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Neurodegeneration



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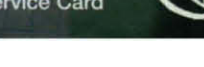
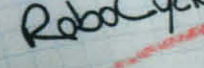
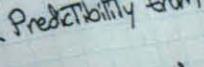
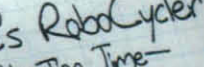
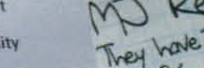
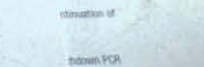
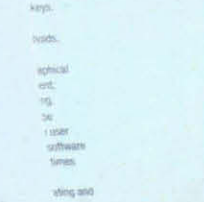
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COVER Coronal magnetic resonance image of the brain of an Alzheimer's disease patient. Accurate realignment and subtraction of two scans of this patient taken 1 year apart reveal substantial widespread cerebral loss, indicated by the red overlay. This graphically enhanced image is related to the special section on Neurodegeneration, which begins on p. 1071. [Image: W. R. Crum, N. C. Fox, M. N. Rossor, Dementia Research Group, National Hospital for Neurology and Neurosurgery, London, U.K.]



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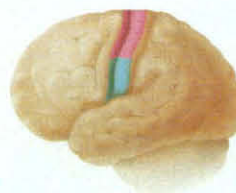
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IMPROVING HOLOGRAPHIC MATERIALS

Although holography can be used to store huge amounts of digital data, the process of reading the hologram also erases it unless the material is "fixed" in some way, just as development fixes photographic film. Hesselink *et al.* (p. 1089) recently described an all-optical fixing method in which the energy from two light beams is used to write holograms. The weaker infrared beam, used in the reading mode, is too weak to erase the material. They now describe the underlying mechanism of this approach and ways to optimize the composition of the storage material, lithium niobate, to improve its sensitivity, gated recording efficiency, and dark-condition storage times.

THE BIRTH OF BROWN DWARFS

Since the discovery of the first bona fide brown dwarf, Gliese 229B, observers have searched for other candidate brown dwarfs to determine how they form and to characterize their mass and age. Tamura *et al.* (p. 1095) conducted two near-infrared wavelength surveys of the nearby (about 500 light years away) molecular clouds, Taurus and Chamaeleon, and found a dozen brown dwarf candidates. Some of these candidates had inferred masses as low as 0.012 solar masses, and some were also inferred to be as young as 1 million years old. Thus, the low mass and young age of these brown dwarf candidates suggest that these images captured brown dwarfs just after birth and that, like stars, brown dwarfs can form in molecular clouds.

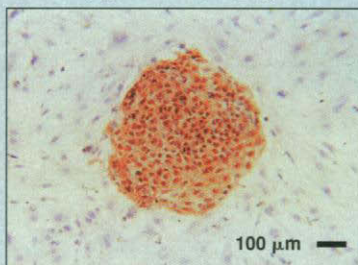
PARTICLE BALLET IN NEPTUNE'S RING

Neptune has four arcs of concentrated dusty, subkilometer-sized particles confined within a diffuse ring of particles that orbits about 63,000 kilometers away from the planet. It has been difficult to understand how this arc-ring system can be maintained over long periods of time. Salo and Hänninen (p. 1102) have developed a numerical model that reproduces several key structures of the arc-ring system that are stable for long time scales. They show that gravitational attraction between particles within the arcs actually keeps them from impacting each other under the influence of the major confining forces applied by Neptune and Neptune's moon, Galatea. Thus particle self-gravity allows the arcs to maintain their shape. This unexpected result removes an assumed

source of dust (by particle-particle impacts) for the arcs, however. The authors suggest that kilometer-sized particles between the arcs are impacted by smaller particles. The subtle gravitational presence of the larger particles then confines the dusty ejecta into specific regions, and simulations show that multiple regions may intersect one arc. Thus, the large particles help to explain the width and high concentration of dust in the arcs.

HARNESSING HUMAN STEM CELLS

The early embryo contains cells that have unlimited growth and differentiation potential. In mice, these embryonic stem (ES) cells have been cloned and used to generate mice with specific genetic changes. Thomson *et al.* (p. 1145; see the editorial, news story by Marshall, and the Perspective by Gearhart) generated long-term cell



lines from early human embryos. Although the cells remain undifferentiated in culture and express primate ES cell markers, they can be induced both in vitro and in vivo to differentiate into recognizable tissue from all three major lineages: ectoderm, mesoderm, and endoderm. Cell lines such as these may be useful for generating replacement human cells and tissues.

FIELDS OF NANOTUBES

Carbon nanotubes are receiving much attention as components in nanoscale electronic devices. A key requirement for such applications is the synthesis of highly ordered arrays of the tubes and to use the synthesis conditions and substrates that are compatible with the intended applications. For example, flat panel displays use glass substrates, which constrains the highest temperatures that can be used in the nanotube synthesis. Ren *et al.* (p. 1105) show that nanotube arrays of high regularity and wide spatial extent (several square millimeters) can be grown directly

on glass substrates at low enough temperatures (below 700°C) so that the glass properties were not affected.

EARLY FOIL FASHIONING

Metalworking, including the fashioning of intricate copper and gold ornaments, has been well known since about 2500 years ago in Andean civilizations, but the origins of this culture have been uncertain. Burger and Gordon (p. 1108; see the Perspective by Quilter) now describe simple copper and gold artifacts dating to about 3400 years ago from Mina Perdida, Peru. The foil artifacts seem to have been produced by shaping native metal and indicate that metalworking significantly predated ore smelting.

TRAUMA RESPONSE IN THE BRAIN

What is the capacity for long-term change in the primate brain? Two reports provide anatomical and physiological results from monkeys that have suffered trauma to an upper limb, thus altering the sensory input to the brain (see the Perspective by Merzenich). Jones and Pons (p. 1121) find that the thalamus, the first station through which sensory input passes, experienced massive reorganization that resulted in the sensory representations of the face and trunk coming together along with an expansion of the corresponding areas. Florence *et al.* (p. 1117) find that similarly large-scale changes of representation and neuronal expansion occurred in the somatosensory cortex.

CLUES FROM THE MALARIA PARASITE GENOME

The complete sequence of a chromosome of the malaria parasite, *Plasmodium falciparum*, is presented by Gardner *et al.* (p. 1126). Chromosome 2 is 945 kilobases in length and contains 209 predicted genes. Its highly A+T-rich (80.2 %) nature had suggested that established procedures for whole-genome "shotgun" strategies would not work; however, accurate assembly was accomplished. Several *Plasmodium*-specific genes, including a family of rifins that may be involved in antigenic variation, were identified.

UNDERPINNINGS OF ADAPTIVE MUTABILITY

In 1988, Cairns described a series of experiments, which seemed to show that an organism could respond to stress by increasing the rate of mutation in one or more genes that would help it to deal

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1005

with that stress. This "adaptive mutability" hypothesis itself has created a large increase in the amount of seeking to confirm or refute the premise. Andersson *et al.* (p. 1133) present experiments to show that there can be selective amplification of a mutant gene that is partly functional. This selective amplification increases the number of targets and makes it appear like the mutation rate has increased after exposure to stress, when, in reality, the mutability of locus is unchanged.

BUILDING THE BITE

Tooth development in mammals depends on finely regulated interactions between the ectoderm and the underlying mesenchyme. Further specifications must define the particular type of tooth and the order relative to other teeth, placing incisors in the front of the mouth and molars in the rear. Tucker *et al.* (p. 1136) have identified the peptide signal BMP4 and the homeobox gene *Barx-1* as some of the components

that determine tooth identity in the mouse. Fine differences in structure between members of an array of otherwise similar structures can be specified and adjusted by the timing and balance of relevant peptide signals and homeobox gene expression.

