

AMERICAN
ASSOCIATION FOR THE
ADVANCEMENT OF
SCIENCE

SCIENCE

28 JUNE 1991

\$6.00

VOL. 252 ■ PAGES 1757-1886



cDNA Cloning Technology... That Towers Above The Rest

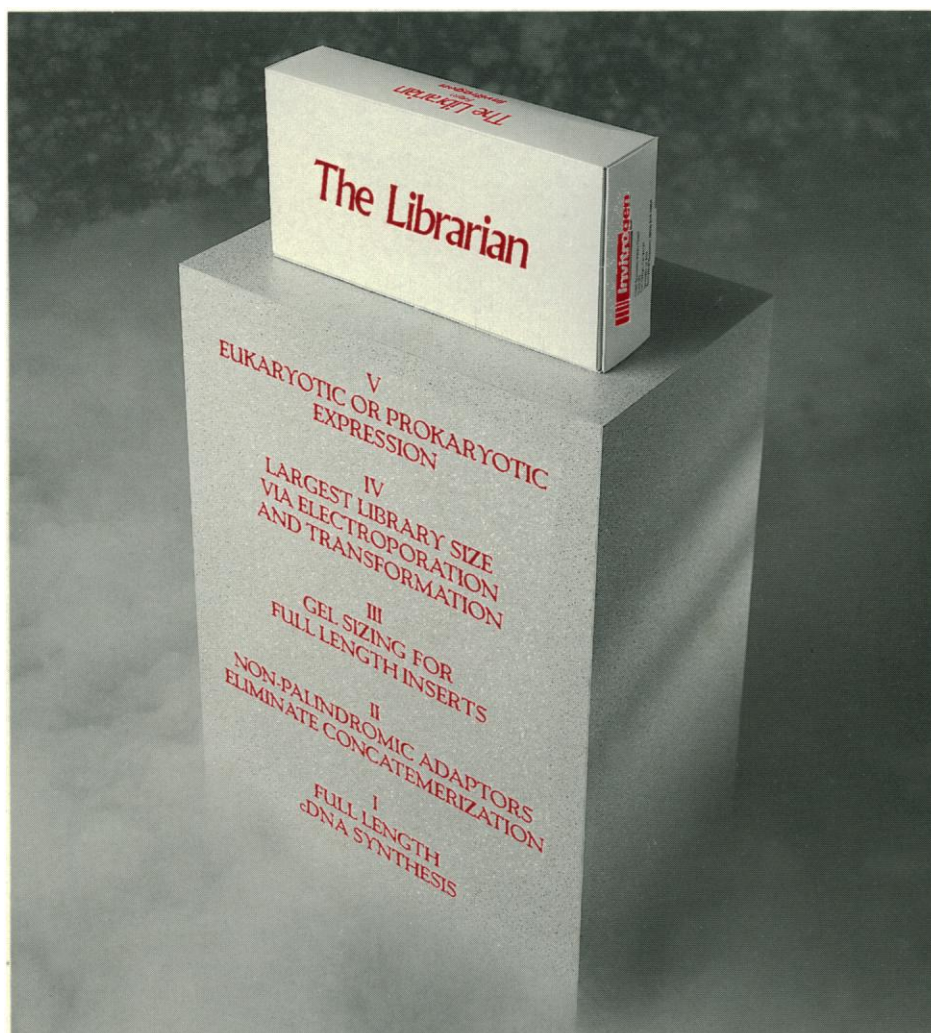
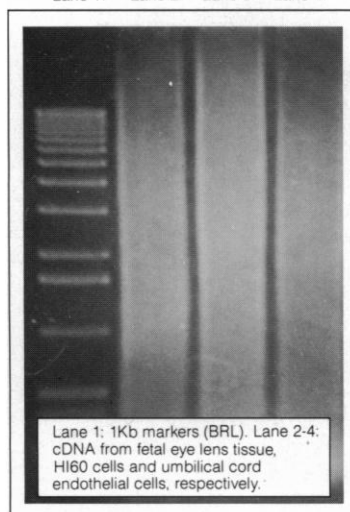
The Librarian cDNA construction system offers direct eukaryotic or prokaryotic expression, uni or bidirectional cDNA insertion and chemical or electrocompetent E.coli transformation.

Librarian Vectors Features	pcDNA 1	pcDNA II	pYES 2	λ gT10	λ gT11
Eukaryotic	•	•	•	•	•
Prokaryotic	•	•	•	•	•
Yeast	•	•	•	•	•
Unidirectional	•	•	•	•	•
Bidirectional	•	•	•	•	•
RNA Promoters	•	•	•	•	•
M13 Origin	•	•	•	•	•
NA Screening	•	•	•	•	•
Ab Screening	•	•	•	•	•
Panning	•	•	•	•	•

In addition, each Librarian kit contains every reagent needed to turn RNA to recombinants plus;

- Eukaryotic and Prokaryotic Expression Cloning Using Multifunctional Phagemid and Lambda Vectors.
- Highly Efficient cDNA Synthesis and Non-palindromic Ligation for Complete Representation.
- Electroporation or Chemical Transformation for Increased Numbers of Recombinants.
- Accurate cDNA Sizing for Greater Representation and More Information per Clone.
- Full Length cDNA >10Kb using MeHgOH Denaturation and AMV Reverse Transcriptase.

Lane 1. Lane 2. Lane 3. Lane 4.



For over three years Invitrogen's Librarian has led the way in cDNA synthesis. Each kit is guaranteed and each reaction is fully optimized to provide the highest efficiencies. Our technical service people can help you determine which kit is right for your research.

Put the most advanced cDNA technology available to work for you today.

1-800-955-6288

Invitrogen
CORPORATION

3985-B Sorrento Valley Blvd. • San Diego, CA 92121 • (619) 597-6200 • (619) 597-6201 Fax

BRITISH BIOTECHNOLOGY LTD, UK - TEL: 44-235529449 • AMS BIOTECHNOLOGY UK LTD, UK - TEL: 44-993822786 • BDH INC., CANADA - TEL: 800-268-0310 • BIO-TRADE, AUSTRIA - TEL: 43-2228284694 • CELBIO, ITALY - TEL: 39-24048646 • FUNAKOSHI PHARMACEUTICALS, JAPAN - TEL: 81-356841622 • ITC BIOTECHNOLOGY GMBH, GERMANY - TEL: 06221-303907 • KEBO LABS AB, SWEDEN - TEL: 46-86213400 • MEDOS COMPANY PTY LTD, AUSTRALIA - TEL: 61-38089077

Circle No. 244 on Readers' Service Card

Pure mRNA in Minutes...

...Directly from Small or Large Samples of Cells or Tissue.

FastTrack™ and MicroFastTrack™ set the industry standard in high quality mRNA isolation.

MicroFastTrack™*: 20 Reactions

- Ideal for PCR, Northern and cDNA synthesis
- Isolation from samples ranging in size from 10^3 - 10^6 cells or 10-250mg of tissue.
- Reproducible yields of high quality mRNA.

FastTrack™*: 6 Reactions

- mRNA isolation for Northern, cDNA, library construction, PCR, microinjection, RNA protection studies and *in vitro* translation.
- Isolation from samples ranging in size from 10^7 - 10^8 cells or 0.4-1.0 gram of tissue.
- Fast, efficient recovery of large amounts of polyA+ RNA from a variety of sources.

Both systems offer:

- High yields of intact mRNA with low ribosomal contamination.
- Eliminate the need for total RNA isolation or the use of toxic chemicals.
- The most cost effective means of generating high quality mRNA.
- Consistency, convenience and the fastest isolation time.

