

A microscopic image showing a complex network of green, filamentous structures, possibly bacteria or fungi, against a dark red background. The structures are interconnected, forming a web-like pattern.

Science

21 May 1999

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Microbes
& Immunity
& Disease



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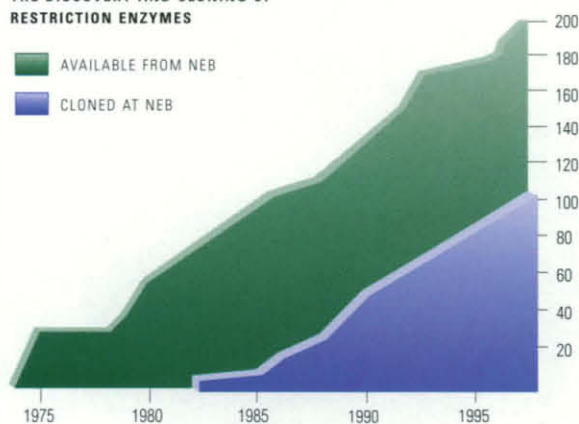
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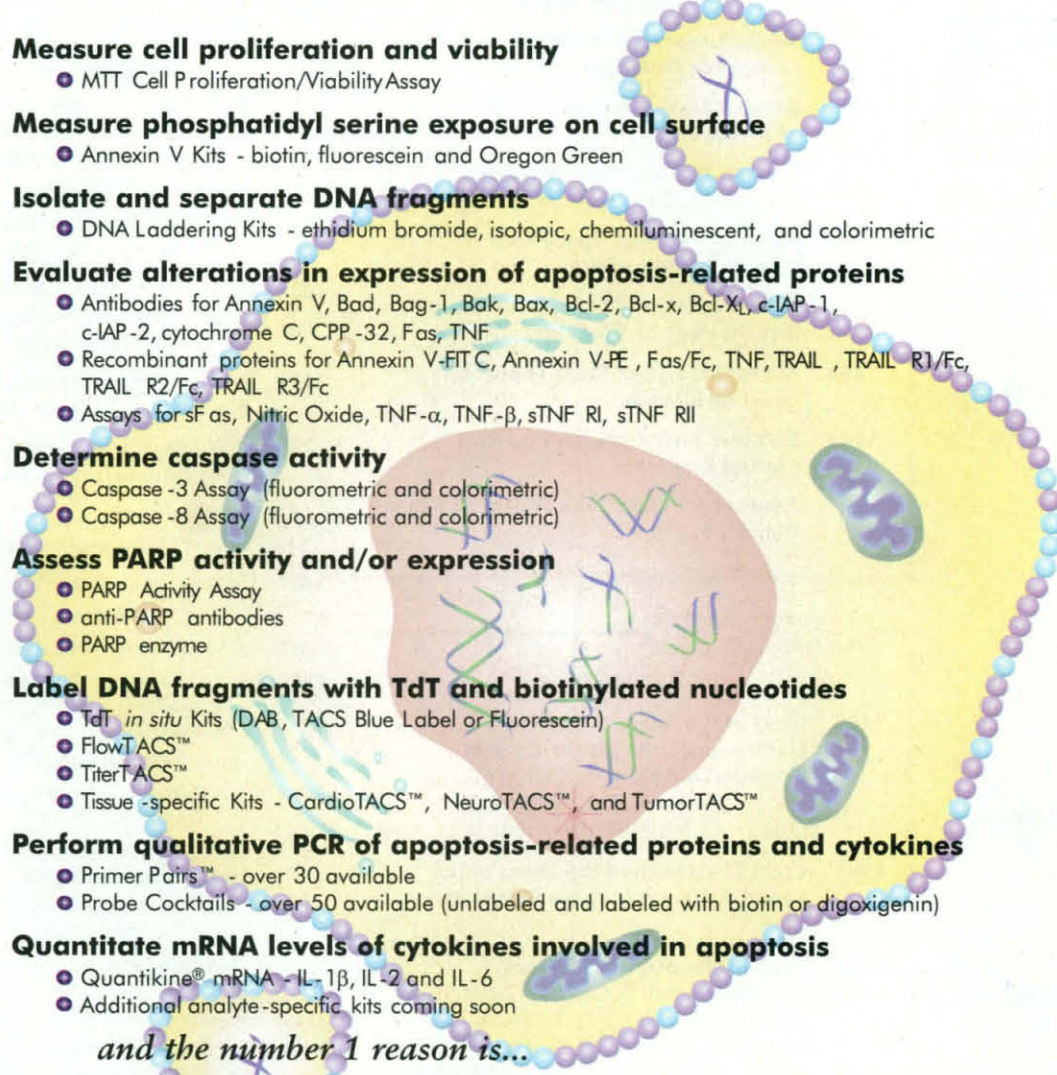
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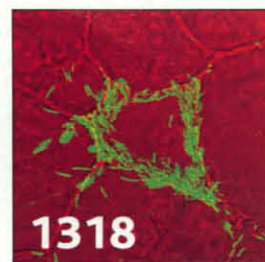


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COVER Initial stage of *Pseudomonas aeruginosa* biofilm formation on an explant of human lung tissue. Green shows *P. aeruginosa*, tagged with a fluorescent protein, on the epithelial surface (red-light microscopic image). The bacteria (2 to 3 μm long) form microcolonies in the intercellular junctions around injured cells. A special section on microbes, immunity, and disease begins on p. 1301. [Image: P. Singh, M. Parsek, T. Moninger, E. P. Greenberg, University of Iowa]



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The oldest Australian

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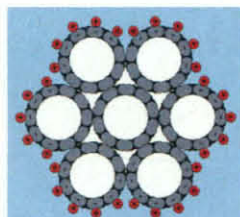
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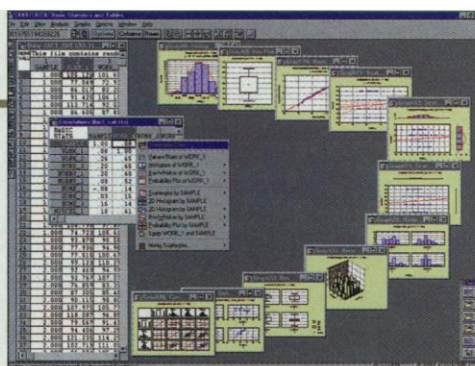
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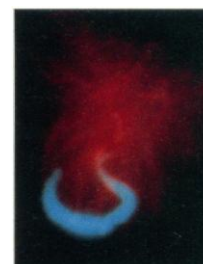
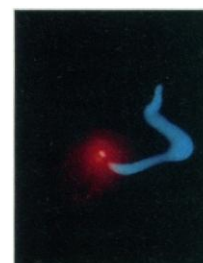
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Ran runs spindle formation

