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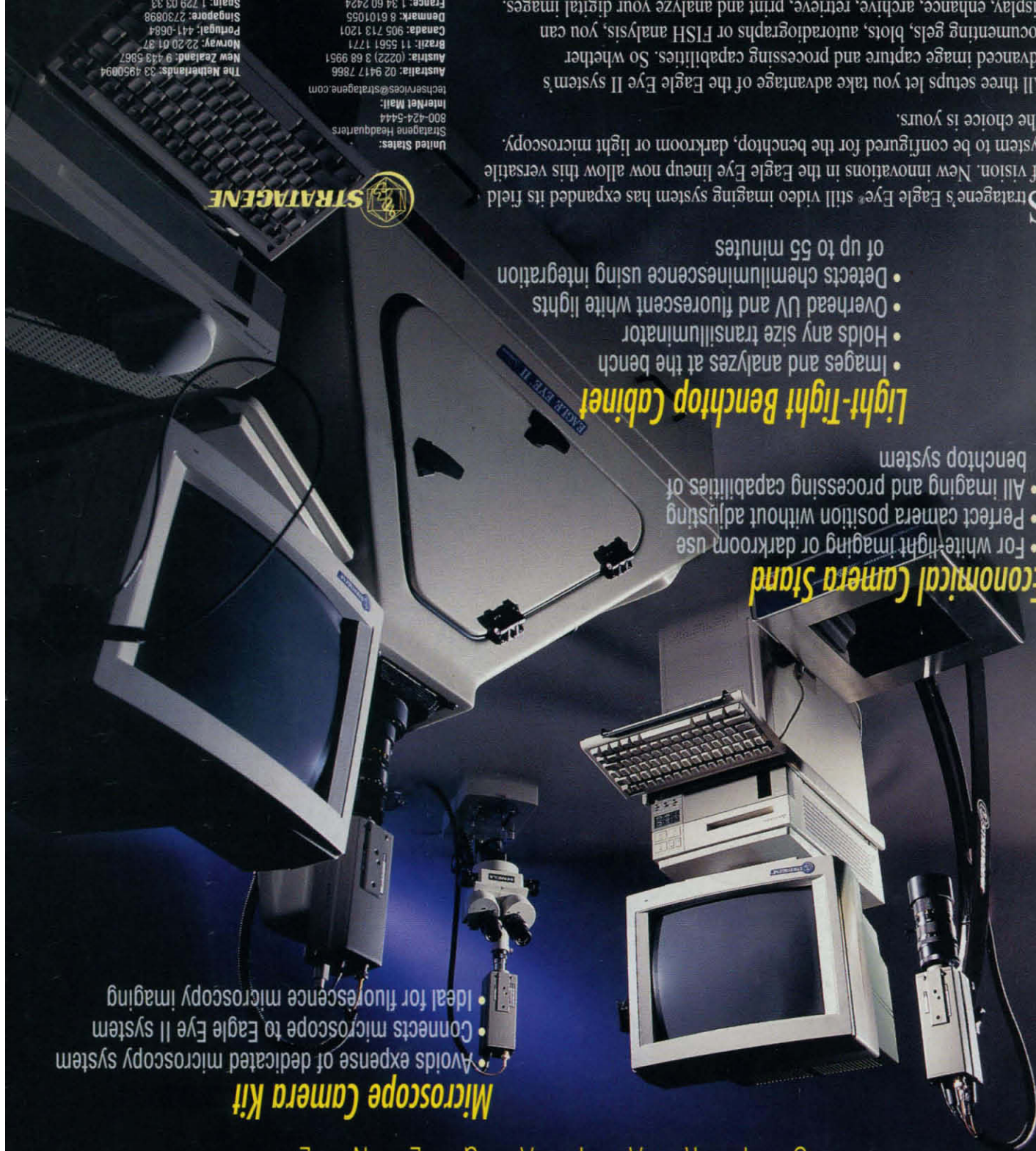
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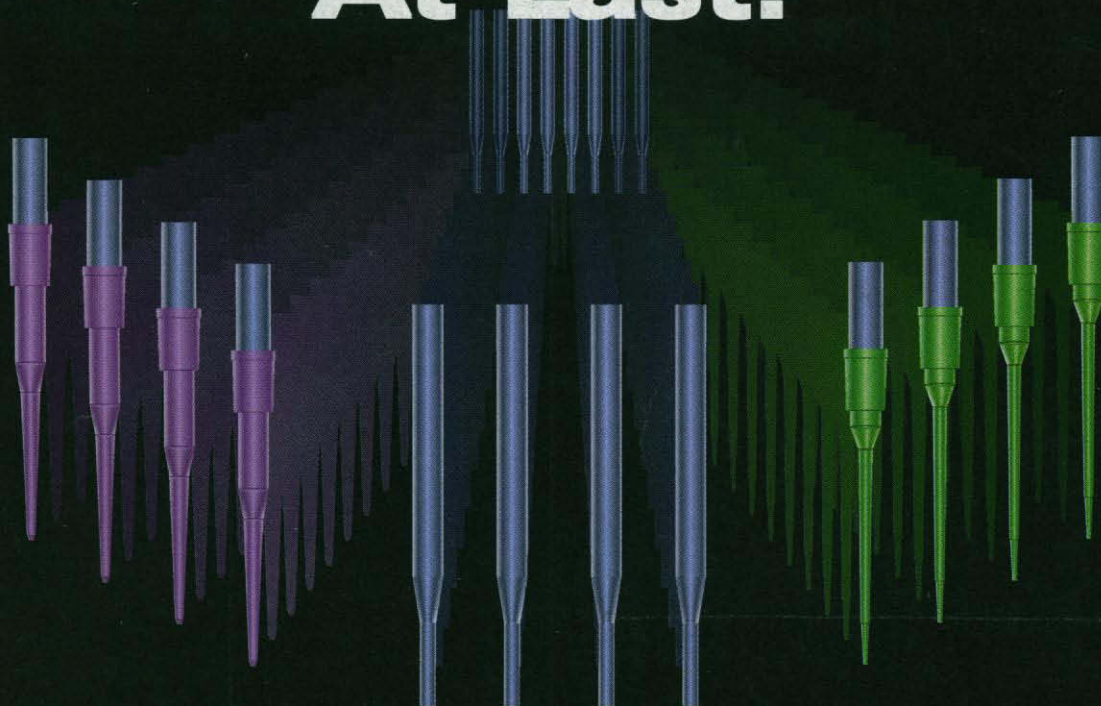
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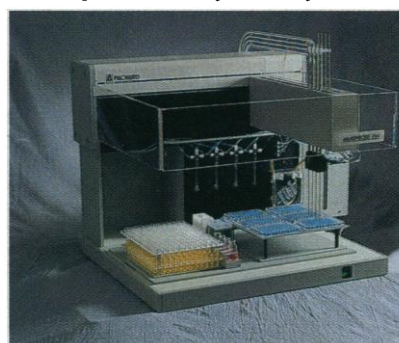
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Estrogen: a
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COVER

Enteropathogenic *Escherichia coli* (~3 micrometers long) adhere to human epithelial (HeLa) cell surfaces by inducing the formation of a "pedestal." Bacterial pathogens communicate with each other and with the cells they are attempting to colonize by secreting signals that

make conditions more permissible for infection. The rich diversity of microbes, how best to use the latest techniques, and applications to industry and medicine are discussed in the special section beginning on page 699. [Image: B. B. Finlay, A. Abe, and I. Rosenshine]



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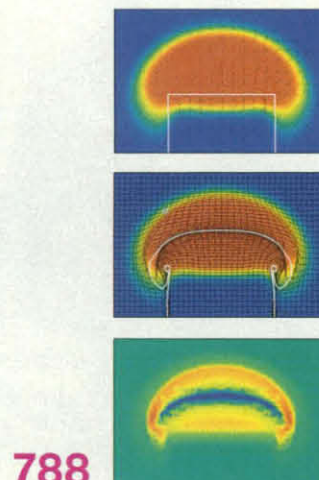
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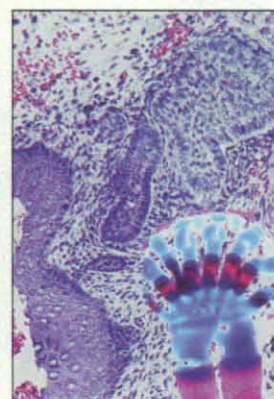
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Deformation in eastern Tibet



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Mouse model for basal cell carcinoma

Indicates accompanying feature

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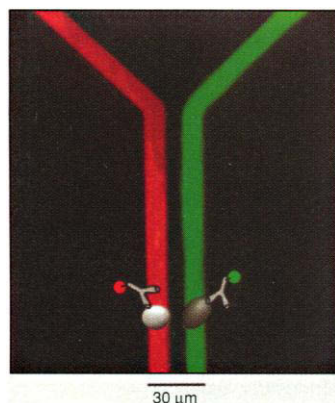
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Bright infrared lasers

Infrared lasers that are bright and whose wavelength can be precisely tuned could have important applications in communications. Scamarcio *et al.* (p. 773) describe a long-wavelength (8 micrometers) infrared laser based on semiconductor superlattices formed by molecular beam epitaxy. Photons are emitted when electrons tunnel between two superlattice conduction bands; different wavelengths can be achieved by changing the energy gap between these minibands. The use of bands rather than discrete states allows the laser to operate at high powers.

