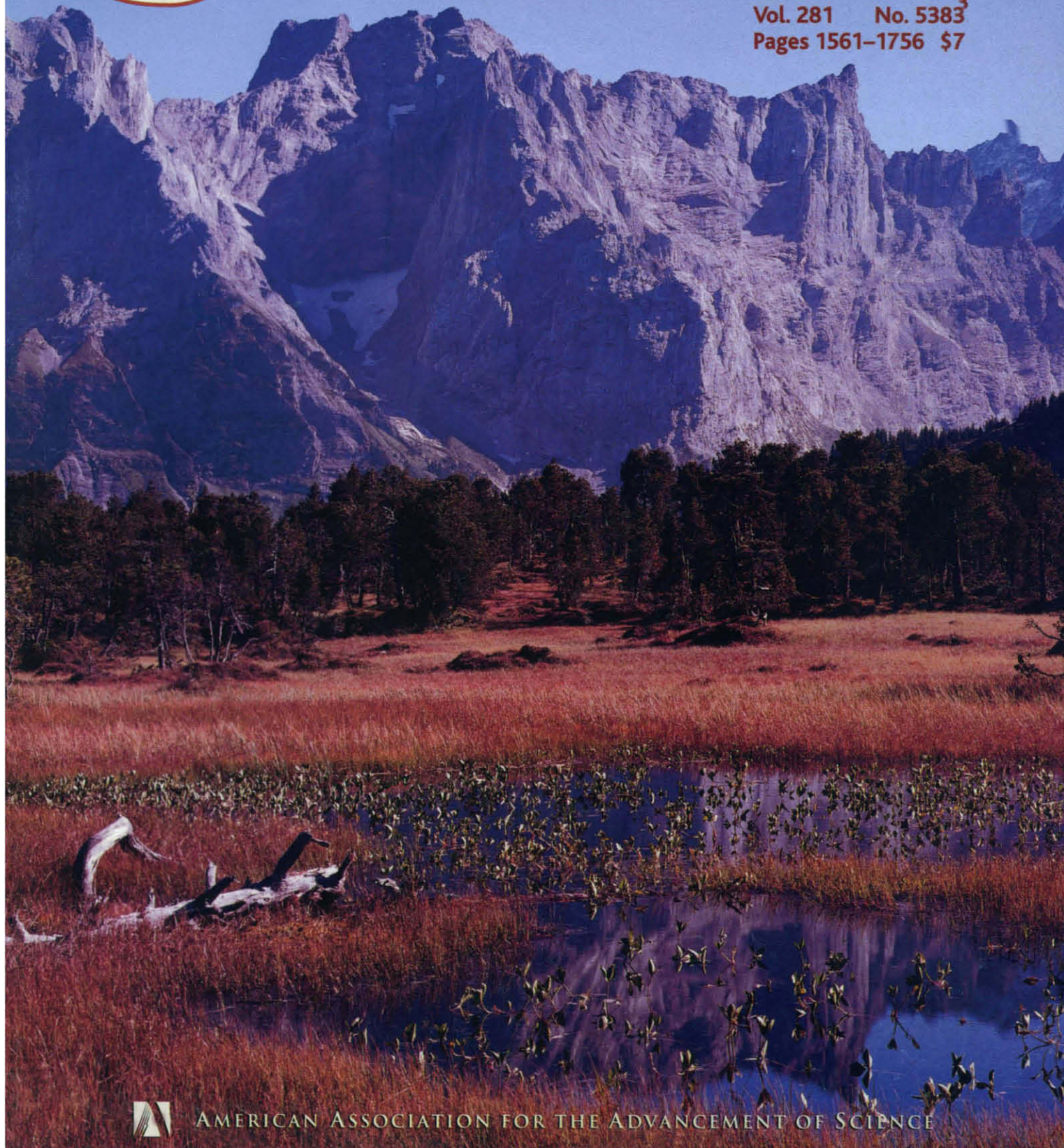


Science

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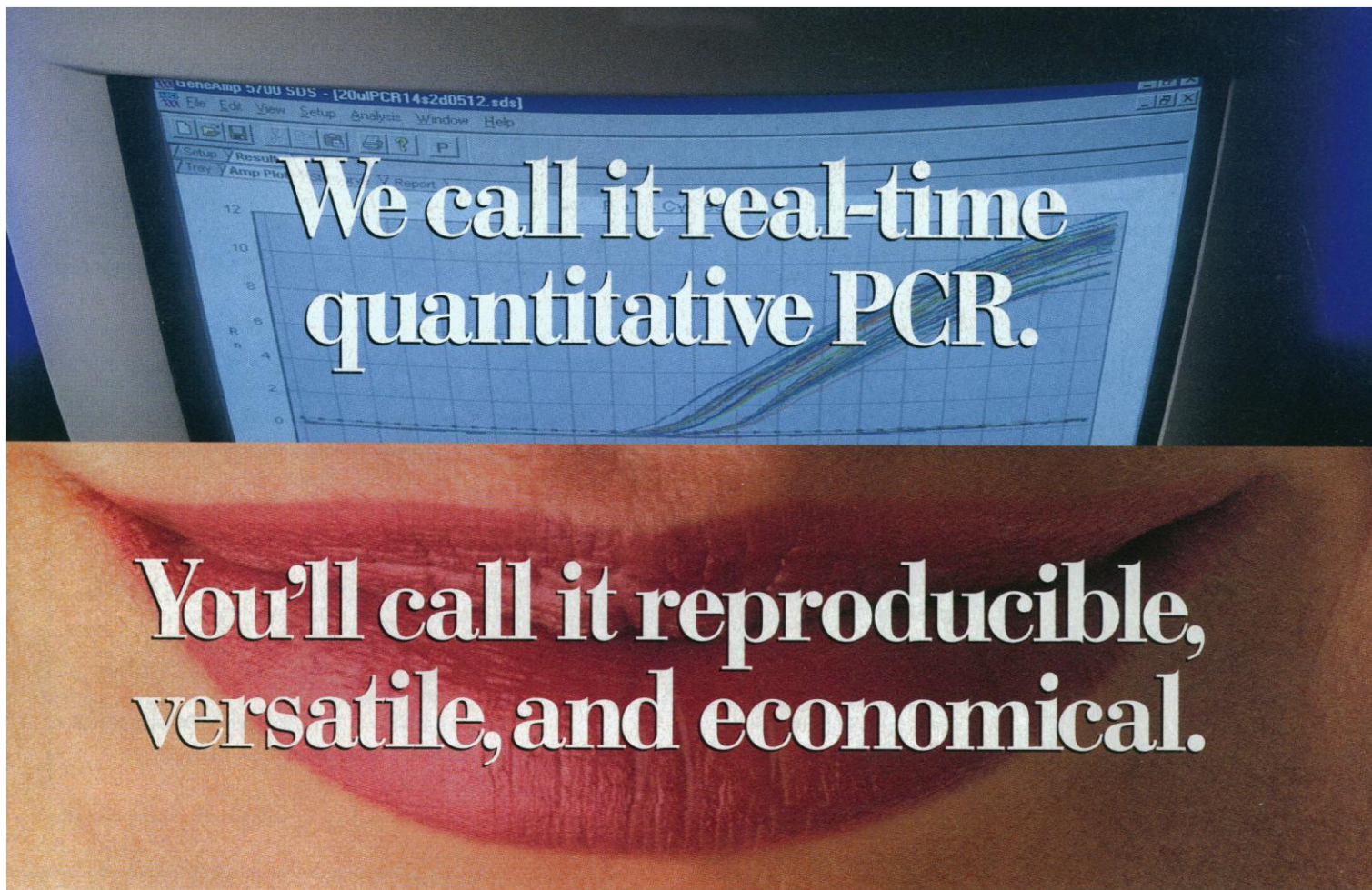
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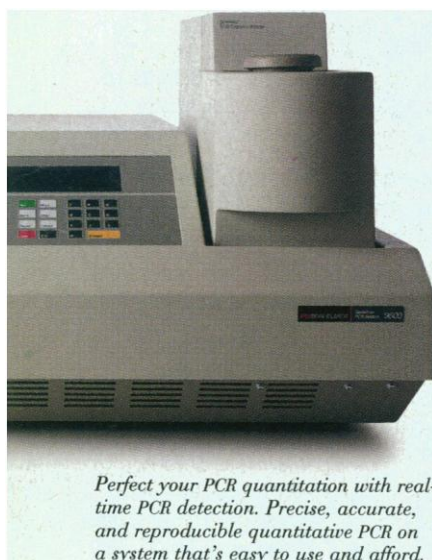
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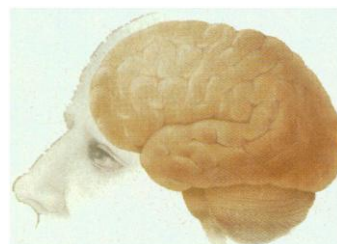
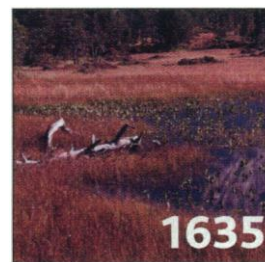


