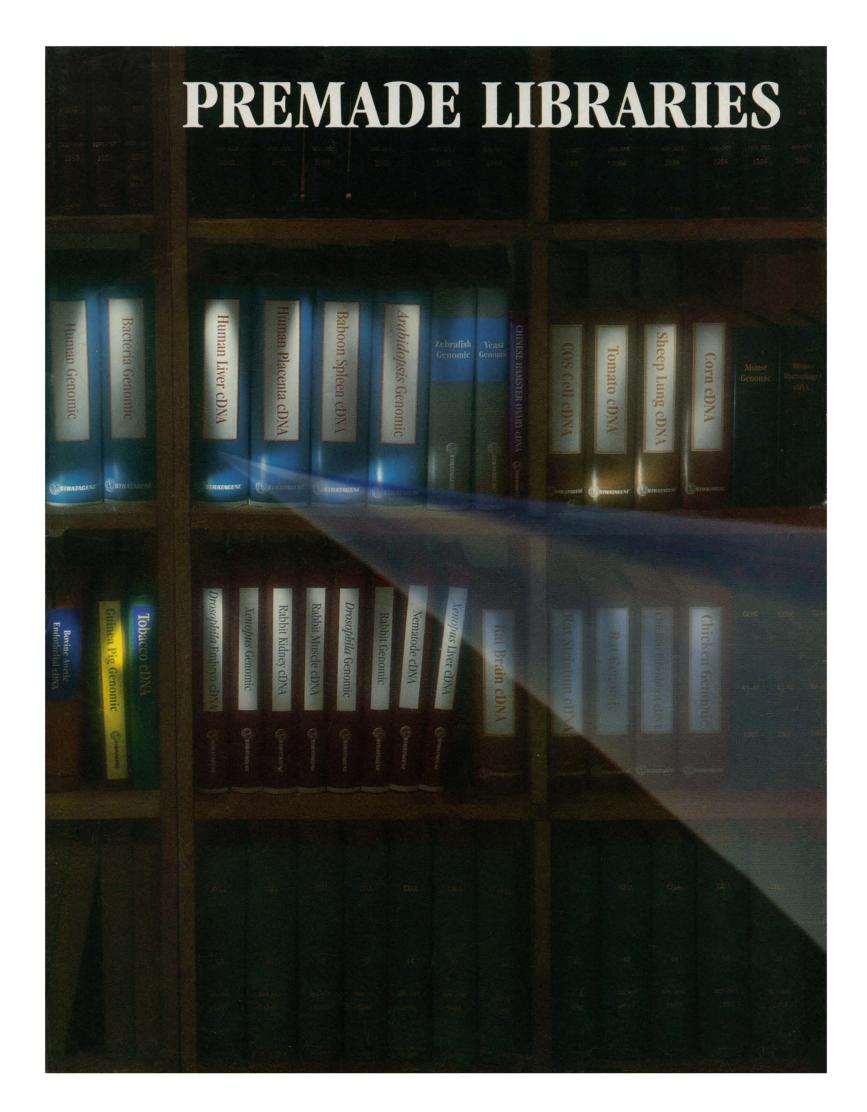
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

# SCIENCE

16 DECEMBER 1994 Vol. 266 • Pages 1777–1916 \$6.00



# TO MEET YOUR SPECIFIC RESEARCH NEEDS.

- Constantly Growing, Diverse Collection
- Actin Screened for Quality
- Packaged for Optimal Efficiency and Representation
- Custom Library Service Also Available

Stratagene Constructs the Highest Quality Libraries Available

# <image>

#### **Novel Vectors**

Stratagene's libraries are constructed using novel vectors that simplify screening and analysis. For cDNA libraries, our exclusive Lambda ZAP<sup>®</sup> Vectors\* combine the high efficiency of lambda cloning with the ease of a plasmid system. Clones isolated from Lambda ZAP<sup>®</sup> Vectors can be easily excised into the pBluescript<sup>®</sup> Vector, eliminating time-consuming subcloning. For genomic libraries, our Lambda DASH<sup>®</sup> II, Lambda FIX<sup>®</sup> II and Cosmid Vectors contain T3 and T7 promoters flanking the inserts, allowing rapid genomic walking and restriction mapping. To simplify gene manipulation and mapping, the insert can be removed as a cassette by using *Not* I to digest these vectors.

#### **Host Strains**

Our libraries are provided with powerful host strains like XL1-Blue and SRB(P2). Our new SOLR<sup>™</sup> strain facilitates single-clone and mass library excisions. Stratagene is constantly developing new strains to clone the previously unclonable.

#### **Actin Screened**

All cDNA libraries are actin screened for quality. Since actin is a common sequence with considerable homology between species and tissues, screening with an actin cDNA probe provides valuable information about the probability of finding your clone.

#### **Amplified Only Once**

Stratagene's libraries are amplified only once, avoiding the problem of skewed representation caused by overamplification. Single amplification prevents fast-growing clones from "taking over" and making rare clones harder, if not impossible, to find. Our newest libraries are amplified in the SURE<sup>™</sup> strain to minimize rearrangements and deletions.

#### **Custom Library Service**

Stratagene's growing collection of libraries is updated continually. We also offer a Custom Library Service and high quality reagents for constructing your own libraries.