Microdelivered molecules

The controlled delivery and immobilization of small quantities of reactants is a necessary step in many biological assays and combinatorial screening techniques. Delamarche *et al.* (p. 779) have designed micro-



fluidity networks that allow controlled delivery and immobilization with submicrometer control. A network of capillaries was formed from an elastomeric mold; molecules such as immunoglobulins were introduced by flow and were immobilized onto the substrate. Af-

Collaring circadian clocks

Most organisms contain internal circadian clocks that keep track of the day-night cycle even in constant light or darkness. Several clock components are known—*frequency* in the fungus *Neurospora* and *period* and *timeless* in *Drosophila*. Crosthwaite *et al.* (p. 763; see the Perspective by Kay, p. 753) report that two genes from *Neurospora*, *white collar-1* (*wc-1*) and *wc-2*, also encode key components of the clock. In addition to keeping time, *wc-1* and *wc-2*, which are transcriptional activators with PAS domains, are required for *Neurospora*'s responses to light, suggesting that circadian clocks evolved from early organisms' light-regulated pathways.

ter removing the mold, the patterned areas showed high specificity and contrast.

Paleo plant patterns

Paleovegetation changes in the tropics have been used to estimate that coolings by up to about 5°C occurred during the last glacial maximum (LGM), but other paleoclimate data and climate models have suggested that temperature changes were not so great. However, atmospheric CO₂ levels were also much lower during the LGM, and how this effect changed vegetation has been unclear. Jolly and Haxeltine (p. 786), using a coupled climate-biosphere model, found that the much lower CO₂ levels alone could account for the shift in vegetation.

Calcium signaling and heart disease

High blood pressure leads to cardiac hypertrophy and heart failure, which is a leading cause of death in developed countries. However, the underlying defects in excitation-contraction coupling mechanisms that control and coordinate contraction of individual heart cells have been unknown. Gómez *et al.* (p.

800; see the Perspective by Yue, p. 755) studied two forms of cardiac dysfunction in rats and found that much of the mechanism by which excitation (depolarization of membrane potential) leads to contraction was functioning normally. However, calcium ions flowing into the cell through channels in the plasma membrane were less effective in opening calcium-dependent channels on intracellular stores of calcium (which would ordinarily cause release of more calcium and promote contraction). At least in the models tested, the results define a potential site for therapeutic intervention that might reduce an unresponsiveness at the cellular level that can eventually lead to heart failure.

Making DNA late

When cells divide, some portions of the DNA are replicated earlier than others. In yeast, telomeres, the specialized structures at the ends of chromosomes, seem to be responsible for delaying the process origins of DNA replication near them. Raghuraman *et al.* (p. 806) show that this effect must be re-established anew with each cell cycle. A replication origin located near a telomere in one cell cycle will replicate late, but

when removed from the vicinity of the telomere by inducible recombination, it replicates earlier in the very next cell cycle.

Reaction centers in action

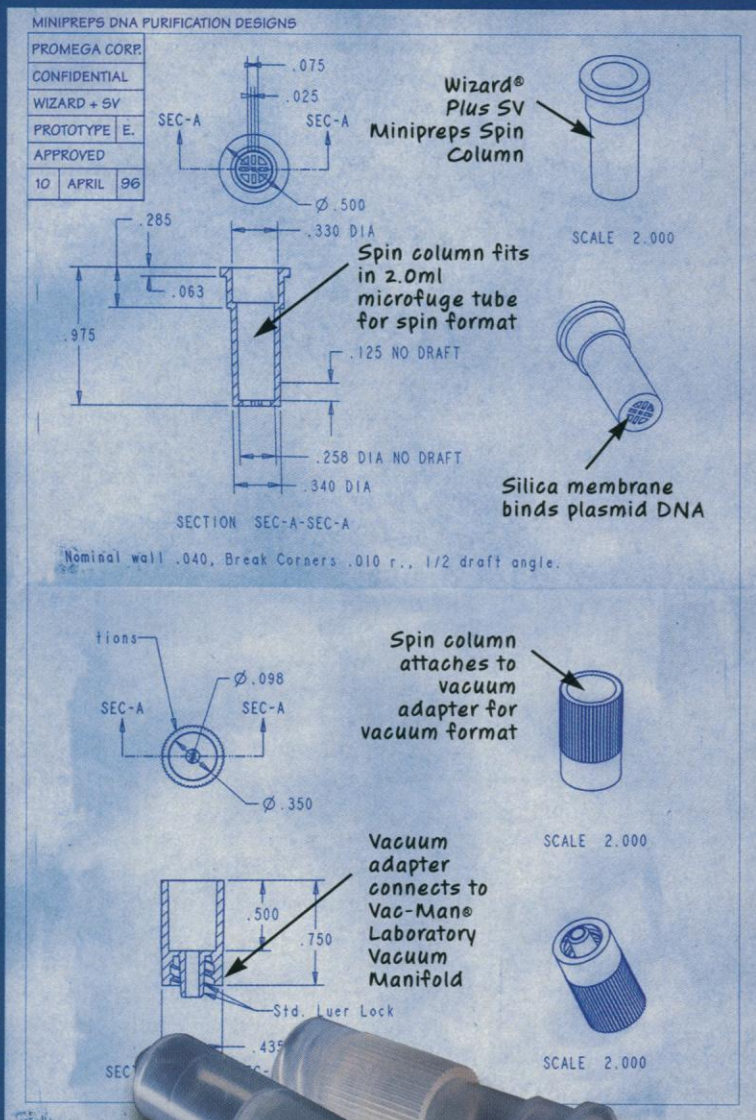
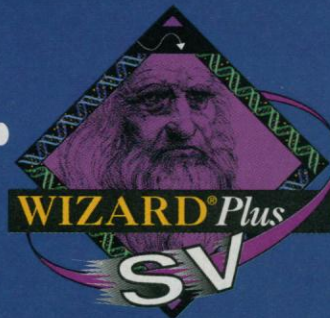
In the bacterial photosynthetic reaction center (RC), light absorption causes charge to transfer from a primary donor group to the ubiquinone acceptor groups, Q_A and Q_B; the resulting charge separation thus converts photon energy into a chemical gradient. Stowell *et al.* (p. 812) obtained x-ray crystal structures of the RC grown in the dark and then activated by light. Light activation moves the terminal acceptor Q_B⁻ about 5 angstroms and rotates it roughly 180°, and a kinetic model based on the observed structural changes can account for the electron transfer rates.

Mice, hedgehogs, and skin cancer

Basal cell nevus syndrome (BCNS) is an inherited disease characterized by developmental defects and a predisposition to certain cancers, including basal cell carcinoma (BCC). Patients with BCNS have mutations in the patched gene, which codes for a transmembrane receptor that, in lower organisms, transmits critical developmental signals. Oro *et al.* (p. 817) have generated transgenic mice that overexpress in their skin a ligand for this receptor, called Sonic hedgehog (SHH). The mice developed many features of BCNS, including multiple BCCs and skeletal abnormalities. A putative mutation in the *Shh* gene was identified in a small number of human tumors.

