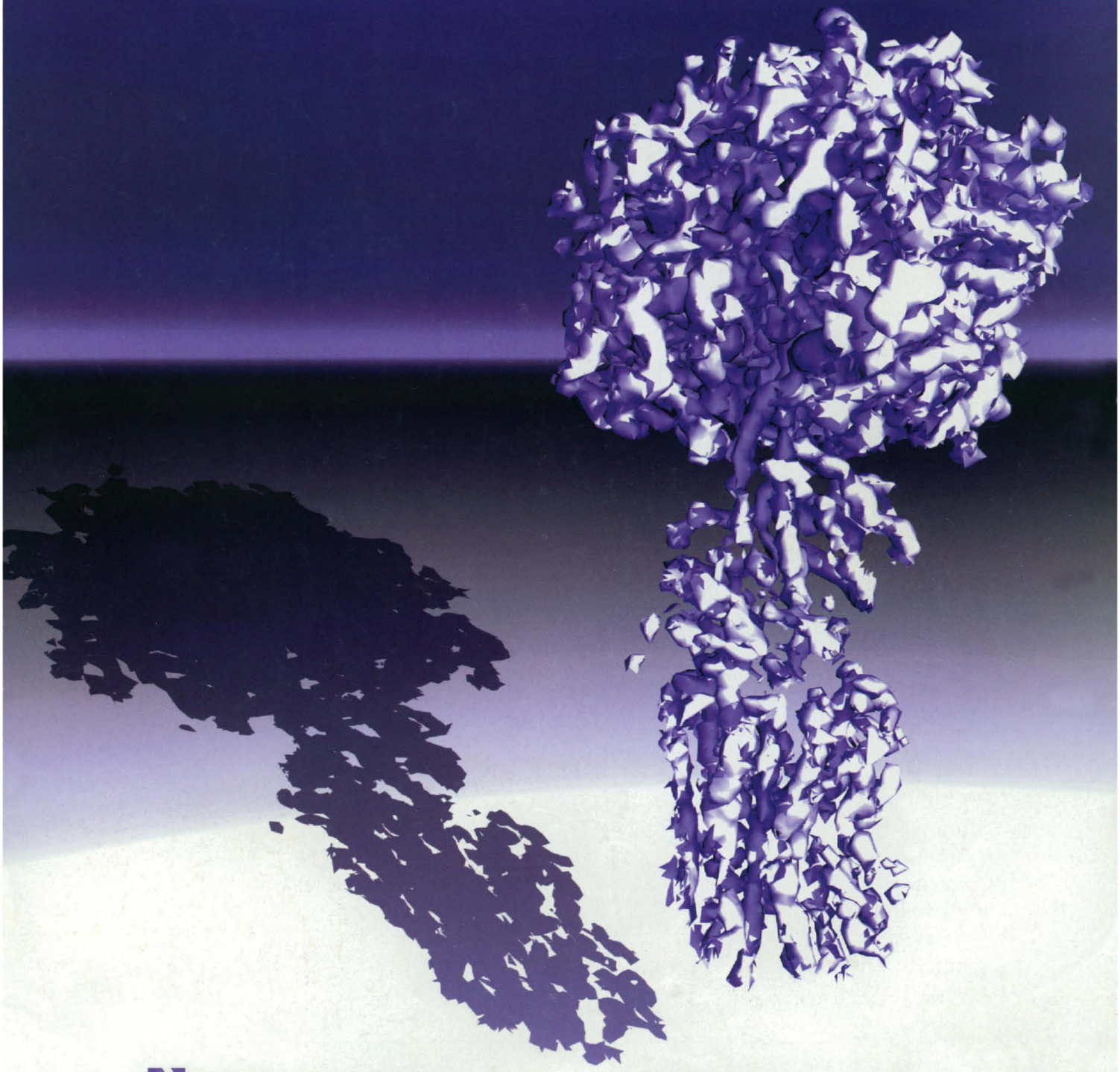
26 November 1999

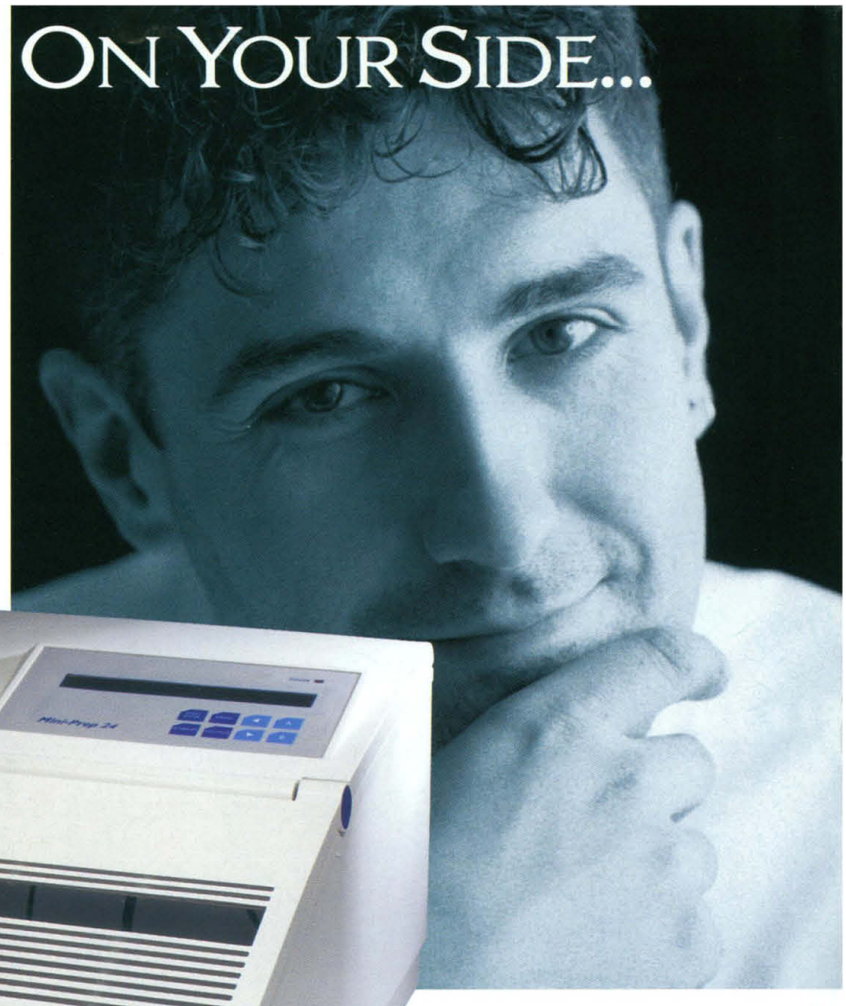
Science

Vol. 286 No. 5445
Pages 1637–1804 $8



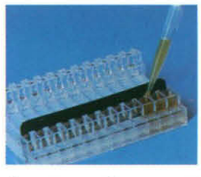
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

NOW, TIME IS ON YOUR SIDE...



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

The Mini-Prep 24 uses a new method of plasmid purification based on agarose electrophoresis and subsequent recovery by electroelution.

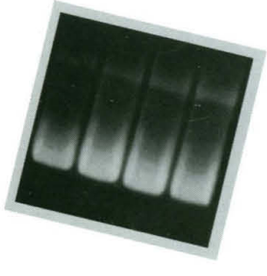


The Mini-Prep 24 uses premanufactured sample cassettes that come ready for direct loading of up to 2 ml of culture.

Call now to learn how the new Mini-Prep 24 can give you quality DNA while saving you more time than you can imagine.

NO CENTRIFUGATION STEPS

High Purity - sufficient for automated fluorescent and manual sequencing.
Consistent Results - up to 6 µg of plasmid per ml.
Fast - up to 24 preps per hour.
Quality - time and time again.



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

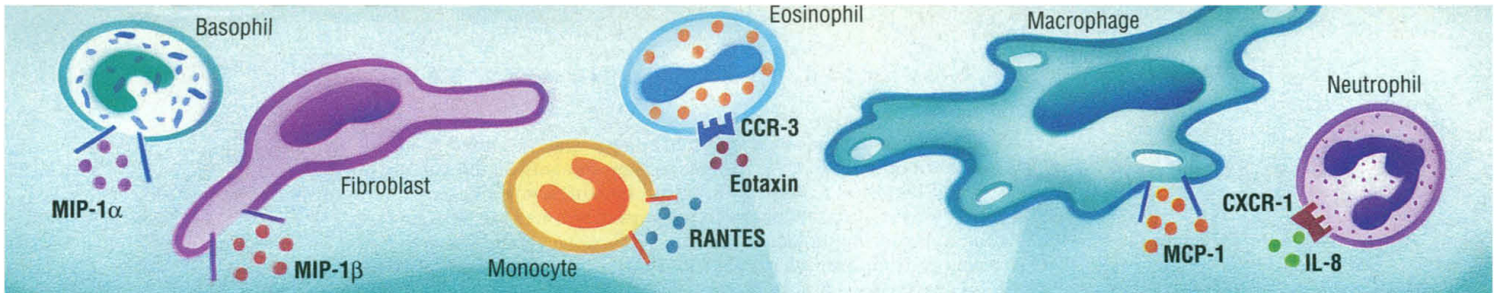
MACCONNELL RESEARCH

1-800-466-7949

11339 SorrentoValley Rd • San Diego, CA 92121

Phone: (619) 452-2603 Fax (619) 452-6753
www.macconnell.com

Circle No. 62 on Readers' Service Card



Chemokines & Receptors

R&D Systems Expanding Line of Chemokine Reagents Include:

