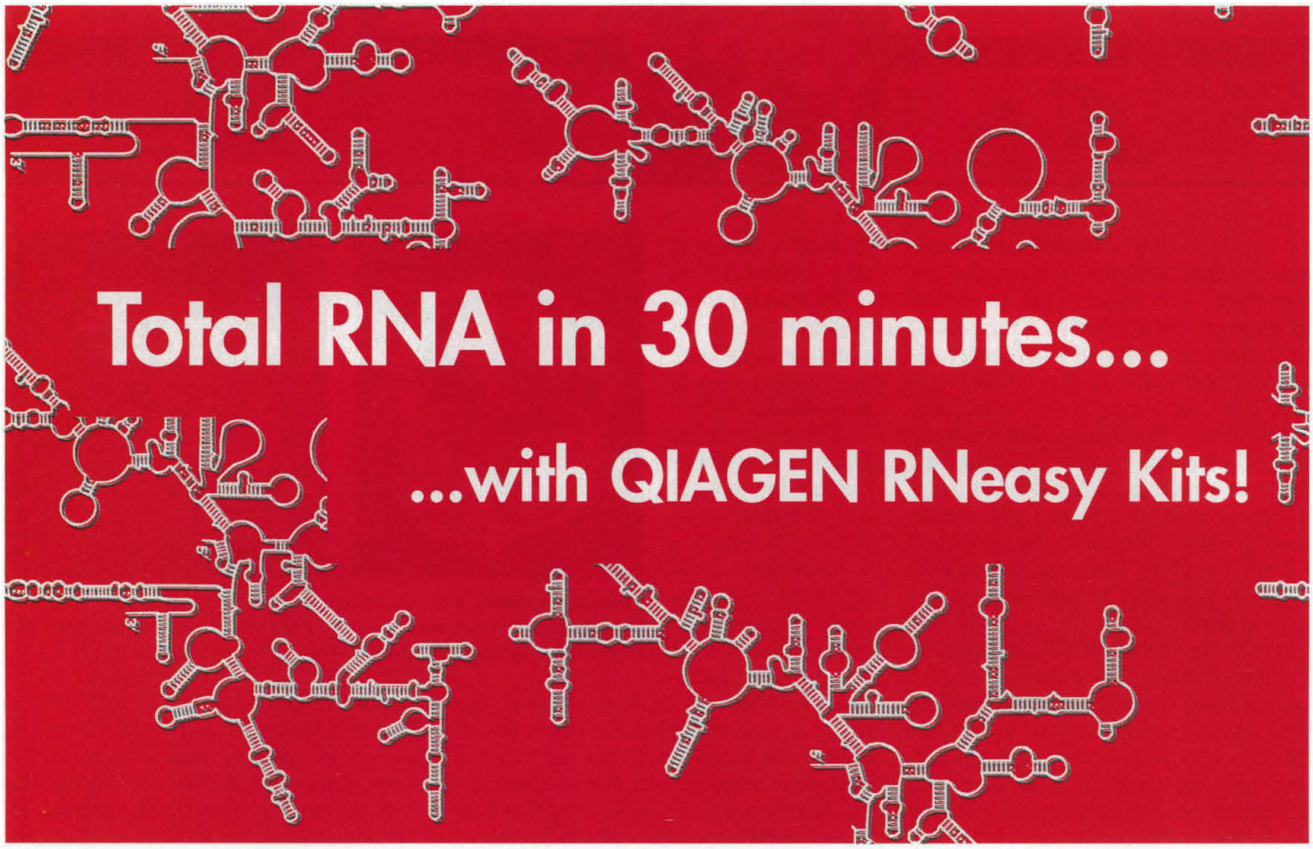
Over 3 Hours of Multimedia, Animated Overviews and Examples



StatSoft®

2300 East 14th Street • Tulsa, OK 74104 • (918) 749-1119
Fax: (918) 749-2217 • WEB: http://www.statsoft.com
e-mail: info@statsoft.com