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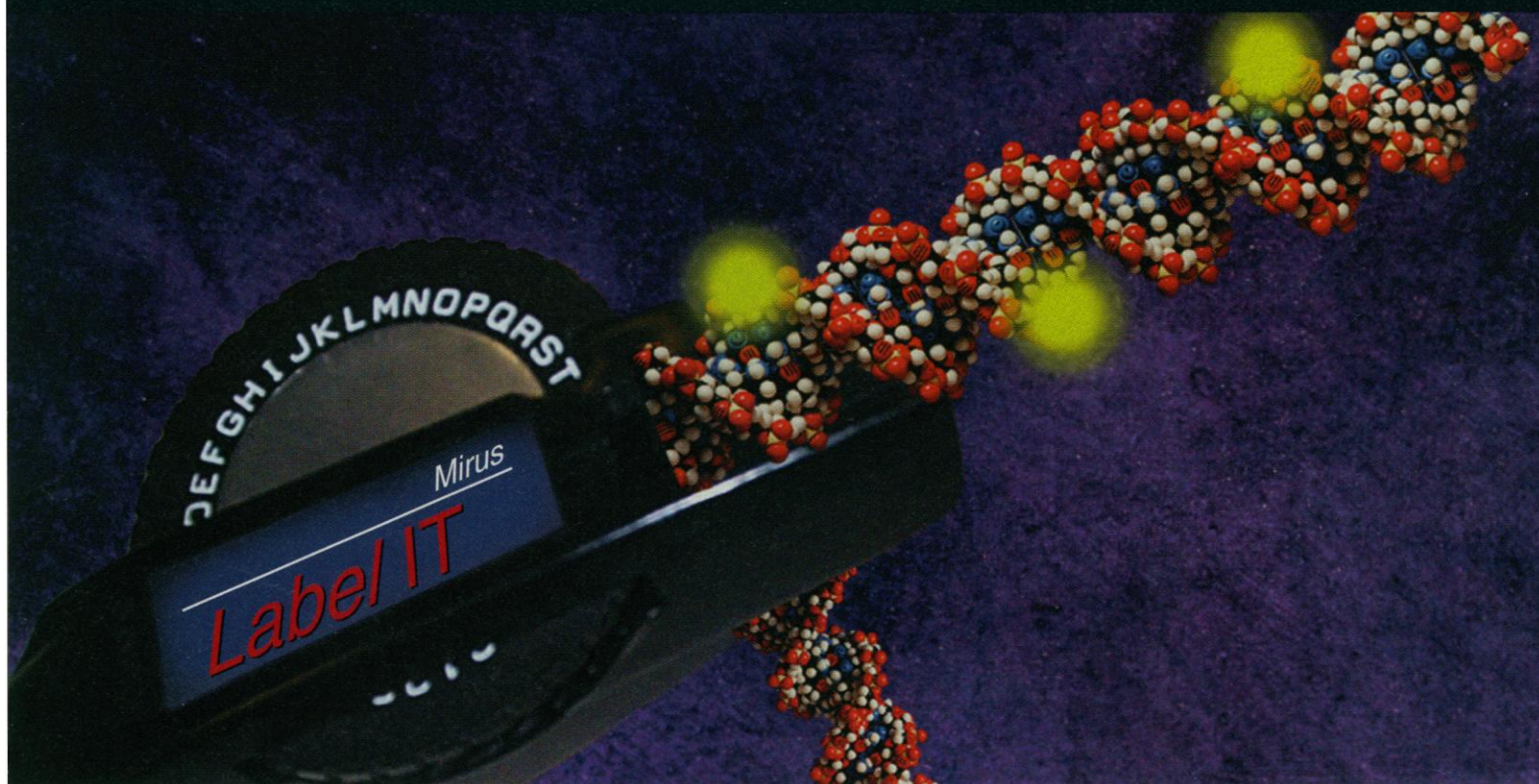


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RAPID PARENT BODY FORMATION

Meteorites are classified either as undifferentiated, which represent the most primitive components of the early solar system, and differentiated, which represent fragments from larger parent bodies that have undergone additional heating and differentiation. All meteorites initially formed from melts, and it was suggested in the 1950s that the heat source for this melting was the decay of radiogenic nuclide aluminum-26 (^{26}Al). Recently, evidence for ^{26}Al was found in undifferentiated meteorites, but not in differentiated ones. Srinivasan *et al.* (p. 1348; see the news story by Stokstad) have found evidence for ^{26}Al in a differentiated meteorite, Piplia Kalan, with a measured formation age of about 4.6 billion years that fell in India in 1996. The presence of ^{26}Al in Piplia Kalan suggests that its parent body (inferred to be the asteroid 4 Vesta) accreted, melted, and differentiated within 5 million years after the formation of the solar system. This result would indicate that planetesimal formation was very fast and would reduce the possible time scales that should be considered for at least our solar system.

MAGNETORESISTANCE VIA ELECTROCHEMISTRY

Although much recent attention in magnetic sensing has focused on spin-dependent magnetoresistive (MR) materials (which change resistance in a magnetic fields), bismuth metal does so simply because its electrons can travel faster in an applied field in induced cyclotron orbits. Thin films are needed for applications, however, and good quality films that do not scatter the electrons have proven expensive to fabricate—ultrahigh vacuum processing conditions are needed. Yang *et al.* (p. 1335) now show that electrochemical deposition can create large-grain films that can be annealed into single-crystal films; both exhibit good room-temperature MR properties.

GIVING NANOTUBES THE PUSH

Motors are the common way to convert electricity into mechanical work, but for many microscopic systems, electromechanical actuators, in which an applied voltage creates a mechanical strain in materials such as ferroelectrics or conducting polymers, are a simpler alternative. Baughman *et al.* (p. 1340; see the Perspective by Inganäs and Lundström) show that single-wall carbon nanotubes may be a promising actuator material. Charge injection and depletion into parallel sheets of nanotube

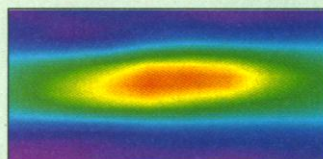
"paper," separated by an insulating layer and immersed in salt water, led to large deflections at low voltages (typically 1 volt) as one sheet expanded and the other contracted. Because the nanotubes on the inside of the sheets likely experienced little charging, the work densities produced by even smaller nanotube assemblies may be substantially higher.

FAST CRACKS

When cracks travel through a material, the speed at which they proceed has long been believed to be limited by inherent properties of the material, that is, to be slower than the speed at which shear waves can travel. Rosakis *et al.* (p. 1337) show that crack growth in a brittle polyester resin proceeded at speeds faster by a factor of nearly the square root of two times the material's shear wave speed. Similar processes may be observed in earthquake events.

MAGNETISM AND HIGH- T_c SUPERCONDUCTIVITY

The origin of high-temperature superconductivity is controversial. To help address this problem experimentally, Dai *et al.* (p. 1344; see the Perspective by Scalapino) have made comprehensive neutron scattering and nuclear



magnetic resonance measurements on cuprate superconductors ($\text{YBa}_2\text{Cu}_3\text{O}_{6-x}$) with various amounts of doping. They find good qualitative agreement between the thermodynamics of the magnetic fluctuations and the electronic specific heat. These results provide evidence for magnetism being the driving force behind high-temperature superconductivity.

SETTING UP THE SPINDLE

The small guanosine triphosphatase Ran regulates import and export of RNA and other macromolecules across the nuclear membrane. Two reports provide evidence for a new role of Ran in the regulation of the formation of the mitotic spindle (see the news story by Pennisi). Wilde and Zheng (p. 1359) report that either wild-type Ran in the active, guanosine triphos-

phate (GTP)-bound form, or a mutant, activated form of Ran stimulated the formation of microtubule asters when added to *Xenopus* egg extract. Formation of asters associated with added sperm centrosomes, as well as independently of the sperm nuclei, were both observed. Ohba *et al.* (p. 1356) altered Ran function by manipulating the RCC1 protein, a nucleotide exchange factor for Ran. Depletion of RCC1 from *Xenopus* egg extracts reduced formation of asters. However, addition of RanGTP to such extracts restored aster formation. Thus, Ran, which is apparently released from the nucleus as mitosis is initiated and the nuclear membrane breaks down, promotes polymerization of microtubules and spindle formation. Consistent with such a role, the Ran-binding protein RanBP1 and the RanGTPase-activating protein RanGAP1 are localized to the centrosome and mitotic spindles, respectively.