- Recombinant Proteins
- Antibodies
- ELISA Kits
- Flow Cytometry Reagents
- Probe Cocktails
- Primer Pairs

CC Chemokines

6CKine • C10 • Eotaxin • Eotaxin-2 (MPIF-2) • HCC-1 • HCC-4 • I-309 • JE • Lkn-1
MARC • MCP-1 (MCAF) • MCP-2 • MCP-3 • MCP-4 • MCP-5 • MDC • MIP-1α • MIP-1β
MIP-1γ • MIP-1δ • MIP-3α • MIP-3β • MPIF-1 • PARC • RANTES • TARC • TECK

CXC Chemokines

BLC/BCA-1 • CINC-1 • CINC-2α • CINC-2β • CRG-2 • ENA-78 • GCP-2 • GROα • GROβ
GROγ • I-TAC • IL-8 • IP-10 • KC • MIG • MIP-2 • NAP-2 • SDF-1α/PBSF • SDF-1β/PBSF

C Chemokines

Lymphotactin

CX_3C Chemokines

Fractalkine

Viral Chemokines

MIP-I • MIP-II • MIP-III
CCI • CMV UL146

Chemokine Receptors

CCR-1 • CCR-2 • CCR-3 • CCR-5 • CCR-6 • CXCR-1 (IL-8RA) • CXCR-2 (IL-8RB) • CXCR-3 • CXCR-4 • CXCR-5

Circle No. 57 on Readers' Service Card

www.rndsystems.com

FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC OR THERAPEUTIC PROCEDURES.

North America
R&D Systems, Inc.
614 McKinley Place NE
Minneapolis, MN 55413, USA
Tel: 612 379-2956
Fax: 612 379-6580
info@rndsystems.com

Europe
R&D Systems Europe Ltd.
4-10 The Quadrant, Barton Lane
Abingdon, OX14 3YS, UK
Tel: +44 (0)1235 529449
Fax: +44 (0)1235 533420
info@rndsystems.co.uk

Germany
R&D Systems GmbH
Borsigstrasse 7
65205 Wiesbaden, Germany
Tel: +49 (0)6122 90980
Fax: +49 (0)6122 909819
infogmbh@rndsystems.co.uk

Europe Free Phone
Belgique/België: 0800 10 468
Danmark: 80 01 85 92
France: 0800 90 72 49
Nederland: 060 225607
Norge: 800 11033
Sverige: 020 79 31 49
Switzerland: 0800 55 2482

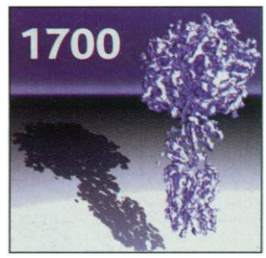
R&D SYSTEMS

1-800-343-7475

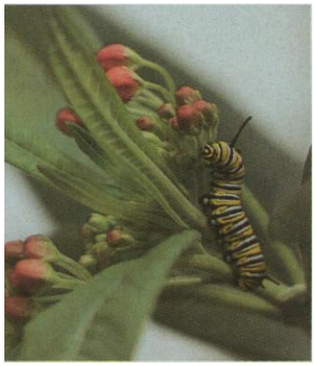
VOLUME 286 26 NOVEMBER 1999 NUMBER 5445

Science

www.sciencemag.org



COVER Life depends on a supply of energy, which is stored in adenosine triphosphate (ATP). The image shows details of the submicroscopic biological ATP-synthesizing machine (at 5 Å resolution), found in life-forms from microbes to humans. It provides the first glimpse of the rotating molecular motor (the lower cylinder), which uses energy from food to propel ATP synthesis in the spherical head. [Image: D. Stock, A. G. W. Leslie, J. E. Walker]



1662

GM foods: Science, stakes, and risks

NEWS

NEWS OF THE WEEK

NEWS FOCUS

DEPARTMENTS

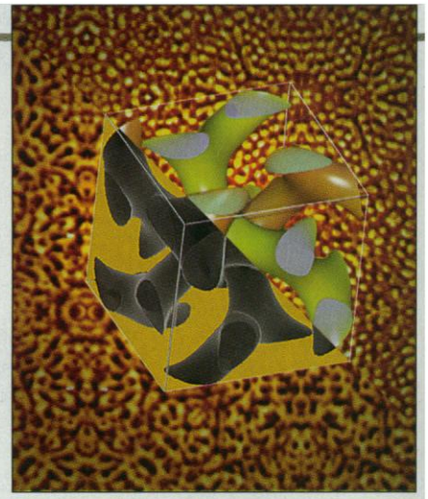
RESEARCH

RESEARCH ARTICLES

REPORTS

1716

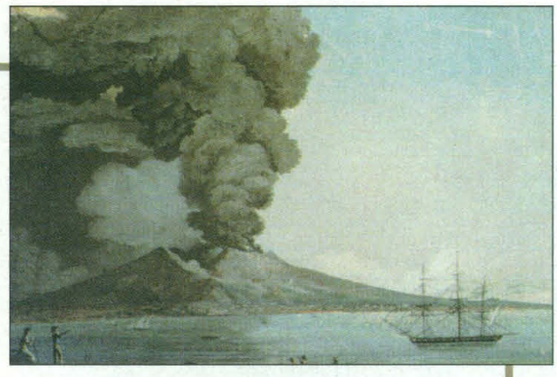
Converting polymers into nanoporous ceramic films



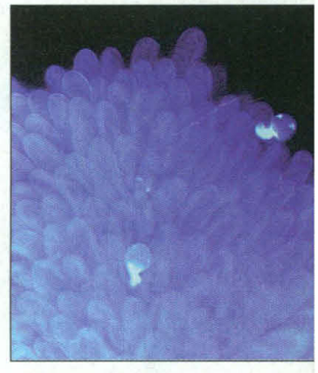
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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



1685
Harbinger of future eruptions?



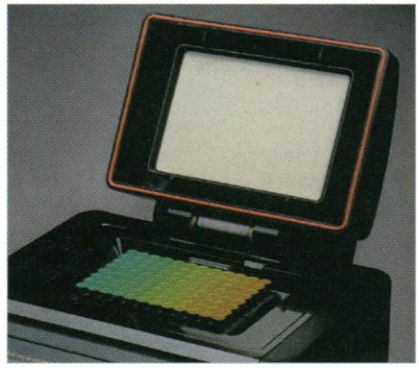
1697
Regulation of self-incompatibility

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.

THE MJ RESEARCH NOTEBOOK

Volume IX...No. 3 *A Bulletin of Technological Advance in Molecular Biology* *Autumn 1999*

NEW GRADIENT HELPS OPTIMIZE ANNEALING AND DENATURATION



DNA Engine™, with the thermal gradient shown in artificial colors from data collected by an IR camera.

Optimized Denaturations Surprisingly Important

It is well known in the biological community that DNA amplification reactions should have optimized annealing temperatures for best results. Denaturation is quite important as well—but only the savvy optimize this step.

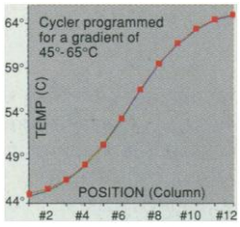
Too bad. MJ's scientific staff finds that denaturation often leads to problems. Use of a lower denaturation temperature, such as 90°-92°C, is generally recommended whenever possible. Not only does it preserve enzymatic activity for later cycles, it also reduces breakdown of fluorescent dyes in cycle sequencing. On the other hand, higher temperatures, such as 95°-96°C, may be required for GC-rich templates from organisms such as Mycobacteria.

Gradient Calculator Especially Useful

Easy to Transfer "Golden" Parameters to Actual Protocols

Most researchers would agree that gradient cyclers are great in concept—but their utility is significantly compromised if an optimized protocol does not transfer well to normal, non-gradient operation. This "Achilles heel" of gradient cyclers can often be traced to imprecise knowledge of either incubation time or incubation temperature during the gradient step. Whatever technology is used, there will always be lags—often not well known—before samples reach the new temperature.

MJ has long had an excellent reputation for delivering time/temperature control with precision, so extra efforts were expended to address these issues. Thus time control includes "dynamic ramping" (see below), while temperature control incorporates a new software feature called the "gradient calculator".



Reported temps (dots) vs. independently acquired thermal data in 4 cyclers (lines).

This calculator is so precise and accurate that it reports the temperatures in individual columns to within ±0.4°C of the NIST standard, making transfer of values to normal operation *very* reproducible. Just look above how reported temperatures from the gradient calculator superpose *almost perfectly* with independent NIST-traceable data from 4 different cyclers.

ALL EXISTING DNA ENGINES & TETRADS CAN BE UPGRADED

Standard Feature on New Thermal Cyclers

WALTHAM, Mass. — MJ RESEARCH is pleased to announce the introduction of an advanced gradient feature that is now standard on all DNA Engine & Tetrad thermal cyclers. This powerful new function allows precision thermal gradients as high as 24°C to be developed across 96-well blocks, at any temperature between 30° and 105°C. This greatly assists in developing robust protocols, for the optimal annealing and denaturation temperatures give strong results without lots of "ampli-schmutz" or other unwanted artifacts appearing in the gel.