- **StatSoft Ltd. (London, UK), ph: +44 1234 341226, fax: +44 1234 341622**
- **StatSoft GmbH (Hamburg, Germany), ph: +49 40/468866-0, fax: +49 40/468866-77**
- **StatSoft France (Paris, France), ph: +33 01-45-185-999, fax: +33 01-45-185-285**
- **StatSoft Polska Sp. z o.o. (Krakow, Poland), ph: +48 12-391120, fax: +48 12-391121**
- **StatSoft Italia (Padova, Italy), ph: +39 49-893-4654, fax: +39 49-893-2897**
- **StatSoft Pacific Pty Ltd. (Australia), ph: +613 9521 4833, fax: +613 9521 4288**
- **StatSoft Japan (Tokyo, Japan), ph: +813 3667 1110, fax: +813 3668 3100**
- **StatSoft Taiwan (Taipei, Taiwan, R.O.C.), ph: +886 2 5786587, fax: +886 2 5793179**



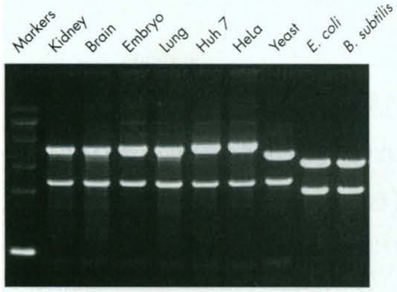
In the hands of an expert or a novice, RNeasy® Total RNA Kits are the fastest, easiest way to purify high-quality RNA.

RNeasy simplifies small- to large-scale total RNA isolation by combining the stringency of GITC lysis with the speed of silica-membrane spin technology.

The RNeasy Total RNA purification system requires **no tedious phenol extractions or precipitations** — just load, spin, and elute.

User variability has no effect, so RNeasy gives **high-quality RNA and reliable results every time.** For pure RNA in as little as 30 minutes, order RNeasy today!

Purified Total RNA

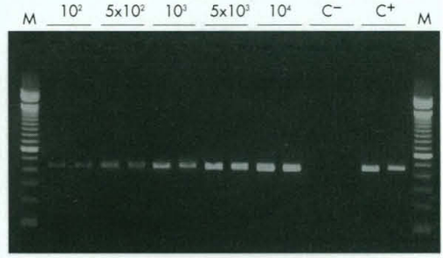


Formaldehyde agarose gel of total RNA isolated with the RNeasy Maxi Kit from the indicated sources. All tissues were from mouse.

RNeasy Spin Columns

Mini 100 µg RNA | **Midi** 1 mg RNA | **Maxi** 6 mg RNA

RT-PCR of RNA from ≥100 cells



RT-PCR amplification of total RNA. RNA was isolated with the RNeasy Mini Kit from the indicated numbers of HeLa cells.

Try RNeasy at no risk — we guarantee your satisfaction!

The PCR process is covered by US patents 4,683,195 and 4,683,202 or equivalent in other countries, owned by Hoffmann-La Roche AG.

