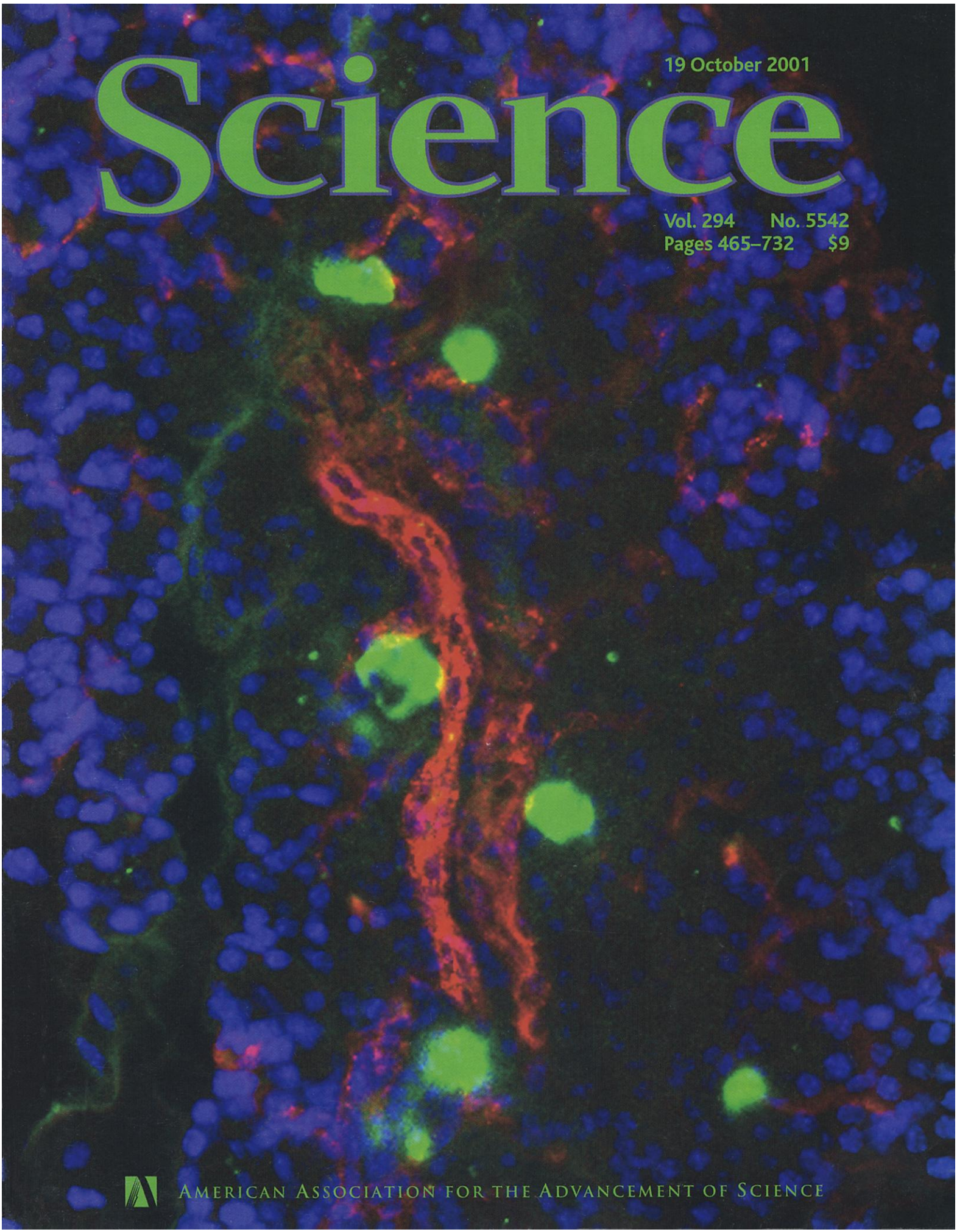

19 October 2001

Science

Vol. 294 No. 5542
Pages 465–732 $9

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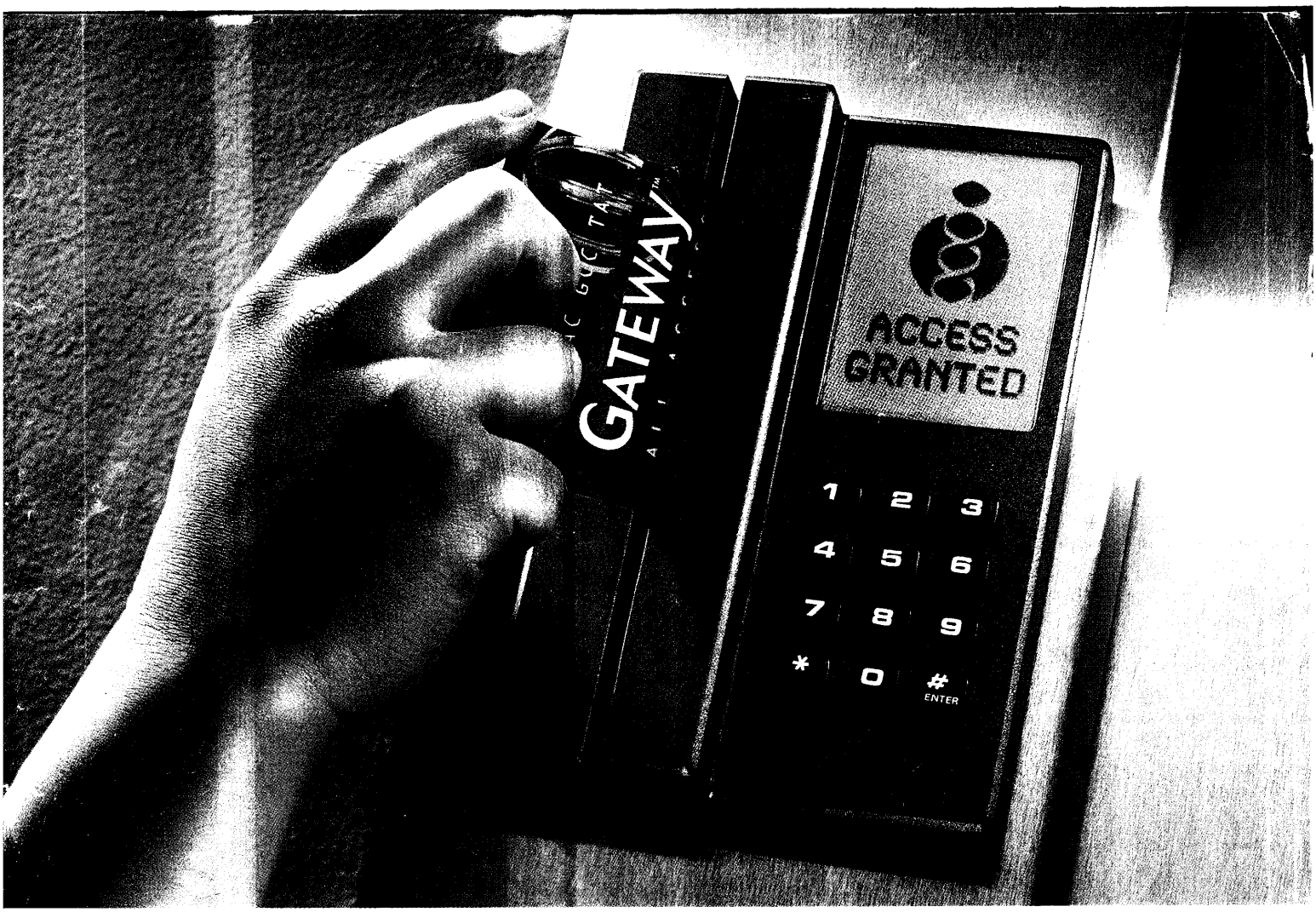

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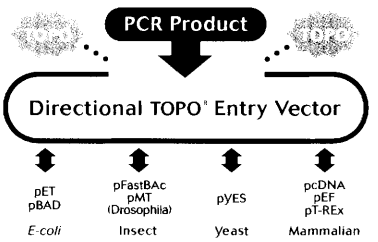

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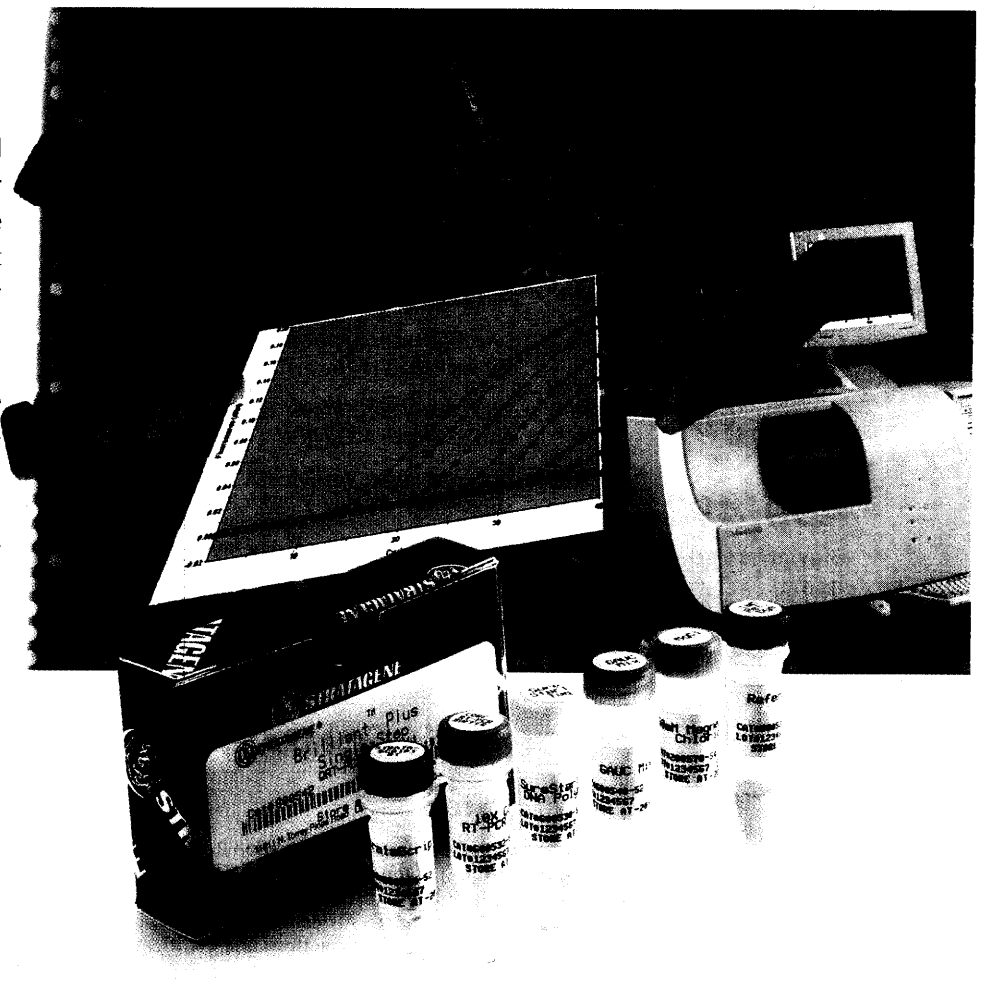

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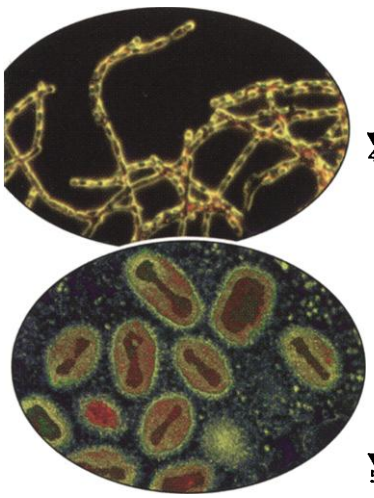

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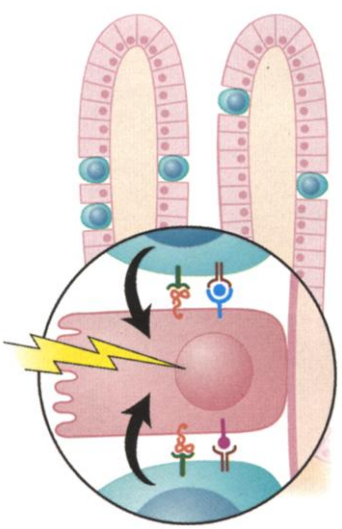

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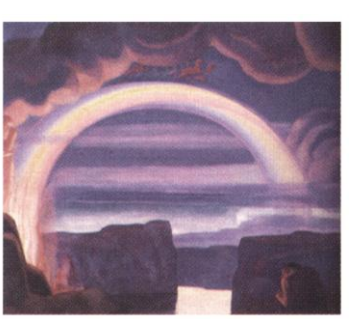

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Rainbows in art and science

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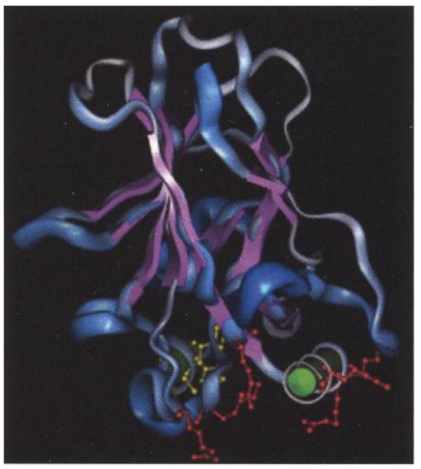

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A p53 homolog in worms

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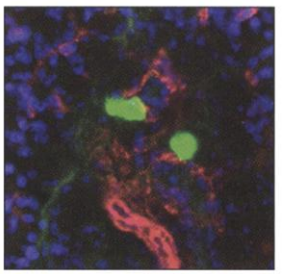
Cloud forests at risk