For the very best in direct mRNA isolation FastTrack™ and MicroFastTrack™ are the choice of thousands of research labs worldwide. When the quality of your mRNA is important, turn to the original source for purity, reliability and convenience; turn to Invitrogen.

Toll Free 1-800-955-6288

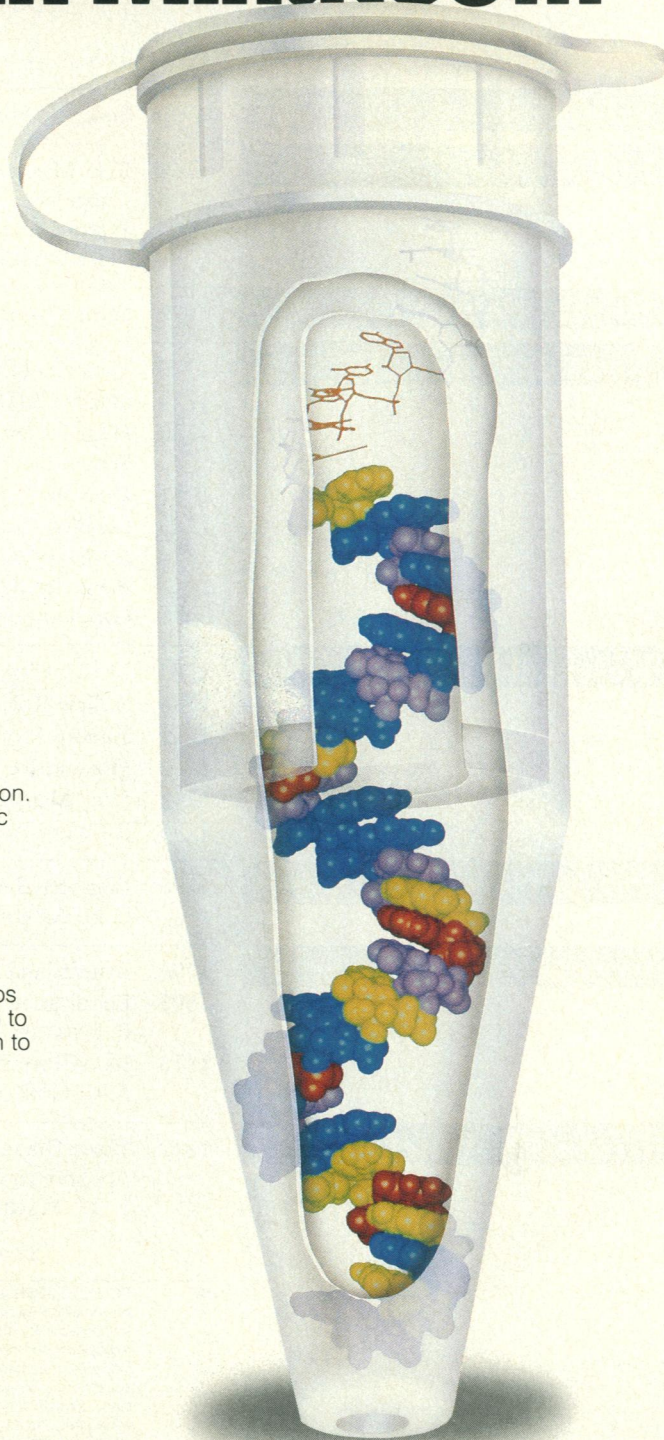


3985 • B Sorrento Valley Blvd. • San Diego, CA 92121
(619) 597-6200 Phone • (619) 597-6201 Fax

BRITISH BIOTECHNOLOGY LTD, UK - TEL: 44-235529449 • AMS BIOTECHNOLOGY UK LTD, UK - TEL: 44-993822786 • BDH INC., CANADA - TEL: 800-268-0310 • BIO-TRADE, AUSTRIA - TEL: 43-2228284694 • CELBIO, ITALY - TEL: 39-24048646 • FUNAKOSHI PHARMACEUTICALS, JAPAN - TEL: 81-356841622 • ITC BIOTECHNOLOGY GMBH, GERMANY - TEL: 06221-303907 • KEBO LABS AB, SWEDEN - TEL: 46-86213400 • MEDOS COMPANY PTY LTD, AUSTRALIA - TEL: 61-38089077

*patent pending. mRNA model courtesy of BIOSYM

Circle No. 243 on Readers' Service Card



1763 This Week in *Science*

Editorial

1765 Federally Funded Research

Letters

1768 PHS Misconduct Procedures: B. C. HANSEN AND K. D. HANSEN ■ International Congress of Entomology: Another Opinion: Y. ITÔ AND S. MASAKI ■ Westinghouse Awards: E. D. SCHEIRER ■ Citations and Careers: J. JANICK ■ Uhl's Deification: A. M. SHAPIRO

ScienceScope

1775 Science policy boosting at DOE; detector backbiting at the SSC; etc.

News & Comment

1776 Labstyles of the Famous and Well Funded
1779 Seventh AIDS Conference: Mostly "Fine Tuning"
1780 Huge Eruption May Cool the Globe
Whom Do Yew Trust?
1781 Does the Harrison Case Reveal Sexism in Math?
1783 Funding Cutoff Threatens Thai Science
1784 *Briefings*: Oil and Water ■ Senate Boosts SSC, Main Injector Funding ■ Borderless Grants ■ Can-do Bugs ■ Logger's Dismay ■ Can PR Cool the Greenhouse? ■ A Transforming Look at C₆₀ ■ Please Sir, \$250 Million More

Research News

1786 Untwinkling the Stars
1788 A New Role for Gases: Neurotransmissions
1789 Famous Monkeys Provide Surprising Results
1790 Fire and Ice: Under the Deep-Sea Floor
1792 How Many Genes Had to Change to Produce Corn?
1794 A Call to Action on a Human Brain Project

Perspective

1796 Engineered Metal-Binding Proteins: Purification to Protein Folding:
F. H. ARNOLD AND B. L. HAYMORE

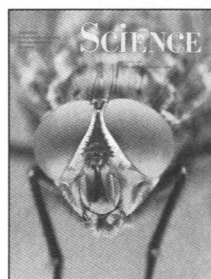
Articles

1798 Benefits and Costs of HIV Testing: D. E. BLOOM AND S. GLIED
1805 Localization and Its Absence: A New Metallic State for Conducting Polymers:
P. PHILLIPS AND H.-L. WU
1813 Blood Pressure Control—Special Role of the Kidneys and Body Fluids:
A. C. GUYTON

Research Articles

1817 Three-Dimensional Structure of the LDL Receptor-Binding Domain of Human Apolipoprotein E: C. WILSON, M. R. WARDELL, K. H. WEISGRABER, R. W. MAHLEY, D. A. AGARD

- **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 1991 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$82 (\$50 allocated to subscription). Domestic institutional subscription (51 issues): \$150. Foreign postage extra: Canada \$46, other (surface mail) \$46, air freight \$90. First class, airmail, school-year, and student rates on request. **Change of address:** allow 6 weeks, giving old and new addresses and 11-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 2033, Marion, OH 43305-2003. **Single copy sales:** \$6.00 per issue prepaid includes surface postage; Guide to Biotechnology Products and Instruments, \$20. 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 the base fee of \$1 per copy plus \$0.10 per page is paid directly to CCC, 27 Congress Street, Salem, Massachusetts 01970. The identification code for *Science* is 0036-8075/93 \$1 + .10. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.
- 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.



