American Association for the Advancement of Science

SCIENCE

9 August 1996
Vol. 273 • Pages 709–840
$7.00

STRATAGENE®

QuikChange™
SITE-DIRECTED MUTAGENESIS KIT

Stratagene Times

QuikChange Site-Directed Mutagenesis Kit
Mutagenesis made easy!

MUTAGENESIS BREAKTHROUGH

150 Times More Accurate than PCR-based Mutagenesis!

REPLICATES *ONLY* PARENTAL DNA

Stratagene has just revolutionized site-directed mutagenesis with the QuikChange site-directed mutagenesis kit. You can now complete your mutagenesis in one day, with a simple 4-step method.

No more single-stranded DNA templates, subcloning into specialized vectors, unique restriction sites, or multiple transformations. And the extreme efficiency of this method cuts your screening time in half!

Call Stratagene or your Stratagene distributor for the complete picture.

QuikChange™ Site-Directed Mutagenesis Kit

Near 100% Efficiency
- Eliminates background
- Cuts screening time in half
- Highest efficiency method
- Mutation in virtually all transformants

150 Times More Accurate than PCR-based Mutagenesis
- Extends without PCR
- Uses high fidelity *Pfu* DNA polymerase
- Replicates only parental DNA
- Reduces second-site mutations 150 fold

1-Day Method

Gene in plasmid with target site for mutation

1. Mix
Denature plasmid and anneal primers containing the desired mutation

2. Cycle
Temperature cycle to extend and incorporate mutation primers resulting in nicked circular strands

3. Digest
Digest parental DNA template

4. Transform
Transform the resulting annealed double-stranded nicked DNA molecules

After transformation the XL2-Blue *E.coli* cell repairs the nicks in the plasmid

MUTAGENSIS MADE EASY!

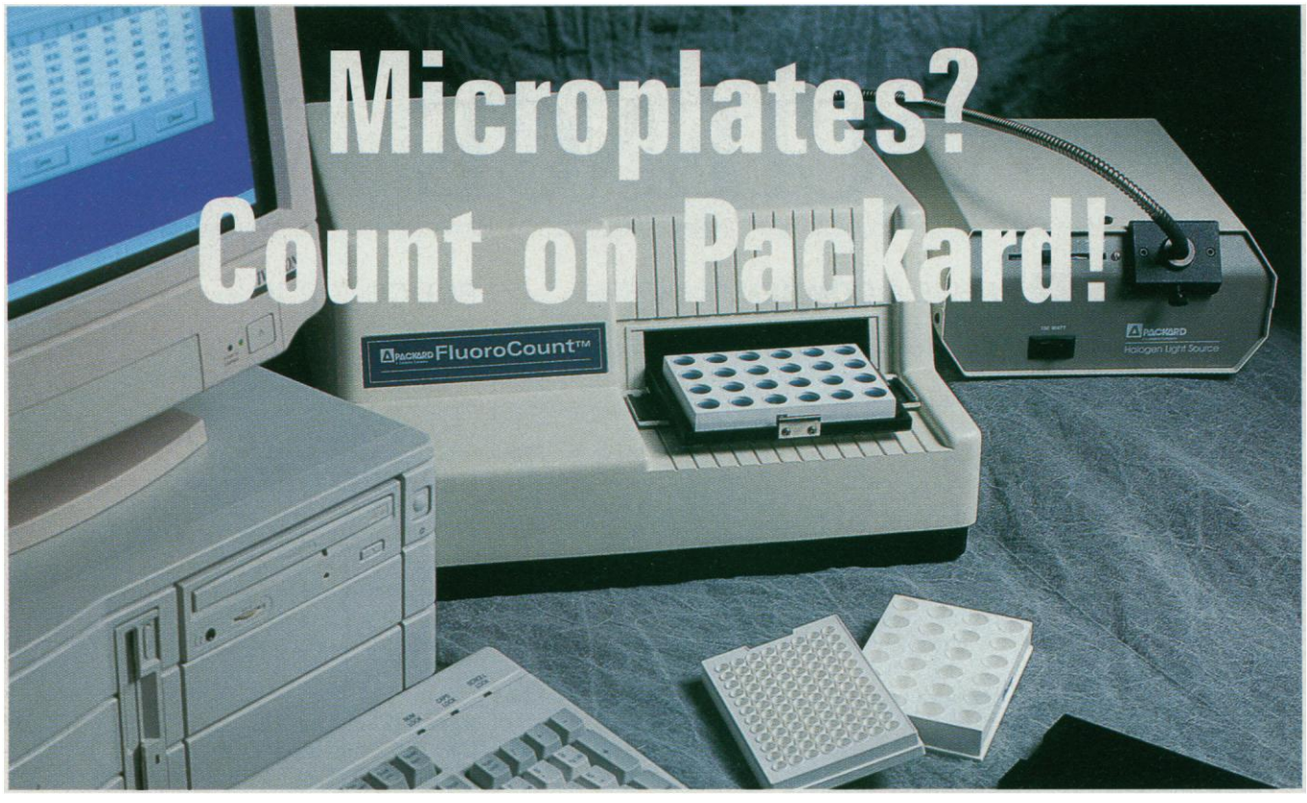
QuikChange™ Site-Directed Mutagenesis Kit catalog #200518

*Patent pending

Circle No. 35 on Readers' Service Card

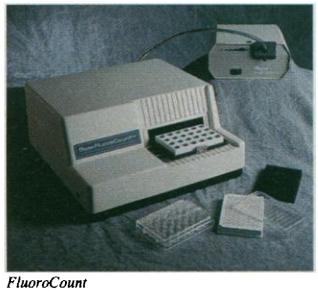
UNITED STATES:
Stratagene Headquarters
800-424-5444
INTERNET MAIL:
techservices@stratagene.com
AUSTRALIA: 1800-252-204
AUSTRIA: 1 5332666
BRAZIL: 11 530 7833
CANADA: 905 713 1201
DENMARK: 8 6101055
FRANCE: 1 34 60 2424
GERMANY: 0130-840911
HONG KONG: 5785839
ISRAEL: 3 7521687
ITALY: 258013409
JAPAN: (Toyobo) 3 3660 4819
(Funakoshi) 3 5684 1622
KOREA: 2 5560311
MALAYSIA: 37031888
THE NETHERLANDS: 33 4950094
NEW ZEALAND: 9 443 5867
NORWAY: 22715090
PORTUGAL: 1-4581641
ROC: 2 694 0066 or 2 720 2215
SINGAPORE: 2730898
SPAIN: 1 729 03 33
SWEDEN: 8 680 0845
SWITZERLAND: 3641106
THAILAND: 23080611
UNITED KINGDOM: 0800 585370
OTHER COUNTRIES CALL STRATAGENE U.S.A.