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COVER Ombrotrophic peat bogs receive material exclusively from the atmosphere in the form of rain and soil dust, but pollutants also. As the peat accumulates over thousands of years, it preserves many changes in the chemical composition of the atmosphere. From a 650-centimeter-long core from a peat bog in the Jura Mountains, a record of atmospheric lead deposition was constructed extending back 12,370 radiocarbon years before the present. [Photo: Chaltenbrunnen mire, Swiss Alps, by S. Eigstler]



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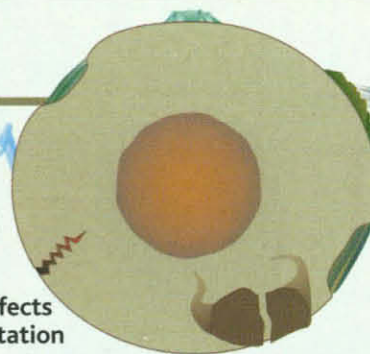
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The complexity of dissolving blood clots

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TRACES OF LEAD

Human activities have introduced lead into the atmosphere for thousands of years. A 12,000-year record of atmospheric lead deposition obtained from a peat bog in Switzerland is presented by Shotyk *et al.* (p. 1635; see the cover, the Perspective by Nriagu, and a discussion of recent environmental lead poisoning in a Policy Forum by Lanphear). About 5000 years ago, agriculture increased lead loading to the atmosphere through dust production, and lead emissions increased further when mining and smelting became widespread 3000 years ago. Switzerland began receiving dust from the Baltic Shield areas when glaciers retreated there, but this dust waned when vegetation expanded.

NYLON SANS NITROUS OXIDE

Adipic acid is the precursor to the more than 2 million tons of nylon produced annually. However, the formation of adipic acid requires the oxidation of cyclohexanol or cyclohexanone by nitric acid, a process that produces nitrous oxide (N_2O), an ozone-depleting greenhouse gas. Despite abatement efforts, this synthetic route contributes 5 to 8 percent of anthropogenic N_2O emissions. Sato *et al.* (p. 1646) describe an alternative synthesis of adipic acid that uses 30 percent hydrogen peroxide as the oxidant and eliminates N_2O emissions and the need for organic solvents. Such green chemistry comes at a price in that hydrogen peroxide is currently much more expensive to use than nitric acid.

TRAPPED AT LONG RANGE

Electrostatic interactions of molecules in solution with a nearby surface can play an important role in biological processes at cell surfaces and in chromatographic assays. Xu and Yeung (p. 1650) tracked the motion of individual protein molecules in solution and found that they were influenced by a charged silica surface at distances much greater than the electrical double layer distance that is usually assumed to be the limit for charge interactions. The charged surface, rather than immobilizing more proteins through adsorption at the surface, slows down their motion, which indicates that long-range trapping is the dominant mechanism for sorting molecules in chromatography.

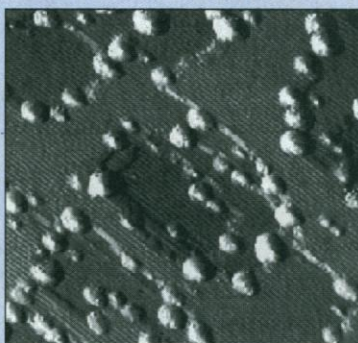
ALL IN A DAY

Most of the short-term changes in Earth's angular momentum (less than 10 years), as measured as a change in its rotation

rate, are driven by Earth's atmosphere, but some contribution comes from other sources and has been difficult to explain. Marcus *et al.* (p. 1656; see the Perspective by Wilson), using two independent ocean models and long-term length of day measurements, show that large-scale changes in ocean circulation can account for much of this residual.

JUST THIN ENOUGH

Unlike platinum or palladium, gold is usually not thought of as an important metal for industrial catalysts. Recently, however, it has been found that gold dispersed as extremely fine particles on supports such as titanium dioxide can catalyze reactions such as partial oxida-



tion of hydrocarbons and the reduction of nitrogen oxides. Valden *et al.* (p. 1647) offer an explanation for this increased activity from scanning tunneling and spectroscopy studies of gold clusters on a single-crystal titania surface. The maximum activity for carbon monoxide oxidation occurs for clusters (about 300 atoms) approximately two monolayers in thickness, and this cluster size corresponds to the onset of nonmetallic behavior. Unlike larger clusters, these smaller ones exhibit a band gap of 0.2 to 0.6 electron volts.

TWO PHOTONS AT A TIME

Molecules that have a high probability for excitation after absorbing two laser photons have numerous applications, such as in two-photon fluorescence microscopy and in optical data storage in three dimensions. Strategies for synthesizing molecules with high two-photon absorption cross sections, δ , have been limited, however. Albota *et al.* (p. 1653) show that symmetric charge transfer between the ends and the middle of a conjugated molecule can lead to very high δ values.

Bis(styryl)benzene derivatives were synthesized that have δ values up to ~600 times greater than that for *trans*-stilbene, and quantum-mechanical calculations indicate that two-photon excitation of these molecules leads to substantial charge redistribution in the molecule.

COOKING UP AMINO ACIDS

At ambient conditions (cool, oxidized sea water), synthesis of amino acids is not favored energetically. Amend and Shock (p. 1659), however, show that at conditions representative of those near ocean hydrothermal vents (moderately reducing and hot), the synthesis of 11 of the 20 protein-forming amino acids can be energetically favored. These data may help rationalize the rapid doubling rates of some thermophilic organisms and are also consistent with an origin of such amino acids in high-temperature vent environments.

TREATING DEPRESSION

All of the drugs currently used to treat depression work in the brain monoaminergic system and often cause unpleasant side effects. Kramer *et al.* (p. 1640; see the Perspective by Wahlestedt) describe the development of new drugs that block receptors for substance P, a widely distributed neurokinin in the brain. In preclinical studies, they showed that these substance P antagonists were acting as antidepressants. In a controlled clinical trial, they observed significant improvement in patients with major depression and found less severe side effects than those encountered in classical drug therapy.