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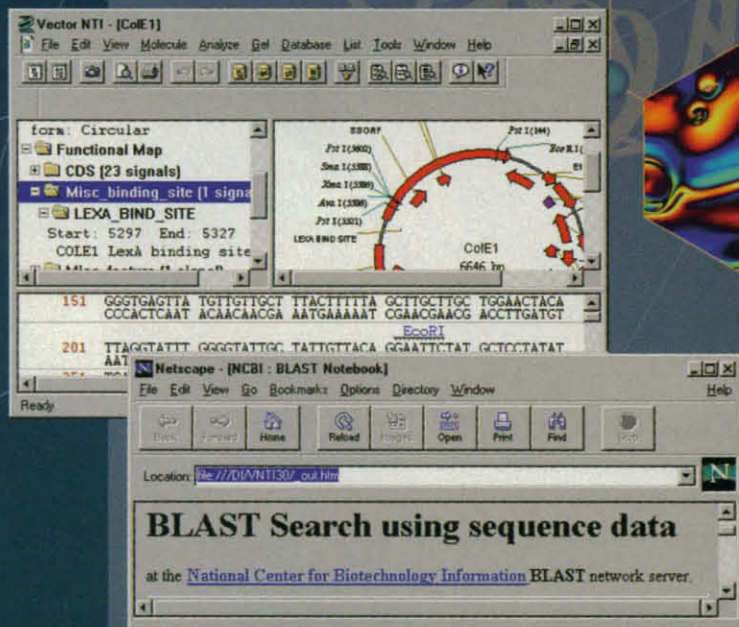
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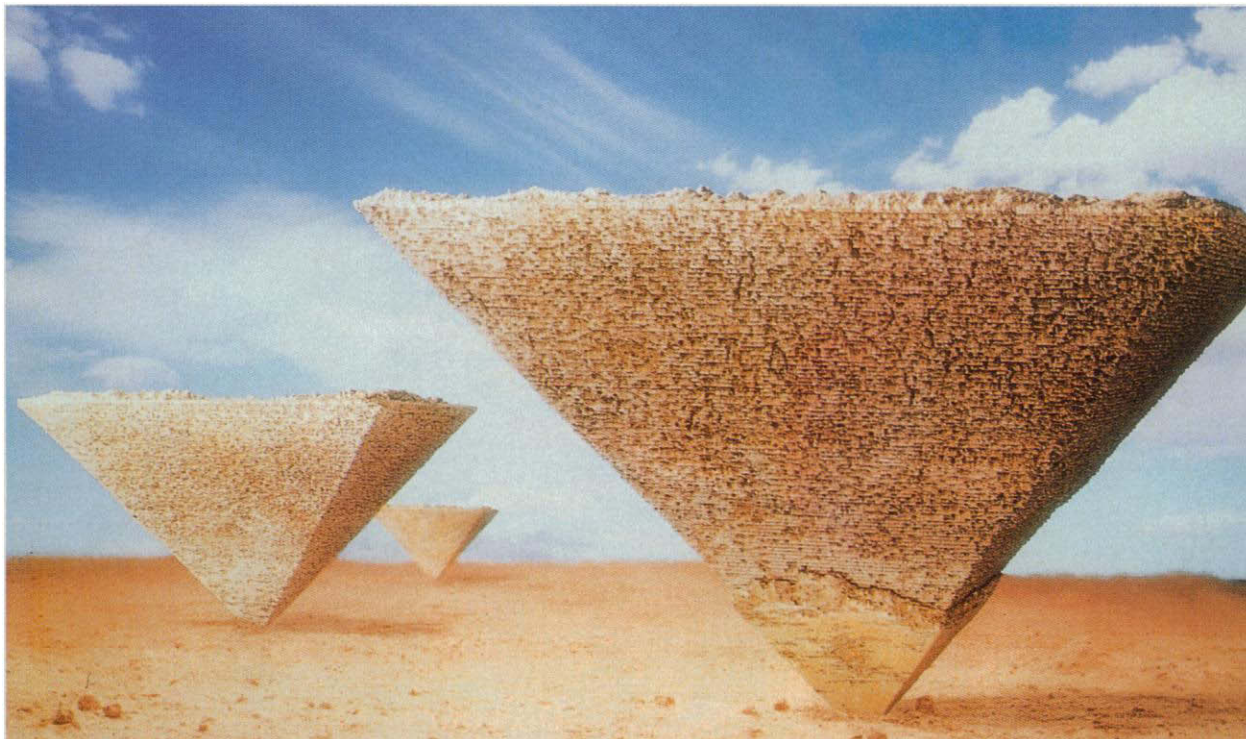


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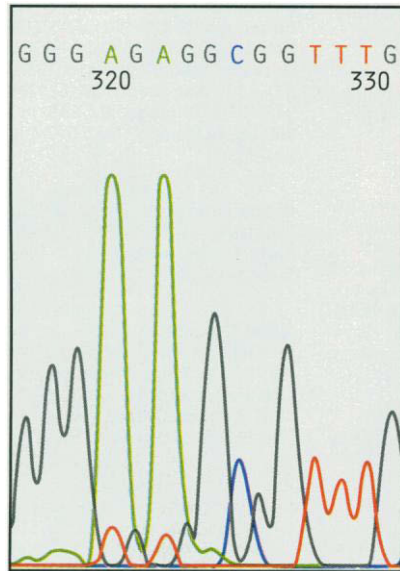
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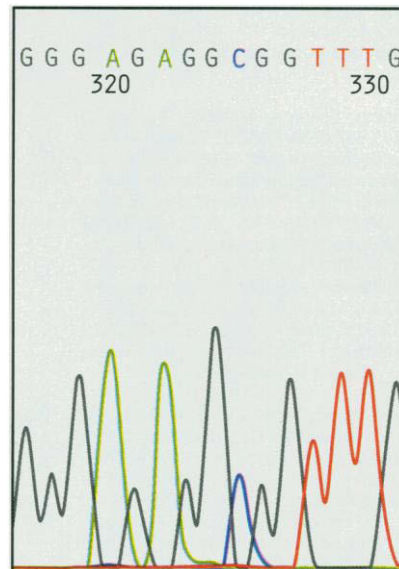
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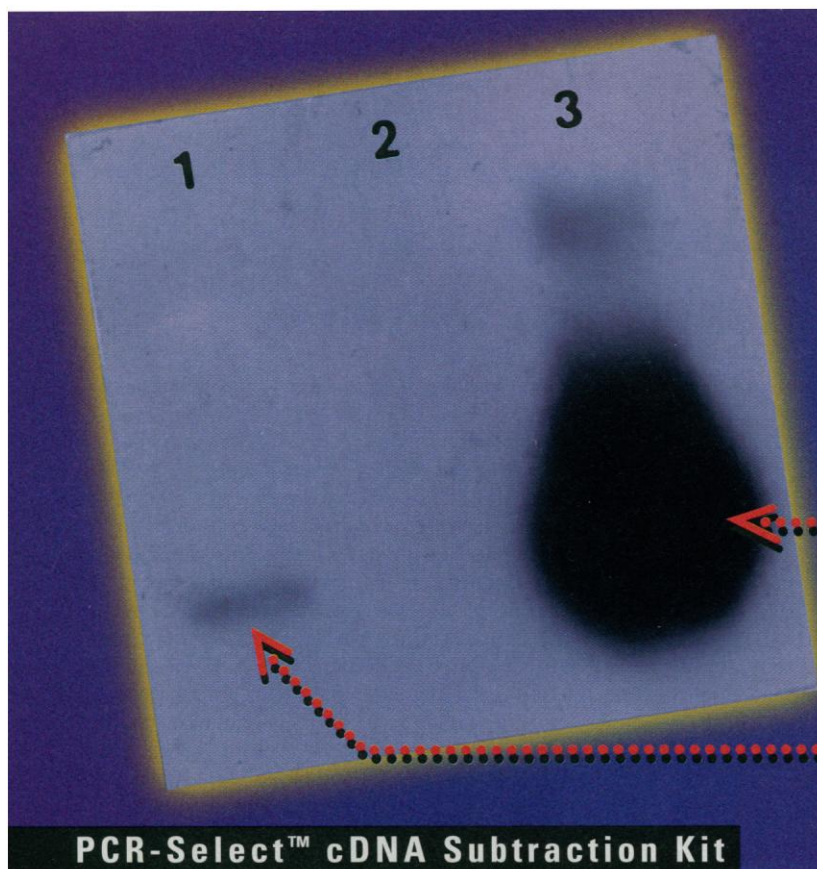
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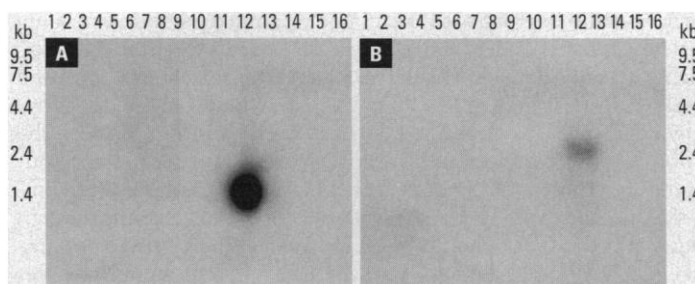
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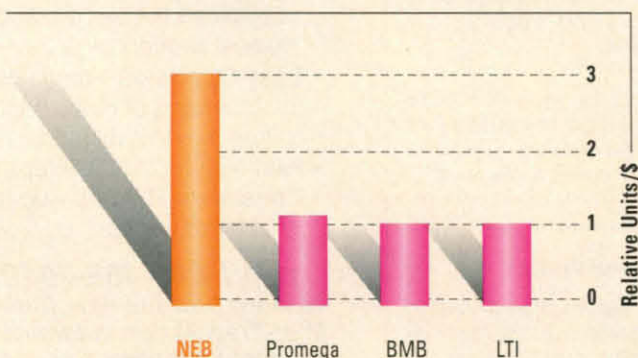
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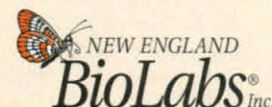