IMPROVING SURVEILLANCE

Major efforts are being made to treat or prevent cancer by manipulation of the immune system. "Cancer vaccines" could theoretically boost an individual's immune system by making the immune system highly reactive to any existing tumors. However, to develop a vaccine, antigens generally need to be identified. Methods exist to identify tumor antigens that bind to major histocompatibility complex (MHC) class I. Wang *et al.* (p. 1351) have now devised a method to find antigens that bind to MHC class II proteins. With specific knowledge of which tumor peptides the MHC proteins present to T cells, vaccines, and treatments could be designed to take advantage of the patient's own immune system.

BRCA1 AND ESTROGEN SIGNALING

The protein encoded by the breast cancer susceptibility gene *BRCA1* has been implicated in general cellular processes such as DNA repair and transcription, but its role in tumorigenesis remains unclear. In experiments with transfected cancer cells in culture, Fan *et al.* (p. 1354) show that *BRCA1* inhibits estrogen-induced signaling by estrogen receptor- α and blocks the receptor's transcriptional activation function. These observations suggest a hypothesis that can now be tested in animal models—that *BRCA1* functions in part to suppress estrogen-dependent transcriptional pathways related to breast epithelial cell growth.

CONTINUED ON PAGE 1235

...Eradicate pathogens in human plasma



Request for Proposals

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1233

CLOSING THE LOOP ON CHOLESTEROL

Cholesterol is enzymatically degraded into bile acids to prevent accumulation of fat in the body. These cholesterol by-products not only clear dietary fat from the body, but are also known to somehow regulate cholesterol metabolism and bile acid transport in the digestive system. Parks *et al.* (p. 1365) and Makishima *et al.* (p. 1362) report that bile acids may control these two physiological processes through an orphan nuclear receptor called the farnesoid X receptor (FXR) (see the Perspective by Gustafsson). When bound to bile acids, FXR can interact with another nuclear steroid receptor. This complex can control the transcription of two genes, one that encodes a regulatory enzyme of bile acid synthesis and one that encodes a bile acid transporter protein. Hence, nuclear bile acid signaling may regulate cholesterol homeostasis.

IN SERIES AND IN PARALLEL

Microbial enzyme complexes are responsible for the synthesis of natural products, including important polycyclic antibiotics such as tetracycline. These compounds generally are constructed from simple two-

and three-carbon units that are joined in repetitive linkages, modified by hydroxylation or reduction, and then cyclized. The complexes fall into two classes: In one, serially arranged enzyme active sites are highly specific for substrate and different modification reactions are enacted on each unit added, and in another the growing polymer is cycled iteratively around a core of relatively nonspecific active sites. Kennedy *et al.* (p. 1368) find that the cholesterol-lowering drug lovastatin, a fungal natural product, is made using a combination of these serial and iterative modes.

STICKING WITH IT

All eukaryotic cell surfaces display proteins and lipids that are decorated with carbohydrate moieties. This modification is particularly critical for molecules involved in cell adhesion. Keppler *et al.* (p. 1372) show that in hematopoietic cell lines, the addition of sialic acid residues to specific cell surface molecules depends on an epimerase that regulates sialic acid biosynthesis. Epimerase activity was required for the binding of adhesion molecules to leukocytes. Epimerase expression may therefore regulate cell activation and adhesion events in the immune system.

TECHNICAL COMMENT SUMMARIES

Evaluating Evidence of Ancient Animals

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5418/1235a

A. Seilacher *et al.* (Reports, 2 Oct. 1998, p. 80) studied "bedding plane features" in "the Mesoproterozoic Chorhat Sandstone" of central India. They interpreted these trace fossils "as the burrows of wormlike undermat miners," which suggests that "triploblastic animals existed more than a billion years ago."

V. Rai and R. Gautam comment that "these markings are more likely pseudo-trace fossils or casts of some megascopic algae, for several reasons," and note that they have found fossils of *Grypania* species of algae from the same beds, "a little higher up in the succession. ..."

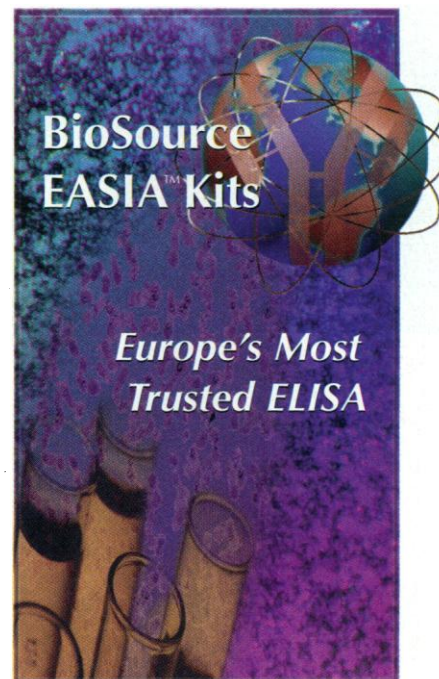
In response, Seilacher *et al.* "agree that pseudofossils are a major problem in Precambrian paleontology," but state that the structures described in their report "do not fall into the morphospace and tapofacies of macroalgae such as *Grypania*, or of shrinkage cracks, or of any other known physical structures." They "look forward to new radiometric ages from ash beds, currently being determined by other groups."

Role of Ceruloplasmin in Cellular Iron Uptake: Addendum

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5418/1235b

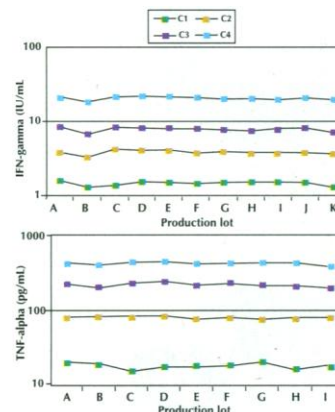
C. K. Mukhopadhyay *et al.* (Reports, 30 Jan. 1998, p. 714) found that ceruloplasmin (Cp) increased "iron uptake by HepG2 cells." Cp synthesis was transcriptionally regulated.

In an addendum, P. L. Fox *et al.* (co-authors of the report) note that the "anti-transferrin receptor monoclonal antibody H68.4 [which was used in the report] is not the preferred reagent for determining the role of the receptor in iron uptake by intact cells," and they thank I. S. Trowbridge for raising the issue. Control experiments with a more effective antibody, 42/6, support the report's original findings. Their complementary studies "provide compelling evidence that Cp-stimulated iron uptake is transferrin- and transferrin receptor-independent."



