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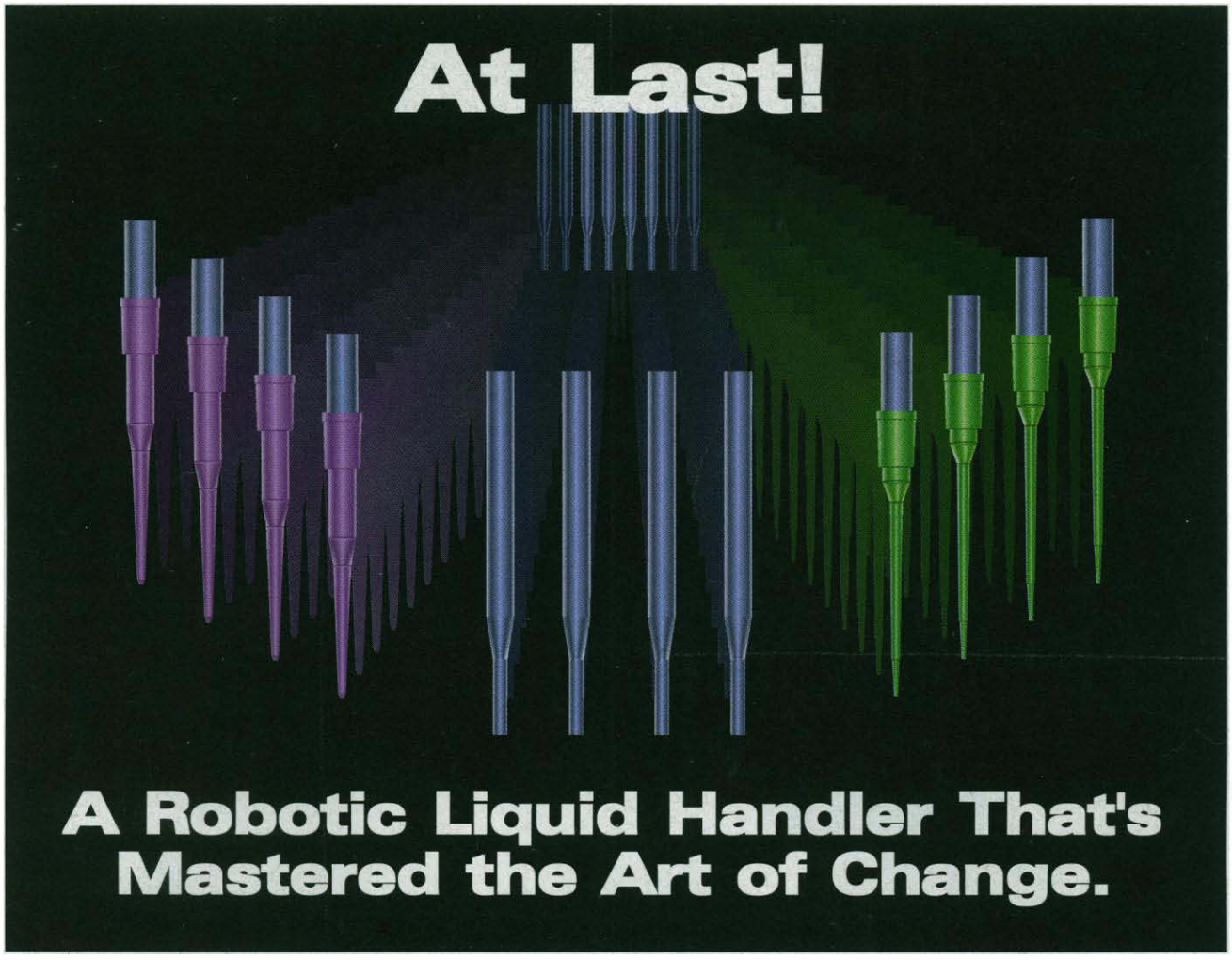

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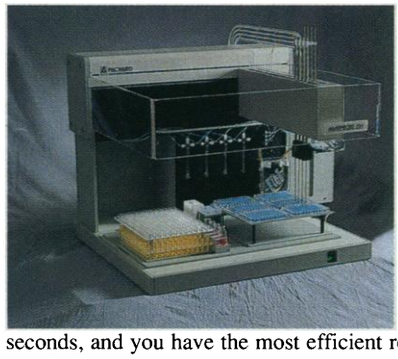

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COVER

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]

RESEARCH ARTICLE

REPORTS

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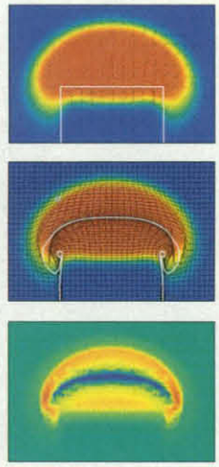

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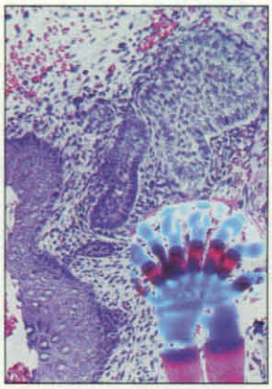
Deformation in eastern Tibet



817

Mouse model for basal cell carcinoma

◩ Indicates accompanying feature

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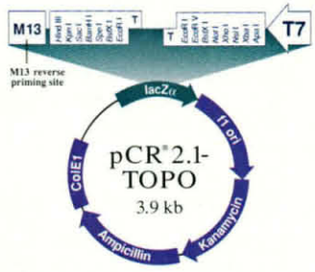

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

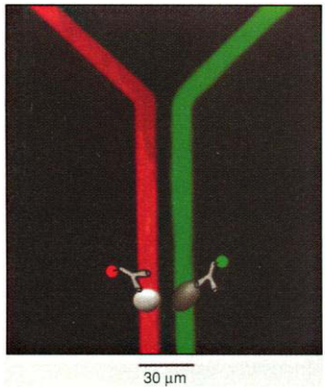
Bright infrared lasers

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



■

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.

