5 October 2001

Science

Vol. 294 No. 5540
Pages 1–252 $9

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American Association for the Advancement of Science

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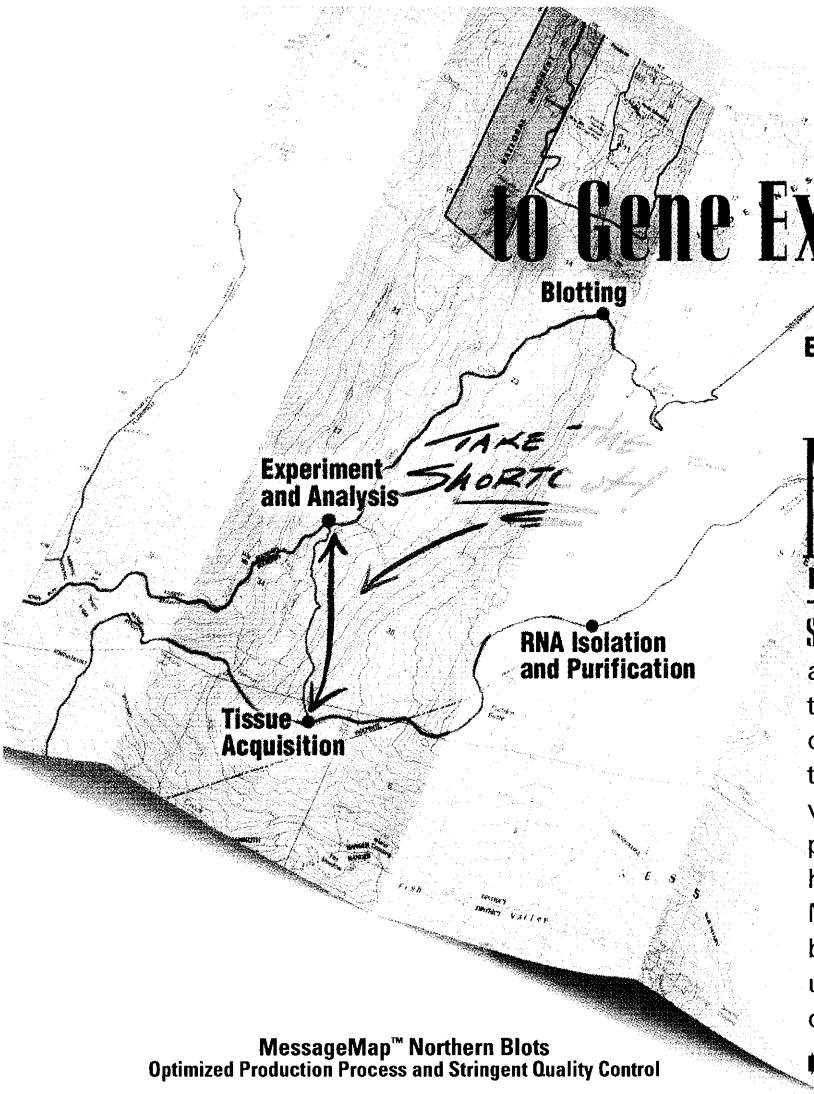

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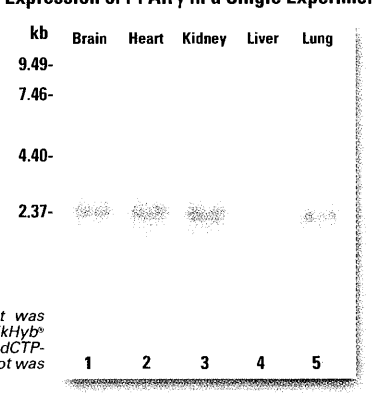

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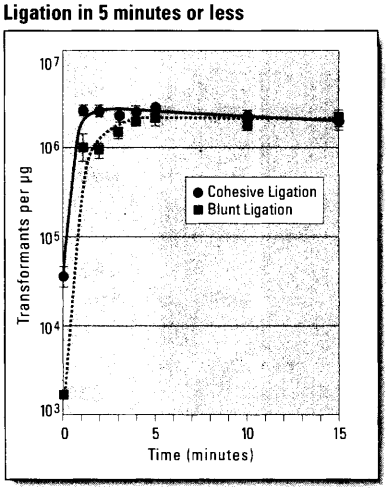

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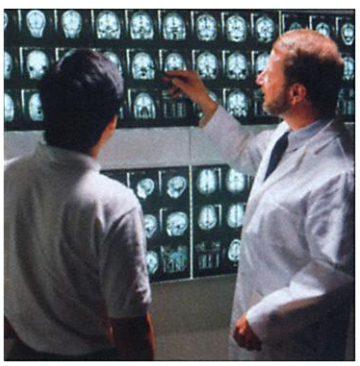
Science

Volume 294 5 October 2001 Number 5540

NEWS



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Autism's many roots and guises

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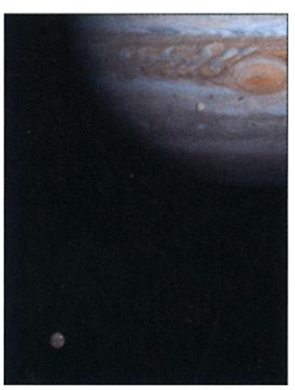
McClintock in context



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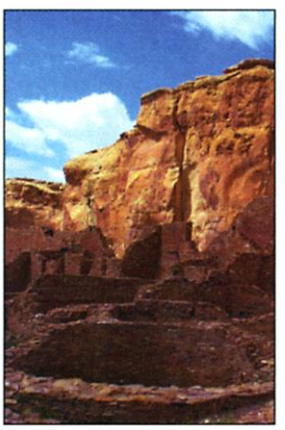
COVER 81

Sequencing genomes is only the first step to unlocking their secrets. This issue examines new ideas, approaches, and research related to genomic information. [Art: C. Slayden]



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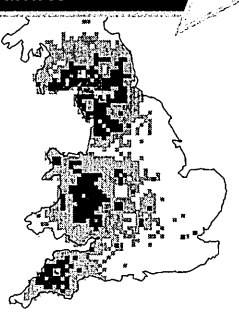
Chaco Canyon abandoned pueblo

New on *Science* Express Foot and mouth: modeling disease dynamics



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CONTENT HIGHLIGHTS AS OF 5 OCTOBER 2001

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SCIENCE EXPRESS www.sciencexpress.org

Dynamics of the 2001 UK Foot and Mouth Epidemic: Stochastic Dispersal in a Heterogeneous Landscape M. J. Keeling *et al.*
26 Spatial models of the dynamics of foot-and-mouth disease offer new insights into the pattern of spread, and possible control, of the current UK epidemic.

Logic Circuits with Carbon Nanotube Transistors A. Bachtold, P. Hadley, T. Nakanishi, C. Dekker

A local-gate layout for logic circuits with carbon nanotube transistors enables integration of multiple devices on a single chip.

Regulation of Receptor Fate by Agonist-Dependent Ubiquitination of the β_2-Adrenergic Receptor and β-Arrestin
S. K. Shenoy, P. H. McDonald, T. A. Kohout, R. J. Lefkowitz

The β_2-adrenergic receptor and its negative regulator β-arrestin are modified by ubiquitination, resulting in distinct effects on receptor internalization and degradation.

TECHNICAL COMMENTS

Archaeology and Australian Megafauna

In a study that dated megafaunal burial sites across Australia, Roberts *et al.* (8 June 2001) concluded that all large animals on the continent were extinct by around 46,400 years ago, and suggested that remains at some sites have been disturbed and therefore must be dated with caution. A comment by Field and Fullagar disagrees with the "argument for disturbance made by Roberts *et al.*" for at least one site, Cuddie Springs, stating that "stratigraphic integrity of a site cannot be assessed by dating alone." In response, Roberts *et al.* reaffirm their claim that "reliable ages . . . can only be determined by direct dating," and offer a proposal to reconcile the discrepancy between the optical dates cited by Field and Fullagar and the ages reported in the Roberts *et al.* study.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/294/5540/7a

SPECIAL FEATURE

***Science* Functional Genomics** www.sciencegenomics.org
How to Close Those Pesky Genome Gaps C. O'Keefe

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science's next wave www.nextwave.org

October Feature: Careers in Patent Law

Looking for a challenging career involving the very latest scientific breakthroughs? A career in patent law may be perfect for you. We hear from patent professionals from around the world, and look at hiring trends in the field.

Germany: Pioneering Engineers Flock to Rural Germany J.-F. Lévesque

A unique collaboration of universities on three continents is pushing forward the emerging field of mechatronics—with exciting training and research opportunities for young scientists.

US: American Postdocs Abroad A. Agrawal

American graduates seeking to broaden their horizons can find plenty of opportunities by studying in labs outside the country. And there's plenty of money, too, if you know where to look for it.

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News Synthesis: Life Extension—Our Salvation or Our Ruin? M. Barinaga

Scientists and ethicists peek inside Pandora's box.

Perspective: Biomarkers of Aging R. A. Miller

A generally optimistic but not too gullible appraisal.

science's stke www.stke.org

Perspective: Cell Signaling—The Proteomics of It All K. Ashman *et al.*

A discussion of the methods and techniques for analyzing protein interactions on a global scale.

Protocol: Identification of Cell Signaling Molecules by Expression Cloning M. L. Matter, M. H. Ginsberg, J. W. Ramos

A method that describes how to find new participants in signal transduction from cDNA libraries.

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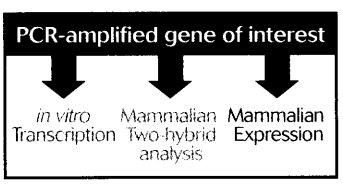

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THIS WEEK IN Science

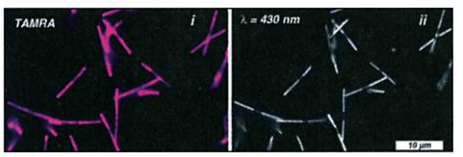
edited by Phil Szuromi

Quasar Double Helix

Relativistic jets of collimated hot plasma from active galactic nuclei provide information about the physical and chemical properties that drive these energetic structures. Lobanov and Zensus (p. 128) used the HALCA radio telescope spacecraft and an array of ground-based radio telescopes to create a high-resolution image of the structure of the jet from quasar 3C273. The jet's exquisite double-helix structure, which results from different modes of a Kelvin-Helmholtz instability, should provide an important test for improving models of the difficult-to-observe active galactic nuclei.

137 Speeding Those Laboratory Checkout Lines

Small metal barcodes have been developed for labeling large sample arrays. Nicewarner-Peña *et al.* (p. 137) electrochemically synthesized metal rods a few tenths of a micrometer in diameter and several micrometers in length in which different metals are stacked sequentially. The different reflectivity of metals such as gold, silver, copper, and nickel allows numerous sequences to be read out with ordinary light microscopy (with three metals, about a quarter million different codes can be created). The noble metal surface can be readily derivatized for use with fluorescence bioassays.



Evolving a Balancing Act

Elongation factor Tu (EF-Tu) is responsible for supplying amino acid–transfer RNA (aa-tRNA) conjugates to the ribosome, where they are used in protein synthesis. Because there is only one EF-Tu and there are at least 20 different varieties of aa-tRNA, it had been thought that this would be a relatively nonspecific interaction. LaRiviere *et al.* (p. 165; see the Perspective by Ibba) took a closer look and found that the binding affinities of EF-Tu for different aa-tRNAs do indeed fall within a narrow range. However, this uniformity results from the compensatory adjustment of pairing a stronger binding amino acid with a weaker binding tRNA, and vice versa. The authors suggest that EF-Tu may be a site for kinetic proofreading; incorrectly matched aa-tRNA conjugates either dissociate from EF-Tu before reaching the ribosome or bind so tightly as to be undeliverable.