ACTIVATING PLASMINOGEN

Streptokinase is a bacterial protein that binds to and activates plasminogen. This complex hydrolytically converts the inactive plasminogen to the serine protease plasmin, which hydrolyzes fibrin, a protein that is the basic constituent of blood clots. Wang *et al.* (p. 1662) present the crystal structure of the plasmin catalytic domain in complex with streptokinase. Streptokinase appears both to conformationally resculpt the cryptic active site of plasminogen and to provide an augmented binding surface that helps to corral the susceptible peptide bond of the zymogen.

SAFER MEAT THROUGH CATTLE FEED

Differences in the pH and bacterial flora in the guts and rumen of cattle have been found to depend on their feed. Diez-Gon-

CONTINUED ON PAGE 1571

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1569

zalez *et al.* (p. 1666; see the news story by Couzin) found that a grain diet increased the number of *Escherichia coli* shed by cows and promoted acid-resistance and bacterial survival. Switching the cows' diet to hay a few days before they were slaughtered might help to prevent *E. coli* contamination of the carcasses and thus reduce the prevalence of food-related illnesses in humans.

PEPTIDES AND BEHAVIOR

Peptides, when used as neurotransmitters, often are encoded by larger precursors that contain related family members. Differential expression and processing can lead to a bewildering repertoire of activities. Nelson *et al.* (p. 1686) have provided an initial understanding of the linkage of a spectrum of molecules to complex behaviors in the nematode *Caenorhabditis elegans*. The peptide family is defined by Phe-Met-Arg-Phe-amide with at least 14 genes and 44 distinct encoded peptides. The analysis of the *flp-1* gene, with gain of function and loss of function locomotory phenotypes, suggests that it acts upstream of the molecule $G\alpha_o$ and downstream of serotonin.

ATM ACTING ON P53

The gene encoding the ATM protein is mutated in the human disease ataxia telangiectasia, and this defect causes symptoms that include genetic instability and a predisposition to cancer. The ATM protein is a member of a family of proteins with similarity to phosphatidylinositol-3 kinases, but the physiological substrates of ATM have not been identified. Banin *et al.* (p. 1674) and Cunman *et al.* (p. 1677) present evidence that purified ATM in fact phosphorylates another protein, p53,

which is a transcription factor also required for appropriate responses of cells to DNA damage. This protein kinase activity is lost in cells with mutated ATM, and the ATM phosphorylation site on p53 is the same as the one phosphorylated *in vivo* in response to DNA damage. These and other results indicate that regulation of p53 by ATM-mediated phosphorylation may be a critical step in the cellular response to DNA damage.

FAT TIMES FOR ANGIOGENESIS

Leptin is a hormone that regulates food intake and energy expenditure, and its effects are thought to be mediated primarily through a receptor that is expressed in the hypothalamus. Sierra-Honigsmann *et al.* (p. 1683; see the news story by Barinaga) show that the leptin receptor is also expressed in endothelial cells and that leptin has angiogenic activity *in vitro* and in corneal assays in rats. By providing a local angiogenic signal, leptin may help maintain an appropriate balance between blood supply and fat tissue mass.

INHIBITED HEARTS

Hypertrophic cardiomyopathy (HCM) is an inherited heart disease that affects one in 500 individuals and is the leading cause of death in young athletes. Sussman *et al.* (p. 1690) show that inhibitors of calcineurin, a calcium-regulated phosphatase, prevent the development of HCM in four distinct rodent models of the disease. These results suggest that calcineurin is a key signaling molecule in the pathogenesis of HCM and that calcineurin inhibitors such as cyclosporin, a drug already in clinical use, merit attention as a potential therapy for certain forms of HCM in humans.

TECHNICAL COMMENT SUMMARIES

Ferromagnetic Superlattices

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/281/5383/1571a

K. Ueda *et al.* (Reports, 15 May, p. 1064) fabricated a ferromagnetic double perovskite, achieving "ferromagnetic spin order" in the $\text{LaCrO}_3\text{-LaFeO}_3$ superlattices.

W. E. Pickett comments that "the unusual behavior of the material bears a strong resemblance to [his] theoretical predictions for precisely that artificial compound," and he follows "the comparison as far as the current data allow." G. I. Meijer states that Ueda *et al.* "seem to use the magnetic units incorrectly in interpreting of their magnetization data," which "makes it questionable that ferromagnetic order occurs" in the proposed superlattice.

In response to Pickett, Ueda *et al.* state that further measurements show their sample to be a ferromagnetic insulator. In response to Meijer, they agree that the units in question were "miscalculated; however, this error does not affect the conclusion of [their] report."

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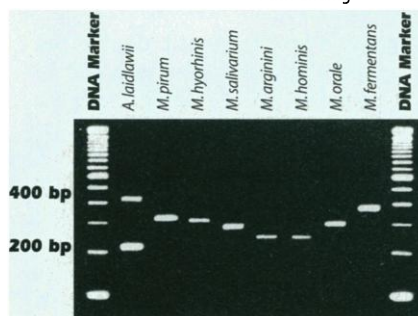
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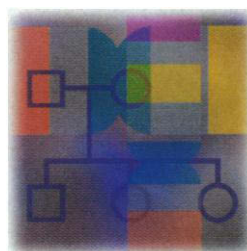
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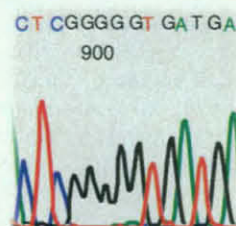
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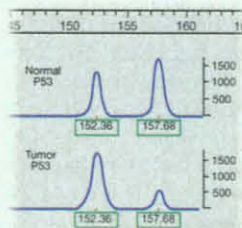
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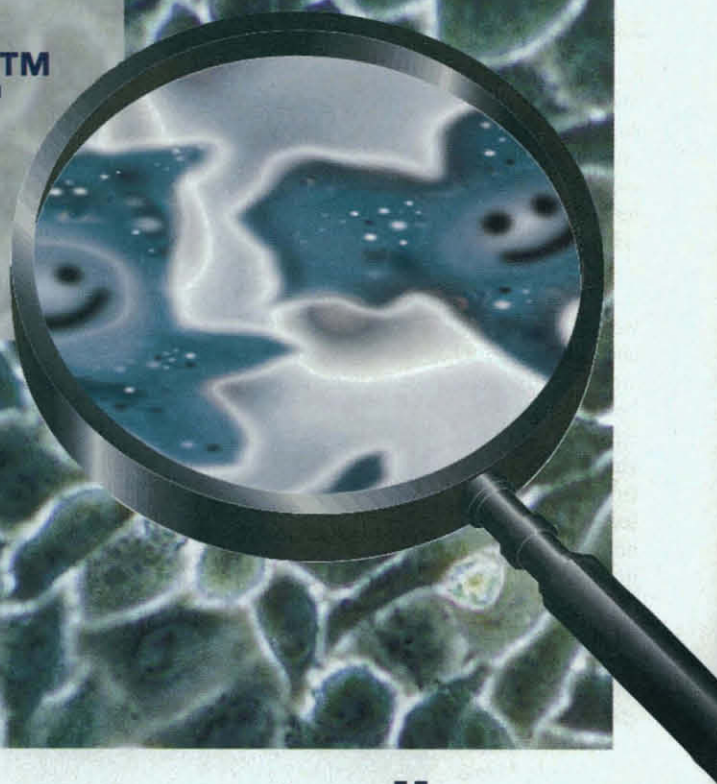