COVER The head of the blowfly *Calliphora erythrocephala* with its large compound eyes. Each eye contains about 5000 ommatidia, which provide the fly with all its information about the visual world. Because it is highly regular and easily accessible for electrophysiology, the fly visual system is widely used in the study of the fundamental aspects of neural information processing. See page 1854. [Photograph by H. L. Leertouwer]

Reports

- 1823 RNA Secondary Structure Repression of a Muscle-Specific Exon in HeLa Cell Nuclear Extracts: B. CLOUET D'ORVAL, Y. D'AUBENTON CARAFA, P. SIRAND-PUGNET, M. GALLEG0, E. BRODY, J. MARIE
- 1829 Pressure Dependence of Superconductivity in Single-Phase K_3C_{60} : G. SPARN, J. D. THOMPSON, S.-M. HUANG, R. B. KANER, F. DIEDERICH, R. L. WHETTEN, G. GRÜNER, K. HOLCZER
- 1831 Environmental Patterns in the Origins of Higher Taxa: The Post-Paleozoic Fossil Record: D. JABLONSKI AND D. J. BOTTJER
- 1834 Quaternary Raised Coral-Reef Terraces on Sumba Island, Indonesia: P. A. PIRAZZOLI, U. RADTKE, W. S. HANTORO, C. JOUANNIC, C. T. HOANG, C. CAUSSE, M. B. BEST
- 1836 Development of Diapiric Structures in the Upper Mantle Due to Phase Transitions: M. LIU, D. A. YUEN, W. ZHAO, S. HONDA
- 1839 Regulation of B Cell Antigen Receptor Signal Transduction and Phosphorylation by CD45: L. B. JUSTEMENT, K. S. CAMPBELL, N. C. CHIEN, J. C. CAMBIER
- 1842 Tissue-Specific Splicing in Vivo of the β -Tropomyosin Gene: Dependence on an RNA Secondary Structure: D. LIBRI, A. PISERI, M. Y. FISZMAN
- 1845 Subunit Communication in the Anthranilate Synthase Complex from *Salmonella typhimurium*: M. G. CALIGIURI AND R. BAUERLE
- 1848 A Corticosteroid Receptor in Neuronal Membranes: M. ORCHINIK, T. F. MURRAY, F. L. MOORE
- 1851 An Analog of Myristic Acid with Selective Toxicity for African Trypanosomes: T. L. DOERING, J. RAPER, L. U. BUXBAUM, S. P. ADAMS, J. I. GORDON, G. W. HART, P. T. ENGLUND
- 1854 Reading a Neural Code: W. BIALEK, F. RIEKE, R. R. DE RUYTER VAN STEVENINCK, D. WARLAND
- 1857 Massive Cortical Reorganization After Sensory Deafferentation in Adult Macaques: T. P. PONS, P. E. GARRAGHTY, A. K. OMMAYA, J. H. KAAS, E. TAUB, M. MISHKIN

Book Reviews

- 1863 The Surgical Solution, reviewed by J. REED ■ Living Fossil, J. E. MCCOSKER ■ Longevity, Senescence, and the Genome, T. B. L. KIRKWOOD ■ Biological Mass Spectrometry, P. WILLIAMS ■ Books Received

Products & Materials

- 1866 Sonic Wind System ■ Automated Coordination Tester ■ Medium for Peptide and Protein Separations ■ Microbiological Decontamination Station ■ Cellulose Acetate Electrophoresis Membranes ■ New Version of ChiWriter ■ Messenger RNA Purification Kit ■ Literature

Author Index for Volume 252 is on pages i-x

Board of Directors

Donald N. Langenberg
Retiring President,
Chairman

Leon M. Lederman
President

F. Sherwood Rowland
President-elect

Mary Ellen Avery
Francisco J. Ayala
Eugene H. Cota-Robles
Robert A. Frosch
Joseph G. Gavin, Jr.
Florence P. Haseltine
Jean'ne M. Shreeve
Warren M. Washington

William T. Golden
Treasurer

Richard S. Nicholson
Executive Officer

Editorial Board

Charles J. Arntzen
Elizabeth E. Bailey
David Baltimore
William F. Brinkman
E. Margaret Burbidge
Pierre-Gilles de Gennes
Joseph L. Goldstein
Mary L. Good
Harry B. Gray
John J. Hopfield
F. Clark Howell
Paul A. Marks
Yasutomi Nishizuka
Helen M. Ramey
Robert M. Solow
Edward C. Stone
James D. Watson

Board of Reviewing Editors

John Abelson
Frederick W. Alt
Don L. Anderson
Stephen J. Benkovic
Floyd E. Bloom
Henry R. Bourne
James J. Bull
Kathryn Calame
Charles R. Cantor
Ralph J. Cicerone
John M. Coffin
Robert Dorfman
Bruce F. Eldridge
Paul T. Englund
Fredric S. Fay

Douglas T. Fearon
Harry A. Fozzard
Theodore H. Geballe
Roger I. M. Glass
Stephen P. Goff
Corey S. Goodman
Stephen J. Gould
Eric F. Johnson
Stephen M. Kosslyn
Konrad B. Krauskopf
Charles S. Levings III
Richard Losick
Anthony R. Means
Mortimer Mishkin
Roger A. Nicoll
William H. Orme-Johnson III
Yeshayau Pocker

Dennis A. Powers
Erkki Ruoslahti
Thomas W. Schoener
Ronald H. Schwartz
Terrence J. Sejnowski
Thomas A. Steitz
Robert T. N. Tjian
Emil R. Unanue
Geerat J. Vermeij
Bert Vogelstein
Harold Weintraub
Zena Werb
George M. Whitesides
Owen N. Witte
William B. Wood
Keith Yamamoto

express

Go QIAexpress

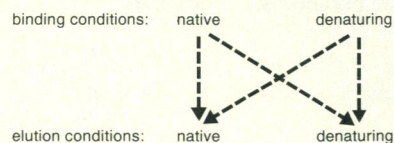
QIAexpress is:

Overexpression and one-step purification of chemical amounts of recombinant proteins and peptides for:

- Functional studies
- Antibody Production
- Epitope mapping
- Immunodetection methods

The QIAexpress Method:

- Places a histidine hexamer as a negligibly antigenic affinity tag onto recombinant polypeptides.
- Makes use of patented NTA resin, for a unique, one step purification by metal chelate chromatography.
- Makes no distinction as to whether denaturing or native conditions are used in either binding or elution :



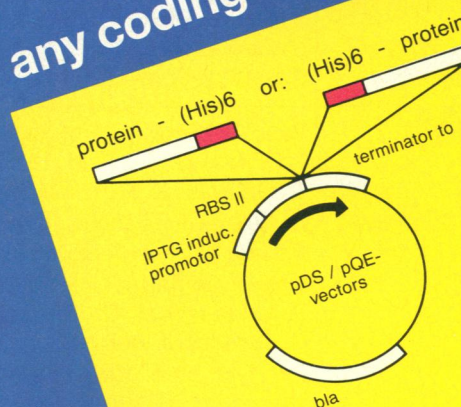
QIAexpress comes in a kit containing:

- Expression vectors allowing insertions in all reading frames
- Special vectors encoding DHFR for enhanced antigenicity of recombinant polypeptides
- Bacterial strains for overexpression
- Resin for Ni²⁺-affinity chromatography of up to 10mg of protein
- Numerous application protocols