■

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 CO_2 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 CO_2 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 reestablished 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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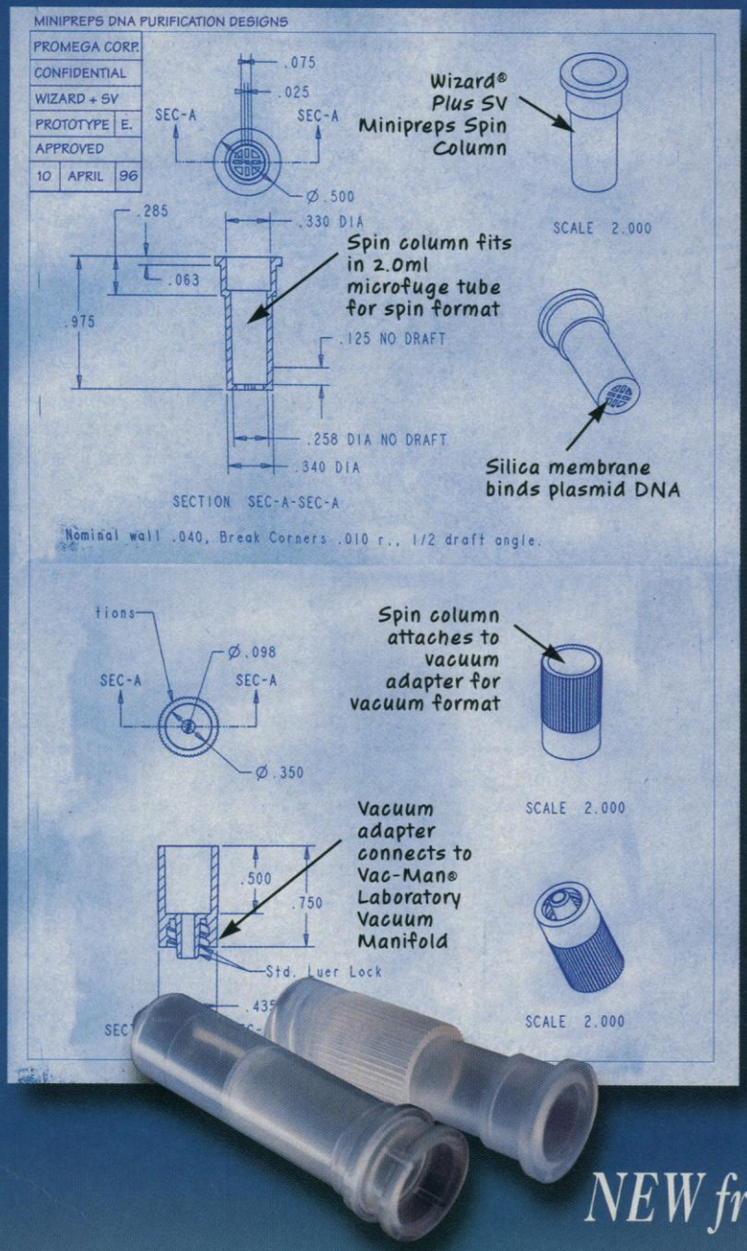

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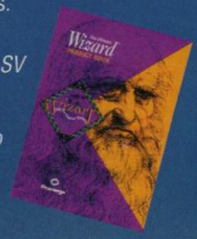

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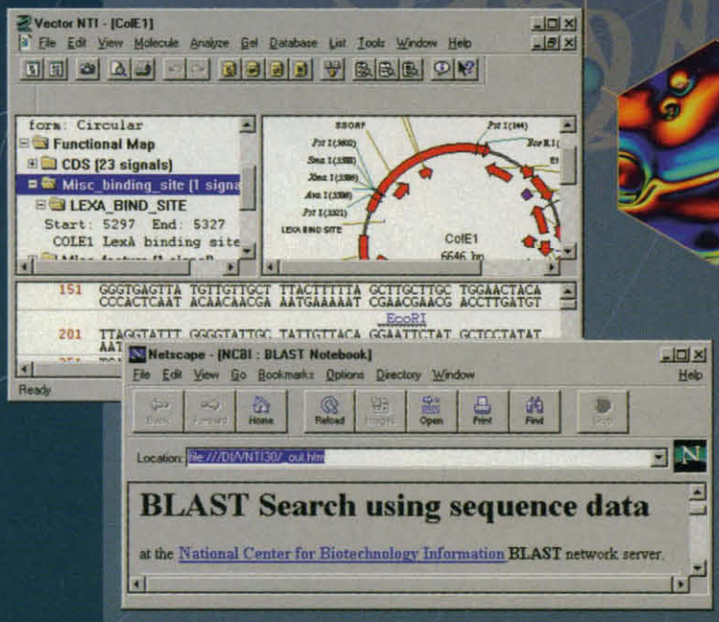

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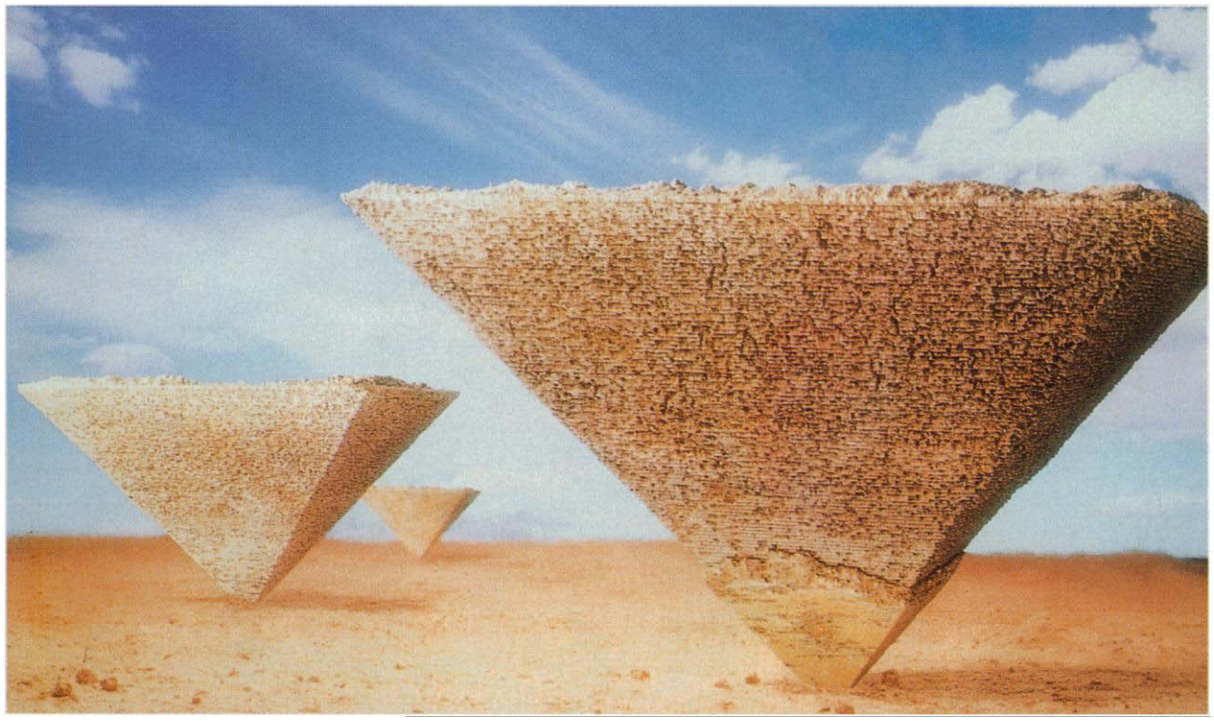

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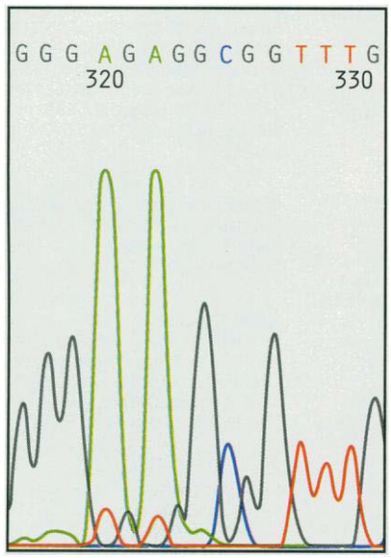

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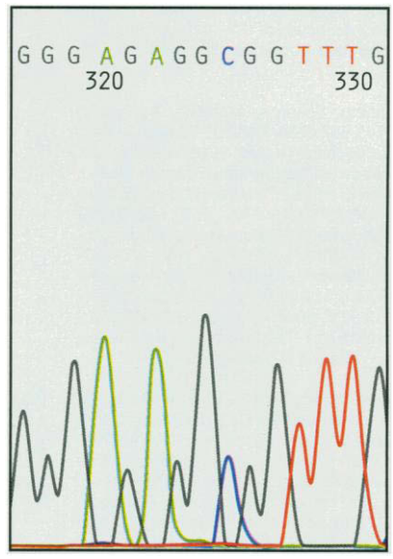