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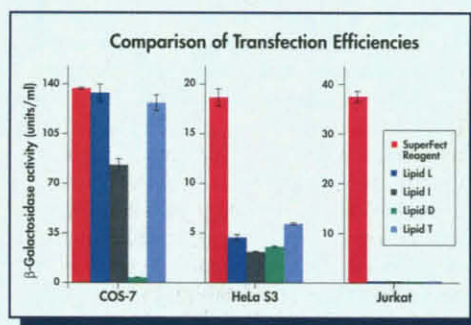


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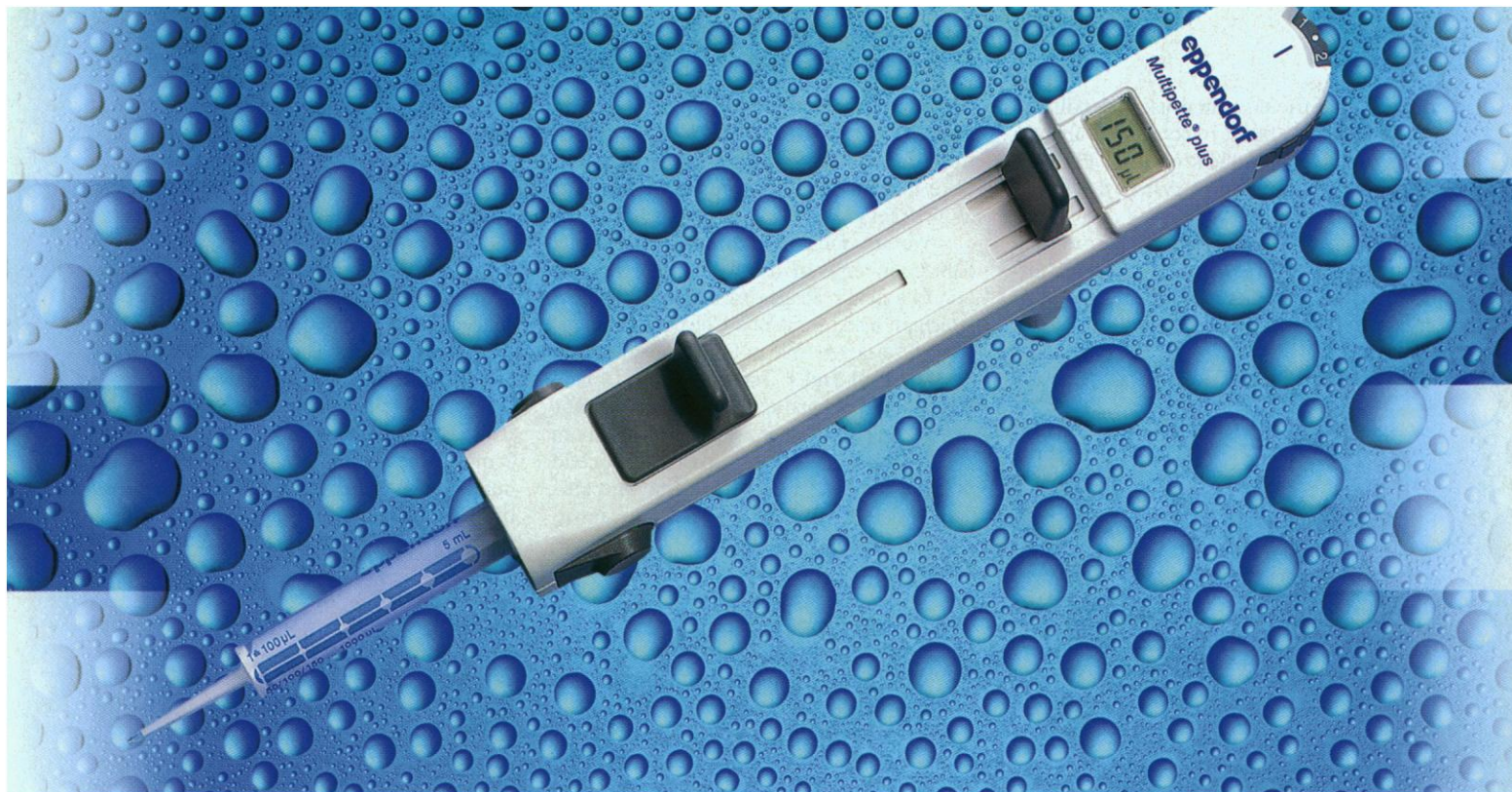
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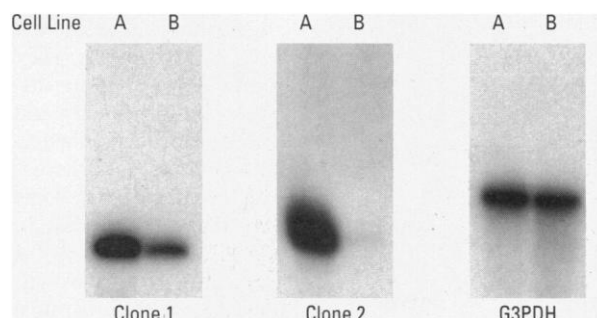
