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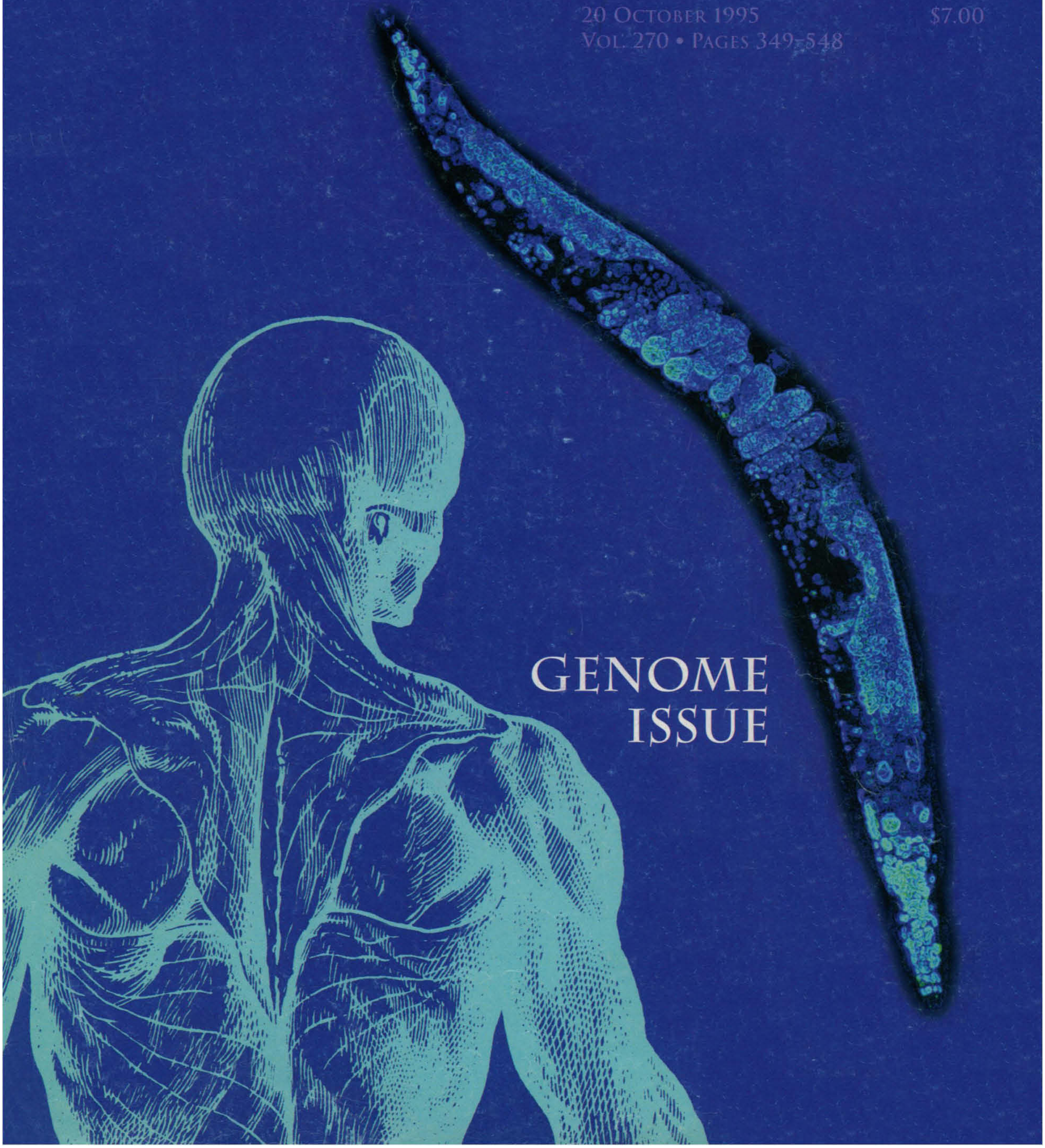

GENOME ISSUE

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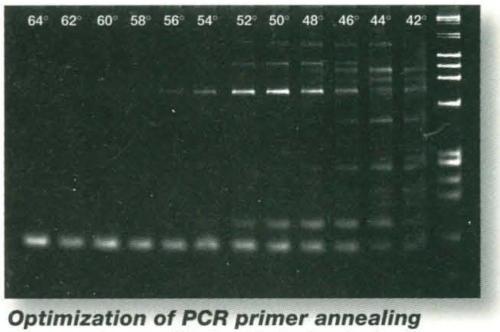
No temperature ramping because robotic arm moves samples from one pre-equilibrated block to another.



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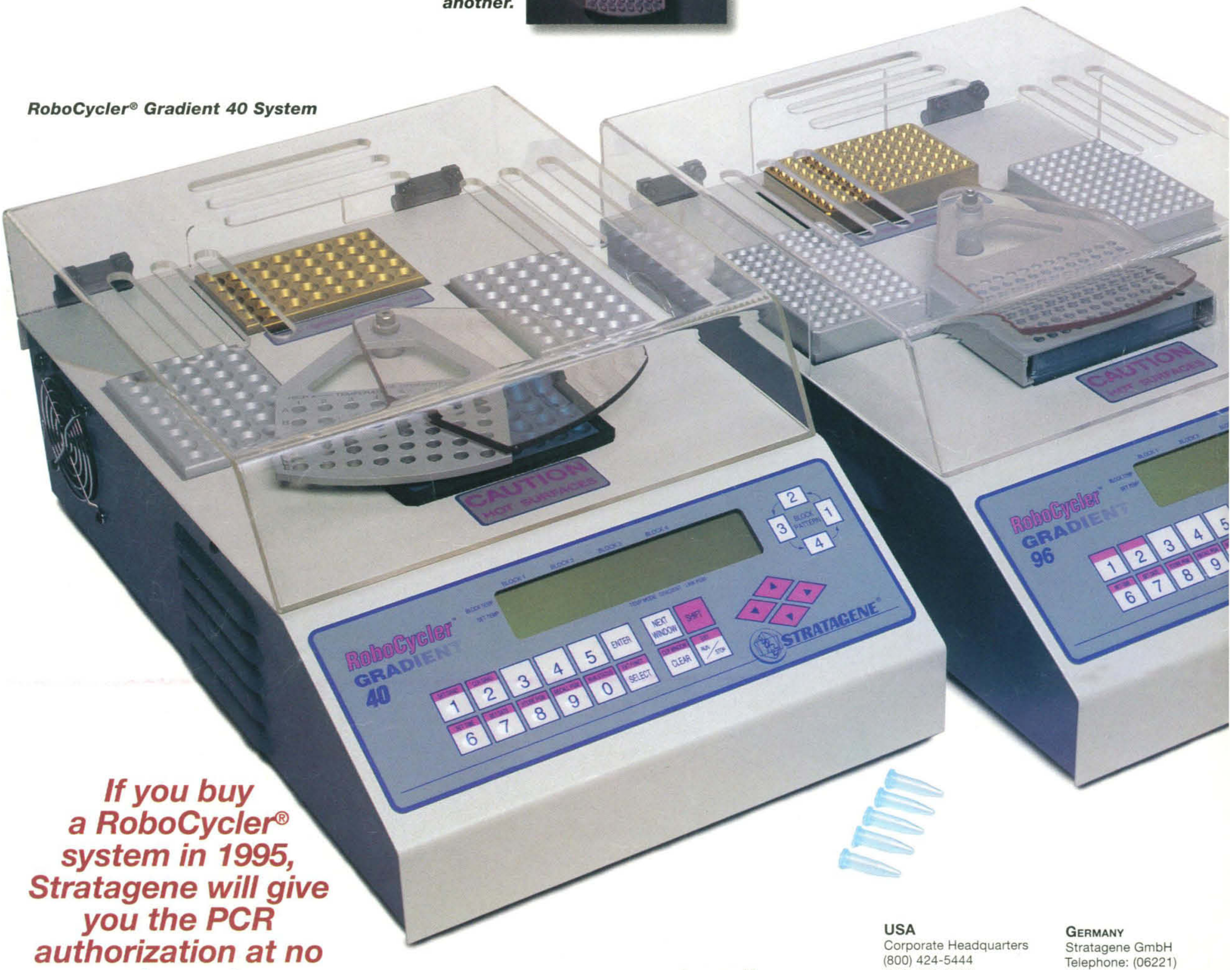

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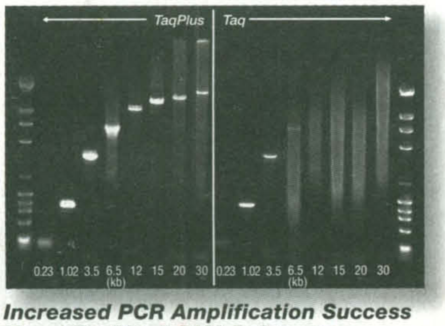

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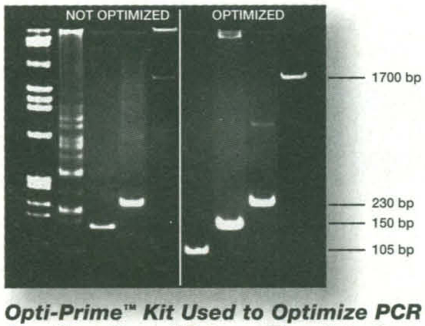

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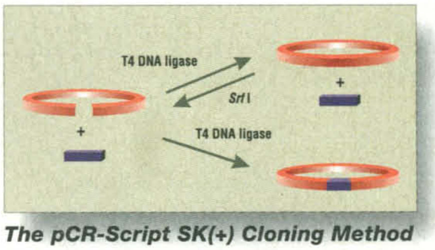

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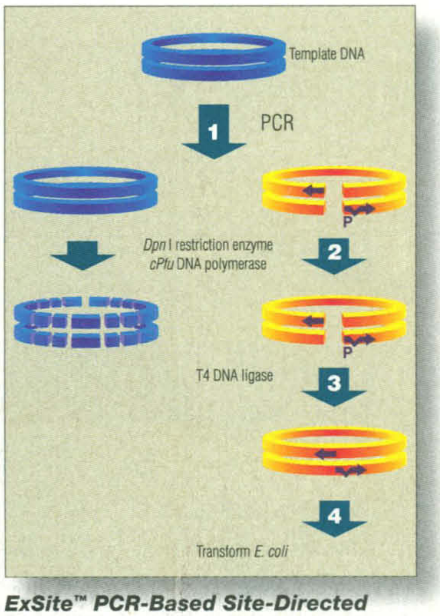

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† Purchase of these enzymes is accompanied by a license to use them in the Polymerase Chain Reaction (PCR) process in conjunction with an Authorized Thermal Cycler.
Stratagene's PCR products are sold under licensing arrangements with Roche Molecular Systems, Inc., F. Hoffmann-La Roche Ltd. and The Perkin-Elmer Corporation.

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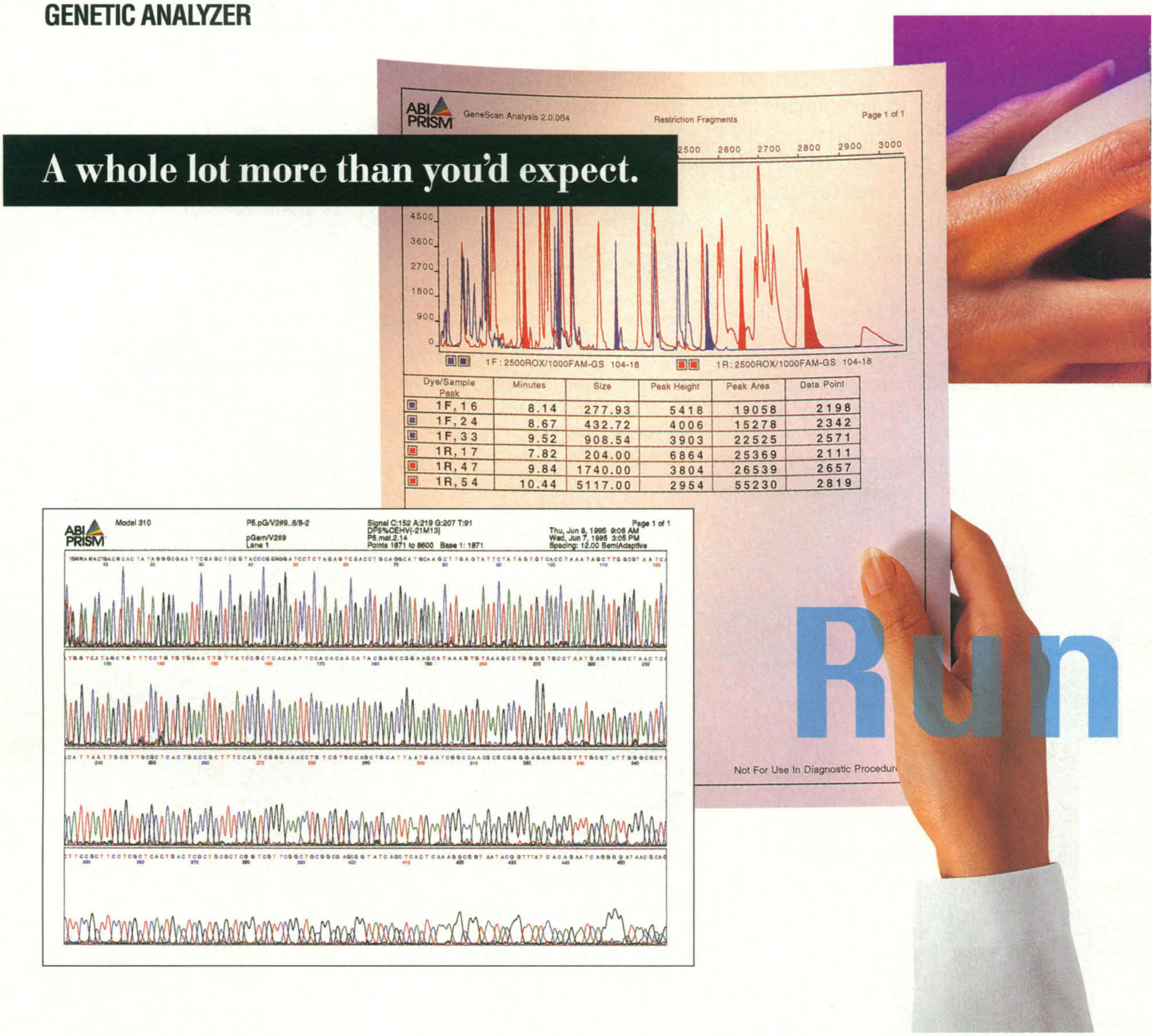
* Patent(s) pending