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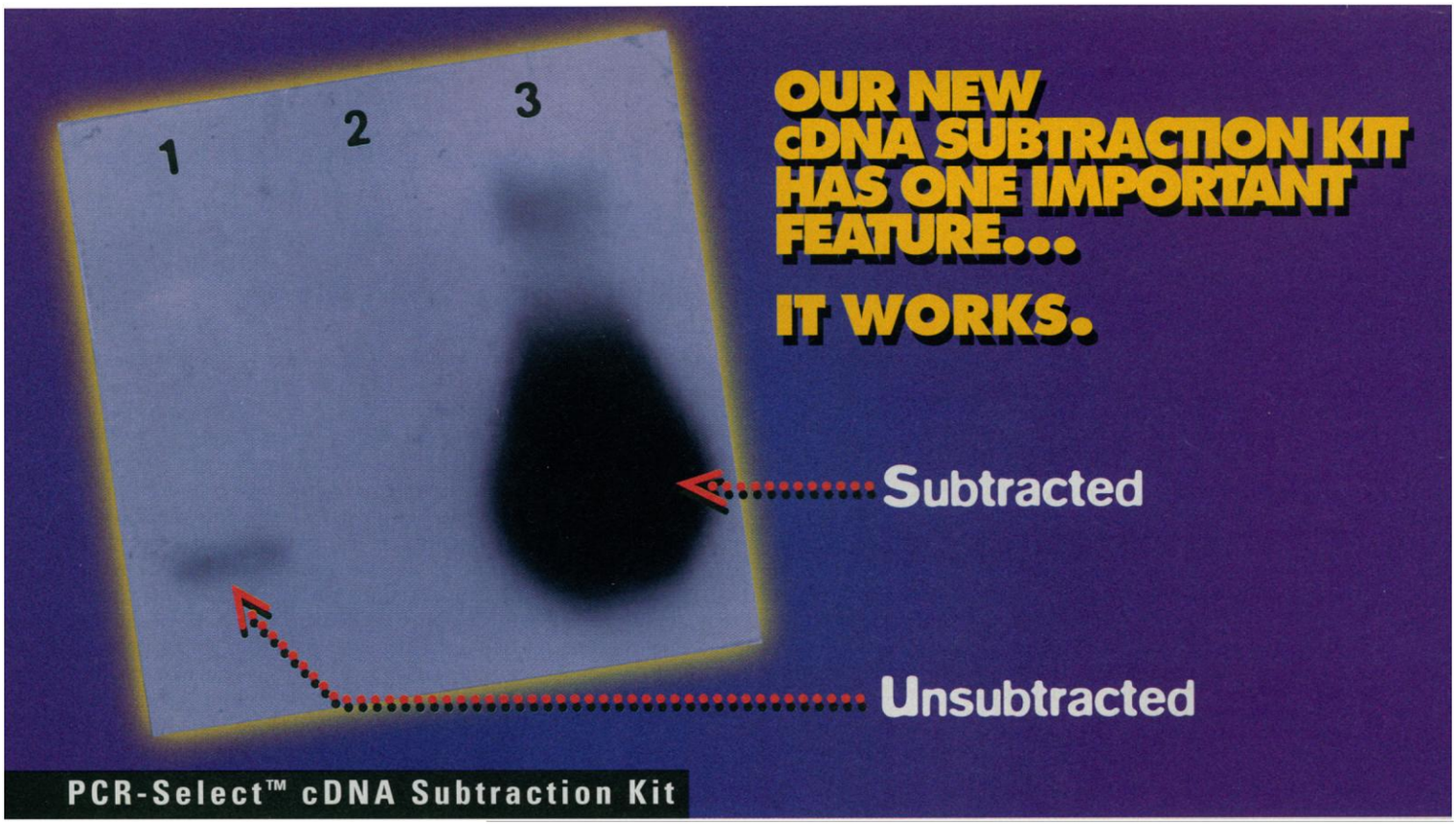
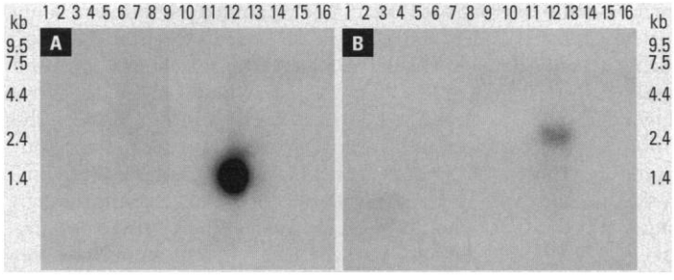


Above photo: Southern blot analysis showing enrichment of IL-2 receptor, known to be activated in human Jurkat T-cells by PHA/PMA treatment. Lane 1: unsubtracted cDNA, treated cells. Lane 2: unsubtracted cDNA, untreated cells. Lane 3: subtracted cDNA, treated cells. A dramatic reduction of the abundant housekeeping gene, G3PDH, was also seen (data not shown).



Northern blot analysis of two selected representative cDNA clones from a testis-specific library. Testis cDNA was subtracted against a mixture of cDNAs from 10 different tissues. The subtracted testis-specific cDNA was cloned into a plasmid vector, and 10 randomly selected clones were used to probe Human Multiple Tissue Northern Blots containing 2 µg of poly A^+ RNA from the indicated tissues. All 10 clones hybridized only to testis RNA. The exposure times needed to generate signal ranged from 5 hr (Panel A) to 7 days (Panel B), indicating that abundant and relatively rare cDNAs were obtained. Lanes 1-16: heart (1), brain (2), placenta (3), lung (4), liver (5), skeletal muscle (6), kidney (7), pancreas (8), spleen (9), thymus (10), prostate (11), testis (12), ovary (13), small intestine (14), colon (15), peripheral blood leukocyte (16).

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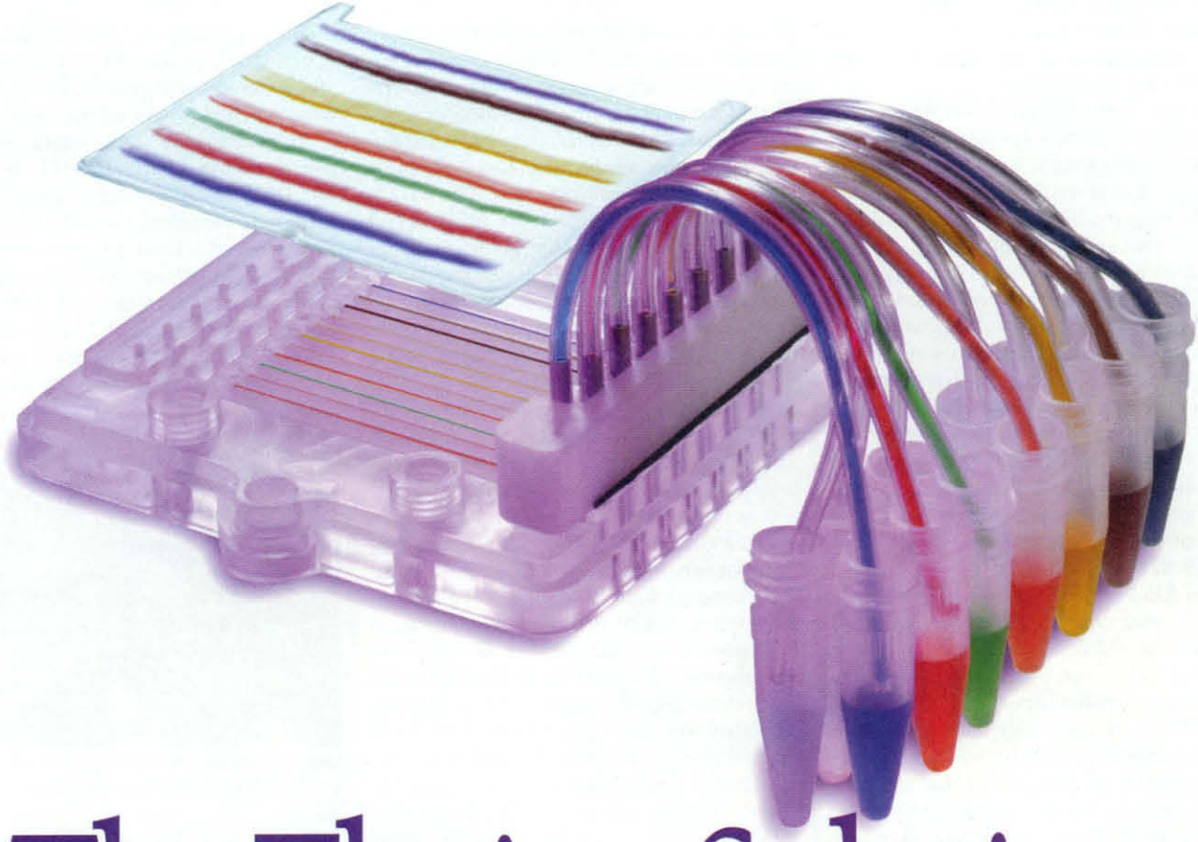