COVER 564

Confocal image showing the close association of immature pancreatic islets of Langerhans (green fluorescence) with blood vessels (red fluorescence) during embryogenesis; cell nuclei are blue. Blood vessels induce the formation of the islets during development, which leads to the intimate contact that allows islets to secrete insulin directly into the bloodstream in response to blood glucose levels. [Image: Ondine Cleaver]

New on *Science* Express

Clustering on both sides of the synapse

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CONTENT HIGHLIGHTS AS OF 19 OCTOBER 2001

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TECHNICAL COMMENTS

Variation in Food Supply, Time of Breeding, and Energy Expenditure in Birds

One effect of global warming is to hasten the availability of food for birds each year, and many species have responded by advancing their breeding dates. By measuring metabolic rates and life-spans in bird populations with variable breeding times, Thomas *et al.* (Reports, 30 March 2001, p. 2598) concluded that the excessive parental metabolic effort resulting from mismatching of breeding time to peak food supply lowers reproductive efforts in adult birds. In a comment, Verhulst and Tinbergen protest these conclusions, suggesting that the Thomas *et al.* report suffers from "the problem of interpretation" in comparing persistence of birds in populations and that "only experiments can demonstrate a causal relationship between timing of breeding" and "any other parameter." In response, Thomas *et al.* clarify their original presentation of "a unique natural experiment," and state that their data were "consistent with theory predicting tradeoffs between current effort and future reproductive prospects."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/294/5542/471a

SPECIAL FEATURE

Celebrating the 2001 Nobel Physics Laureates

Classic *Science* papers, news, and commentary on the accomplishments of prizewinners Cornell, Wieman, and Ketterle—as well as many others—in the field of Bose-Einstein condensates. www.sciencemag.org/feature/data/nobelprize/2001/physics.shtml

SCIENCE EXPRESS www.sciencexpress.org

Bose-Einstein Condensation of Potassium Atoms by Sympathetic Cooling G. Modugno *et al.*

502 A Bose-Einstein condensate of potassium atoms is realized by a technique of sympathetic cooling, whereby a different atomic species, rubidium, is used to cool the potassium atoms through favorable collisions.

Rapid Increase in Clusters of Presynaptic Proteins at Onset of Long-Lasting Potentiation I. Antonova *et al.*

Short-term LTP, a cellular correlate of fast synaptic plasticity, is accompanied by surprisingly rapid changes in synaptic organization in both presynaptic and postsynaptic cells.

science's next wave www.nextwave.org

career resources for scientists

US: Job Search Bliss—A Happy Job Seeker Is a Successful Job Seeker D. Jensen

In *Tooling Up*, advice about how to gear up for the job search, and keep stress to a minimum, when the rest of the world seems to be going out the window.

Singapore: Career Opportunities for Ph.D.'s J. Wong

What are the best job options for Singapore's Ph.D.'s?

Germany: The Challenges of Intensity and Excellence E. von Ruschkowski

The University of Göttingen's collaborative neuroscience and molecular biology programs attract international students and scholars—but how do they get used to life in Germany?

UK: The Secrets of Research Success P. H. Dee

To our *Yours Transferably* columnist, the secret of developing into an independent researcher is being selective about what you communicate to your peers.

Canada: Ontario's Biotech Community L. McKarney

In this installment of *Under One Roof*, we examine Ontario's emerging biotech clusters and how government funding initiatives are supporting industry expansion.

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News Focus: Get Some Glasses, Ump! K. Miller

Long judged unfairly, research on aging might finally get its own NIH study sections.

Neurodegenerative Disease Case Study: Dementia with Lewy Bodies H. Posner, S. Chin, K. Marder

Patients mistake inanimate objects for people.

science's stke www.stke.org

signal transduction knowledge environment

Perspective: Highlights of Alternative Splicing Regulation Session—Yes, No, Maybe: A History of Paradigm Shifts T. A. Cooper

New insights into the proteins that dictate exon inclusion or exclusion.

Perspective: Insulin Signaling—Lessons from the *Drosophila* Tuberous Sclerosis Complex, a Tumor Suppressor J. Montagne, T. Radimerski, G. Thomas

Connections between cell size, the cell cycle, and the tuberous sclerosis complex.

Connections Map: The Jasmonate Biochemical Pathway Pathway Authorities: E. E. Farmer and R. Liechti

A pathway describing the biosynthesis of the jasmonate plant signaling molecules.

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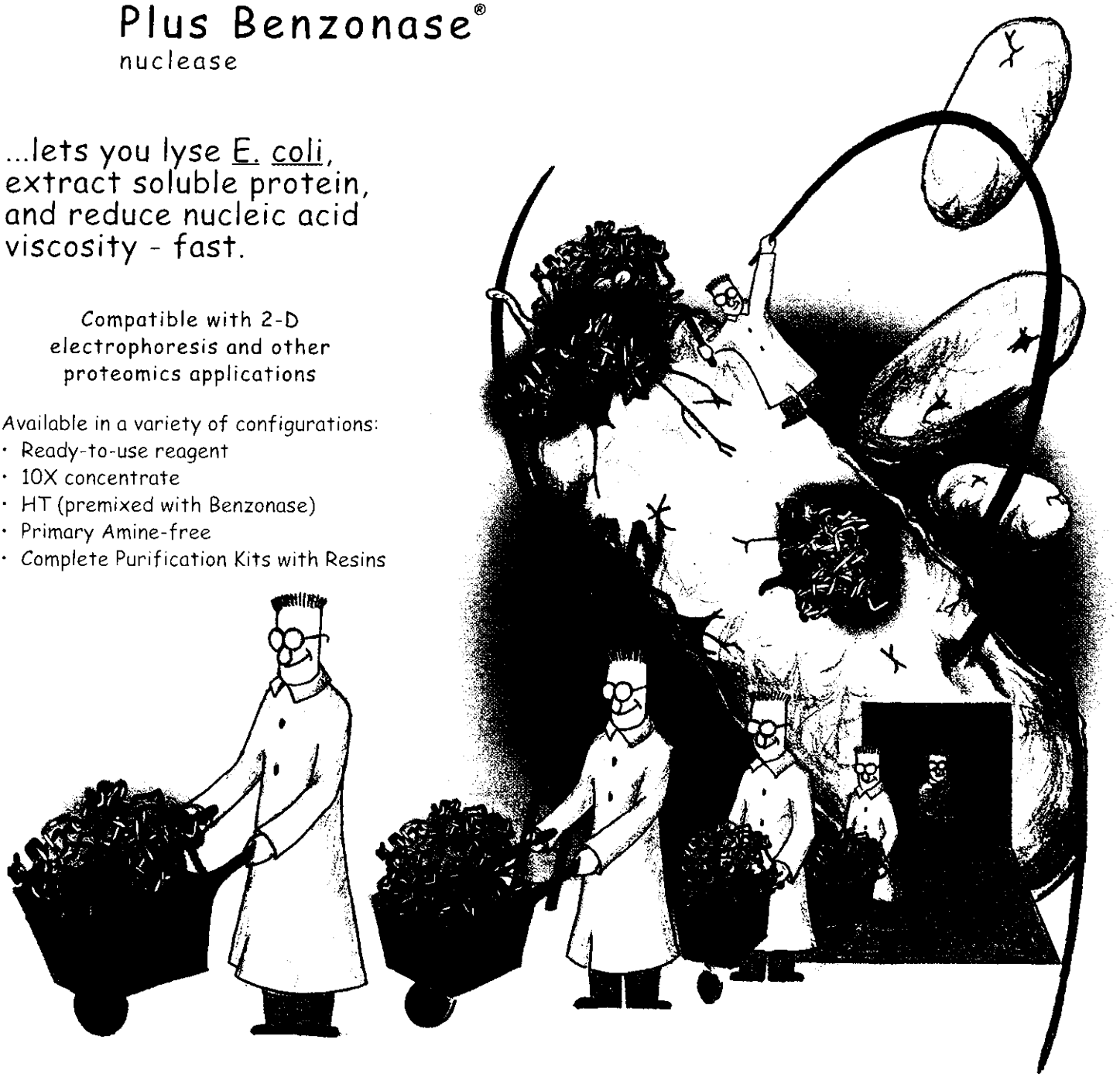

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THIS WEEK IN Science

edited by Phil Szuromi

Ion-Gated Carrier Transport in DNA

Many experimental and theoretical studies have been aimed at elucidating the mechanism for the transport of electrons and holes through DNA. Barnett *et al.* (p. 567) have now used molecular dynamics simulations and first-principles structure calculations to show that even the hydrated counterions that interact with phosphate groups can exert a large effect on the rate of hole transport. Inclusion of the hydrated ion favors correlated motions of the helix that facilitate transport. Experimental studies revealed that electron transport rates are reduced in DNA strands containing uncharged methylphosphonate bridges.

574 Crustal Shortening and Extrusion

The major continent-to-continent collision of India into Eurasia has created the high-standing Tibetan plateau, major fault zones, and a natural laboratory for a crustal deformation study. Wang *et al.* (p. 574) combine 10 years of geodetic data into a comprehensive kinematic model of crustal motion throughout China. They find that 90% of the deformation is taken up in crustal shortening to create the plateau and most of the remaining 10% is taken up by eastward extrusion and rotation of the crust into southeastern China.

Stratospheric Effects on Weather

Vigorous circulation in the troposphere makes predicting the weather more than 1 week in advance difficult. The stratosphere, which lies immediately above the troposphere, is far more stable but is not often considered to have much effect on surface weather patterns. Baldwin and Dunkerton (p. 581, see the news story by Kerr) present evidence that strong variations in stratospheric circulation at altitudes above about 50 kilometers can descend into the troposphere and affect the weather there. These events may be followed by months during which patterns of surface pressure are systematically altered, as reflected in large-scale atmospheric pressure patterns called the Arctic Oscillation and the North Atlantic Oscillation. This effect may allow storminess and storm tracks to be predicted more accurately.

Lemur Origins

Small, nocturnal lemurs are divided into two extant orders, the Lemuriformes, isolated in Madagascar, and the Lorisiformes, found in Africa and Asia. The fossil and molecular record of how and when these orders may have evolved is poorly sampled and contradictory. Marivaux *et al.* (p. 587) have discovered a lemuriform fossil, *Bugtilemur mathesoni*, in Oligocene sand deposits in Pakistan. Diversification of lemuriforms outside of Madagascar thus occurred at least 30 million years ago, which is more than 50 million years after the continental breakup of Madagascar from India. Hence, the lemuriforms either found land bridges from Madagascar to Asia or they evolved in Asia before the continental breakup.

Making Better Contacts

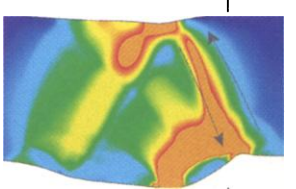
Studies of single-molecule conductivity yield a wide range of values, in part because of the difficulties of making reliable contacts to individual molecules. Cui *et al.* (p. 571; see the Perspective by Hipps) now describe a method for covalently attaching gold nanoparticles to alkane thiol molecules self-assembled on a gold surface. Current-voltage curves are observed that can be attributed to making contact with one to five molecules, and these scale as multiples of the single contact curve. The results are with a factor of 6 of the theoretically expected conductivity.

Out of the Clouds

Tropical deforestation has obvious primary costs, such as reduced carbon sequestration, loss of habitat, decreased biodiversity, and increased erosion, but what are the secondary costs? Lawton *et al.* (p. 584) use satellite imagery of clouds and regional atmospheric modeling to show that clearing lowland forests in Costa Rica alters the surface energy budget enough to diminish dry season cloudiness, which in turn deprives downwind montane cloud forests of the moisture that they need to survive.

Starting Subduction

How does a tectonic plate bend and break to initiate a subduction zone? Regenauer-Lieb *et al.* (p. 578) developed a nonlinear elasto-visco-plastic finite element model to examine the initiation of subduction. In their model, a sedimentary load was piled onto the lithosphere (similar to a passive continent-ocean margin), and the water content of the lithosphere was varied. The addition of water promoted the development of a narrow shear zone through the lithosphere that started the subduction process.



CREDIT: REGENAUER-LIEB *ET AL.*

Sex and Fitness

The experimental evaluation of the adaptive significance of sexual recombination has been hampered by inconsistent experimental results. Rice and Chippindale (p. 555; see the Perspective by Lensky) present a set of *Drosophila* experiments that directly compared nonrecombining and freely recombination replicates. In the nonrecombining population, the variability among lines was very large, as expected, but the average increase in the favored allele was slight and seemed to saturate after about eight generations. In the recombining strain, the fitness continued to increase throughout the experiment.