Many reactions benefit from careful temperature optimization, especially sensitive ones, such as dye-terminator cycle sequencing. GC-content, length of molecule, concentration of magnesium—all these lead to differences in optimal "heat" for annealing and denaturation. This is why empirical experiments can almost always enhance even the *best* calculations for T_m.

But who wants to do a dozen runs of slightly variant protocols? Gradient cyclers make this chore much easier by allowing a dozen different incubation temperatures in a single run. The user simply selects a range of temperature, and the cycler does the rest. The optimal temperatures become obvious in the gel—with thick "meaty" bands unbracketed by artifact.

How to Get Upgrade

In a nutshell, visit the MJ website. For DNA Engines manufactured after 1/1/99, the gradient feature is a simple software upgrade that is provided free and can be installed by users. For older DNA Engines or Tetrads, a new logic board is also required, and this upgrade is available inexpensively from MJ or its distributors.

WWW.MJR.COM • INFO@MJR.COM

MJ RESEARCH, INC.

Manufacturer of Products for Molecular Biology

590 Lincoln St. • Waltham MA 02451 USA

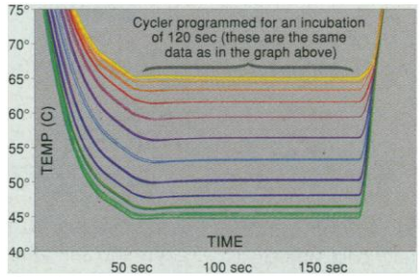
(888) 729-2164 • Fax (617) 923-8080

Precision Control of Time as well as Temp

"Dynamic Ramping" Incubates Each Sample for Same Period

In some gradient cyclers, the gradients develop gradually. When cooling to an annealing gradient, for example, the highest temperature stabilizes long before the lowest one does. This means that the time spent at incubation is different at each temperature—thus two critical parameters are being varied at the same time.

Not so with MJ cyclers. Careful engineering has led to "dynamic ramping" where each column of wells ramps at a different rate, for ramp rates are much less critical. The results are consistent incubation times column-to-column, with only temperature varying among samples.



Data from four cyclers are superposed in this graph, with each trace representing the average temperature measured in a column of wells. Note the consistency of incubation periods, the cycler-to-cycler reproducibility (each trace is made up of *four* separate lines), and the even spread of incubation temperatures between the programmed targets of 45° and 65°C.

POLLEN PREFERENCES

Self-incompatibility in certain plants allows a plant to distinguish its own pollen from among that of other plants of the same species, and preferentially react to nonself pollen in order to limit inbreeding (see the Perspective by Dickinson). Stone *et al.* (p. 1729) have analyzed the activities of ARC1, which shows a phosphorylation-dependent interaction with a kinase located in the stigmatic plasma membrane. Their in vivo studies show that ARC1 is a key regulator of self-incompatibility from the female side. Schopfer *et al.* (p.1697) have now identified a critical component from the pollen side—a polymorphic protein expressed in the pollen that interacts with the stigmatic proteins to determine whether the outcome will be fertile.

CRANKING OUT ATP

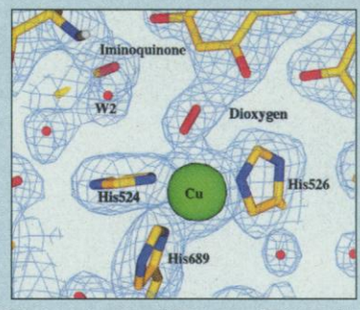
Although the common form of energy used in cells is adenosine triphosphate (ATP), energy is stored both in chemical forms such as fat or starch and in electrochemical forms such as ion gradients across cellular membranes. Fat and starch are metabolized to produce small amounts of ATP and large amounts of energy in the form of a gradient of protons, which is then converted into ATP by an enzyme known as ATP synthase. Stock *et al.* (p. 1700; see the cover) present the crystal structure of the membrane-bound portion (F_0) of the synthase and the axle that connects it to the ATP-synthesizing part (F_1). F_0 transforms the energetically downhill movement of protons into rotation of an internal axle (the γ subunit of F_1) as shown by Sambongi *et al.* (p. 1722). These workings of a nanogenerator are discussed in a Perspective by Fillingame.

THE SUN, THE MOON, AND THE PLUMES

There have been several episodes of large-scale volcanism recorded on Earth's surface, and many of these events are thought to have been initiated by the upwelling of a major thermal anomaly (a plume) from the core-mantle boundary. Greff-Lefftz and Legros (p. 1707) have modeled a possible connection between episodes of volcanism and the initiation of a plume by the interplay of the gravitational forces between Earth, the moon, and the sun. They show that fluid outer-core oscillations set up by the lunar-solar tides and core rotation resonated with the solar tidal waves and that these resonances, which could initiate a plume, occurred at about the same time as three episodes of volcanism in the Precambrian.

OXYGEN IN ACTION

Despite the importance of oxygen as an electron acceptor in many enzymatic reactions, the mechanism of oxygen activation by redox enzymes is not well understood. Wilmot *et al.* (p. 1724) determined x-ray structures



of freeze-trapped intermediates related to the oxidative half-reaction of copper amine oxidase. They also determined the oxidation state of the quinone cofactor for each structure by using single-crystal spectrophotometry. Their studies reveal the binding site for dioxygen and the hydrogen peroxide product and show the proton transfer pathways to the oxygen. The product aldehyde inhibits enzyme reoxidation in the crystal, and thus the release of the aldehyde is rate-determining.

THE WINDS OF CHANGE

The subdecadal variability of climate in the region of the tropical North Atlantic Ocean during the past century is thought to be well understood, but longer term variations that occur over decades to centuries are more difficult to resolve because instrumental records do not extend far enough into the past and most existing sedimentary records do not have sufficient temporal resolution. Black *et al.* (p. 1709) present a 825-year-long record from a southern Caribbean sediment core that reveals decadal and century-scale trade wind variations which indicates that natural climate changes also occurred abruptly in the preindustrial past. These findings also highlight the link between thermohaline circulation in the Atlantic Ocean and other tropical climatic variations.

NANOPOROUS CERAMIC FILMS VIA POLYMERS

Block copolymers, in which segments (blocks) of different chemical composition are connected, can phase-separate at the nanometer scale and form intricate structures. Chan *et al.* (p. 1716) show that copolymers containing two hydrocarbon blocks separated by a block made from a silicon-containing polymer can form an open nanoporous network with a double gyroid morphology. A single-step process that uses ozone and ultraviolet light converts the silicon-containing block into a ceramic framework and removes the remaining hydrocarbon material to create nanoporous ceramic films.

MOLECULAR SHUTTLE

The scanning tunneling microscope (STM) allows great control over atomic and molecular manipulation on surfaces. The microscope tip can also be used to record vibrational spectra that allow the identification and characterization of single adsorbed molecules and the bonds they form with the substrate. Lee and Ho (p. 1719) used these combined capabilities of their low-temperature STM to study the bond formation between single iron atoms on a silver surface and carbon monoxide (CO) molecules delivered with the STM tip. Complexes of iron with one or two CO molecules were formed and characterized.