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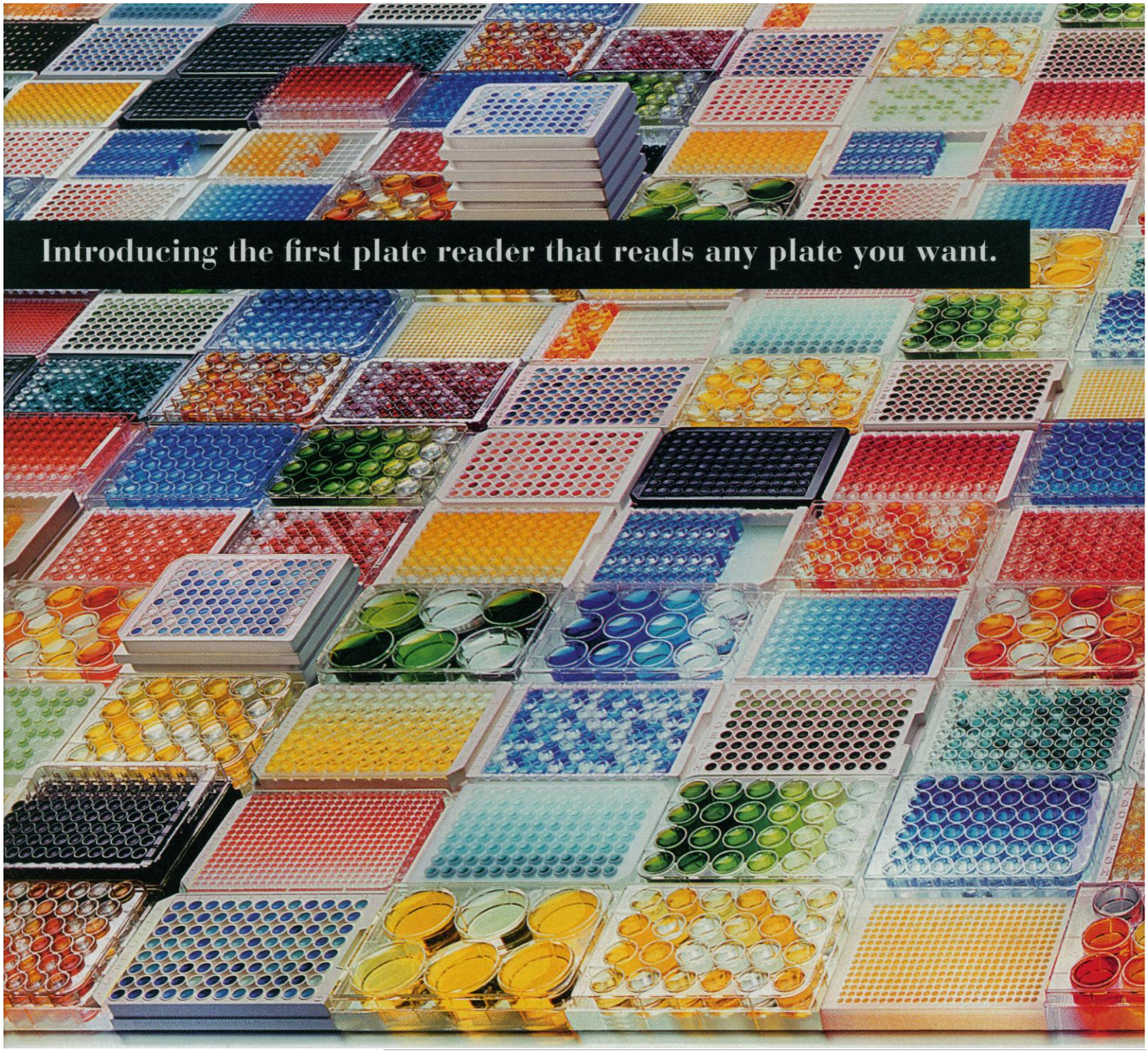

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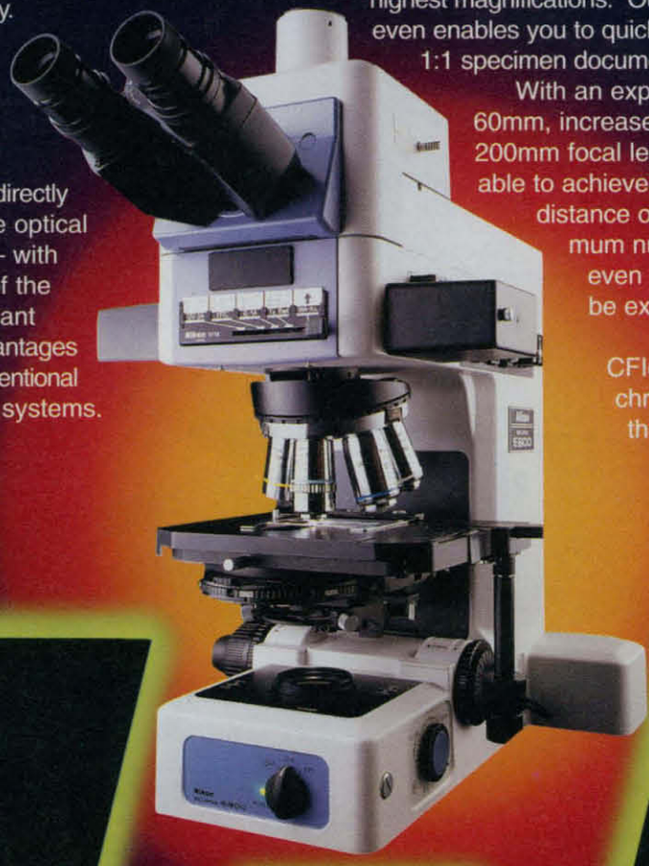

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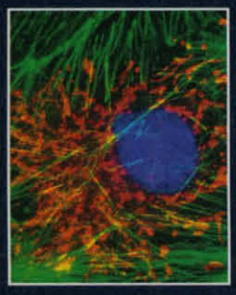