#### **Gigapack® Packaging Extract**

All of Stratagene's libraries are made with Gigapack<sup>®</sup> Packaging Extracts, which allow high packaging efficiency and construction of representative libraries. Especially critical for genomic libraries, the absence of restriction activity in Gigapack<sup>®</sup> II Packaging Extracts prevents the degradation of methylated sequences.

Please call Stratagene or a Stratagene distributor to discuss your library needs.



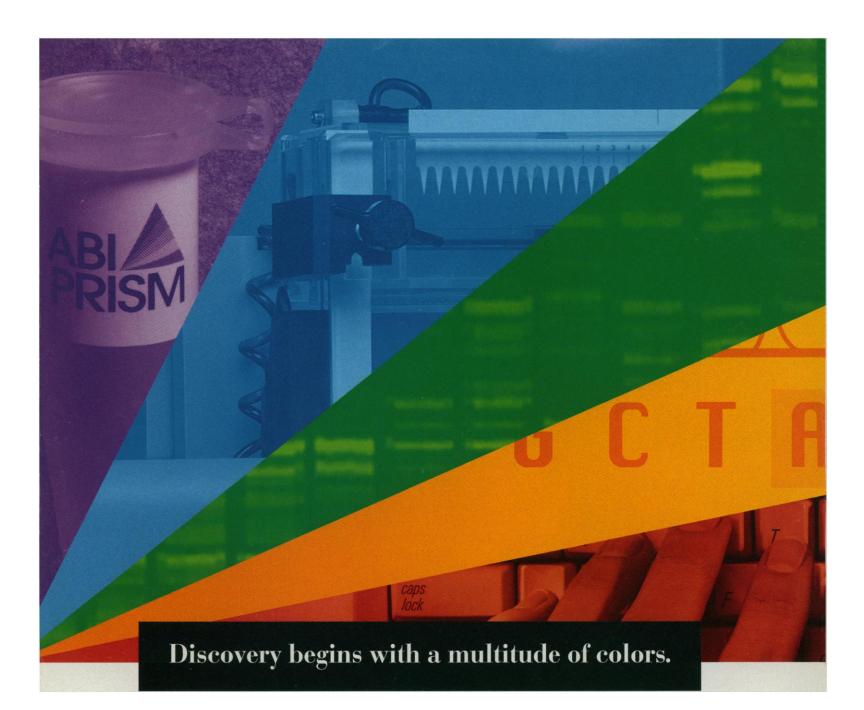
Telephone: 800-424-5444 Fax: 619-535-0034

Germany: Stratagene GmbH Telephone: (06221) 40 06 34 Telefax: (06221) 40 06 39

United Kingdom: Stratagene Ltd. Telephone: (0223) 42 09 55 Telefax: (0223) 42 02 34

France: Stratagene France Telephone: (0590) 72 36 Telefax: (1) 44 28 19 00

Switzerland: Stratagene GmbH Telephone: 01-3641106 Telefax: 01-3657707



Only ABI PRISM<sup>\*\*</sup> genetic analysis products bring you the power of multicolor analy-

sis. Because with our line of ABI PRISM instruments, reagents, and software, multicolor labeling is part of your DNA analysis from start to finish. So you harness the power of automation to generate more data and turn it into meaningful results.

All other DNA analysis methods determine only position (and perhaps



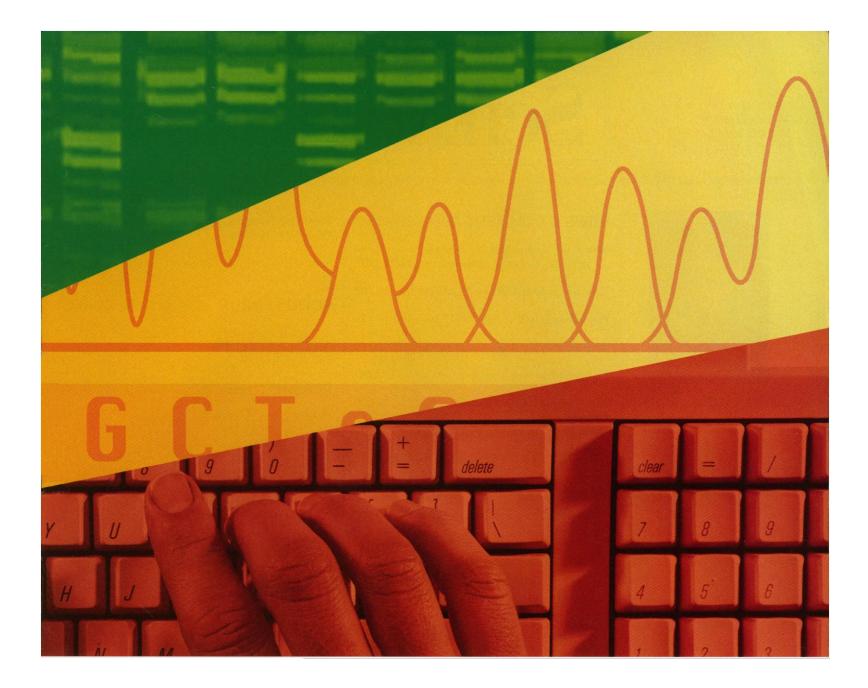
intensity) of a gel band. But multicolor fluorescent labeling allows you to track the *color* of bands as well. This additional information

enables ABI PRISM systems to separate a complex molecular mixture *run in a single gel lane*—into a spectrum of molecular species.