NEW ABI PRISM™ 310
GENETIC ANALYZER



ABI PRISM GeneScan Analysis 2.0.0b4 Restriction Fragments Page 1 of 1

1F: 2500ROX/1000FAM-GS 104-18 1R: 2500ROX/1000FAM-GS 104-18

Dye/Sample Peak	Minutes	Size	Peak Height	Peak Area	Data Point
🟦 1F, 16	8.14	277.93	5418	19058	2198
🟦 1F, 24	8.67	432.72	4006	15278	2342
🟦 1F, 33	9.52	908.54	3903	22525	2571
🟥 1R, 17	7.82	204.00	6864	25369	2111
🟥 1R, 47	9.84	1740.00	3804	26539	2657
🟥 1R, 54	10.44	5117.00	2954	55230	2819

ABI PRISM Model 310
P5.pG/V2#9..6/8-2
pGem/V2#9
Lane 1
Signal C:152 A:219 G:207 T:91
DP5%CEHV{-21M13}
P5.mat.2.14
Points 1871 to 8600 Base 1: 1871
Page 1 of 1
Thu, Jun 8, 1995 9:06 AM
Wed, Jun 7, 1995 3:05 PM
Spacing: 12.00 SemiAdaptive

The new ABI PRISM™ 310 Genetic Analyzer is changing a lot of expectations about automated genetic analysis.

To begin with, it gives you a lot more versatility. The 310 system automates all the applications you now perform on acrylamide or agarose—and a whole lot more—without limitations.

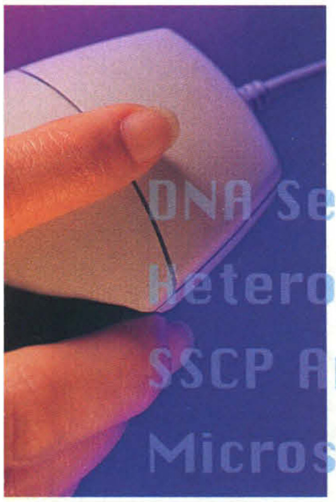
At the same time, the 310 Genetic Analyzer makes genetic analysis a lot less work. You'll never have to pour another slab gel. Instead of conventional gels, the 310 system uses revolutionary new polymers that are injected into a capillary before each run. Not only do these polymers make automation possible, their uniform consistency eliminates guesswork and helps to ensure reproducibility.

You don't even have to pipet your samples into the gel. Just perform your

ABI PRISM 310 GENETIC ANALYZER

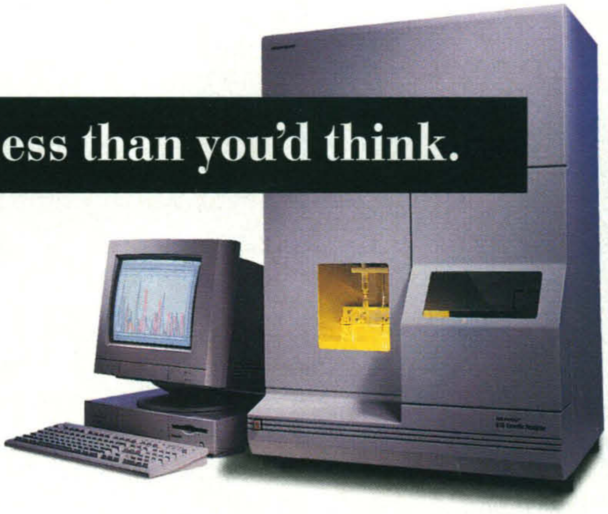
Application	Performance
Cycle Sequencing	425 nt, 98.5% base calling accuracy
Microsatellites	2 nt resolution, 0.5% sizing precision
SSCP	0.5% pattern matching precision
Quantitative RT-PCR	4.0% peak height precision

A lot more, for a lot less. *You can automate virtually any DNA electrophoresis application on the ABI PRISM 310 system. Here are just a few examples.*



DNA Sequencing
Heterozygote Detection
SSCP Analysis
Microsatellite Analysis
Long PCR
RT-PCR

For a whole lot less than you'd think.



reactions, and place your labeled samples in the sample tray. The 310 system automatically injects your samples in whatever order you specify. You can even add samples during a run.

Sample preparation is a lot less trouble, too. ABI PRISM kits for fluorescent PCR and DNA sequencing reduce pipetting steps and variability. And there's no radioactivity or ethidium bromide.

Most importantly, the 310 Genetic Analyzer makes it a whole lot easier to get the results you want. In fact, the results are so accurate, you can transfer data directly to specialized programs for genotyping, mutation detection, and sequence assembly.

But if you expect the 310 Genetic Analyzer to cost a lot, you'll be surprised to find the price is well within the budget of individual laboratories. The ABI PRISM 310 system costs about half as much as the ABI PRISM 377 system, our high-throughput DNA sequencing system.

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AMERICAN
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SCIENCE

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Dates for fans and faults

NEWS

NOBEL PRIZES

GENOME ISSUE

POLICY FORUMS

ARTICLES

PERSPECTIVES

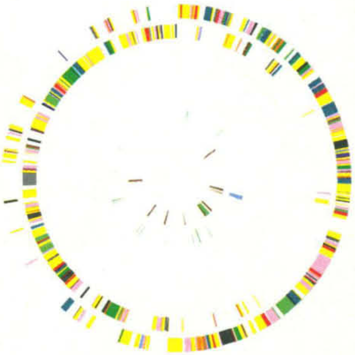
DEPARTMENTS

COVER

The Genome Project adds a new dimension to questions on gene expression in humans and model systems. A chart on page 415 summarizes progress in the *Caenorhabditis elegans* Genome Project and indicates some ways information about sequences can be used. News stories, Articles, Perspectives, Policy Forums, and Reports focus on technological developments, clinical applications, and ethical concerns resulting from the burgeoning of genomic information. [*C. elegans* image: F. Maduro and D. Pilgrim, University of Alberta]

REPORTS

TECHNICAL COMMENTS



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Good things in small genomes

◩ **Indicates accompanying feature**

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THIS WEEK IN SCIENCE

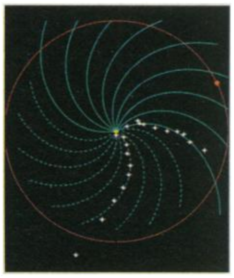
edited by PHIL SZUROMI

Fans and earthquakes

Prominent alluvial fans have formed along the faulted front of many mountain ranges in the western United States. By analyzing cosmogenic isotopes in boulders on fan surfaces, Bierman *et al.* (p. 447) dated fans along the eastern front of the Sierra Nevada in California, some of which were offset by the great 1872 Lone Pine earthquake. The data show that the surfaces of the fans were stabilized at least 8000 years ago, and that the recurrence interval of great earthquakes on the fault is 5800 to 8000 years.

Above the plane

Solar flares and other energetic processes inject electrons and ions into space, where they are guided by the solar magnetic field. Electron interactions with plasma can generate radio emissions (type II radio bursts) whose frequency decreases with distance from the sun. Such emissions are beamed along the solar system plane, so they are best observed from above or below the ecliptic. Reiner *et al.* (p. 461) report radio measurements obtained from the Ulysses spacecraft, which was put into an orbit that takes it over the poles of the sun. Such measurements allow coronal disturbances to be tracked as they move away from the sun, and they also verify theoretical predictions that the solar coronal magnetic field has an Archimedean spiral structure.



Hydrogen ecology deep underground

Nearly all known ecosystems on Earth, including those existing deep in the terrestrial subsurface, are somehow ultimately dependent on photosynthesis for energy. Stevens and McKinley (p. 450; see the news story by Kaiser, p. 377), however, describe bacterial communities in deep aquifers in the Columbia River Basalt Group in the northwestern United States. Their energy source appears to be hydrogen produced by reactions of water and rock in the basalt.

An old warm-up

Measurements of oxygen isotopes in ice cores have provided a detailed record of paleotemperatures at high latitudes during the Holocene; however, factors other than surface temperature may affect oxygen isotope ratios in ice. Because of heat diffusion from the surface, inversion of a borehole temperature record can provide an independent view of changes in surface temperature with time and can be used to calibrate the oxygen isotope thermometer. Cuffey *et al.* (p. 455; see the Perspective by McAyeal, p. 444) analyzed the borehole temperature record from the GISP2 ice core in Greenland. The temperature profile suggests that average temperatures increased by about 15°C from glacial conditions to the Holocene, an increase several times greater than that in the tropics.

Processed for export

Certain proteins, including several interleukins and types of fibroblast growth factor, are secreted directly from cells across the plasma membrane avoiding transport through the traditional secretory. This nonclassical secretory pathway for the production, processing, and transport of these important molecules has been very difficult to characterize in mammalian systems—in particular, the processing of precursors to mature, transport-competent proteins is not well understood. Adames *et al.* (p. 464) examined the export and processing of the yeast pheromone **a** factor, which is secreted by a similar nonclassical pathway. A yeast protease denoted Axl1p, related to the mammalian insulin degrading enzymes, played a critical role in the processing of the **a** factor precursor. The protease also played a role in bud site selection, but this function did not require an active protease. These findings not only bear on the classical pathway but also show that a single protein can regulate distinct signaling pathways—bud site selection and the mating response.

Gene expression by the numbers

Variations in the types and amount of genes expressed at different times in development, between normal and pathological states, or between different tissues can provide clues to gene expression. Two reports describe new methods for speeding the quantitative assessment of gene function (see news story by Nowak, p. 368). Schena *et al.* (p. 467) have developed a robotic system for rapidly generating high-density arrays of complementary DNA clones (in this case, 45 genes from *Arabidopsis thaliana*). By labeling samples with different dyes, differences in mRNA expression (such as between root and leaf) could be quantified. Velculescu *et al.* (p. 484) took a different approach to this problem which they call serial analysis of gene expression, or SAGE. They developed a system for producing concatenates of short diagnostic sequence tags; more than 1000 transcripts could be analyzed in a 3-hour period. Expression levels of tags corresponding to known genes were consistent with known mRNA expression, and new pancreatic transcripts were identified.

Gene therapy in SCID

A form of severe combined immune deficiency (SCID) results from defects in the gene for adenosine deaminase (ADA); deoxyadenosine then accumulates and is toxic to T cells. Bone marrow transplants can cure this disease but donors are usually not available; some symptomatic relief can be afforded by the use of enzyme replacements, such as ADA conjugated to polyethylene glycol (PEG-ADA). Two reports discuss the results of separate clinical trials in which the ADA gene has been transferred with retroviral vectors to two children with SCID during 2-year treatment periods. Blaese *et al.* (p. 475) targeted T cells and showed that vector integration and ADA expression persisted 2 years after gene treatment ended. Bordignon *et al.* (p. 470) used two different vectors to target peripheral blood lymphocytes and bone marrow cells. T cells derived from the marrow gradually dominated the population after treatment stopped. In each trial PEG-ADA was also given, but both reports conclude that gene therapy has contributed to therapeutic improvements in SCID.