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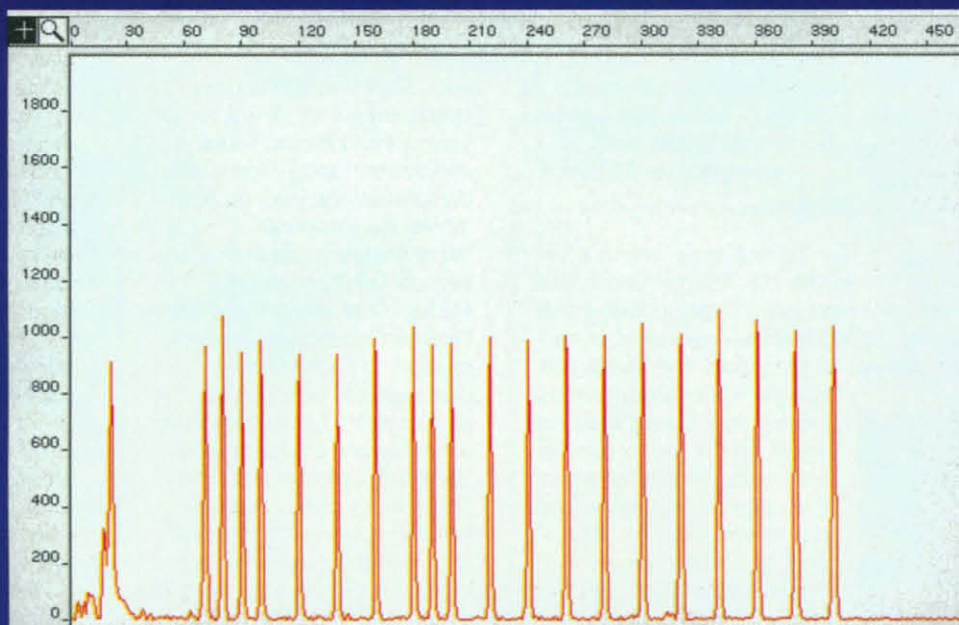
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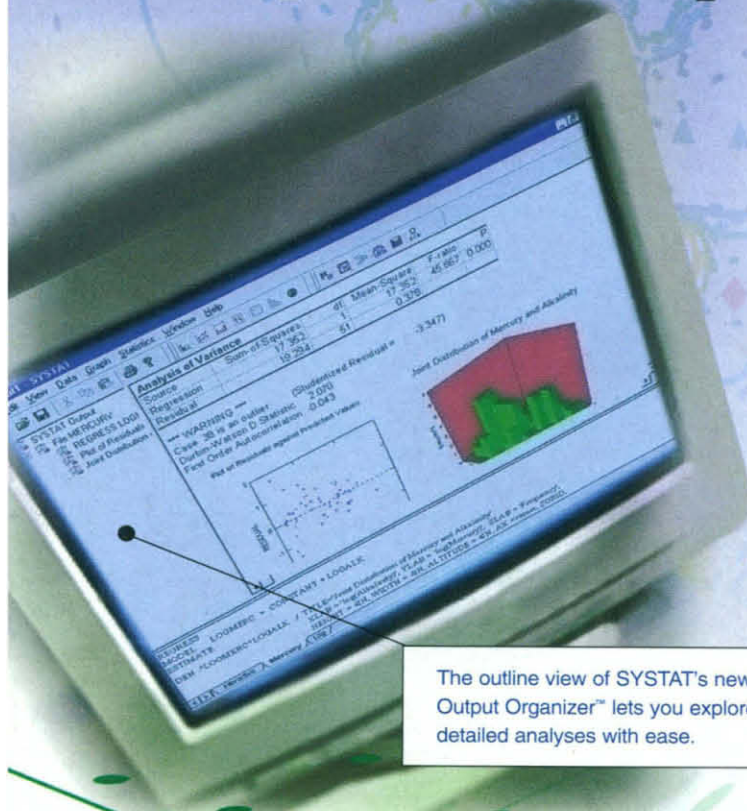
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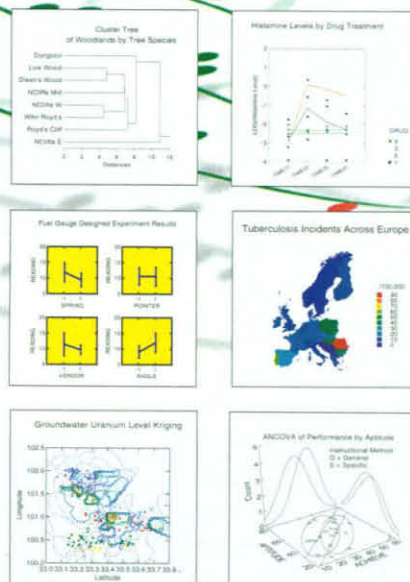
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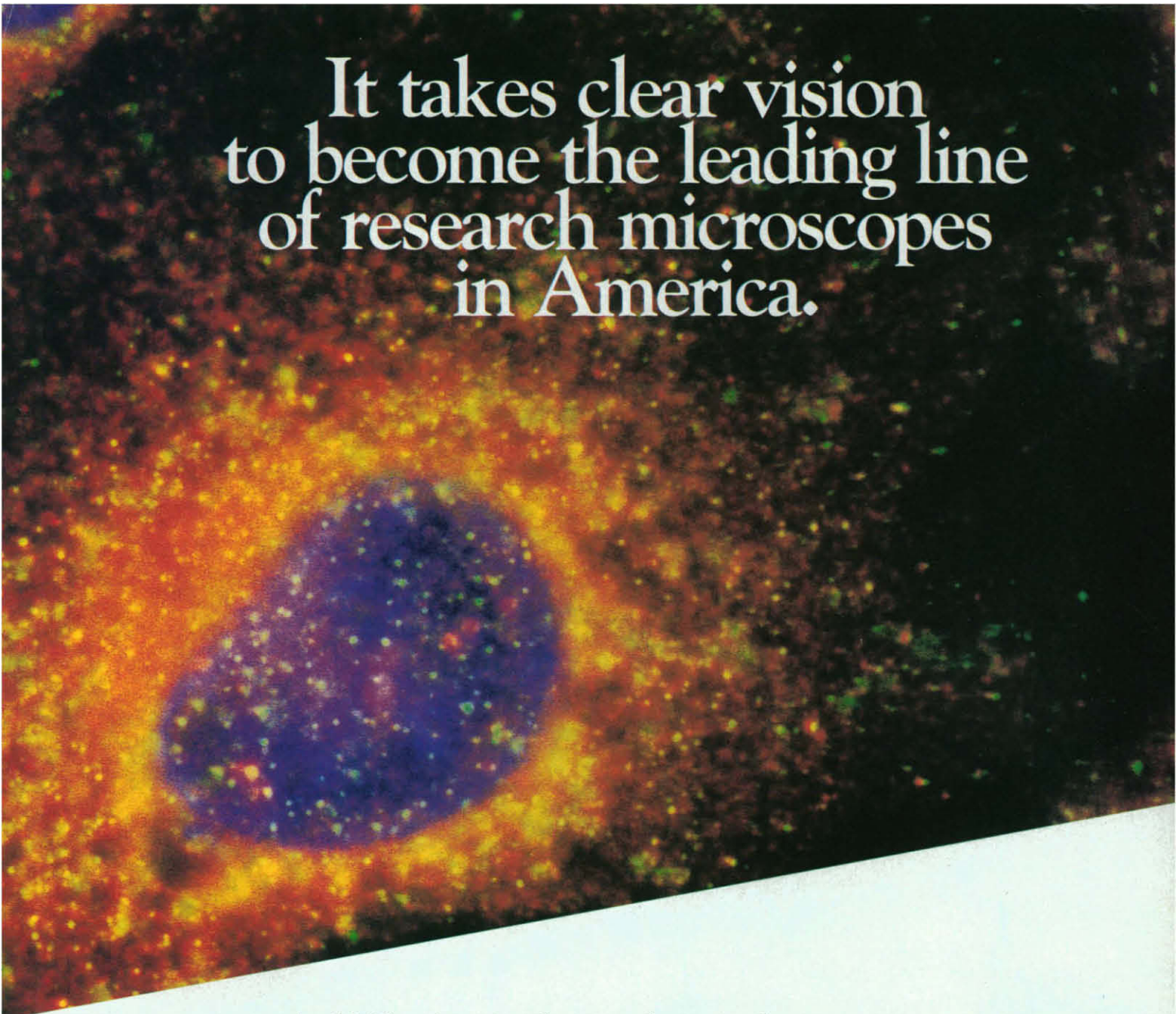