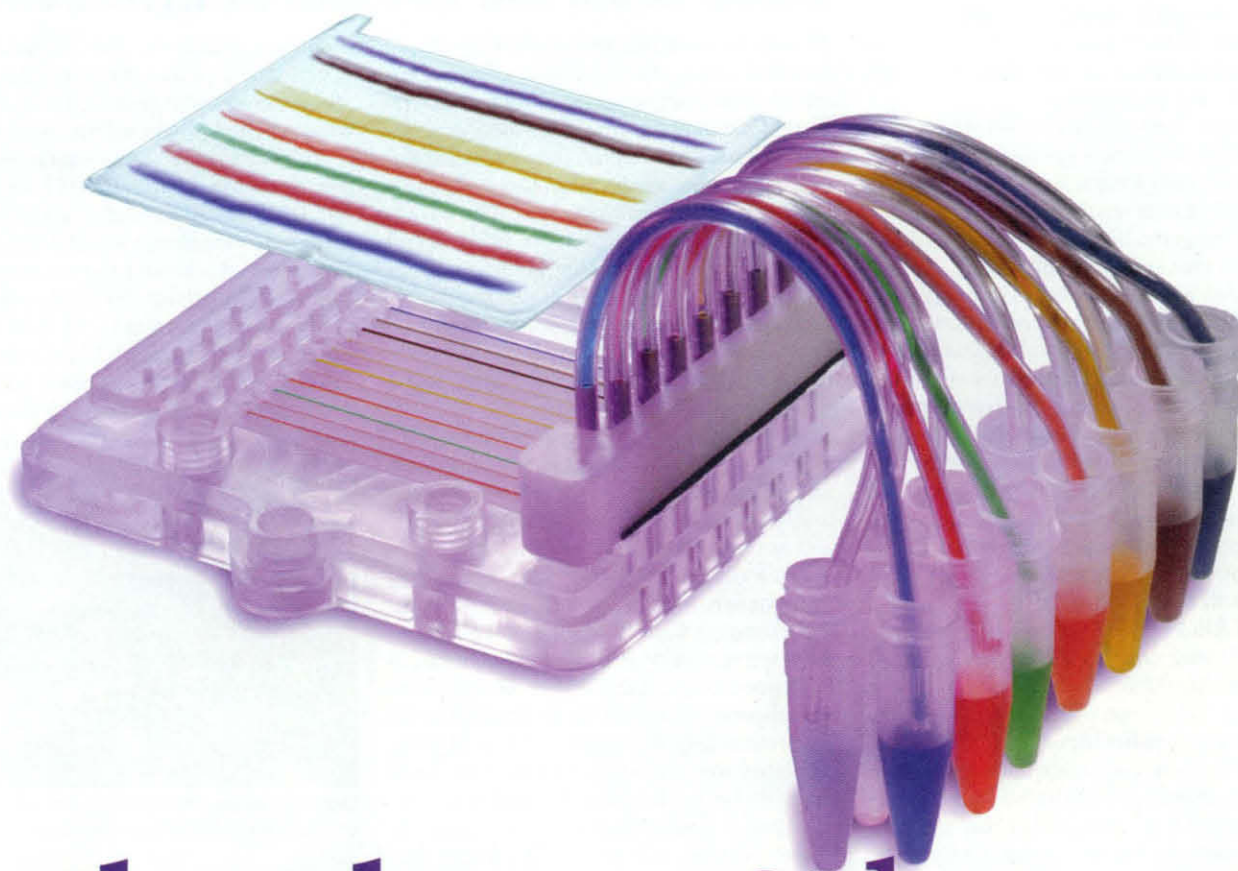
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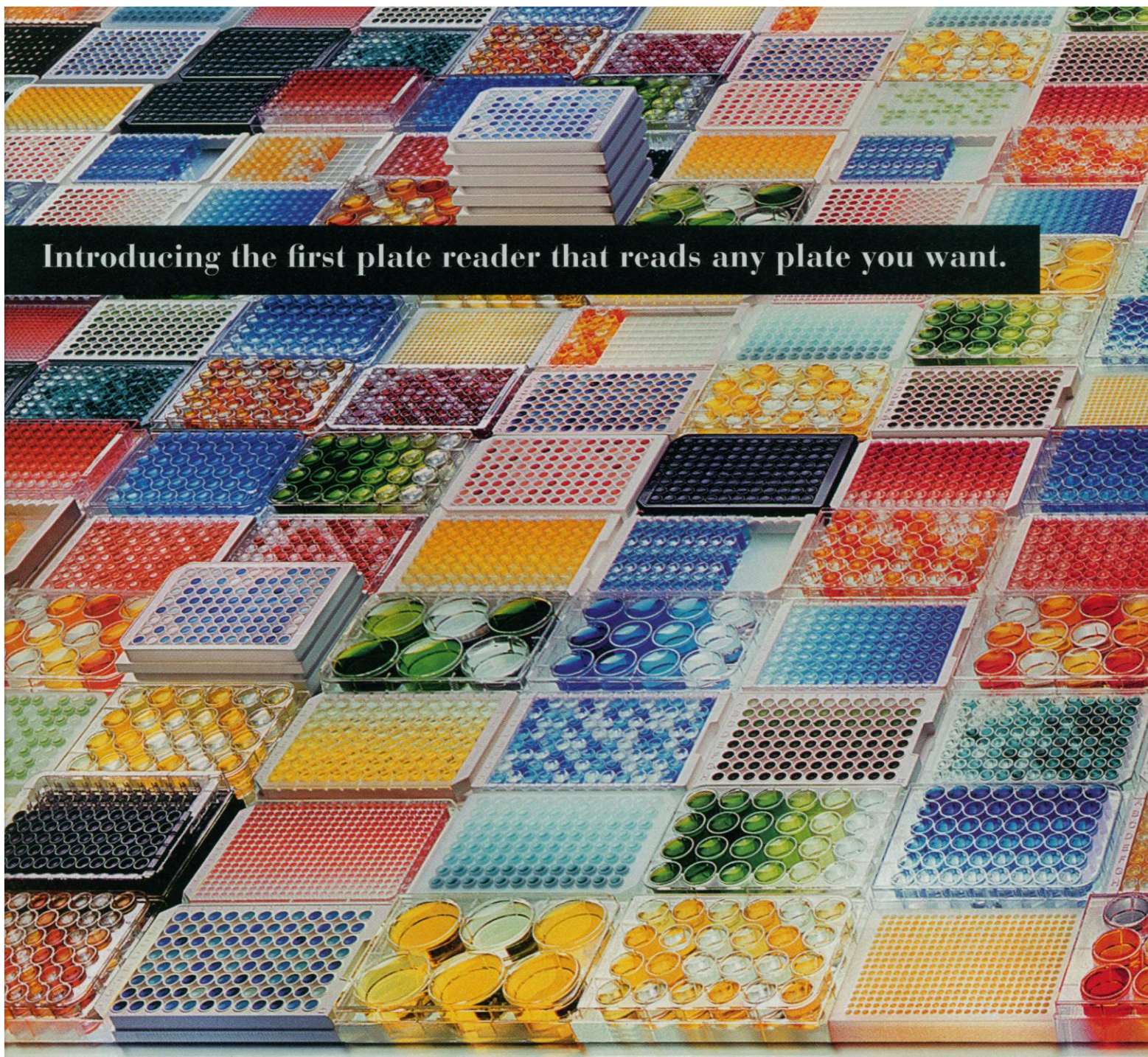
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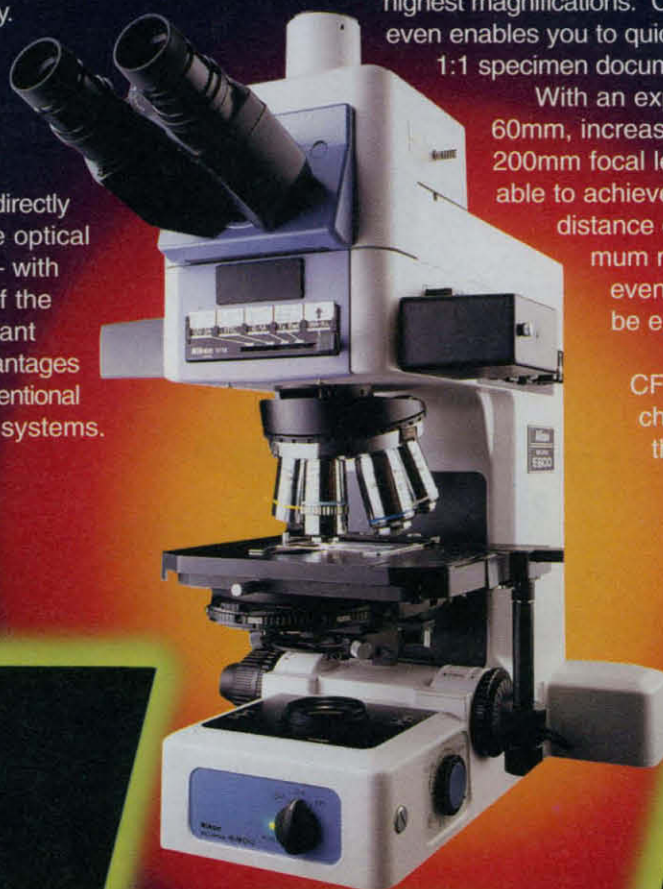
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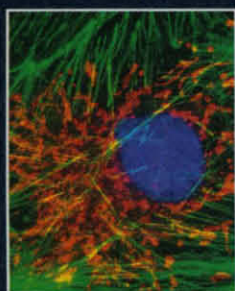
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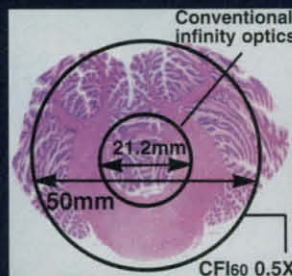