ENERGY AND EXCITATION

In many tissues, potassium (K^+) channels are modulated by adenosine triphosphate (ATP). The metabolism of the cell can thus control the membrane resting potential and hence its excitability. The mismatch between ATP sensitivity of these K^+ channels and the ATP concentration found in many cells suggests that other endogenous factors influence this modulation. Baukowitz *et al.* (p. 1141) and Shyng *et al.* (p. 1138) show that the phospholipids PIP and PIP₂ strongly control ATP and K^+ channel interaction (see the Perspective by Ashcroft). This finding may be another example for the fine-tuning of cellular excitability by its metabolic state.

TECHNICAL COMMENT SUMMARIES

Calcineurin Inhibition and Cardiac Hypertrophy

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5391/1007a

M. A. Sussman *et al.* (Reports, 11 Sept., p. 1690) found that "administration of the calcineurin inhibitors cyclosporin and FK506 prevented disease in mice that were genetically predisposed to develop hypertrophic cardiomyopathy." "Cyclosporin had a similar effect in a rat model of pressure-overload hypertrophy."

J. G. Müller *et al.* comment that, in their experiments, with high serum concentrations of cyclosporin in a mouse model of pressure-overload hypertrophy, "all treated animals developed hypertrophy within 3 weeks." They conclude that "activated calcineurin is sufficient, but not necessary, for the induction of cardiac hypertrophy."

In response, J. D. Molkentin (Sussman *et al.*) agrees "that calcineurin is not necessary for the induction of pressure-overload hypertrophy." The original report was a 6-day study. Molkentin now observes that "rats treated with cyclosporin for longer periods, 21 days, did not show a significant prevention of the pathologic response."

Detecting Strain in the Yucca Mountain Area, Nevada

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5391/1007b

B. Wernicke *et al.* (Reports, 27 Mar., p. 2096) used data from Global Positioning System (GPS) satellite surveys and from trilateration surveys to measure the rate of strain in the Earth's crust in the Yucca Mountain area, which is under consideration as a site for the permanent disposal of highly radioactive waste. The strain rates they found were "at least an order of magnitude higher than would be predicted from the Quaternary volcanic and tectonic history of the area."

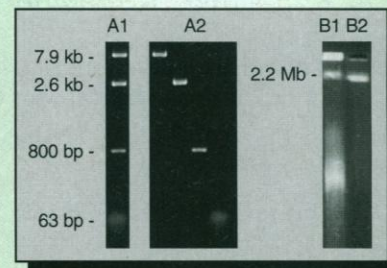
J. C. Savage comments that Wernicke *et al.* "did not include the effects of monument instability in their error budget" and "did not give proper weight to the coseismic and postseismic effects of the Little Skull Mountain earthquake" of 1992. C. B. Connor *et al.* state that high-precision isotopic dates of Lathrop Wells basalts indicate an age much older than that cited by Wernicke *et al.* They propose "three alternatives to the suggestion by Wernicke *et al.*" that the GPS-derived strain rates indicate that the area is experiencing an anomalous strain accumulation.

In response to Savage, J. L. Davis *et al.* give details of their "four different solutions for the rate of strain using different methods" to account for coseismic effects. Davis *et al.* state that the "several alternatives" offered by Connor *et al.* are "plausible, but also speculative." (Davis *et al.* also correct a value of one of the trilateration measurements.)

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(Pulsed-field CHEF gels B1 & B2 courtesy of L. Chen & A. Atherly, Zoology & Genetics, Iowa State Univ., Ames, IA.)

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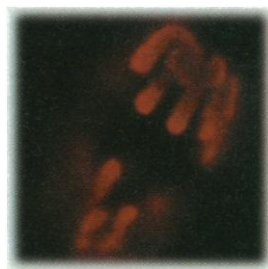
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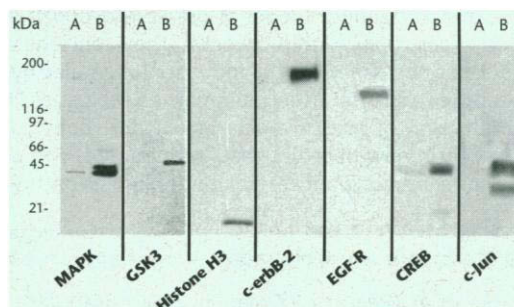
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Specific Immunocytochemical Labeling of Mitotic Cells.

Exponentially-growing kangaroo rat Ptk1 cells were fixed with methanol and stained with Upstate Biotechnology polyclonal anti-phospho-Histone H3 (Mitosis Marker) and visualized with a rhodamine-conjugated secondary antibody. An anaphase nucleus is shown at high magnification.



Western Blot Analysis. Lysates of unstimulated cells (Lane A) and stimulated cells (Lane B) were resolved by electrophoresis, transferred to nitrocellulose and probed with phosphorylation state-specific antibodies.

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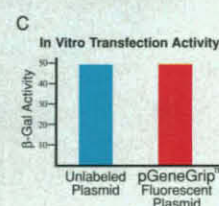
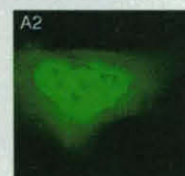
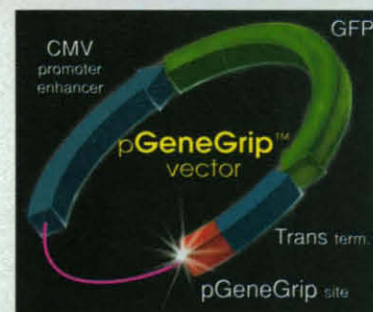
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Figures:

- A.** Fibroblasts transfected with pGeneGrip™ Rhodamine/GFP vector:
1. Rhodamine labeled DNA
2. GFP expression
- B.** Electrophoresis of pGeneGrip™ Rhodamine labeled fluorescent vector
Lanes: 1. β-gal, 2. GFP, 3. Blank
- C.** Plasmid expression with and without fluorescent label.