Dial M for Spin Control

The ability to coherently control an ensemble of carriers in a semiconductor in response to an external magnetic field is a fundamental issue for spintronics, where not just the charge but the spin states of the carriers will be exploited for information processing. Kawakami *et al.* (p. 131) show that a ferromagnetic layer deposited on GaAs exerts an unexpectedly strong influence on the spin dynamics of excited carriers within the semiconductor. Interpreted as a feedback mechanism of dynamic nuclear polarization, the results indicate the adjacent ferromagnetic layer "imprints" a nuclear magnetic moment in the semiconductor that influences the spin dynamics of the photogenerated carriers.

Customized Chemical Patterns

Chemical waves, such as reaction fronts on metal surfaces or Ca waves in cells, can be modified in many ways, such as by pulsing reactants or introducing physical barriers. Wolff *et al.* (p. 134) show that localized surface heating can be used to control the evolution of chemical waves produced during the oxidation of CO on a Pt surface. Wave fronts can be launched and redirected, either under operator control or feedback optimized under computer control.

One Layer at a Time

Our understanding of how climate influenced culture in the southwestern United States during the latter half of the Holocene would be improved by a more complete record of regional precipitation, but for the period before written records, we must rely on proxies to determine moisture variations. Polyak and Asmerom (p. 148) analyzed data from five New Mexican stalagmites, covering the past 4000 years, to reconstruct precipitation changes, which they relate to records of cultural development in the region.

Can Plants Keep Up with Climate?

How rapidly can organisms adapt to global climate change? From an experimental study on a native legume of the American Great Plains, Etterson and Shaw (p. 151) have calculated the number of generations needed for adaptive changes to take place, and compare this estimate with the trajectory of predicted climate change. Adaptive evolution in response to global change is constrained by antagonistic genetic correlations among traits within populations of the plant, which suggests that plants of this kind might not adapt sufficiently rapidly to projected climate changes.

How to Copy a Genome

Replication of genomic DNA occurs during the S or synthesis phase of the cell cycle. Although we have detailed knowledge of the dynamics of a few specific replication origins, little is known about how replication occurs for an entire genome. Raghuraman *et al.* (p. 115) developed a DNA microarray assay that allowed them to analyze the replication of the entire yeast genome. Replication of the ends of each chromosome are highly correlated, and, unlike mammalian cells, there is essentially no correlation between replication and transcription.

Finding the Heart of the Centromere

The high content of repetitive sequences in the centromere, which is vital for normal partitioning of chromosomes during cell division, has made it one of the most intractable regions of the human genome. Schueler *et al.* (p. 109; see the news story by Pennisi) developed a genomic map from the X chromosome arm to its centromeric satellite DNA. Human chromosome rearrangements were used to infer the

CREDIT: NICEWARNER-PEÑA *ET AL.*

Published online in *Science* Express

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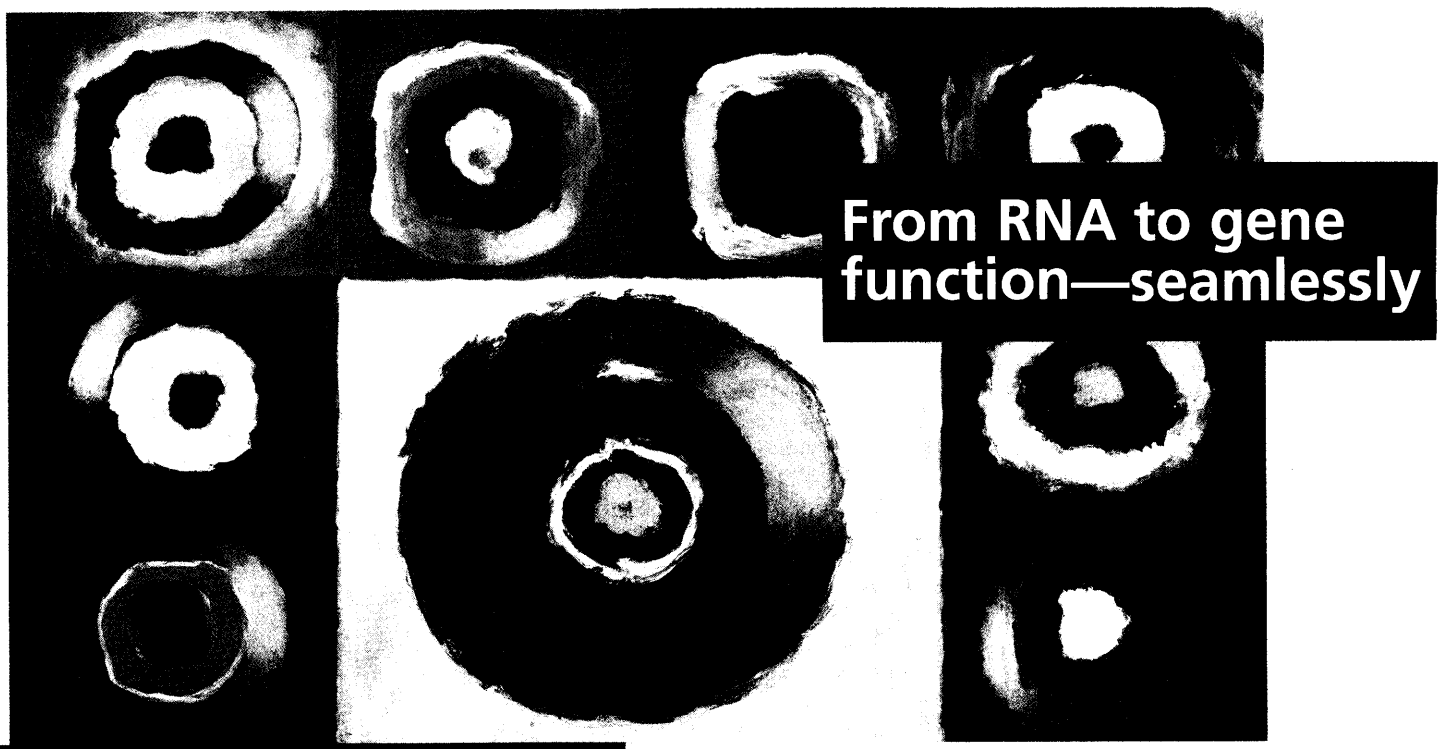

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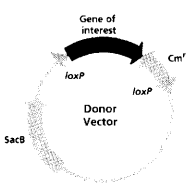

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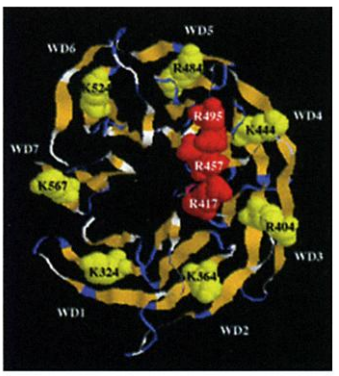
region essential for centromere function, and that definition was tested in an artificial chromosome assay. Analysis of sequences in this region provided clues to the evolution of the centromere as well as the potential for a recent origin for the functional sequences.

Tracking Triglyceride Genes

The apolipoprotein gene cluster on human chromosome 11 has been extensively studied as a region known to exert effects on triglyceride levels and cardiovascular disease. Pennacchio *et al.* (p. 169; see the news story by Seydel) have used comparative genomics between mouse and human sequences to identify a new apolipoprotein gene, *APOAV*, located near the cluster. When the human gene was expressed as a transgene in mice, plasma triglyceride decreased. In contrast, knockout mice had increased plasma triglyceride levels compared to wild-type mice. Studies of single nucleotide polymorphisms (SNPs) in the *APOAV* region in two independent human populations also indicated that this gene may influence triglyceride levels in humans.

Regulating Cell Proliferation



Increased amounts of cyclin E and its protein kinase partner cyclin-dependent kinase 2 (CDK2) promote progression of cells from G1 to S phase of the cell cycle, and the abundance of cyclin E is regulated by proteolysis. Koepp *et al.* (p. 173; see the Perspective by Bartek and Lukas) have identified the human ubiquitin ligase subunit, named Fbw7, that binds phosphorylated cyclin E and targets it to the SCF complex, where it is ubiquitinated and later degraded. Thus, similar mechanisms are used in yeast, worms, flies, and mammals to regulate abundance of cyclin E. The functional characterization of Fbw7 suggests that it could function as a tumor suppressor.

A Beneficial Triplet Repeat

Triplet repeat expansions occur in several human genetic diseases and always result in a deleterious phenotype. Studying the bacterium *Escherichia coli*, Ritz *et al.* (p. 158) describe a triplet repeat expansion that is beneficial. An *E. coli* strain that grows poorly because of a defect in the reduction of protein disulfide bonds undergoes a phenotypic reversion at high frequency because of reversible expansion of a TCT repeat sequence in the *ahpC* gene. Remarkably, this genetic alteration restores normal cell growth because it introduces a single amino acid into the AhpC protein that converts it from a peroxidase to a disulfide reductase. The ready mutational interconversion of these two enzyme activities may allow the bacteria to survive conditions of oxidative or disulfide stress.

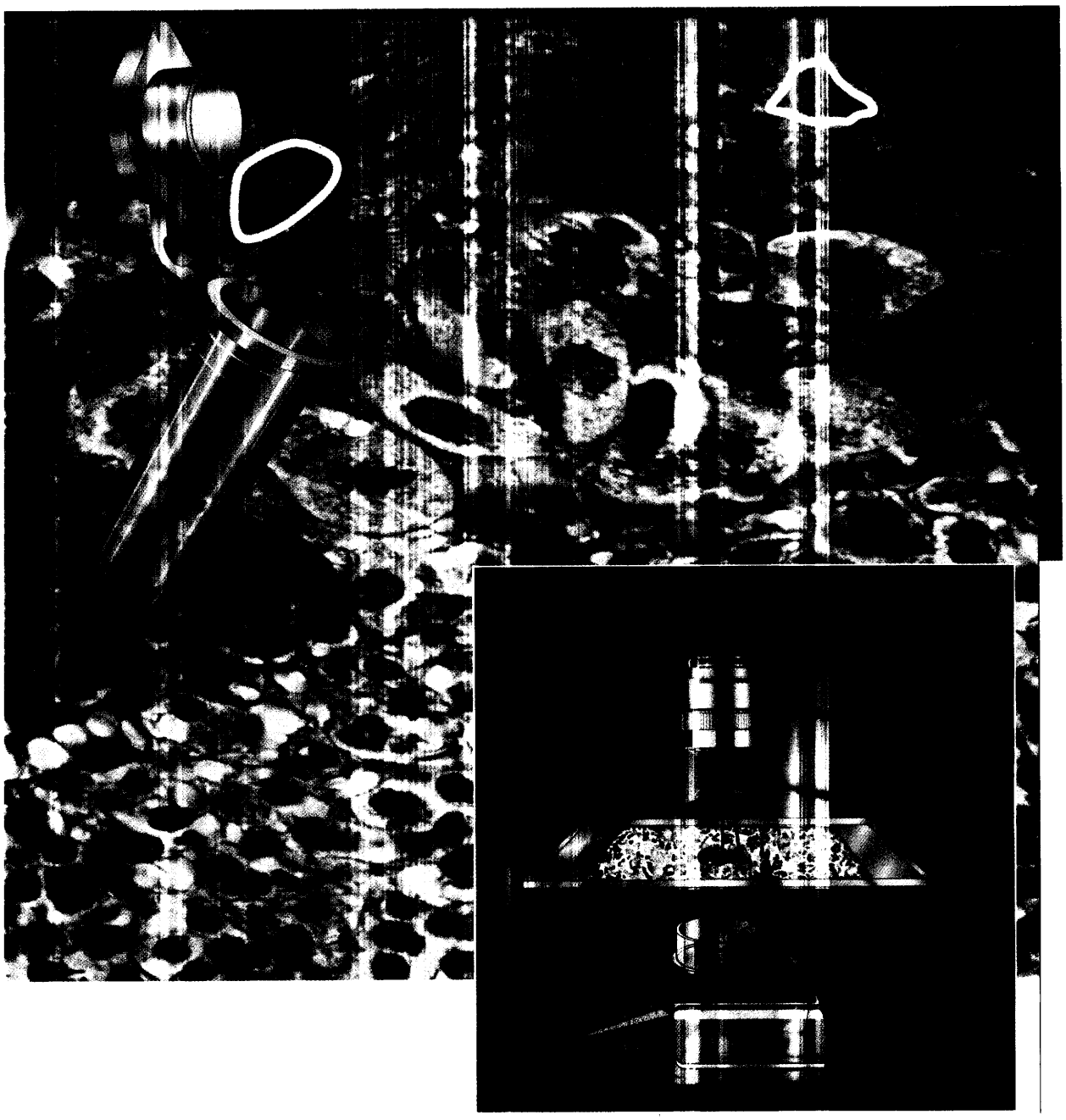
Evolution of Virulence in Toxoplasma

Toxoplasma, which undergoes sexual reproduction and might be expected to show a high degree of genetic mixing among strains, exists as only a few genetically distinct "clonal types." Grigg *et al.* (p. 161) analyzed polymorphic loci and found that the three major types originated from rare crossing events between two ancestors. Such reassortment may have been crucial in the development of virulence, as a cross between two avirulent strains resulted in an organism that was highly virulent in mice. Virulence is likely to be attributable to a combination of factors rather than a single gene.