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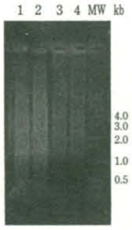
Figure 1.



mRNA isolated from 8×10^7 HeLa cells.
Each pellet was resuspended in 50 µl RNase-free H_2O. 5 µl was loaded onto a 1% agarose gel.
Lanes 1 and 2: FastTrack® 2.0
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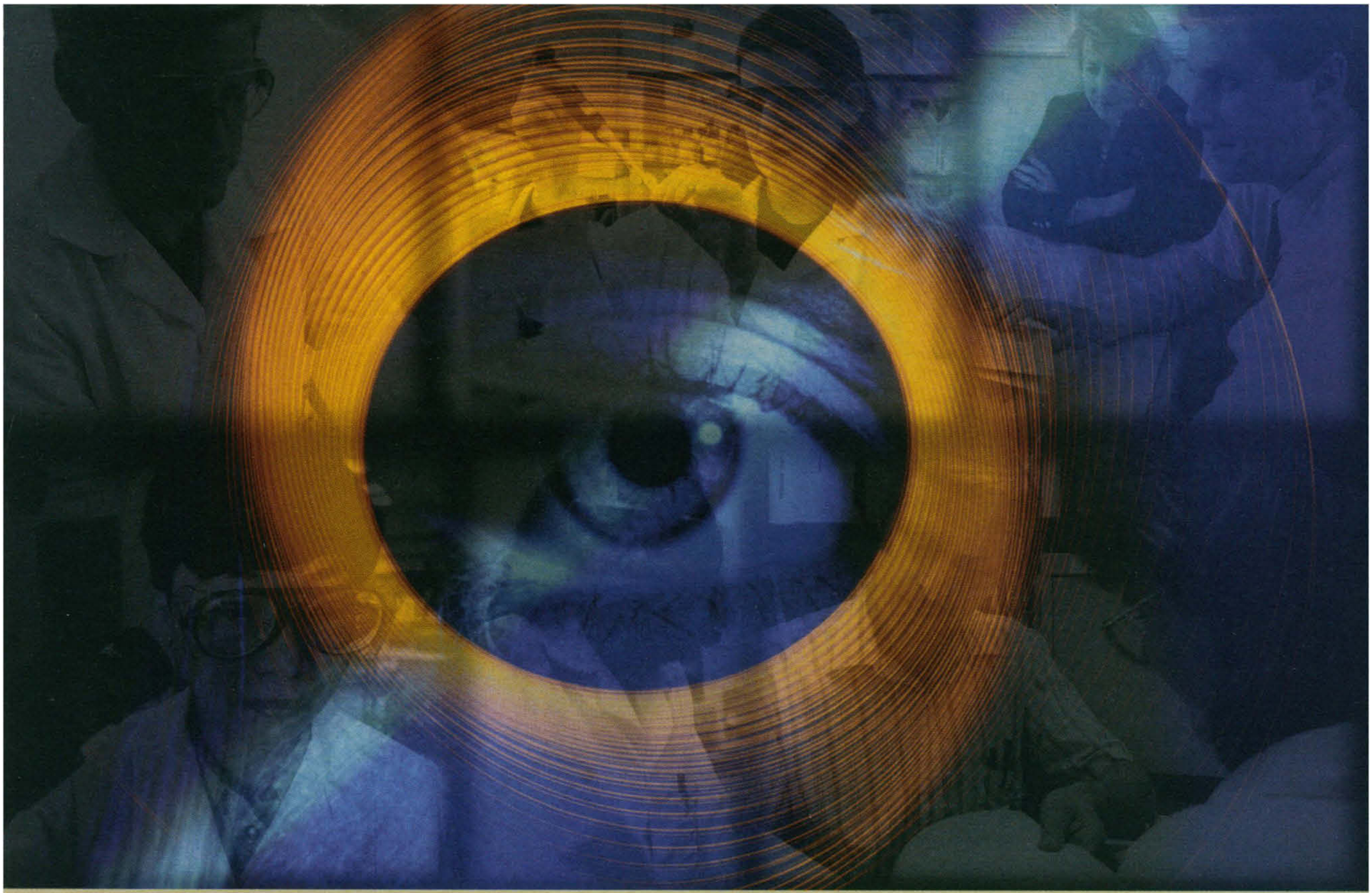

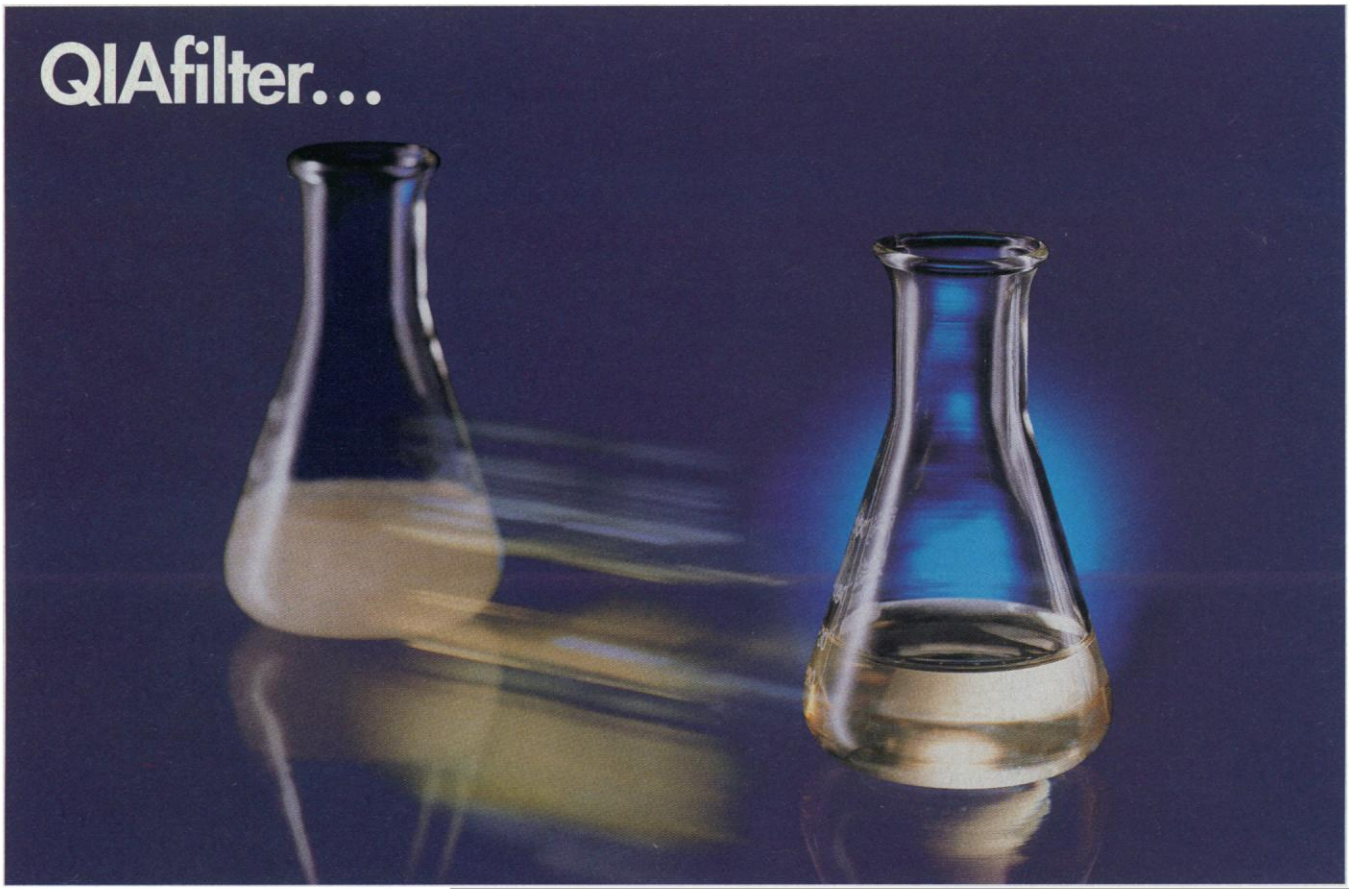

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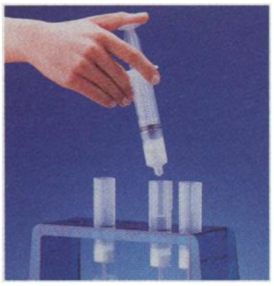

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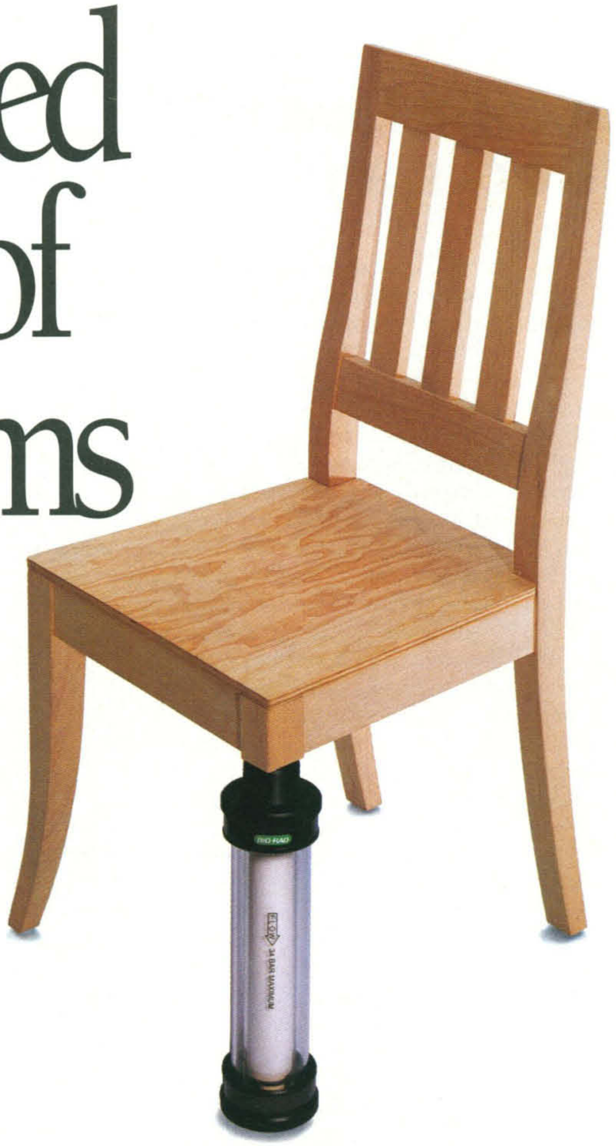

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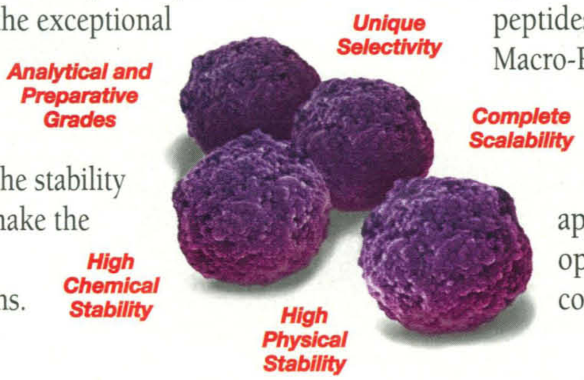

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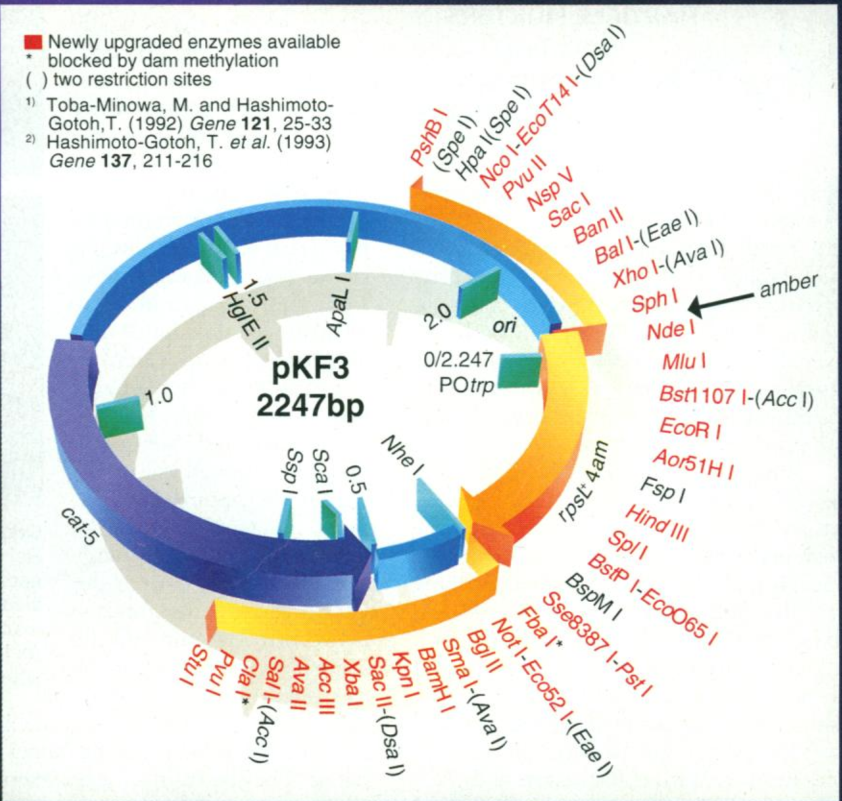

🟥 Newly upgraded enzymes available
* blocked by dam methylation
( ) two restriction sites

[1] Toba-Minowa, M. and Hashimoto-Gotoh, T. (1992) *Gene* **121**, 25-33
[2] Hashimoto-Gotoh, T. *et al.* (1993) *Gene* **137**, 211-216