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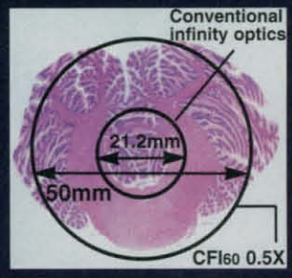

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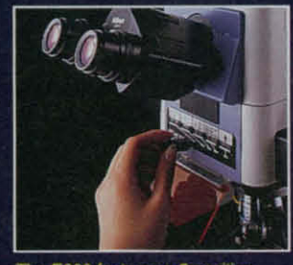

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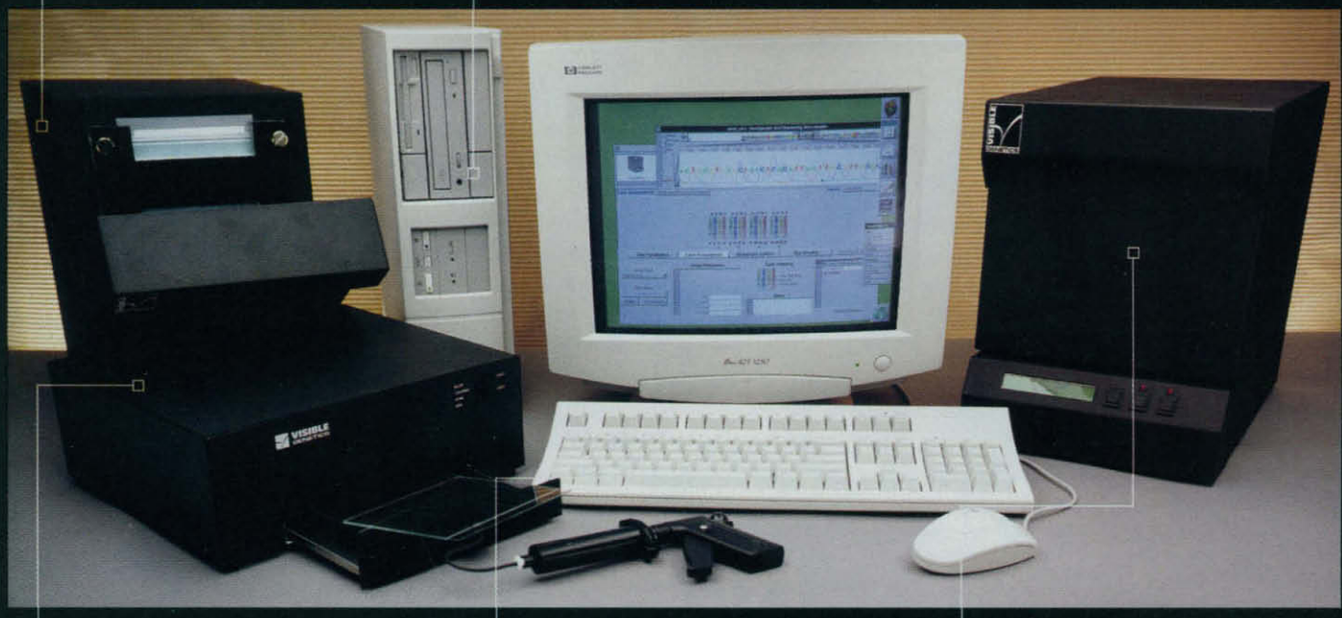

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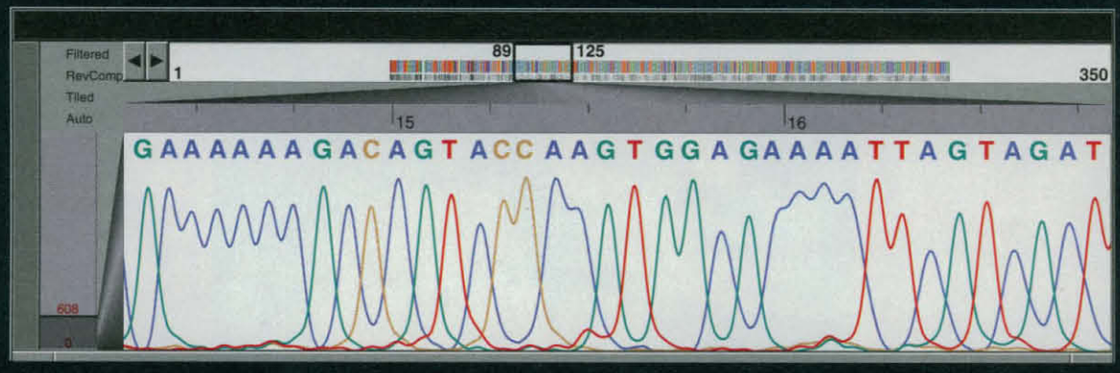

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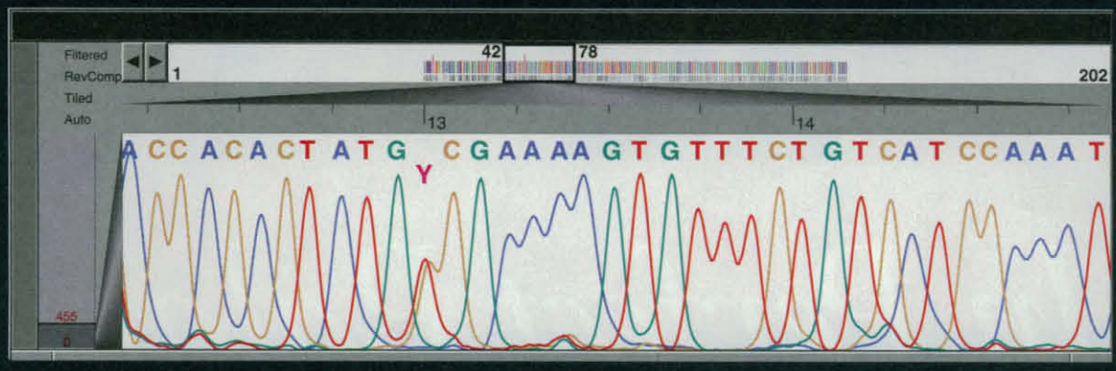

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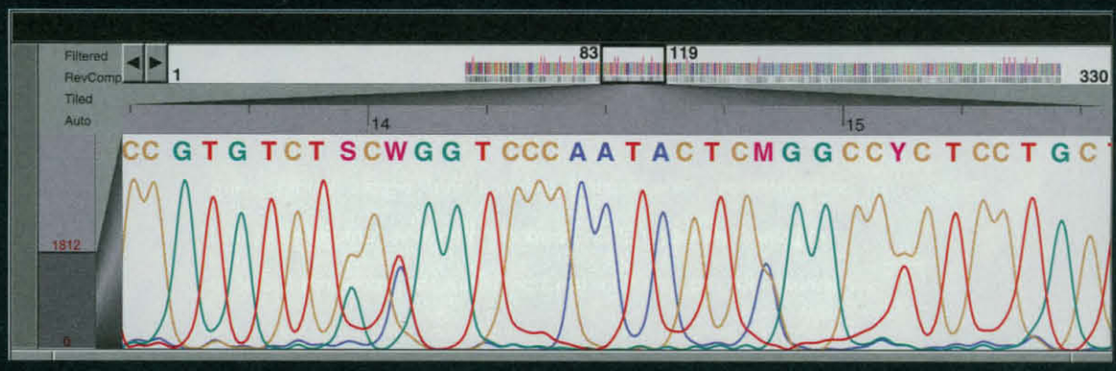