Adapt your own expression vectors to QIAexpress

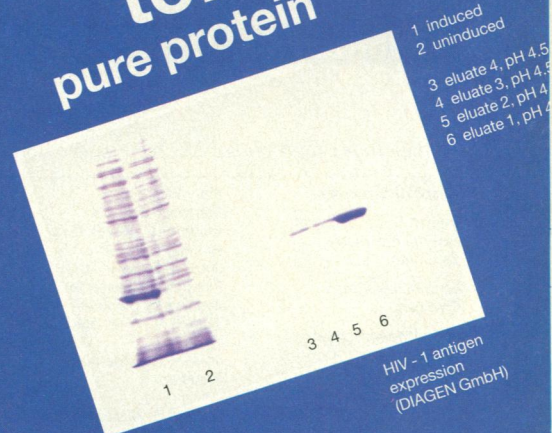
using site directed mutagenesis to introduce the histidine hexamer.

from:
any coding sequence



NTA resin ••• Ni ••• His-protein

to:
pure protein



USA/CANADA: QIAGEN Inc., Chatsworth, CA 91311, Phone (800) 426-8157, (818) 718-9870, Fax (818) 718-2056
GERMANY: DIAGEN GmbH, Niederheider Str. 3, D-4000 Düsseldorf 13, Phone (0211) 79 30 37, Fax (0211) 79 04 44
DISTRIBUTORS: AUSTRALIA: Phoenix Stansens Scient.Div. (3) 544 8022 AUSTRIA: Bio-Trade (222) 828 46 94
BENELUX: Westburg B.V. (NL-33) 95 00 94 FRANCE: Cogem (1) 45 33 67 17 ISRAEL: Bio-Lab Laboratories Ltd.
(2) 52 44 47 ITALY: Genenco (M-Medical) (55) 67 64 41 JAPAN: Funakoshi Co., Ltd. (3) 5684 1622
KOREA: LRS 924-8697 PORTUGAL: Izasa Portugal, S.A. 758 07 40 SCANDINAVIA: Kebo Lab: Denmark: (44) 68 18 00,
Finland: (90) 437 56 40, Norway: (02) 30 11 20, Sweden: (08) 621 34 00 SPAIN: Izasa S.A. (3) 401 01 01
SWITZERLAND: Kontron Instruments AG (1) 733 5 733 TAIWAN: Formo (2) 736 7125 UK: Hybaid Ltd. (81) 977 3266



Circle No. 47 on Readers' Service Card

Economics of HIV testing

IN July 1992 the Americans with Disabilities Act will take effect, and preemployment medical screening of any kind will be severely limited. In the meantime, many companies require job candidates to be screened for certain medical conditions; recently tests to detect infection with the AIDS virus HIV have become available. In 17 states no laws currently exist to prohibit the use of HIV test results for denying jobs to candidate employees. Bloom and Glied assess the economic costs and benefits of HIV tests in the workplace and conclude that for most firms it is not cost-effective either to test prospective employees or to periodically retest employees for HIV (page 1798). HIV testing incurs large direct and indirect costs on companies (some of the latter are quite subtle, such as whether a policy of testing will deter qualified individuals from applying to that company) and only a fraction of all firms—large ones in high-risk areas of the country that offer good benefit packages—would realize economic benefits from testing. The authors also discuss social costs and benefits of HIV tests, which are quite separate from the company costs and benefits.

Primary role for secondary structure

THERE are three isoforms (related forms) of the chicken protein β -tropomyosin. Skeletal muscle contains one of these forms; smooth muscle and all other tissues contain the other forms of the protein. All three are produced from the same gene through a process called alternative splicing: in skeletal muscle cells a segment of the gene called exon 6B is used, whereas in other tissue exon 6A is incorporated into the pre-messenger molecule. What determines how the splicing will occur? In vitro studies by Clouet d'Orval *et al.* show that secondary structural features of the RNA transcript near the exon 6 insertion site affect the accessibility of the site: in muscle cells only muscle-

specific exon 6B can be incorporated and incorporation of alternative exons is blocked; in other tissue, the reverse is true (page 1823). Libri *et al.* illustrate the same phenomenon with an in vivo system (page 1842). Exactly how big a part secondary structure plays in tissue-specific splicing is not yet clear; secondary structure probably acts in concert with trans-acting factors and exon competition to promote different forms of gene splicing.

Superconductor under pressure

THE superconductivity of alkali-doped buckyballs— K_3C_{60} —is pressure-dependent: the onset temperature for superconductivity gets higher as the pressure used in the preparation of the compound is decreased (page 1829). Bulk superconductivity in K_3C_{60} was monitored by measurements of the fractional diamagnetic shielding of sample materials. Samples prepared under atmospheric conditions showed a transition temperature of 19.3 K; in other samples the transition temperature was observed to drop as pressure was increased, and a low transition temperature of less than 8 K was recorded at the highest pressure, 21.2 kilobars. Sparr *et al.* discuss similarities and differences in the behaviors of K_3C_{60} and other superconducting materials, noting that current hypotheses for the mechanism of superconductivity may not be adequate to explain the strong negative pressure dependence of this new material.

Potential trypanosome drug

AN analog of myristic acid, called O-11 because oxygen is substituted for the number 11 methylene group of the molecule, has proved to be toxic to African trypanosomes in vitro (page 1851). This suggests that the analog might have a future role as a chemotherapeutic agent against these parasites, which are responsible for the lethal disease African sleeping sickness.

Myristates are the only fatty acids present in the trypanosome's membrane anchor that holds the variant surface glycoprotein in the membrane; without this glycoprotein the parasite would not be able to survive long in the host's bloodstream. Trypanosomes are dependent on their hosts for myristate because they cannot synthesize myristates *de novo* and may be able to produce only tiny amounts from precursors. Studies by Doering *et al.* show that trypanosomes that have incorporated the analog instead of myristic acid into their anchors die. Related studies have shown that the analog is not toxic to mammalian cells and should not, therefore, induce toxic side effects in a mammalian host.

Brain reorganization after deafferentation

HOW much "rewiring" can go on in the brain after neuronal connections have been severed? Brains of infants are known to be quite plastic, but neuronal connections in brains of adults were thought to be capable of only marginal reorganization. However, Pons *et al.* discovered that in macaque monkeys years after limb nerves had been cut at their entry point into the spinal cord (a process that leads to peripheral deafferentation) the zone of the brain that originally had responded to the limb area was now responding to sensory stimulation of the face (page 1857). The area that was newly responsive to face stimulation was more than 10 millimeters beyond the original face-responsive zone; this extent of reorganization is an order of magnitude greater than had been observed previously. The next step is to determine how reorganization is brought about and whether the mechanisms involved might be exploited for rerouting inputs to undamaged zones of the brain to restore function after strokes or similar pathologic brain lesions. Palca discusses these experiments on the "Silver Spring monkeys" further on page 1789.

■ RUTH LEVY GUYER

NONRADIOACTIVE LABELING

LIGHTSMITH™ 1 *Luminescence Engineering for Oligonucleotides*

Non-radioactive labeling system for oligonucleotides

- Sensitivity greater than ^{32}P
- Extremely low background
- Rapid hybridizations
- Probe stable for six months.
- One Lightsmith kit yields probe for up to 4 liters of hybridization solution

Additional Products...