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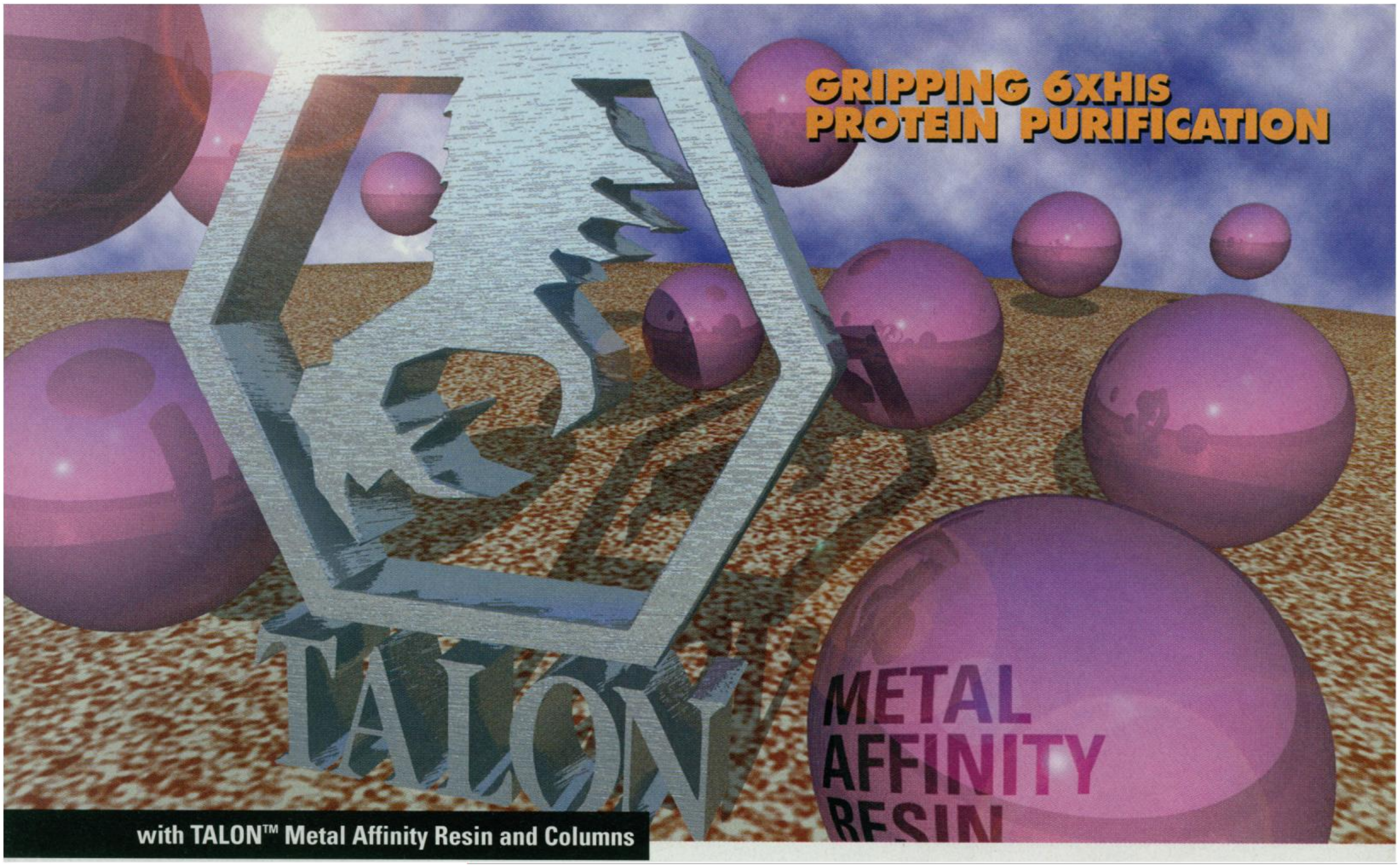
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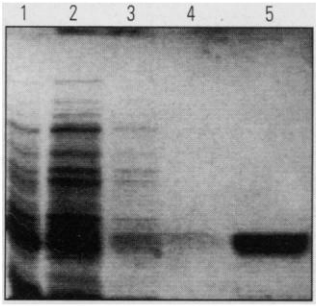
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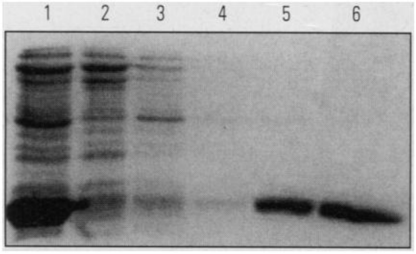
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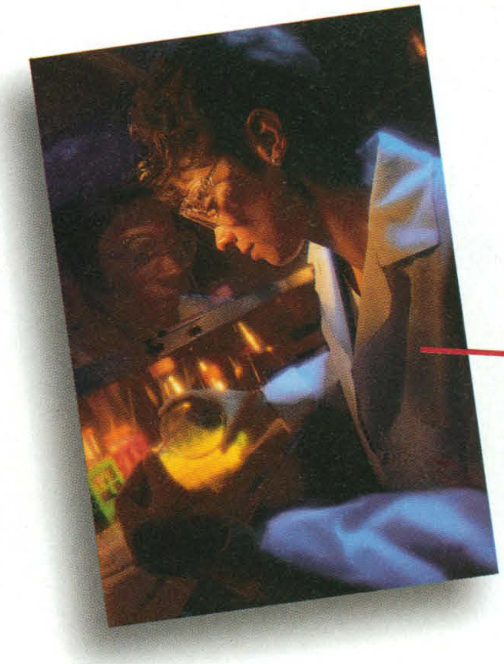


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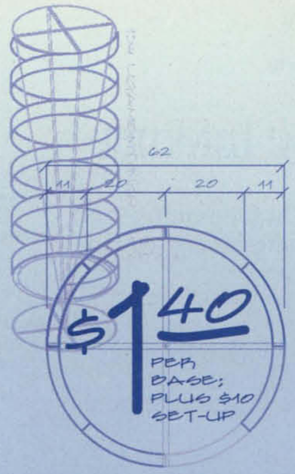

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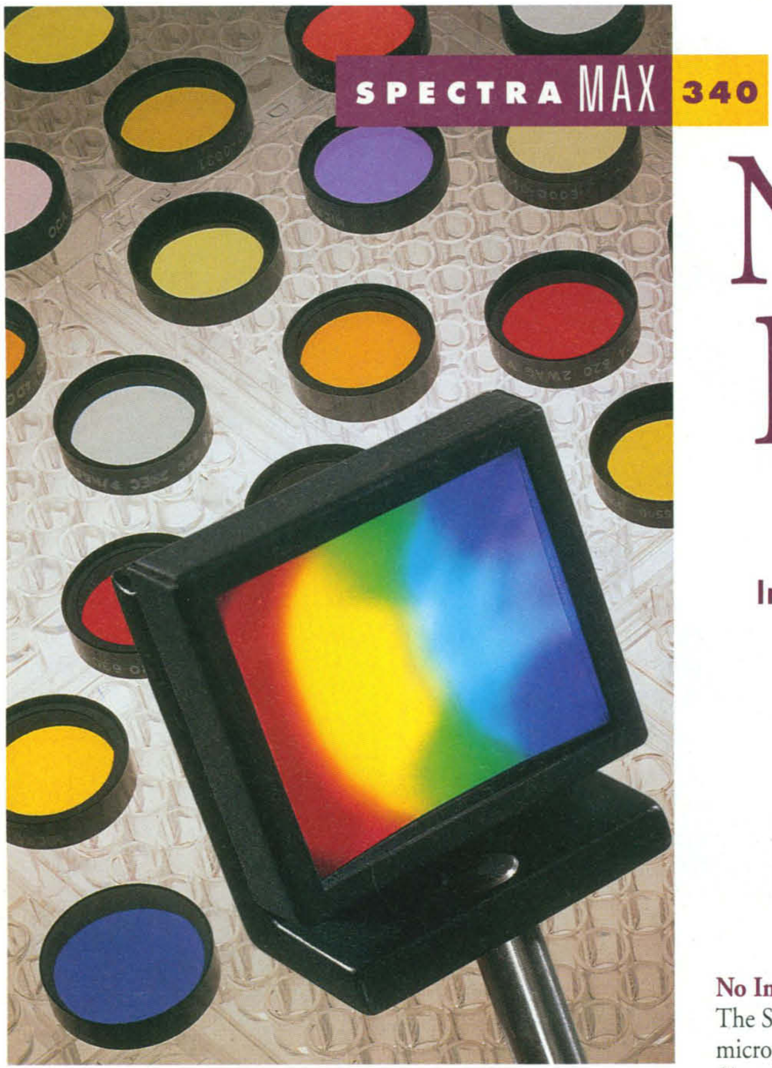
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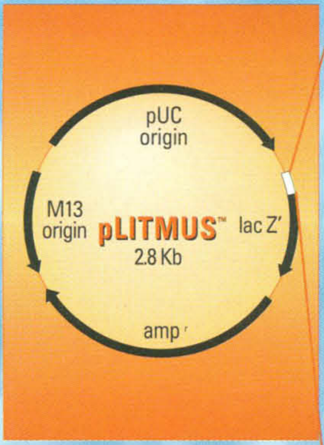
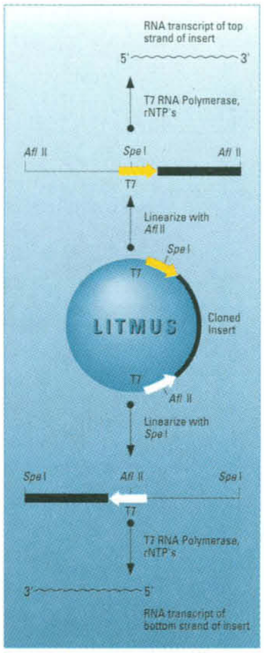


LITMUS 28	LITMUS 29
Spe I **T7** ↓	*Spe* I **T7** ↓
Bgl II	*Kpn* I-*Acc*65 I
Nsi I-*Ppu*10 I	*Sac* I
*Bss*H II	*Avr* II
*Bsi*W I	*Xba* I
Xho I	*Age* I
*Eco*R I	*Aat* II
Pst I	*Nco* I
*Eco*R V	*Hind* III
*Bam*H I	*Bam*H I
Hind III	*Eco*R V
Nco I	*Pst* I
Aat II	*Eco*R I
Age I	*Xho* I
Xba I	*Bsi*W I
Avr II	*Bss*H II
Sac I	*Nsi* I-*Ppu*10 I
Kpn I-*Acc*65 I	*Bgl* II
Stu I	*Stu* I
Afl II **T7** ↑	*Afl* II **T7** ↑

LITMUS 38	LITMUS 39
Spe I **T7** ↓	*Spe* I **T7** ↓
Apa I-*Bsp*120 I	*Sal* I
Mfe I	*Sph* I
*Ngo*M I	*Bsr*G I
Kas I	*Bsp*E I
Hind III	*Mlu* I
Pst I	*Eag* I
*Eco*R V	*Nhe* I
*Bam*H I	*Eco*R I
*Eco*R I	*Bam*H I
Nhe I	*Eco*R V
Eag I	*Pst* I
Mlu I	*Hind* III
*Bsp*E I	*Kas* I
*Bsr*G I	*Ngo*M I
Sph I	*Mfe* I
Sal I	*Apa* I-*Bsp*120 I
Stu I	*Stu* I
Afl II **T7** ↑	*Afl* II **T7** ↑

Polylinker cloning sites in LITMUS Vectors

And RNA Probe Production.



Simple To Optimize.