With multicolor labeling, all four DNA sequencing reactions can run in one lane. Likewise, controls and PCR products run in the same lane. So there's no interference from electrophoresis variables. The inherent accuracy of multicolor analysis provides the basis for reliable automation, allowing our ABI PRISM software to turn data into definitive answers. Your results are so reproducible you can reliably compare them from lane to lane and gel to gel.



The power of multicolor analysis—only with ABI PRISM Systems.



The ABI PRISM integrated approach to genetic analysis streamlines the entire process for you. Sample preparation is flexible and fast with our comprehensive range of ABI PRISM kits for DNA sequencing and fragment analysis. The kits are convenient at the bench, or on our automated ABI PRISM 800 lab station. Electrophoresis and detection take place on the proven ABI PRISM 373 DNA Sequencer—the heart of the system. And ABI PRISM software collects and analyzes your data. Our complete systems are so easy to use, you do less work to get data that's better. You'll complete research projects much faster, too.

Every ABI PRISM product is backed by our commitment to helping you advance your research. And as part of Perkin-Elmer, the Applied Biosystems Division offers the most comprehensive range of products, services and support for DNA analysis.

ABI PRISM genetic analysis systems are unmatched in throughput, accuracy, and convenience. Begin your next discoveries with the power of multicolor analysis. Only with ABI PRISM systems. Call your local Perkin-Elmer representative today.

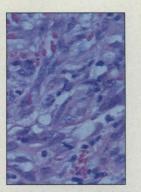
#### PERKIN ELMER

U.S. Foster City, U.S. Tel: 800-345-5224 Fax: 415-572-2743 Europe Langen Germany Tel: 49-6103-708-0 Fax: 49-6103-708-210 Canada Mississauga, Canada Tel: 905-821-8183 Fax: 905-821-8246 Japan Tokyo, Japan Tel: 81-473-80-8500 Fax: 81-473-80-8505 Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223 Australia Melbourne, Australia Tel: 61-3-212-8585 Fax: 61-3-212-8502

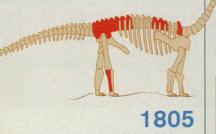
ABI PRISM is a trademark and Perkin-Elmer is a registered trademark of The Perkin-Elmer Corporation. ISSN 0036-8075 16 DECEMBER 1994 VOLUME 266 NUMBER 5192



AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



1803 & 1865 Herpes link to Kaposi's?



It could be a contender

NEWS & COMMENT	
New GOP Chairs Size Up Science Two Senators Target Defense Research	1796 1797
Italy Keeps EMBL Anxiously Waiting	1798
Piot Named Head of New UN Unit	1798
Thrashing Out a Compromise on the LHC	
To Mars, But Not Together The Company That Genome	1799
Researchers Love to Hate Terms for a Dip Into TIGR's Database	
RESEARCH NEWS	
Is a New Virus the Cause of KS?	1803

Can Sound Drive Fusion in a Bubble? 1804 Argentine Dinos Vie for 1805 Heavyweight Titles

The Space Telescope Spies on Ancient 1806 **Galaxy Menageries** 

THIS WEEK IN SCIENCE
EDITORIAL Scientific Evidence in Court
<b>LETTERS</b> Funding of Newly Submitted NIH Grant A cations: H. G. Mandel • EMBL and Eur Cooperation in the Life Sciences: F. C. Kaf Expressed Sequence Tags: M. M. Cohen,

op ato B. Emanuel et al. • Crystalline Polymorph Constr tion: Correction: L. Leiserowitz • Malaria Vacc Research: W. R. Ballou, C. L. Diggs, S. Land B. F. Hall • Correction: D. Stokoe

Capturing Sound, Light, and Strength With New Materials	1807
Even a Robot Cricket Always Gets Her Mate	1809
POLICY FORUM	
A Need to Reinvent Biotechnology Regulation at the EPA H. I. Miller	1815
PERSPECTIVE	
Upsetting the Balance of Forces in DNA D. M. Crothers	1819
ARTICLE	ISO ISO

Cell Cycle Control and Cancer 1821 L. H. Hartwell and M. B. Kastan

#### RESEARCH ARTICLE

DNA Bending by Asymmetric **1829 Phosphate Neutralization** J. K. Strauss and L. J. Maher III

#### DEPARTMENTS

17

17

17 Ap

785	SCIENCESCOPE 1795	
787	RANDOM SAMPLES 1810 Questions About French Cancer Fund • Vertebrate Vibrations • Imaging Alabaimar's • Imagina Kari	
789 pli-	Vibrations • Imaging Alzheimer's • Imanishi-Kari to Leave Tufts • Scholars Defend Bell Curve • Crème de la Crème (cont'd), etc.	
os• . S. ruc-	BOOK REVIEWS       1888         QED and the Men Who Made It, reviewed by D. S       Saxon • Antoine Lavoisier, R. L. Kremer • Other         Books of Interest • Vignettes • Books Received	
dry,	PRODUCTS & MATERIALS 1893	

#### Board of Reviewing Editors

Frederick W. Alt Don L. Anderson Michael Ashburner Stephen J. Benkovic David E. Bloom Floyd E. Bloom Piet Borst Henry R. Bourne Michael S. Brown James J. Bull

Kathryn Calame C. Thomas Caskey Dennis W. Choi John M. Coffin F. Fleming Crim Paul J. Crutzen James E. Dahlberg Robert Desimone Bruce F. Eldridge Paul T. Englund