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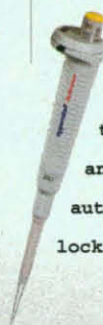


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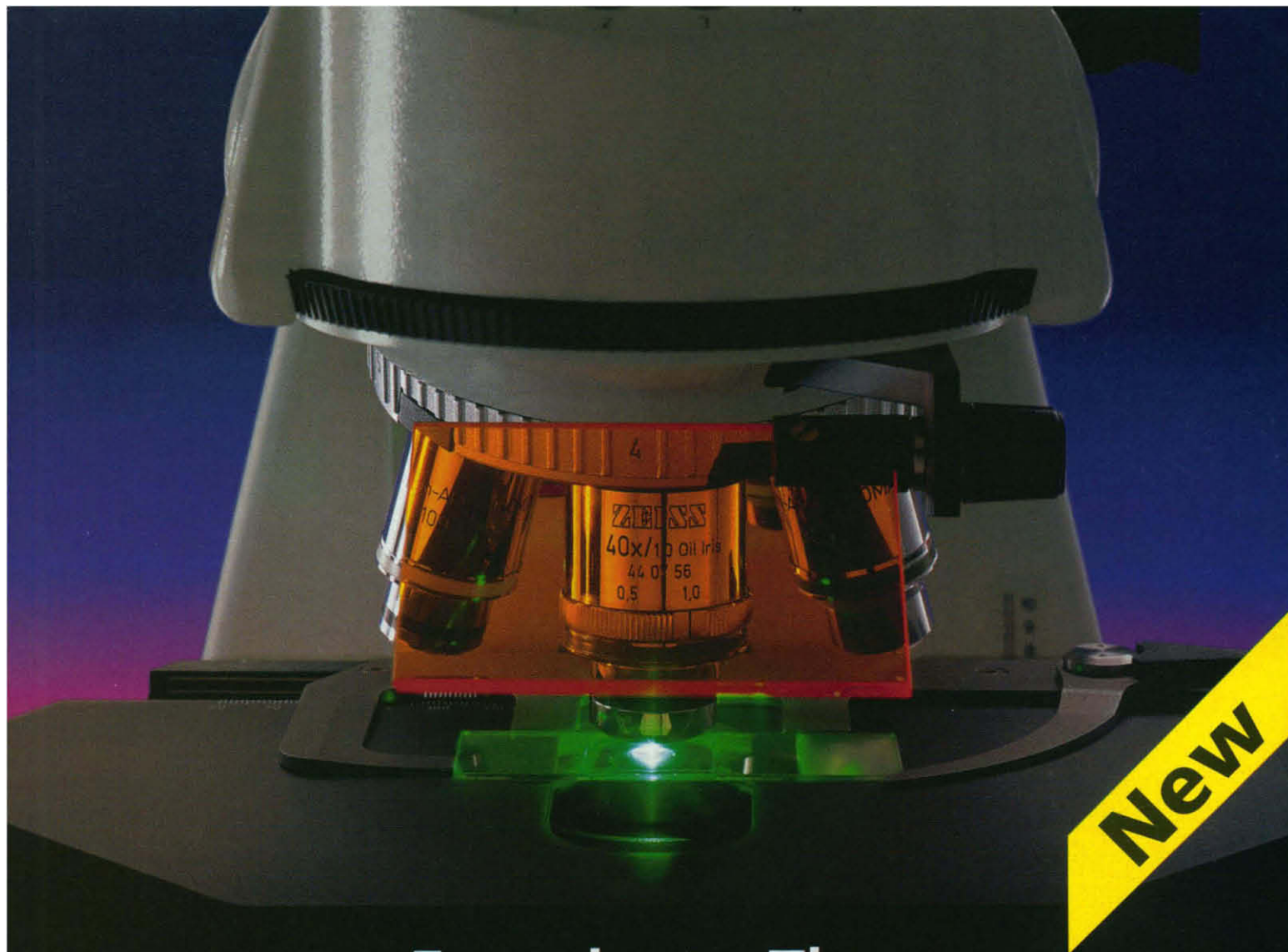
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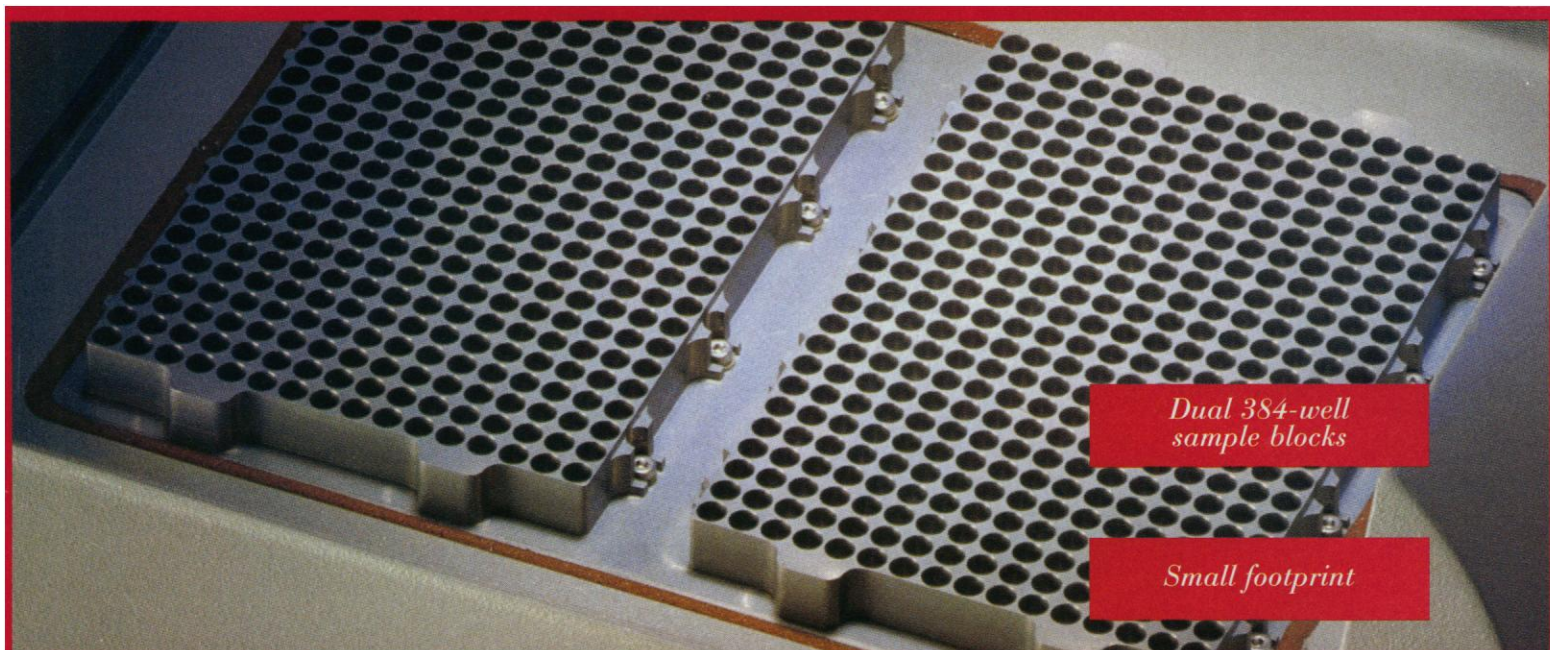
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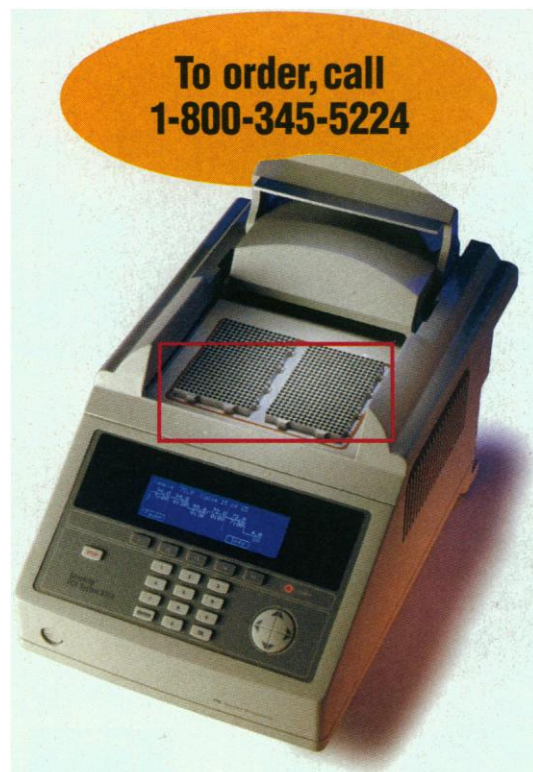
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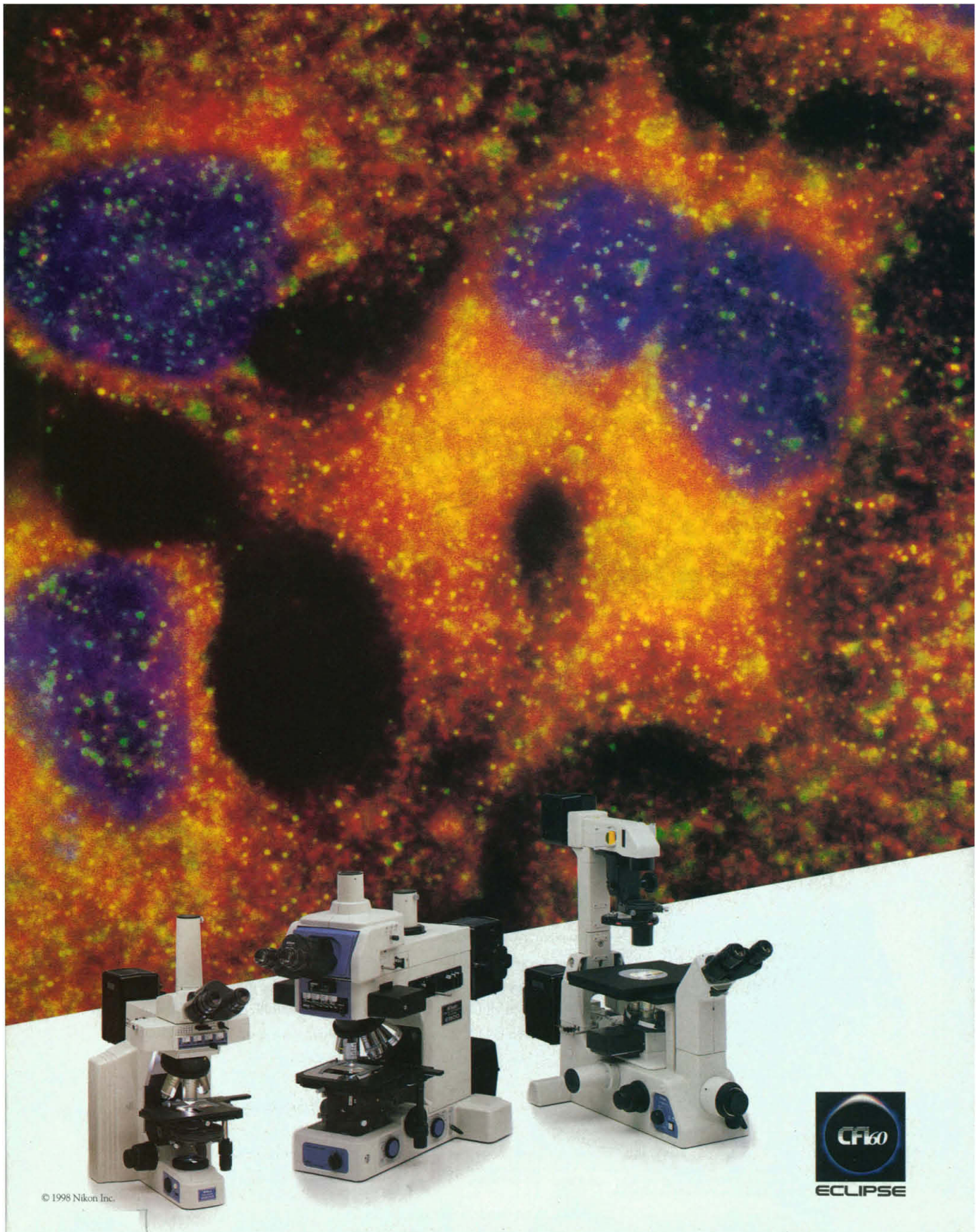
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2. Andre, P. et al. (1997) *Genome Res.* **7**, 843.
3. Slater, M. et al. (1998) *Promega Notes* **68**, 7.