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#306-29	20 µg	LITMUS 29
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GENOME MAPS VI

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SCIENCE COORDINATOR
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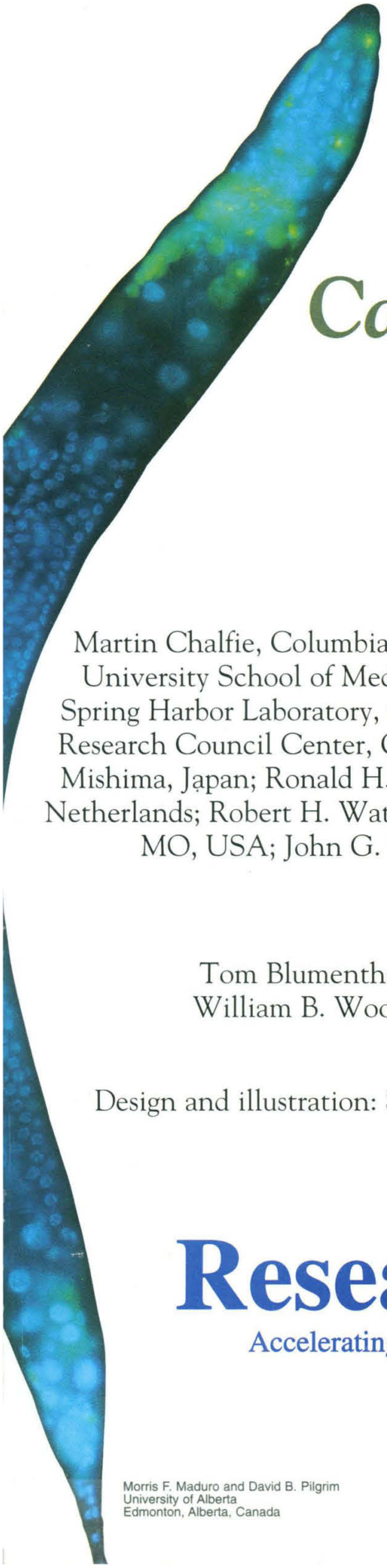

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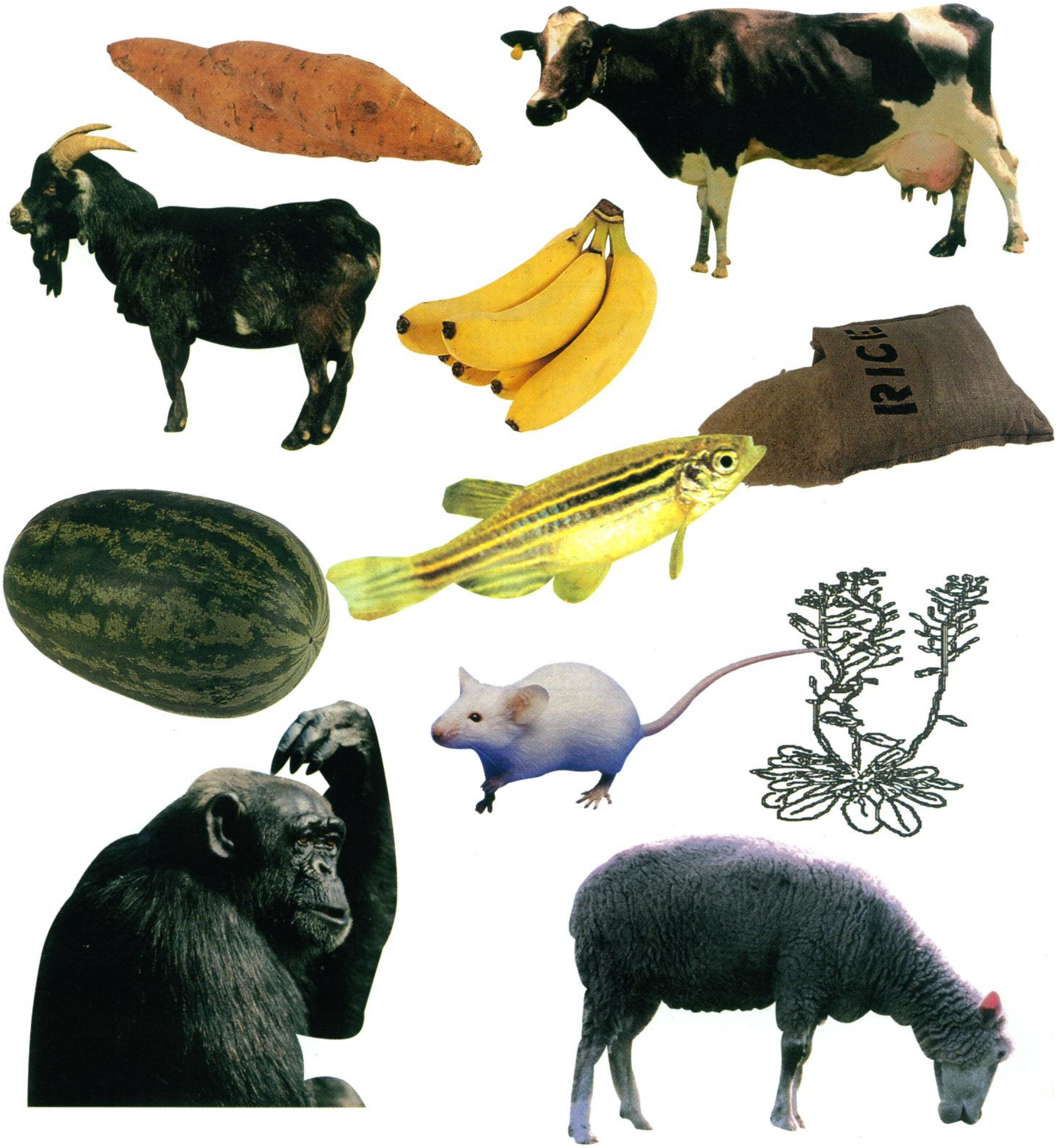
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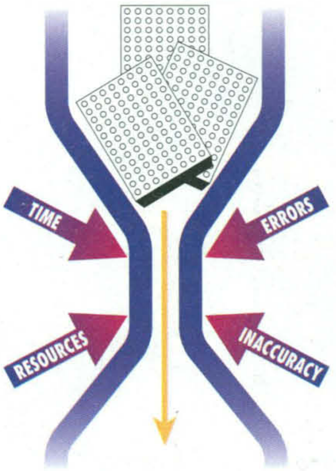
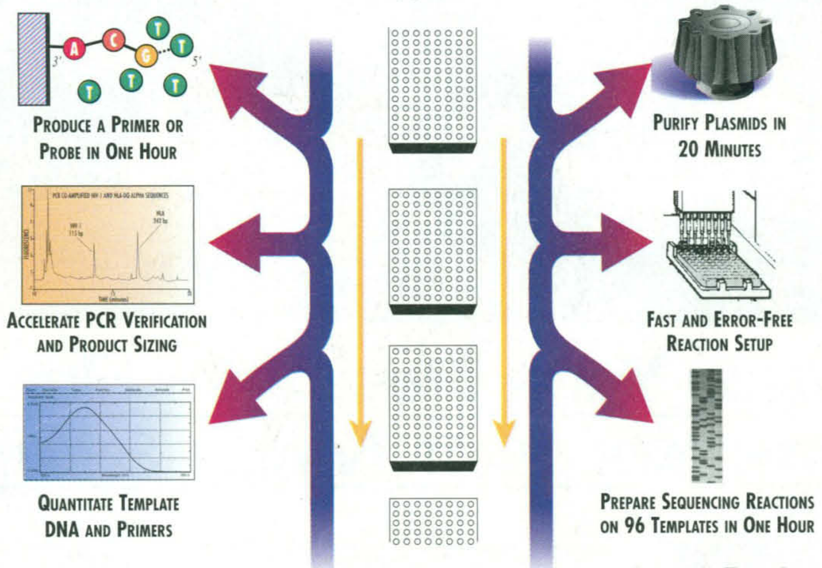


Research workflow can be restricted by any number of factors.



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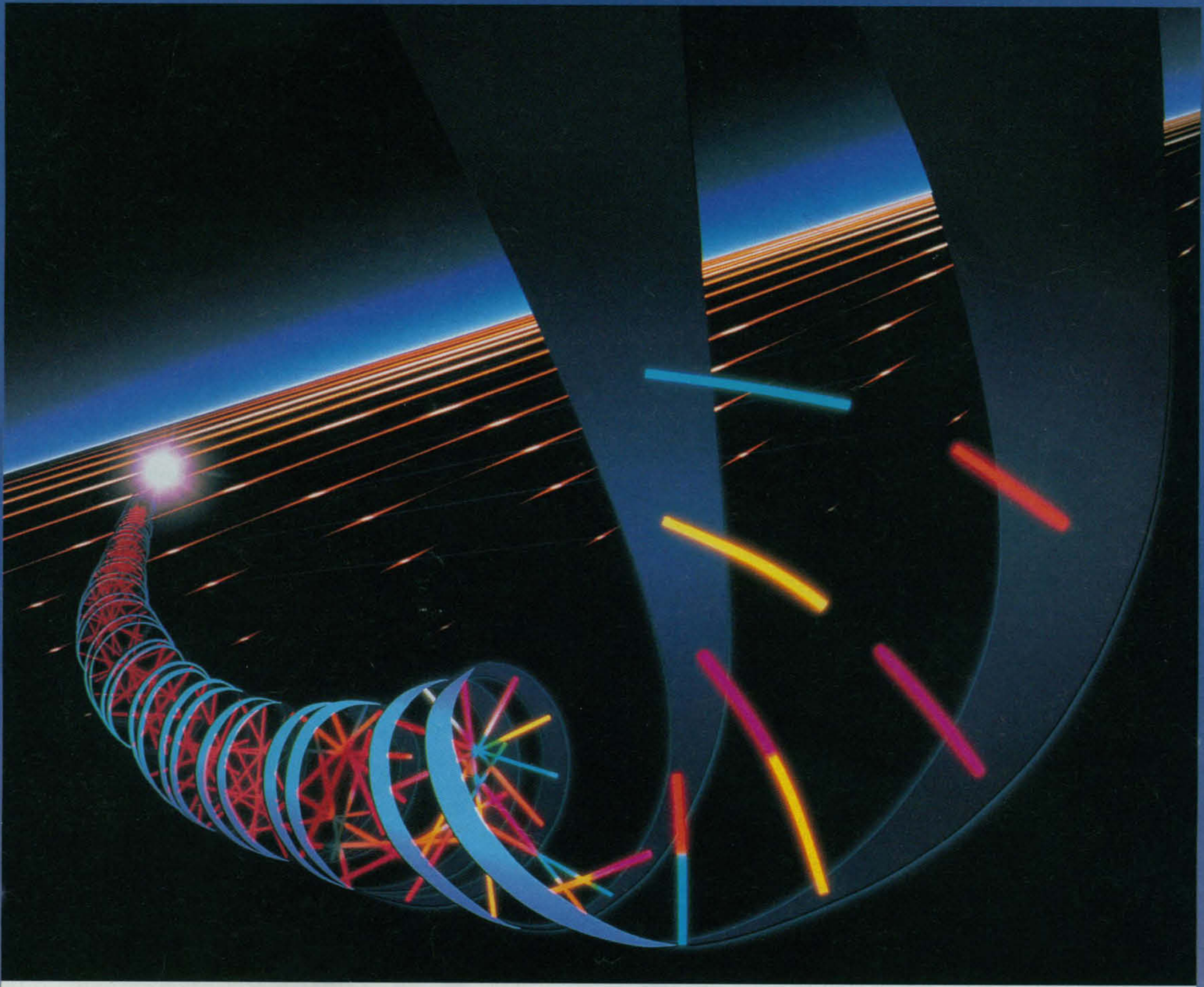

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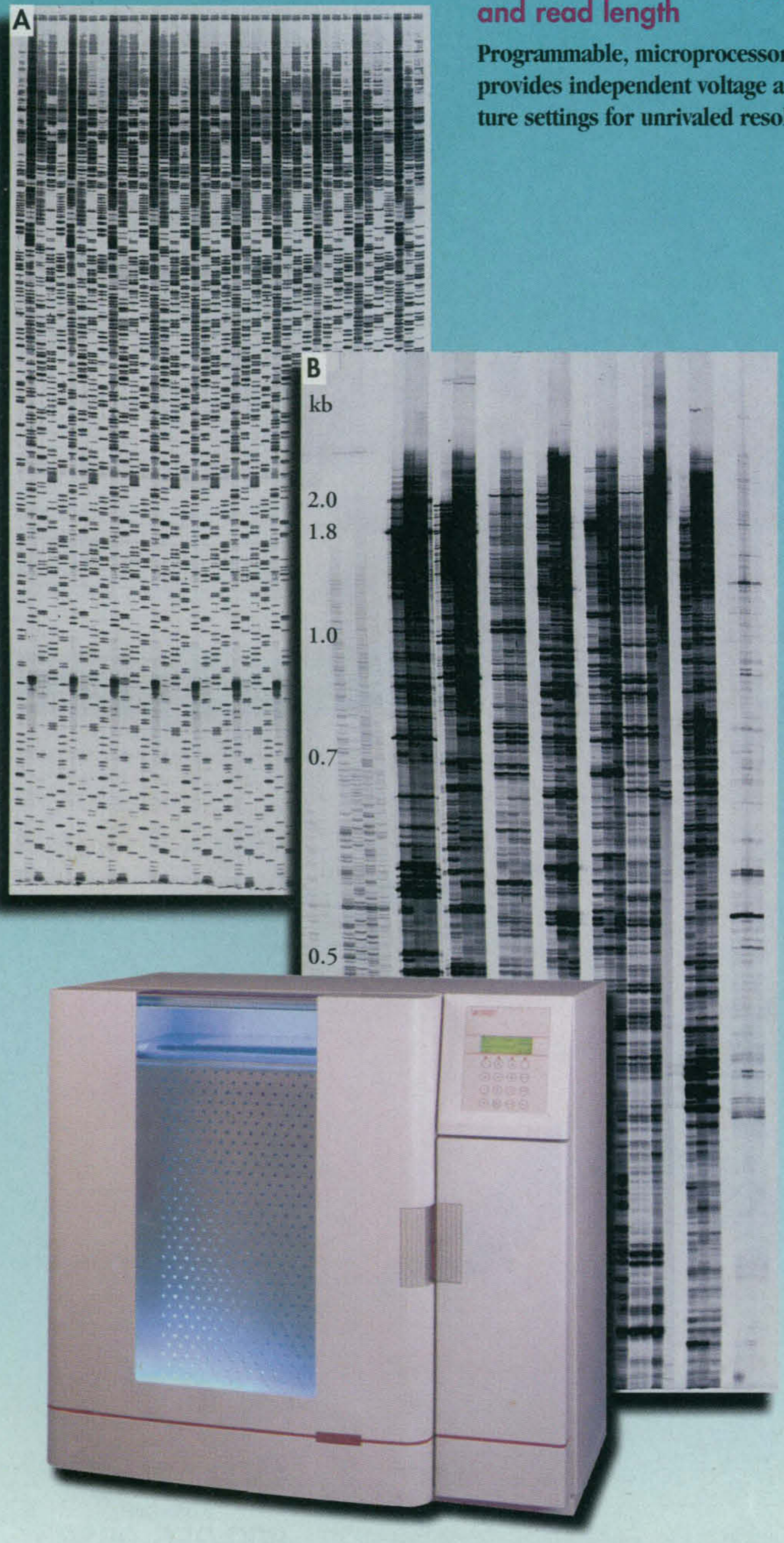

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Registration

Completely even cDNA fragment migration across entire gel assures accurate pattern determination across entire width of gel.