STRATAGENE®



Introducing a Complete Line of Microplate Counters for Non-Isotopic Assays

Packard, the company that revolutionized the microplate assay market with its TopCount™ microplate scintillation and luminescence counter, introduces three new non-isotopic microplate instruments.



FluoroCount

SpectraCount™ Photometric Microplate Counter features unique single beam detection to extend the linear range of UV/VIS measurements and to handle a greater variety of microplates, including 6, 12, 24, 48 and 96-well plates.

LumiCount™ Microplate Luminometer uses digital photon integration technology to measure glow luminescence assays with high sensitivity. Combined with Packard's enhanced chemiluminescence technology, LumiCount makes it possible to measure a wide variety of assays in both 24 and 96-well plates.

FluoroCount™ Microplate Fluorometer is the only fluorescence microplate counter with a user selectable external excitation source. FluoroCount gives unmatched sensitivity for a wide range of assays. Its unique close-proximity detection design can be configured for either top or bottom reading, for both solution and cell-based assays.

LumiCount

Total System Support for microplate counters is only as dependable as the company that provides it. Packard's unique range of luminescence and fluorescence reagents, its specialty microplates, and its service and applications support will ensure the performance you need today and tomorrow.

SpectraCount

For complete details please call Packard at 1-800-323-1891 (U.S. only), 203-238-2351 or visit our web site.

Count on Packard... we bring you solutions.

PACKARD
A Canberra Company

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

Packard Instrument, Co. SYSTEM CERTIFIED ISO 9001

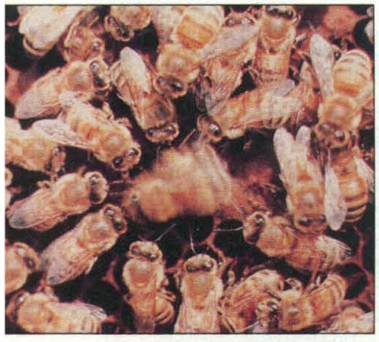
Packard International Offices:
Australia, Mt Waverley 61-3-9543-4266; **Austria**, Vienna 43-1-2702504; **Belgium**, Brussels 32-2-4668210; **Canada**, Ontario 1-800-387-9559; **Central Europe**, Schwadorf, Aus. 43 456 2230 015; **Denmark**, Greve 45-42909023; **France**, Rungis (33) 1 46.86.27.75; **Germany**, Dreieich 49 6103 385-0; **Italy**, Milano 39-2-33910796/7/8; **Japan**, Tokyo 81-3-3866-5850; **Netherlands**, Groningen 31-50-5413360; Tilburg (013) 5423900; **Russia**, Moscow, 7-095-238-7335; **Switzerland**, Zurich (01) 481 69 44; **United Kingdom**, Pangbourne, Berks (44) 01734 844981.

Circle No. 25 on Readers' Service Card

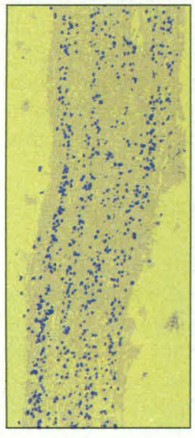
ISSN 0036-8075
9 AUGUST 1996
VOLUME 273
NUMBER 5276

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



739
Teamwork in evolution



784
Neurofilaments in motion

NEWS & COMMENT

RESEARCH NEWS

POLICY FORUM

PERSPECTIVES

ARTICLE

DEPARTMENTS

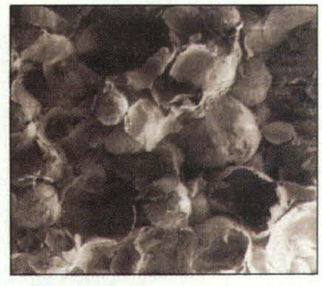
■ **SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005**. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Domestic individual membership and subscription (51 issues): $102 ($55 allocated to subscription). Domestic institutional subscription (51 issues): $250. 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. **Printed in the U.S.A.**

COVER

Chondrule (850 μm in diameter) from the unmetamorphosed Chainpur meteorite, containing excess ^{26}Mg from decay of ^{26}Al 4.6 billion years ago. Initial abundance of ^{26}Al is one-fifth of that in Ca-Al inclusions, the oldest solids formed in the solar system, implying that chondrules formed—and the solar nebula lasted—for more than 2 million years. The chondrule includes glass (dark magenta), brightly colored olivine and dendritic pyroxene, and blocky spinel (light magenta). See page 757. [Transmitted polarized light (plus gypsum plate) photo: G. J. MacPherson]