Protection from Prions

Prions are the likely causative agents in new variant Creutzfeldt-Jakob disease (vCJD) and bovine spongiform encephalopathy (BSE), as well as scrapie. Experimental vaccination against prion disease in mice has been impaired by poor immunogenicity of the prion protein (PrP^{Sc}) resulting from partial immune tolerance to the endogenous host form of the protein, PrP^{c}. Heppner *et al.* (p. 178) generated transgenic mice in which the clonal antibody repertoire was skewed toward prion recognition. Immunization of these animals with PrP^{Sc} resulted in protection from neuropathic changes associated with scrapie, even when genes for endogenous PrP^{c} were reintroduced.

CREDIT: KOEPP *ET AL.*



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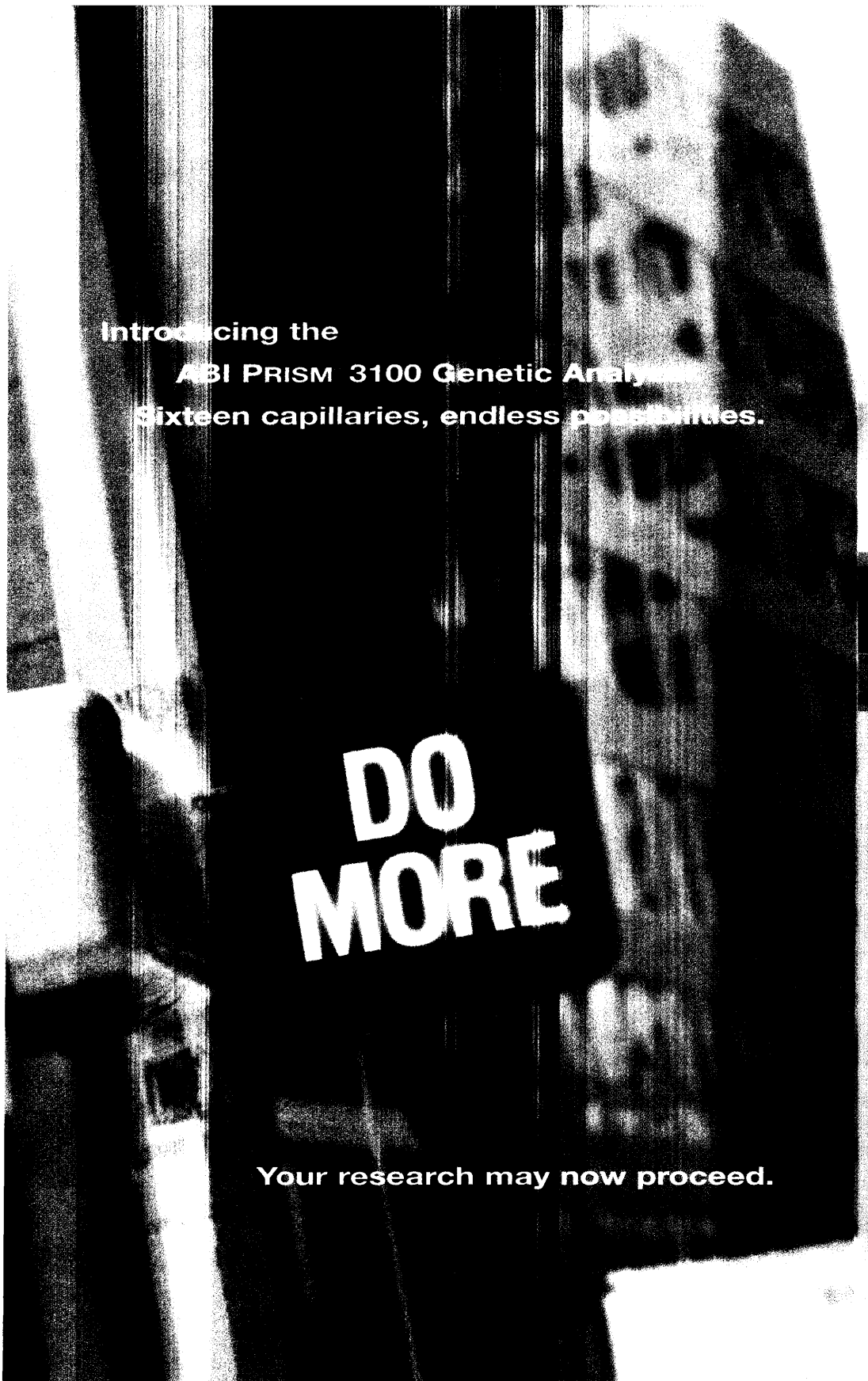

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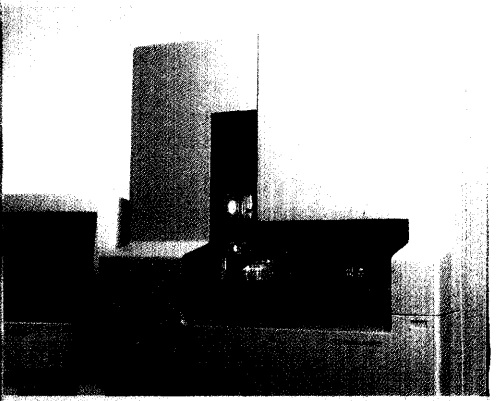

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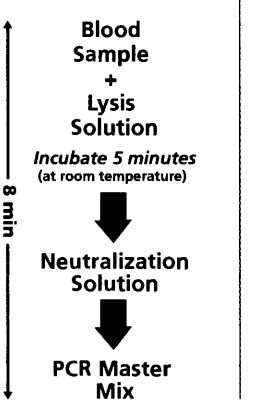

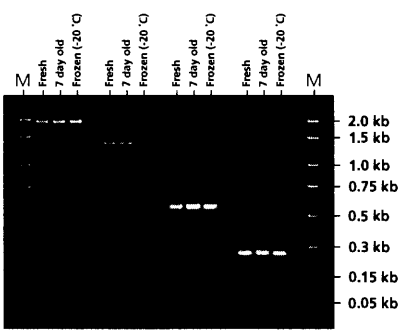

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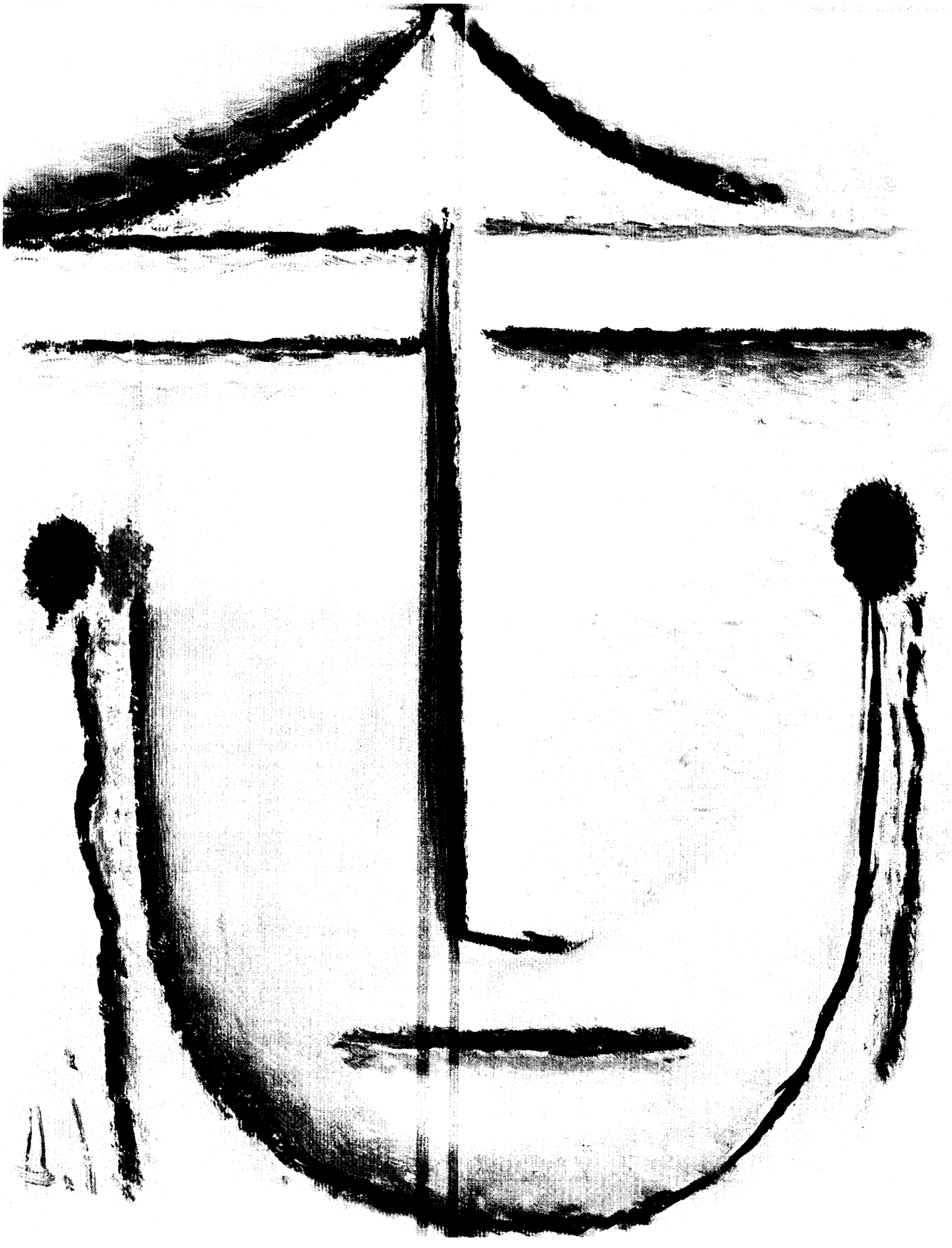