Blood Vessels Originating Organs

Blood not only sustains and oxygenates organs—two reports show how blood vessel endothelium plays important roles in organ development (see the Perspective by Bahary and Zon and the 28 September news story by Seydel). Lammert *et al.* (p. 564; see the cover) found that the endothelium supplies signals that are necessary for pancreatic differentiation and insulin expression. Removal of the dorsal aorta in *Xenopus* embryos led to a failure in insulin expression, whereas vascularization in transgenic mice in the posterior foregut led to ectopic islet formation and insulin expression. Matsumoto *et al.* (p. 559) used

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CONTINUED ON PAGE 475

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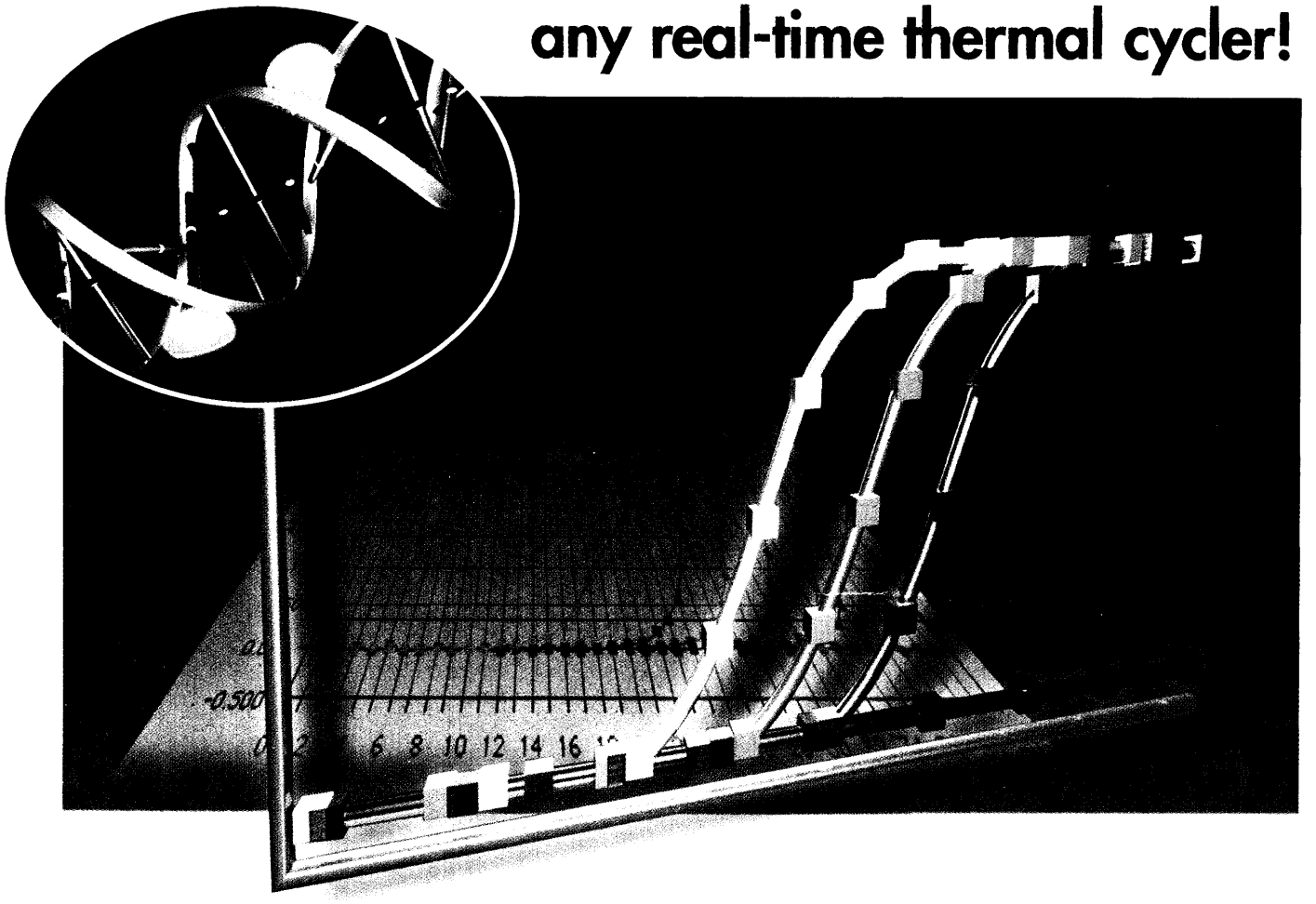

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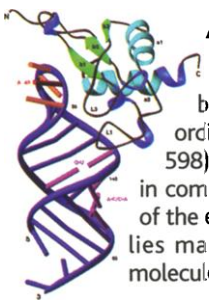
flk-1 mutant mice, an embryo tissue explant system, and an angiogenesis inhibitor to show that endothelial cells promote liver development prior to vascular blood flow.

Worming Secrets Out of p53

The *p53* tumor suppressor gene is among the most frequently mutated genes in human cancer. Although much has been learned about p53 from studies of mammalian cells, progress in understanding its function and regulation has been hampered by the lack of a genetically accessible system. Derry *et al.* (p. 591) have identified a p53 homolog in the nematode *Caenorhabditis elegans*, an organism previously thought to be devoid of p53. This gene, *cep-1*, functions in apoptosis and meiotic chromosome segregation in the germ line and mediates responses to environmental stress in somatic cells. The genetic potential offered by the *C. elegans* system is likely to lead to new insights into *p53* and other cancer-related genes.

Riding the Neural Crest

Stitching together the circuitry that connects central and peripheral nervous systems requires a wiring diagram with complex assembly instructions. Begbie and Graham (p. 595) now show that, in the chick, neurons extending from peripheral epibranchial placodes toward the hindbrain find their way by following tracks defined by neural crest cells migrating in the opposite direction, from the hindbrain outward. These ganglionic connections later relay sensory information such as taste from the oral cavity to the brain.



A Signal Assembly

The signal recognition particle (SRP) is an RNA-protein complex that bridges active ribosomes and internal membranes and enables the coordinated synthesis and insertion of membrane proteins. Wild *et al.* (p. 598) have solved the structure of one of the protein components, SRP19, in complex with helix 6 of the SRP RNA. This complex, postulated to be one of the early intermediates in assembly of the SRP, reveals that recognition relies mainly on shape complementarity, meditated by a layer of water molecules, rather than direct nucleotide–amino acid contacts.

CREDIT: WILD *ET AL.*

Everybody Counts

Organisms are discrete entities in space and time, but most ecological models simulate populations as a continuum. Lattice models can handle populations that have discrete numbers, and by this means Henson *et al.* (p. 602) have shown in laboratory populations of the flour beetle, *Tribolium*, that it does matter whether organisms are treated as points rather than smears. Accounting for lattice effects can dramatically alter the predictions of ecological models, especially those with complex dynamics used in conservation biology and wildlife management.

γδ T Cells Get Under the Skin

T cells bearing the γδ T cell receptor reside in large numbers within the epidermis of the skin. The growing evidence that γδ T cells contribute to dermal integrity is supported by the study by Girardi *et al.* (p. 605; see the Perspective by Pardoll), who show these lymphocytes can protect against cutaneous malignancy. Thus, in the absence of γδ T cells, mice coped poorly with experimentally induced forms of skin carcinoma. Induction of malignancy correlated with the up-regulation of the protein Rae-1, which contributed to the killing of carcinoma cells by a γδ T cell line in vitro. Binding studies revealed that Rae-1 interacts with the NKG2d receptor on γδ T cells, which suggests that this ligand may be a functional homolog of tumor-related MICA/B proteins in humans.

The Past Molds the Future

Trypanosomes possess a characteristic flagellum that winds helically around the cell. How is this complex structure passed on to the resulting daughter cells during cell division? Moreira-Leite *et al.* (p. 610) examined the process and found that the new and the old flagella are physically linked during division such that the structural form is passed directly from mother to progeny. This type of morphogenetic inheritance is known as cytotaxis.

Impressed?
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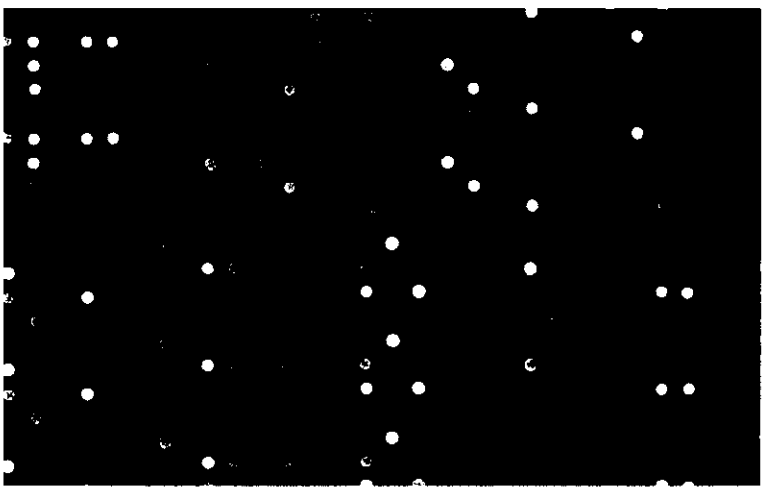

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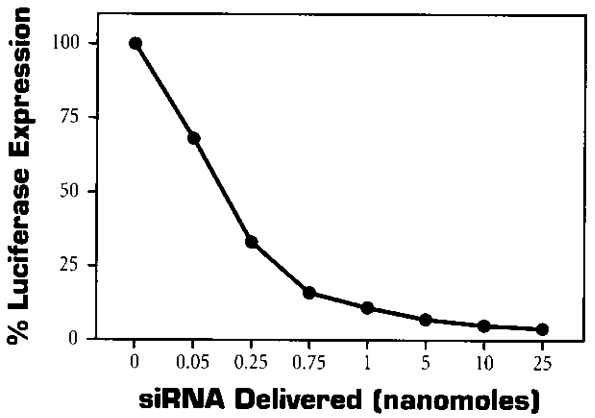

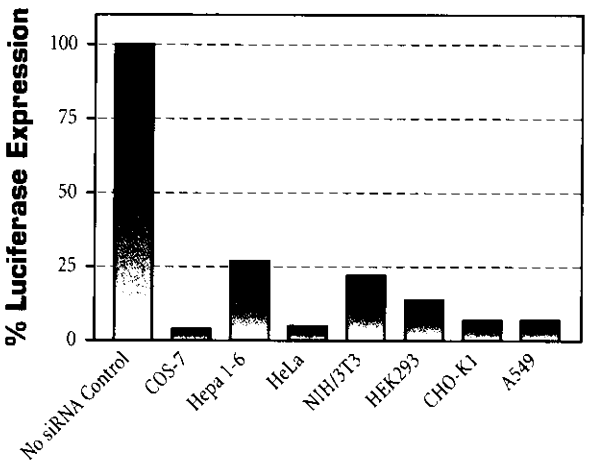

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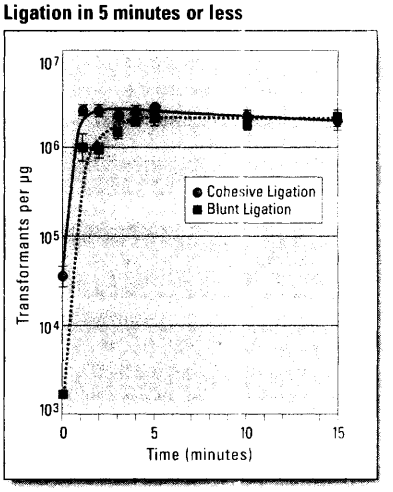

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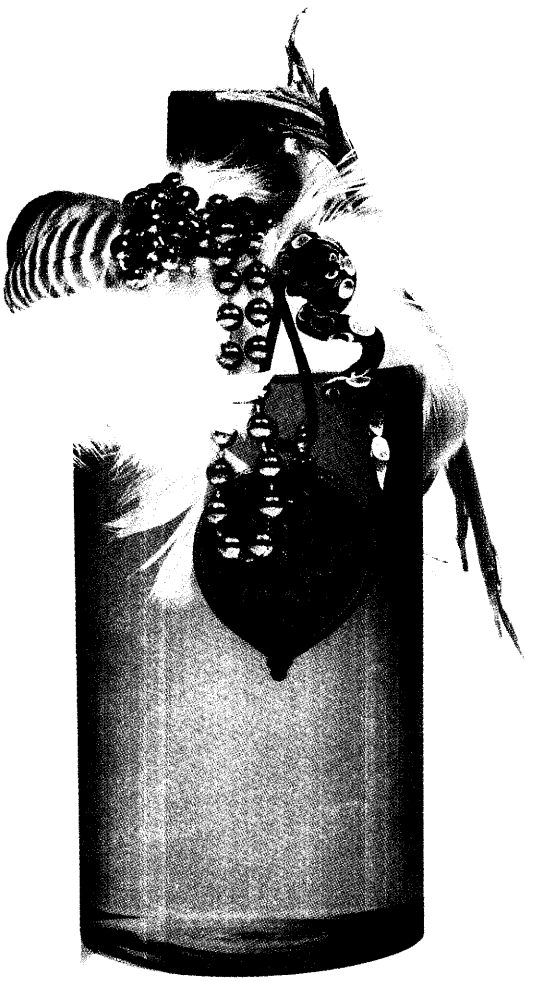

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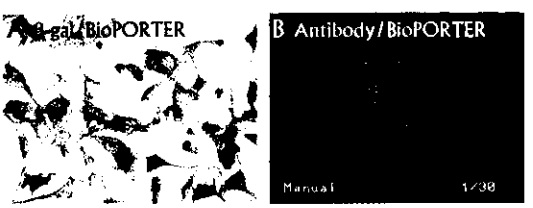

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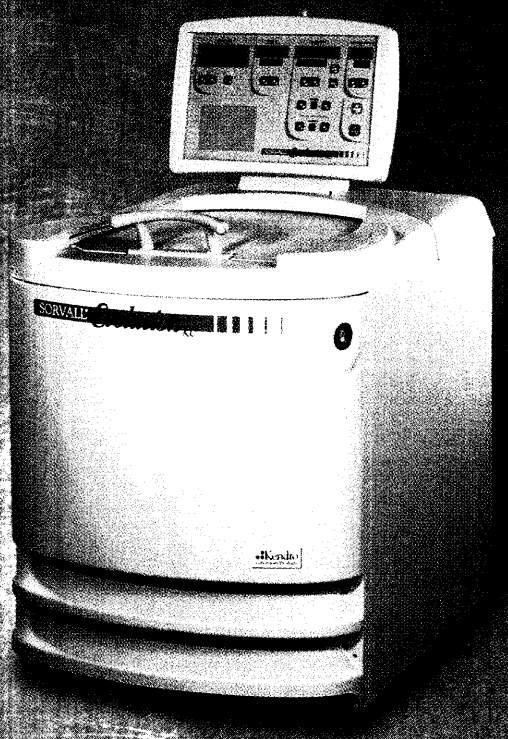