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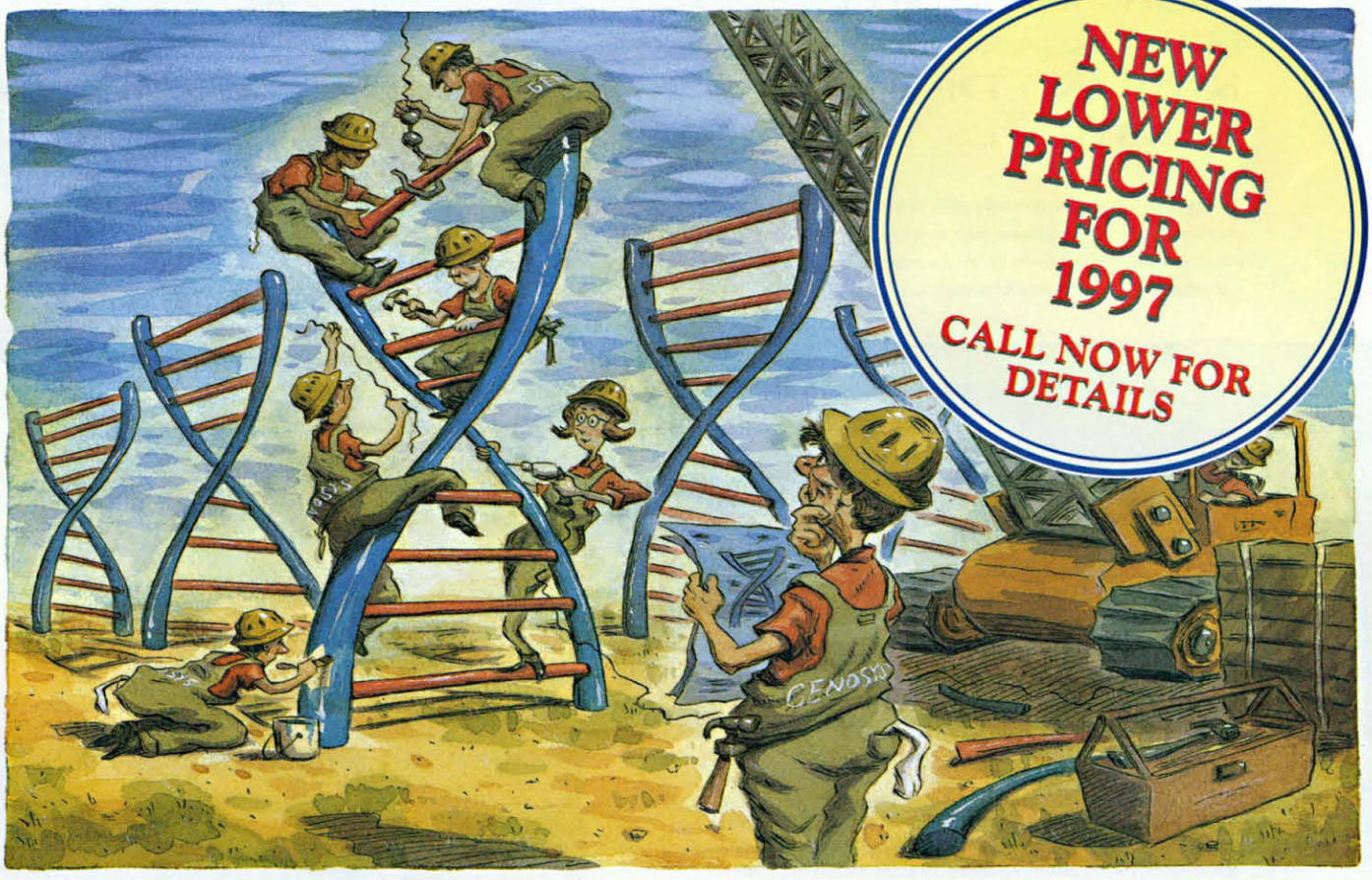

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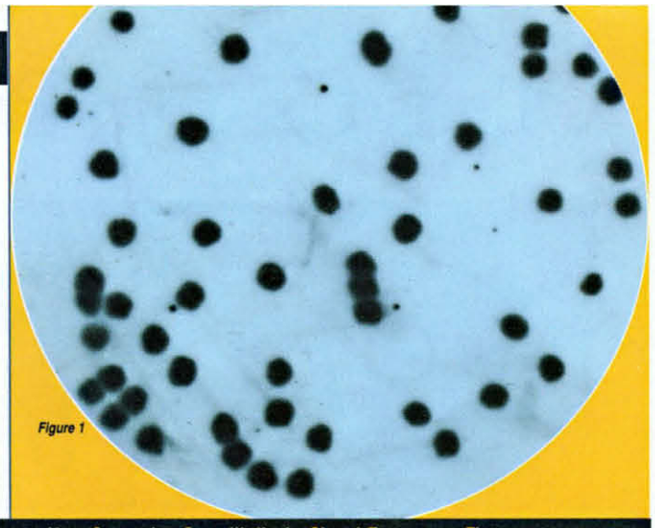

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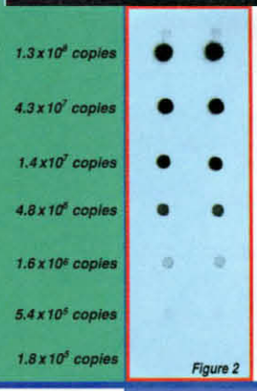

Figure 2

Figure 1. Colonies were screened for the TGF- ß1 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. Mouse ß-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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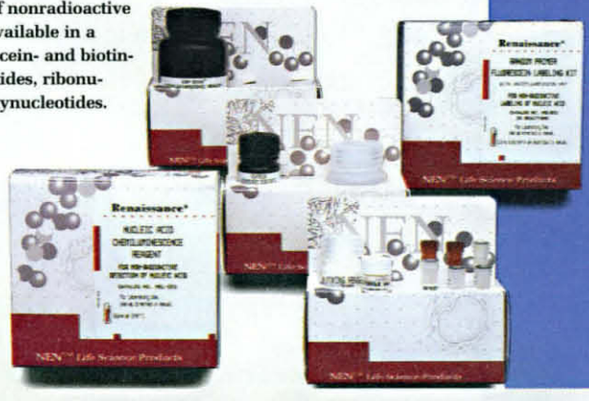