- **LIGHTWORKS™ DNA**
Detection Reagents
- Complete nucleic acid
hybridization reagent kit,
including chemiluminescent
substrate
- Individual reagents
available separately
- **EquiLadder™ DNA Size**
Markers and Probe



Promega

Promega Corporation

2800 Woods Hollow Road
Madison, WI 53711-5399 USA
Toll Free 800-356-9526
Telephone 608-274-4330
FAX 608-273-6967
Telex 62057092

800-356-9526

Convince yourself! For a limited time, Promega is offering a substantially reduced price on oligonucleotides for use with the Lightsmith™ 1 Luminescence Engineering system. For details of this offer, call toll-free 1-800-356-9526.

Circle No. 262 on Readers' Service Card

KEY FORUM FOR BIOTECHNOLOGY

BIO TECHNICA

About 500 exhibitors from 20 countries will present their latest problem-solving techniques and the present state of biotechnology in the following fields:

Research, Processes, Products, Laboratory and production techniques, Bioinformatics, Services, Applications.

Particular emphasis will be placed upon applications in the following areas, especially in the accompanying programme of events

- Health and medicine
- Agriculture
- Food
- Environment and recycling

BIOTECHNICA Hannover '91 is the most important international platform for information and communication of the year for experts in the research and industrial sectors.

NEW PRIORITIES OF THE ACCOMPANYING PROGRAMME (Participation for all trade fair visitors is free of charge):

BIO CONGRESS

Leading international experts will give lectures on current topics in the fields of **health/medicine, agriculture and environment/recycling.**

BIO SCIENCE

This scientific seminar programme is devoted to the key topic of bioinformatics.

FOREIGN MARKETS

International seminars presented by groups of exhibitors from particular countries.

CORPORATE LECTURES

Within the framework of corporate lectures, exhibitors will present and explain their latest problem-solving techniques.

BIO PATENTS

Databases for patent applications. A seminar programme dealing with inventions and their assessment.

BIO BUSINESS

Workshops, seminars and contact stands will deal with questions of financing (BIO FINANCING), cooperation between companies (BIO PARTNER) and vocational orientation (BIO JOB).

Upon request, we shall be glad to provide you with more detailed information on the trade fair and accompanying programme.



BIOTECHNICA '91★

INT. TRADE FAIR
FOR BIOTECHNOLOGY

HANNOVER 22.-24.10.91

★ BIOTECHNICA is an official event of DEUTSCHE MESSE AG, HANNOVER/GERMANY

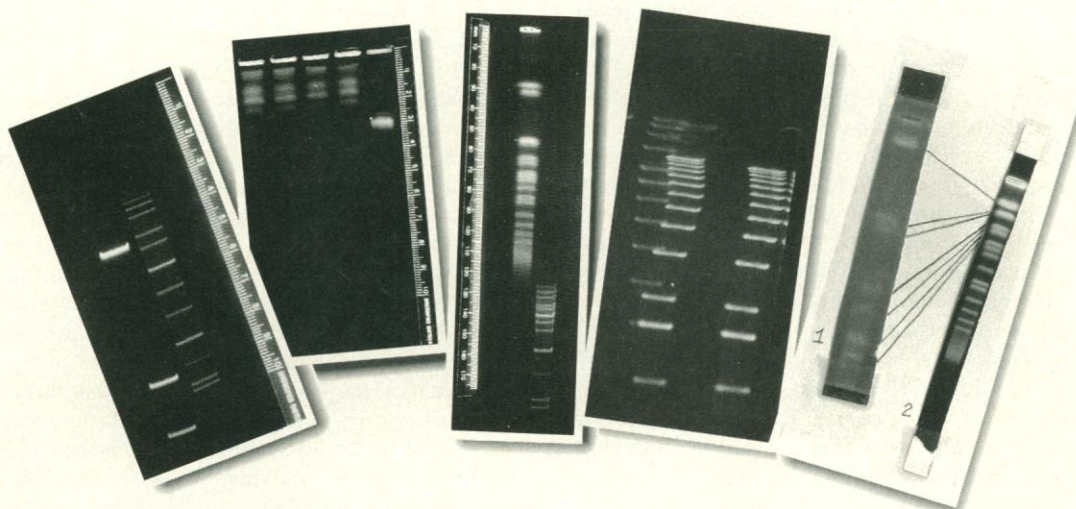


DEUTSCHE MESSE AG, HANNOVER/GERMANY

Further information: Hannover Fairs USA, Inc. 103 Carnegie Center, USA-Princeton, New Jersey 08540, P.O. Box 7066,
Tel. (6 09) 9 8712 02, Telex 51 01 0117 51, Fax (6 09) 9 87 00 92

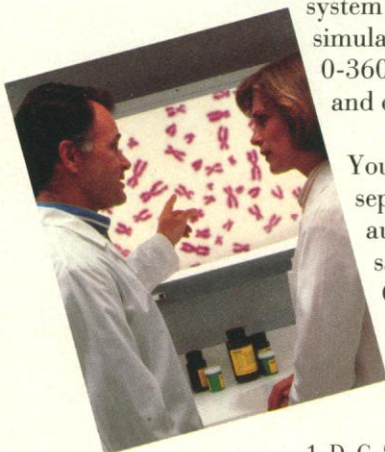
Circle No. 188 on Readers' Service Card

Introducing the Most Important Invention in PFGE Since the Invention of PFGE



Left to right: Asymmetric voltage FIGE, 5-50 kb; *S. pombe* 24 hrs, 106° angle; 8kb - 2.2 mb; 2-D separation of linear and supercoiled DNA; 8 state high resolution separation of *S. cerevisiae*.

Pulsed field electrophoresis (PFGE¹) is the most powerful method ever developed for genome and small DNA mapping. And the CHEF Mapper™ system is the ultimate PFGE tool. Its incredible PACE² architecture lets you simulate any PFGE technique. Or create any technique you want using 0-360° angles, multi-state vectors, asymmetric voltages, rapid switching, and other unique capabilities.



You don't need to be a PFGE expert to get fast, high resolution separations. A built-in algorithm based on 5 man-years of PFGE expertise automatically selects optimum conditions for the fragments in your sample and gives you results at the push of a button. The interactive CHEF Mapper system also lets you program 11 key variables to suit your specific separations.

The possibilities are unlimited.

1. D. C. Schwartz and C. R. Cantor. *Cell*, **67** (1984).
2. Programmed Autonomously Controlled Electrodes. See S. M. Clark, E. Lai, B. W. Birren and L. Hood. *Science*, **241**, 1203 (1988).

1-800-4BIORAD

CALL TODAY OR FAX 1-800-950-4BIO FOR CHEF MAPPER BROCHURE.

BIO-RAD

**Chemical
Division**

U.S. (800) 4BIORAD • California • Ph. (415) 232-7000 • Fx. (415) 232-4257; New York • Ph. (516) 756-2575 • Fx. (516) 756-2594; Canada • Ph. (416) 624-0713 • Fx. (416) 624-3019; Australia • Ph. 61-2-805-5000 • Fx. 61-2-805-1920; Austria • Ph. 43/222/82 89 010 • Fx. 43/222/82 85 629; Belgium • Ph. 32/2/91 85 55 11 • Fx. 32/2/91 82 65 54; France • Ph. 33/1/49 60 68 34 • Fx. 33/1/46 71 24 67; Germany • Ph. 49/89/31 88 40 • Fx. 49/89/31 88 41 00; Kowloon • Ph. 852/789/3300 • Fx. 852/789/1257; Italy • Ph. 39/2/213 87 51 • Fx. 39/2/213 90 32; Spain • Ph. 34/1/661 7085 • Fx. 34/1/661 9698; Japan • Ph. 81-3-534-7240 • Fx. 81-3-534-8037; The Netherlands • Ph. 31/8385-40666 • Fx. 31/8385-42216; Switzerland • Ph. 41/1/810 16 77 • Fx. 41/1/810 19 33; England • Ph. 44/442/23 25 52 • Fx. 44/442/59118; New Zealand • Ph. 64/9/443/3099 • Fx. 64/9/443/3097

Circle No. 194 on Readers' Service Card

(CAN YOU AFFORD TO WAIT FOR YOUR COMPUTER?)