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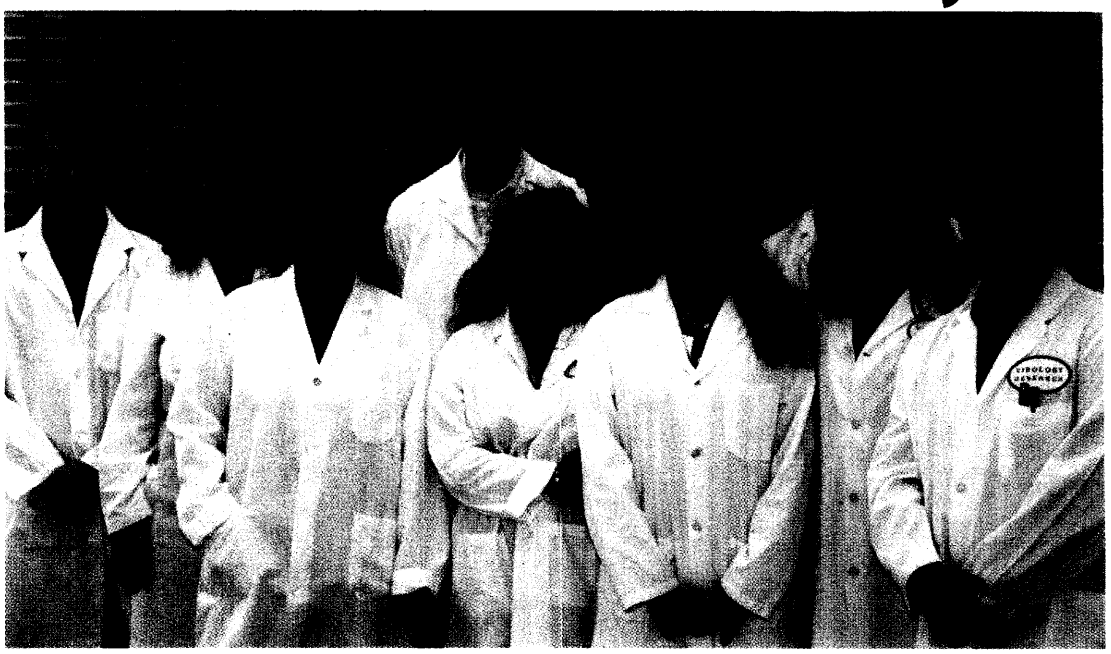

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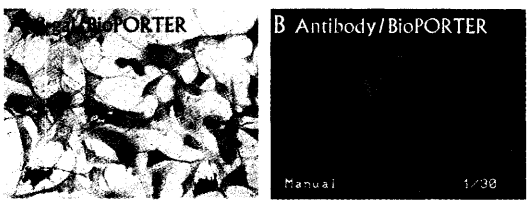
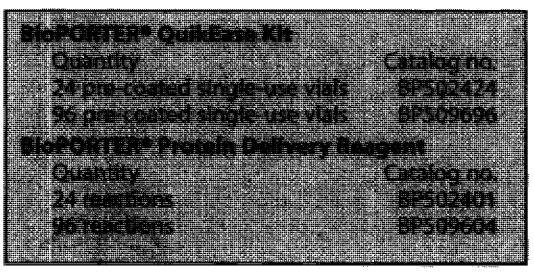


Fig. A/B FITC-Antibody or β-gal Delivery Into Mouse Fibroblasts



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1. Zelphati, O *et al* (2001) Paper in press: *J. Biol Chem.* published on July 10, 2001 as manuscript M104920200

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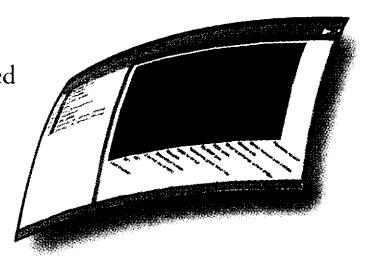

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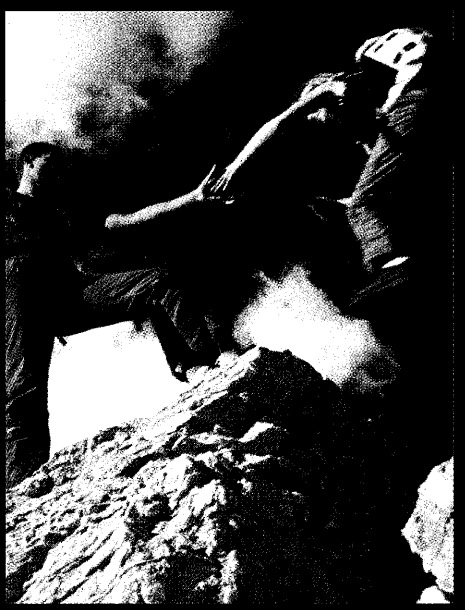

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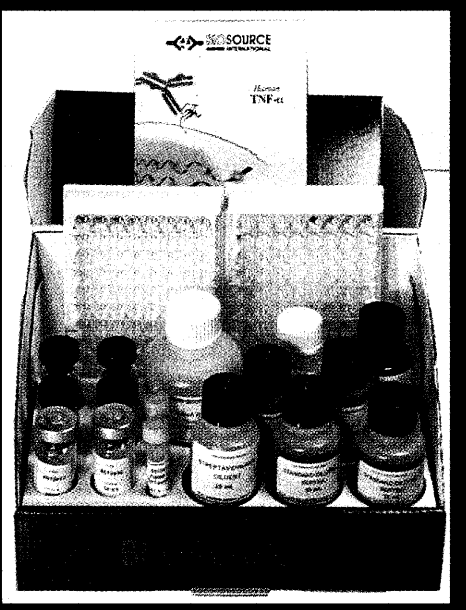

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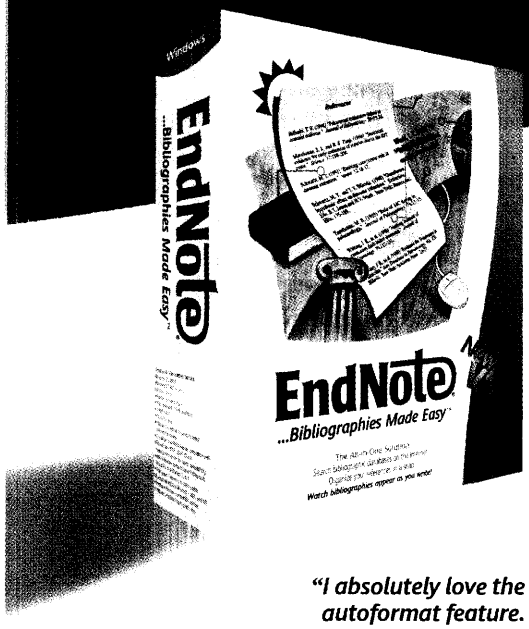

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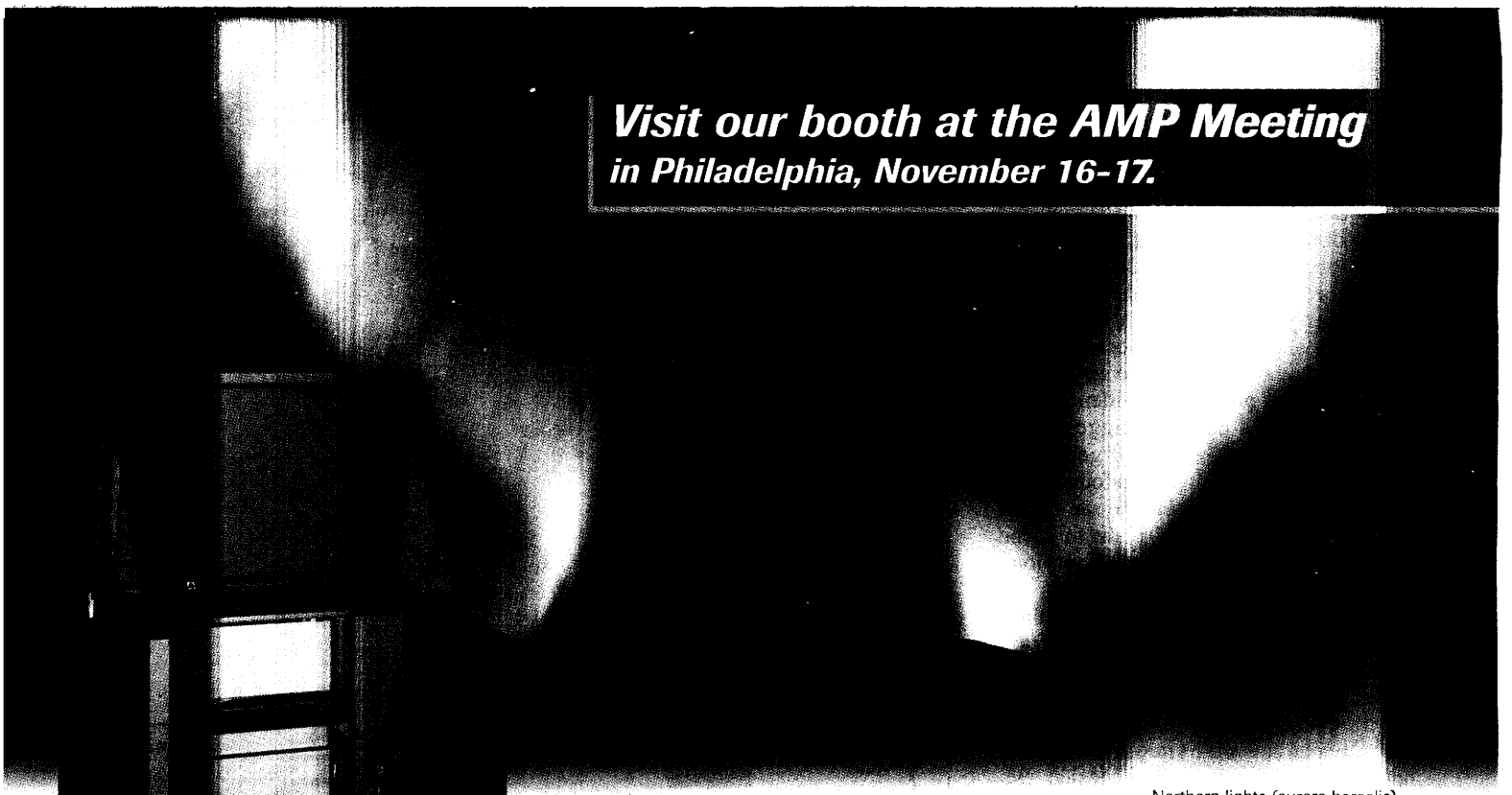

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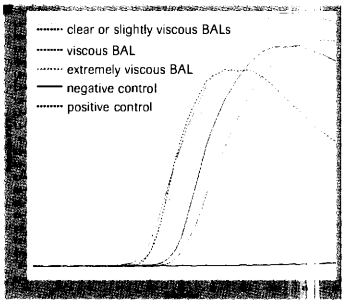
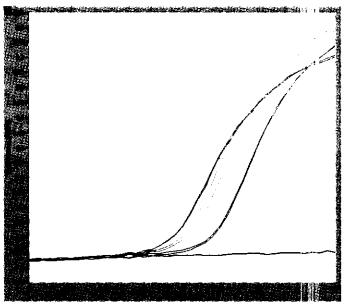


DNA from six different *S. aureus*-positive BAL research samples, analyzed by LightCycler PCR.