Richard G. Fairbanks Douglas T. Fearon Harry A. Fozzard Klaus Friedrich Theodore H. Geballe John C. Gerhart Roger I. M. Glass Stephen P. Goff Peter N. Goodfellow Corey S. Goodman

Ira Herskowitz Eric F. Johnson Stephen M. Kosslyn Michael LaBarbera Nicole Le Douarin Charles S. Levings III Alexander Levitzki Harvey F. Lodish Richard Losick Reinhard Lührmann

Diane Mathis Anthony R. Means Shigetada Nakanishi Roger A. Nicoll Stuart L. Pimm Yeshayau Pocker Dennis A. Powers Ralph S. Quatrano V. Ramanathan Douglas C. Rees

T. M. Rice David C. Rubie Erkki Ruoslahti Gottfried Schatz Jozef Schell Ronald H. Schwartz Terrence J. Sejnowski Ellen Solomon Thomas A. Steitz Michael P. Stryker

Robert T. N. Tjian Emil R. Unanue Geerat J. Vermeij Bert Vogelstein Harold Weintraub Arthur Weiss Zena Werb George M. Whitesides Owen N. Witte William A. Wulf

#### COVER

1835

1848

1851

1858

Mosaic of three image sets from the Clementine spacecraft ultraviolet-visible camera of the lunar impact crater Tycho (85-kilometer diameter). A color composite is shown in mirror format on the left. The colors emphasize variations in surface units, where blues and greens indicate relatively recently exposed material, and green

CLEMENTINE

S. Nozette, P. Rustan, L. P. Pleasance, D. M.

Horan, P. Regeon, E. M. Shoemaker, P. D. Spudis, C. H. Acton, D. N. Baker, J. E. Blamont, B. J.

Buratti, M. P. Corson, M. E. Davies, T. C.

Duxbury, E. M. Eliason, B. M. Jakosky, J. F. Kordas, I. T. Lewis, C. L. Lichtenberg, P. G.

Lucey, E. Malaret, M. A. Massie, J. H. Resnick,

C. J. Rollins, H. S. Park, A. S. McEwen, R. E

Priest, C. M. Pieters, R. A. Reisse, M. S.

Robinson, R. A. Simpson, D. E. Smith, T. C.

Sorenson, R. W. Vorder Breugge, M. T. Zuber

The Shape and Internal Structure of the 1839

M. T. Zuber, D. E. Smith, F. G. Lemoine, G. A.

A Sharper View of Impact Craters from 1844

C. M. Pieters, M. I. Staid, E. M. Fischer, S.

E. M. Shoemaker, M. S. Robinson, E. M. Eliason

Topographic-Compositional Units on the 1855

P. G. Lucey, P. D. Spudis, M. Zuber, D. Smith,

A. S. McEwen, M. S. Robinson, E. M. Eliason, P. G. Lucey, T. C. Duxbury, P. D. Spudis

Moon from the Clementine Mission

Ancient Multiring Basins on the Moon

P. D. Spudis, R. A. Reisse, J. J. Gillis

The South Pole Region of the Moon as

Moon and the Early Evolution of the

Clementine Observations of the

Aristarchus Region of the Moon

Revealed by Clementine Laser Altimetry

The Clementine Mission to the Moon:

REPORTS

Scientific Overview

Neumann

**Clementine** Data

Tompkins, G. He

Seen by Clementine

Lunar Crust

E. Malaret

indicates a higher abundance of iron-bearing minerals.

The red area surrounding Tycho is a ring of lower

albedo impact melt. See page 1844 and related Re-

ports on Clementine data beginning on page 1835.

[Color composite image: produced at Brown University]

An Alternative to SH2 Domains for 1862 **Binding Tyrosine-Phosphorylated Proteins** W. M. Kavanaugh and L. T. Williams

Identification of Herpesvirus-Like **Z** 1865 **DNA** Sequences in AIDS-Associated Kaposi's Sarcoma

Y. Chang, E. Cesarman, M. S. Pessin, F. Lee, J. Culpepper, D. M. Knowles, P. S. Moore

#### Toxic Shock Syndrome Toxin-1 1870 Complexed with a Class II Major

Histocompatibility Molecule HLA-DR1 . Kim, R. G. Urban, J. L. Strominger, D. C. Wilev

#### Subsets of HLA-DR1 Molecules 1874 Defined by SEB and TSST-1 Binding Thibodeau, I. Cloutier, P. M. Lavoie, N.

Labrecque, W. Mourad, T. Jardetzky, R.-P. Sékaly

Specification of C/EBP Function During 1878 Drosophi Development by the bZIP **Basic Region** P. Rørth

Potentiated Transmission and 1881 Prevention of Further LTP by Increased CaMKII Activity in Postsynaptic **Hippocampal Slice Neurons** D. L. Pettit, S. Perlman, R. Malinow

#### **TECHNICAL COMMENTS**

Seasonal Precipitation Timing and	1885	
Ice Core Records		
E. J. Steig, P. M. Grootes, M. Stuiver		

Indicates accompanying feature

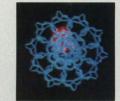
1886

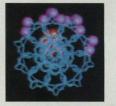
Successful Biological Control B. A. Hawkins and H. V. Cornell

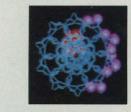
Maximum Parasitism Rates and

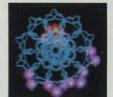


SCIENCE









#### 1819 & 1829 **DNA** bending

AAAS Board of Directors Eloise E. Clark Retiring President, Chairman Francisco J. Avala