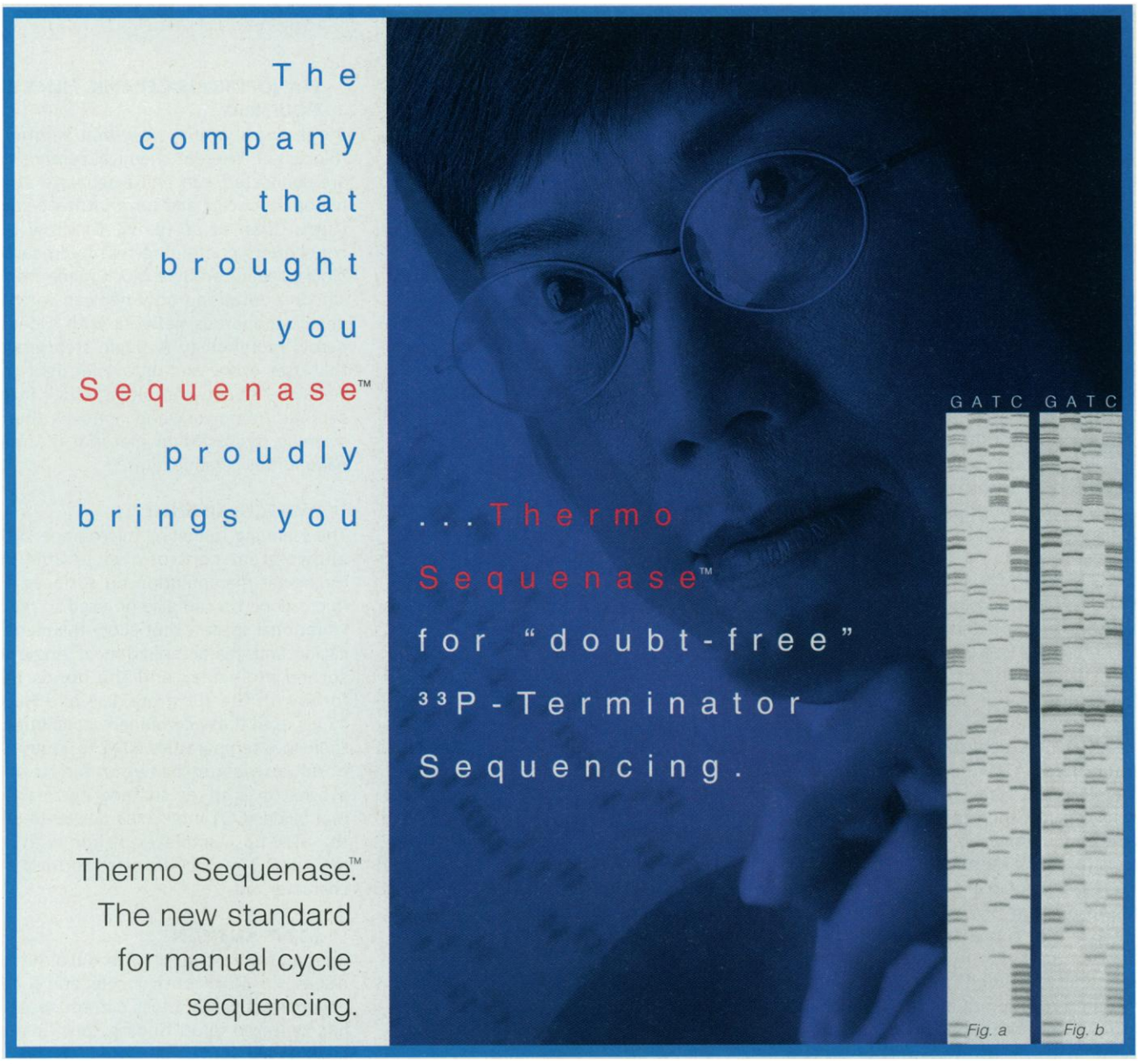
JOINT ANTIGEN

Rheumatoid arthritis is an autoimmune disease in which both T cells and B cells become activated. Most current research has centered upon finding specific antigens of the joint that could be the immunogenic targets for T cell–mediated damage. In a mouse model of arthritis that seems to mimic many of the features of the human condition, Matsumoto *et al.* (p. 1732) have determined that the antigen with the arthritogenic activity for the B cells as well as the T cells is from the same protein, glucose-6-phosphate isomerase, a ubiquitously expressed enzyme. Thus, local autoimmunity need not be caused by a tissue-specific antigen.

DEATH IS ROLE WITHIN A NORMAL LIFE

Proteins of the Bcl-2 family play both roles in apoptosis, either promoting or inhibiting cell death. The smaller proteins that contain only the third Bcl-2 homology domain (BH3-only proteins, such as

CONTINUED ON PAGE 1647



Are your cycle sequencing results leaving you in doubt? Strong stops, background sequence causing problems?

Thermo Sequenase Radiolabelled Terminator Cycle Sequencing Kit

The combination of USB's Thermo Sequenase Terminator Cycle Sequencing Kit with Amersham Pharmacia Biotech's radiolabelled terminators will give you sequencing results beyond a shadow of a doubt.

Thermo Sequenase - gives excellent performance at cycle sequencing temperatures. Helps eliminate secondary structure artifacts.

^{33}P-labelled terminators - yield detection of only truly terminated sequencing fragments. False terminations are not visible because these fragments are not labeled.

- Eliminate stops and BAFLs. (Bands Across all Four Lanes)
- Read the first base after the primer.
- Crisp, clean sequence.
- Detect heterozygotes and mutants more easily.
- Sequencing directly from bacterial colonies is possible.

No other combination for manual cycle sequencing gives more information per gel — long reads, accurate sequence. Doubt-free results.

Above: Elimination of bands across all four lanes (BAFLs) in plasmid template.

Fig. a) Using the Thermo Sequenase Radiolabelled Terminator Cycle Sequencing Kit.

Fig. b) Compared to standard ^{35}S-dATP cycle sequencing where a strong BAFL is observed.

To order within the United States contact USB directly at 1-800-321-9322 or e-mail us at customerserv@usbweb.com. For your authorized USB distributor outside the United States, please contact your local Amersham Pharmacia Biotech office.

USB Corporation, 26111 Miles Road
Cleveland, OH 4412
800-321-9322
www.usbweb.com

usb™
Rediscover the chemistry

Circle No. 51 on Readers' Service Card

CONTINUED FROM PAGE 1645

Bim) are thought to have pro-death properties, but their role in normal apoptotic functions in vivo, such as homeostasis and immune function, has been unclear. Bouillet *et al.* (p. 1735) now report results for a gene-targeted Bim-deficient mouse which show that this BH3-only protein is critical for normal homeostasis of white blood cells, cytokine withdrawal, and calcium-induced apoptosis and also acts as a barrier against autoimmune disease. Thus, Bim is a part of the physiological apoptosis machinery.

WORKING IT OUT DOWNSTREAM

A cell's response to a particular growth factor or hormone involves a relay of signals between the cell surface and the nucleus. The small GTP-binding protein Ras is activated by numerous growth factor receptors and can regulate more than one signaling pathway in response to a single growth factor, depending on the cell type. Hence, Ras can serve as a branch point for signal propagation, and tight regulation of the pathways it stimulates is needed to ensure the proper biological outcome. Two reports describe the cross communication that occurs between two pathways that lie downstream of Ras, the Raf kinase–MEK (mitogen-activated protein kinase)–ERK (extracellular-regulated kinase) pathway and the PI3K (phosphatidylinositol 3-kinase)–Akt kinase pathway. Zimmermann and Moelling (p. 1741) demonstrate that Akt inhibited Raf activity by phosphorylating a known regulatory site on Raf. In breast cancer cells, Akt directly interacted with Raf, and inhibition of Akt resulted in increased Raf activity. The authors suggest that in these cells, this mechanism may regulate growth response to insulin-like growth factor (IGF). Rommel *et al.* (p. 1738) also reveal that Akt associated with Raf and inhibited the Raf signaling pathway in differentiated muscle cells (myotubes) but not in undifferentiated precursor cells. Activation of the Akt pathway or inhibition of the Raf pathway resulted in a hypertrophic phenotype (thickening) similar to that induced by IGF on muscle cells. These studies suggest that integration of these two pathways into a particular cellular response may depend on cell type or the stage of cell differentiation.

FORCE OF HABIT

Patterns of behavior can be learned and become so routine as to occur unconsciously. Jog *et al.* (p. 1745) monitored neural activities within the basal ganglia, a portion of the brain known to be involved in the control of movement. These neural activities changed over time in rats learning a T-maze (the rats associated a tone cue with the correct direction in which to turn at a T-junction toward a food reward). As the rat's accuracy and speed improved, the ensemble of neurons appear to fire most actively at the beginning and at the end of what became a habitual behavior. The representation of entire sequences of motor commands within the basal ganglia may relate to the difficulties that Parkinson's patients experience in beginning or ending movements.

TECHNICAL COMMENT SUMMARIES

Species and Regular and Irregular Areas

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full//286/5445/1647a

Harte *et al.* (Reports, 9 Apr., p. 334) argued that the probability distribution of species is self-similar with respect to area and use this notion to reconcile and address several common species-area relations. Maddux and Athreya comment that the model of Harte *et al.* "implies that species are distributed in one of three trivial ways" and thus conclude that the law is "in general...invalid." Harte *et al.* respond that "patch...shape does matter" and that the prediction made by [their] theory about the dependence of species richness on patch shape is reasonable."

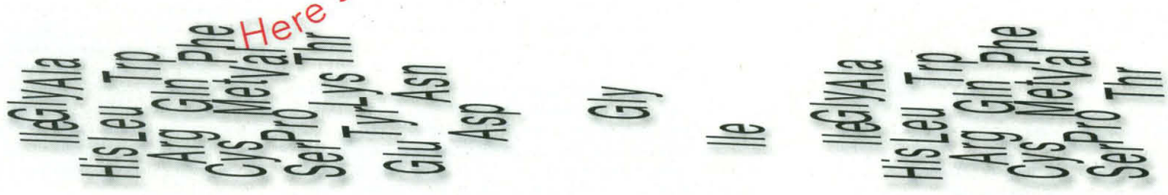
Polymorphisms Return in the IL-13 Promoter

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full//286/5445/1647b

Interleukin-13 (IL-13) plays an important role in allergic responses. In a previous Technical Comment and Response (28 May 1999), Anderson *et al.* and Wills-Karp and Rosenwasser examined part of the IL-13 promoter region, found no polymorphisms there, and concluded that the promoter region was not a susceptibility locus for atopy. Van der Pouw Kraan *et al.* now report that they find evidence of polymorphism just outside the region examined earlier, a finding that Gillespie *et al.* confirm.

Need Custom PEPTIDES?

Here's An Attractive Offer.



We believe if you try our custom peptide and/or antisera services just once, you'll stick with us. In fact, we'll send you a free amino acid micrograph magnet just for calling and requesting more information!

Peptide Service

We're proactive. Before we put your sequence together, we'll take it apart and thoroughly analyze it to prevent surprises later. Because your project depends on our peptide, we'll offer suggestions for increased success. Of course, you can choose from a variety of purity levels and scales. Since every Sigma-Genosys peptide comes with mass spectral analysis and HPLC documentation, you're bound to be 100% satisfied. Guaranteed.

Antisera Service

We'll take care of it from start to finish. Whether you're a peptide novice or pro, we'll help you design your target sequence, synthesize your peptide and conjugate it to a carrier protein. And yes, we also handle the immunization and sera collection. Hassle-free.

Provide us with your sequence and leave the rest to us.

SPECIAL OFFER!

Free micrograph magnet when you call for more information.

SIGMA GENOSYS

1442 Lake Front Circle • The Woodlands, Texas 77380-3600 • Tel: 1-800-498-2098 or (281) 363-3693 • Fax: (281) 363-5923
Email: ginformation@sial.com • http://www.genosys.com

Micrographs are courtesy of Michael W. Davidson, director of the Optical Microscopy Division of the National High Magnetic Field Laboratory.