http://www.qiagen.com

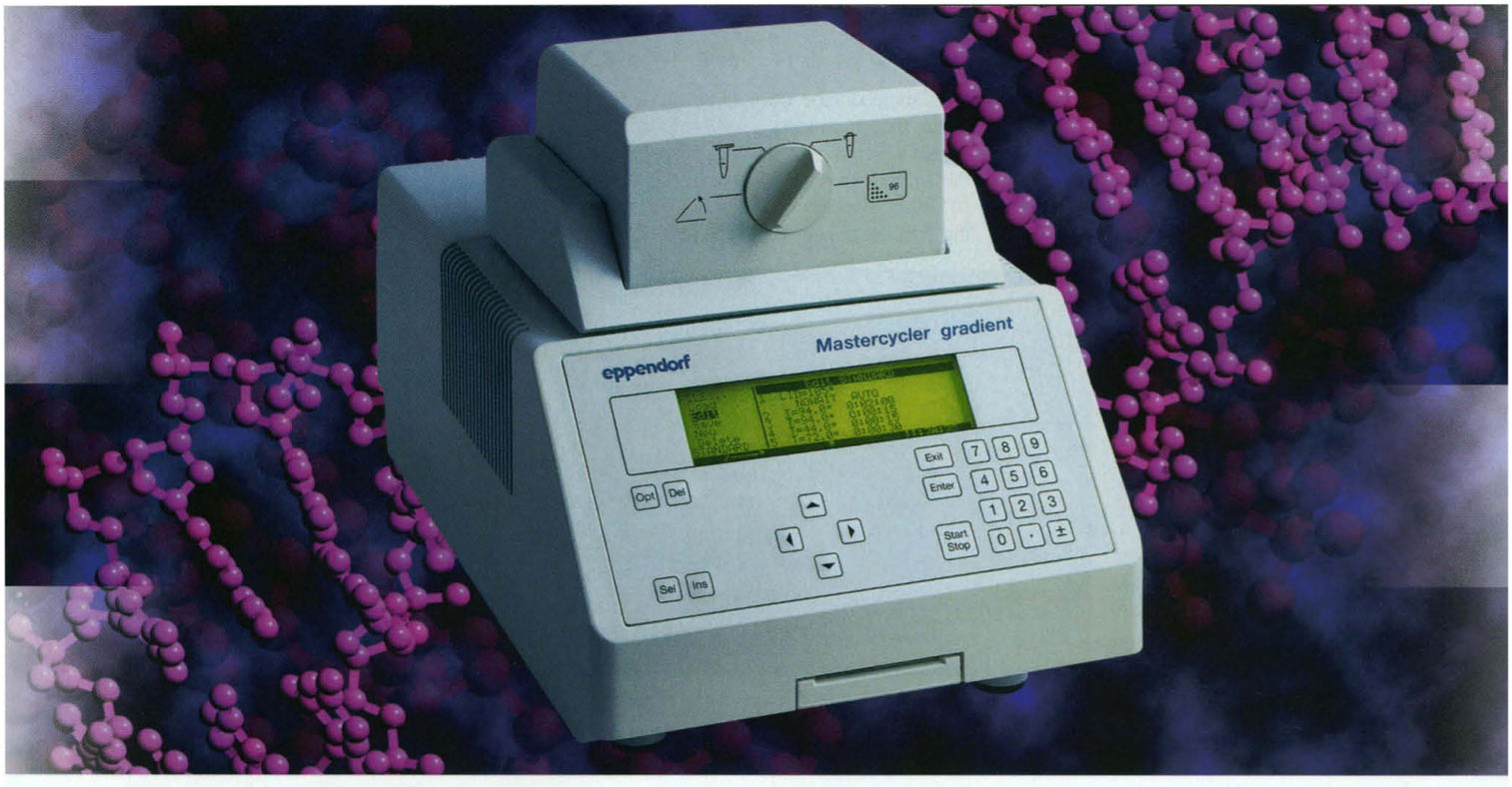
Germany:	USA:	Australia:	Canada:	France:	Japan:	Switzerland:	UK:
QIAGEN GmbH	QIAGEN Inc.	QIAGEN Pty Ltd	QIAGEN Inc.	QIAGEN S.A.	QIAGEN K.K.	QIAGEN AG	QIAGEN Ltd.
Tel. 02103-892-240	Tel. 800-426-8157	Tel. 03-9489-3666	Tel. 800-572-9613	Tel. 01-60-920-930	Tel. 03-5805-7261	Tel. 061-319-30-31	Tel. 01293-422-999
Fax 02103-892-255	Fax 800-718-2056	Fax 03-9489-3888	Fax 905-501-0373	Fax 01-60-920-925	Fax 03-5805-7263	Fax 061-319-30-33	Fax 01293-422-922