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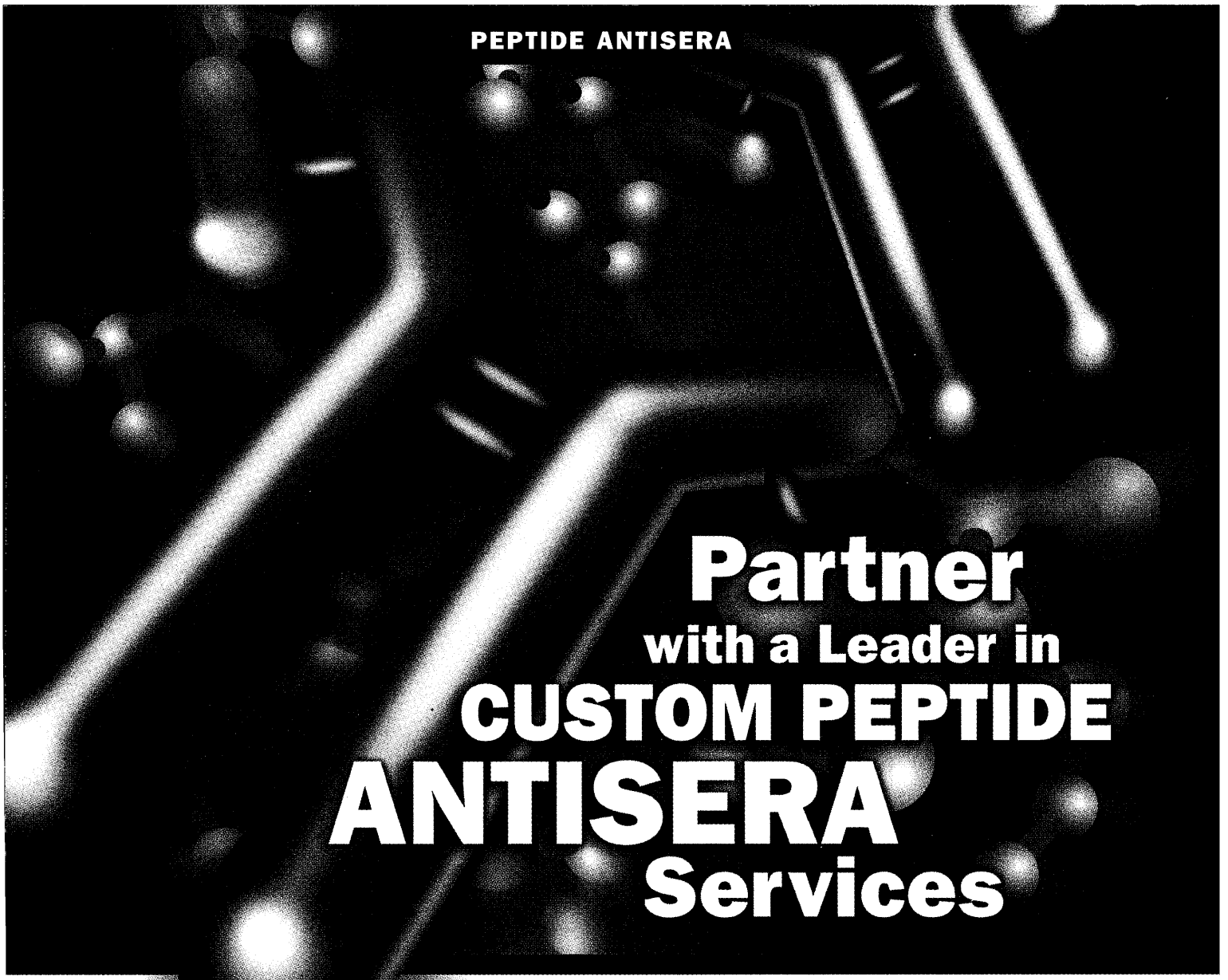

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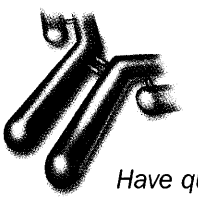

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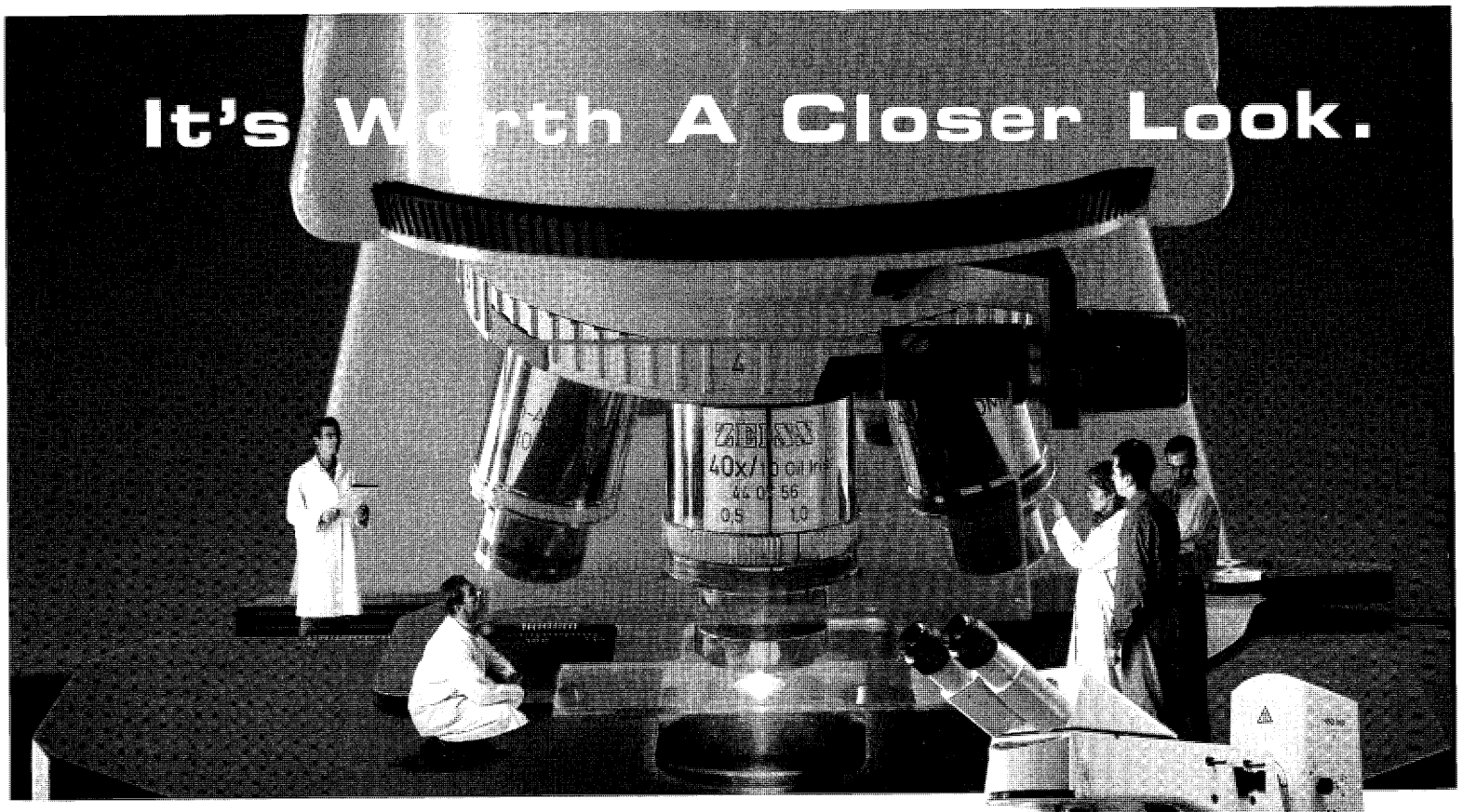

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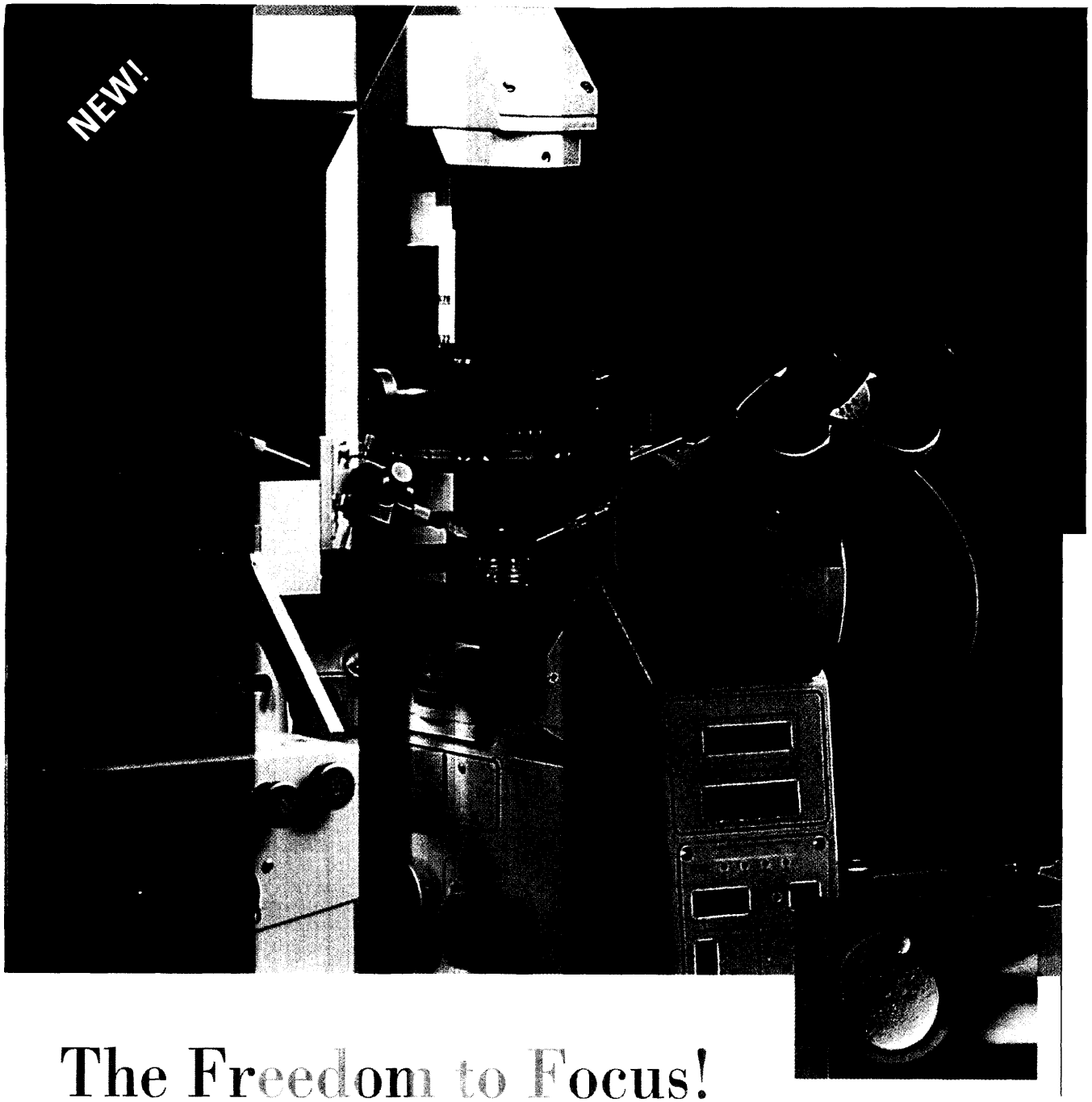

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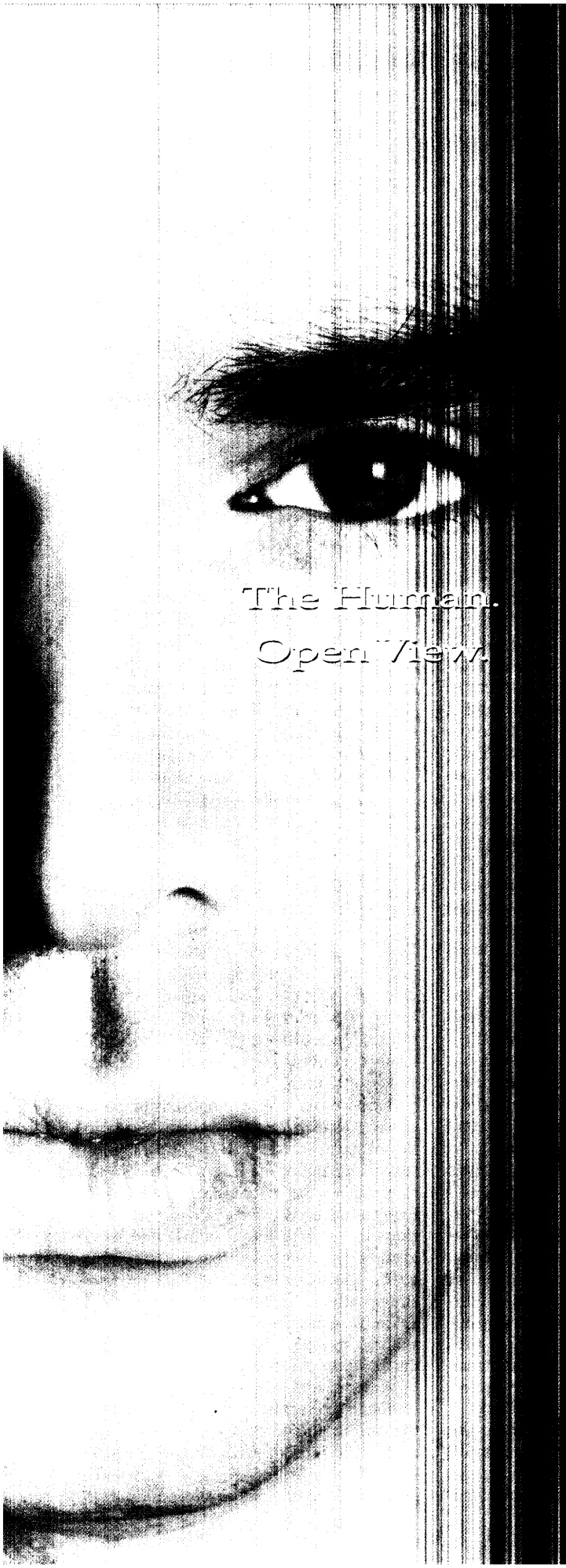