President Rita R. Colwell President-elect

William A. Lester Jr. Simon A. Levin Anna C. Roosevelt

Alan Schriesheim Jean'ne M. Shreeve Chang-Lin Tien Warren M. Washington Nancy S. Wexler

William T. Golden Treasurer Richard S. Nicholson Executive Officer

SCIENCE (ISSN 0036-8075) is published weekly on Friday, except In Science (ISN 003-6075) 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 © 1994 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): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$29 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues): \$20 (S50 allocated to unbencified). Demettic individual membership and subscription (51 issues). \$20 (S50 allocated to unbencified). to subscription). Domestic institutional subscription (51 issues): \$215. Foreign postage extra: Mexico, Caribbean (surface mail) \$50; other countries (air assist delivery) \$95. First class, airmail, student and emeritus rates on re-quest. Canadian rates with GST available upon request, GST #1254 88122. Printed in the U.S.A.

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 43305-2033. Single copy sales: \$6.00 per issue prepaid includes surface postage; Guide to Biotechnology Products and Instruments, \$200. 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 Planamon Conter (CCO) Transactional Benefiting Senter provides and the senter of the Copyright Planamon Conter (CCO) Transactional Benefiting Senter provides and the senter of t 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, MA 01970. The identification code for *Science* is 0036-8075/83 \$1 + .10. *Science* is indexed in the *Reader's Guide to Peri*odical Literature and in several specialized indexes

# A SOLID REPUTATION FOR LIQUID HANDLING.

0.

23456780

10

Pipettes and dispensers for volumes from 0.5 μL to 100 mL.

Adjust

Peptitive, and electronic models.Bottletop dispensers that are

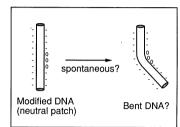
certified pyrogen-free, RNase-free, DNA-free, ATP-free and sterile.

#### THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

#### Bending DNA

Protein binding can bend a DNA double helix. In some cases, it is thought that cationic peptide side chains on the protein neutralize the negative charge on phosphate groups on one backbone; this charge im-



balance leads to a force that bends the helix. Strauss and Maher (p. 1829; see the Perspective by Crothers, p. 1819) tested this idea by synthesizing DNA double helixes that contained short segments of neutral methylphosphonates instead of phosphates in one of the backbone strands. They show that such DNA strands are bent in toward the chargeneutralized surface.

#### -

#### Put differently

Activation of growth factor receptors or other tyrosine kinases leads to formation of complexes of signaling proteins. The tyrosine phosphorylated substrates, which include the receptors themselves, can be bound by other proteins that contain SH2 domains-100-residue regions that recognize phosphotyrosine in the context of specific adjacent residues. Kavanaugh and Williams (p. 1862) show that SHC-a protein that has an SH2 domain and appears to participate in activation of Ras-has another domain that recognizes phosphotyrosine. This phosphotyrosine-binding (PTB) domain allows SHC to interact with a 145-kilodalton protein of un-

#### Clementine's view of the moon

Earlier this year Clementine, a lightweight spacecraft developed by NASA and the Defense Department, orbited the moon for more than 2 months, mapping and surveying the entire surface. Seven Reports in this issue recount the mission and the unprecedented detail of results that it achieved. Nozette et al. (p. 1835) describe the instrumentation Clementine carried, which included multiwavelength imaging capacity from the infrared to the ultraviolet, as well as a laser-ranging system. The latter vielded a topographic survey of the lunar surface, which in conjunction with gravity data derived from the spacecraft's trajectory produced the high-resolution map of the moon's shape and crustal structure discussed by Zuber et al. (p. 1839). Pieters et al. (p. 1844) used ultraviolet and visible light images to investigate the lithography of the impact craters Copernicus, Tycho, and Giordano Bruno. Impact melts and different components of excavated minerals are readily identified. By means of laser altimetry, Spudis et al. (p. 1848) identified several partly obliterated multiring basins due to impacts early in lunar history; some previously tentative identifications are now confirmed, and a number of newly identified basins are described. Shoemaker et al. (p. 1851) offer a wholly new view of the moon's south polar region, much of which is permanently in shadow because of encircling mountains and crater rims. Topographic and geological differences between the near and far sides of the moon are discussed by Lucey et al. (p. 1855). The heavily cratered far side, which does not have the large basaltic plains so prominent on the near side, has significantly different surface mineralogy and a different distribution of elevations. Finally, McEwen et al. (p. 1858) use Clementine's capabilities to study the already much-studied Aristarchus region, showing how detailed mineralogical and stratigraphic information can be used to reconstruct the history of a portion of the moon's surface.

known function in cells stimulated with growth factors. The PTB domain may provide another mechanism by which growth factors and oncogenes lead to interaction of specific proteins and thus to alterations in cellular function.

#### Superantigen binding

Peptide antigens bind to specific types of molecules of the major histocompatibility complex (MHC) in a surface groove, but superantigens, which are proteins produced by many bacteria and viruses, bind less specifically to many types of MHC molecules outside of this

groove. Thibodeau et al. (p. 1874) use mutant MHC class II molecules to show that although two superantigens, enterotoxin B from Staphylococcus aureus (SEB) and toxic shock syndrome toxin-1 (TSST-1), bind to the same region of different subsets of the human class II MHC molecule HLA-DR1, peptide binding into the groove of the MHC molecule affects superantigen binding. Kim et al. (p. 1870) determined the x-ray crystal structure of TSST-1 bound to HLA-DR1 and found that, unlike a previously determined structure for SEB bound to HLA-DR1, the TSST-1 binding site extends over half of the peptide binding site.