Recovery

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Panel A: pTTQ plasmid template samples run on **genomyxLR DNA Sequencer** (2 hr, 100 W, 3000 V, 50°C, 6% HR-1000™ denaturing gel).

Panel B: Large fragment DD-PCR samples run on **genomyxLR DNA Sequencer** (18 hr, 100 W, 703 V, 40°C, 6% HR-1000 denaturing gel). Lanes represent total RNA prepared from untreated and treated human cell line cultures. DD-PCR carried out with GenHunter RNAimage™ Kit. Data provided by Dr. Karen Lowe (Genomyx Corporation).

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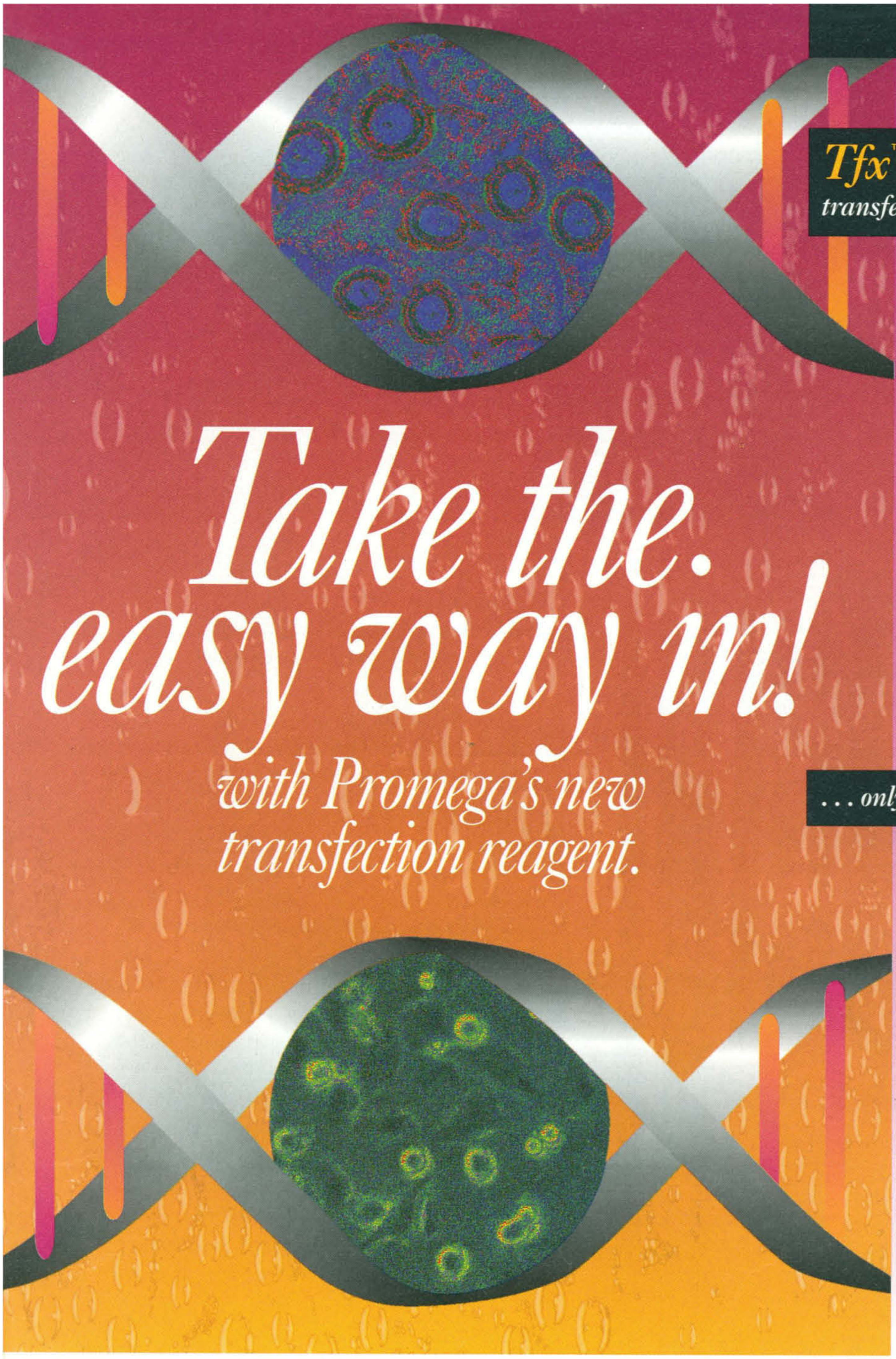

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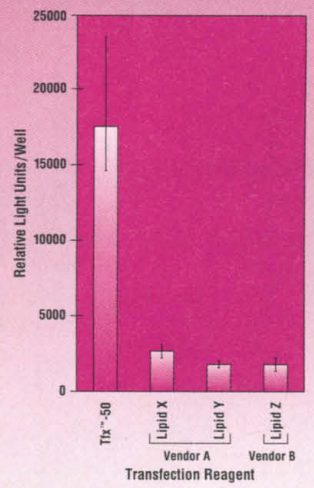

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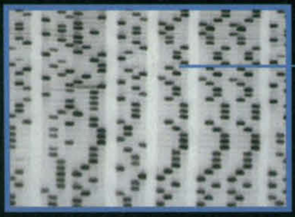

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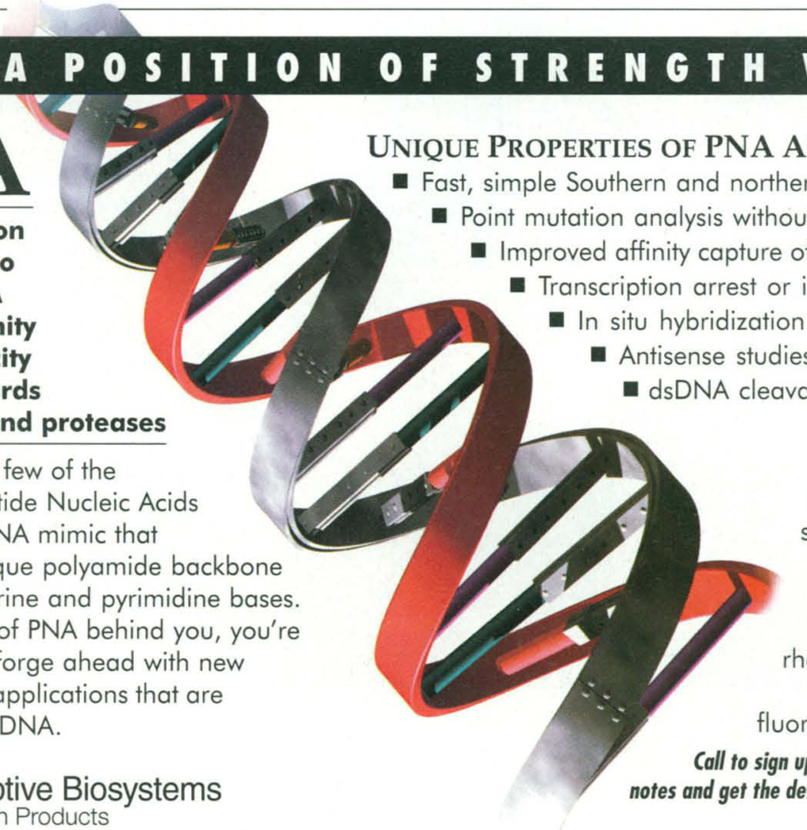

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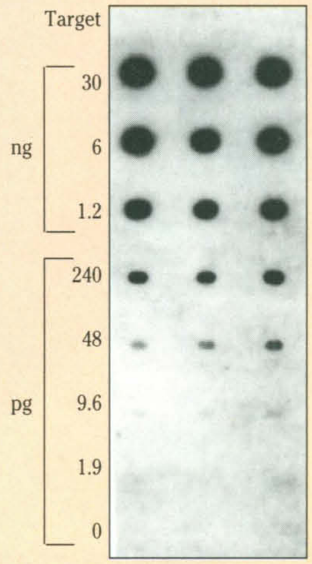

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† Psoralen-based probes are covered by US Patent Number 4,599,303 licensed from Naxcor, Menlo Park, CA.

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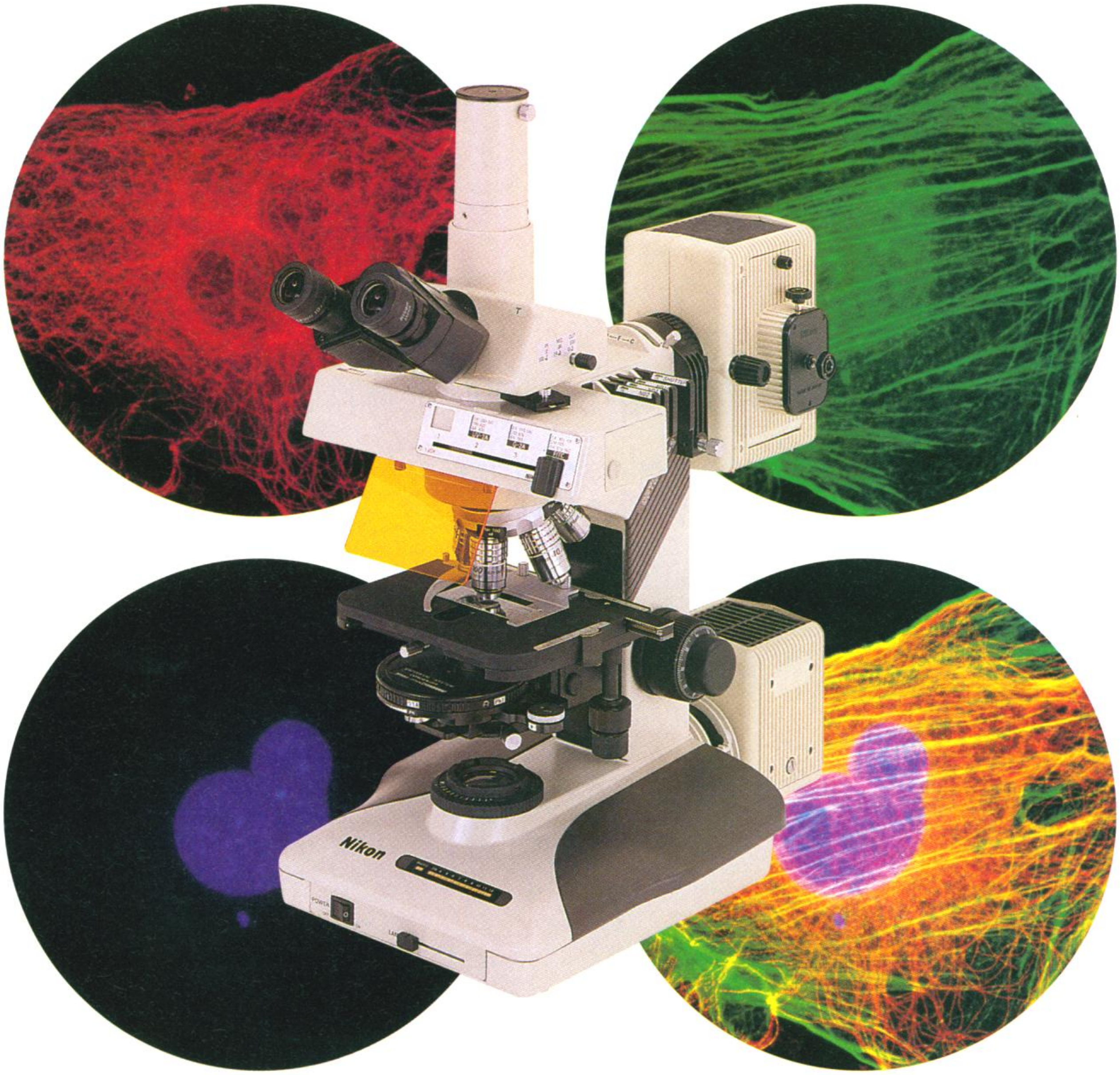
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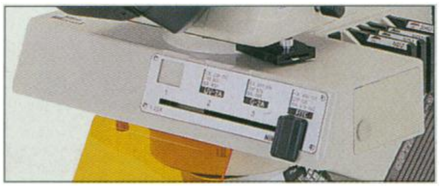