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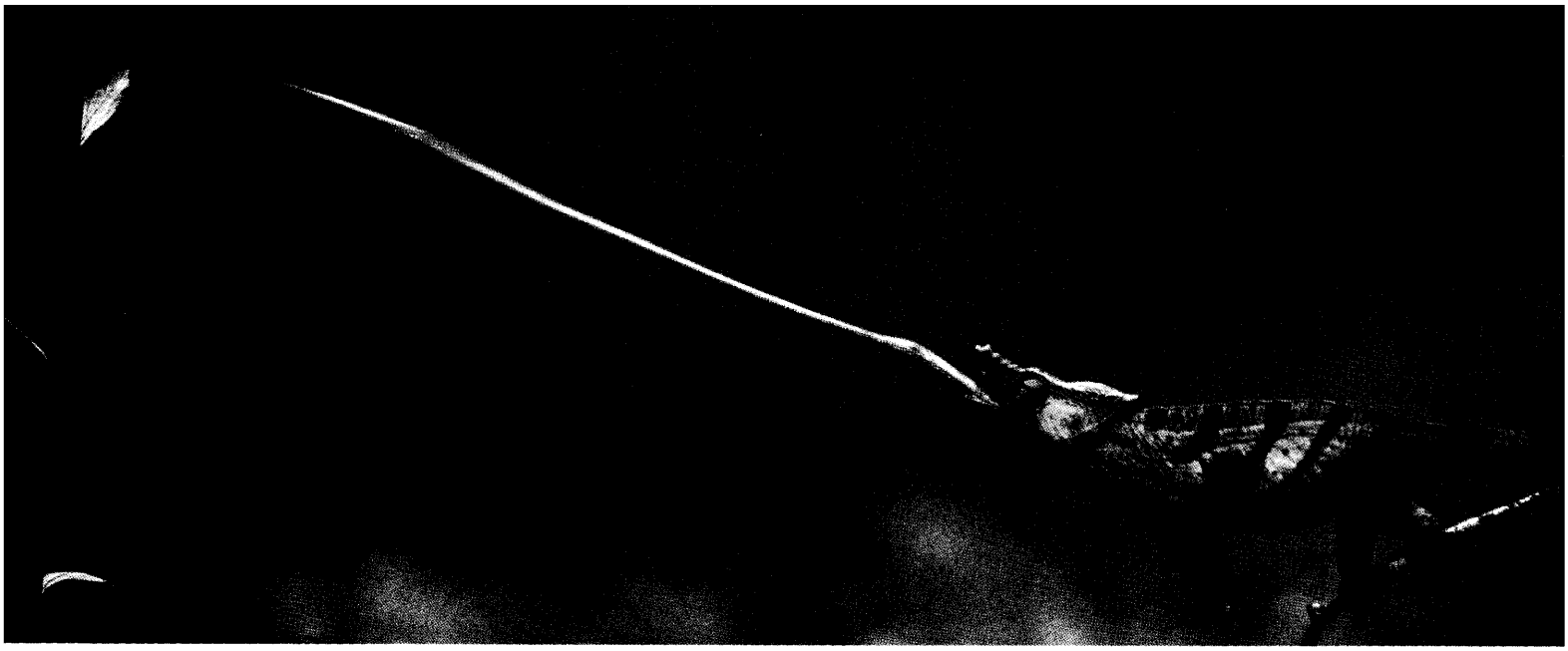

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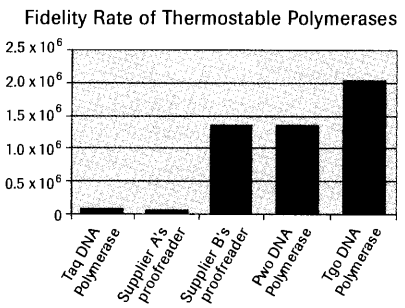

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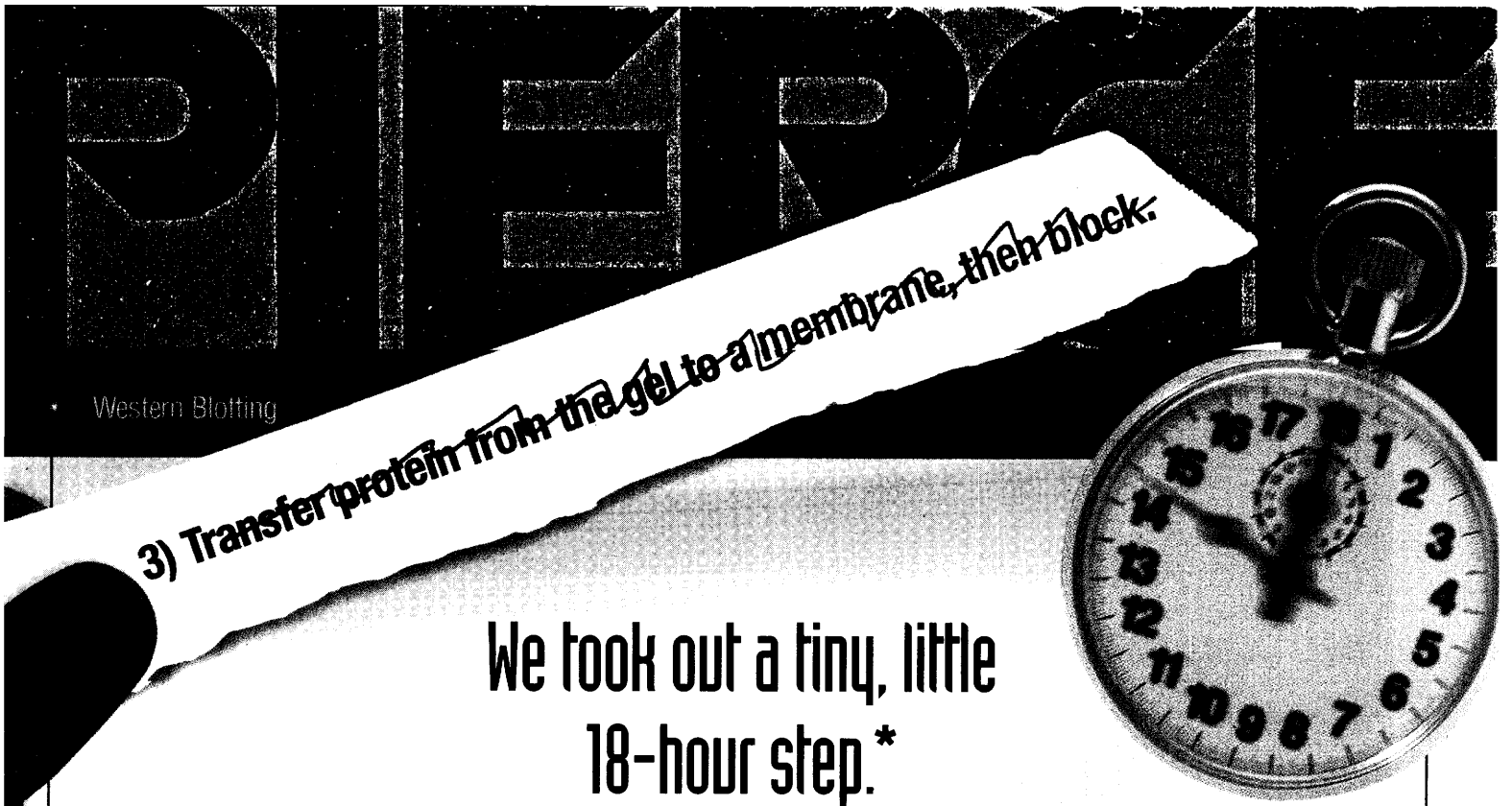

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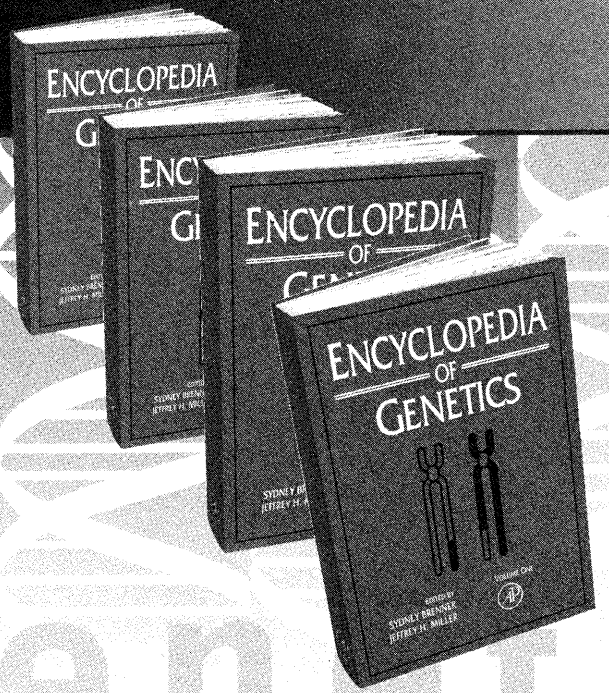

EDITED BY

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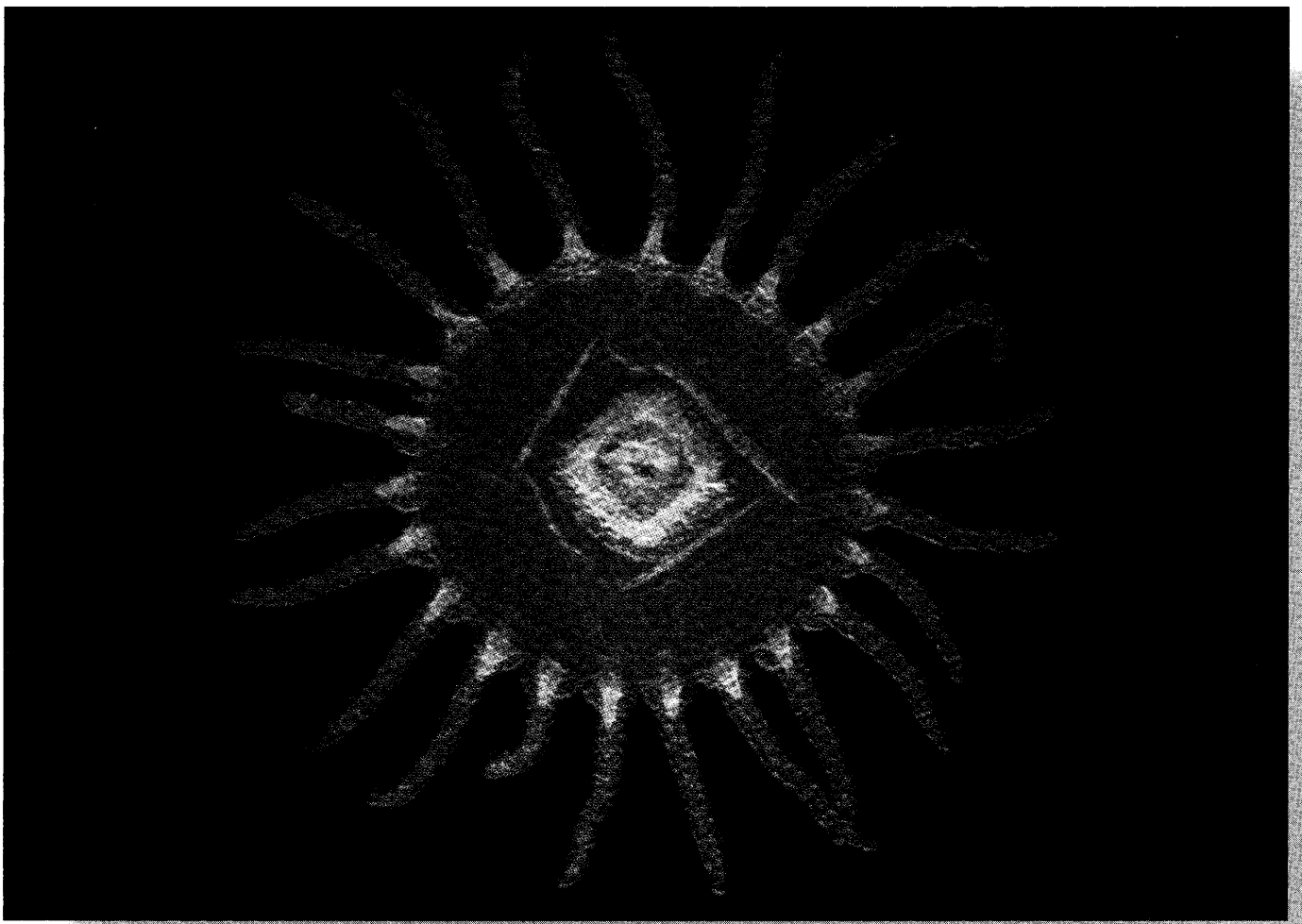