Circle No. 34 on Readers' Service Card

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.

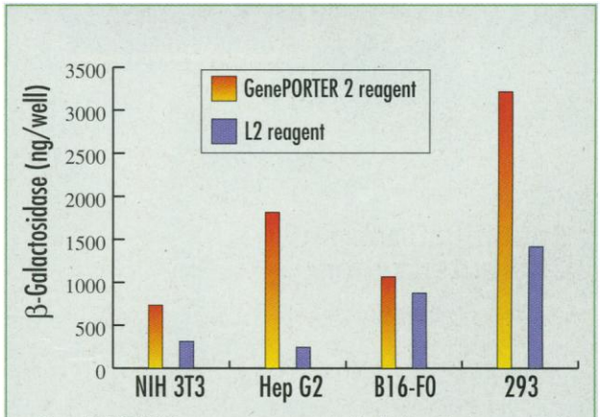
The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objectives are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of 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.

Works great with or without serum

Highest levels of transfection available

Best results with hard-to-transfect cell lines

Alienated by hard-to-transfect cell lines? GenePORTER™ 2 transfection reagent has out-of-this-world results for a variety of cell lines. This new reagent yields higher efficiencies than GenePORTER reagent, even in the presence of serum. Order GenePORTER 2 reagent today and make contact with the next generation of transfection reagent.



GenePORTER 2 reagent or a competitor's transfection reagent was used to deliver the β-gal expression plasmid into cells in 24-well plates. Each manufacturer's protocol was followed. Following transfections (48 hours), a colorimetric assay was used to measure β-galactosidase.

GenePORTER™ 2
Transfection Reagent

75 reactions (0.75 ml) • T202007
150 reactions (1.5 ml) • T202015
750 reactions (5 x 1.5 ml) • T202075

Now available on our web site:

✓ Gene Therapy Systems, Inc. 1999 Catalog
✓ Updated list of sucessfully transfected cells

GTS
Gene Therapy Systems
"the art of innovation"

To Order: 888-428-0558
Fax: 858-623-9494
10190 Telesis Court, San Diego, CA 92121, USA
Check out the Gene Therapy Systems web site @
http://www.genetherapysystems.com

Circle No. 49 on Readers' Service Card

Gene Therapy Systems International Distributors

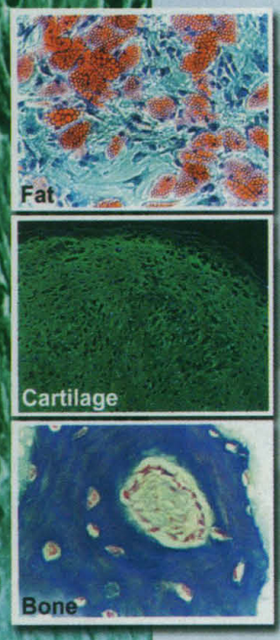
Australia • Astral 61-2-9540-2055 **Austria** • BIO-TRADE +43 1 889 18 19 **Benelux** • BIOzymTC BV +31 +(0)45 532 77 55 **China** • Shanghai Haojia Tech. 86-21-5453-0107 **Denmark** • KEBO Lab A/S +45 43 86 87 88 **Finland** • Kebo Lab +358 9 8045 5300 **France** • OZYME +33 1 30 85 92 92 **Germany** • PEQLAB 49-9131-691-470, Biozym +49 5152-9020 **Israel** • Biotech Appl. 972 8 928 5353 **Italy** • Duotech 39 02 331 066 30 **Japan** • Funakoshi 81-3-5684-1622, Takara +81-77-543-7231 **Korea** • Core Bio 82 2 841-7530 **Norway** • Kebo Lab A/S +47 22 90 00 00 **Sweden** • KEBO Lab +46 8 621 35 07 **South Africa** • Millinium 27 12 8034-876 **Spain** • bioNova +34 91 551 54 03 **Switzerland** • Axon Lab AG +41 56/484 80 80 **Taiwan** • PROtech 886-2-23810844 **United Kingdom** • Lifescreen Ltd 01895 453700

BIOWHITTAKER
A CAMBREX Company

Now Available, Exclusively From POIETICS™

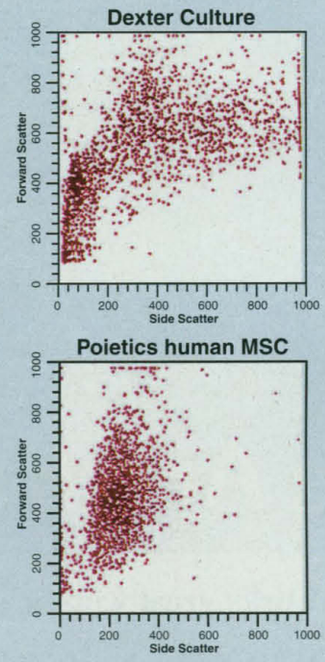
Normal Human
Mesenchymal Stem Cells

Standardized Cell Culture System containing Cells and Medium
Quality Tested and Guaranteed



QC Tested for:

- Adipogenic Lineage as indicated by Neutral Lipid
- Chondrogenic Lineage as indicated by Collagen Type II
- Osteogenic Lineage as indicated by Calcium Mineral

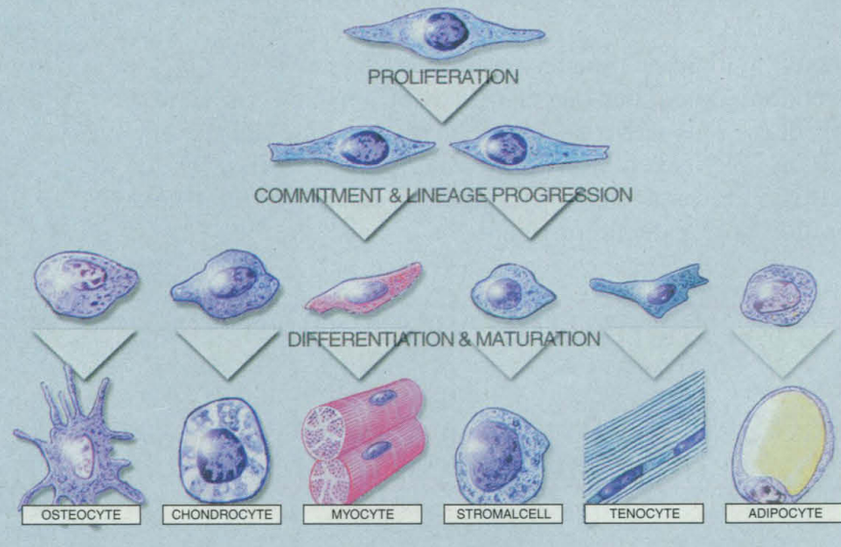


Poietics human MSCs are more homogeneous than a Dexter Culture

Specifications and Characterization:

- Cells cryopreserved in passage two
- Recover 750,000 cells/amp
- Flow cytometric analysis of surface antigens:
  Positive for:
  SH2; SH3; CD29; CD44
  Negative for:
  CD14; CD34
- Cells test negative for HIV-1, hepatitis B & C, mycoplasma, bacteria, yeast and fungi
- Performance guaranteed using Poietics Mesenchymal Stem Cell Growth Medium (MSCGM™)

* Not for use in humans. For research use only.



BioWhittaker is a certified ISO-9001 Quality Management System Company
USA, Can.:(800) 852-5663 • **UK:** 011 8 979 5234
Europe: 32 87 32 16 11 • **All others:** 301-898-7025
E-mail: cs@biowhittaker.com
www.biowhittaker.com, www.clonetics.com or www.poietic.com

OSIRIS Under license from Osiris Therapeutics, Inc.

Circle No. 42 on Readers' Service Card

THE RNA COMPANY™

Make time stand still

WITH RNA*later*™

RNA*later*™ eliminates the need to immediately process or snap-freeze tissue samples for RNA isolation

•

Rapidly inactivates RNases in solid tissue samples

•

RNA is stable in tissues stored for weeks at 25°C, months at 4°C, or indefinitely at -20°C

•

Thaw and refreeze tissue samples without RNA degradation

•

No more freezing and grinding

•

Dissect and weigh tissues at room temperature

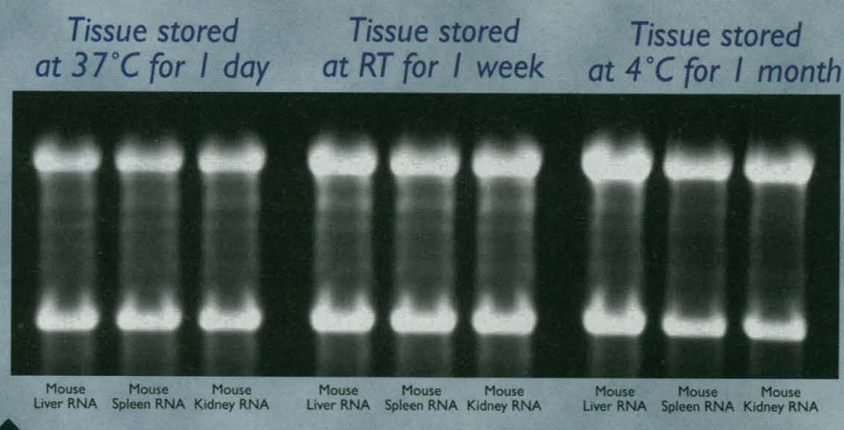
•

Perfect for field collection and clinical samples

•

Ship samples at room temperature

No more quick-freezing of samples to preserve RNA



DO YOU ISOLATE RNA FROM TISSUE?