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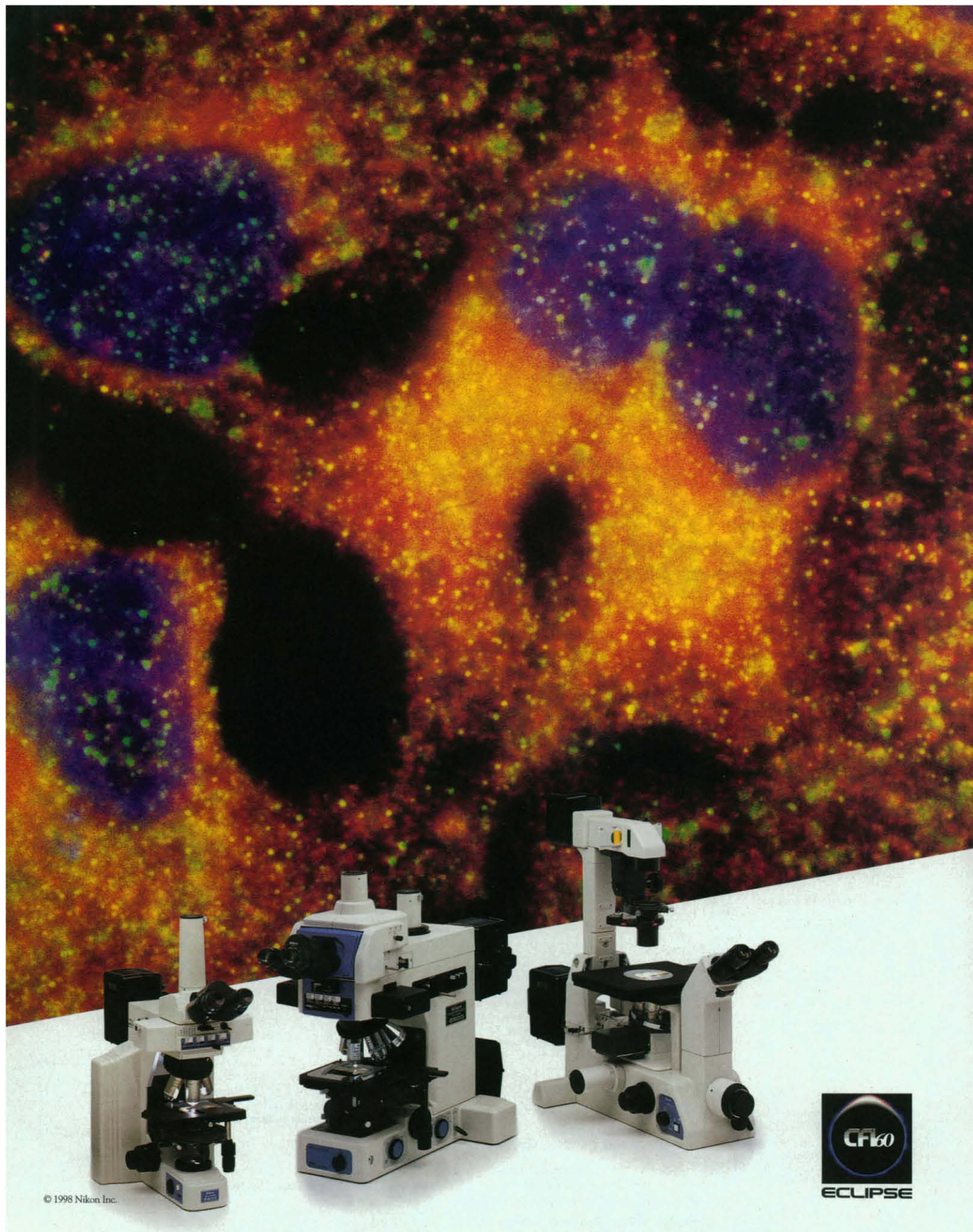
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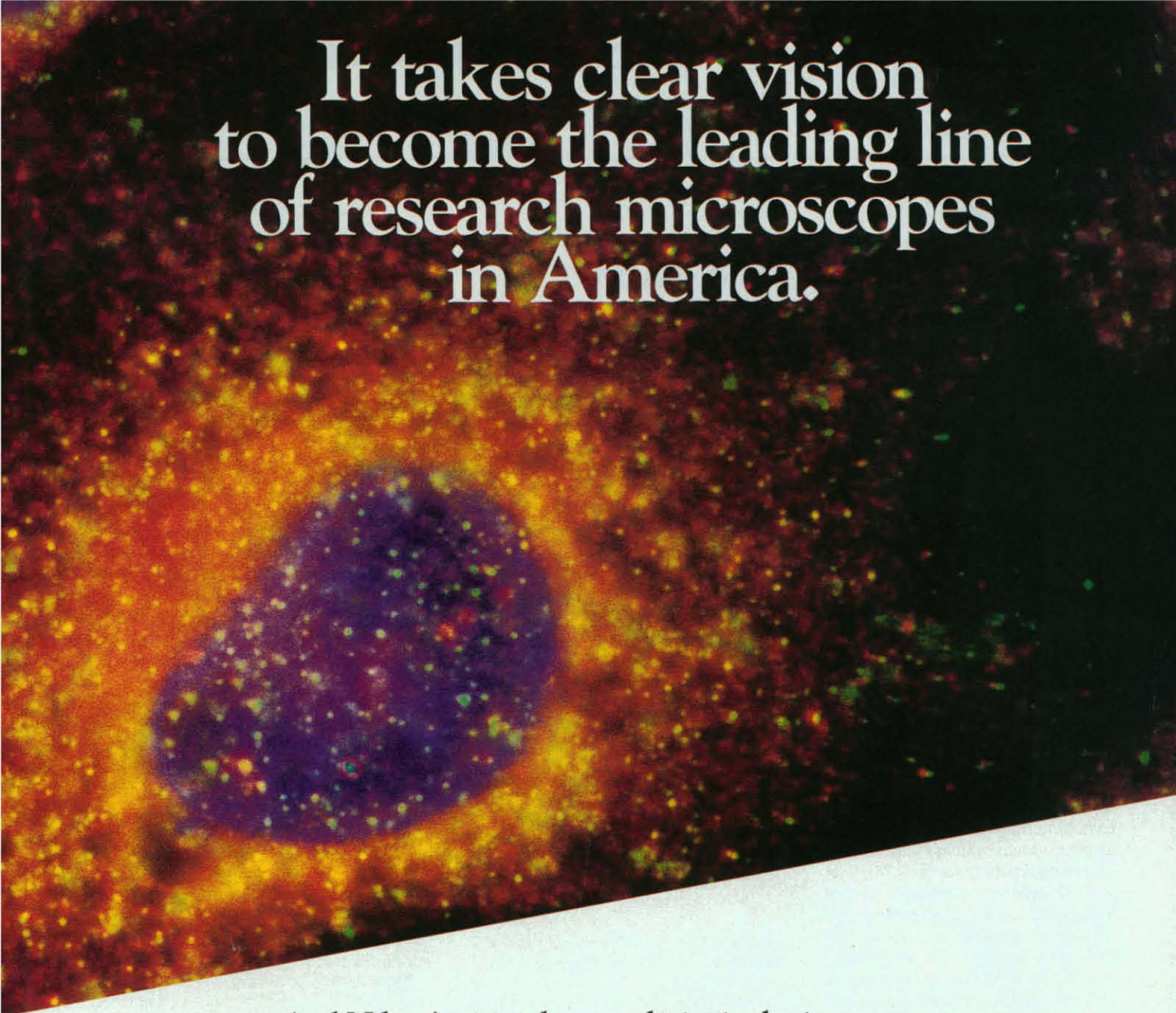
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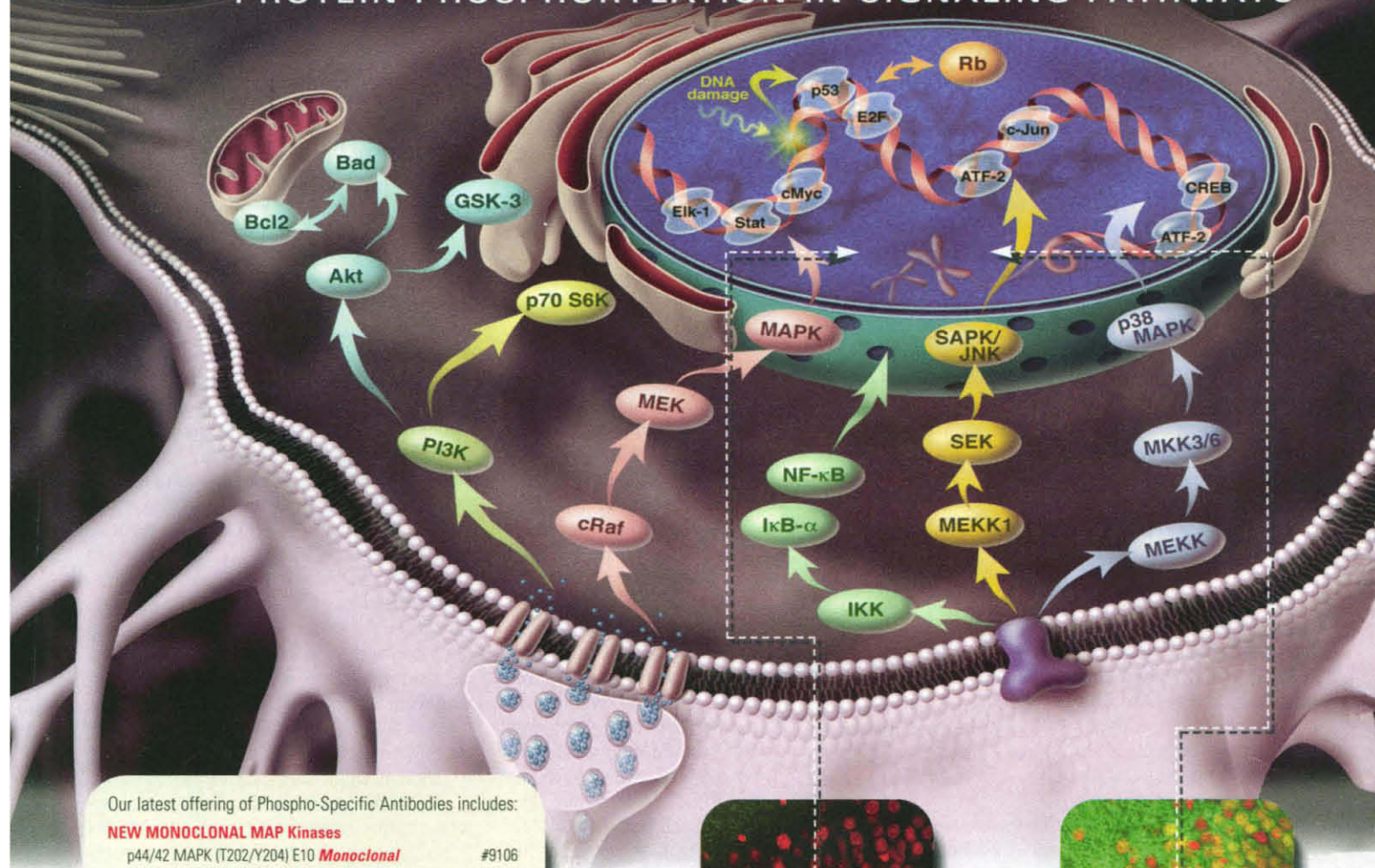
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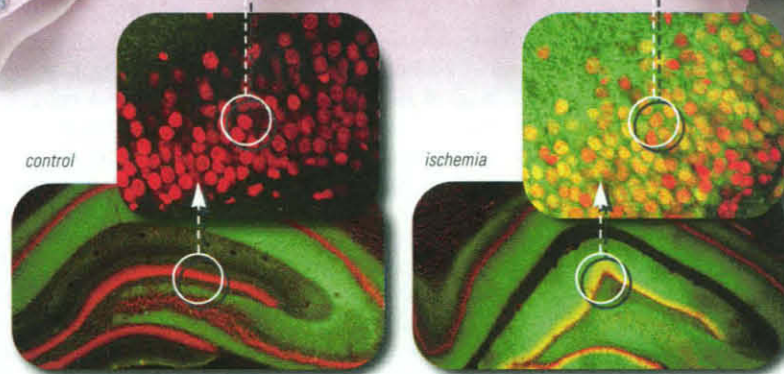
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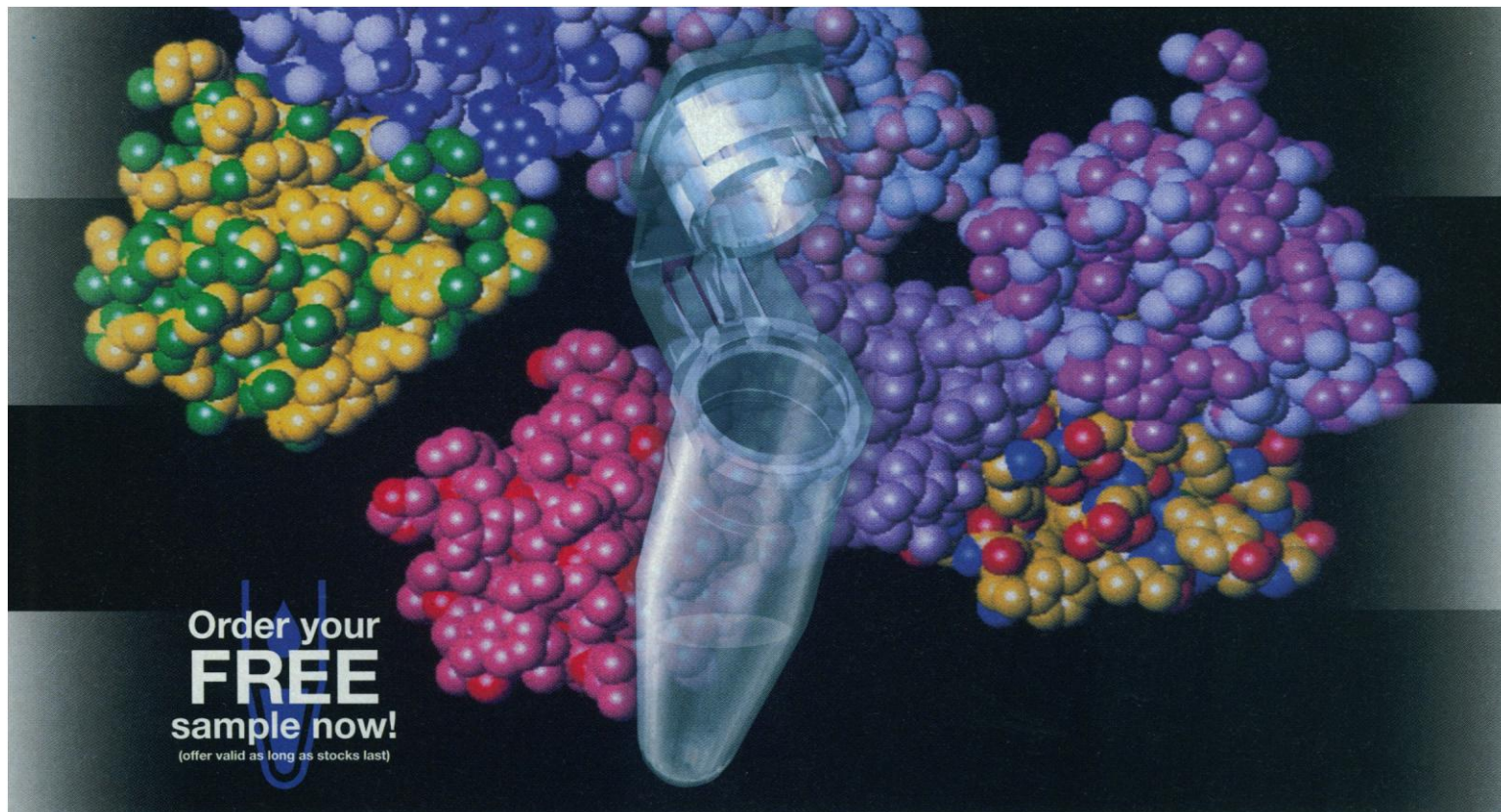
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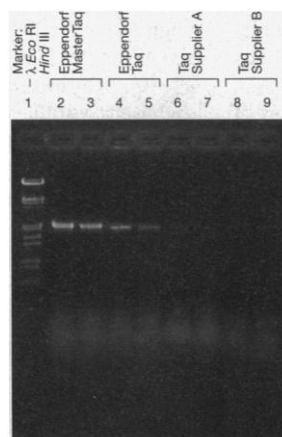
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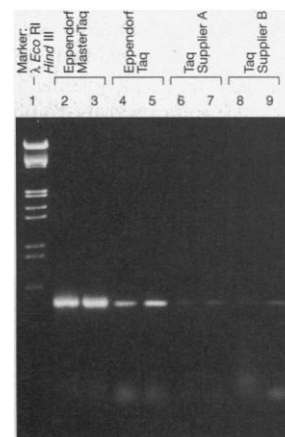
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● Fig. 1: Amplification of a SSU rRNA gene from total genomic algae DNA. PCR was performed from genomic algae using different Taq DNA Polymerases. Equal volumes of the PCR reactions were analyzed by gel electrophoresis.