RESEARCH ARTICLE

REPORTS



768
Controlling shapes of mesoporous films

◩ Indicates accompanying feature

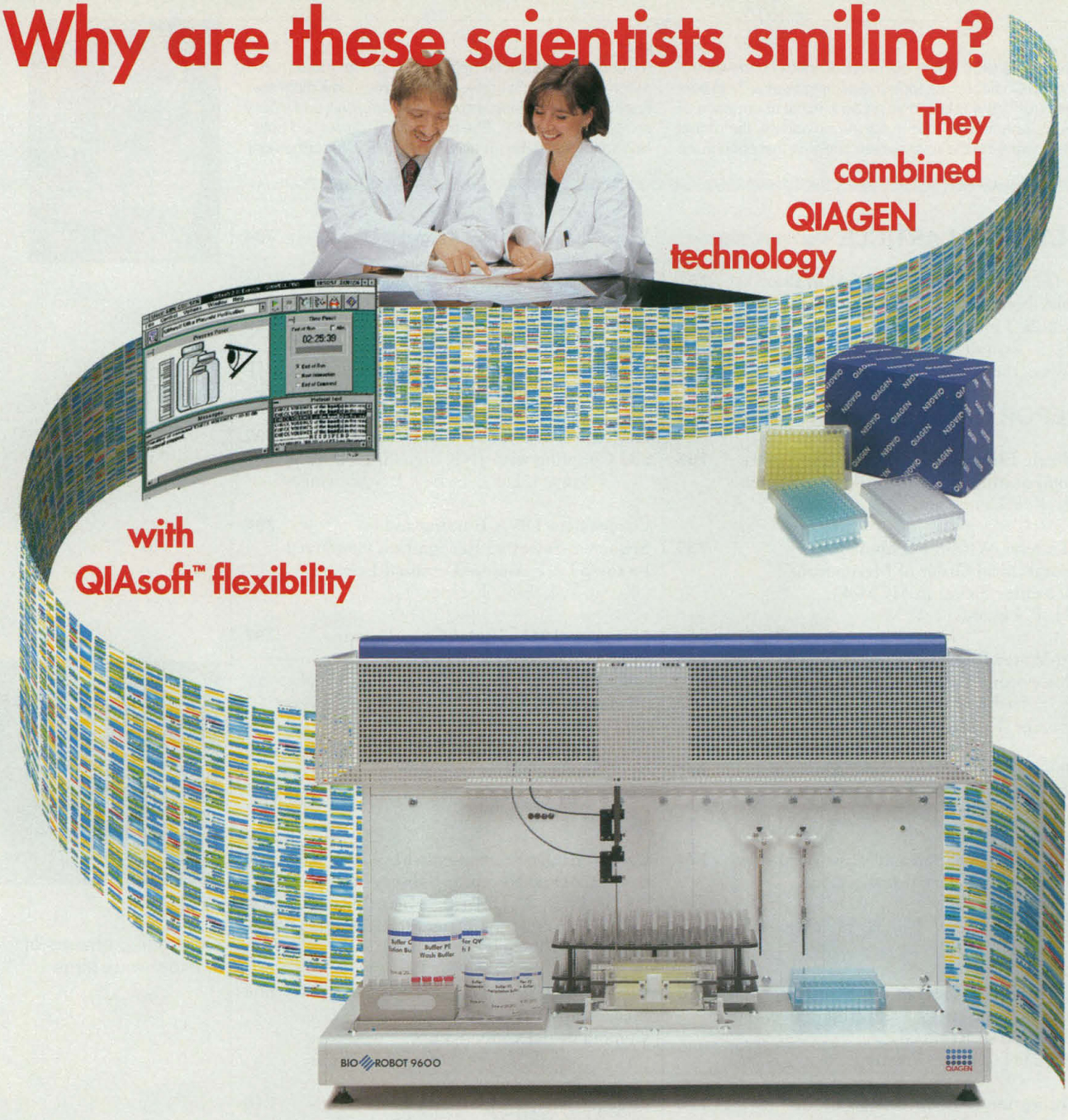
Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $7.00 per issue prepaid includes surface postage; bulk rates on request.

On the Web

Breaking News: Possible Life on Mars?
A special electronic preprint of the McKay *et al.* paper is available at http://www.sciencemag.org/

Why are these scientists smiling?

They combined QIAGEN technology with QIAsoft™ flexibility



on the BioRobot™ 9600

Call today to find out more about cost-effective miniprep automation — from the world leaders in nucleic acid purification.

QIAGEN Inc.
9600 De Soto Avenue
Chatsworth, CA 91311, USA
Orders 800-426-8157
Fax 800-718-2056
Technical 800-362-7737

QIAGEN

Circle No. 32 on Readers' Service Card

THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Nanopores in tubes and through films

Mesoporous materials can contain porous networks of parallel nanoscale cylinders. Two reports show how such materials can be assembled into hollow structures on the micrometer scale. Lin and Mou (p. 765) tailored the mesoporous aluminosilicate MCM-41 into micrometer-diameter tubules in which its cylindrical pores are coaxial with the tube. Schacht *et al.* (p. 768) assembled mesoporous films at oil-water interfaces to create hollow micrometer-scale fibers and spheres as well as thin sheets. The pores generally align perpendicular to the film.

■

American origins

The eastern margin of North America was first defined in the Precambrian, when rifting created the Iapetus Ocean. Closure of this ocean formed the Appalachian-Ouachita mountains; subsequent reopening formed the Atlantic Ocean. As a result of this history, original fragments of North America are now attached to other continents. Thomas and Astini (p. 752) synthesize recent geologic data to show that one such fragment, originally from the region of the Ouachitas, is now part of western South America. Tracing this connection allows a better understanding of the timing of the formation of the Iapetus Ocean and the past geography of continents.

■

Solar system origins

A key for reconstructing events in the early solar system is the recognition of daughter isotopes of short-lived radioisotopes in meteorites. One such important isotope is ^{26}Al, which decays to ^{26}Mg with a half-life of 0.73 million years. Russell *et al.* (p. 757) searched for the original presence of ^{26}Al in chondrules and calcium-aluminum–rich inclusions (CAIs), two particles that formed early in the solar nebula and are contained in ordinary chondrites, a primitive class of meteorites. The CAIs had the highest amounts of ^{26}Mg, some chondrules had lesser amounts, and some had no evidence of original ^{26}Al. Chondrule formation likely lasted more than 5 million years in the solar nebula.