Figure 3

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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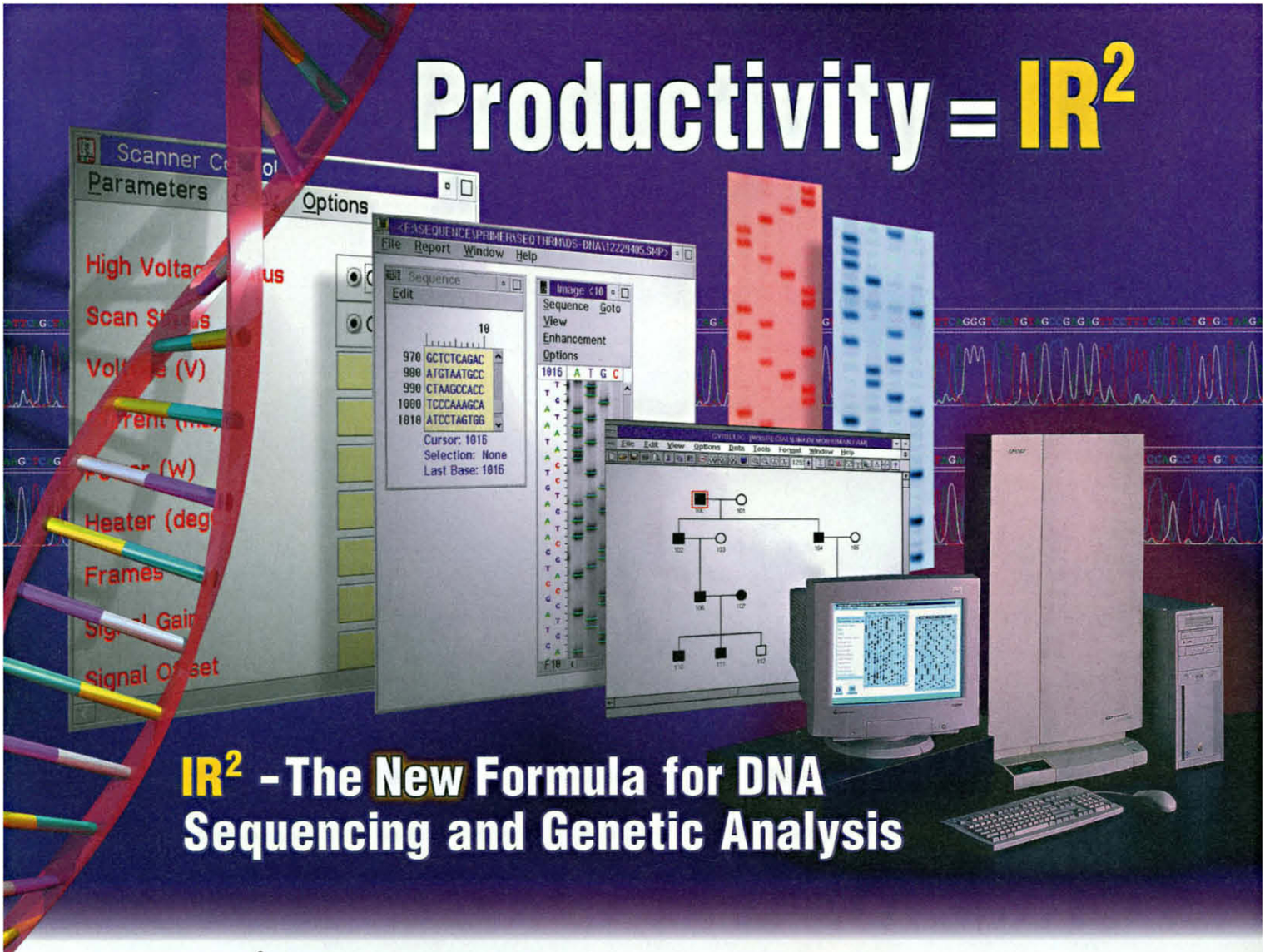

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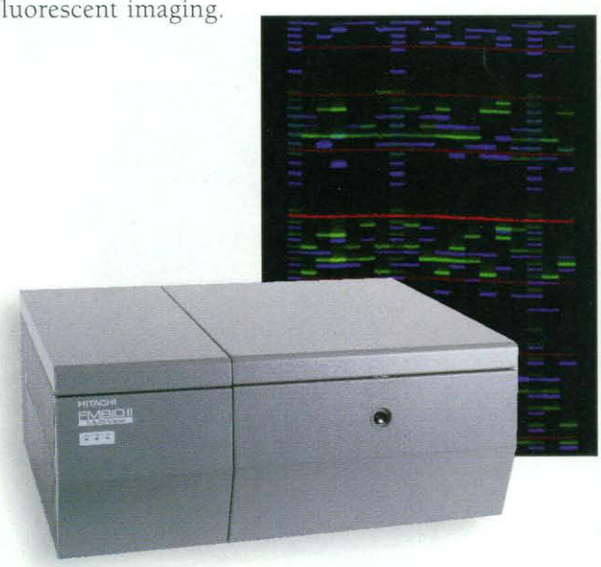

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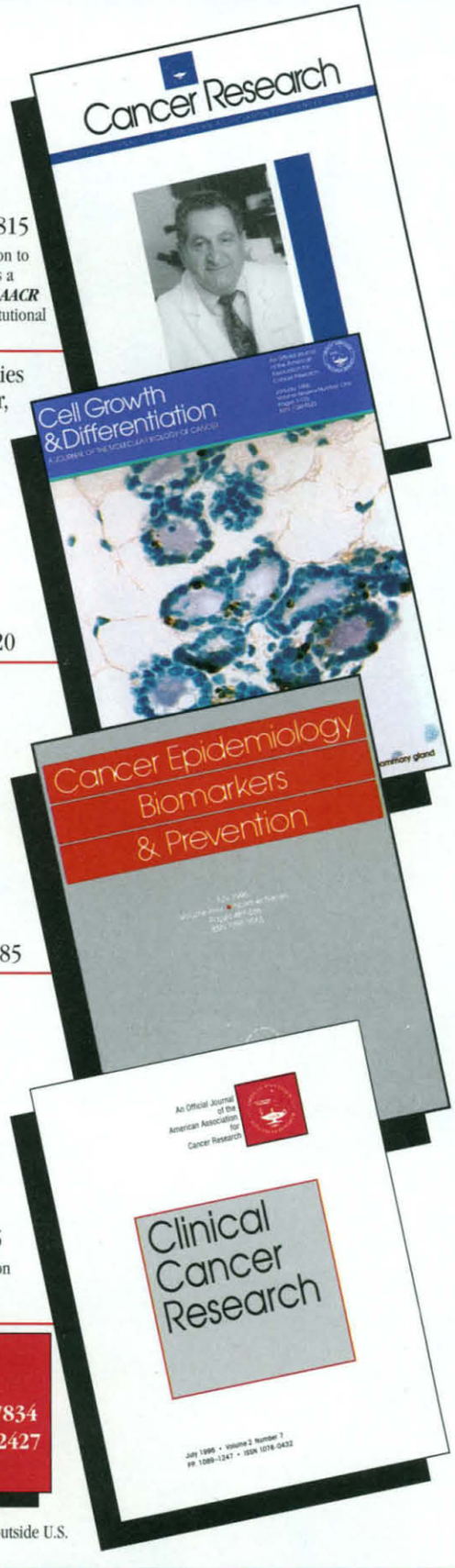