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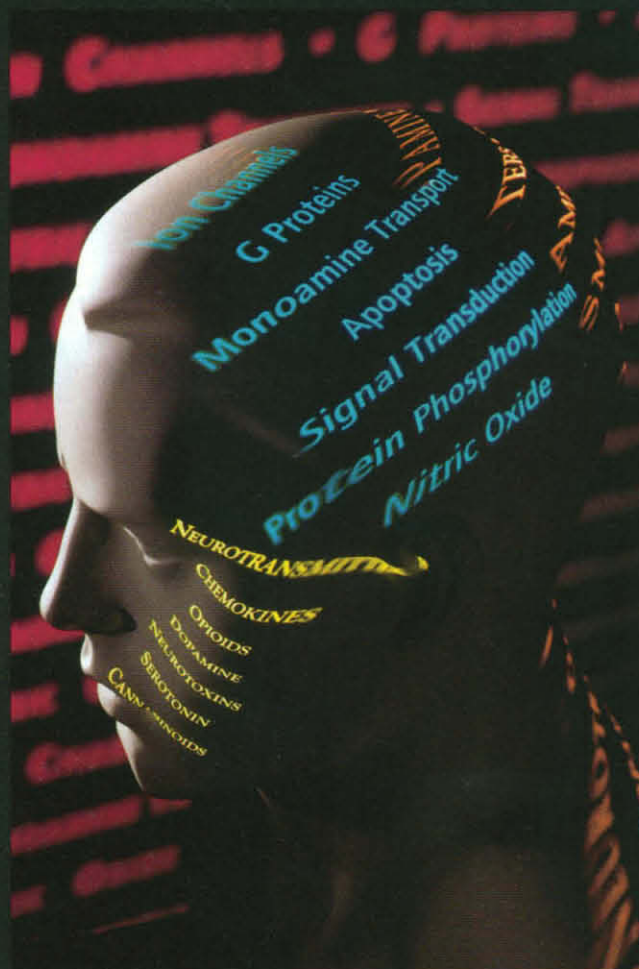
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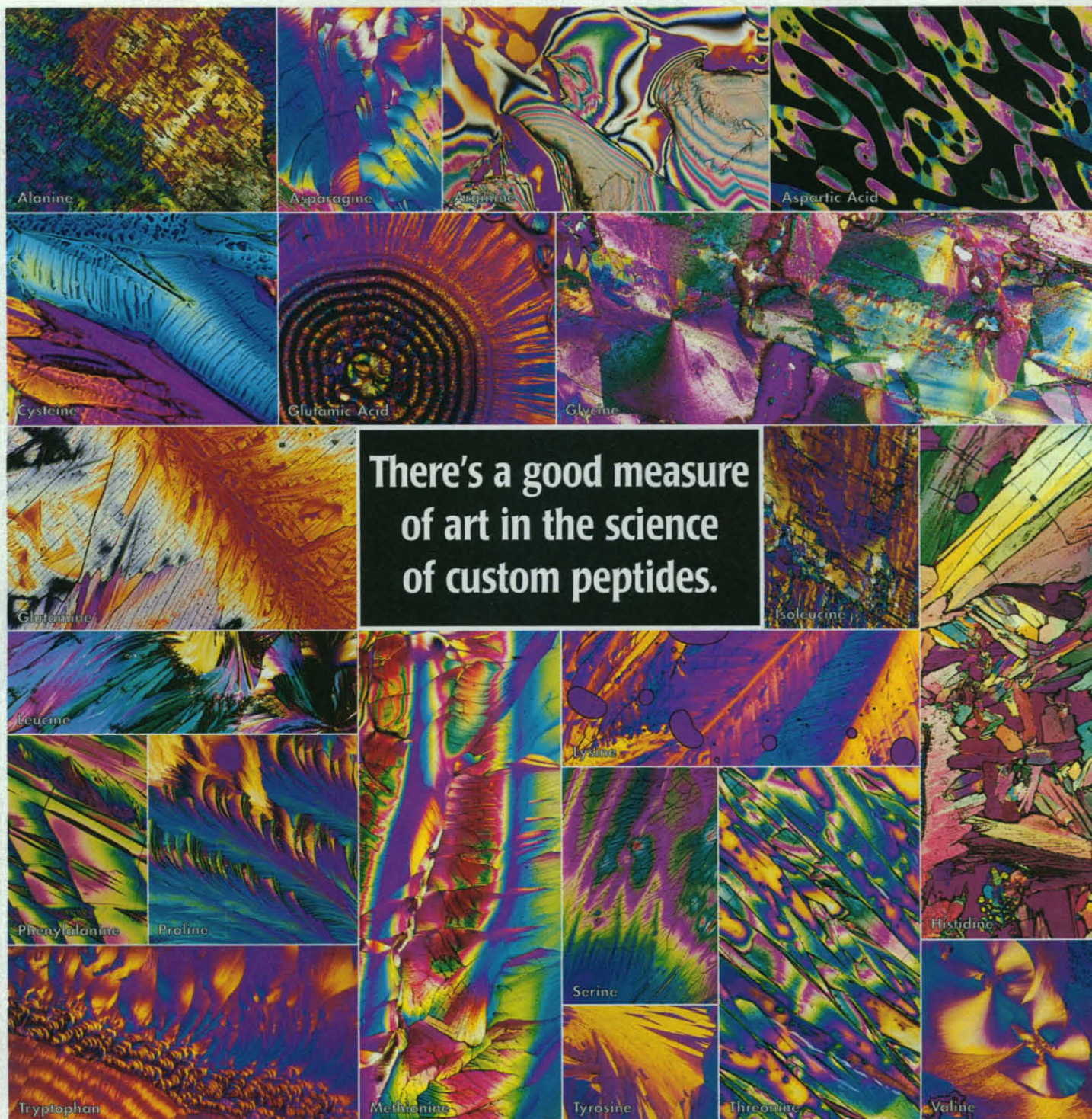
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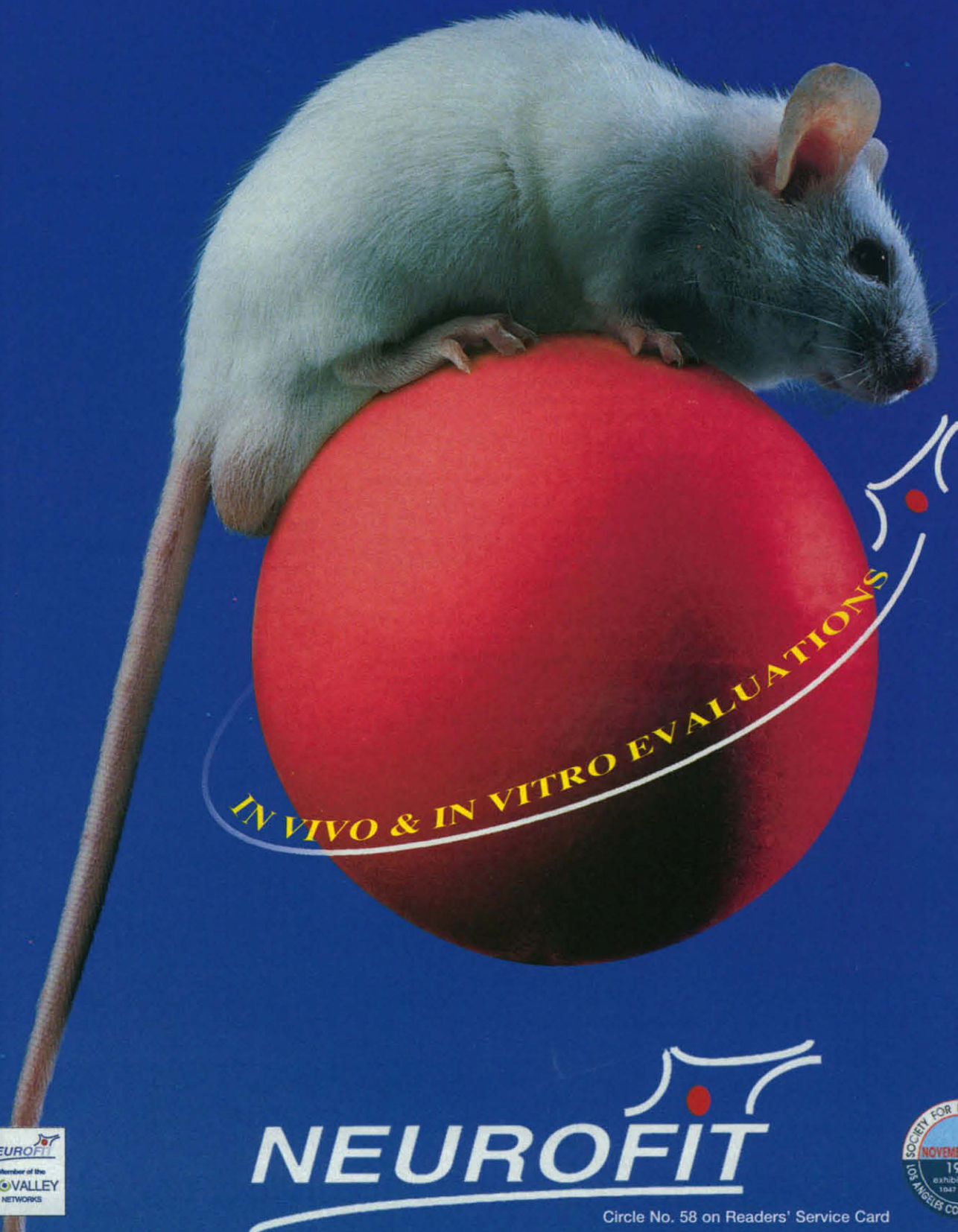