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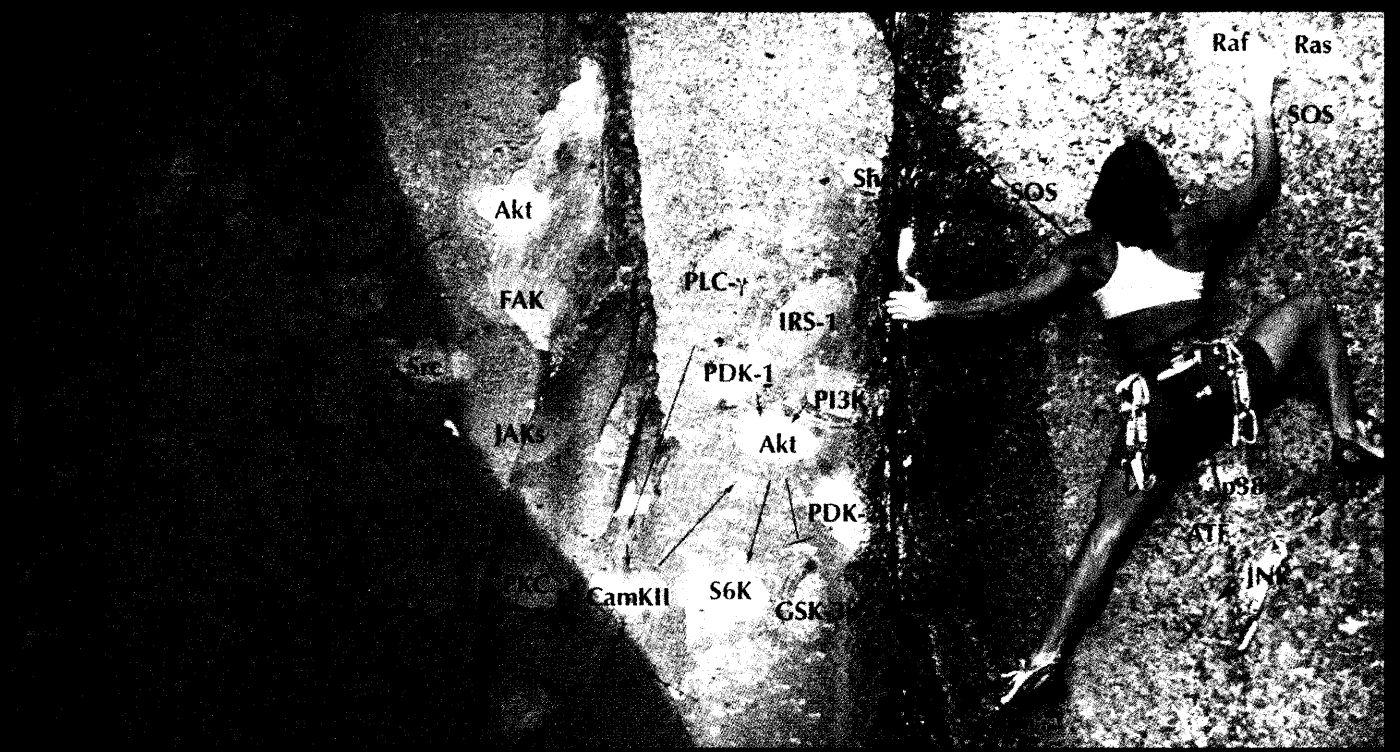

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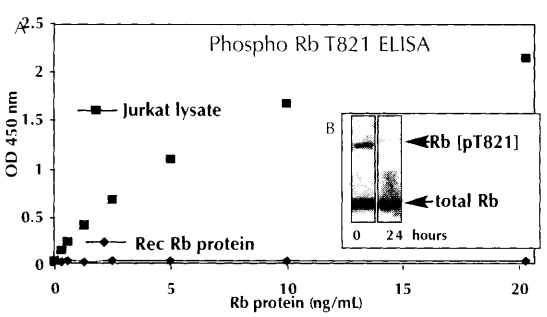

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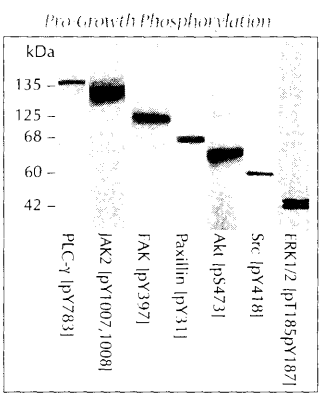
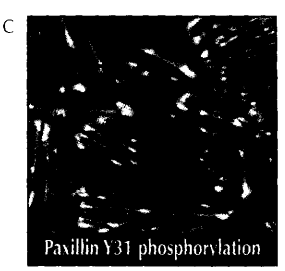
Pro Growth Phosphorylation





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CB1	IκB-α	PKR
cdc2	Insulin-R	PLCγ-1
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EGF-R	Integrin-β_3	Rb
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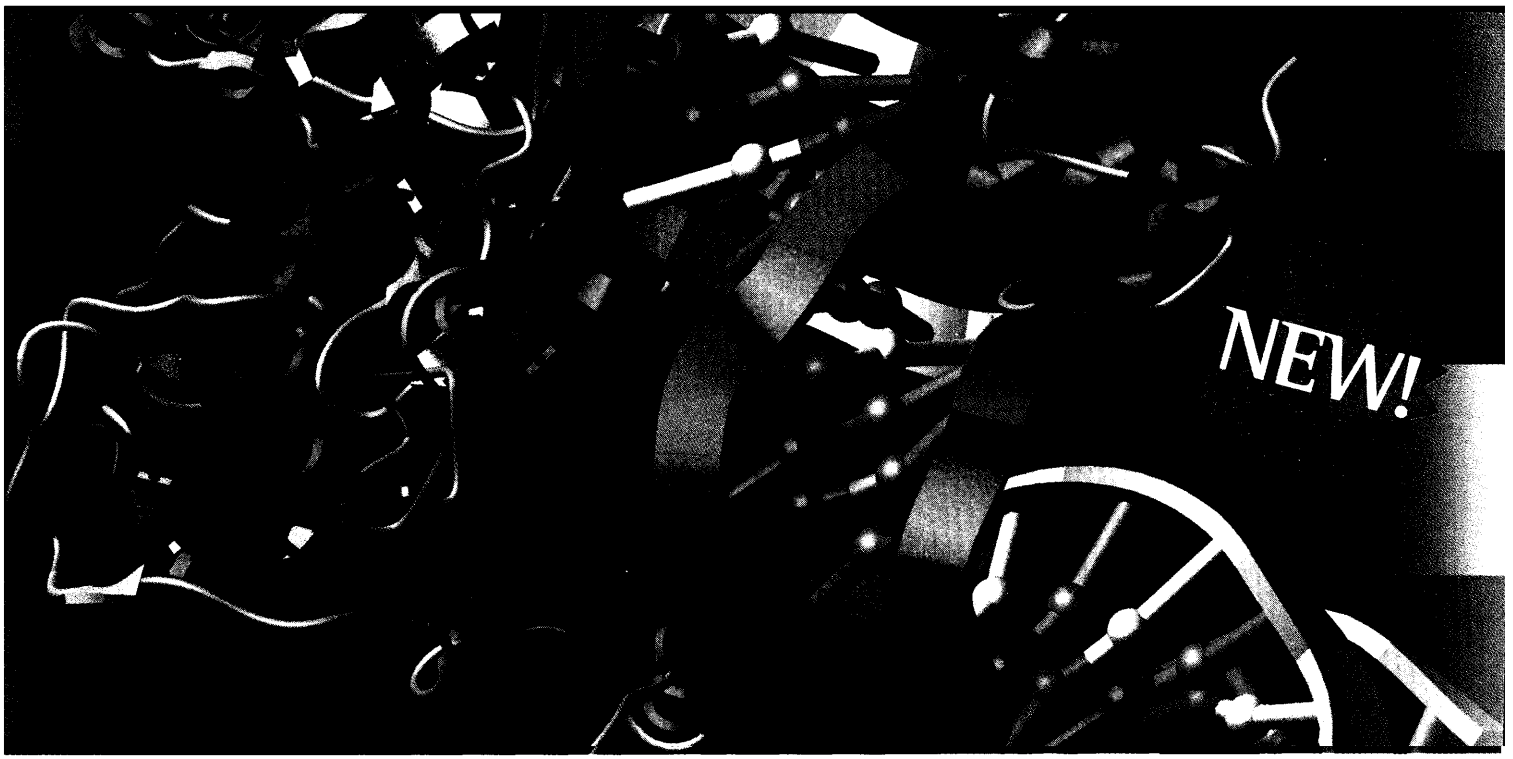

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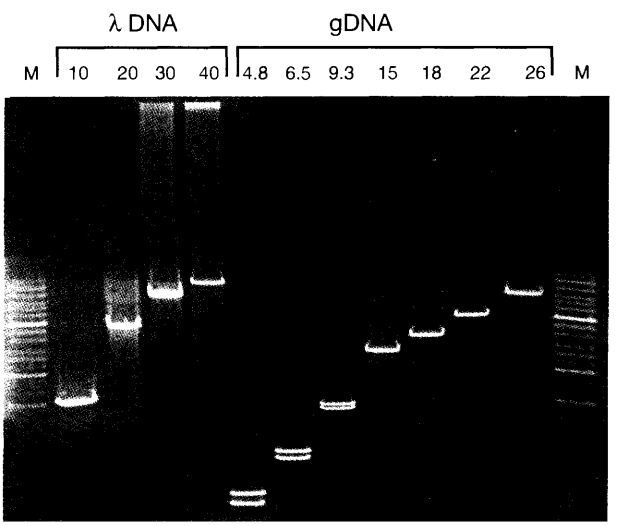

Amplification of 10–40 kb fragments from λ DNA and 4.8–26 kb fragments from human DNA with TripleMaster PCR system using the special Tuning Buffer™. Double bands (gDNA) are caused by amplification of the two different allels.

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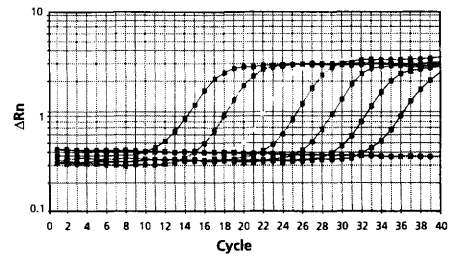
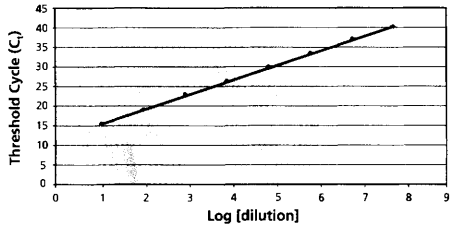
Quantitative PCR (qPCR) performed on pBac-2cp. Initial template copy number was 10^6, diluted 10-fold in subsequent wells. Threshold cycles (Cts) determined using the ABI PRISM 7700 Sequence Detection software.



Linearity of pBac-2cp ten-fold dilutions with SYBR Green JumpStart Taq ReadyMix



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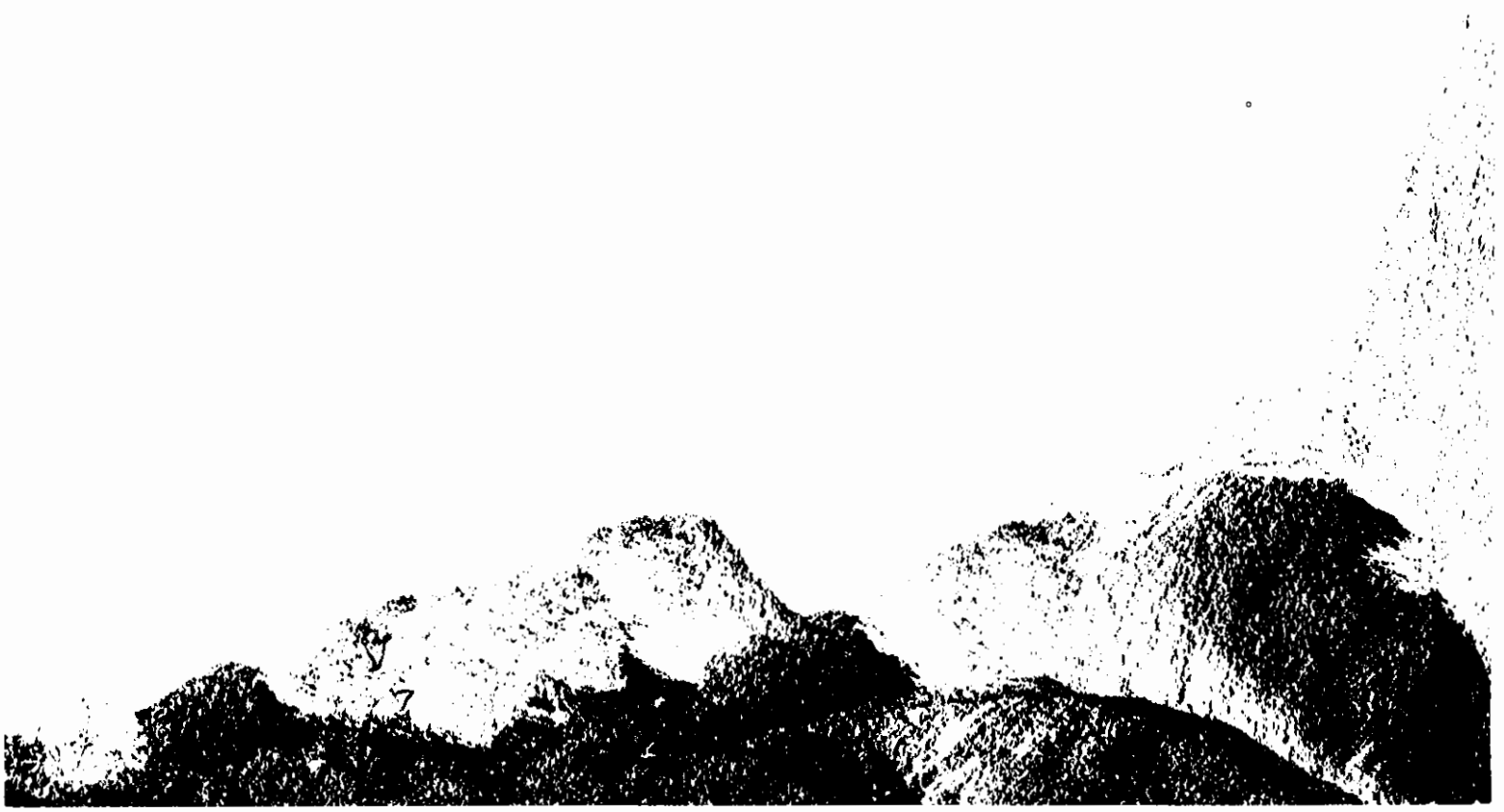