These results suggest that peptide antigens can play a role in the activation of T cells by superantigens.

#### Kaposi's sarcoma and herpesvirus

Because gay and bisexual men are much more likely to develop Kaposi's sarcoma (KS) tumors than other people with acquired immunodeficiency syndrome, it has been thought that a sexually transmitted infection agent may underlie its cause. Chang et al. (p. 1865) identified DNA sequences in KS tissues that are rare or absent in healthy tissue. These sequences are homologous to but distinct from other herpesviruses and may represent a new human herpesvirus. In a newsstory, Cohen (p. 1803) discusses whether such a virus could be an infectious agent that causes KS or is a virus that colonizes KS lesions.

#### **Back to basics**

In order to understand how a transcription factor functions in a specific context in vivo, it is necessary to define the domains of the protein that are required. Rørth (p. 1878) has substituted various domains in CCAAT/enhancer binding protein (C/EBP) of Drosophila with heterologous domains and tested if the chimeric proteins could substitute for wildtype C/EBP during development. The chimeras could rescue a C/EBP mutant if they contained the C/EBP-specific basic region, but could contain heterologous activation and leucine zipper dimerization domains. These experiments support the model that the basic region dictates C/EBP-specific activity in vivo.

# GET A WHOLE NEW VIEW OF "BIO" SPECTROPHOTOMETRY.

our life science research deserves a spectrophotometer without limitations. Beckman "bio" spectrophotometers give you more flexibility and operational simplicity than any other system in their class. They deliver final results the easiest way possible graphically. No other "bio" spectrophotometer can pass this screen test!

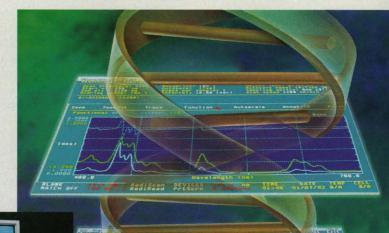
Simply select one of many pre-defined methods on the graphical "windowing" interface to perform a DNA or Protein analysis, such as:

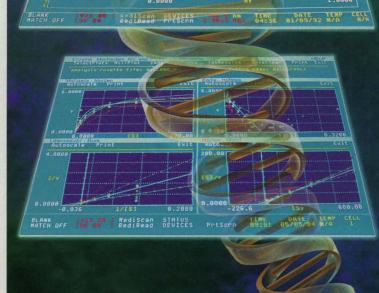
- Quantitative Total Protein Analysis
- Nucleic Acid/Protein Ratios
- DNA/Oligonucleotide Quantitation
- Theoretical T<sub>m</sub>
- Enzyme Mechanisms, K<sub>m</sub>, V<sub>max</sub>, K<sub>i</sub>
- Gel Scanning

Fully adaptable, fully programmable, and loaded with applications power, Beckman "bio" spectrophotometers are easily tailored to your needs. So look no further than Beckman—the leader in life science bioresearch instrumentation—for answers to your specific applications needs.

Easy final results for bioresearch — another part of the Beckman Plus, that extra level of personalized service and support available only from Beckman. For free information about the DU<sup>®</sup> Series 600 or DU Series 7000, contact your local Beckman office.



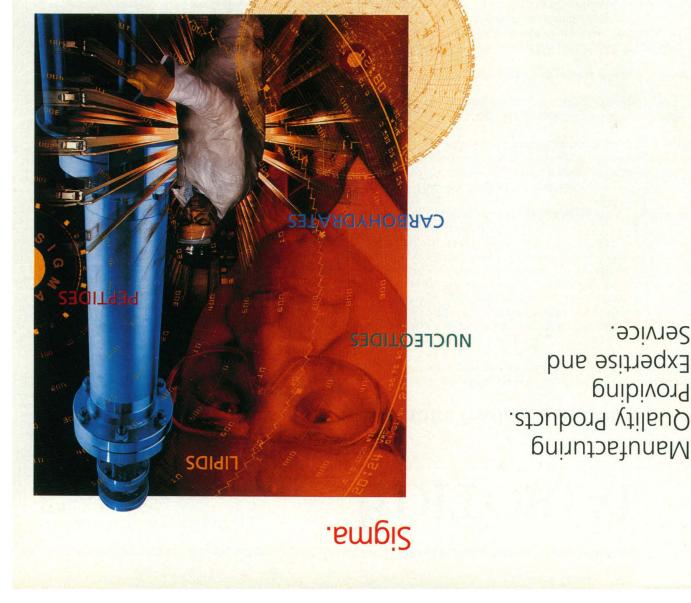




# BECKMAN

Worldwide Offices: Africa, Middle East, Eastern Europe (Switzerland) (22) 994 07 07. Australia (61) 02 816-5288. Austral (2243) 85656-0. Canada (800) 387-6799. China (861) 5051241-2. France (33) 1 43 01 70 00. Germany (49) 89-38871. Hong Kong (852) 814 7431. Italy (39) 2-953921. Japan 3-3221-5831. Mexico 525 575 5200, 525 575 3511. Netherlands 02979-85651. Poland 408822, 408833. Singapore (65) 339 3633. South Africa (27) 11-805-2014/5. Spain (1) 358-0051. Sweden (8) 98-5320. Switzerland (22) 994 07 07. Taiwan (886) 02 378-3456. U.K. (0494) 441181. U.S.A. 1-800-742-2345.