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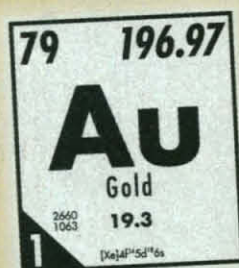
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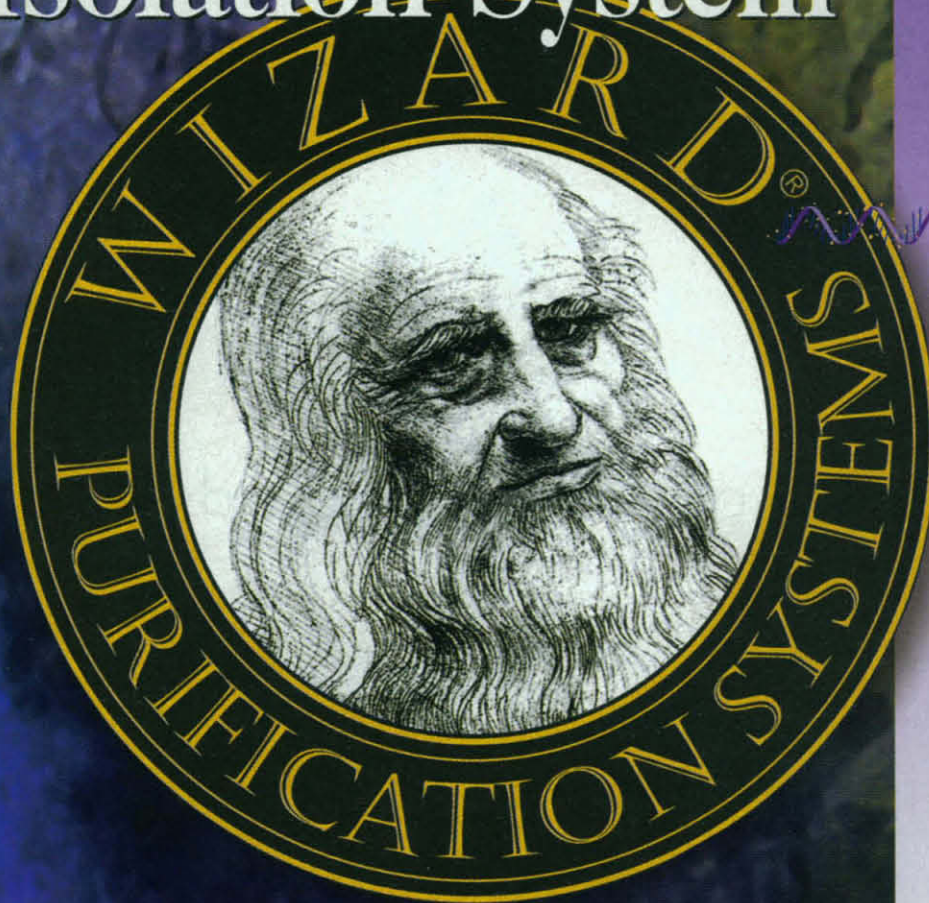
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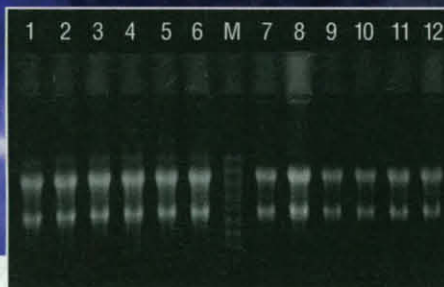
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Product Information