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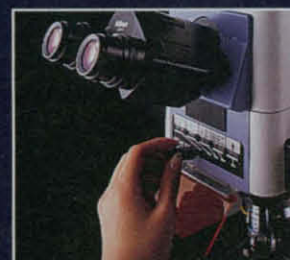
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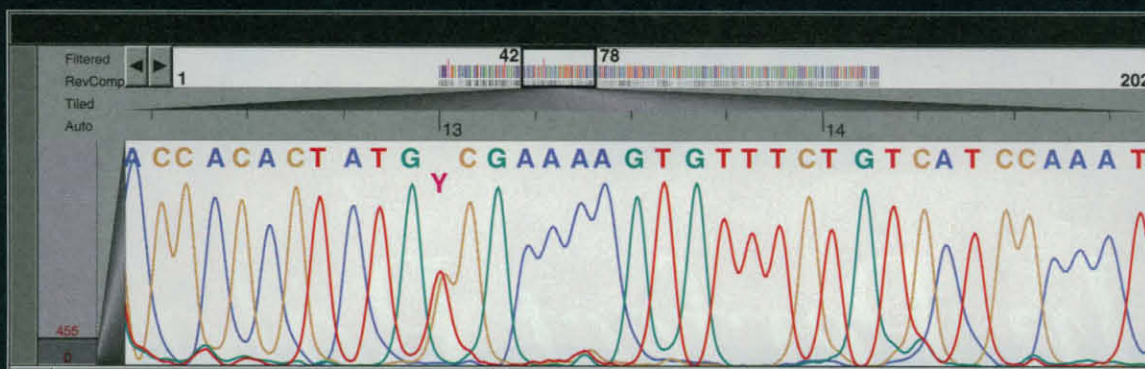
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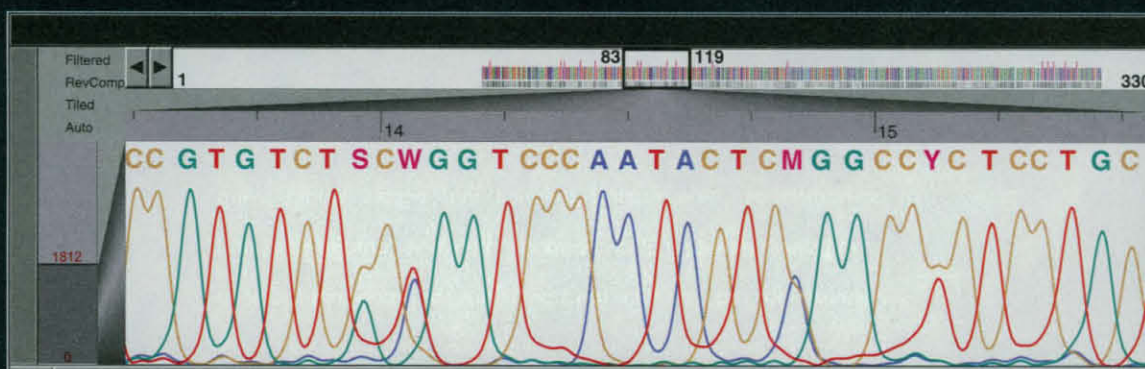
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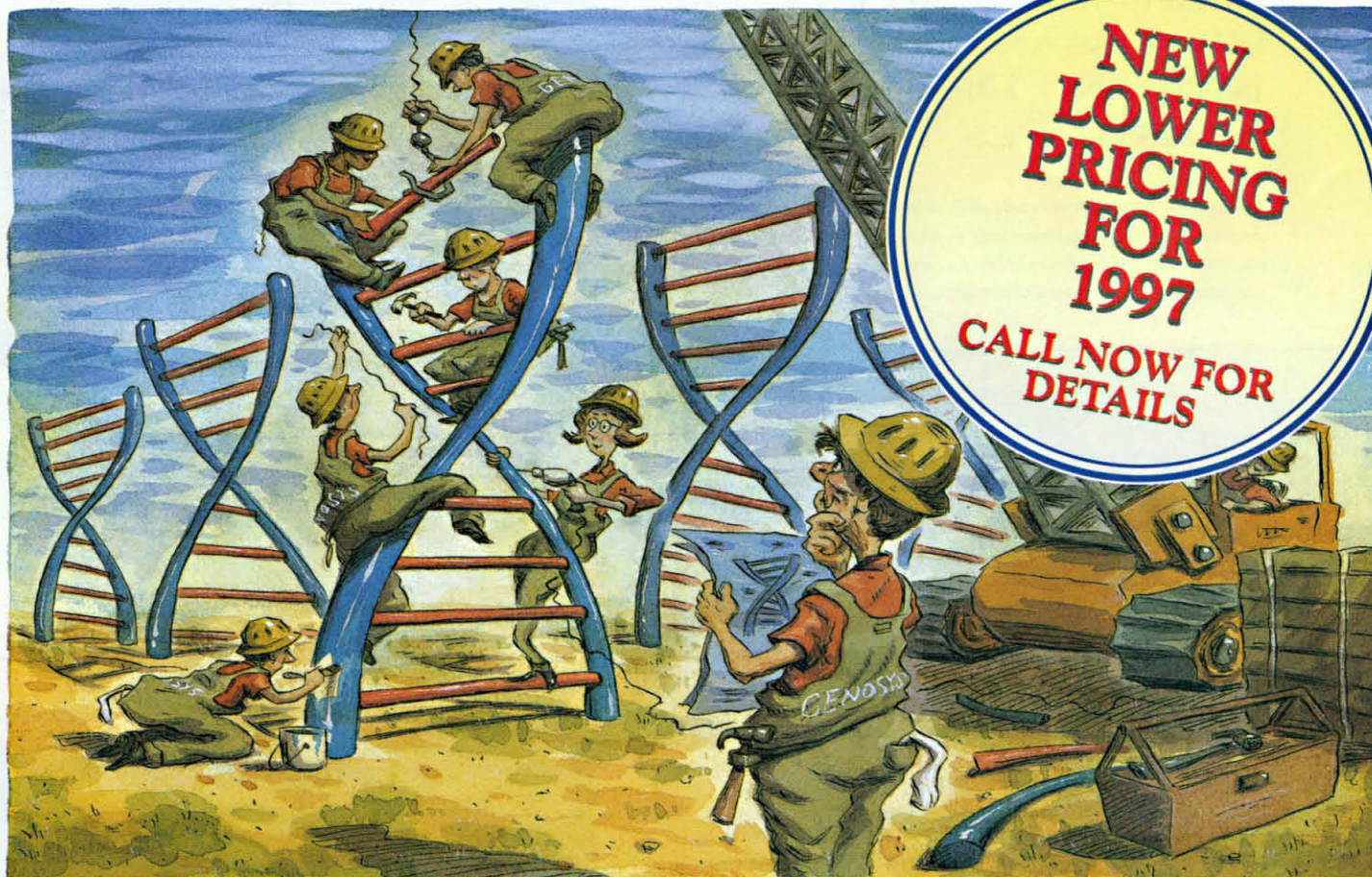
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Figure 1