©1994 Beckman Instruments, Inc.



For nearly half a century, Sigma Chemical Company has been committed to manufacturing quality biochemicals and organic compounds for researchers around the world. Diversity within our multiple manufacturing sites enables our chemists to produce many of the 33,000 research reagents found in the Sigma general catalog. This diversity allows Sigma to formulate custom blends, to produce specific purities and to fulfill milligram to large-scale production requests for our customers.

In order to support the tradition of quality that you have come to expect from Sigma, our chemists closely monitor every stage of manufacturing, and analytical chemists assay every product we



offer. We package experience, service and expertise into every product you receive. But commitment to our customers does not stop here. Sigma continues

to provide exceptional service that includes a large inventory of packaged stock, fast delivery and technical assistance.

Weigh all the advantages. Consider Sigma as your single source for research biochemicals.



Where Science and Service Come Together.

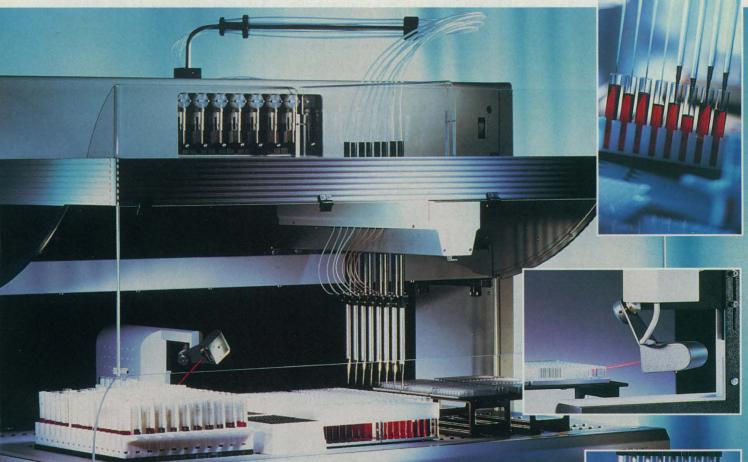
Call collect: 314-771-5750, 800-325-3010, or contact your local Sigma office.

ÌVEVN WEXICO NETHERLANDS SOUTH KOREA SPAIN SWITZERLAND UNITED KINGDOM UNITED STATES AUSTRALIA AUSTRIA BELGIUM BRAZIL CZECH REPUBLIC FRANCE GERMANY HUNGARY INDIA ITALY

Circle No. 9 on Readers' Service Card

A Sigma-Aldrich Company

# A new concept in Robotic Sample Processing



GENESIS Series

Robotic Sample Processors used to be either fast, or flexible - but not both.

That's all changed. The GENESIS Series combines total flexibility with extremely rapid throughput.

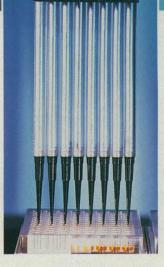
Now you have the freedom to choose tips, carriers and workspace configuration. This choice is extended by a wide range of options. All matched with true high speed processing.

For pharmaceutical and biotechnology work adjustable liquid level detection allows the smallest volumes to be used. For clinical applications, safe and secure processing is guaranteed by Positive Identification. Even the most complex research protocols are simply co-ordinated through Windows<sup>™</sup> - based software.

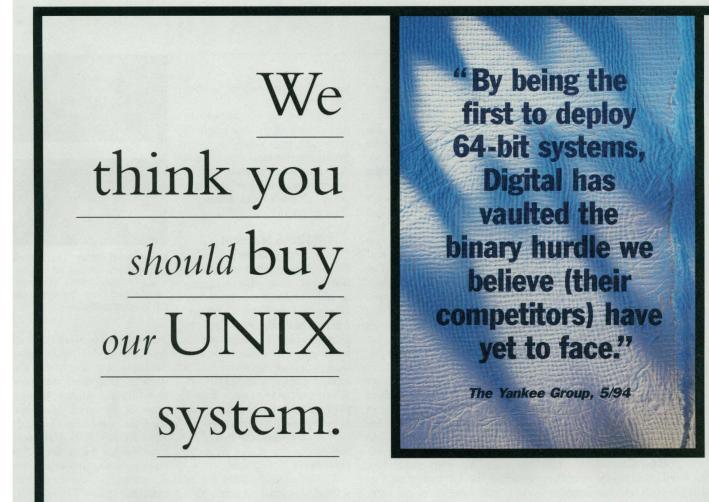
GENESIS Series - the platform for all your applications.

TECAN AG, Tel: 055 41 81 11, Fax: 055 42 38 83, Hotline: 055 41 82 82
 TECAN France SA, Tel: 1 30 64 90 70, Fax: 1 30 64 90 64
 TECAN Asia PTE. Ltd., Tel: 0567 0600, Fax: 0567 2122
 TECAN Ltd., Tel: 01491 875087, Fax: 01491 875087, Fax: 01491 875432
 TECAN Japan Co. Ltd., Tel: 04 2334 1790, Fax: 04 2334 0401
 SLT Labinstruments GmbH, Tel: 07951 5035, Fax: 07951 5038
 TECAN US Inc., Tel. 919 361 5200, Fax: 919 361 5201, Hotline: 800 338 1226

Worldwide sales and support are provided by an additional, extensive and specialist network of Representatives. To find out more information about your local TECAN Representative, contact TECAN AG. Windows is a trademark of Microsoft Corporation

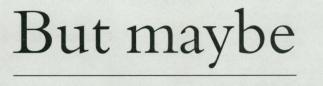


CITECAN.