Product	Cat. #
SV Total RNA Isolation System	Z3100
SV Total RNA Isolation System, Trial Size	Z3101
Miniprep Vacuum Adapters	A1331

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Formaldehyde Gel Electrophoresis of RNA.

RNA was isolated from 30mg liver tissue using Promega's system (Lanes 1-6) and a competitor's system (Lanes 7-12). Promega's system consistently yielded an average of 100µg. The competitor's system yielded an average of 70µg with wide variability. (M = marker lane)



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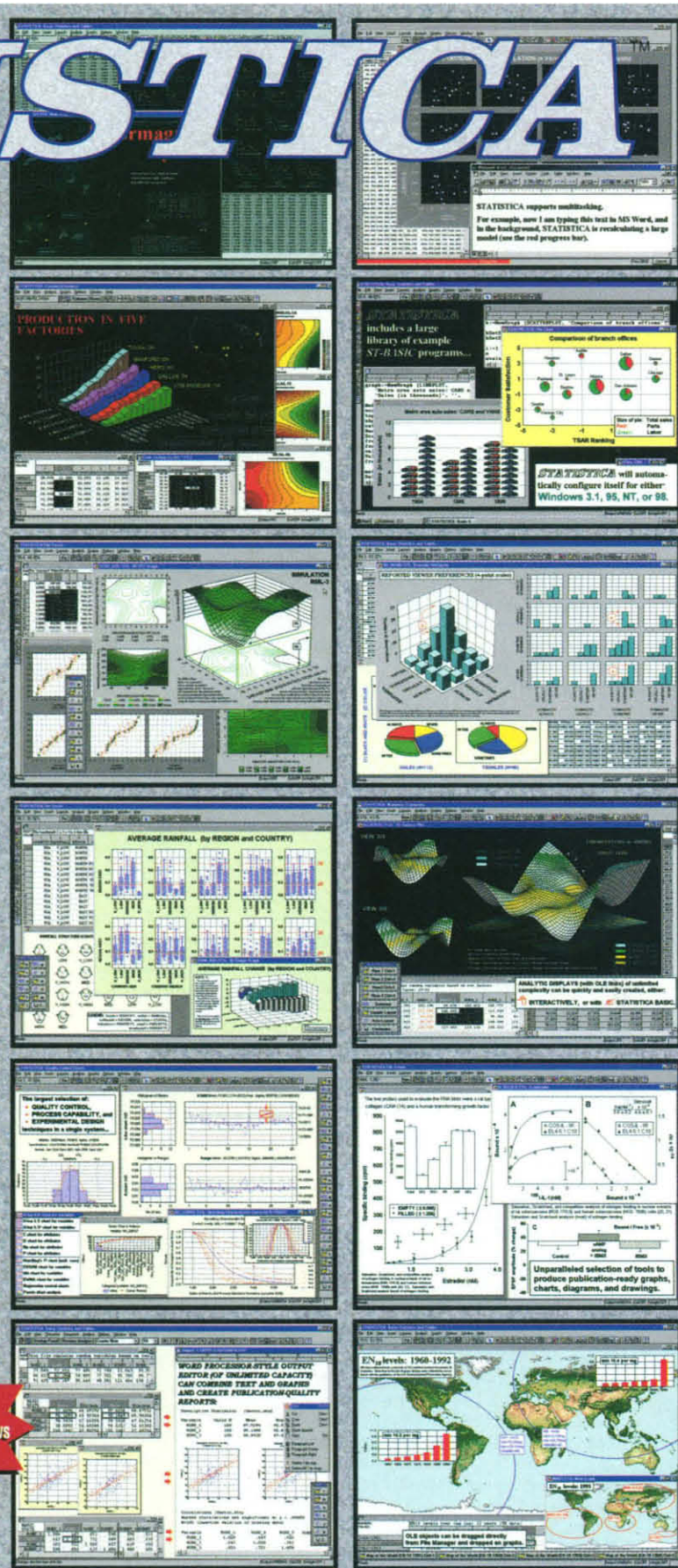
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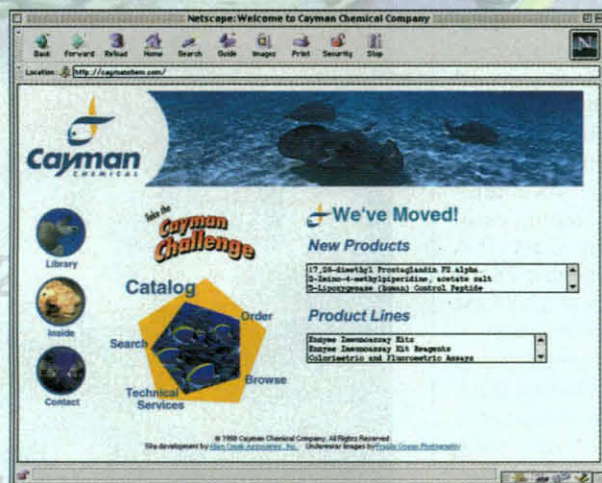
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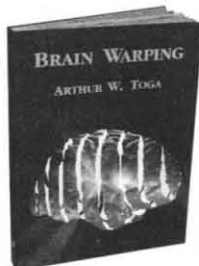
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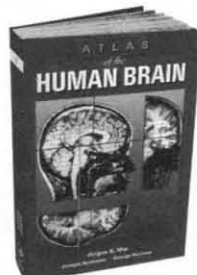
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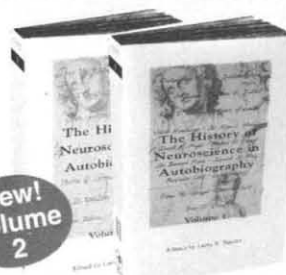
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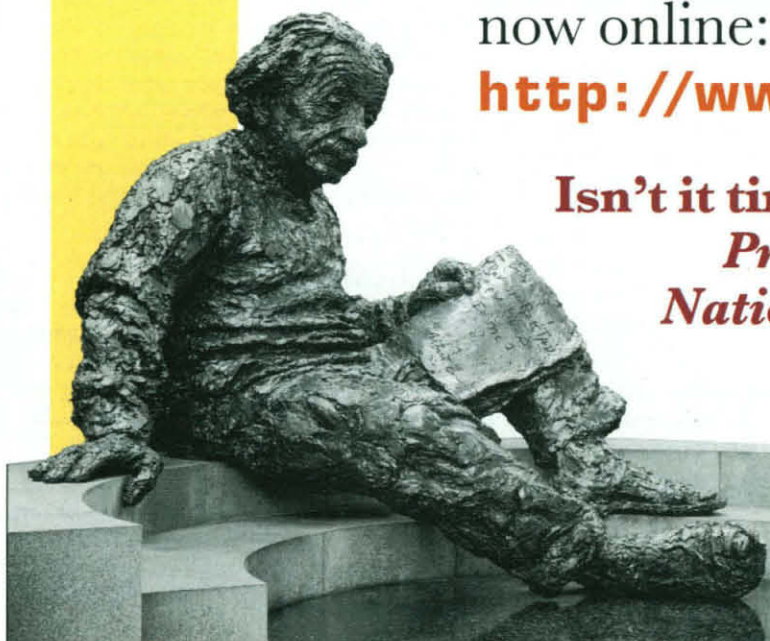
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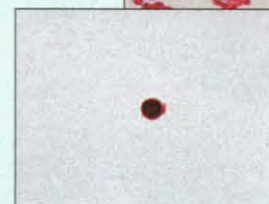