Figure 1. Colonies were screened for the TGF- β 1 gene with a fluorescein-labeled oligonucleotide probe and Enhanced Luminol. This film demonstrates results obtained using the Renaissance 3'-End Labeling Fluorescein Kit with Antifluorescein-HRP (NEL823) and the detection substrate Enhanced Luminol (NEL201). Discs were exposed to Reflection film for 15 minutes.

Figure 2

Figure 2. Mouse β -actin was detected using a fluorescein-labeled ssRNA probe and ready-to-use CDP-Star. This film demonstrates results obtained using Renaissance RNA Fluorescein Labeling Kit with Antifluorescein-AP (NEL633) in conjunction with ready-to-use CDP-Star (NEL601). Blots were exposed to Reflection film for 5 minutes.

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Figure 3

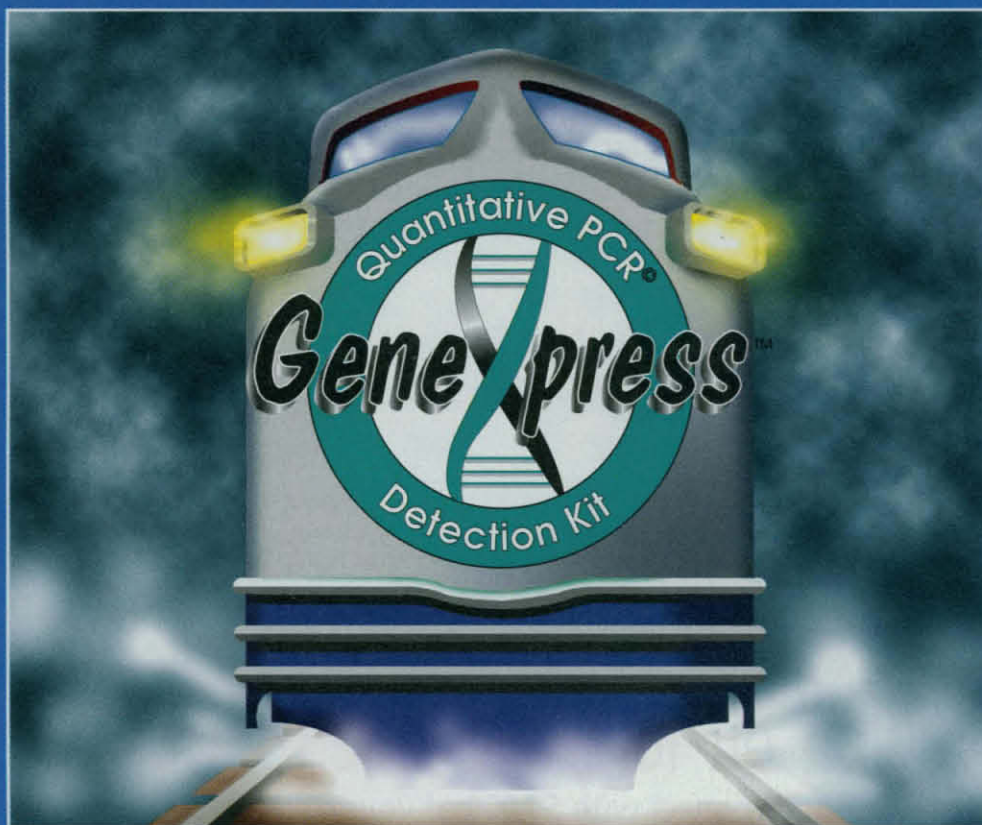
Figure 3. The v-Fos gene was detected in 125 ng of blotted mouse genomic DNA in less than 5 minutes using CDP-Star. This film demonstrates results obtained using the Renaissance Random Primer Biotin Labeling Kit with Streptavidin-AP (NEL604) in conjunction with ready-to-use CDP-Star (NEL601). Blots were exposed to Reflection film for 5 minutes.