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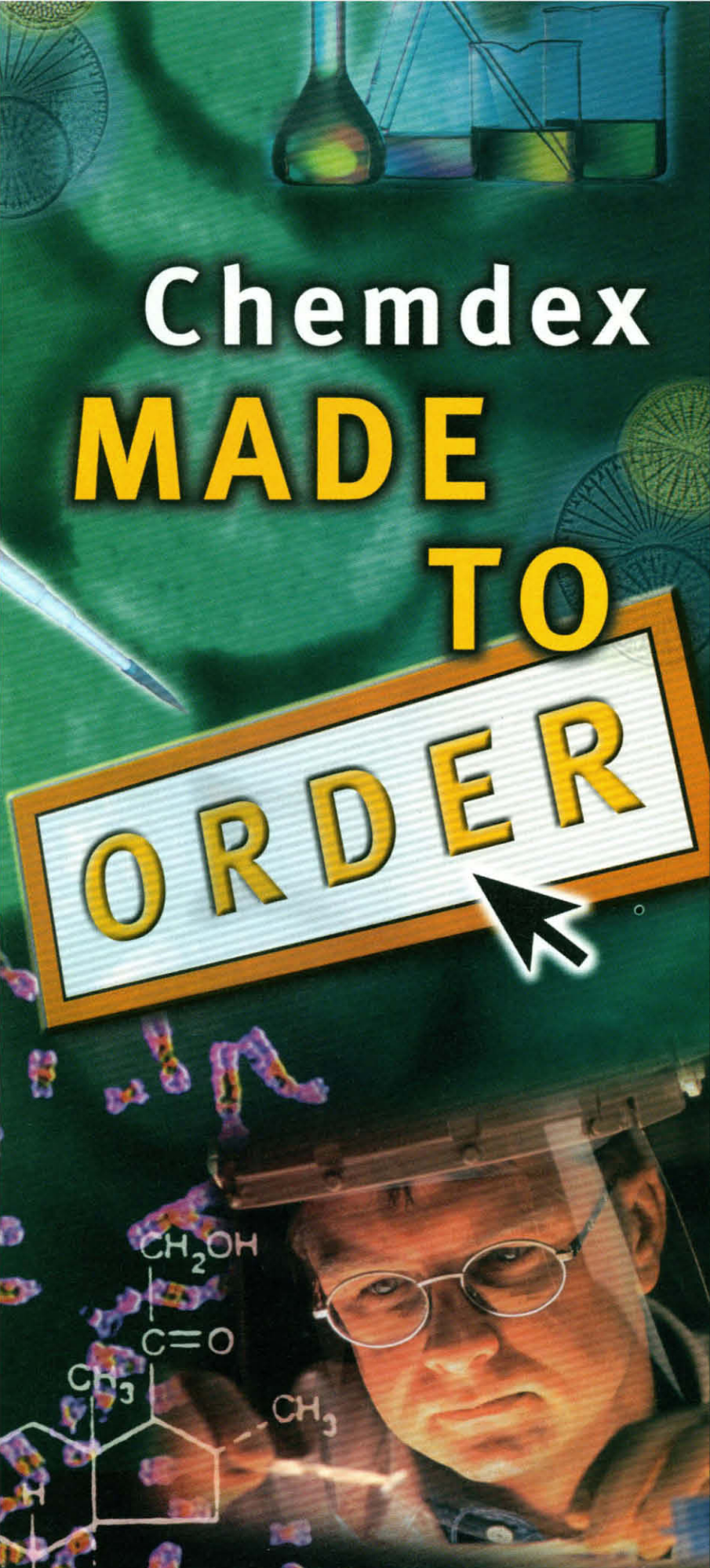
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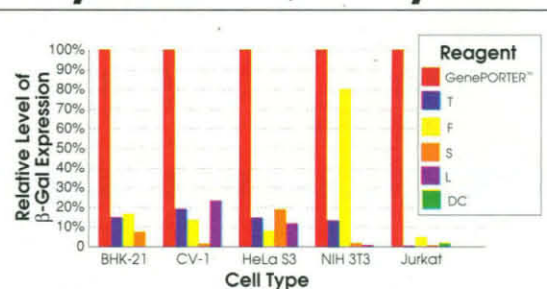
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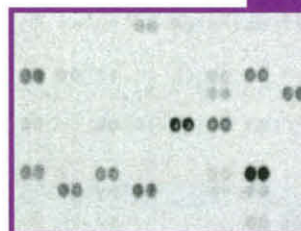
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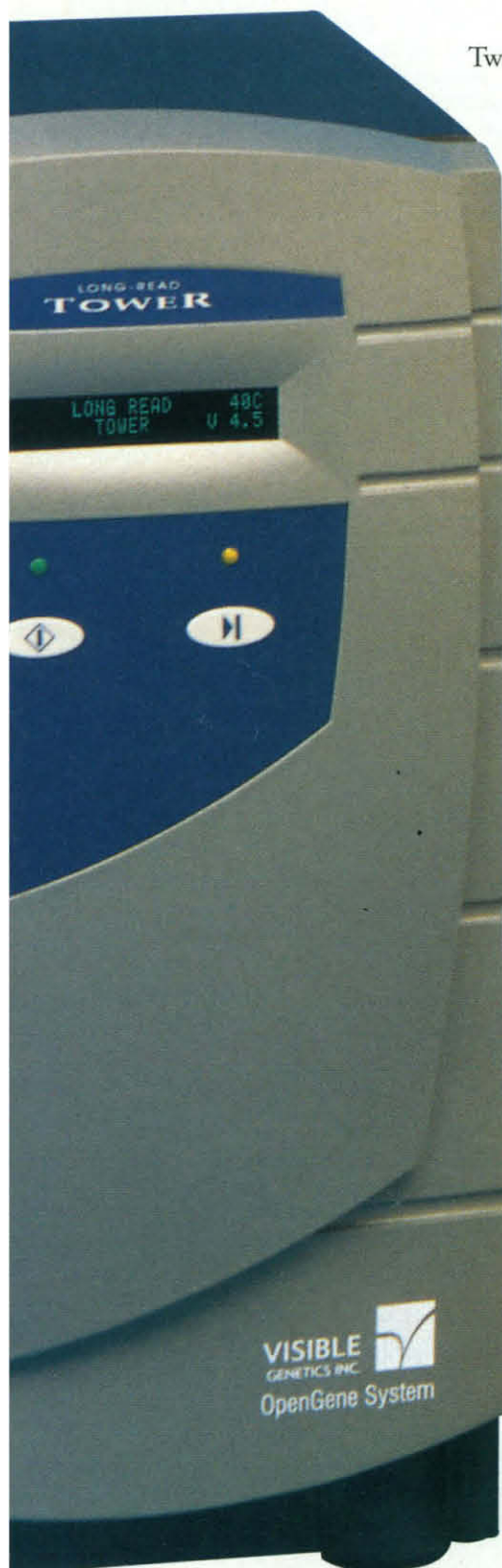