Drugs, receptors, and hypertension

Stimulation of α_2-adrenergic receptors (α_2ARs) causes a decrease in blood pressure, and drugs that activate these receptors are widely used to treat hypertension. However, the role of the three α_2AR subtypes (α_{2a}, α_{2b}, and α_{2c}) and possibly other receptors in the physiological effects of α_2AR agonists has been unclear. Link *et al.* (p. 803) and MacMillan *et al.* (p. 801) describe the specific roles of the α_2AR subtypes revealed by studies of genetically engineered mice deficient in one of the α_2AR subtypes. The α_{2a} subtype is mainly responsible for the antihypertensive action of α_2AR agonists, whereas the α_{2b} subtype mediates an undesirable opposite, or hypersensitive, effect. Drugs designed to be selective for the α_{2a} receptor may be more effective in treating hypertension.

■

Delivery systems

Most neuronal proteins are synthesized in the cell body. Proteins that are required at the synapse must be transported along the axon—many by a process known as slow axonal transport. Terada *et al.* (p. 784) examined the transport of neurofilament proteins along the axons of living neurons. Their findings suggest that neurofilament subunits can be transported along axonal microtubules, rather than requiring a preexisting neurofilament track for their own transport.

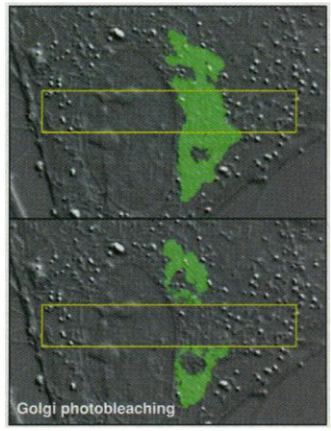
Sending a message

With so many neurotransmitters activating so many receptors that are coupled to so many second messengers, how do signals overcome the intracellular bureaucracy to produce an effect? Brezina *et al.* (p. 806) describe a model of combinatorial control of a muscle in the buccal mass of *Aplysia*. In this system, a relatively small number of identified neurons make it possible to interpret neuromuscular events in terms of behavioral circumstances. The authors were able to predict and confirm experimentally the cellular changes caused by the release of several neurotransmitters, which allows them to explain why, for instance, unpalatable food triggers only a gentle biting, and voracious feeding enforces an increase in muscle relaxation rate .

■

Free to move about the membrane

The Golgi complex is comprised of a set of flattened cisternae. Many theories have been put forward to explain how the Golgi morphology and the distinctive membrane composition of each cisterna is established and maintained in the face of rapid membrane traffic. Cole *et al.* (p. 797) examined the lateral mobility of engineered fluorescently labeled Golgi membrane protein in a living cell. Surprisingly, all of the proteins studied showed

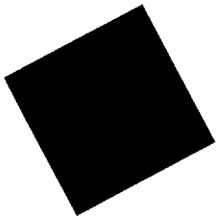


very rapid movement, which suggests that lateral restriction of diffusion of membrane components is unlikely to explain the distribution of specific Golgi membrane proteins in specific Golgi cisternae.

■

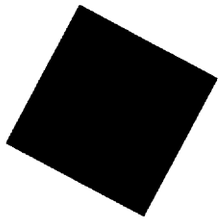
Pox strategies

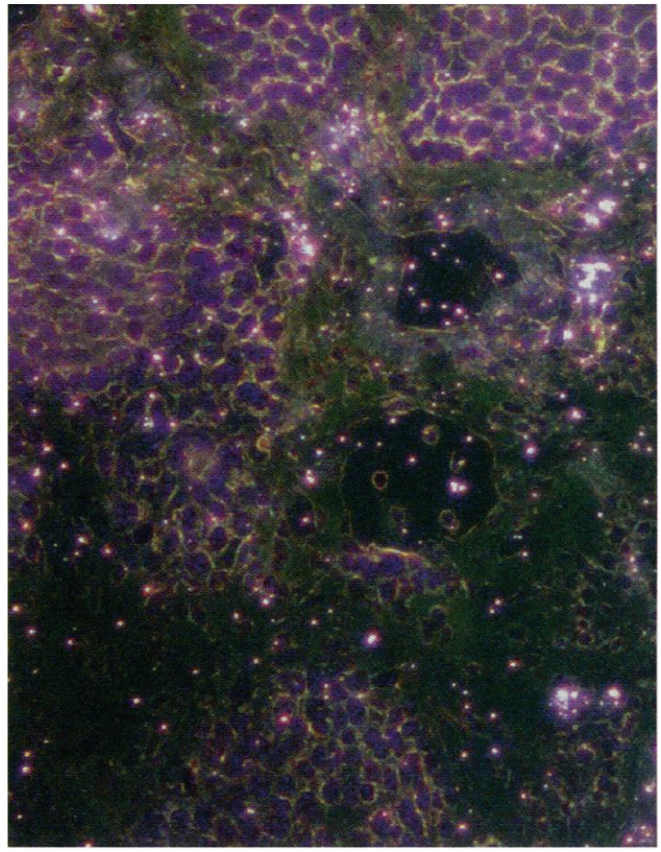
Only two pox viruses have been known to infect humans—variola virus, which was responsible for smallpox, and molluscum contagiosum virus (MCV), which normally causes asymptomatic skin papules but leads to opportunistic infection when it infects persons with AIDS. Senkevich *et al.* (p. 813) have sequenced the MCV genome and have found important differences in the genes involved in host infection, nucleotide biosynthesis, and cell proliferation. This study not only provides a genetic basis for understanding the very different strategies by which these viruses evade the host immune system but may also provide clues for drug therapies.



SEE

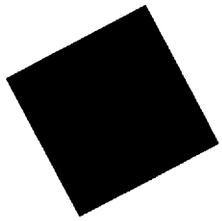
WHAT YOU'VE BEEN MISSING.





Pixera Professional System/John Bagley Photography

CAPTURE IT, ENHANCE IT, SHARE IT.



Pixera Studio: Compose your picture with a through-the-lens motion viewfinder. Manipulate and enhance the acquired image and regions of interest with a wide variety of built-in high-performance tools, filters and effects. Compress it and store it in JPEG format or convert it into TIFF, PICT, BMP, or DIB.