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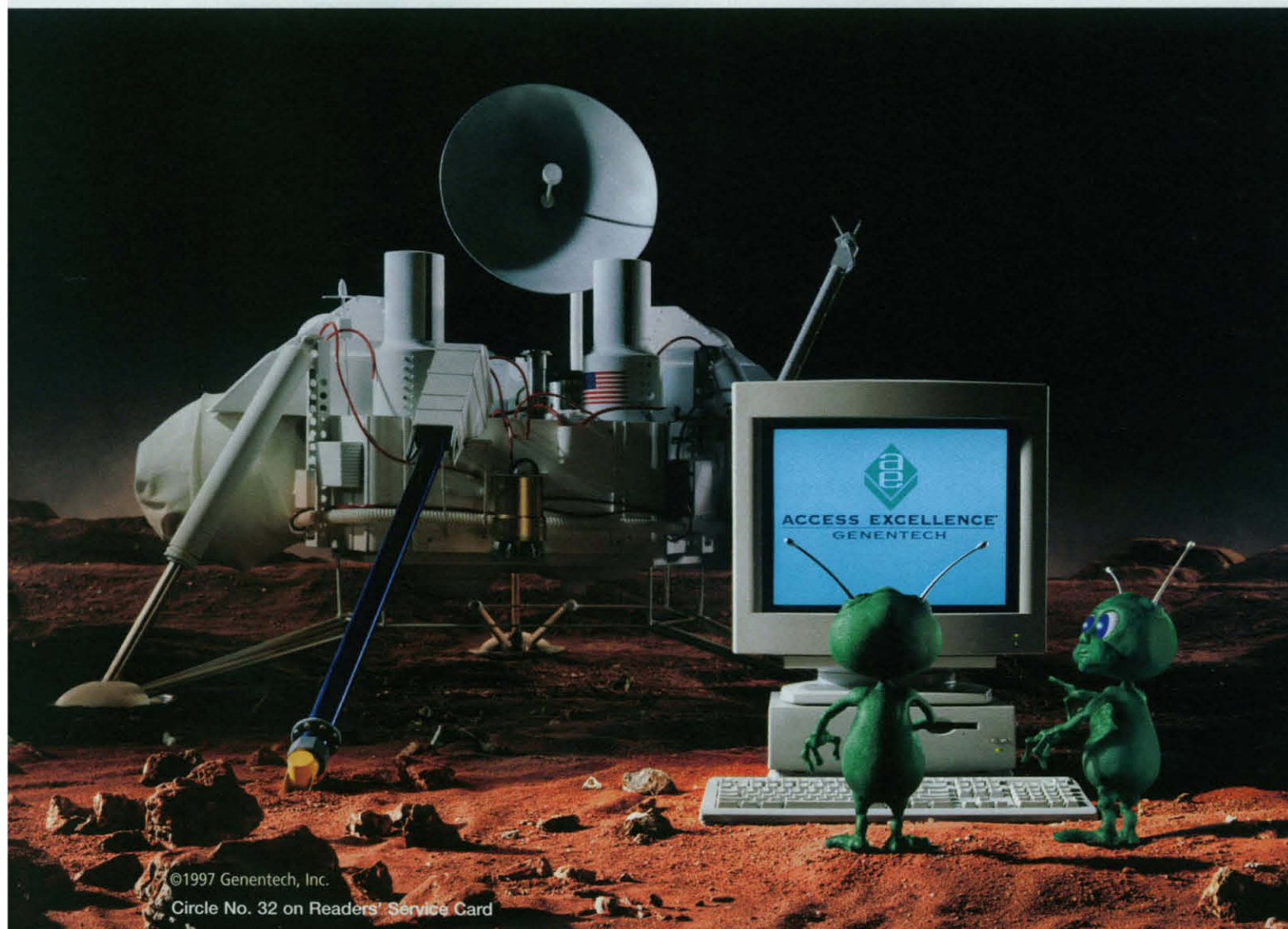
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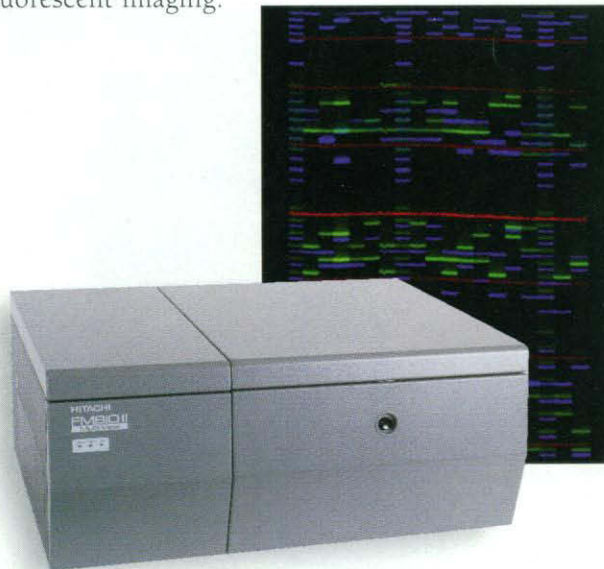
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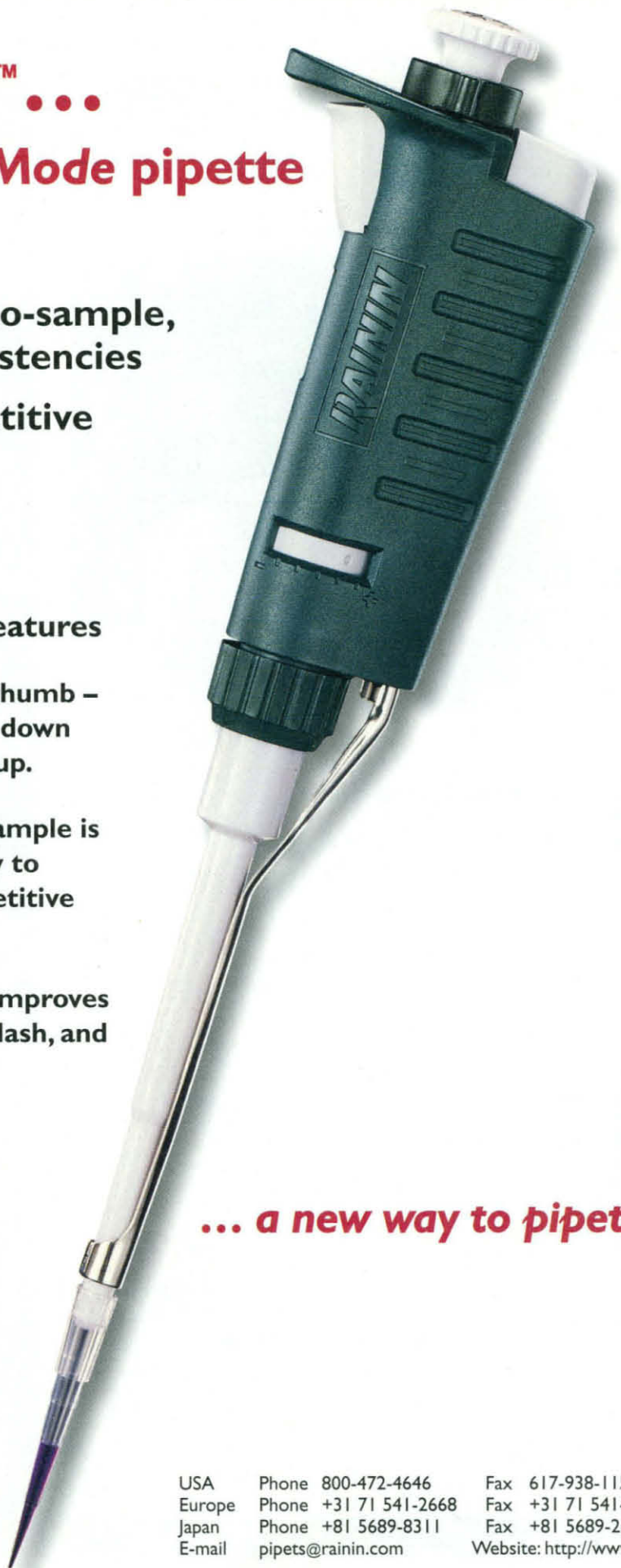
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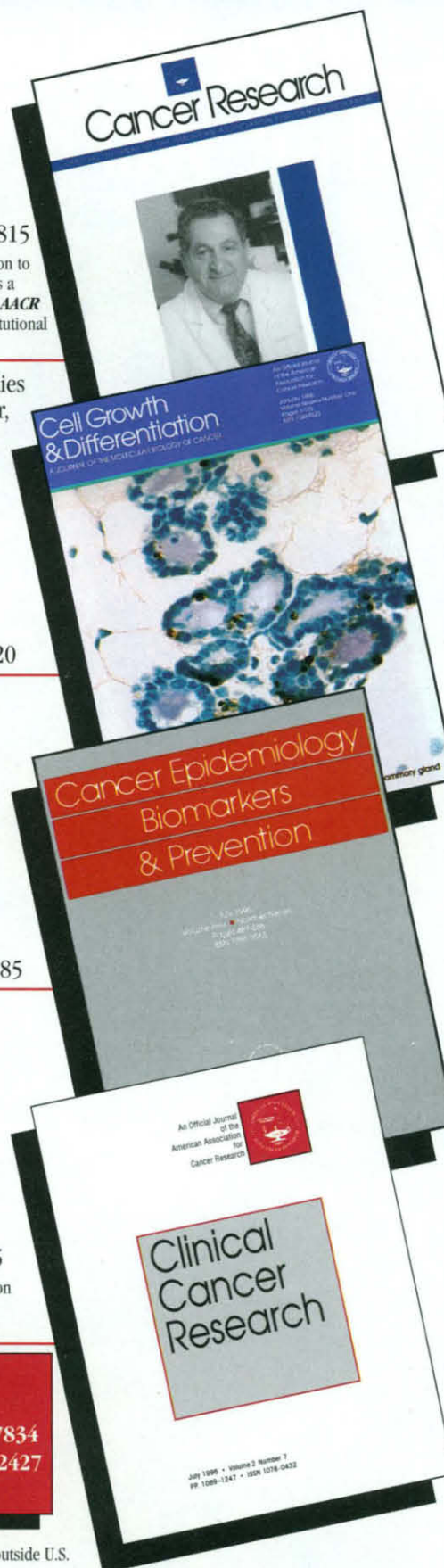
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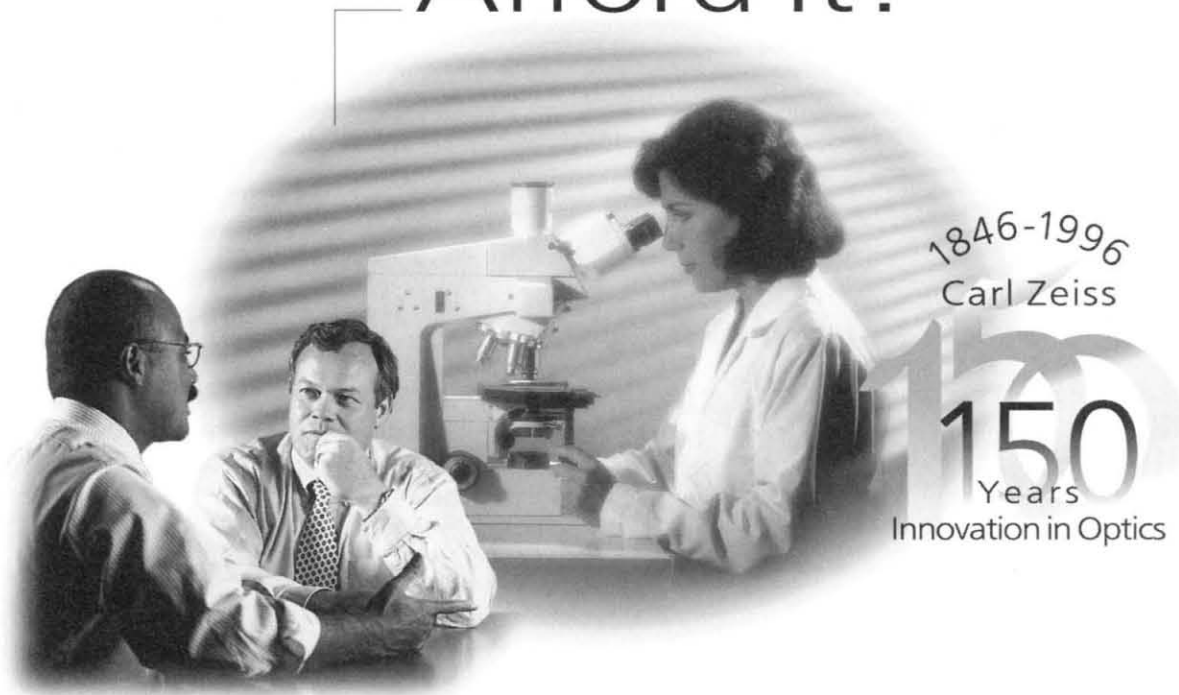
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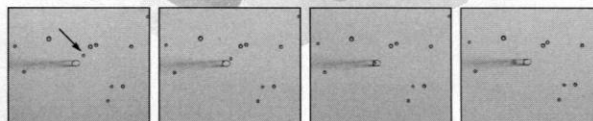
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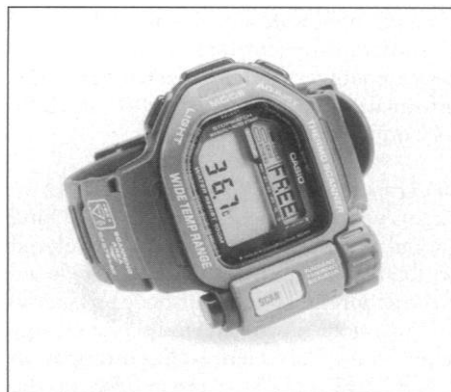
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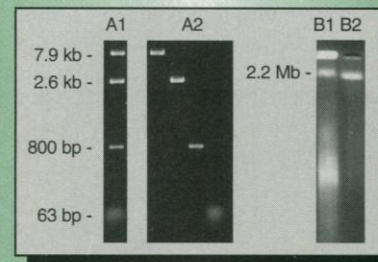
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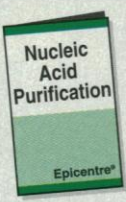
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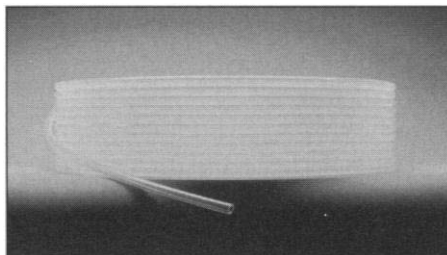
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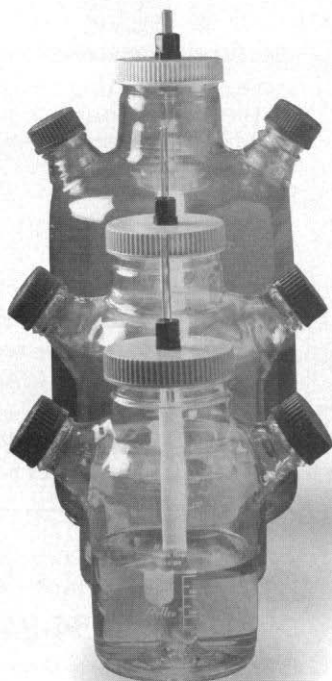


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Literature

Counting Aqueous Samples by LSC provides technical tips on liquid scintillation counting. *Use of the TopCount for Radioactivity Determinations in Wipe Test* describes the use of this microplate scintillation and luminescence counter. **Packard Instrument.** For information call 800-323-1891 or circle 149 on the reader service card.

Biochemical Catalog 1997-1998 describes an extensive line of dyes, biological stains, and specialty products. It features polyclonal antibodies, reagents for polyacrylamide gel electrophoresis, and several grades of agarose for immunochemistry and molecular biology applications. **Polysciences.** For information call 800-523-2575 or circle 150 on the reader service card.