RNA*later*™ rapidly inactivates RNases and stabilizes RNA in tissues for subsequent RNA isolation.

Ambion's novel Tissue Collection:RNA Stabilization Solution, RNA*later*™, is an aqueous, non-toxic, room temperature reagent that replaces liquid nitrogen for tissue collection prior to RNA isolation. Simply harvest tissues and submerge them in RNA*later*. Store tissues for weeks at 25°C, months at 4°C or indefinitely at -20°C without jeopardizing the quality or quantity of RNA obtained from subsequent RNA isolation. Because RNA*later* immediately inactivates RNases, RNA yield may even increase.

Once saturated in RNA*later*, tissues can be dissected and weighed at room temperature then returned to RNA*later* or placed at -80°C for archival storage. RNA in tissue remains intact after 10 freeze/thaw cycles. RNA*later* is compatible with all RNA isolation procedures tested.

Use RNA*later* and eliminate the rush of tissue harvesting, the worry of long-term tissue storage and the difficulty of freezing and grinding tissue in liquid nitrogen.

For more information, see the 1999 Ambion Product Catalog, call Technical Service, or visit the Ambion website at http://www.ambion.com/ProdInfo/rnalater.html.

U.S. (800)888-8804
Canada (800)445-1161

For a complete list of distributors visit our website, http://www.ambion.com

Order Today

100 ml	Catalog # 7020	$ 50.00
500 ml	Catalog # 7021	$175.00

Ambion®
THE RNA COMPANY™

Ambion, Inc. • 2130 Woodward St. • Austin, TX 78744-1832 • tel(512)651-0200 • fax(512)651-0201 • email: moinfo@ambion.com • www.ambion.com

Circle No. 66 on Readers' Service Card

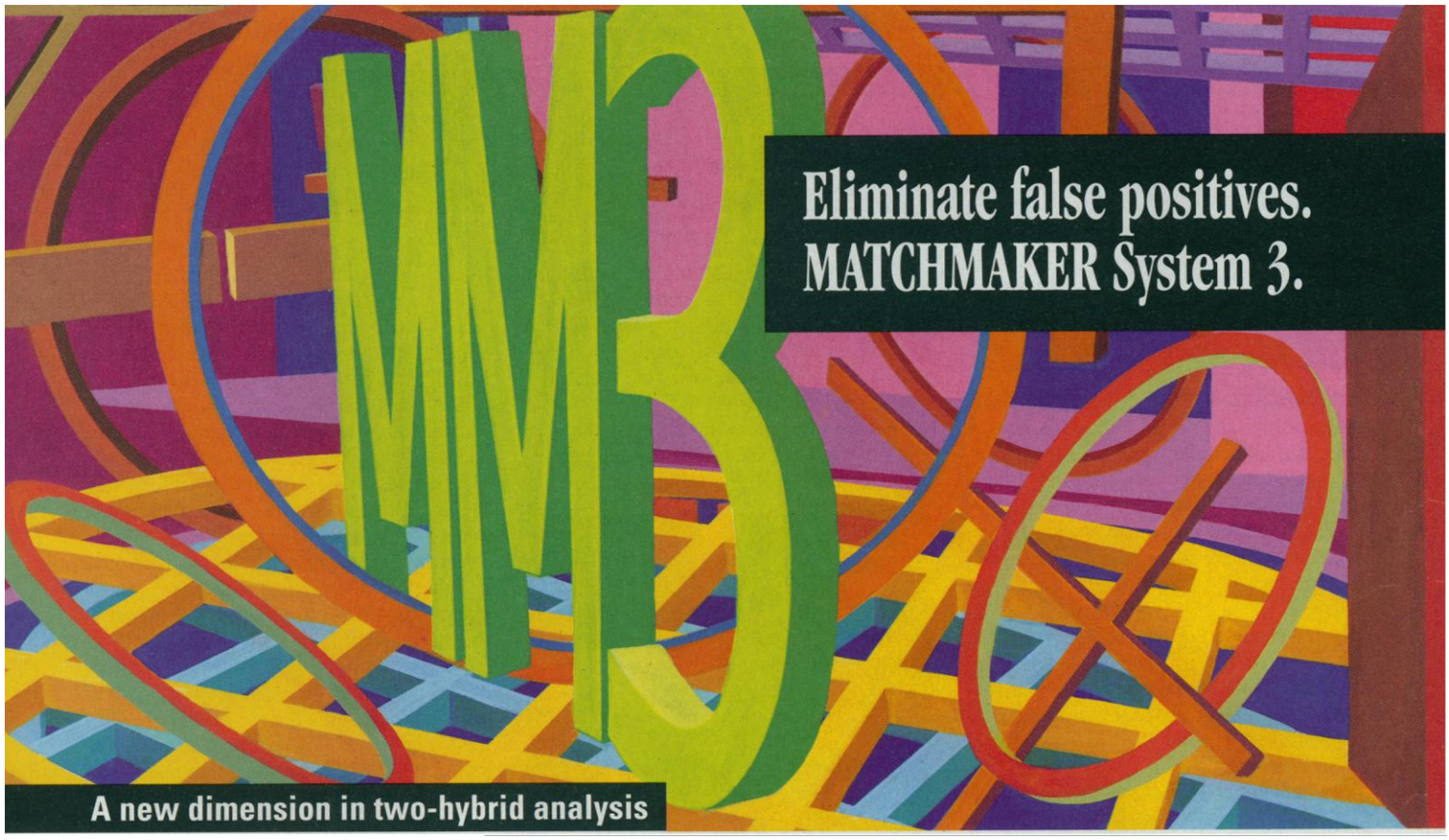
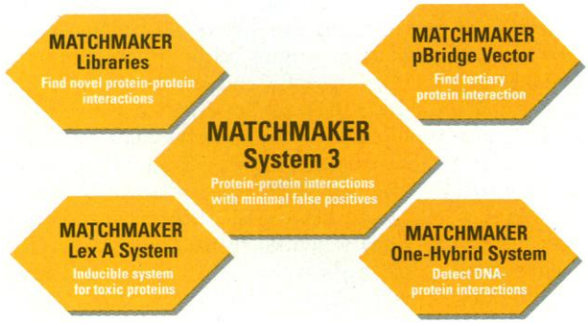


Illustration inspired by the art of Al Held.



Use our high-quality yeast media and convenient nutritional dropout supplements!

Try YEASTMAKER™ Kits for high efficiency yeast transformation and reliable plasmid isolation.

Also available: GAL4 and LexA Monoclonal Antibodies

Germany & East Europe: CLONTECH GmbH • Tel: 06221 34170 Fax: 06221 303511
United Kingdom: CLONTECH UK Ltd. • Tel: 01256 476500 Fax: 01256 476499
Japan: CLONTECH Japan Ltd. • Tel: 03 3523 9777 Fax: 03 3523 9781
Switzerland: CLONTECH AG • Tel: 061 68354 50 Fax: 061 68354 52
Austria: CLONTECH GmbH • Tel: 01 310 6688 Fax: 01 310 7744