DISTRIBUTORS: Austria/Hungary/Slovenia: Austria (01) 889 18 19 **Belgium/Luxemburg:** 0800-1-98 15 **Brazil:** (5511) 543 1455 or 0800 55 1321 **Central & South America:** USA (305) 828-3818 **China:** (852) 2896-6283 **Czech Republic:** (02) 4447 1239 **Denmark:** 43-86 87 88 **Finland:** (09)-804 551 **Greece:** (01)-643 6138 **India:** (011)-542 1714 **Israel:** (02)-652 44 47 **Italy:** (055) 500 1871 **Korea:** (02) 924-8697 **Malaysia:** (03)-731 2099 **Mexico:** USA (805) 294-7940 **The Netherlands:** (033)-495 00 94 **New Zealand:** (09) 418 3039 or 0800 807 809 **Norway:** 22 90 00 00 **Poland:** (071) 735 813 **Portugal:** (1)-751 6000 **Singapore:** 445 7927 **Slovak Republic:** (07) 54 01 336 **South Africa:** (021) 615166 **Spain:** (93) 401 01 01 **Sweden:** (08) 621 34 00 **Taiwan:** (02) 880 2913 **Thailand:** (02) 412 5672 **In other countries contact:** QIAGEN GmbH, Germany

QIAGEN

S1A9161ONA

Circle No. 27 on Readers' Service Card



PCR optimization in one single experiment

licensed and PCR authorized

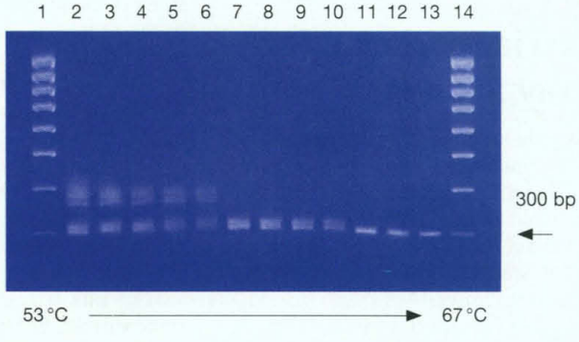
The determination of the right annealing temperature is crucial for establishing a new PCR experiment. The new all-round genius **Mastercycler® gradient** is an innovative, compact thermal cycler for even the most demanding PCR* applications. Its gradient function enables a temperature gradient of up to 20 °C to be generated across the block, thus optimizing the annealing, denaturation, or extension temperature in one single experiment. Its 96-position all-in-one universal block can accommodate 96 x 0.2 ml tubes, 77 x 0.5 ml tubes, or one 96-well plate – without block exchange.

The exact block homogeneity ensures reproducible results. Variable, high incubation speeds as well as time and temperature increments for hot-start, touch-down, and long PCR provide maximum programming flexibility.

The **Mastercycler® personal** is designed to meet personal applications. Its 25-position all-in-one universal block holds 25 x 0.2 ml tubes, 16 x 0.5 ml tubes, or one microplate in a 5 x 5 grid.

Personal memory cards for 10 individually developed protocols allow an easy and comfortable method transfer between both Mastercycler models.

Of course, both Mastercyclers are licensed and authorized for PCR.



● Experimental determination of optimal annealing temperature. The calculated primer annealing temperature was 56.5 °C, the actual annealing temperature is 63.5 °C. The ribosomal spacer region of mycoplasms from H9 cell cultures was amplified.

*PCR (Polymerase Chain Reaction) is protected by patent. The patent is held by Hoffmann-La Roche. Practice of the patented Polymerase Chain Reaction (PCR) process requires a license. The Eppendorf Thermal Cyclers are Authorized Thermal Cyclers and may be used with PCR licenses available from the Perkin-Elmer Corporation. Their use with Authorized Reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents.

Circle No. 11 on Readers' Service Card

eppendorf

ISO CERTIFIED 9001

Eppendorf – Netheler – Hinz GmbH · 22331 Hamburg · Germany · Phone (+49) 40-53801-0 · Fax (+49) 40-53801-556
website: www.eppendorf.com · e-mail: eppendorf@eppendorf.com
Eppendorf Scientific, Inc. · One Cantiague Road · Westbury, NY 11590-0207 · USA · Phone 800-421-9988 or 516-876-6800 · Fax 516-876-8599
website: www.eppendorfsi.com · e-mail: eppendorf@eppendorfsi.com

Imagine a simple oligo probe with more resolution, more versatility, and more sheer analytical power than cDNA.