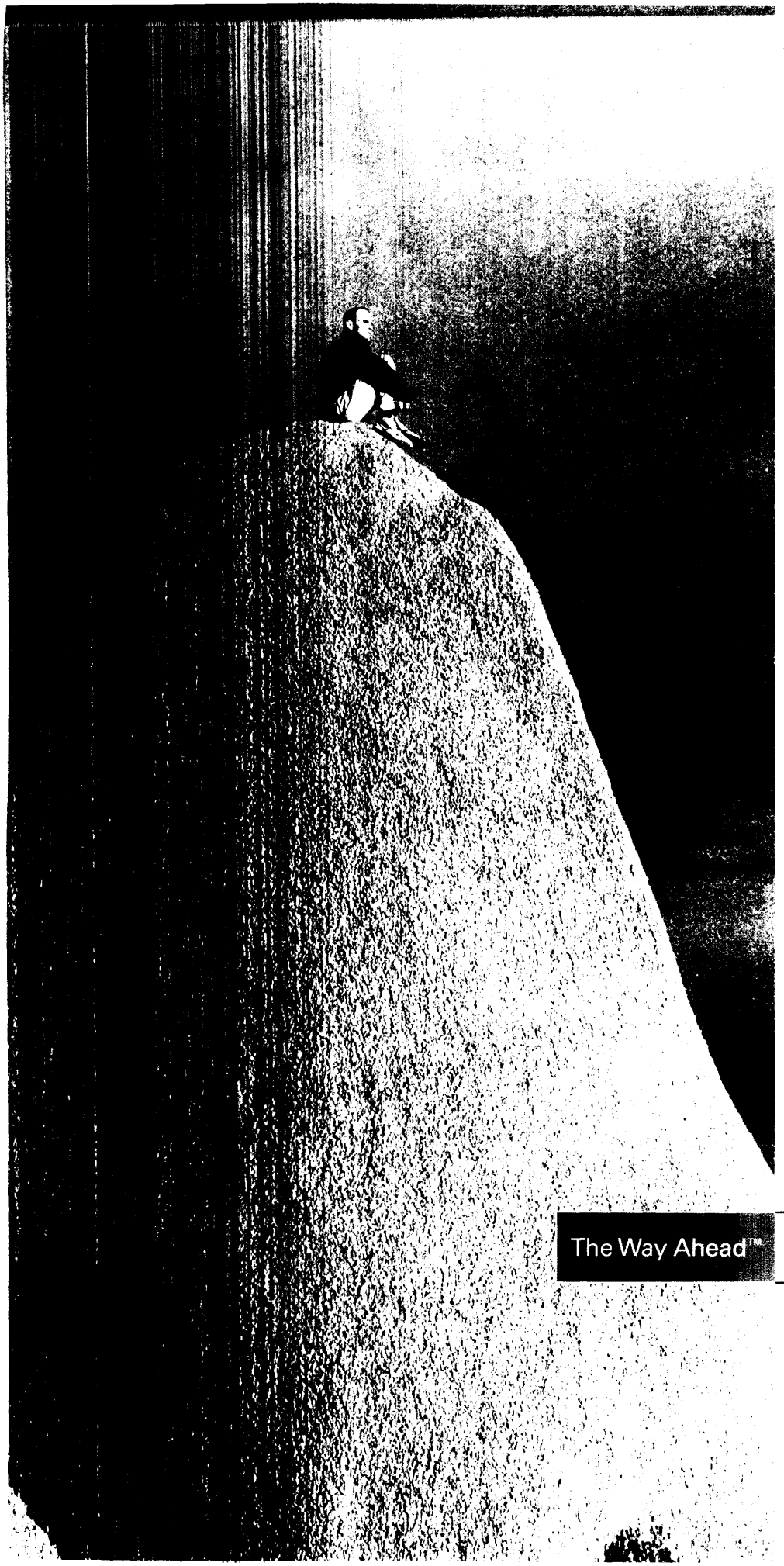

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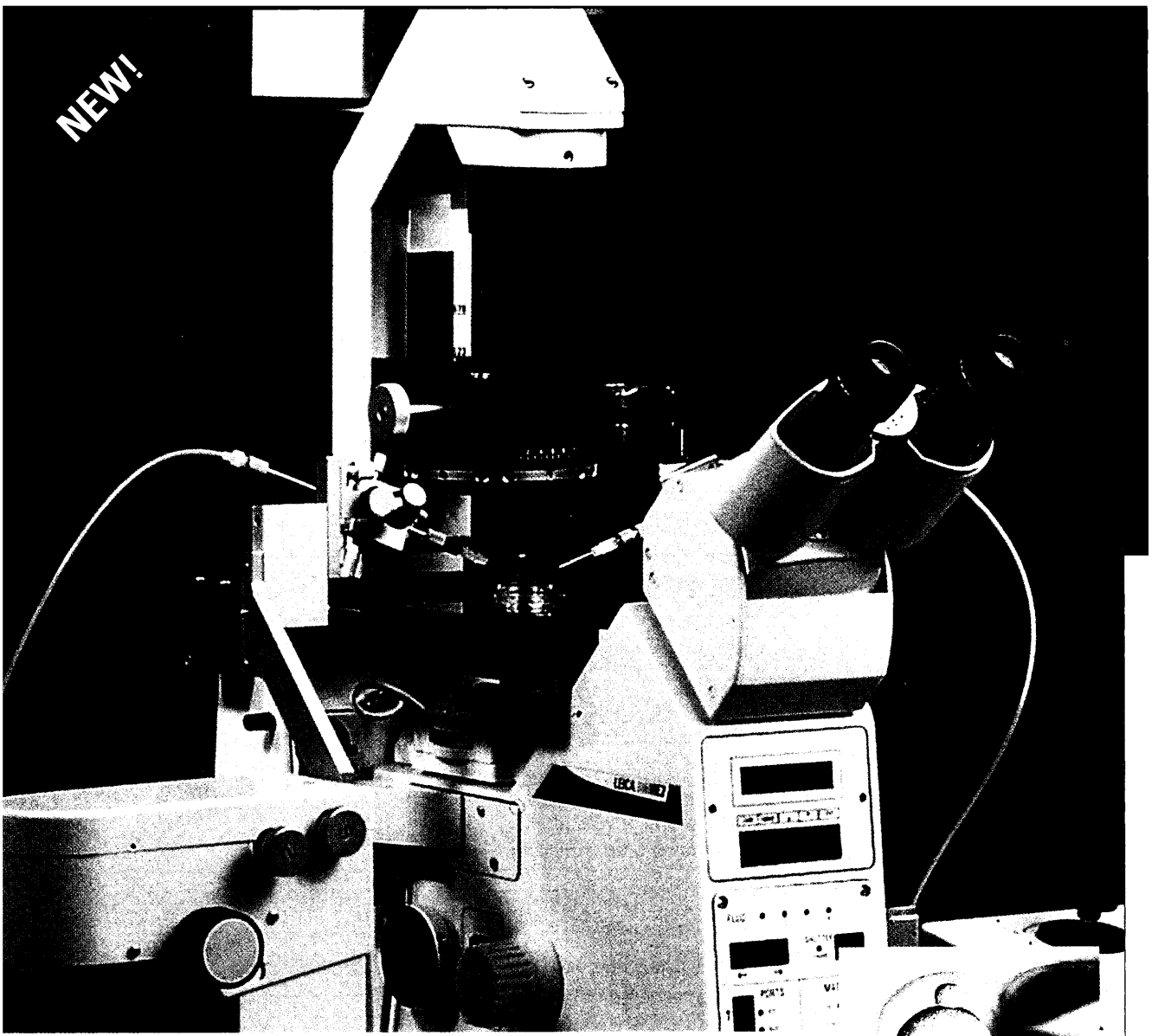

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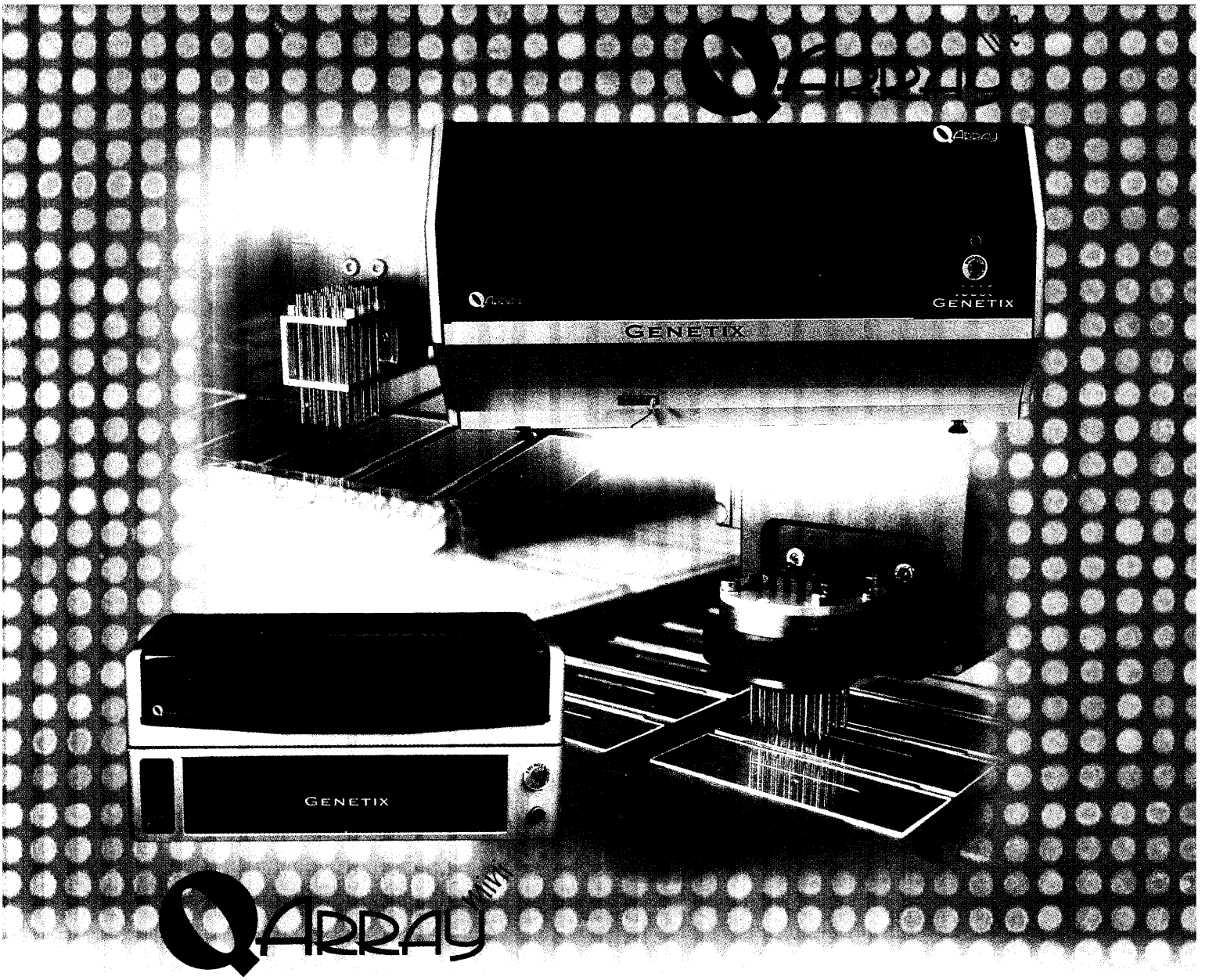

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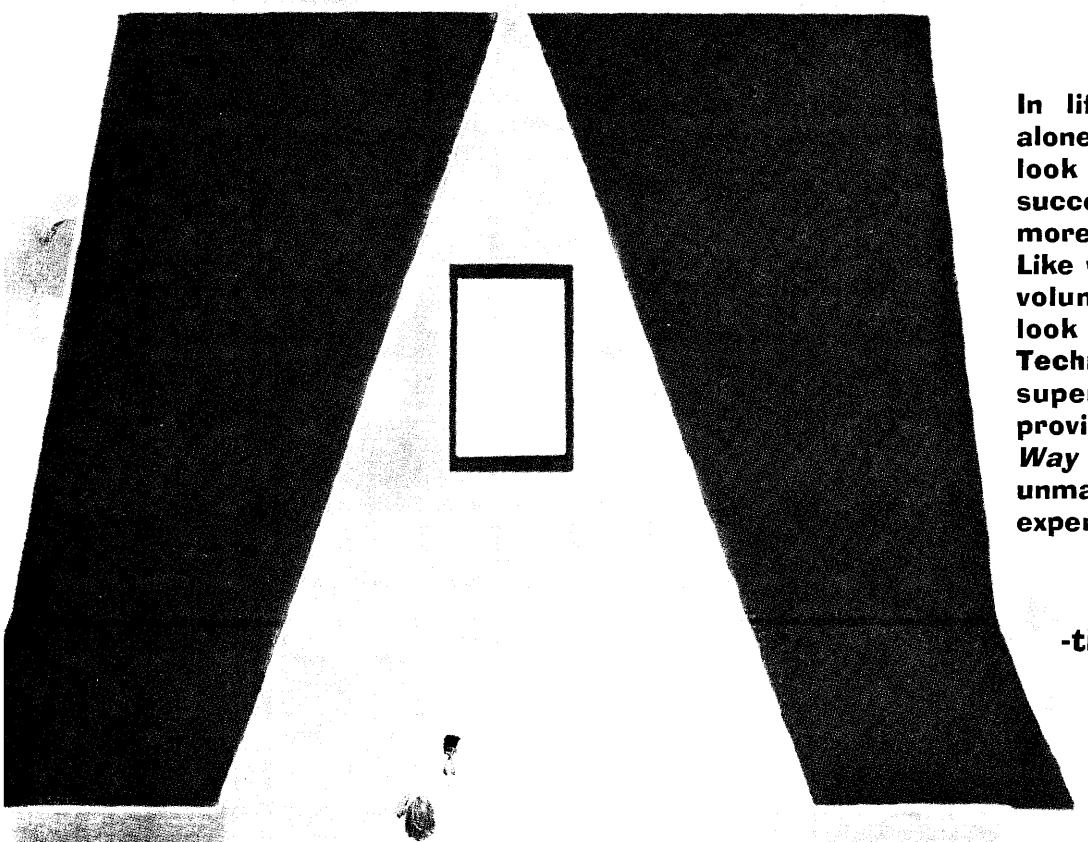