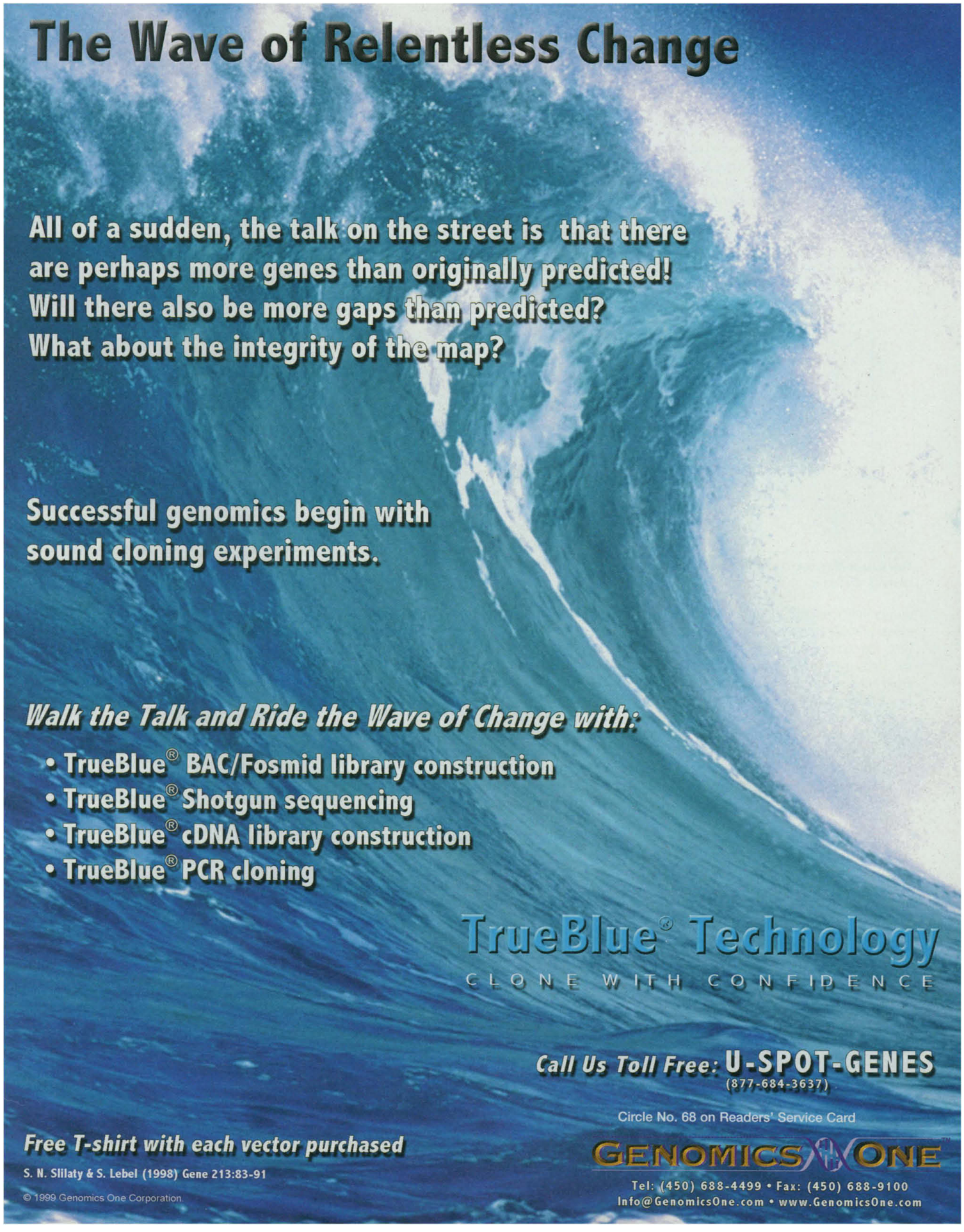
Distributors: Australia: 61 7 3273 9100 ■ **Belgium/Luxembourg:** 0 800 1 9815 ■ **Brazil:** 55 11 66940539 ■ **Canada:** Now call CLONTECH direct • 800 662 2566 ■ **Chile:** 56 2 209 6770 ■ **China:** BEIJING YUANGPING BIOTECH • 86 10 68187551; GENE CO. LTD. • 021 6428 7163; GENETIMES TECHNOLOGY • 86 21 6402 2371 ■ **Czech Republic:** 420 19 7265214 ■ **Egypt:** 202 349 8311 ■ **Finland:** 358 9708 596 19 ■ **France:** 33134 602424 ■ **Greece:** 301 51 53882 ■ **Hong Kong:** 852 2646 6101 ■ **Hungary:** 36 1 280 3728 ■ **India:** 91 11 54 21714 ■ **Israel:** 972 4 9960595 ■ **Italy:** 39 55 5 001871 ■ **Korea:** 82 2 556 0311 ■ **Malaysia:** 603 787 72611 ■ **Mexico:** 525 281 4718 ■ **The Netherlands:** 31 33 495 00 94 ■ **Norway:** 47 22 421 520 ■ **Poland:** 49 6221 34170 ■ **Portugal:** 351 361 36 20 ■ **Scandinavia:** 46 8 728 00 65 ■ **Singapore:** 65 775 7284 ■ **South Africa:** 27 21 671 5166 ■ **Spain:** 34 9 1 630 0379 ■ **Taiwan:** 886 2 27202215 ■ **Thailand:** 662 530 3804 4 ■ **Turkey:** 90 216 385 8321 rev.8/16/99

MATCHMAKER System 3 (#K1612-1) breaks through the barrier of false positives that has encumbered two-hybrid analysis. System 3 eliminates false positives, increases sensitivity, and facilitates independent confirmation of protein interactions. Three reporters with distinct control regions yield strong and specific responses to activation. Inserts can be expressed *in vitro* immediately from a T7 promoter and are tagged with c-Myc or hemagglutinin (HA) for easy analysis. Streamline your analysis even further by using **MATCHMAKER Pretransformed Libraries.** Call and order today!

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
 (AD91807)

Circle No. 64 on Readers' Service Card


The Wave of Relentless Change
All of a sudden, the talk on the street is that there are perhaps more genes than originally predicted! Will there also be more gaps than predicted? What about the integrity of the map?
Successful genomics begin with sound cloning experiments.
Walk the Talk and Ride the Wave of Change with:
• TrueBlue® BAC/Fosmid library construction
• TrueBlue® Shotgun sequencing
• TrueBlue® cDNA library construction
• TrueBlue® PCR cloning
TrueBlue® Technology
CLONE WITH CONFIDENCE
Call Us Toll Free: U-SPOT-GENES
(877-684-3637)
Circle No. 68 on Readers' Service Card
Free T-shirt with each vector purchased
S. N. Slilaty & S. Lebel (1998) Gene 213:83-91
© 1999 Genomics One Corporation
GENOMICS ONE
Tel: (450) 688-4499 • Fax: (450) 688-9100
Info@GenomicsOne.com • www.GenomicsOne.com

BD BIOSCIENCES
LIFE SCIENCE RESEARCH

Antibodies for Cell Adhesion Research

Specific for transmembrane and signaling proteins

BD Biosciences provides a comprehensive portfolio of reagents and systems for the study of signal transduction. Included in the reagent program are antibodies and molecular probes specific for cell adhesion molecules, extracellular matrix proteins, and cytoplasmic peripheral membrane proteins.

- High Quality BD Transduction Laboratories Monoclonal Antibodies for Cell Adhesion Research
- Applications in Western Blotting, Immunoprecipitation, Immunofluorescence, and Immunohistochemistry

Specificities Include:

Cell Adhesion Molecules
- Cadherins
- Integrins
- Catenins

Extracellular Matrix Proteins
- Fibronectin
- Laminin B2
- Kalinin B1

Cytoplasmic Peripheral Membrane Proteins
- Paxillin
- FAK
- P130^{Cas}

Related Materials and Products:

- Now Available — Cell Adhesion Mailer with Information About the Entire BD Transduction Laboratories Cell Adhesion Product Line
- Sampler Kits — 10µg Quantities of Cell Adhesion Antibodies Grouped into Areas of Zonula Adherens, Focal Adhesion, and Integrins
- BD RiboQuant™ — A Novel Molecular Application for Monitoring Genes Associated with Cell Adhesion

BD Biosciences
www.bdbiosciences.com

For more information regarding BD Transduction Laboratories™ products, please call **1-800-227-4063**, or fax to **1-606-259-1413.** For more information regarding BD RiboQuant™, please call **1-800-848-6227.**

BD
Indispensable to human health

For research use only. Not for use in diagnostic or therapeutic procedures.

Circle No. 43 on Readers' Service Card

unleash the power

Incyte Contract Sequencing

What if you had the power to discover 10 thousand genes in 2 months?

What if you had the power to generate 25 million high quality bases in 2 weeks?

What if you had the power to achieve 8x coverage of a microbial genome in 2 days?

Incyte has one of the world's largest high-throughput sequencing facilities.

You *do* have the power: Incyte Contract Sequencing.

At Incyte we have successfully transformed the science of sequencing and bioinformatics into an efficient and streamlined manufacturing process that consistently generates high volume, high quality sequencing results. Now, this state of the art infrastructure that is used to satisfy the discovery needs of the world's leading pharmaceutical and biotechnology companies is available to you.

[*How will you use the power of Incyte Contract Sequencing?*]

877.746.2983 (U.S.) | **650.621.8588** (International) | **www.incyte.com/sequencing**

INCYTE Pharmaceuticals, Inc.

Circle No. 32 on Readers' Service Card

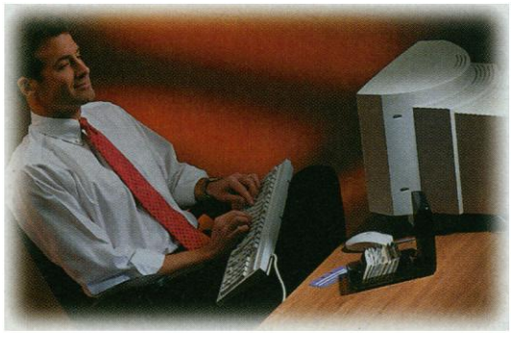
TRY OUR eCOMMERCE SOLUTION @ **www.sigma-aldrich.com**

EASY ON-LINE ORDERING

The Sigma-Aldrich PipeLine™ eCommerce system offers simple, on-line access to over 200,000 products from the Sigma-Aldrich brands: Sigma, Aldrich, Fluka, Supelco and Riedel-de Haën. Now you can place multi-brand orders for biochemicals, chemicals, equipment and laboratory supplies from all of our brands in a single transaction.

FIND WHAT YOU NEED FAST

With eight different ways to search, including product name, product number, CAS number, molecular formula and structure, pinpointing products is a snap.



Stop the chase and log on today.
It will make your job easier.
www.sigma-aldrich.com

A TOTAL INFORMATION RESOURCE

Because we are a manufacturer, we offer not only quality products but the technical knowledge and support to back them up.

- Over 90,000 on-line MSDS's
- Over 2 million on-line Certificates of Analysis
- Thousands of data sheets and technical bulletins

SIGMA-ALDRICH

3050 Spruce Street, St. Louis, MO 63103 • 800-521-8956 or 314-771-5765

Circle No. 36 on Readers' Service Card

The future of life science is in your hands.

Agilent Technologies introduces the first generation of the "Lab-on-a-Chip." Developed in collaboration with Caliper Technologies, the revolutionary Agilent 2100 bioanalyzer system automates nucleic acid analysis. Now sample handling, separation and detection all take place within a microchip.