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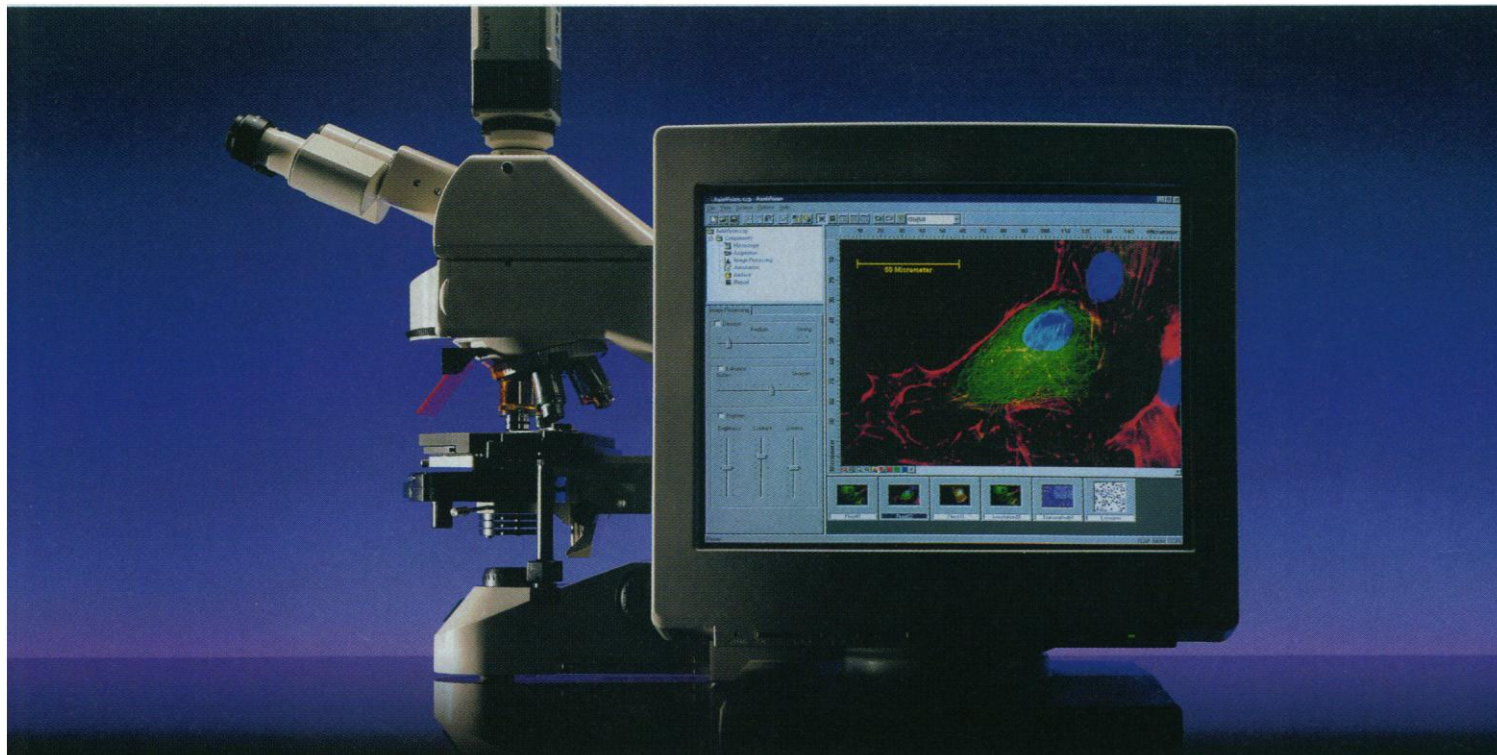
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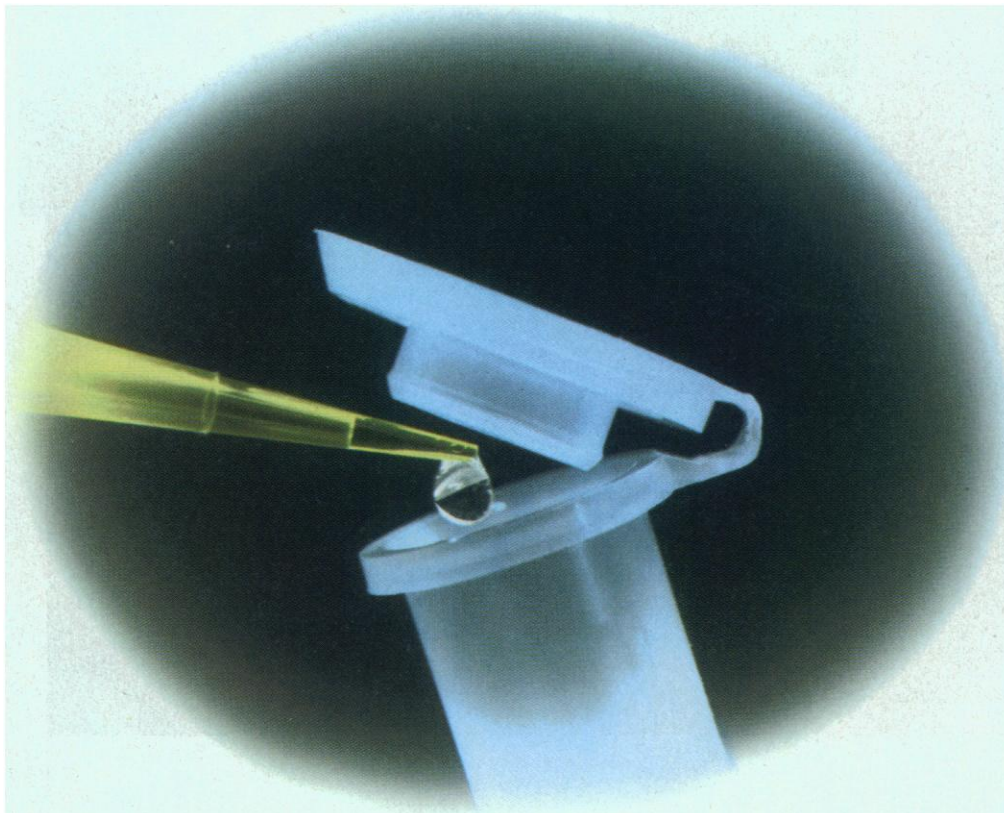
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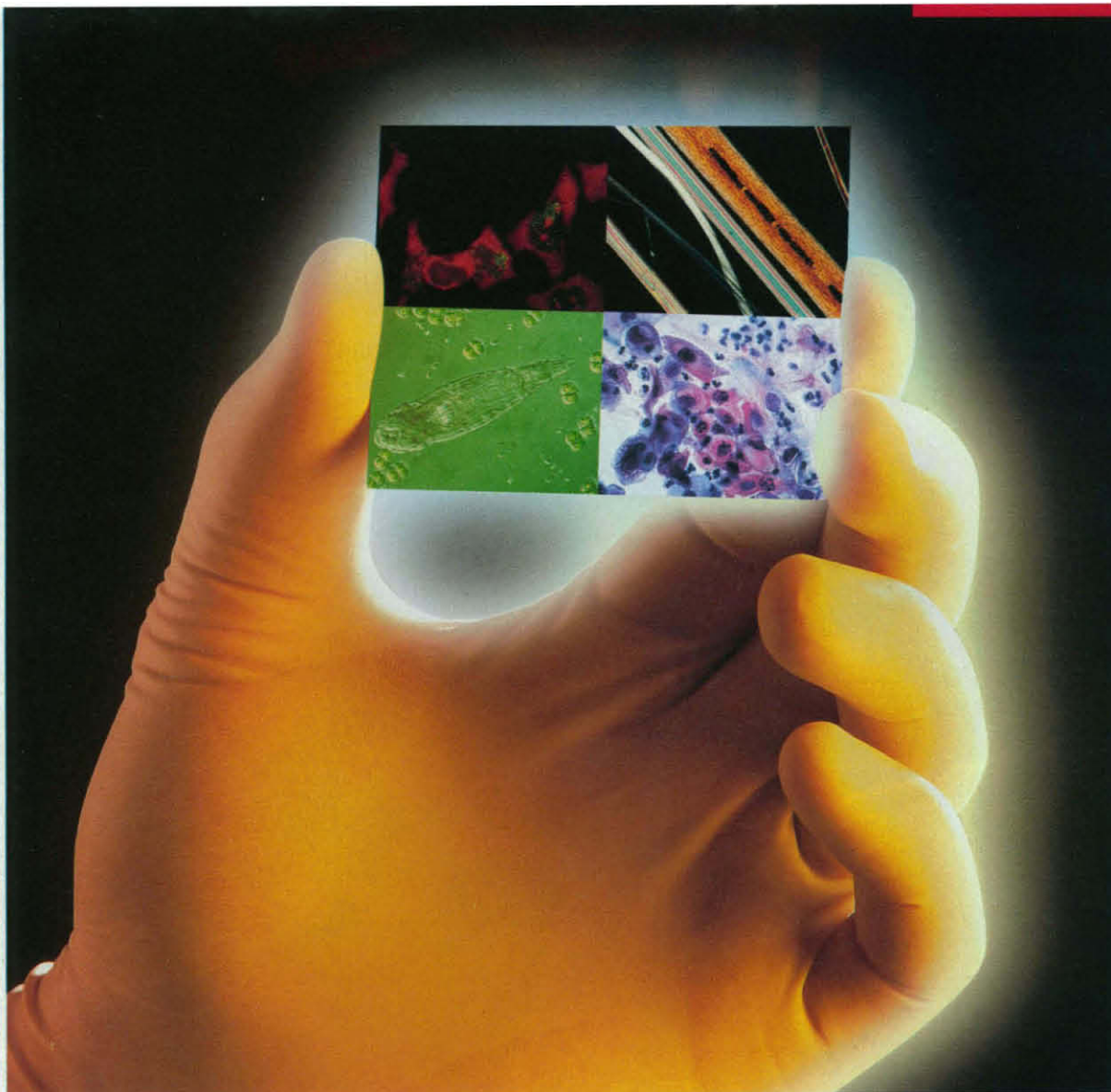
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