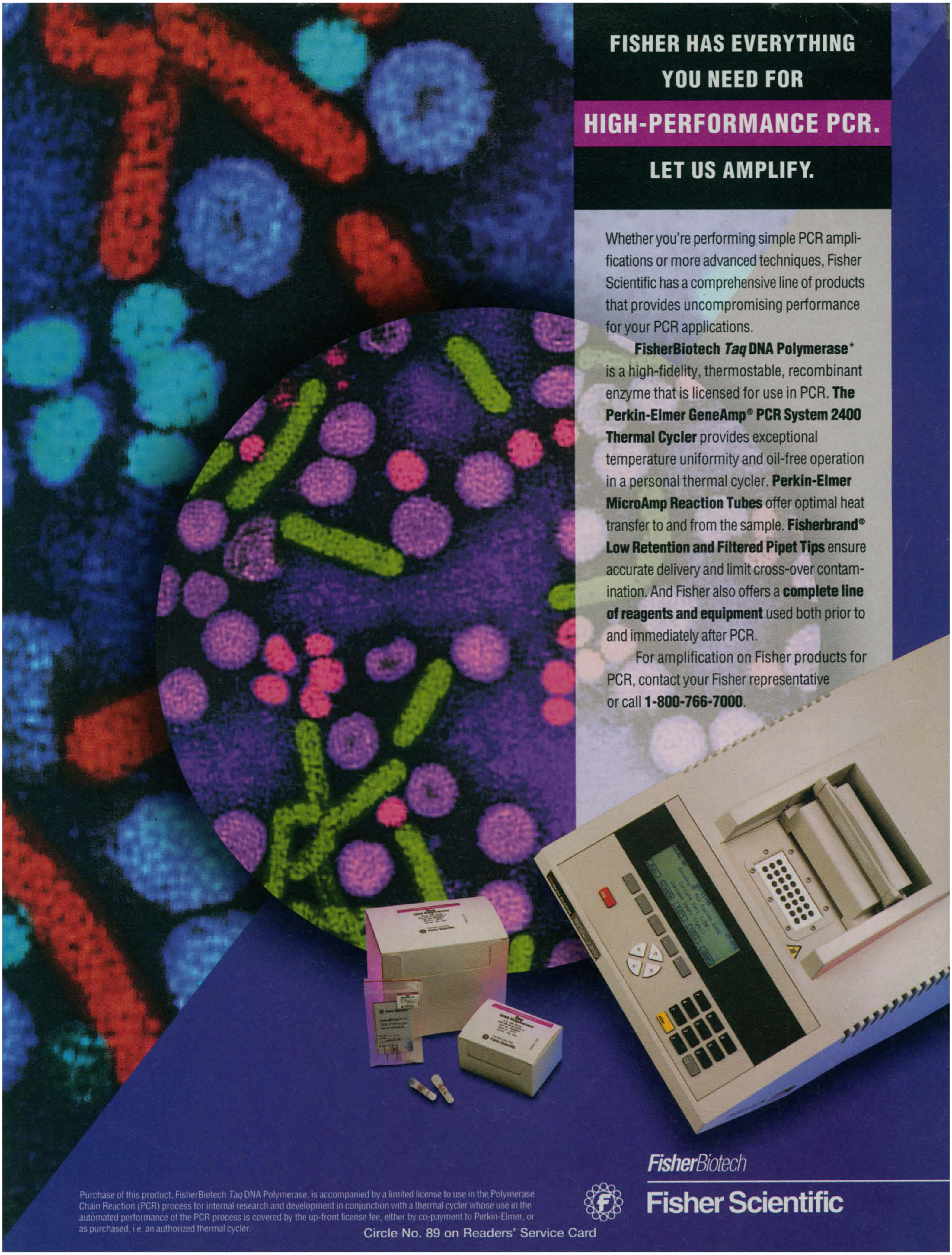

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TIGR
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FACULTY POSITIONS

The Institute for Genomic Research is a not-for-profit research institute with interests in structural, functional, and comparative analysis of genomes and gene products in viruses, eubacteria, pathogenic bacteria, archaea, and eukaryotes, both plant and animal, including humans (see Fleischmann, et al, *Science*, 269: 449-604, 1995, Lee, et al, *PNAS*, 92: 8303-8307, 1995, Adams, et al, *Nature*, 377 Supp: 3-174, 1995, and Fraser, et al, *Science*, this issue). The Institute has recently moved to its new campus in Rockville, MD, in the greater Washington, D.C. metropolitan area, and is close to the National Institutes of Health, Johns Hopkins University, The University of Maryland, and other research institutes and biotechnology companies. The new facility has over 60,000 sq. ft. of laboratory and office space and TIGR plans to expand its research faculty in the following areas:

MICROBIOLOGY.

Applicants are sought with a strong microbiology, molecular biology and/or molecular evolutionary background to lead a research effort in the discovery of new species of archaea and in the comparative characterization of their genomes, metabolism, and physiology. We are also seeking applicants to lead a research program concerned with the discovery and characterization of new species of marine micro–organisms utilizing our research vessel SEA TIGR, a converted 63 ft. North Sea trawler.

CELL BIOLOGY.

Whole genome sequencing of prokaryotes, archaea, and expressed sequence tag (EST) analysis of higher eukaryotes has revealed a large number of new genes with no counterparts in the nucleic acid or protein databases. We are interested in applicants with strong backgrounds in cell/molecular biology to characterize these new gene products, to examine their mode of expression and their structure, and to determine their role in cell metabolism and physiology.

Scientists who have a Ph.D., M.D., or equivalent degree with at least two years postdoctoral experience are encouraged to apply by submitting a cover letter, a *curriculum vitae*, including a bibliography, a statement of research interests, and the names of three references to:

Human Resources Department, The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850, Tel: (301) 838-0200, FAX: (301) 838-0208, e-mail: facpost@tigr.org

TIGR is an equal opportunity employer and encourages qualified women and minority candidates to apply

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SmithKline Beecham, a worldwide leader in pharmaceuticals research, currently has excellent opportunities for several scientists to join our newly organized Molecular Diagnostics Department. All candidates must have a comprehensive understanding of their discipline and relevant literature based on several years of post- graduate experience.

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Scientist/Senior Scientist

Using robotics, this individual will be responsible for synthesizing olignucleotides, automated sequencing of DNA and assisting in arraying clones. Results will be presented at departmental, team and divisional meetings, reflecting accuracy and adherence to SOPs. Candiates must have an B.S./M.S. plus specialist technology/skills, and the ability to apply new techniques and adapt them to relevant research, and be able to apply own research efforts to Program/Feasibility Study goals. Refer to Job Code H0435.

Scientist/Senior Scientist

The successful candidate will independently perform experiments in advanced genetics aimed at constructing and analyzing cDNA libraries, perform subtraction techniques to construct libraries enriched for messages specific to tissues or disease states, develop and evaluate methods for differentially labeling probes in analysis of these cDNA libraries, and evaluate these libraries using high density arrays of clones. Candidates must have a B.S./M.S. plus specialist technology/skills, be able to apply new techniques and adapt them to relevant research, and be able to apply own research efforts to Program/Feasibility Study goals. Refer to Job Code H0434.

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Research Associate (Job #1080) - Grain Traits. The successful candidate will join a team involved in optimizing gene expression in transgenic plants. Applicants must have significant skills in nucleic acid analysis (including DNA/RNA purification, sequencing, cloning, PCR, Southerns and Northerns) and experience with computer analysis programs. Good organizational skills and the ability to interact effectively in a broad multidisciplinary environment will be important. Requirements: BS with 4 years of directly related experience, or an MS with 2 years of experience.

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PLANT MOLECULAR BIOLOGIST- Candidate's expertise should involve the use of molecular and cellular approaches to solve fundamental problems in plant biology. Candidates will be expected to develop a vigorous research program and assume teaching responsibilities in both undergraduate and graduate level courses in plant molecular biology and general plant biology.

Scientists with a Ph.D. and postdoctoral experience are encouraged to apply for either position by sending a curriculum vitae, statement of research interest and arrange for three letters of reference to be sent by December 1 to: **Chairperson (Specify specific position), School of Biological Sciences, 348 Manter Hall, University of Nebraska, Lincoln, NE 68588-0118.** Positions will be open until a suitable candidate is selected. *UNL is committed to a pluralistic campus community through AA/EO and is responsive to the needs of dual career couples. We assure reasonable accommodation under ADA; contact Dr. T. Jack Morris for assistance.*

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- Extensive background in cell and molecular biology
- Ph.D. in life sciences with post doctoral and industrial experience in biological assay development

Please send your resume to **Vical, Inc. Human Resources, 9373 Towne Centre Drive, Suite 100, San Diego, CA 92121 or fax to (619) 453-3452.**

EOE

Faculty Positions in Neurobiology

University of Maryland School of Medicine
Department of Anatomy

The Department of Anatomy is undergoing major expansion and rebuilding. New faculty are being recruited in neurobiology. Positions are available at all ranks.

The Department is located in a newly opened building. Significant expansion of research resources is underway, including core laboratories in molecular biology, tissue culture, neuroanatomy, imaging, and neurophysiology.

Successful candidates will have a Ph.D. or equivalent, outstanding ability in teaching, and exceptional achievement in their field of research, including the potential to attract external funding. Investigators in the Department use approaches ranging from molecular biology to behavior but the common focus is understanding the *organization, function* and *development* of neural networks. We particularly encourage applicants investigating the:

- interplay of gene expression and neural activity in neural network development.
- neurobiological bases of learning and memory.
- development and functional organization of chemosensory systems.

The Department teaches a 9.5 week course - "Structure & Development" - in the medical school curriculum. New faculty are expected to participate 3-5 weeks in this team taught course. Graduate teaching is also encouraged.

For best consideration, applications should be received before February 1, 1996. Candidates should send a C.V., summary of research accomplishments and goals, and the names of 3-5 individuals from whom recommendations may be obtained to:

Dr. David V. Smith
Chair, Faculty Search Committee
Department of Anatomy
University of Maryland School of Medicine
655 West Baltimore Street
Baltimore, MD 21201-1559

The Department is eager to diversify its faculty. We encourage minorities and women to apply. The University of Maryland is an AA/EEO/ADA employer.

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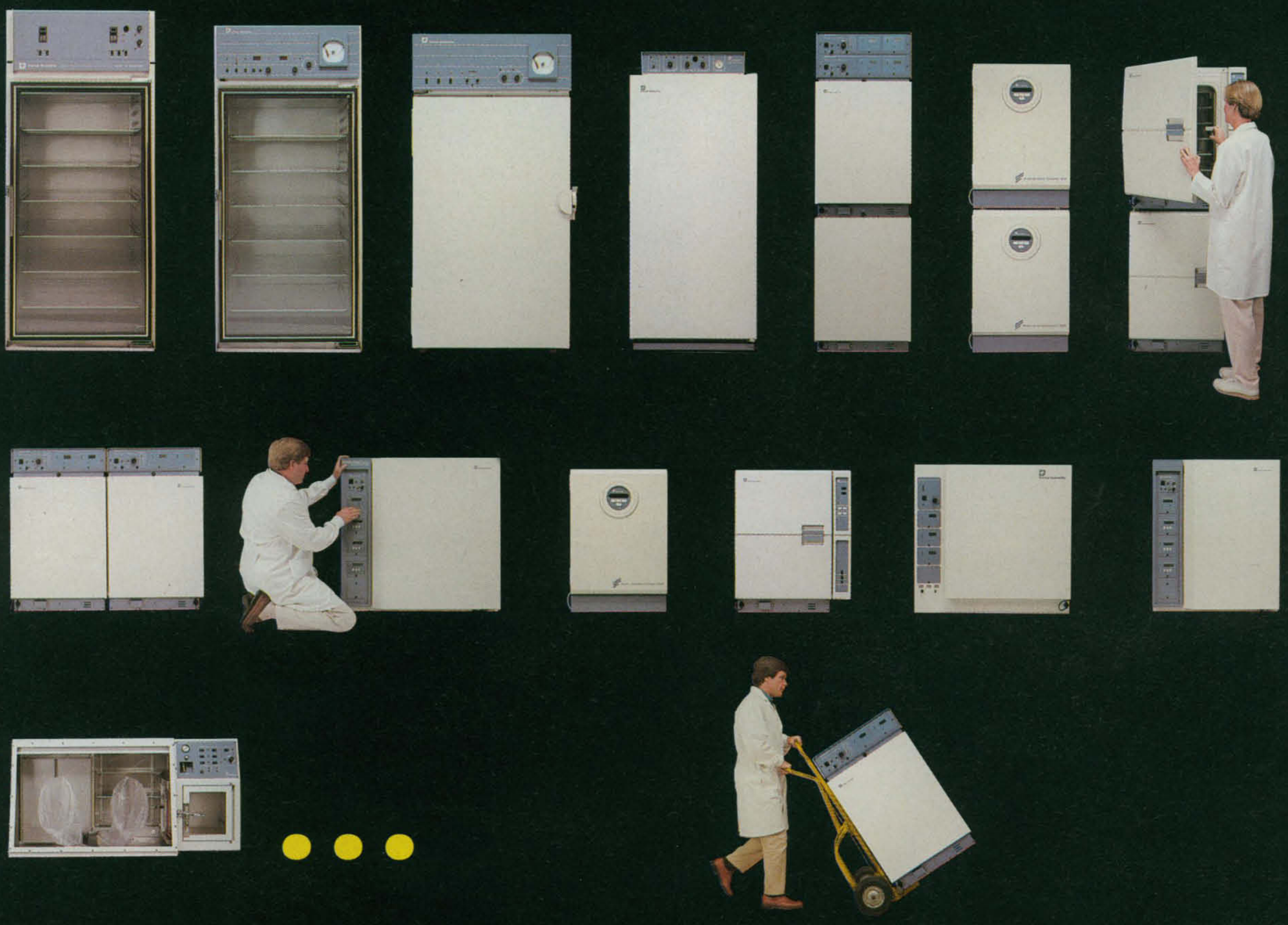