Pixera Album: Store, catalog and manage an unlimited number of images, sound files, even video clips. Organize, sort, query and filter stored objects using a powerful database tool set. Capture, edit or enhance new images with one-button access to the full capability of Pixera Studio.

Sometimes, it's not what you see but what you don't that's critical. You need the best image you can get your eyes on. And no digital camera can give you better image quality at a lower price than a Pixera Professional Visual Communication System. It provides the resolution and image quality of systems costing many times more. Yet you get everything you need at one low price -- including the first digital camera system with million-pixel resolution and a full suite of application software.

The Pixera Professional captures two- or three-dimensional images and can connect to any optical microscope with a standard C-mount interface. Choose from PCI or PCMCIA versions for Windows 95 or Macintosh.

For more information, call toll-free 1-888-4PIXERA or visit our web page at www.pixera.com.

pixera visual SYSTEM communication

Circle No. 21 on Readers' Service Card

http://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.

INFORMATION RESOURCES

SUBSCRIPTION SERVICES
For change of address, missing issues, new orders and renewals, and payment questions, please contact AAAS at Danbury, CT: 800-731-4939 or Washington, DC: 202-326-6417, FAX 202-842-1065. Mailing addresses: AAAS, P.O. Box 1811, Danbury, CT 06813 or AAAS Member Services, 1200 New York Avenue, NW, Washington, DC 20005 • **Other AAAS Programs:** 202-326-6400

REPRINTS & PERMISSION
Reprints: Ordering/Billing, 800-407-9191; Corrections, 202-326-6501 • **Permissions:** 202-326-7074, FAX 202-682-0816

INTERNET ADDRESSES
science_editors@aaas.org (for general editorial queries); science_news@aaas.org (for news queries); science_letters@aaas.org (for letters to the editor); science_reviews@aaas.org (for returning manuscript reviews); science@science_int.co.uk (for the Europe Office); membership@aaas.org (for member services); science_classifieds@aaas.org (for submitting classified advertisements); science_advertising@aaas.org (for product advertising)

INFORMATION FOR CONTRIBUTORS
See pages 93–94 of the 5 January 1996 issue or access http://www.sciencemag.org/science/home/con-info.shtml.

EDITORIAL & NEWS CONTACTS

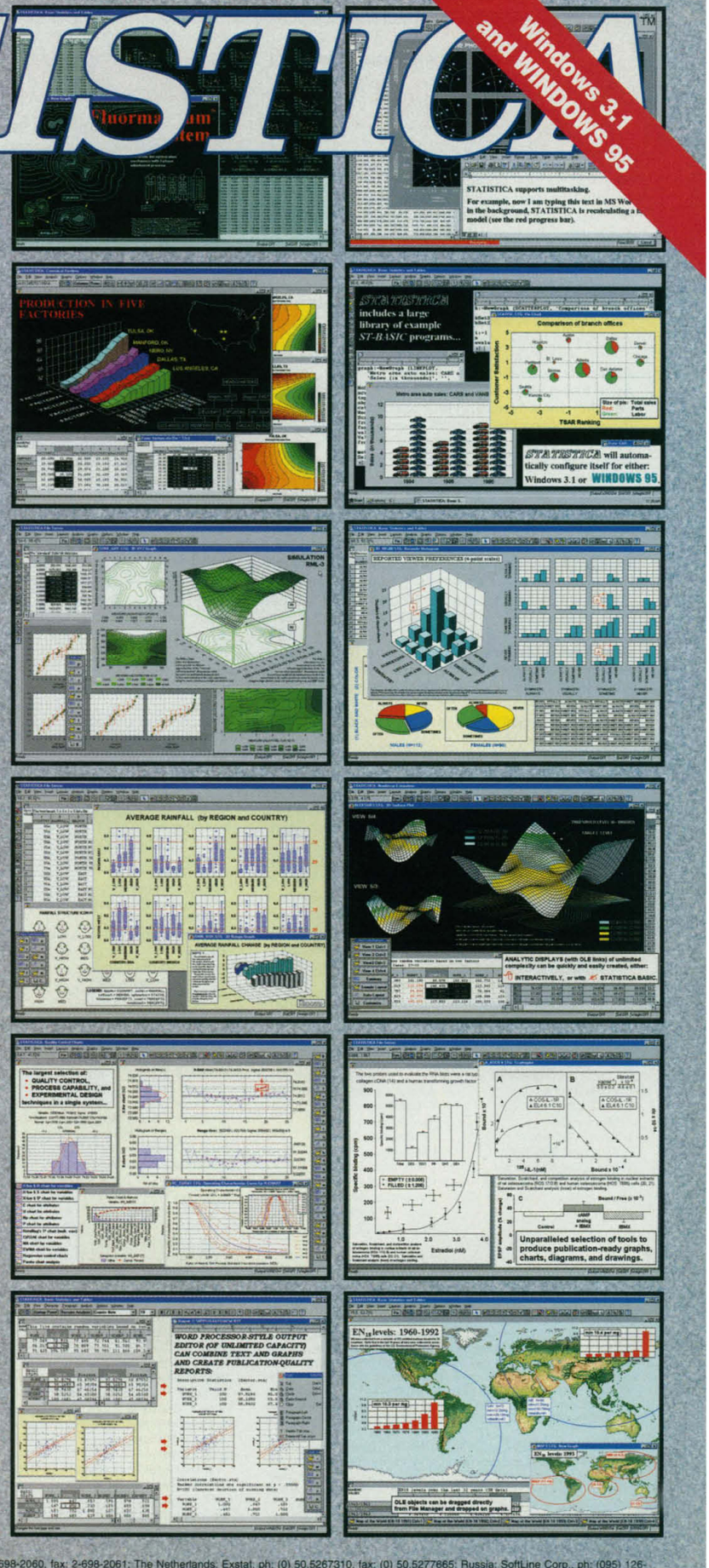
North America
Address: 1200 New York Avenue, NW, Washington, DC 20005
Editorial: 202-326-6501, FAX 202-289-7562
News: 202-326-6500, FAX 202-371-9227 • **Bureaus: Berkeley, CA:** 510-841-1154, FAX 510-841-6339, **San Diego, CA:** 619-942-3252, FAX 619-942-4979, **Chicago, IL:** 312-360-1227, FAX 312-360-0537, **Boston, MA:** 617-566-7137, FAX 617-734-8088