N A S F R O M D I G I T A L .

© DIGITAL EQUIPMENT CORPORATION 1991. THE DIGITAL LOGO, DIGITAL AND VAX ARE TRADEMARKS OF DIGITAL EQUIPMENT CORPORATION. CHARM_m IS A TRADEMARK OF POLYGEN CORP. DISCOVER IS A TRADEMARK OF BIOSYM TECHNOLOGIES, INC.

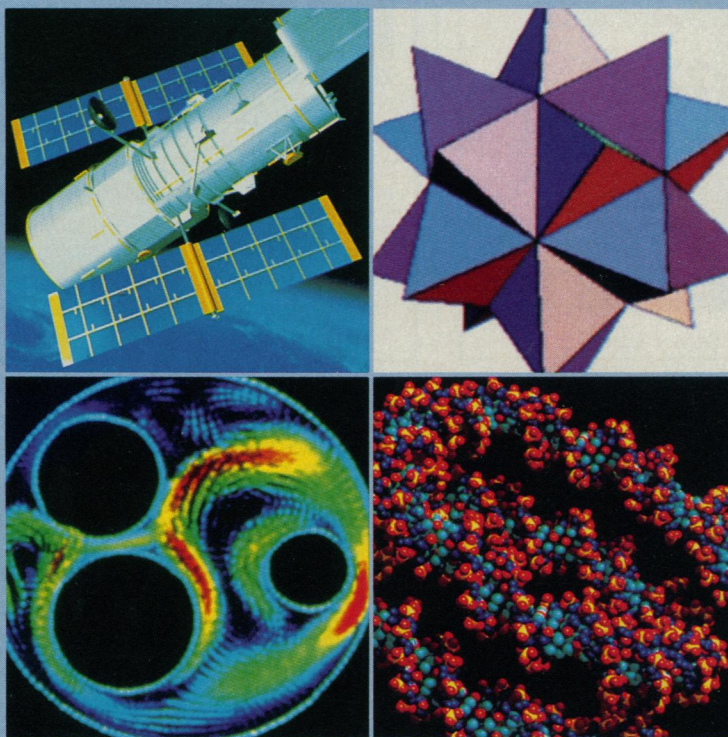
After doing all the research, data acquisition and analysis, you're about to make the biggest breakthrough in your field. But first, you have to wait. And wait. And wait.

What you're waiting for is time on your department's supercomputer - that is, unless you've discovered VAX 6000 and VAX 9000 vector systems.

VAX vectors can prove to be a major boost for you because they perform analyses up to 400 times faster than a general processing system. And they can be added to an existing VAX 6000 or VAX 9000, or purchased as a complete system. Giving you the supercomputing power you need - up to 500 megaflops - at a price that's easy to justify.

VAX vectors also deliver proven performance in two other areas - accessibility and application availability. You get high-speed access to the VAX vectors from your visualization workstation.

VAX SUPER- COMPUTERS AND NAS OPEN A WORLD OF VECTOR PROCESSING POSSIBILITIES.



You can work with your favorite world-class vectorized applications, including CHARMM, DISCOVER, FIDAP, FLUENT, GAUSSIAN 90, IMSL Libraries, MOPAC, NAG Libraries, PHOENICS, and others. And, what's more, you can work with over 10,000

existing VAX applications.

You get breakthrough performance with VAX vectors since they work with Digital's Network Application Support (NAS), the industry's most open computing environment. An environment that's based not only on industry standards, but a commitment to letting different applications on different computing systems from different companies all share information and work together.

With all that VAX vectors offer, it's easy to see why Digital has the lead in supercomputing market share after just one year.

Right now, scientists in research centers all around the world are using VAX vectors for their latest and greatest breakthroughs. So call 1-800-332-4636, extension 289 for more information on VAX vectors. Because you can't afford to wait any longer.

digitalTM

THE OPEN ADVANTAGE.

FIDAP IS A TRADEMARK OF FLUID DYNAMICS INTERNATIONAL. FLUENT IS A REGISTERED TRADEMARK OF creare, x. GAUSSIAN 90 IS A TRADEMARK OF GAUSSIAN, INC. IMSL IS A REGISTERED TRADEMARK OF IMSL, INC. NAG IS A TRADEMARK OF NUMERICAL ALGORITHMS GROUP, LTD. PHOENICS IS A TRADEMARK OF CHAM LTD.Circle No. 209 on Readers' Service Card

DNA by Operon.

**Right Price.
Right Now.** **\$3.60**
per base

Now the world's leading supplier of synthetic DNA is also the price leader. Operon's custom DNA is now \$3.60 per base with a \$20.00 set-up fee per sequence, and free domestic delivery. Same outstanding customer service. Same high product quality. New low price. Call for your free researcher kit.

1-800-688-2248

OPERON

OPERON TECHNOLOGIES, INC.

1000 Atlantic Ave., Suite 108 · Alameda CA 94501
Tel. (415) 865-8644 · Fax. (415) 865-5255—NIHBPA 263-00033233

WORLD'S LEADING SUPPLIER OF SYNTHETIC DNA.

Circle No. 18 on Readers' Service Card

ANNOUNCEMENT

1992 ZIMMERMAN CONFERENCE:

PROGRESS IN VASCULAR BIOLOGY, HEMOSTASIS AND THROMBOSIS

**FEBRUARY
27-29, 1992**

**SPONSORED BY
THE SCRIPPS RESEARCH INSTITUTE AND
RHÔNE-POULENC RORER**

**SHERATON GRANDE TORREY PINES HOTEL
LA JOLLA, CALIFORNIA, USA**

CALL FOR ABSTRACTS

Interested investigators may submit a 250 word abstract for inclusion at Poster Sessions to be held in conjunction with the **1992 Zimmerman Conference**. Abstracts will be selected on scientific merit. **The deadline for abstract submission is November 1, 1991.**

An abstract form and additional conference information may be obtained by contacting by mail or FAX:

Susan J. Buntjer, C.M.P., Department of Academic Affairs
403C, The Scripps Research Institute
10666 North Torrey Pines Road
La Jolla, California 92037 U.S.A.

FAX Number: (619) 554-8841 Telephone: (619) 554-8556

Circle No. 274 on Readers' Service Card

DISCOVER!

1991/92

ANTARCTICA



Call Today for Travel in 1991/92!
(800) 252-4910

Travels with AAAS

For the Inquisitive Traveler

NEW in 1991!