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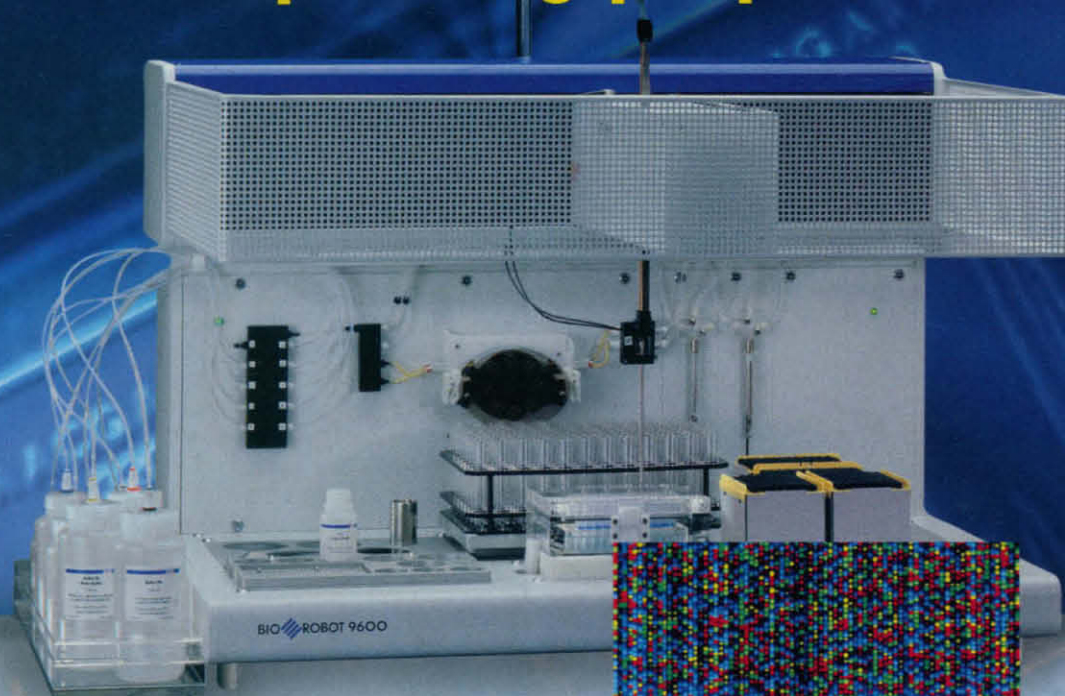
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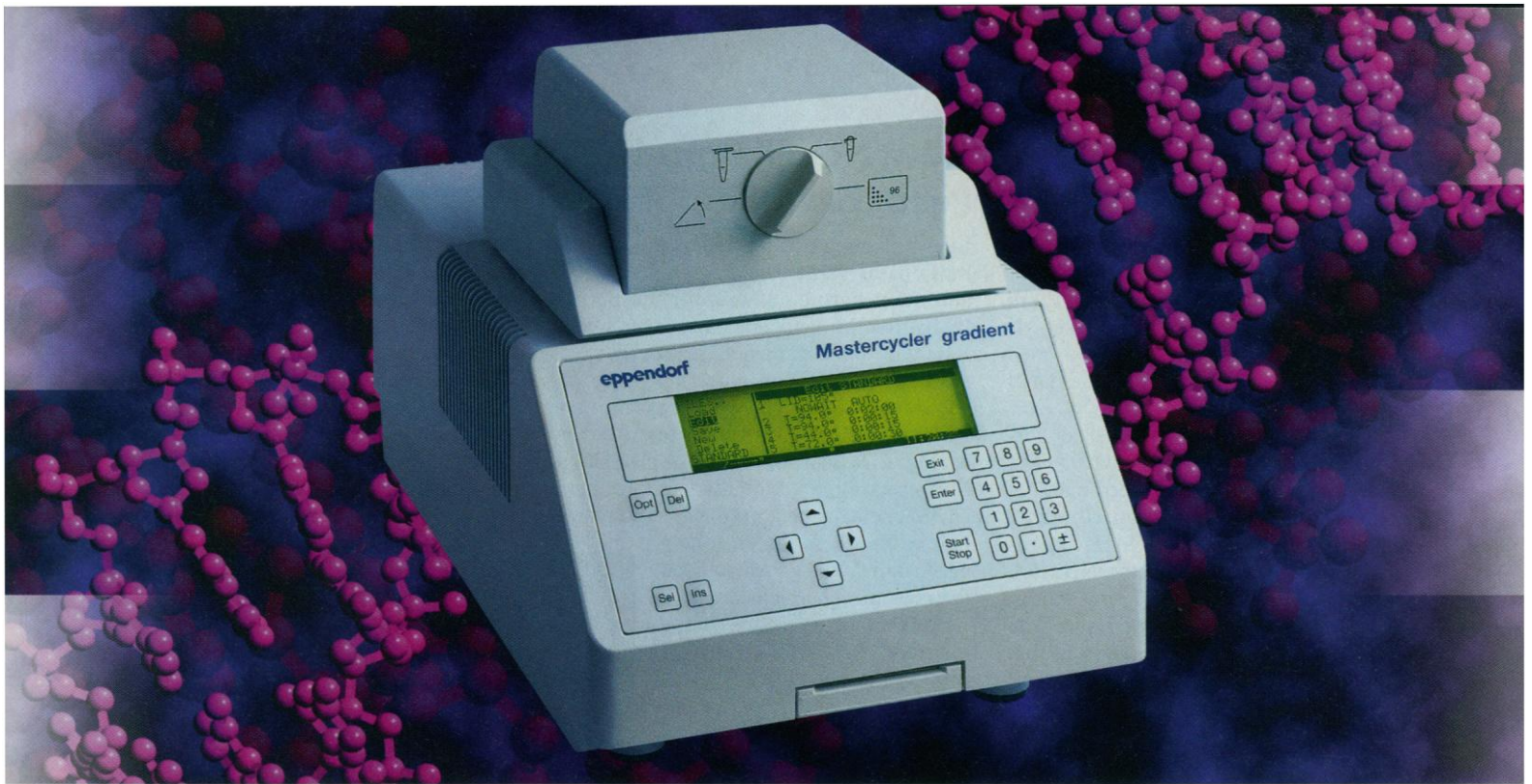
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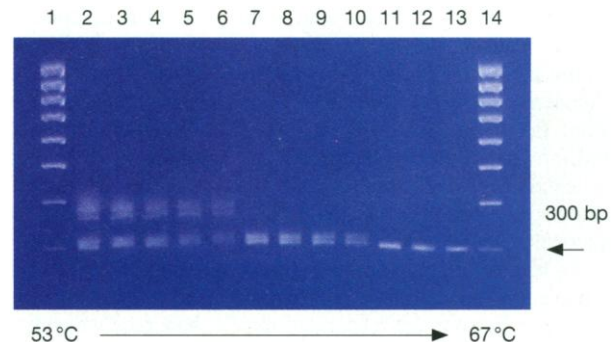