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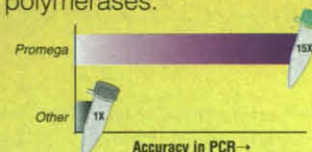
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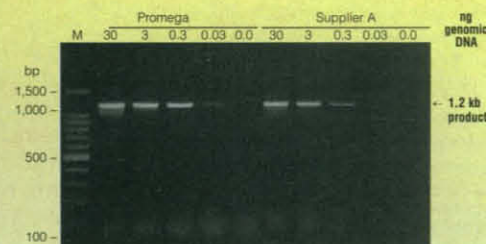
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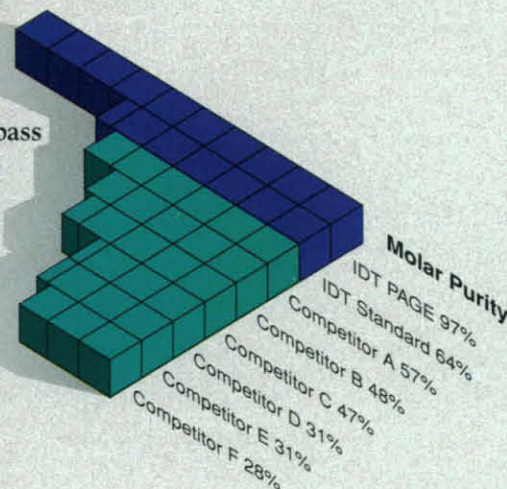
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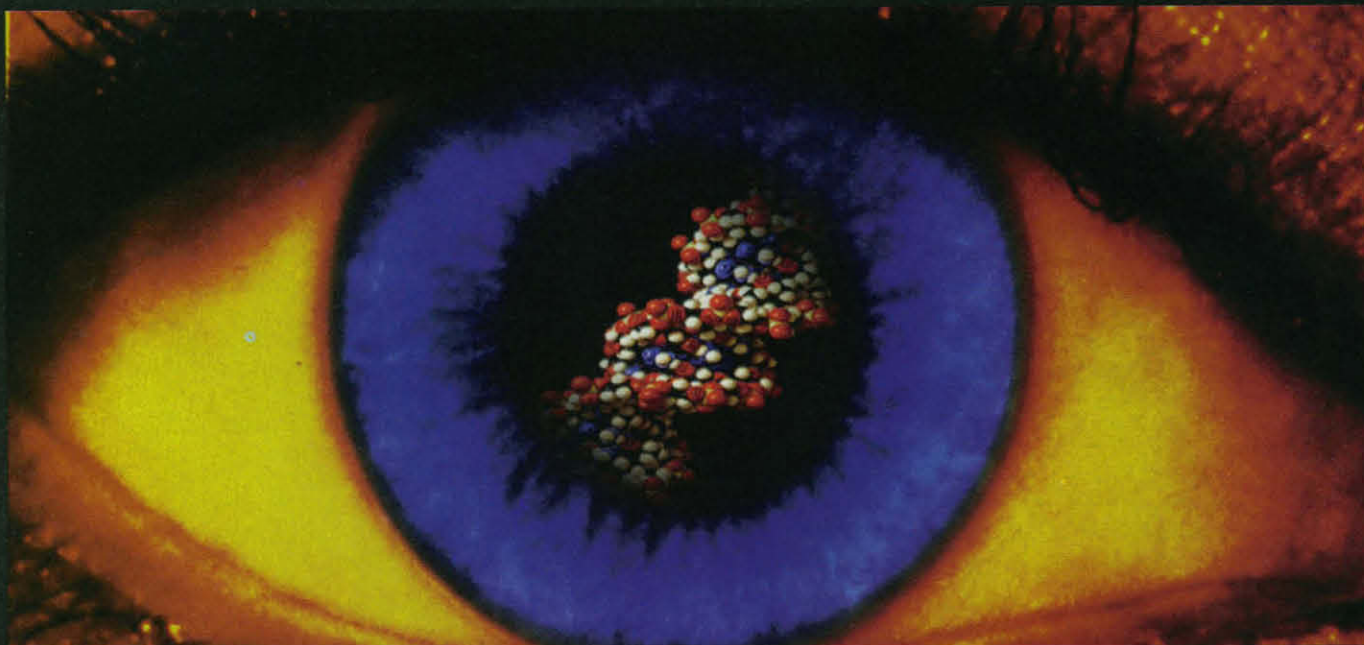
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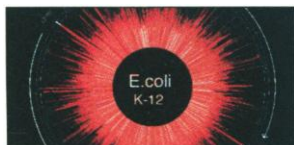
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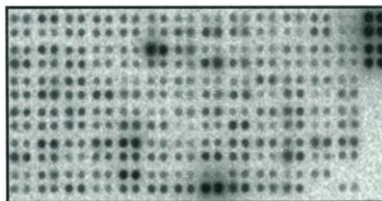
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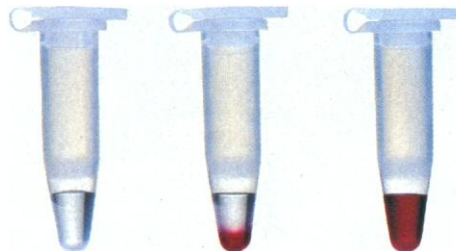
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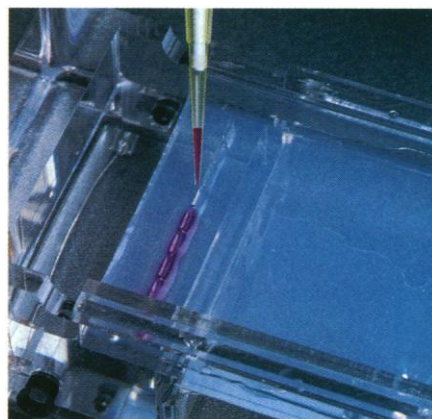
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[†] Patent pending.