- **Ancient Anasazi & Southwest**, Aug. 31–Sept. 9. Explore Chaco Canyon, Santa Fe, Mesa Verde, Hopi & Navajo lands. \$2,290
- **Thailand & Hong Kong**, Nov. 8–24. Bangkok & Chiang Mai cultural treasures, Surin elephant roundup, Khao Yai & Phi Phi Island. \$3,490 (plus air)
- **Amazon & Brazil: Wildlife**, Sept. 11–26. From golden lion tamarins to the rainforest of Amazonia, Manaus, Brasilia, the Pantanal, Emas, and Rio. \$3,490 (plus air)
- **Tahiti with S/V Wind Song**, Sept. 27–Oct. 7. Paradise! Papeete, Raiatea, Bora Bora, and Moorea. \$2,195 (plus air)
- **Voyage to the Sea of Cortez**, Dec. 21–28. For your Christmas holiday! \$2,000+ (plus air)

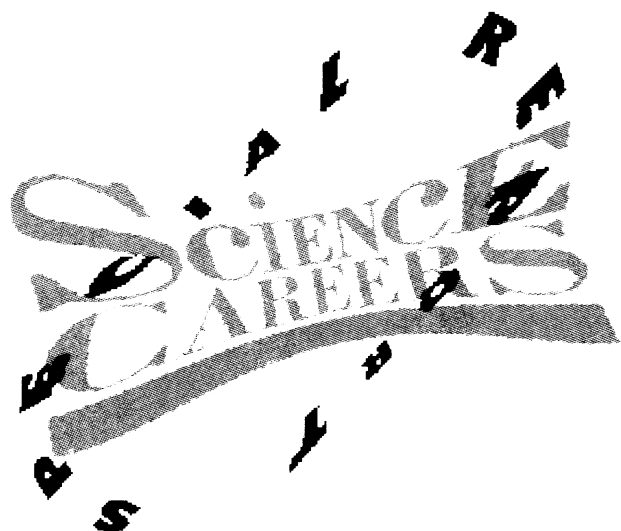
- **Australia**, Oct. 7–18. Koalas, kangaroos, Great Barrier Reef, Sydney and Melbourne. **New Zealand Extension** to Oct. 25. The wonders of Milford Sound and Mt. Cook. \$2,390+ (plus air)

And Coming in 1992:

- **Antarctica**, Jan. 6–20, 1992. Explore the "Great White Continent" aboard *Society Explorer*. See penguins, seals, seabirds, scientific research stations, and the vast spectacle of Antarctica! \$5,950+ (plus air)
- **Galapagos for Budget Travelers**, January 20–29, 1992. On board 10-passenger yachts, 8 glorious days in the Galapagos. \$2,495 including air fare from Miami.
- **Costa Rica**, March 10–22, 1992
- **Belize & Guatemala**, April 1–11, 1992



For Members & Friends of AAAS by
BETCHART EXPEDITIONS INC. • 21601 Stevens Creek Blvd. • Cupertino, CA 95014 • (800) 252-4910



ORDER COUPON

To order additional copies of the Special Careers Issue, please enclose a check payable to Science (U.S. funds only).

Cost: \$1.25 per copy plus postage & handling

ALL ORDERS MUST BE PREPAID

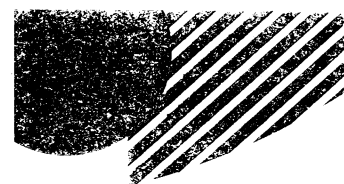
			Cost
Quantity #	X	\$1.25	
Postage and handling			
In the U.S.	\$1.50 first copy		
	\$1.50 each additional copy		
International Air	\$5.00 first copy		
	\$4.00 each additional copy		
International surface	\$1.50 first copy		
	\$1.00 each additional copy		
Total			

Name
Organization
Address
Telephone/Fax

Send orders to: Corrine Harris, Science
1333 H Street NW
Washington, DC 20005

For prices on orders of 30 or more call
202/ 326-6527

Fill the
gap
between
discovery
and
development



Internat.



DEBIO PHARM

You are a researcher and a discoverer in the field of new drugs.

You need help to transform a project into reality.

We have the know-how and money.

We are expecting you.

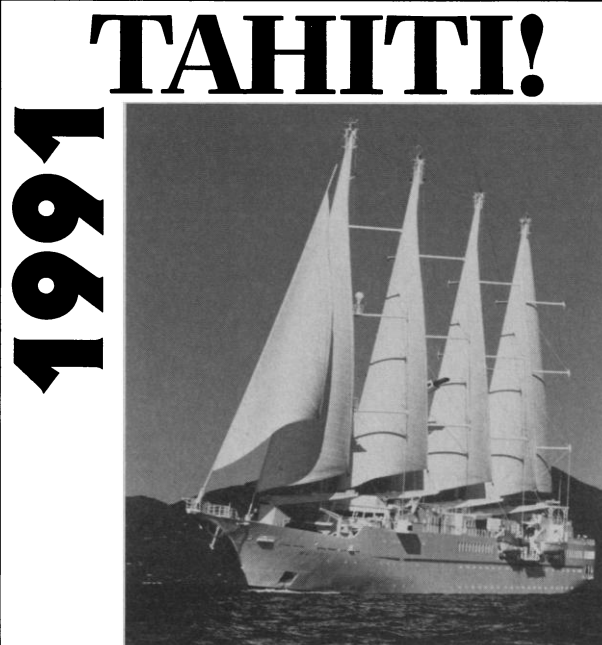
Let's get together.

Contact us at:

DEBIOPHARM*
Rue du Crêt, 2
Case Postale 446
1006 Lausanne
Switzerland
Tel. (41) 21.617.05.86
Fax. (41) 21.617.07.01

* DEBIOPHARM: private and independent research institute for pharmacological and clinical development.

Circle No. 42 on Readers' Service Card



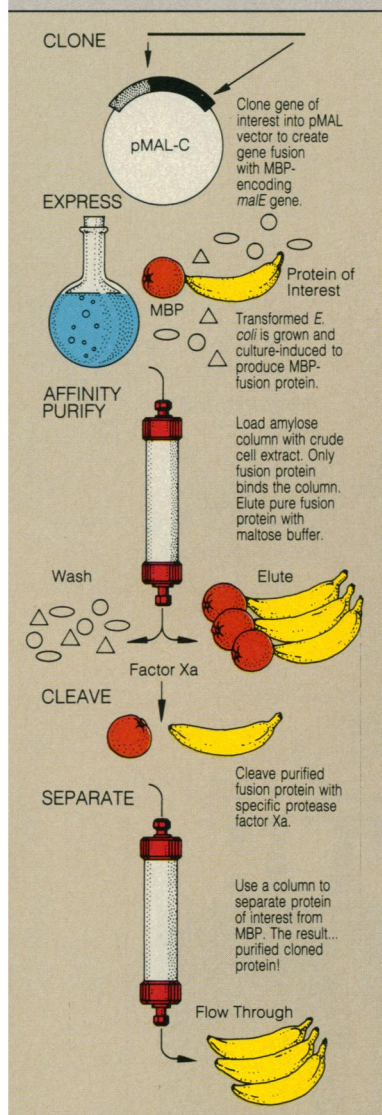
Explore **Tahiti** on board *S/V Wind Song*,
September 27-October 7. Enjoy Papeete
• Raiatea • Bora Bora • & Moorea!
\$2,195 (plus air fare).

(800) 252-4910

Travels with AAAS by BETCHART

Fusion and the Creative Mind.

The New Protein Fusion System from New England Biolabs



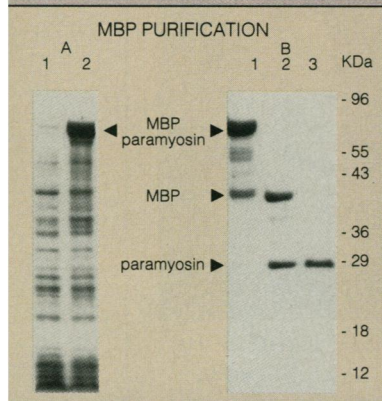
A Creatively Simple Solution for Complex Purification Problems

NEB's Protein Fusion and Purification System (PFP) provides a simple alternative to conventional methods for the expression and purification of recombinant proteins.