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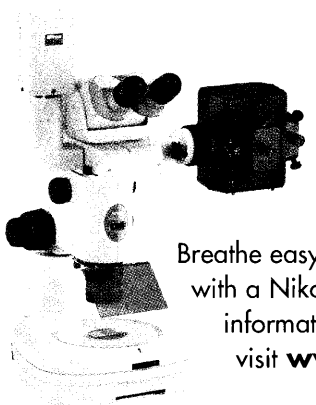

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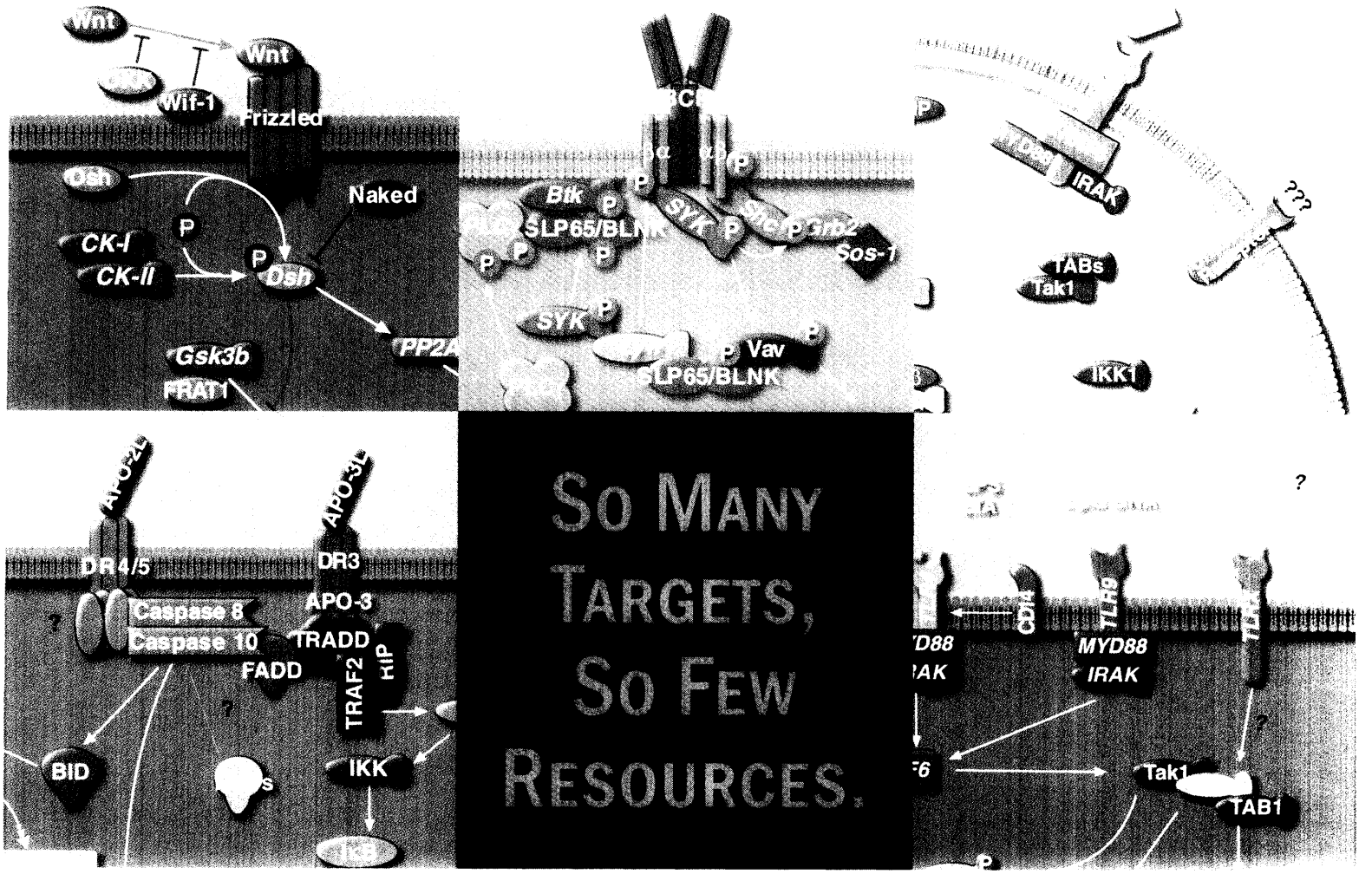

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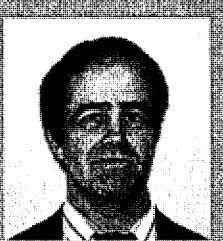

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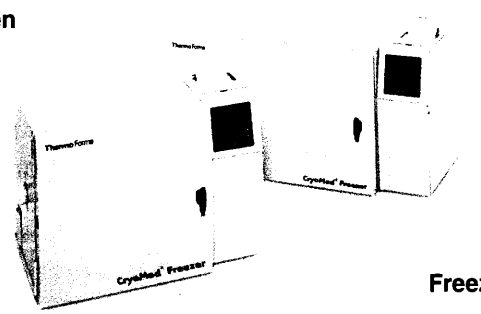

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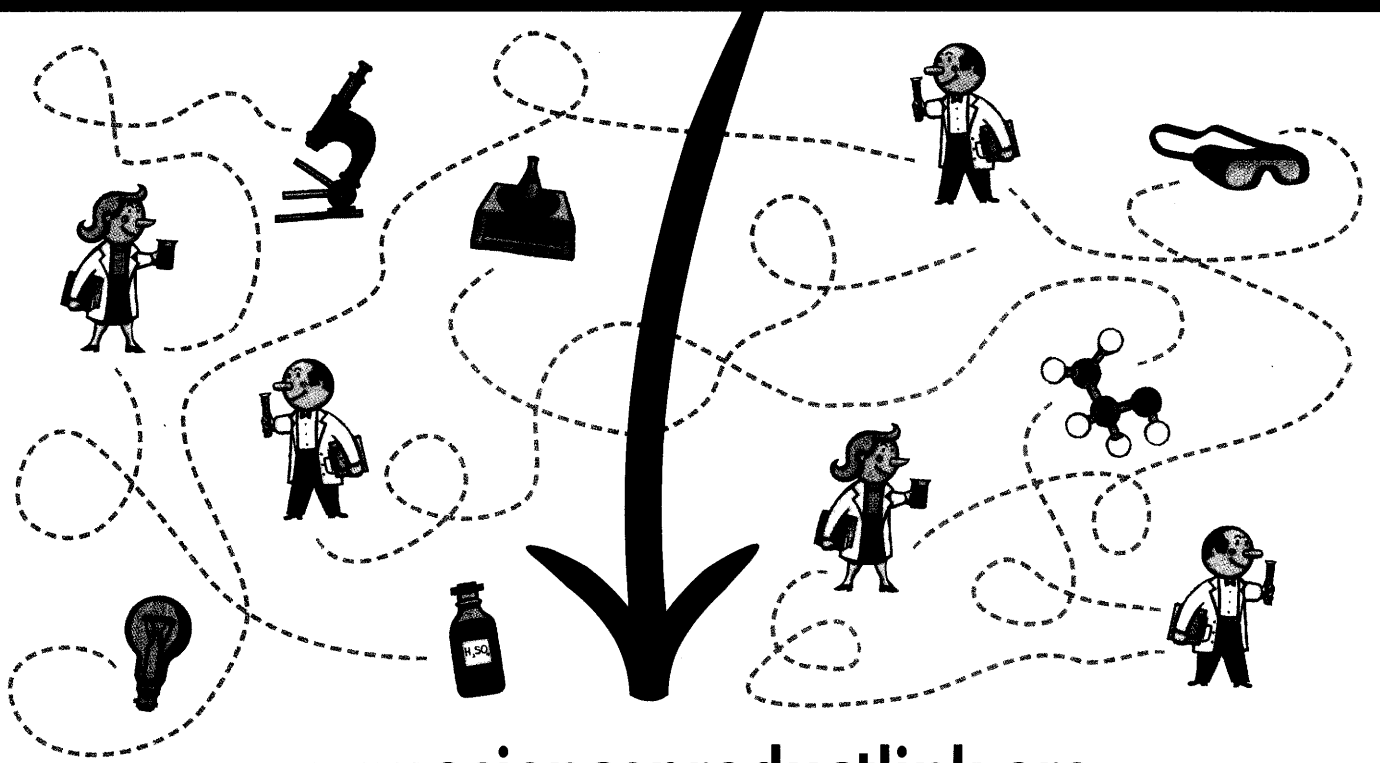

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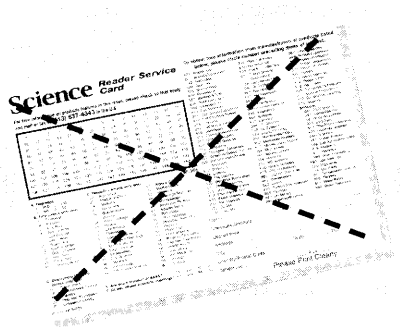

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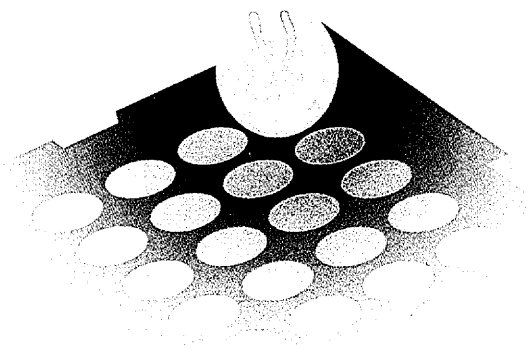