Genisphere introduces 3DNA.

Until now you've had to choose either sensitivity or precision in your blotting experiments. For detection sensitivity in Northerns and Southerns you could use a long probe, like a cDNA. Or for analytic precision you could use a short probe, like an oligonucleotide. Now a remarkable new hybridization probe system called 3DNA gives you the signal strength of a long probe with the analytical power of a short one.

Whether you're studying allelic variations, mapping complex genes, or simply looking for more reliable hybridization results, you'll find 3DNA gives you more analytical power than you've ever had before. Want to find out more? Contact your Fisher Scientific representative at 800.766.7000 or call Genisphere at 877.888.3DNA.

Genisphere™

A DATASCOPE COMPANY

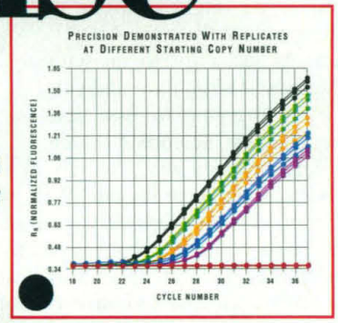
3DNA is distributed by Fisher Scientific.

Circle No. 25 on Readers' Service Card

"A project that used to take weeks can now be completed in a matter of days."

Dr. Charlotte Ip, Senior Research Fellow, Merck Research Laboratories

Real fast Real precise Real-time Quantitative PCR



The ABI PRISM® 7700 system is for real.

There's no doubt about it. Real-time quantitative PCR with the ABI PRISM® 7700 system is gaining worldwide recognition. And it's easy to see why. When it comes to gene expression, the ABI PRISM 7700 system offers real advantages over conventional PCR methods.[1]

Take speed and accuracy. With real-time quantitative PCR, there's no post-PCR processing. So risk of contamination is minimal, and sample throughput is increased dramatically. It takes only about 3.5 hours to analyze 96 reactions!

Then there's precision. In a recent study using the ABI PRISM 7700 system, intra-assay CVs were less than 2%. Interassay CVs were less than 3%. And quantitation of the target was linear over six logs.[2]