Europe
Headquarters: 14 George IV Street, Cambridge, UK CB2 1HH; (44) 1223-302067, FAX (44) 1223-302068
Paris Bureau: (33) 1-49-29-09-01, FAX (33) 1-49-29-09-00

Asia
Japan Office: Carl Kay, Esaka-cho 5-chome 11-10, Suita-shi, Osaka 564 Japan; (81) 6-368-1925, FAX (81) 6-368-6905; science@magical.egg.or.jp • **News Bureau:** (81) 3-3335-9925, FAX (81) 3-3335-4898 • **China Office:** Hao Xin, (86)10-6255-9478; haoxin@sun.ihep.ac.cn

STATISTICA

Windows 3.1 and WINDOWS 95



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

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

STATISTICA/QC - *Industrial statistics add-on package* (requires *STATISTICA* or Quick *STATISTICA* for Windows) ■ The largest selection of industrial statistics in a single package; quality control charts (compatible with real-time data acquisition systems), process capability analysis, R&R, sampling plans, and an extremely comprehensive selection of experimental design (DOE) methods ■ Flexible tools to customize and automate all analyses and reports (incl. "turn-key" system options, and tools to add custom procedures) ■ Price **$495.**

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

Domestic sh/h $12 per product; 30-day money back guarantee.

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

StatSoft®

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

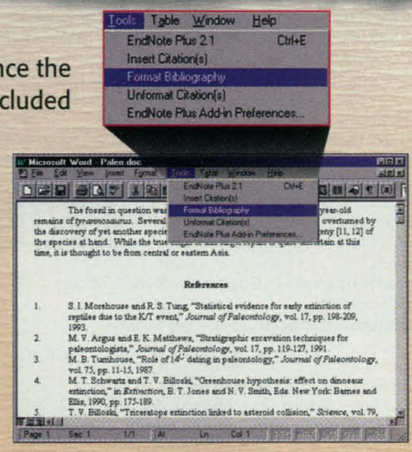
Circle No. 15 on Readers' Service Card

Overseas Offices: StatSoft of Europe (Hamburg, FRG), ph: 040/ 4200347, fax: 040/4911310; **StatSoft UK** (London), ph: 01462/482822, fax: 01462/482855; **StatSoft France,** ph: (1) 34 52 39 22, fax: (1) 34 52 28 48; **StatSoft Polska,** ph: 12-391120, fax: 12-391121; **StatSoft Italia,** ph: 49-893-3227, fax: 49-893-2897; Available from other Authorized Representatives worldwide: Australia: Hearne, ph: (03) 9602 5088, fax: (03) 9602 5050; Sweden: AkademiData Scientific, ph: 018-210035, fax: 018-210039; Finland: Statcon Oy, ph: 24-7334678, fax: 24-7333867; Belgium: Texma NewTech, ph: 010 616 628, fax 010 616 957; South Africa: Osiris, ph: 12-660-2884, fax 12-660-2886; Japan (Macintosh): Three's Company, Inc., ph: 03-3770-7600, fax 03-3770-7784; Japan (Windows): StatSoft Design Technologies, Inc., ph: 03-3667-1110, fax: 03-3668-3110; Taiwan: Intelligent Integration Corp., ph: 2-698-2060, fax: 2-698-2061; The Netherlands: Exstat, ph: (0) 50.5267310, fax: (0) 50.5277665; Russia: SoftLine Corp., ph: (095) 126-9065, fax: (095) 232-0023; Hungary: CheMicro, ph: 1 131-3847, fax: 1 132-9330.

1 step Bibliographies in Microsoft® Word with the new EndNote® Add-in

Create a bibliography in one step:

In some bibliographic programs it takes as many as 10 steps to create a bibliography once the in-text citations have been placed in your document. With the new **EndNote Add-in** (included in **EndNote Plus 2.1**), simply choose *Format Bibliography* from Word's *Tools* menu and **EndNote** will create the bibliography instantly!



To create a bibliography, simply select *Format Bibliography* from Word's *Tools* menu.

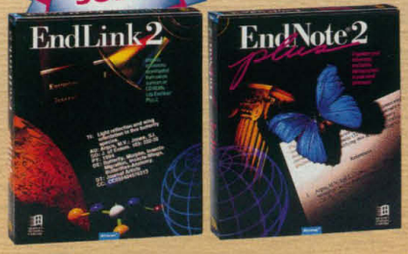
Keep track of only one document:

When formatting bibliographies in some other bibliographic programs, you have to keep track of up to 3 separate documents. Using the **EndNote Add-in,** you can kiss this confusion goodbye!

Revise the same document as many times as you need:

The **EndNote Add-in** has no problem with last-minute revisions that you've made to your document. You can select another bibliographic style or you can even add or delete citations. Each time you choose *Format Bibliography,* the **EndNote Add-in** will automatically update your citations and bibliography in your document.

more than 100,000 SOLD



Available for Macintosh and now for Windows!

- Speedy 32-bit processing
- Works under Windows 3.1, Windows 95, Windows NT and Macintosh
- Works with Microsoft Word 6 and 7 (Windows); 5 and 6 (Macintosh)
- A true Word Add-in (not just a collection of Word Basic macros)

There's More . . .

- **EndNote** is compatible with WordPerfect and other word processors (no Add-in)
- Includes bibliographic styles for more than 300 journals
- **EndLink** (sold separately) imports from more than 100 online databases and CD-ROMS
- Imports from Reference Manager,® PAPYRUS® and some other bibliographic programs
- If you use any bibliographic program, you qualify for a competitive upgrade price. Call us for details.

MICROSOFT® WINDOWS™ COMPATIBLE Mac™ OS

Compatible with Windows 3.1, Windows NT, Windows 95 and the MacOS.