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it's been mixed.*



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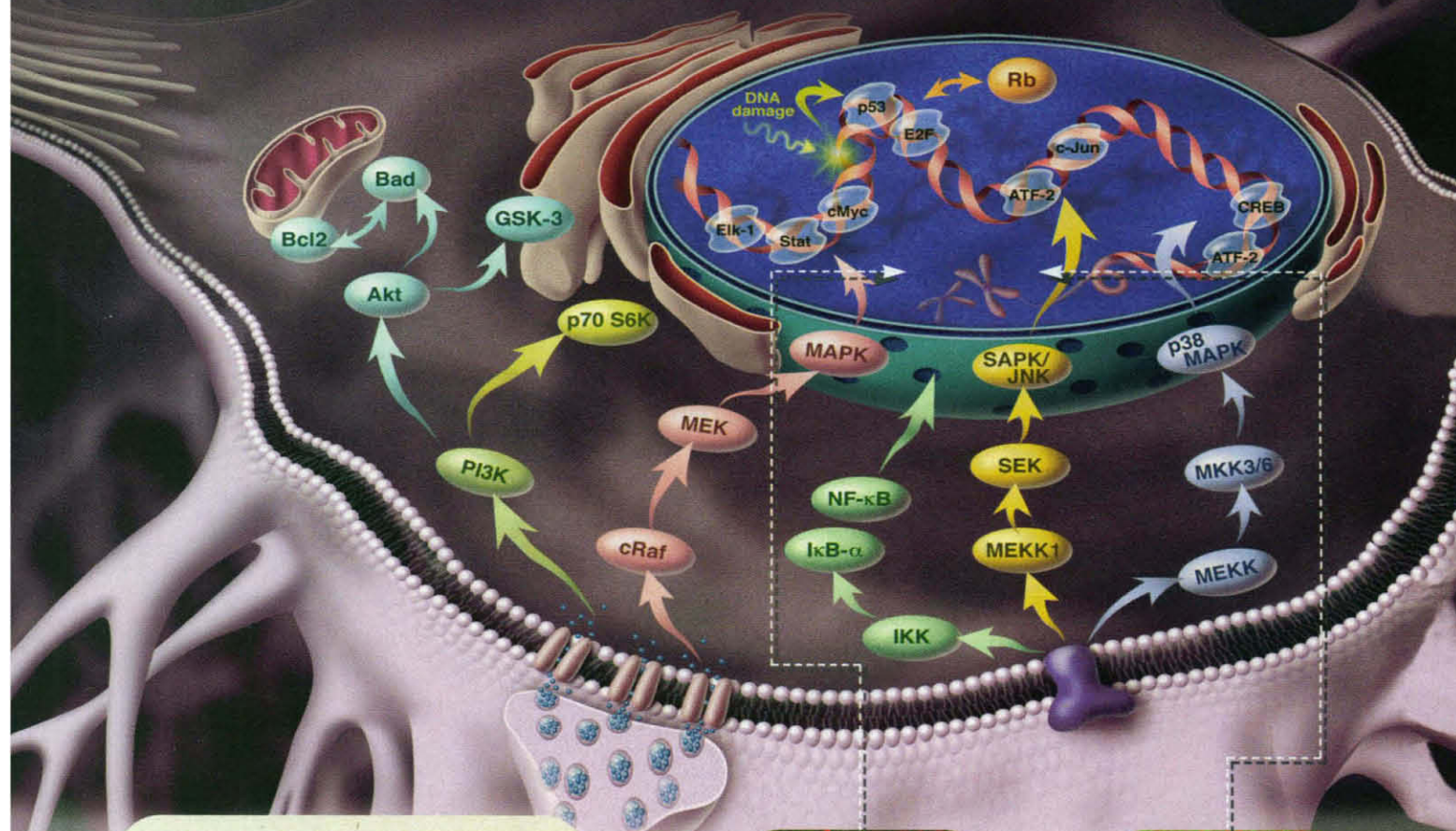
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hs Fas Ligand			▲		
GM-CSF			▲		
ICAM-1			▲		
IFN-α			▲		
IFN-γ	▲	▲	▲	Exclusive	▲*
IL-1 β	▲	▲	▲	Exclusive	▲
IL-1 β US		Exclusive	▲		
IL-2	Exclusive	▲	▲	Exclusive	▲
sIL-2R			▲		
IL-3		▲	▲		
IL-4	Exclusive	▲	▲		
IL-4 US			▲		
IL-5			▲		
IL-6	Exclusive	▲	▲		
IL-6 US			▲		
IL-6 (45-minute)			▲		
sIL-6R			▲		
IL-7		Exclusive	▲		
IL-8			▲	Exclusive	▲
IL-8 US			▲		
IL-10	Exclusive	▲	▲	Exclusive	Exclusive
IL-10 US		Exclusive	▲	▲	
IL-12 Total		Exclusive	▲	Exclusive	▲
IL-12 p70		▲			
IL-12 US			▲		
IL-13			▲		
IL-15			▲		
IL-16		Exclusive	▲		
IL-17			▲		
LIF/HILDA			▲		
MCP-1	Exclusive	Exclusive	Exclusive	▲	
MIP-1α	▲		▲		
MIP-2	▲				
MMP-3	▲				
RANTES	Exclusive	▲*		▲	
SAA		Exclusive	▲		
h Timp			▲		
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