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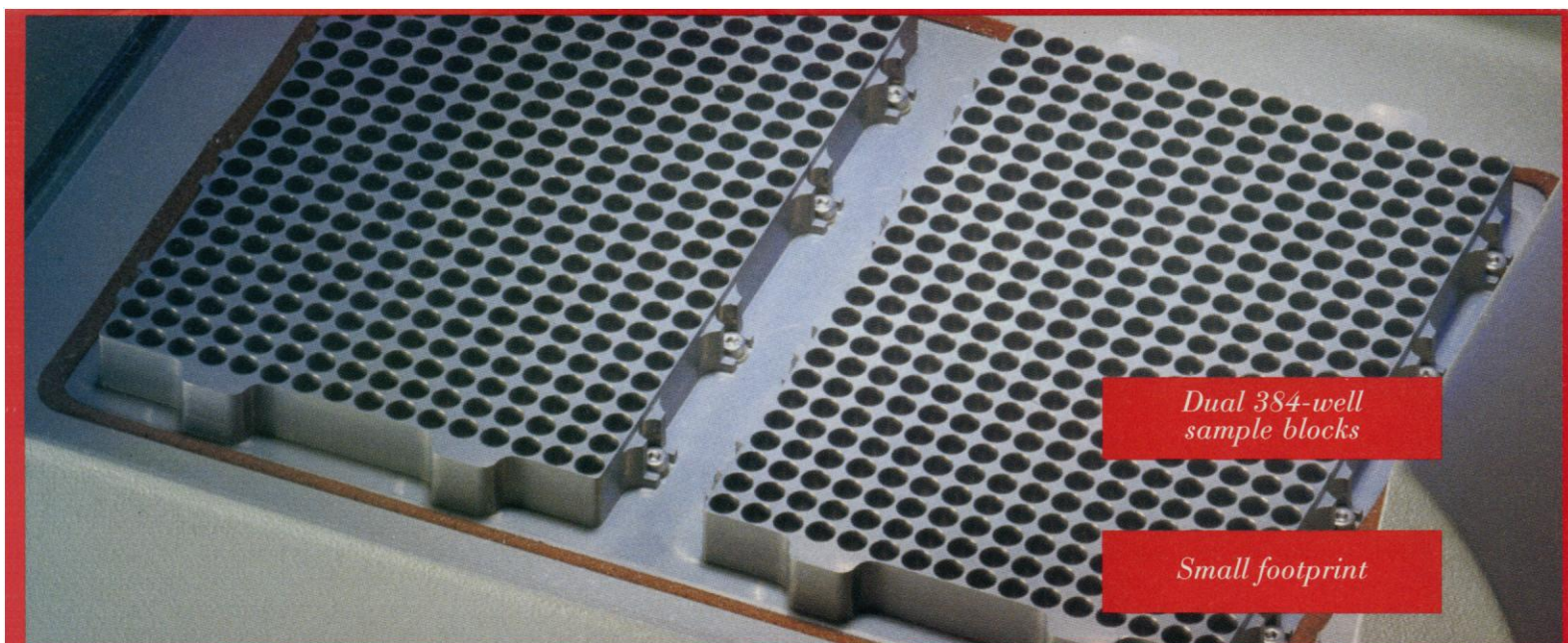
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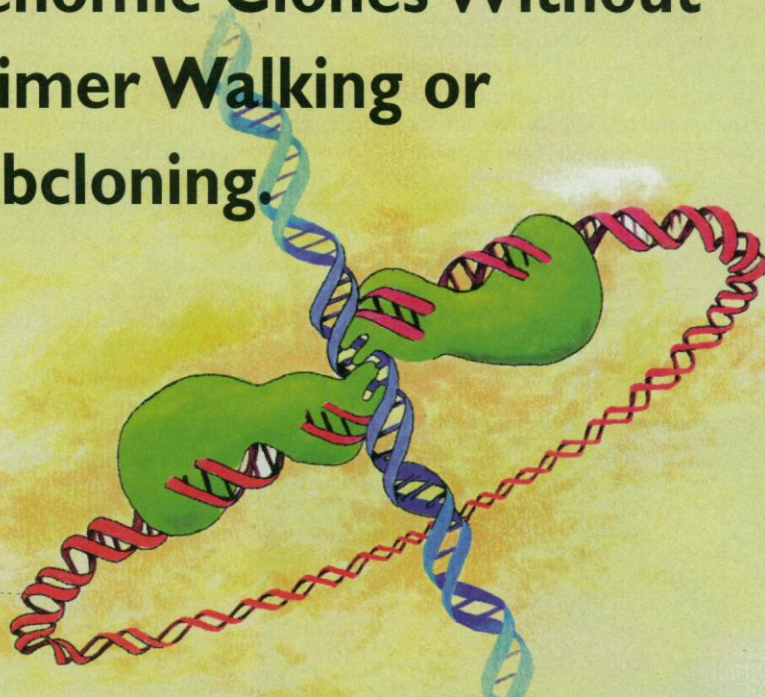
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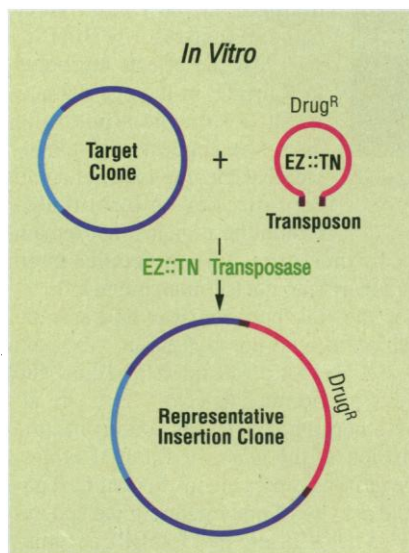
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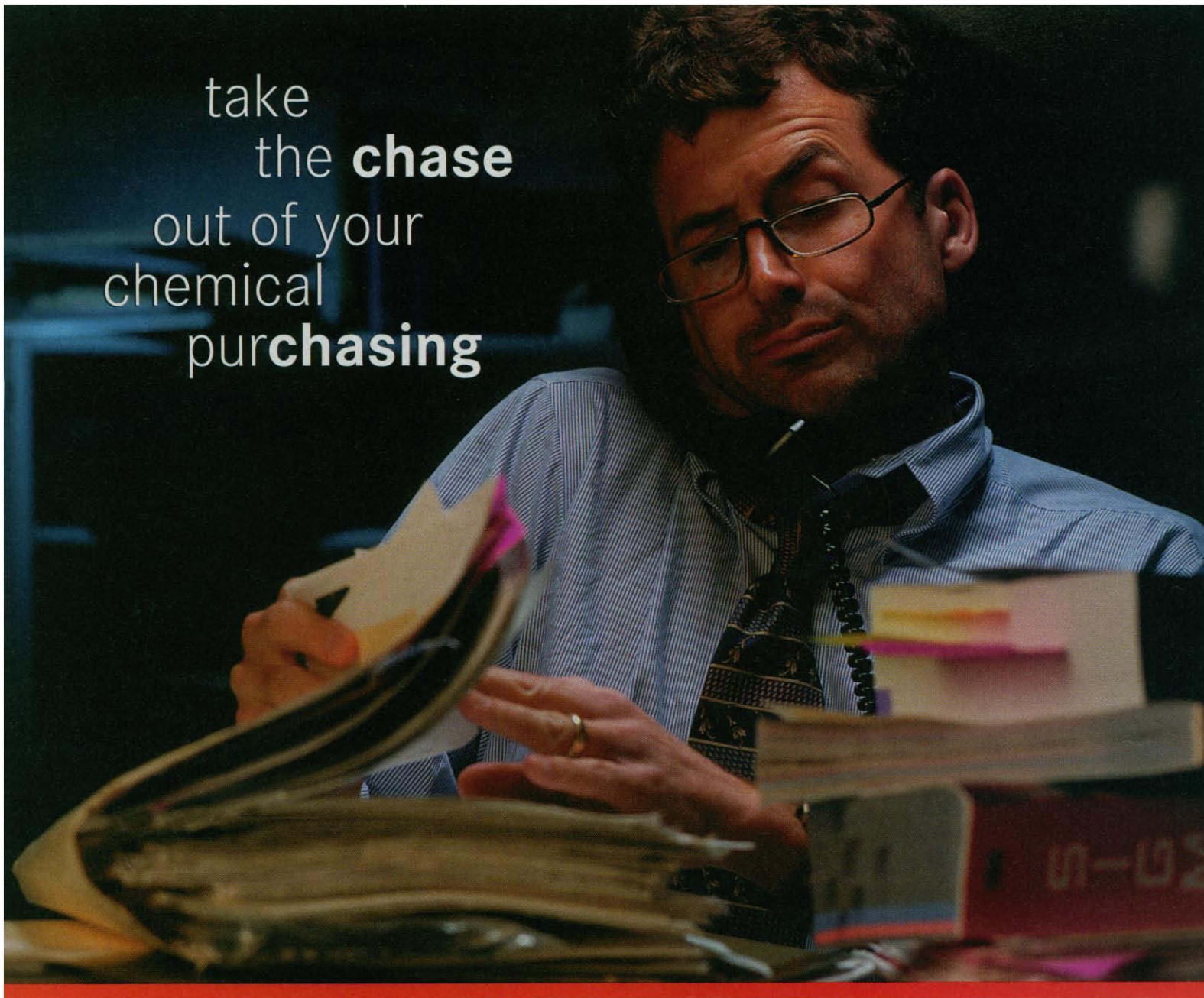