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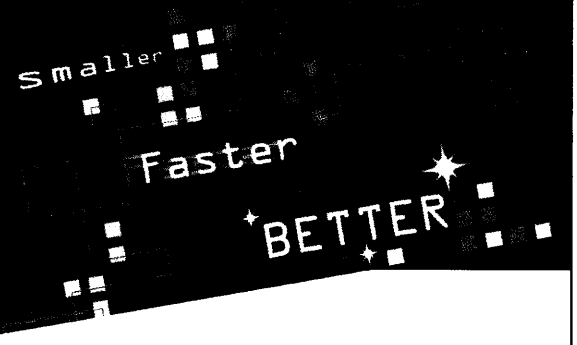

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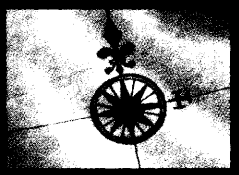

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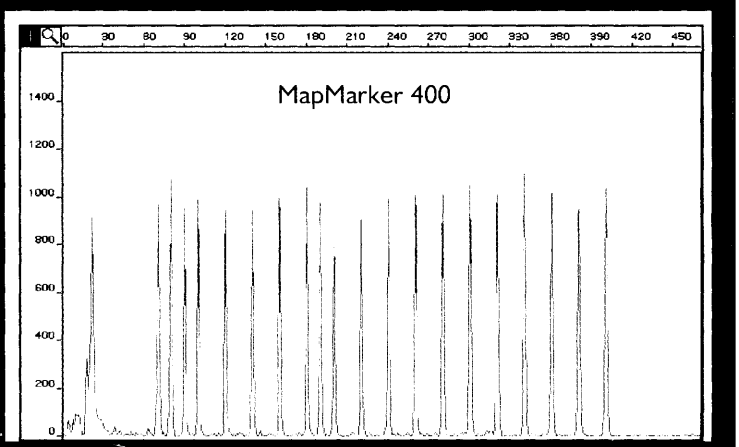

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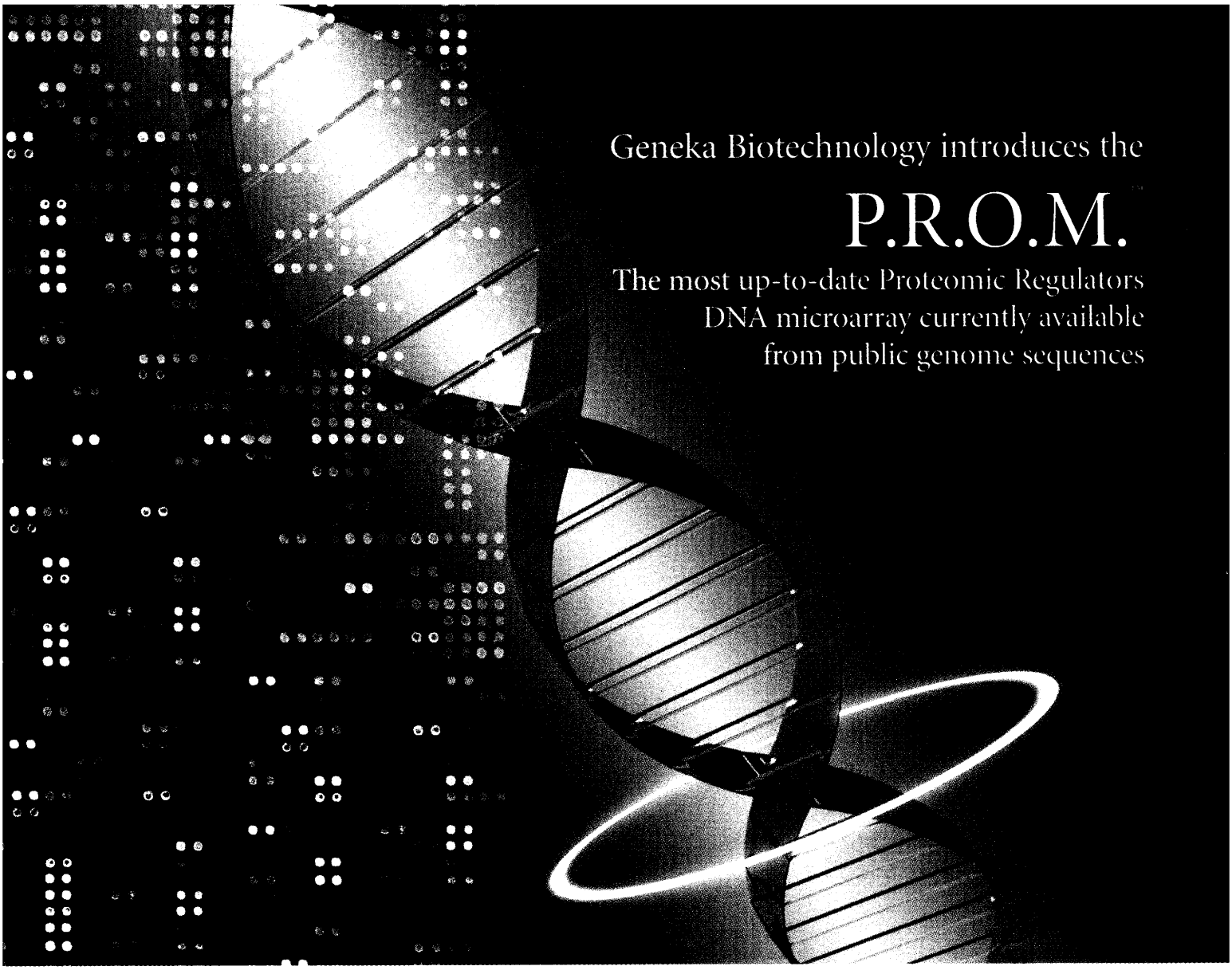

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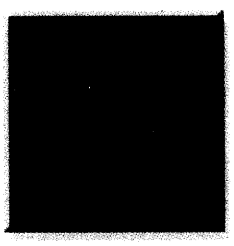

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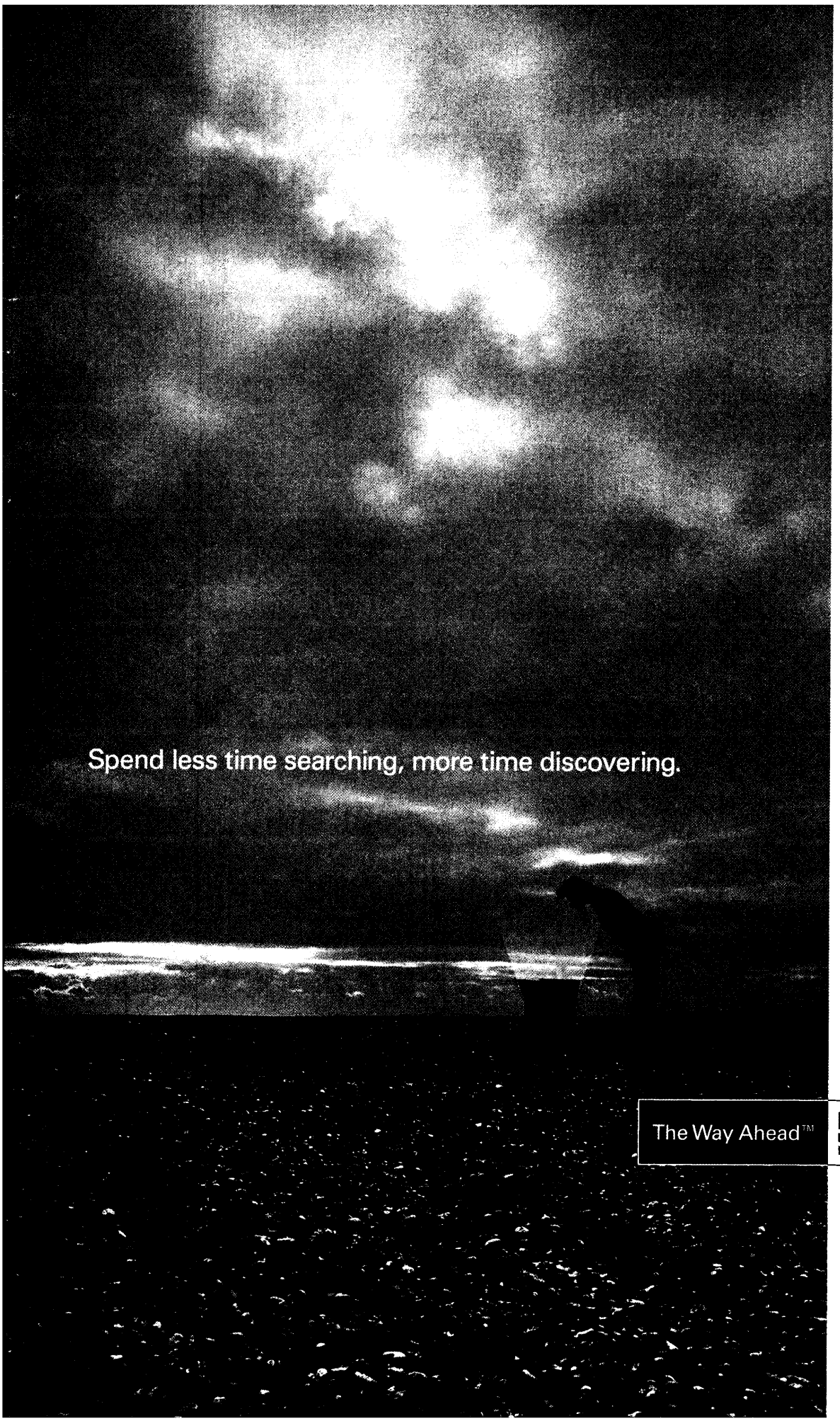

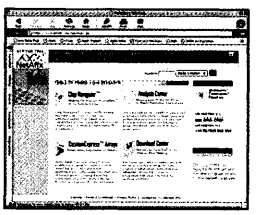

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2) Proc. Natl. Acad. Sci. USA **97**, 1665-1670 (2000)

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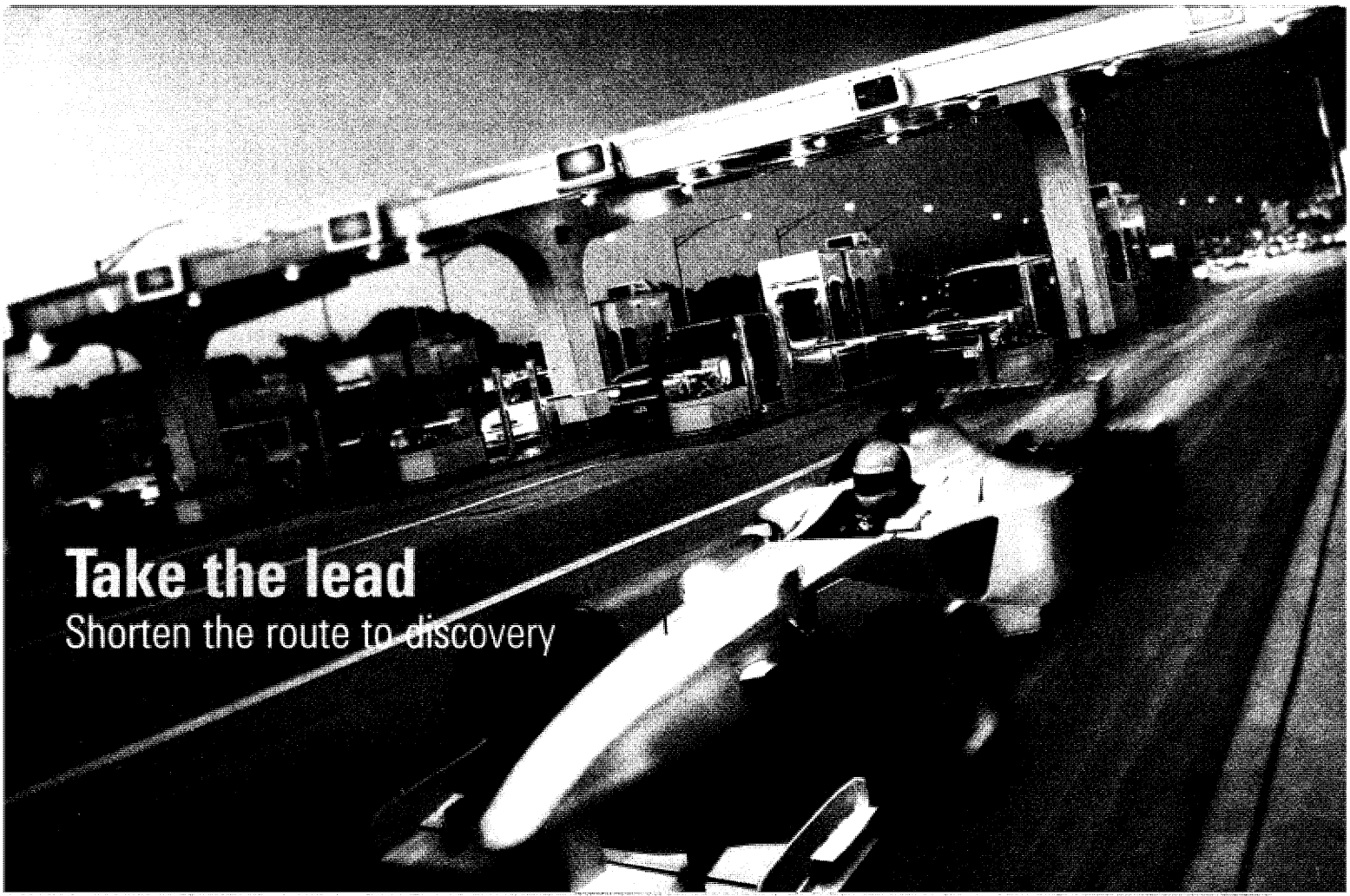