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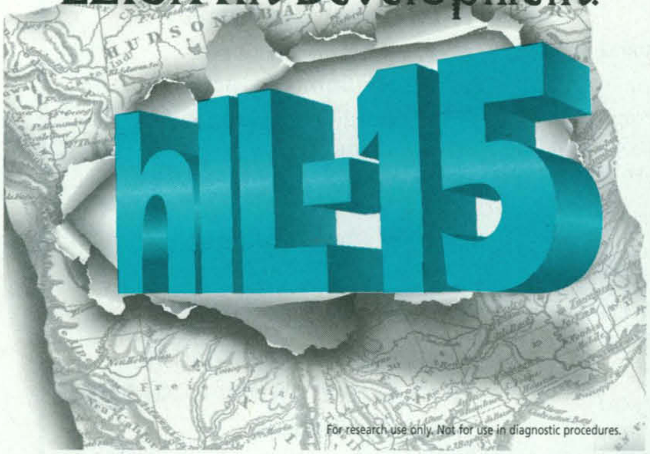

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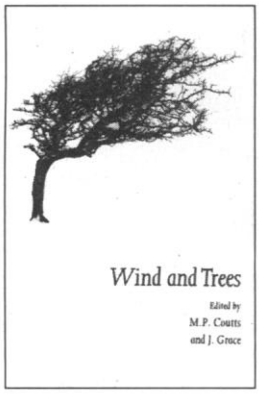
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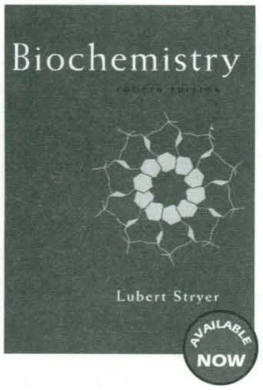

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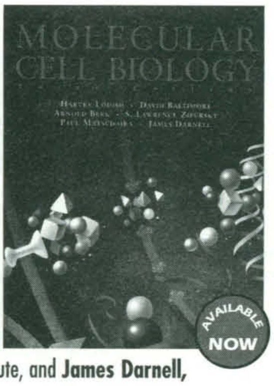

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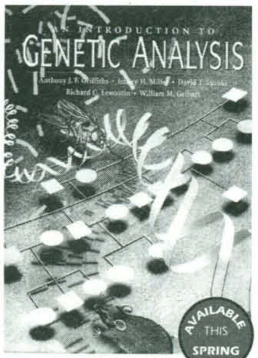

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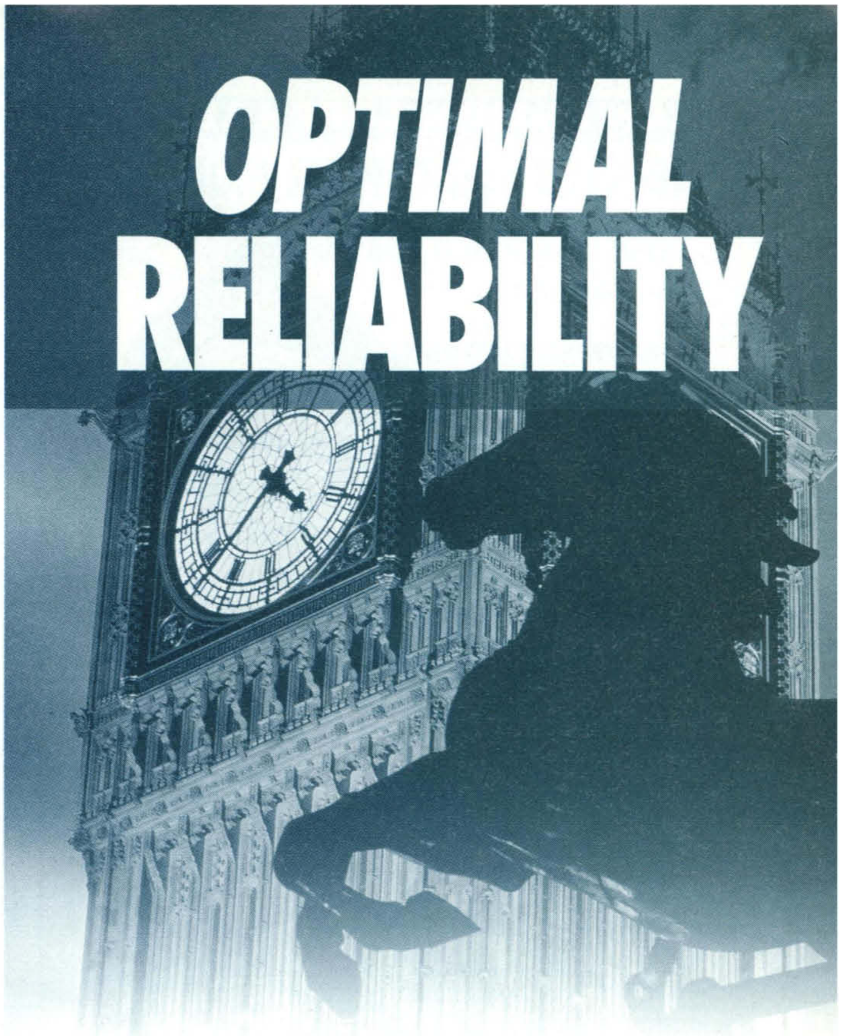

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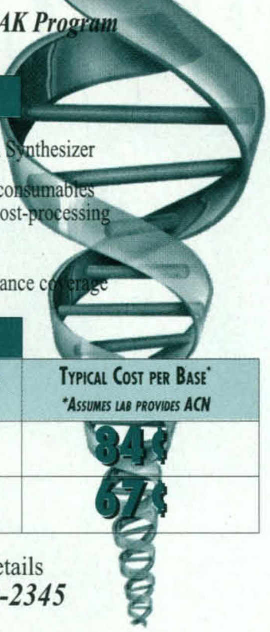

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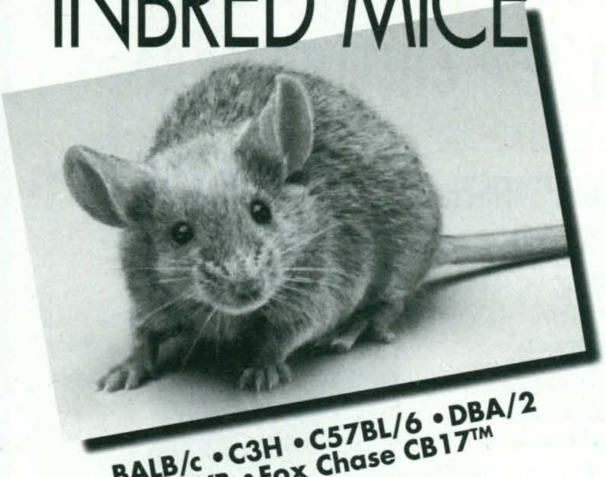

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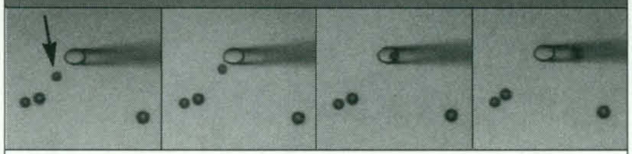

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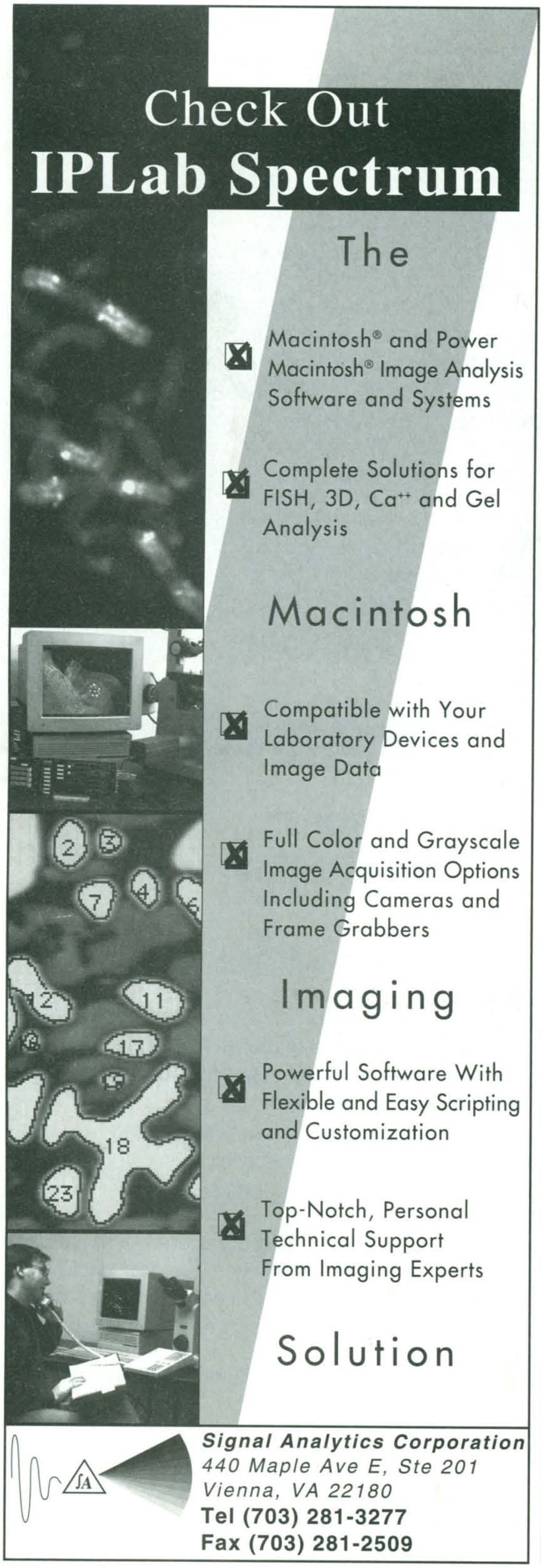

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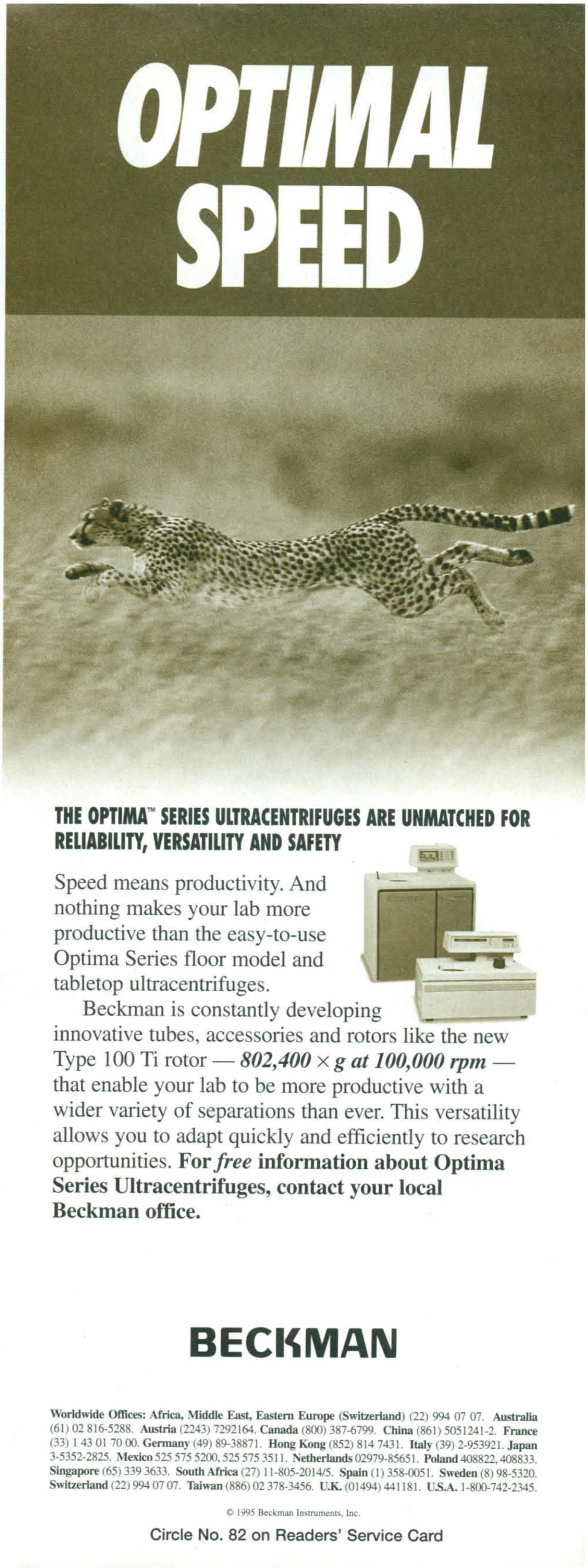

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