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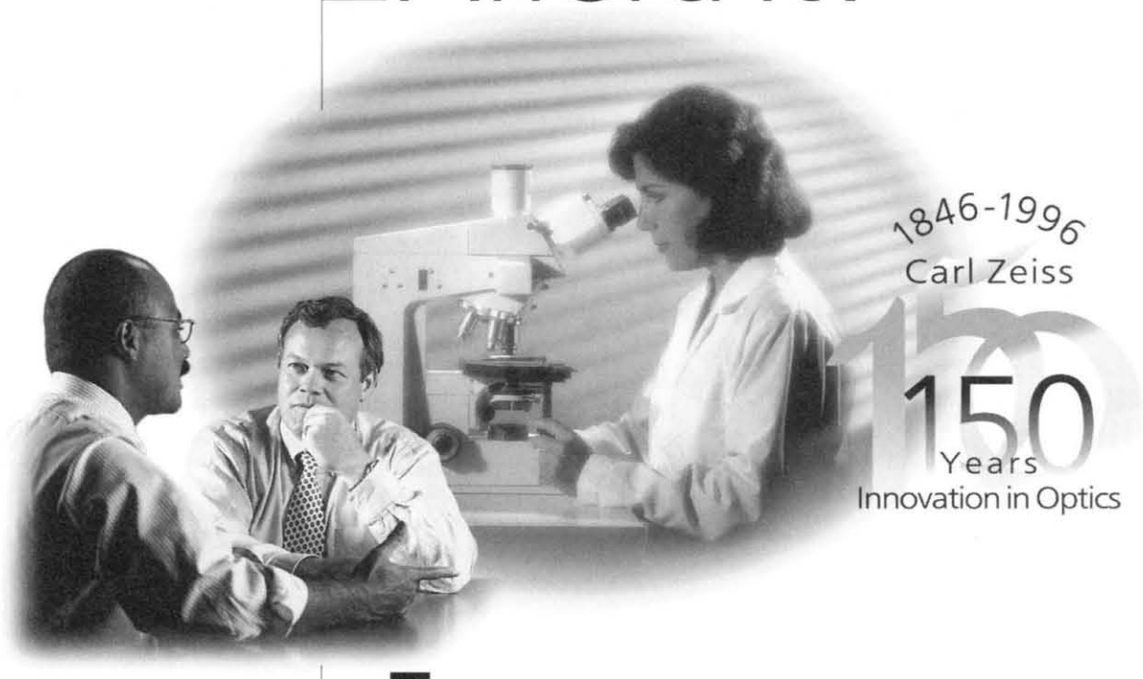

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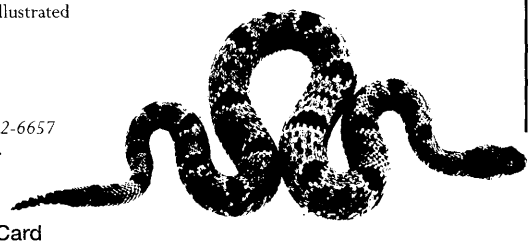

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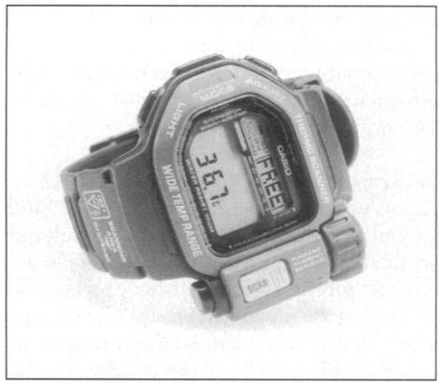

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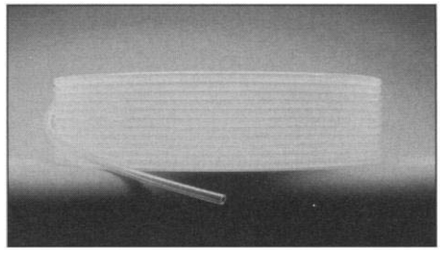

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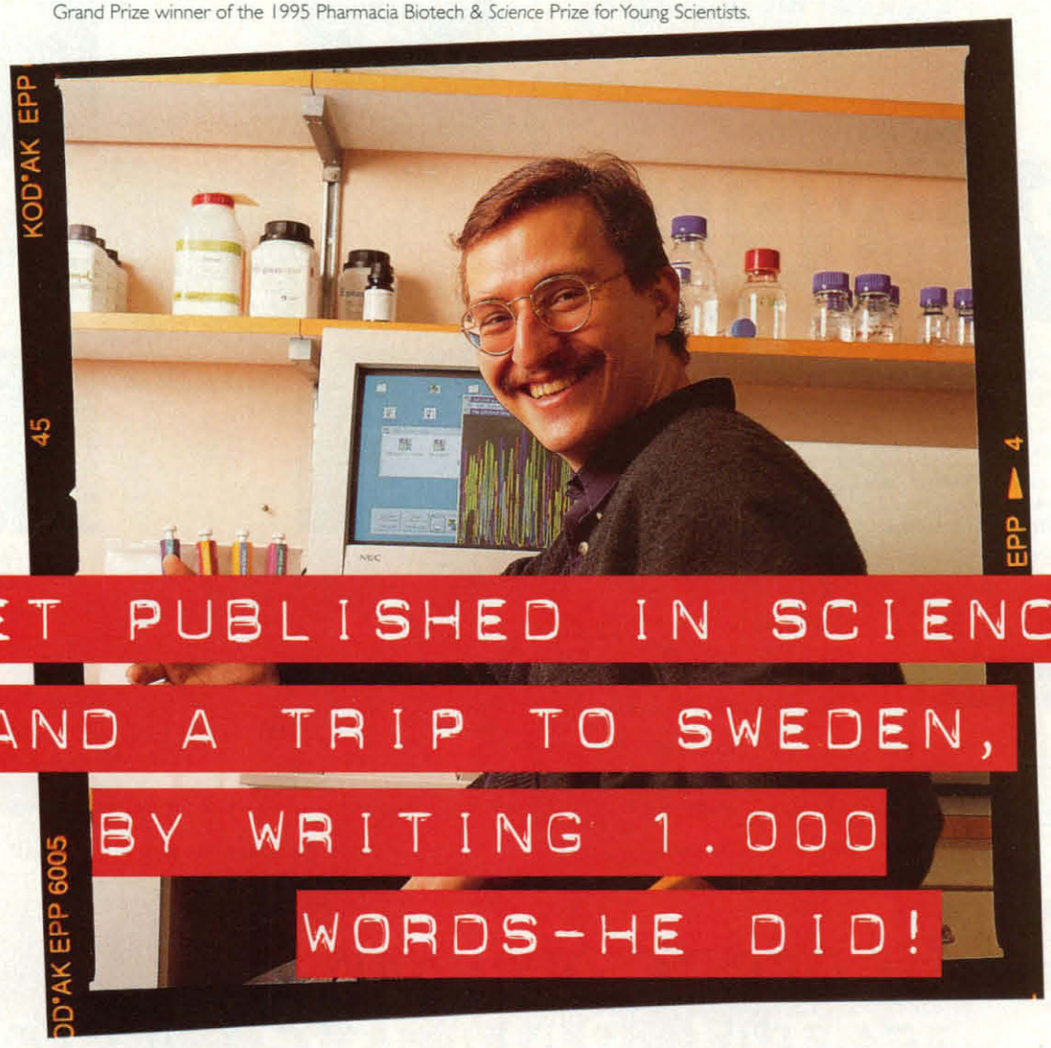

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To be eligible, you must have received your Ph.D. between 1 January and 31 December 1996. Your thesis work must have been in the field of molecular biology. To enter, you must submit a 1,000 word essay that describes your thesis work and places it in perspective with regard to the field of molecular biology. The essay may be submitted in either English, French, German, Spanish, Japanese, or Chinese (Mandarin).

The closing date for entries is 30 June 1997. All prizes will be presented in Sweden in December 1997. Full details and the required entry form can be obtained from:

- the administrator of the Award Committee at the address below
- within the *Science* homepage at http://www.aaas.org/science/prize.htm
- within the Pharmacia Biotech homepage at http://www.biotech.pharmacia.se

Pharmacia Biotech & Science Prize for Young Scientists
IN MOLECULAR BIOLOGY 1997

The Award Committee
Pharmacia Biotech & *Science* Prize for Young Scientists

Enquiries from Europe – *Science* International, 14 George IV Street, Cambridge, CB2 1HH, UK. Tel: +44 1223 302067, Fax: +44 1223 302068
Enquiries from USA and other regions – *Science*, 1200 New York Avenue, NW, Washington, DC 20005 USA. Tel: 202-326-6504, Fax: 202-289-7562