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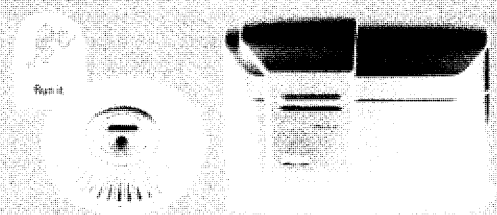

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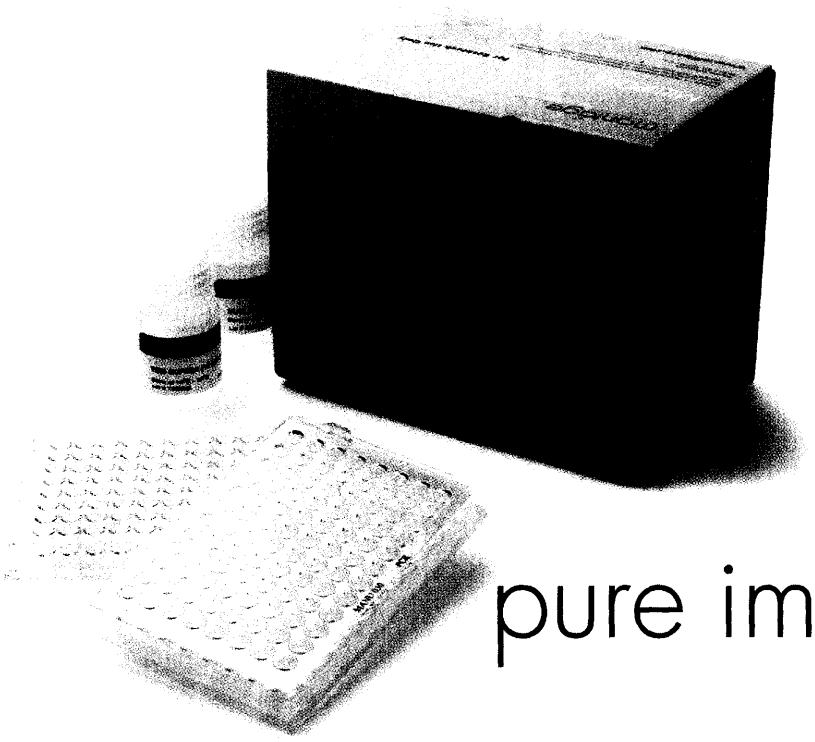

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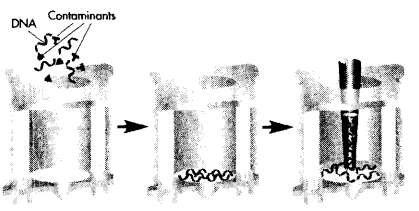

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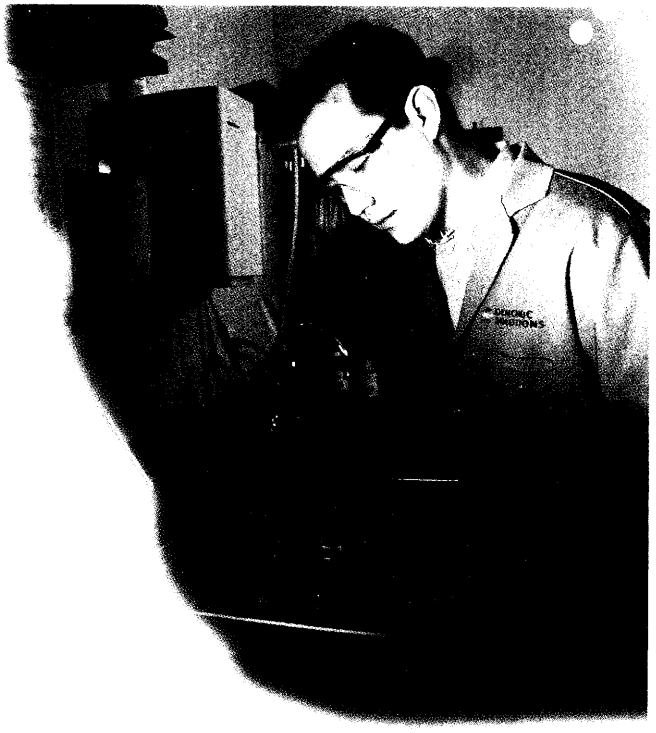

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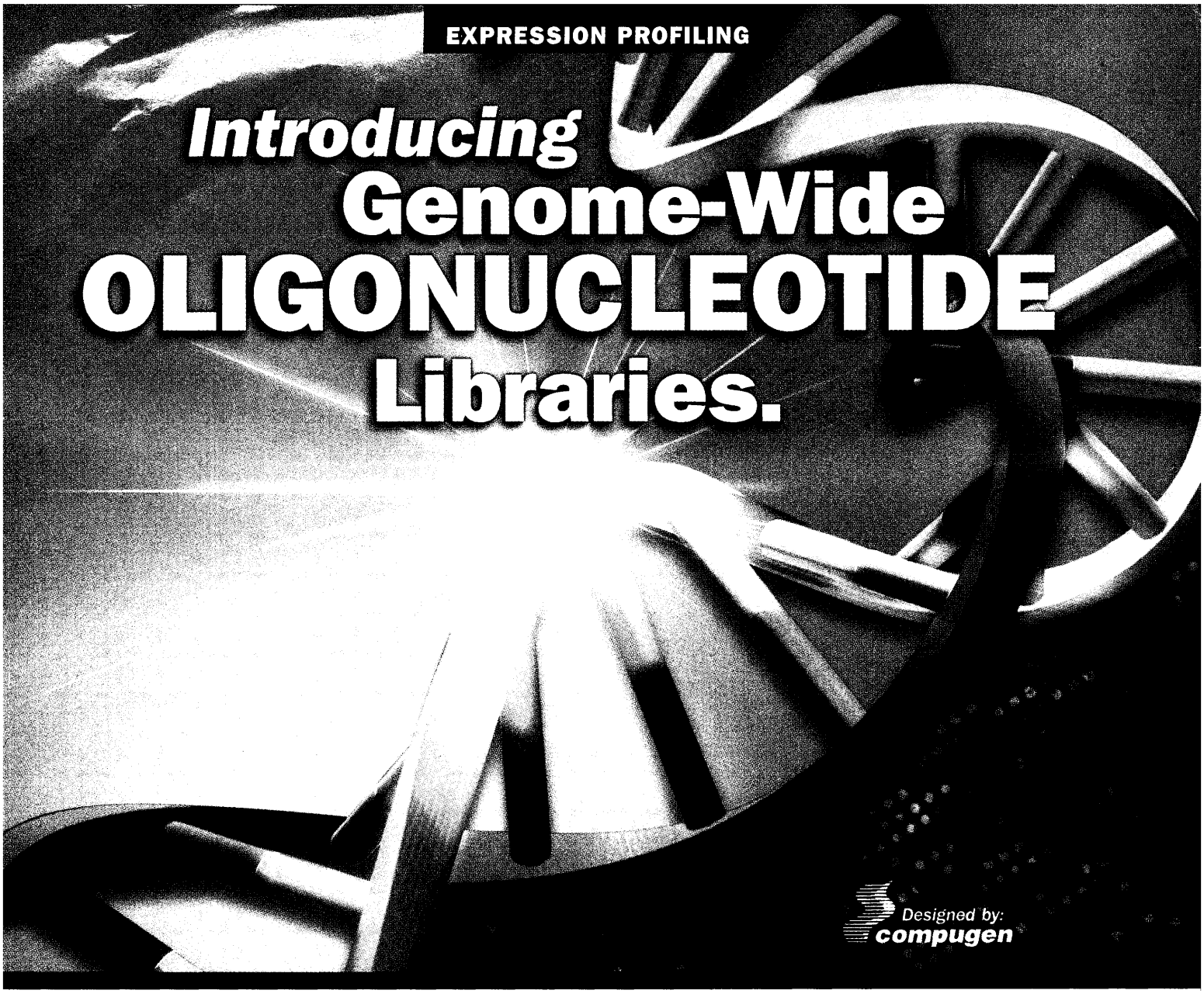

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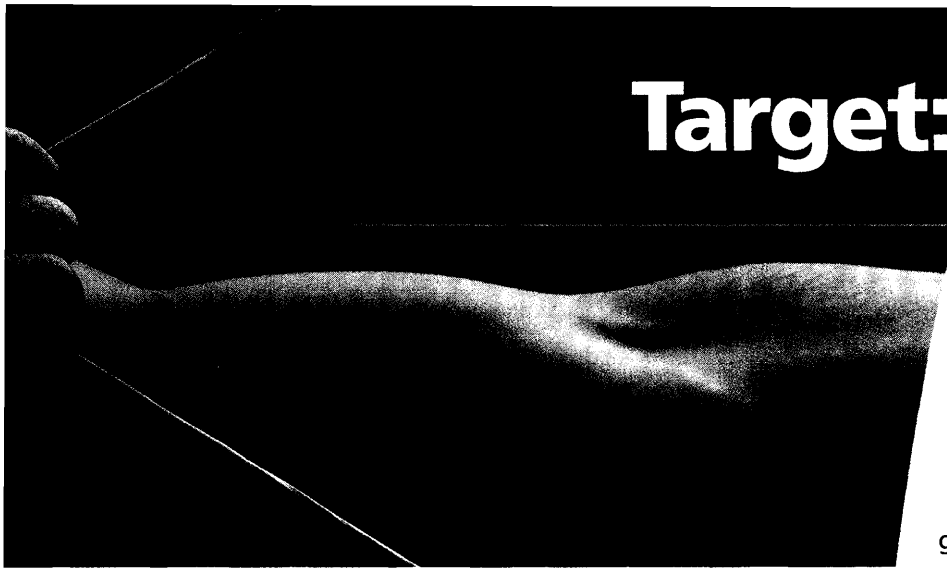
SIGMA GENOSYS



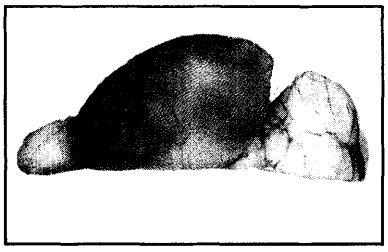
Target: Anxiety response

Focus on gene function

DeltaBase™ is the world's largest searchable database on *in vivo* mammalian gene function. Information in DeltaBase is generated using large-scale mouse gene knockout technology and standardized phenotypic analysis protocols. More than 20,000 data points are collected on hundreds of disease-relevant genes every year. Featured here is just one of those genes.

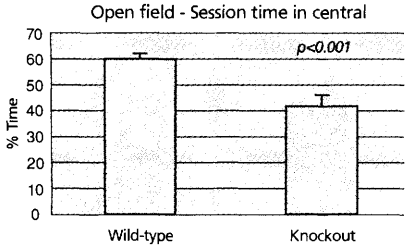
Phenotypic analysis

Gene: Orphan G protein-coupled receptor



The lacZ reporter gene present in the knockout construct allows for the analysis of gene expression. In mutant mice, lacZ expression is detectable in the cortex region of the brain, as shown in this whole-mount image.

Within the brain, lacZ is highly expressed throughout the cortex, hippocampus and amygdala. In normal animals, the hippocampus is essential for spatial processing and some types of exploratory behavior, while the amygdala is important for fear and anxiety behaviors.



The homozygous mutants spent less time in the central region in the open field test, indicating a higher level of anxiety compared to their wild-type siblings.

Phenotypes at your fingertips

Through a browser-enabled interface, DeltaBase subscribers can quickly review and compare phenotypic data, images and analysis summaries from genes belonging to gene families that have demonstrated a high degree of success as drug targets. This information can be used to identify valid targets and to support decisions about therapeutic value. In addition, animal models for all targets in DeltaBase are made available to subscribers for further study.

Discover the power of DeltaBase

For more information on DeltaBase, visit www.deltagen.com and register for the online demo.

With this information, researchers can make informed decisions about which new gene targets to advance into small molecule screening programs. DeltaBase offers the possibility of faster drug discovery and improved overall efficiency in the drug development process.