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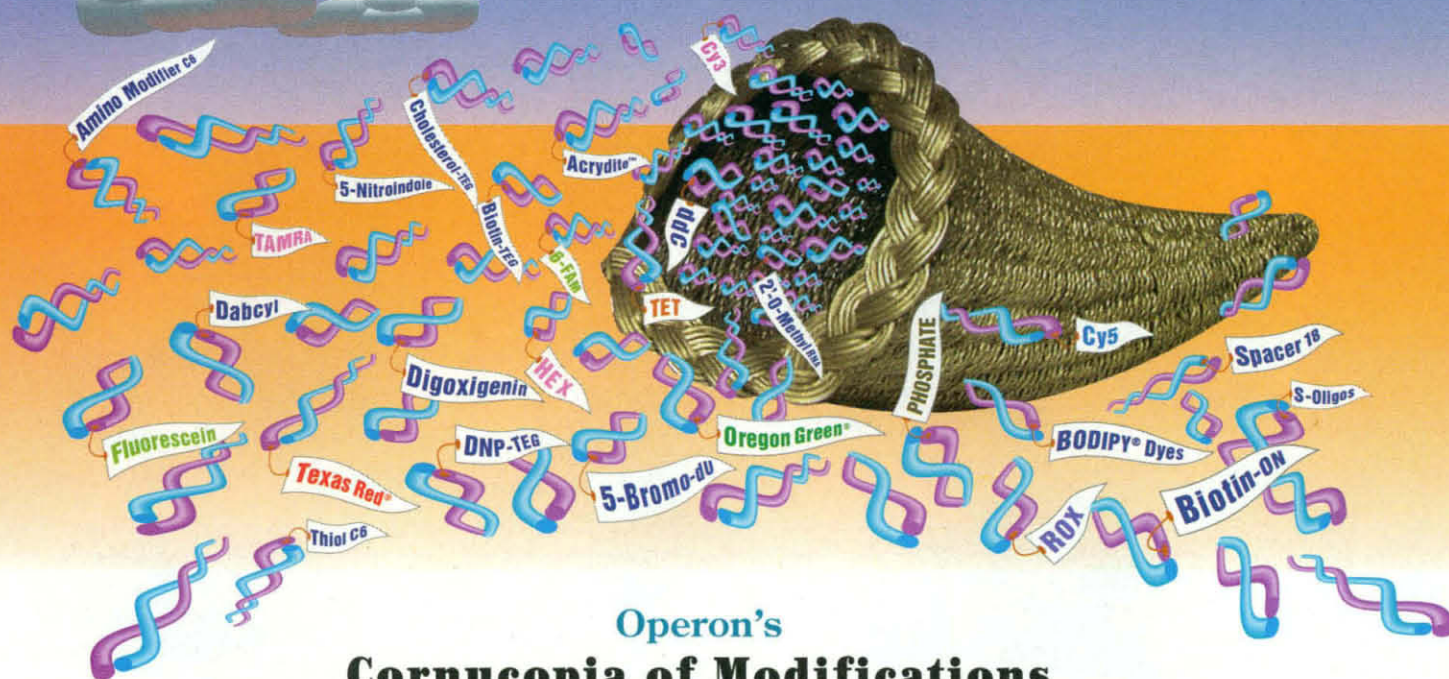
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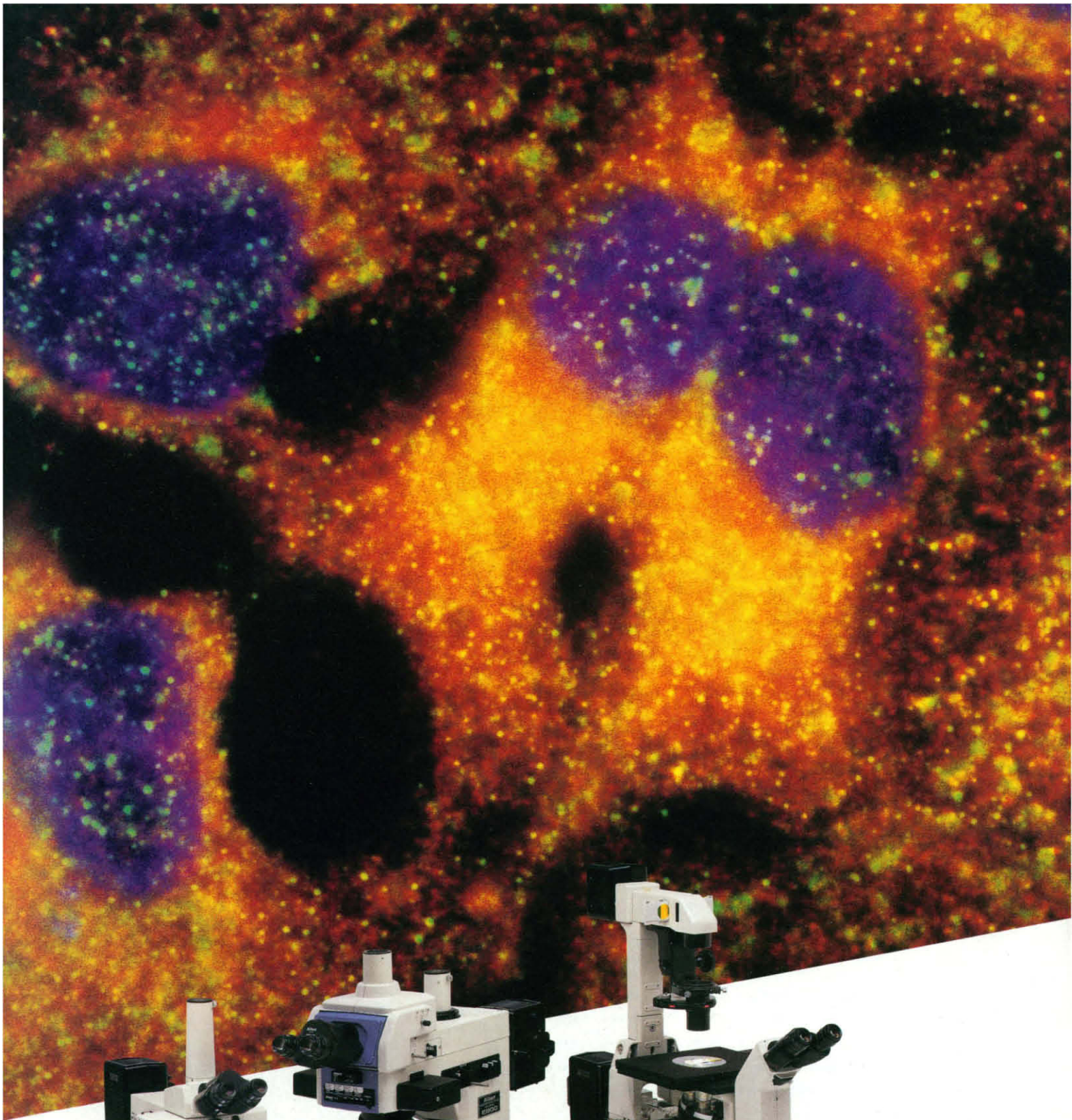
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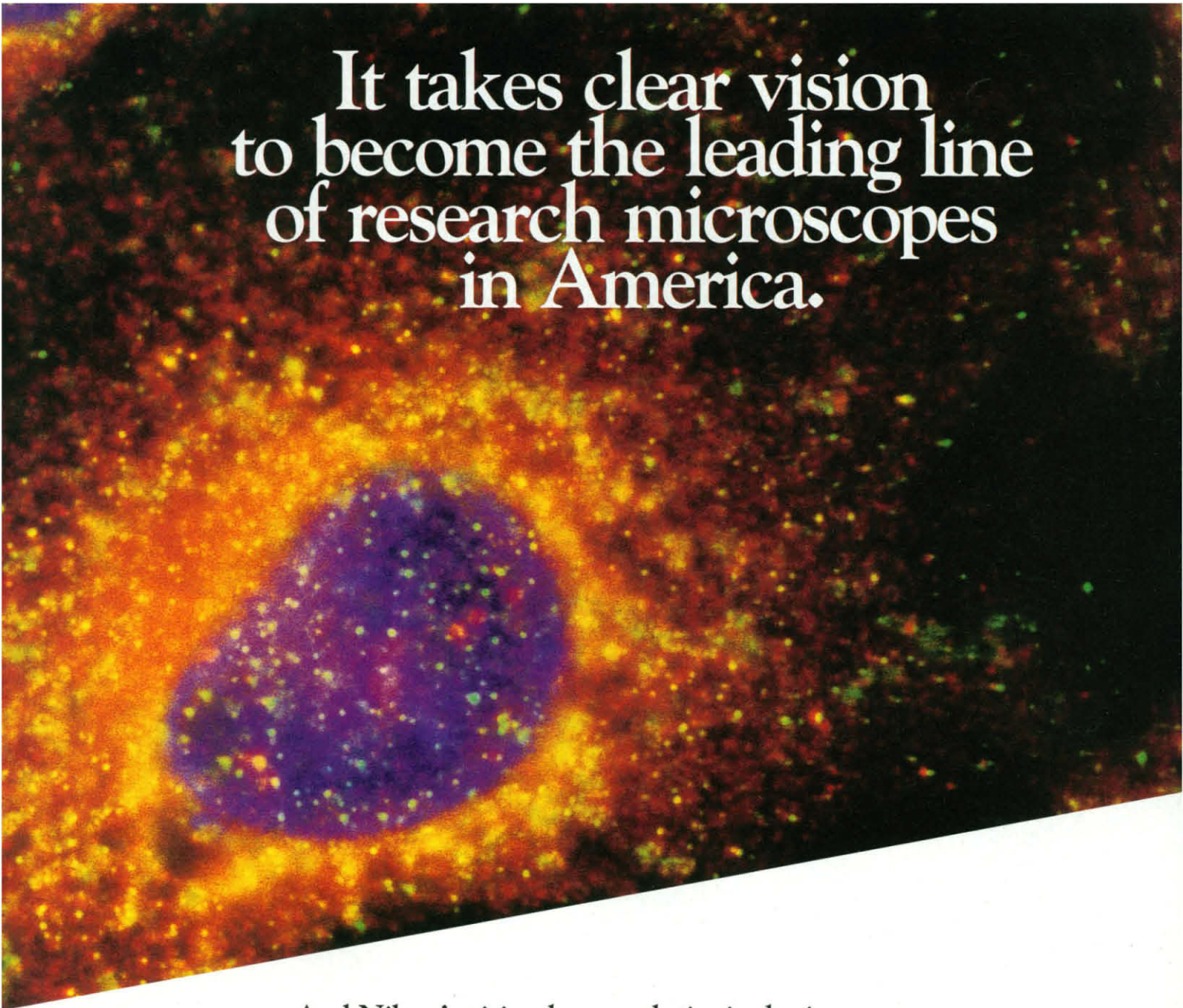