Simply clone, express and purify. Our comprehensive PFP system enables the expression of recombinant proteins in *E. coli* fused to maltose binding protein (MBP). An affinity purification step then allows the recovery of your protein of interest under mild conditions. It's simple, elegant and affordable...and yields up to 100 mgs of fusion protein per liter of culture.

Fully integrated system includes:

- pMAL™ Expression Vectors (5 µg each)
- *E. coli* strain TB1
- Amylose resin (1.5g)
- Factor Xa protease (25 µg)
- Control MBP fusion protein to monitor factor Xa cleavage (100 µg)
- MBP--marker for SDS polyacrylamide gels (10 µg)
- anti-MBP antiserum--for Western blot analysis (25 µg)
- A comprehensive instruction manual

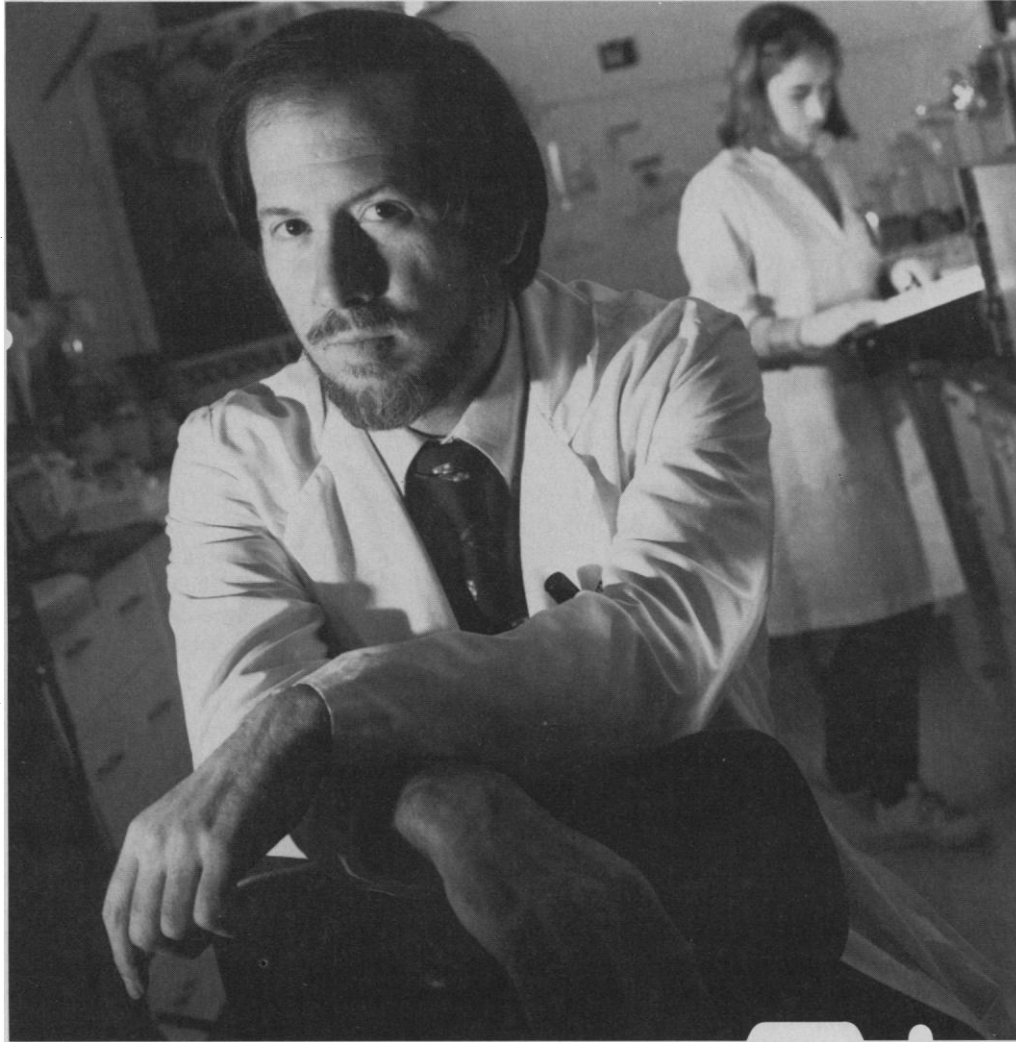


SDS-polyacrylamide gel electrophoresis of fractions from the purification of MBP-paramyosin-ΔSal. A: Lane 1: uninduced cells. Lane 2: induced cells. B: Lane 1: purified protein eluted from amylose column with maltose. Lane 2: purified protein after factor Xa cleavage. Lane 3: paramyosin fragment eluted from second amylose column.

☐ New England Biolabs Inc. 32 Tozer Road, Beverly, MA 01915 USA 800-NEB LABS (US and MA) Tel. (508) 927-5054 Fax (508) 921-1350
☐ New England Biolabs Ltd., Canada Tel. (800) 387-1095 (416) 672-3370 Fax (416) 672-3414
☐ New England Biolabs GmbH, Germany Tel. 49 (06196) 3031 Fax (06196) 83639

DISTRIBUTORS: **AUSTRALIA** GENESEARCh Tel. (075) 37 5499 / **FINLAND, SWEDEN, DENMARK, USSR** FINNZYMES (Finland) Tel. (0) 437-5312 / **FRANCE** OZYME Tel. (1) 30 57 0025 / **INDIA** BIOTECH INDIA Tel. (542) 311473 / **ISRAEL** GAMIDOR Tel. (03) 535-1205 / **ITALY** C.A.M.Bio Tel. (02) 487 06070 / **JAPAN** DAIICHI PURE CHEMICALS CO. LTD. Tel. (03) 3272-0671 / **KOREA** KORAM BIOTECH Tel. (02) 556-0311 / **THE NETHERLANDS** WESTBURG Tel. (033) 95 00 94 / **NEW ZEALAND** BIOLAB SCIENTIFIC Tel. (09) 418-3039 / **NORWAY** ING. F. HEIDENREICH Tel. (02) 22 04 11 / **PEOPLE'S REPUBLIC OF CHINA** CHINA UNITED BIO-TECH. CORP. Tel. (1) 256 1627 / **PORTUGAL** ISODER Tel. (01) 363-8788 / **SPAIN** LANDERDIAGNOSTICO Tel. (01) 594 08 06, (03) 256 9706 / **SWITZERLAND** FLOW LABORATORIES AG Tel. (061) 4814713 / **TAIWAN** LONG CHAIN INTERNATIONAL Tel. (02) 565-2605 / **UK** CP LABORATORIES Tel. (0279) 758200





For more than ten years Bert Vogelstein has been pursuing the genetic basis of cancer. With his publications in Science identifying several tumor suppressor genes, Vogelstein dramatically furthered our understanding of colorectal cancer and its pathogenesis.

*The importance of these discoveries is highlighted by a report from the Institute for Scientific Information placing one of these articles from Science as the most highly cited research paper—across all disciplines—of 1990.**

But Science publishes more than just seminal research. Its News section keeps you up to date on issues from around the world and examines their impact; its Research News and Perspectives review the hottest topics in the scientific community.

Now more than ever Science is your comprehensive guide to the ever changing world of scientific inquiry.

SCIENCE

The international chronicle of scientific progress and thought

* Identification of a Chromosome 18q gene that is altered in colorectal cancer (E.R. Fearon, *et al.*, *Science*, 247; pp. 49-56). For a full report from ISI see *Science Watch*, December 1990.