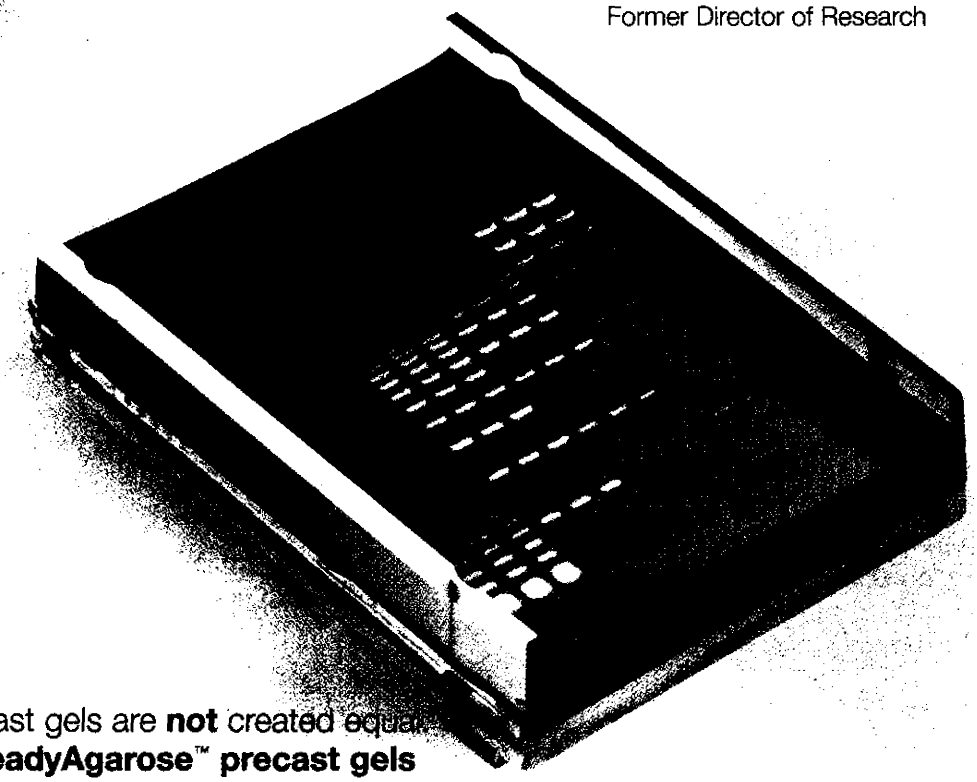
DeltaBase™

Take the lead

Deltagen

All Precast Gels Are Created Equal"

— **Dr. R. U. Kiddingme**
Former Director of Research



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PRIMARY TOPICS

- New approaches to sample preparation, including 2-D gels and chromatographic techniques
- Advances in high-throughput protein identification and analysis
- Array-based measurements
- Structural genomics data related to protein function
- Research on quantitative and structural analysis of proteins and their post-translational modifications
- Metabolic and signal pathway analysis, including metabolomics and peptidomics
- Protein–protein, protein–DNA, and protein–small molecule interactions
- Computational approaches to predict protein function
- Use of bioinformatics/cheminformatics to mine and analyze data
- New tools in proteomic analysis
- Studies on proteomics with an impact on the understanding of disease, diagnosis, and medicine

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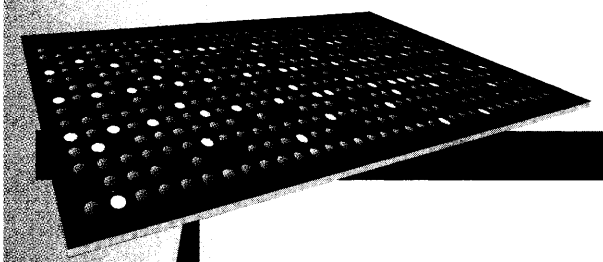
The Total Solution for your Microarray Process



Integrating Sample Prep to Analysis

Sample Prep

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DNATrak™

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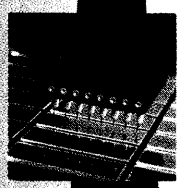
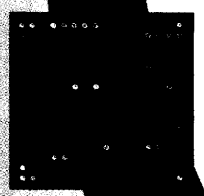


Array Production

SpotArray™ Product Family

- State-of-the-art printhead and pins for high quality genomic arrays
- Non-contact printing for protein and custom array research
- Bench-top and Production models provide throughput flexibility



Scanning/Imaging

ScanArray™

- Microarray Analysis System for up to five color applications
- Confocal design for optimum signal-to-noise ratios

Cyclone®

- Storage Phosphor System for isotopic gene expression applications

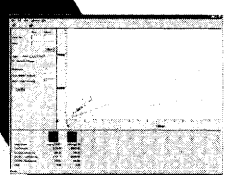
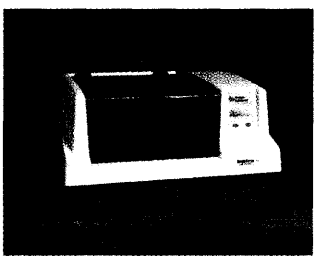


Image Analysis

QuantArray®

- Microarray Analysis Software for gene expression, SNP and protein arrays
- Robust spot finding
- Spot quality measurements for array QC

Focus on Array Production



SpotArray™ 24
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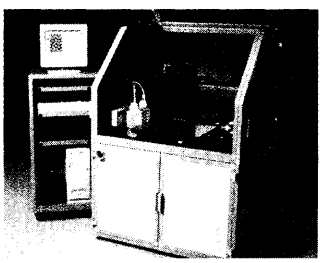
BioChip Arrayer®
Reliable, flexible development tool for non-contact printing applications



SpotArray Enterprise™
High speed, non-contact printing for protein and custom arrays used in HT production applications

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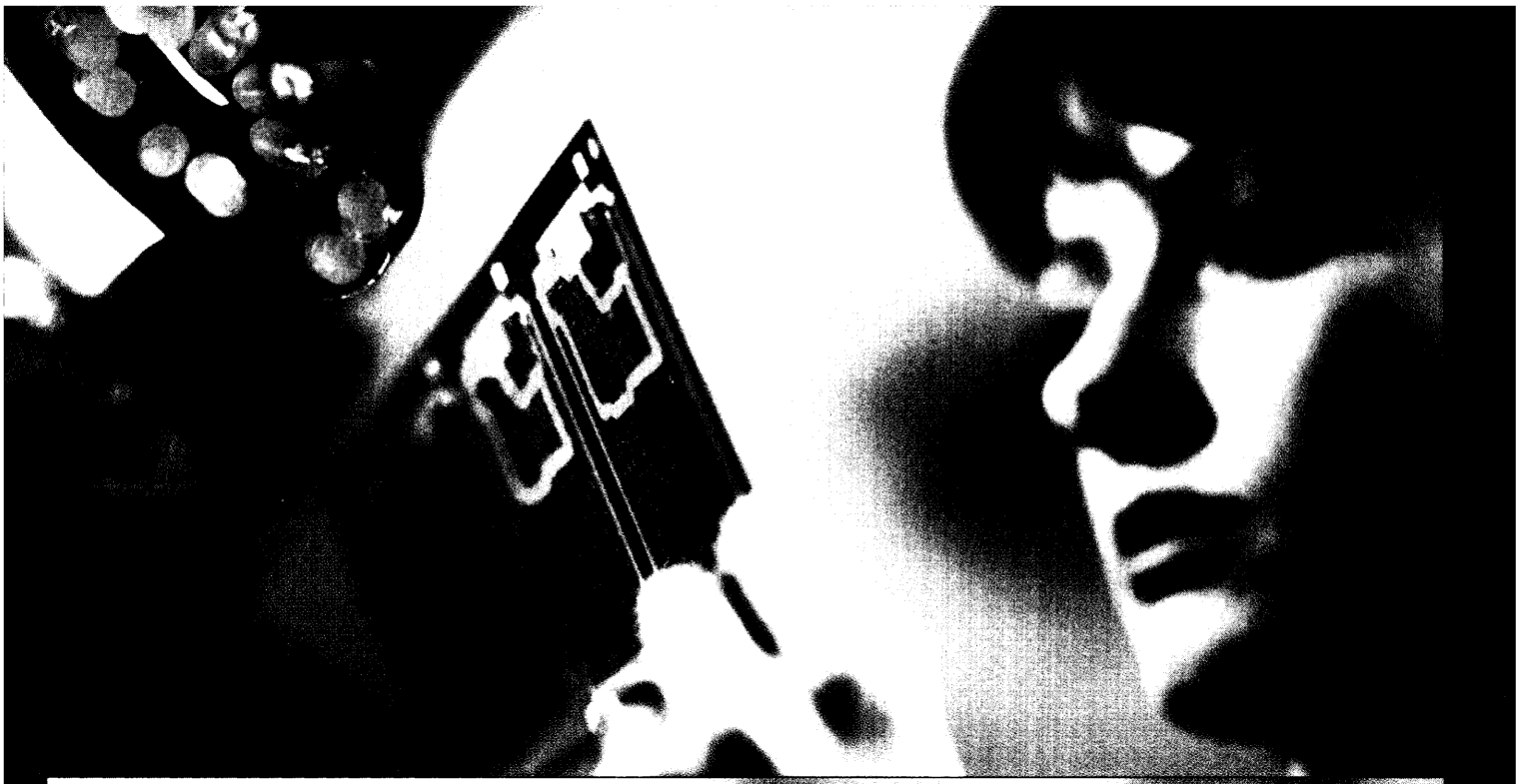


GREAT MINDS DON'T ALWAYS THINK ALIKE.

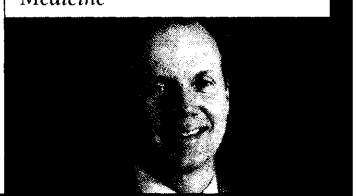
UNDER THE RIGHT CONDITIONS, THEY BREAK NEW GROUND.

Florida State University provides the perfect conditions for pioneers like analytical chemist Alan Marshall. His groundbreaking work at the National High Magnetic Field Laboratory is allowing scientists worldwide to better understand complex molecules like DNA. And internationally acclaimed sociologist Jill Quadagno, who is at the forefront of addressing the challenges and opportunities of an aging population. And Joseph Scherger, M.D., dean of the first new U.S. medical school in 20 years, where doctors are trained to care for those who need them most — the elderly and the underserved in urban centers and rural communities. It's all about ideas that move...minds, hearts and, maybe, mountains.

Sociology Professor Jill Quadagno, above, FSU's Pepper Institute on Aging

Professor Alan Marshall, above, winner of the 2002 American Chemical Society Award in Analytical Chemistry

Joseph Scherger, M.D., below, Dean of the FSU College of Medicine



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IDEAS THAT MOVE

http://minds.fsu.edu

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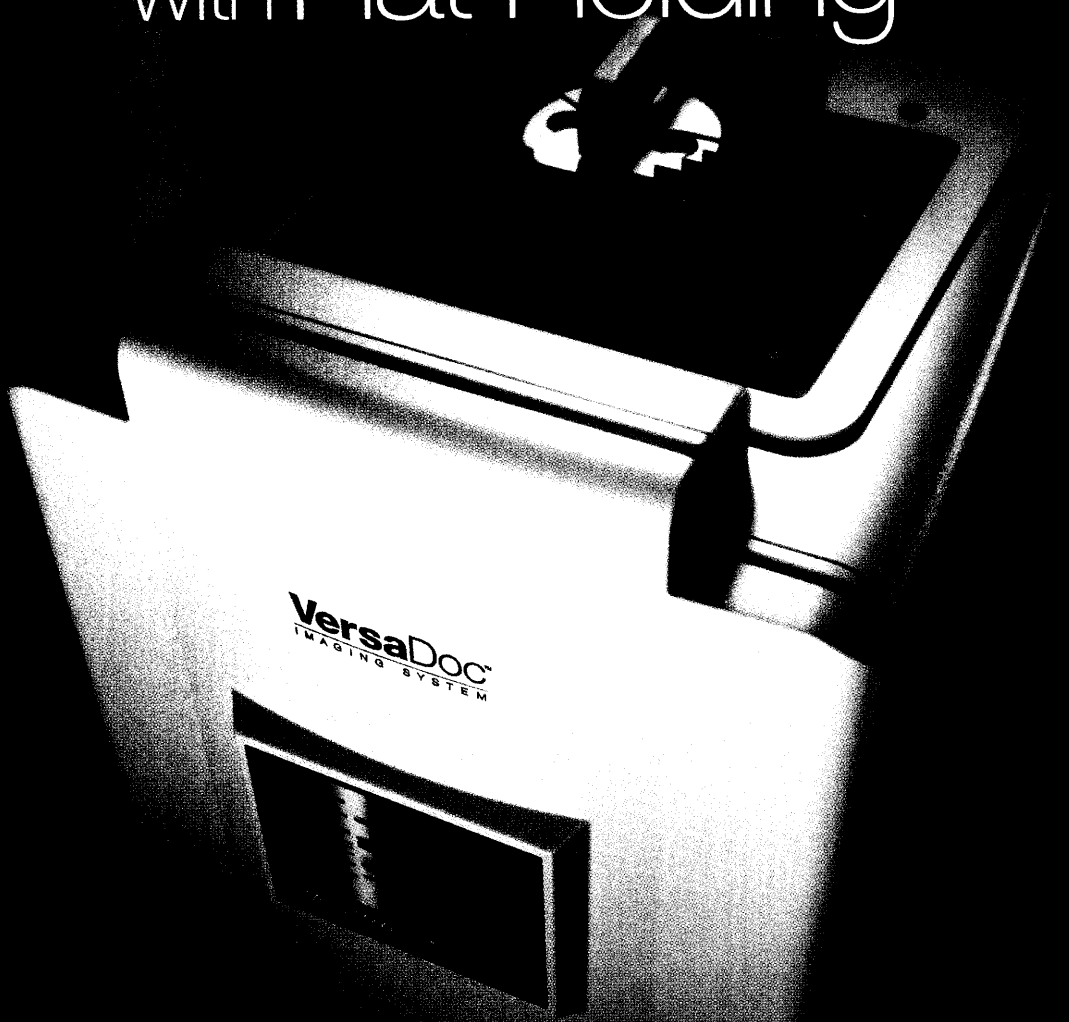

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