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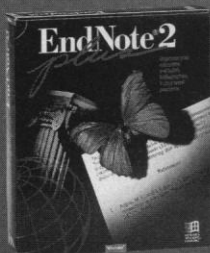
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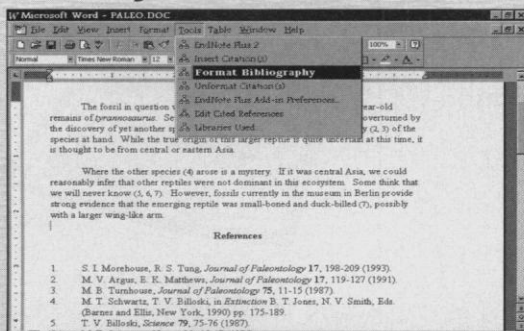
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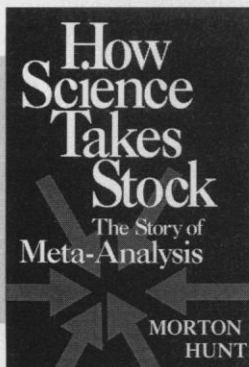
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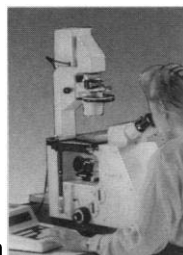
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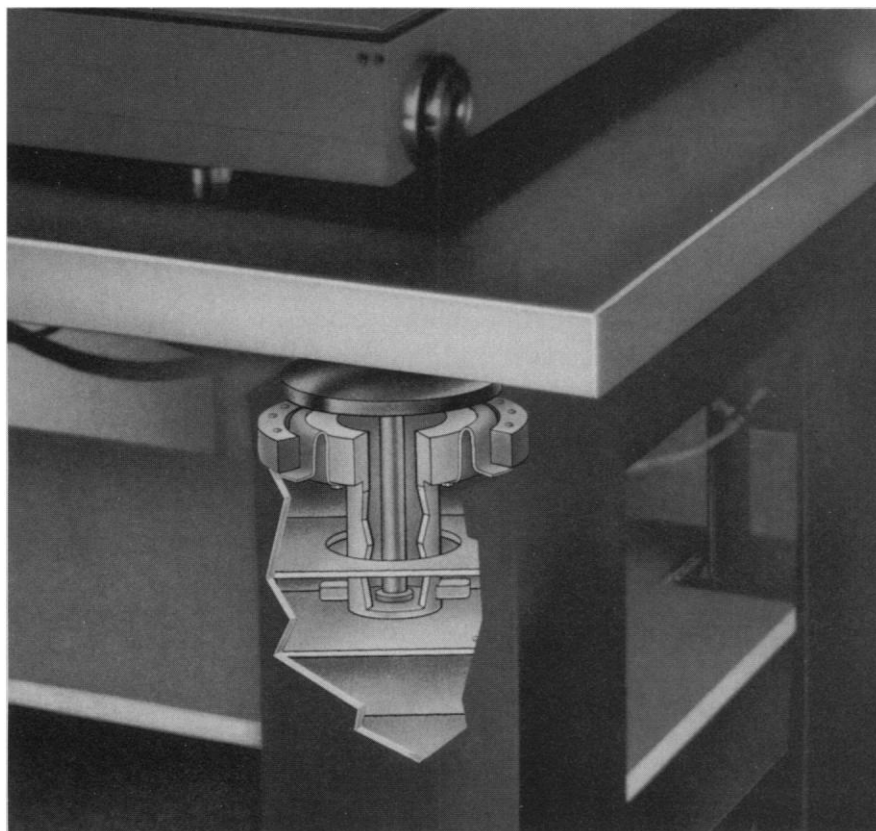
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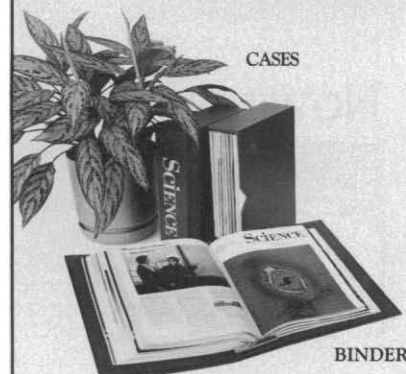
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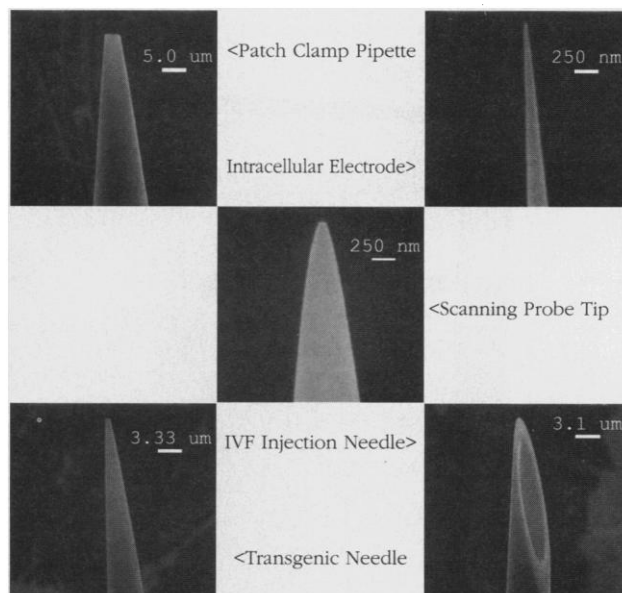
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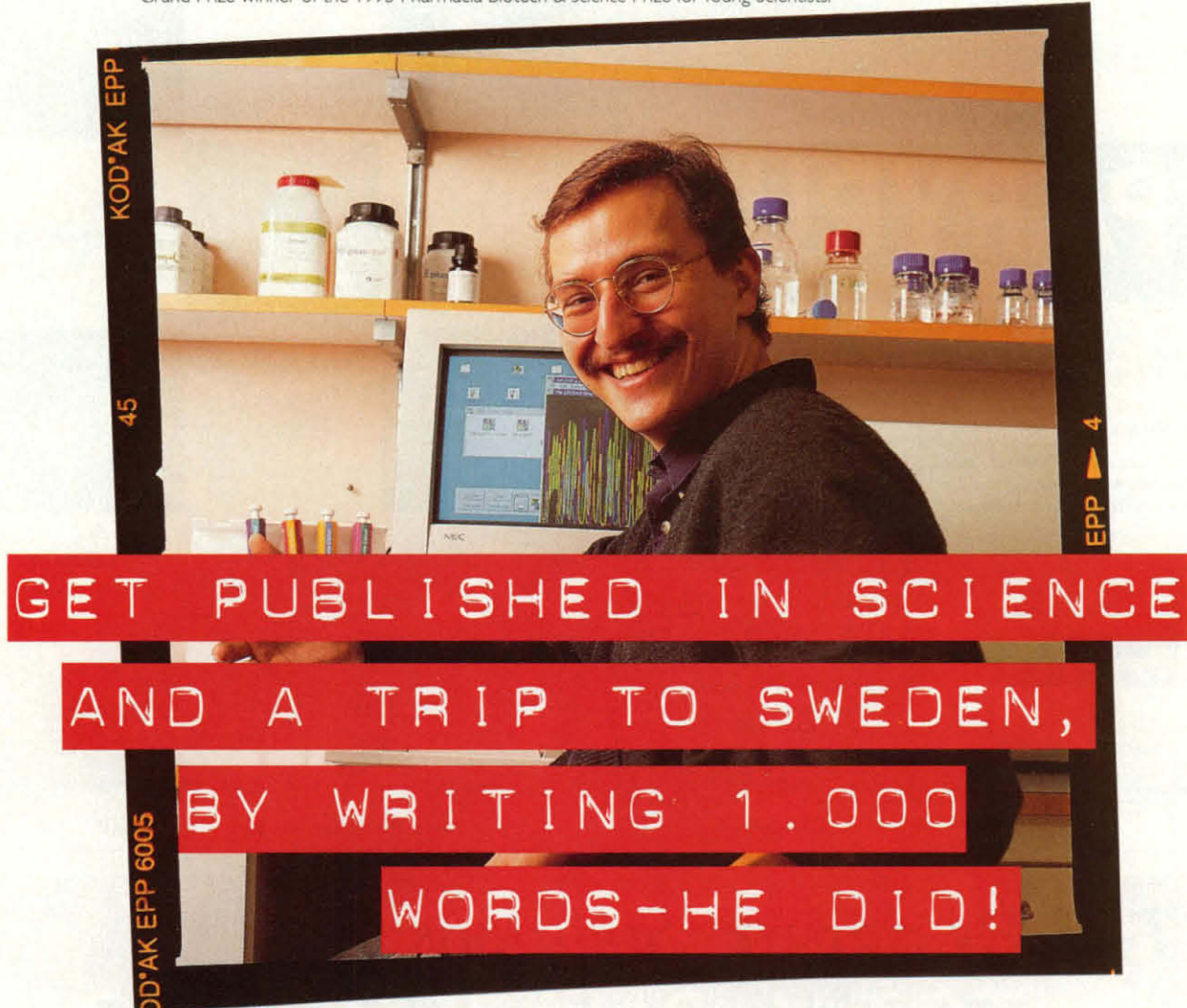
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Dr. Michael Hengartner, a staff member at Cold Spring Harbor Laboratory in New York, was the first Grand Prize winner of the 1995 Pharmacia Biotech & Science Prize for Young Scientists.



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