"... the most powerful citation manager you can find, short of a personal librarian."
— PC Magazine, December 1995

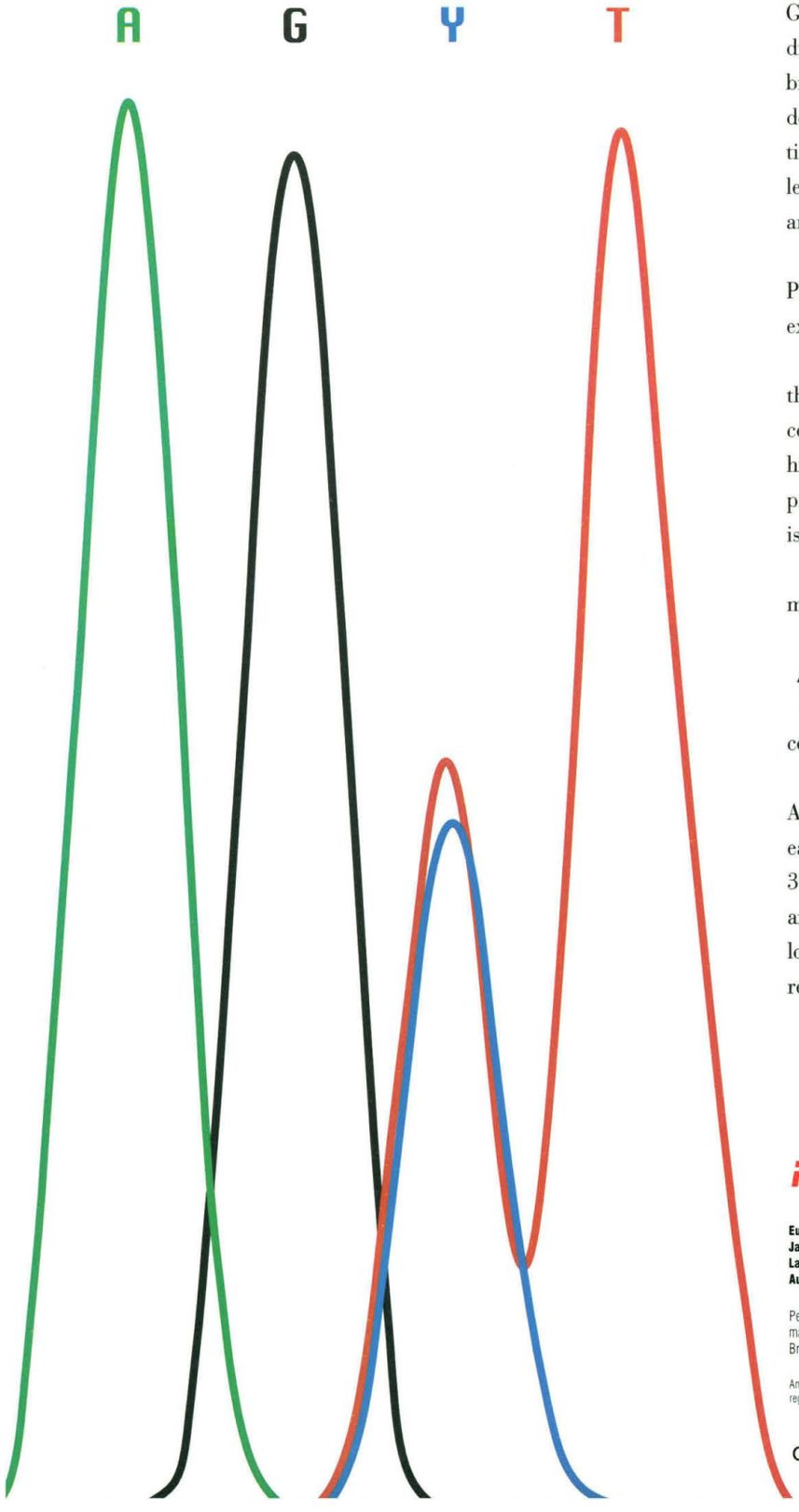
"Despite its power, EndNote Plus remains surprisingly easy to learn and use."
— Macworld, April 1995

"So the next time you need to prepare a bibliography, don't sweat it— use EndNote Plus 2."
— PC/Computing's Windows 95 Buyer's Guide

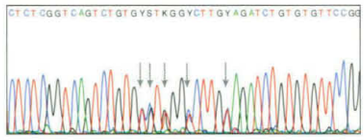
Niles & Associates, Inc.
Circle No. 14 on Readers' Service Card

800 Jones Street Berkeley California 94710 USA Phone 800.554.3049 or 510.559.8592 Fax 510.559.8683
E-mail: info@niles.com World Wide Web: http://www.niles.com
Australia (+61) 66.58.3674 Germany (+49) (0) 69.970841.11 Japan (+81) 3.3384.8861 Scandinavia (+46) 481.511.23 UK (+44) (0) 1865.784800

Even peaks make mutation detection even easier.



Good news for genetic disease researchers. A breakthrough in enzyme design just took mutation detection to new levels of convenience and performance.



Direct PCR sequencing of the highly polymorphic HLA-B gene using a dye primer kit with the AmpliTaq FS enzyme.

That breakthrough is AmpliTaq® DNA Polymerase, FS—an enhanced enzyme developed expressly for automated fluorescent DNA sequencing.

AmpliTaq FS dye primer kits make it easier than ever to directly sequence PCR products. They combine the simplicity of cycle sequencing with high-efficiency ddNTP incorporation to produce precise data with uniform peak heights. The result is accurate detection of mutations.

AmpliTaq FS kits expand the power of ABI PRISM™ multicolor detection technology to sequence-based mutation detection. Together with our reagents and protocols for fluorescent PCR detection, we provide complete DNA analysis solutions for your laboratory.

Find out how PCR-based cycle sequencing with AmpliTaq FS kits makes mutation detection even easier. To order or to request information, call 1-800-345-5224. Outside the U.S. and Canada, contact your local PE Applied Biosystems representative.