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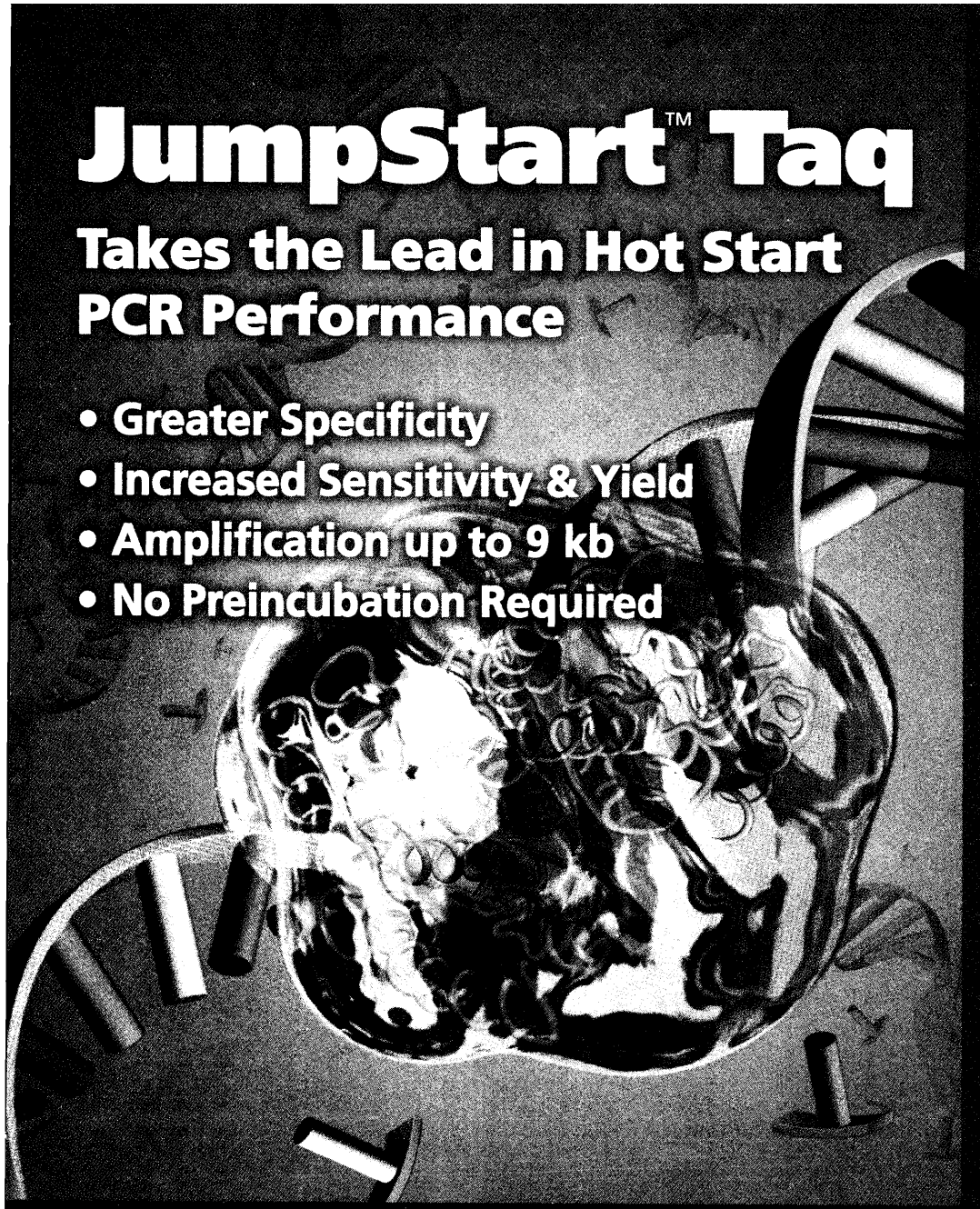

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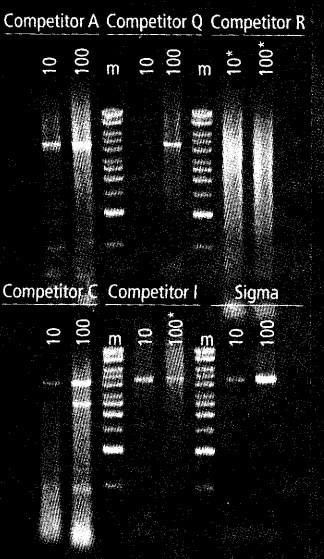

10 or 100 ng total human genomic DNA was amplified with primers targeted to a 5 kb section of β globin. Activation parameters and the number of cycles were altered to fit the supplier's recommendations.

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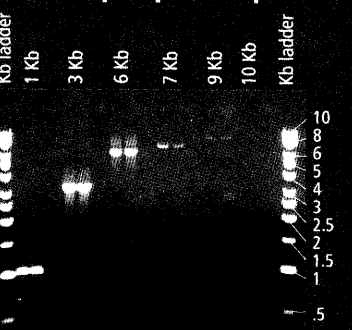

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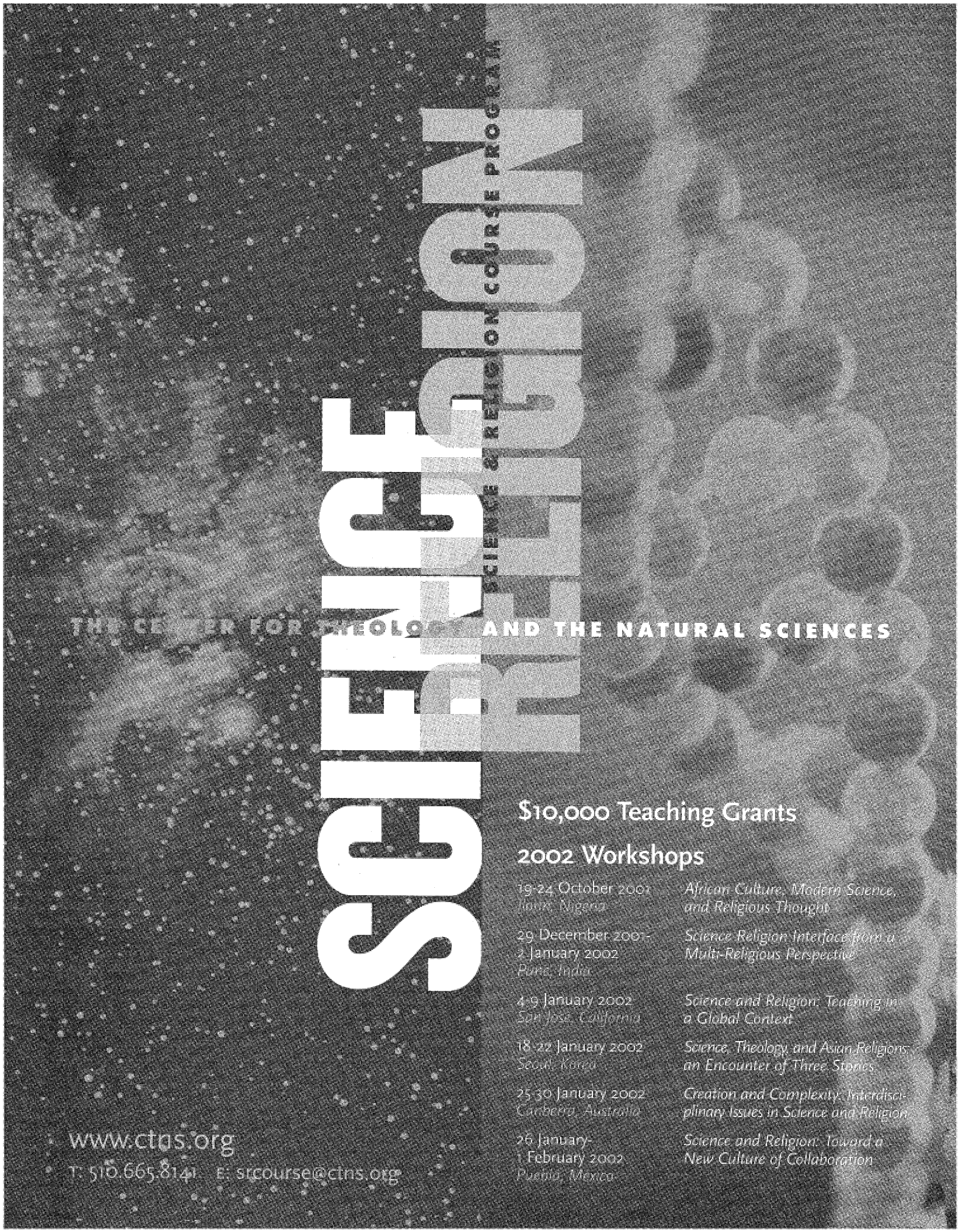
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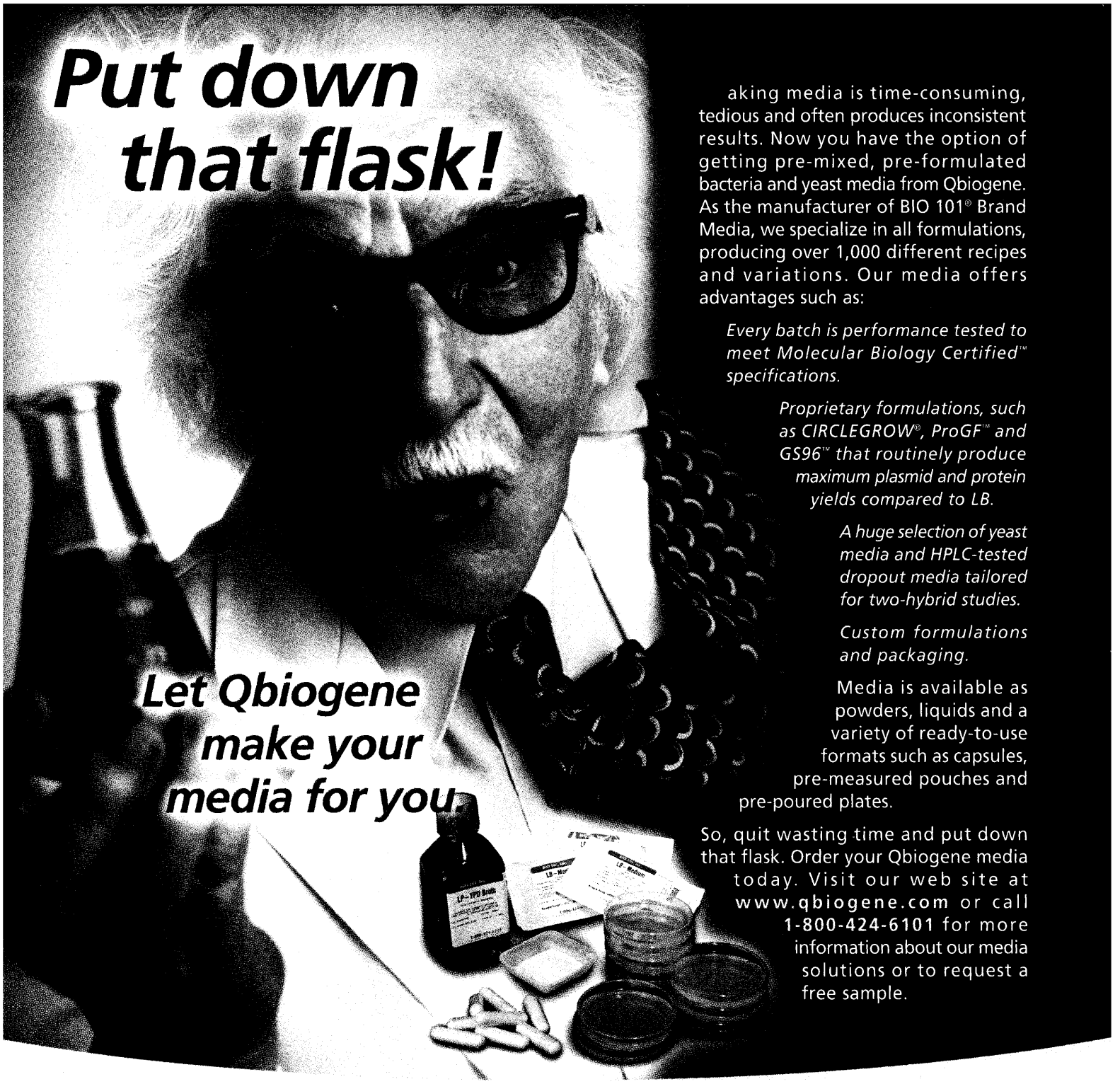

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