"DEC OSF/1 represents a new generation of commercial UNIX...with good functionality, efficiency, modularity, and plenty of room for growth."

> D.H. Brown Associates, Inc., 6/94



you should get

a second opinion.

# And a third.

And a fourth.

No matter how many expert opinions you get, they'll all agree: Digital's DEC OSF/1® is the ideal UNIX® offering for a broad range of businesses. Here's what the experts are raving about:

- Best standards compliance
- Outstanding reliability
- · The highest-level availability
- Incomparable performance
- 64-bit Alpha technology

• Wide variety of applications And, most importantly, no costly future conversions, because you're already where everyone else will be going. "True to its heritage, Digital has managed to engineer its way to a full-featured, high-performance, commercial UNIX offering."

The Yankee Group, 5/94

So if you're looking for a UNIX system to grow with, put DEC OSF/1 on your short list.

Digital has

the best file

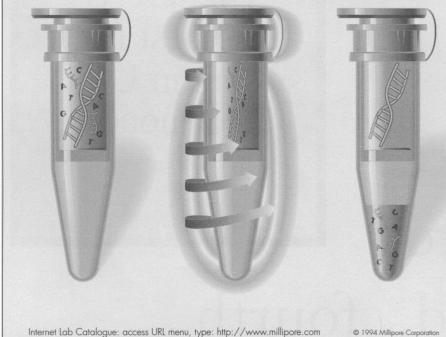
It's a decision everyone will applaud.

To receive copies of these independent evaluations, call 1-800-DIGITAL. For more information, contact your Digital Business Partner or Digital.



#### A New Spin On PCR Cleanup.

# Spin. Spin. Done.



Now you can separate primers and dNTPs from PCR-amplified fragments in just two, five-minute spins in your centrifuge. Simply use Millipore's Ultrafree®-MC (30K Nominal Molecular Weight Limit) centrifugal filters-and your sample is ready. There's no need to run additional purification procedures. No separation method is faster or easier-or gives you higher recovery of amplified product.

Want to give it a whirl? Give us a call and we'll send you a free Ultrafree-MC sample. US and Canada, 1-800-MILLIPORE ext. 8017. Japan, fax to (03) 3474-9141. Europe (fax to our Paris headquarters), +33.1.30.12.71.83.

ILLIPORE

Internet Lab Catalogue: access URL menu, type: http://www.millipore.com

Circle No. 34 on Readers' Service Card

Another first from SCIENCE The 1995				
<ul> <li>From the first experiments with electricity to the genetic revolution, scientists around the globe have looked to the pages of SCIENCE for leading-edge research and scientific news. Now SCIENCE announces another publishing event: The SCIENCE 1995 Calendar. This full-color calendar features:</li> <li>12 full-color mini-poster SCIENCE covers</li> <li>Oversized 9"x 12" format</li> <li>Large date blocks with major holidays</li> <li>An important moment in the history of science highlighted each month Whether you're planning scientific research or researching the perfect gift for your favorite scientist, you'll want to have your own copy of the 1995 SCIENCE Calendar!</li> </ul>				
It's Easy to Order! I want to show my support for SCIENCE. Please send me copies of the 1995 SCIENCE Calendar, for \$12.50 (AAAS Member price \$11.50). I have enclosed a check for the amount of the calendar (plus shipping charges for non-US orders). I understand my order is refundable if I am not completely satisfied.	Payment Information         US dollar check       VISA         Master Card         Important: All payments must be made in US dollars. \$25 minimum order for all credit card orders. Make check payable to AAAS Science Publications, Inc.			
Shipping Address (please print)	Credit card number Expiration date Signature			
Name	Send orders to: Attn: Corrine Harris, AAAS Science Publications, Inc. 1333 H St., NW, Washington, DC 20005			
City/State/Postal Code	(202) 326-6527 • FAX (202) 682-0816 Subtotal			
Please allow 4–6 weeks for delivery. Prices and shipping charges subject to change without notice. Calendars returned must be in salable condi-	DC Sales Tax			
tion. Wash., DC residents please add sales tax.	Outside the US:			
Science	Add \$3.50 per Calendar air delivery			
DUILINE	Total Enclosed			

### We can handle

## clinical trials of any size

# because we have the people

## who know how to get

# the people you need.

Every clinical trial calls for personal attention. No matter how many people, and places, are involved.

That's why we've developed systems for working with tens of thousands of patients. Why we've put together an extensive network of highquality investigator sites.

And why we've assembled a team of over four hundred professionals to oversee it all.

The big picture? Over the years, we've successfully completed projects for a wide range of biotech and pharmaceutical companies, both large and small, on spec, on time and on budget.

We can do the same for you. While making sure that you don't get lost

in the crowd.



Contact: Pharmaceutical Product Development, Inc. 115 N. Third Street, Wilmington, NC 28401 910-251-0081 Fax 910-762-5820 Also RTP, North Carolina and San Antonio, Texas Circle No. 13 on Readers' Service Card