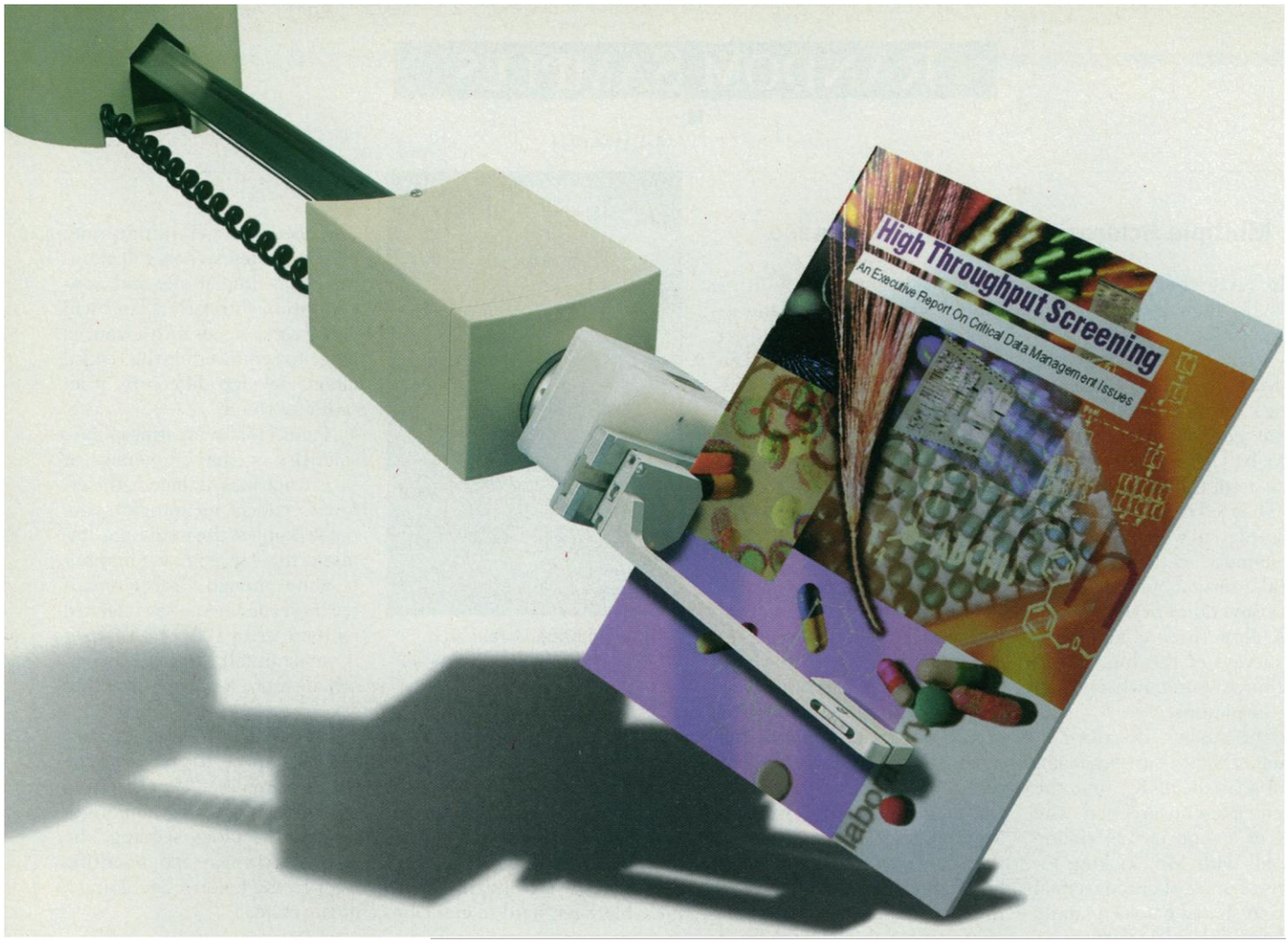
PE Applied Biosystems

Europe Langen, Germany Tel: 49 (0)6103 708 301 Fax: 49 (0)6103 708 310
Japan Tokyo, Japan Tel: (0473) 80-8500 Fax: (0473) 80-8505
Latin America Mexico City, Mexico Tel: 52-5-651-7077 Fax: 52-5-593-6223
Australia Melbourne, Australia Tel: (03) 9212-8585 Fax: (03) 9212-8502

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

Roche

Circle No. 50 on Readers' Service Card



The sooner you get your hands on this executive report, the sooner your HTS investment will pay off.

Life science companies of all sizes are rushing to implement the new discovery technology, high throughput screening (HTS). The promise of higher research productivity and lower R&D costs await those who can effectively manage the unprecedented amounts of information generated by testing up to tens or even hundreds of thousands of compounds.

As the leading provider of integrated chemical information management systems, software, and databases for nearly two decades, MDL Information Systems, Inc. has gathered input from leading HTS scientists like yourself about the critical data management issues your research organization must address when implementing the HTS process.

The knowledge we gained is now available to you in our newly published *High Throughput Screening: An Executive Report on Critical Data Management Issues*.

This informative document offers you valuable insights into managing the HTS process and will help your organization answer questions such as:

"How can HTS enable us to get new drugs to market at less cost?"

"How can we best leverage our huge investment in HTS?"

"How useful is the 'megadata' generated from HTS?"

"How do we use this data to make better decisions?"

We'll also send you the latest information on our comprehensive, high-performance solution for managing HTS information—MDL SCREEN. Simply put, MDL SCREEN is an Oracle-based client-server data management system. It gives you all the functionality, flexibility, and reliability needed to manage information at every stage of the HTS process.

GET THE FACTS ON HTS DATA MANAGEMENT

Call **1-888-888-4635**, for your personal copy of *High Throughput Screening: An Executive Report on Critical Data Management Issues*.

MDL

Information Systems, Inc.

14600 Catalina Street, San Leandro, CA 94577
Tel: (510) 895-1313; Fax: (510) 483-4738
Internet: screen@mdli.com
World Wide Web: http://www.mdli.com

Circle No. 24 on Readers' Service Card