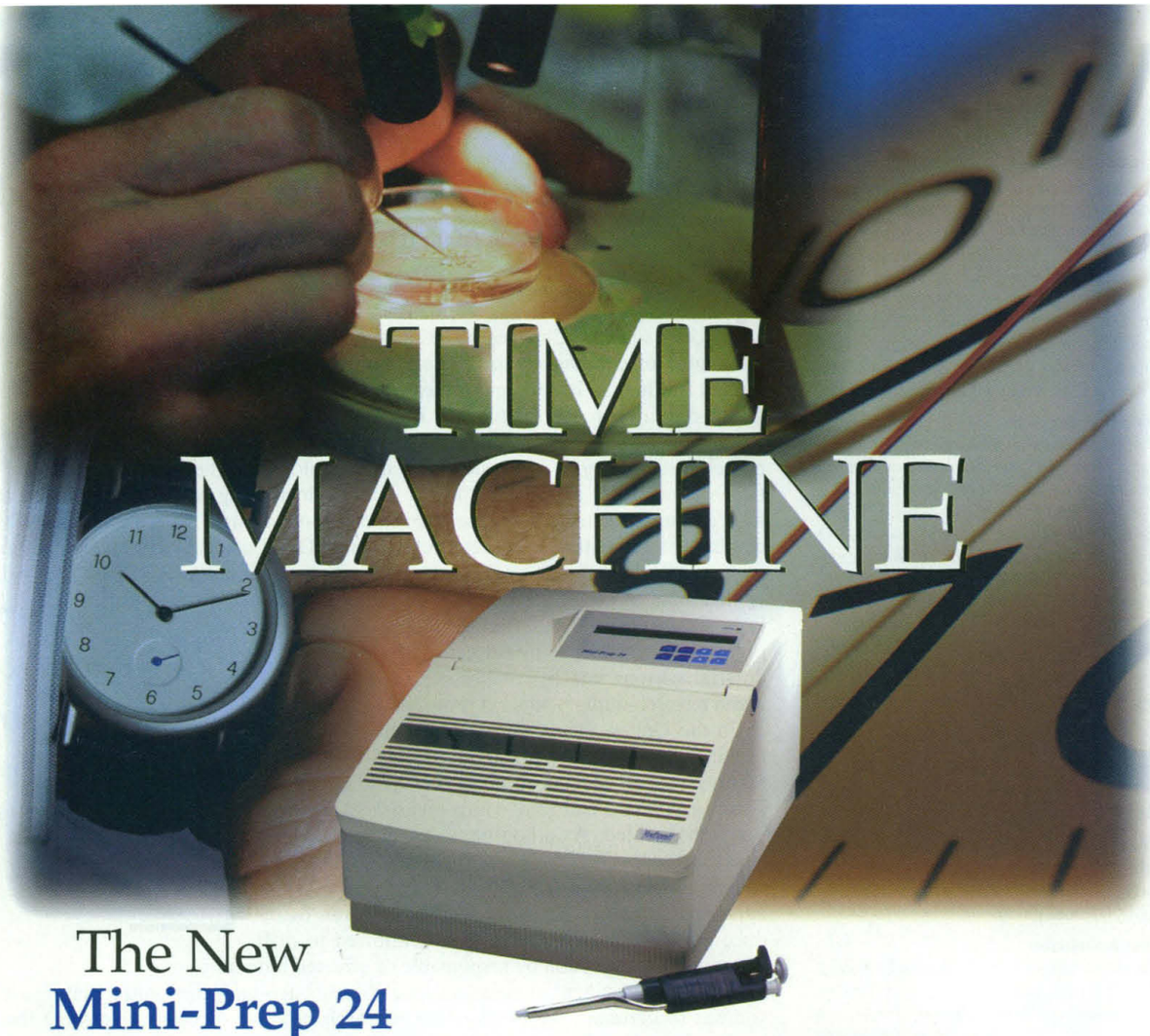
Best of all, the ABI PRISM 7700 system is a complete solution. Each component in the system has been optimized to streamline assay development and ensure that you get the best possible results.

So if you're looking for the best in quantitative PCR, get the real thing—the ABI PRISM 7700 Sequence Detection System. To request more information, call 1-800-345-5224. Outside the U.S. and Canada, contact your local PE Applied Biosystems sales representative, or visit our web site at www.perkin-elmer.com/ab.

1. Heid, Christian A., et al. 1996. Real Time Quantitative PCR. Genome Research 6: 986-994. from Molecular Endocrinology
2. Gibson, Ursula E.M., et al. 1996. A Novel Method for Real Time Quantitative RT-PCR. Genome Research 6: 995-1001

PE Applied Biosystems

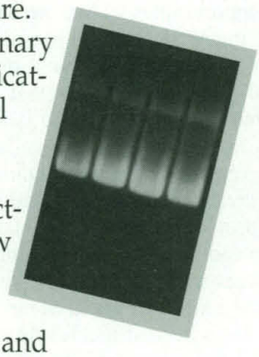
Europe Langen, Germany Tel: 49 (0)6103 708 301 Fax: 49 (0)6103 708 310 **Japan** Tokyo, Japan Tel: (047) 380-8500 Fax: (047) 380-8505 **Latin America** Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223 **Australia** Melbourne, Australia Tel: 1 800 033 747 Fax: 61 3 9212-8502



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

The Mini-Prep 24 is a fully automated bench-top instrument designed for purification of plasmid DNA directly from bacterial culture.

The instrument uses a revolutionary new method of nucleic acid purification based on modified agarose gel electrophoresis and subsequent recovery by electroelution.



The process utilizes premanufactured sample cassettes which allow for direct loading of up to 2 ml of culture.

Call now to learn how the New and Improved Mini-Prep 24 can provide you with great, high-quality DNA...while saving you a lot of time.

High Purity - sufficient for automated fluorescent and manual sequencing.

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

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

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

Quality - time and time again.