The system offers rapid analysis, reduced sample consumption, and enhanced reproducibility for life scientists working with PCR products, restriction enzyme digests, RNA preps, and other types of nucleic acid samples. With standardized assay protocols, digital results, and powerful data analysis tools, the Agilent 2100 bioanalyzer promises to improve your lab's productivity.

To grasp the benefits of an integrated Lab-on-a-Chip system, contact Agilent today. Let LabChip™ technology add a whole new dimension to your work.

www.agilent.com/chem/labonachip

1-800-227-9770, Ext. 3391

Agilent Technologies
Innovating the HP Way

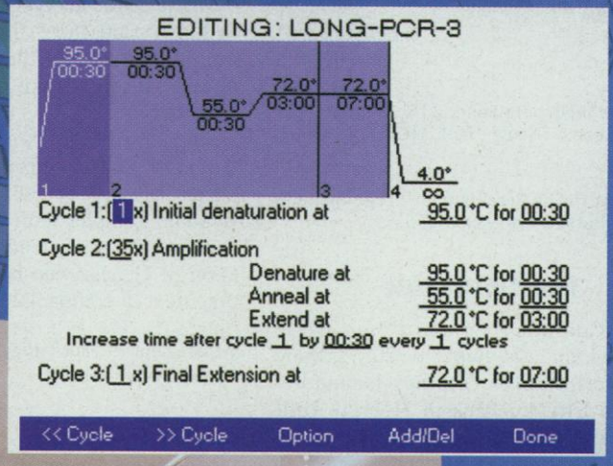
caliper LabChip®

Circle No. 44 on Readers' Service Card

amplify your PCR* expectations

The iCycler™ Thermal Cycler Excels at Performance, Reliability and Ease-of-Use.

The iCycler features the most intuitive interface, including comprehensive informational screens, validation reports and a graphical textual display of a protocol on one screen.



- Effortless interface
- Directly upgradeable for Real Time PCR
- Rapid and reliable cycling
- Interchangeable sample blocks
- Out of the box and running in just minutes

Practice of the patented polymerase chain reaction (PCR) process requires a license. The iCycler includes a licensed thermal cycler and may be used with PCR licenses available from the Perkin-Elmer Corp. Its use with authorized reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents. Some applications may require licenses from other parties.

What Will You Discover Next?

Visit our Life Science web site at discover.bio-rad.com.
Call toll free at 1-800-4BIORAD (1-800-424-6723); outside the U.S., call (510) 741-6996.

BIO-RAD

Circle No. 61 on Readers' Service Card

AVIV
INSTRUMENTS, INC.

750 Vassar Avenue, Lakewood, NJ 08701-6907 U.S.A.
TOLL FREE: 1-888-242-2848
Phone (732) 367-1663 • Fax (732) 370-0032
E-mail: sales@avivinst.com • http://www.avivinst.com

Model 202 Series

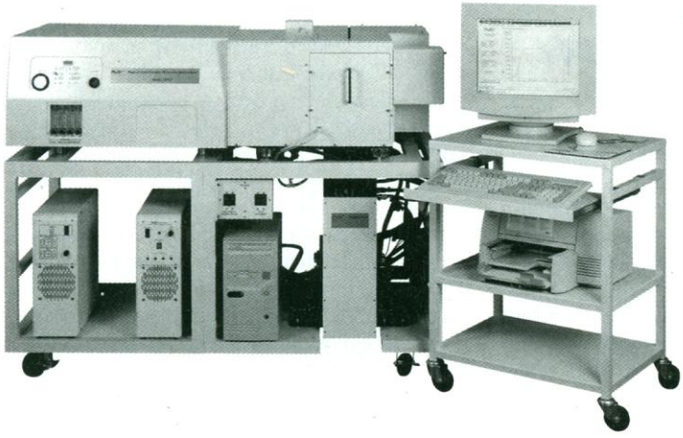
Aviv Model 202 Series instruments record circular dichroism as a function of wavelength, time, temperature and concentration using a double monochromator and containing two UV grade prisms as dispersing elements.

Experiment Modes:

- Wavelength
- Kinetics
- Stopped flow kinetics
- Temperature
- pH
- Titration

Also measures:

- Total Fluorescence
- Fluorescence detected CD
- Absorbance



Model SF 305

An all new Aviv Stopped Flow system used in conjunction with many existing Aviv Circular Dichroism Spectrometers and Spectrofluorometers.

Visit our NEW website for complete details on our entire line of AVIV Instruments

Model ATFF 212

The Aviv Model ATFF 212 is a high stability filter fluorometer for temperature melts, automated chemical denaturation, ligand titration experiments and pH titrations.

Applications:

Determination of thermodynamic parameters and stability measurements.

World Wide Sales

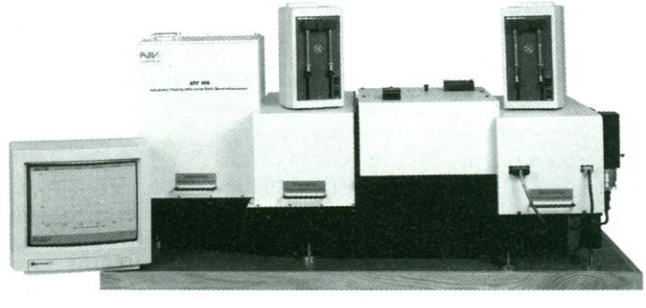
NEW MACRO PROGRAMMING LANGUAGE

Model ATF 105

Experiment Modes:

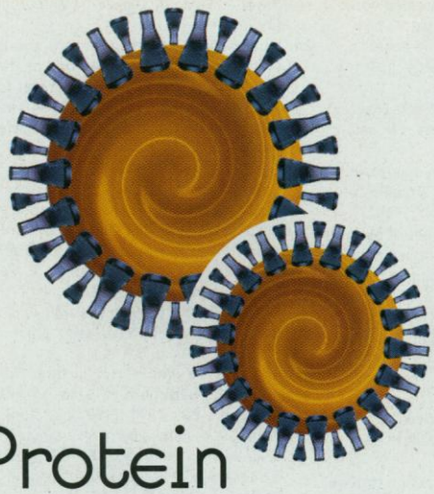
- Excitation Scans
- Emission Scans
- Synchronized Excitation and Emission Scans
- Corrected Excitation Scans
- Corrected Emission Scans
- Temperature Melts with data collected at a single wavelength or as wavelength scans
- Ligand Titrations (absolute or differential measurements)
- Solute Denaturation Titrations (differential measurements option available)
- Steady State Anisotropy Measurements (optional)

Macro Programming for customized experimental modes allows linking and combination of experimental modes. You can perform a titration, scan the spectrum and measure Anisotropy, or any combination, all under temperature control.



Circle No. 21 on Readers' Service Card

ADVERTISER DIRECTORY



Protein + Protein Interactions

The following organizations have placed advertisements in the **Protein-Protein Interactions** Advertising Supplement.

Turn to Page 1759

Science
www.scienceonline.org

NEW PRODUCTS

PROTEIN IMMUNOBLOTS IN 15 MIN

The CodaXcel instrument makes use of flow-through technology to deliver accurate protein immunoblot results for up to eight samples in only 15 min. A specially designed cassette eliminates the need to handle individual strips. The instrument is used with a growing line of CodaXcel test kits; both the instrument and the test kits are for research use only.

Immunetics
For more information call 800-227-4765 or **circle 147** on the Reader Service Card

SIGNAL TRANSDUCTION REAGENT

U0126 is a reagent that can serve as a tool for studying protein kinase–mediated signal transduction. By selectively inhibiting MEK1 and MEK2, U0126 functionally antagonizes AP1-mediated transcriptional activation. Due to its action as a MEK inhibitor, U0126 can also block the production of a variety of cytokines and metalloproteinases involved in the inflammatory response.

RBI
For more information call 800-736-3690 or **circle 148** on the Reader Service Card

AUTOMATIC TUBE LUMINOMETER

The Berthold *flash 'n glow* automatic tube luminometer is for reporter gene assays, ATP/NAD(P)H and enzyme measurements, luminescent immunoassays, and DNA probe assays. The unit features a unique loading mechanism for handling up to 30 samples in a chain. It can be equipped with one, two, or three injectors, each of which is volume-adjustable for greater flexibility in creating new assays. It has its own built-in microprocessor and printer but can work with a personal computer and Windows software for easy protocol setup, data collection and evaluation, and liquid-handling control. Spectral sensitivity is 370 to 620 nm.

EG&G Wallac
For more information call 800-638-6692 or **circle 149** on the Reader Service Card

LITERATURE

Mini-Catalog: Apoptosis Research is a 20-page catalog that features listings and detailed descriptions for more than 250 high-quality reagents and kits. Among the more than 80 new items listed are products for the Fas signaling pathway and caspase substrates and inhibitors. The products are organized by pathway or application, which provides a convenient format for locating them.

Alexis
For more information call 800-900-0065 or **circle 150** on the Reader Service Card

Newly offered instrumentation, apparatus, and laboratory materials of interest to researchers in all disciplines in academic, industrial, and government organizations are featured in this space. Emphasis is given to purpose, chief characteristics, and availability of products and materials. Endorsement by *Science* or AAAS of any products or materials mentioned is not implied. Additional information may be obtained from the manufacturers or suppliers named by circling the appropriate number on the Reader Service Card and placing it in a mailbox. U.S. postage is free.