MACCONNELL RESEARCH

1-800-466-7949

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

Circle No. 14 on Readers' Service Card

challenges for a new century

Call for Contributed Papers

AAAS Annual Meeting and Science Innovation Exposition, January 21-26, 1999, Anaheim, CA

Next January some 5,000 scientists, engineers, educators, and policymakers will gather for the 165th national meeting of AAAS. You are cordially invited to submit an abstract for a contributed poster presentation at this unique event.

The meeting will feature more than 150 scientific symposia, specialized seminars, special lectures by science and engineering leaders, poster sessions, an exhibit hall, career workshops, and a career fair.

1999 Poster Categories

Life and Physical Sciences
including medicine, environment, physiology, biology, cell biology, physics, mathematics, chemistry, geology, information science, engineering or industrial science.

Social and Information Sciences
including policy, economics, social, political, and computer sciences.

Education
Presented in conjunction with the AAAS Forum for School Science.

Student Poster Award Competition
Recognizes the individual efforts of students actively working towards a college degree. Outstanding posters in the Life, Physical, and Social and Information Sciences are awarded.

Deadline for all submissions is September 30, 1998.

Additional information, abstract and registration forms are available on the Web or by contacting the AAAS Meetings Office. All abstracts will be peer reviewed.

Free Registration for Students
Upper division undergraduate and graduate students can obtain a waiver of meeting registration fees by serving as a Session Aide. Applications are available on the Web or from AAAS.

AAAS ANNUAL MEETING AND SCIENCE INNOVATION EXPOSITION

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

www.aaas.org/meetings/scope

AAAS Meetings Office • 1200 New York Avenue, NW • Washington, DC 20005
Phone: 202-326-6450 • Fax: 202-289-4021 • Email: confinfo@aaas.org

For the sea, for the earth, for us.

Each year we select and support ten exceptional

individuals from around the world whose commitment to conservation of life in the oceans helps ensure the future of life on earth.

In this International Year of the Ocean we celebrate the **1998 Pew Fellows in Marine Conservation.**

Richard B. Allen
COMMERCIAL FISHERMAN, RHODE ISLAND
Conserving New England's lobster fishery through computer modeling and science management education for fishermen.

John C. Avise
UNIVERSITY OF GEORGIA, GEORGIA
Creating educational materials on conservation of marine species utilizing genetic markers.

Andrew N. Cohen
SAN FRANCISCO ESTUARY INSTITUTE, CALIFORNIA
Documenting the detrimental effects of marine biological invasions in tropical waters.

Mauro Maida
UNIVERSIDADE FEDERAL DE PERNAMBUCO, BRAZIL
Preserving Brazil's depleted coral reefs through recovery initiatives and multiple-use marine protected areas.

Helene D. Marsh
JAMES COOK UNIVERSITY, AUSTRALIA
Saving Australia's endangered dugongs through participatory indigenous community co-management.

Laurence D. Mee
UNIVERSITY OF PLYMOUTH, UK
Combating marine degradation in the Black Sea region through public outreach and advocacy.

Robert C. Repetto
WORLD RESOURCES INSTITUTE, WASHINGTON, DC
Developing ecological economic accounting models for marine fisheries, habitat and recreation uses.

Robert S. Steneck
UNIVERSITY OF MAINE, MAINE
Introducing co-management initiatives for lobster and urchin fisheries in Maine.

Mia J. Tegner
SCRIPPS INSTITUTION OF OCEANOGRAPHY, CALIFORNIA
Establishing ecosystem approaches for conservation of the collapsed west coast abalone fishery.

Leslie E. Watling
UNIVERSITY OF MAINE, MAINE
Assessing the damaging effects of bottom-trawling on critical benthic habitats to support sustainable fisheries.

PEW FELLOWS PROGRAM
IN MARINE CONSERVATION

A PROGRAM OF THE PEW CHARITABLE TRUSTS IN PARTNERSHIP WITH THE NEW ENGLAND AQUARIUM

Pew Fellows Program in Marine Conservation · New England Aquarium · Central Wharf · Boston, MA · 02110-3399 · USA · TEL 617.720.5100 · FAX 617.720.5102 · E-MAIL pfp@neaq.org