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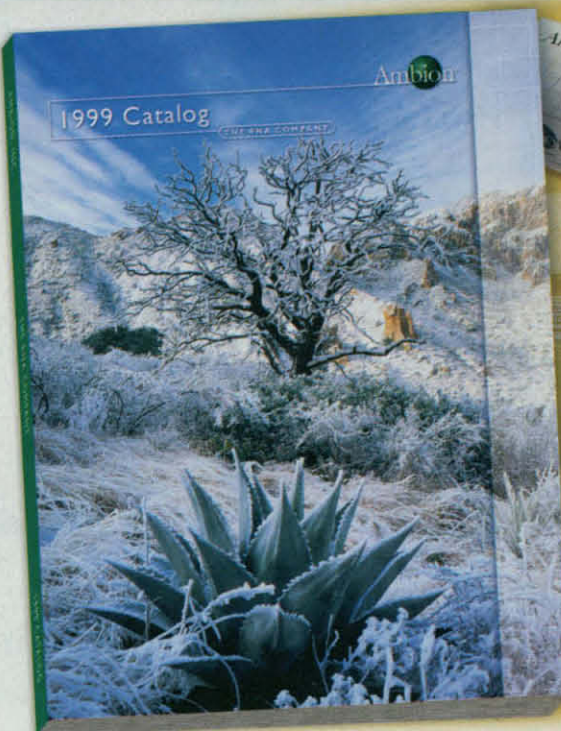
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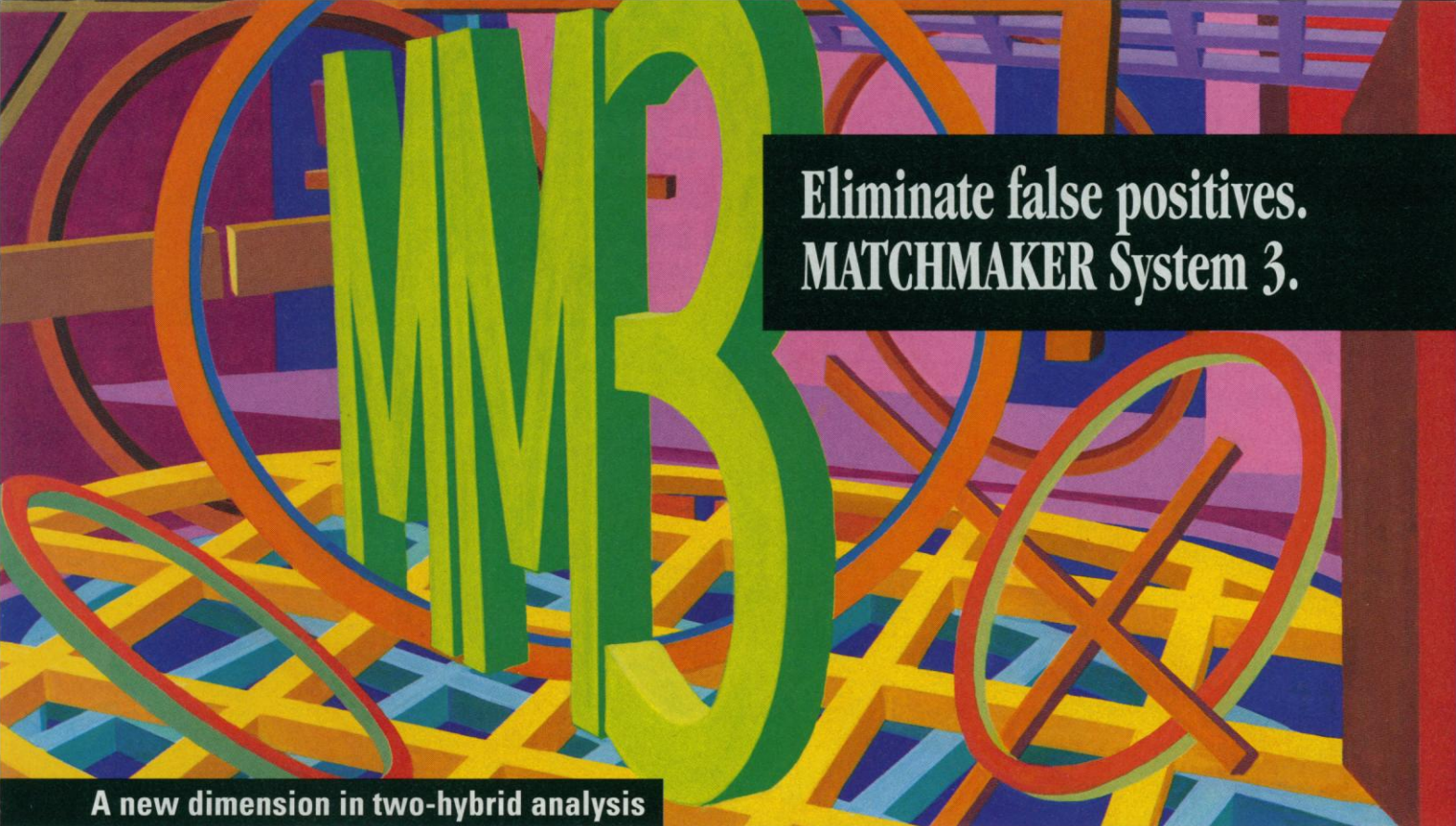


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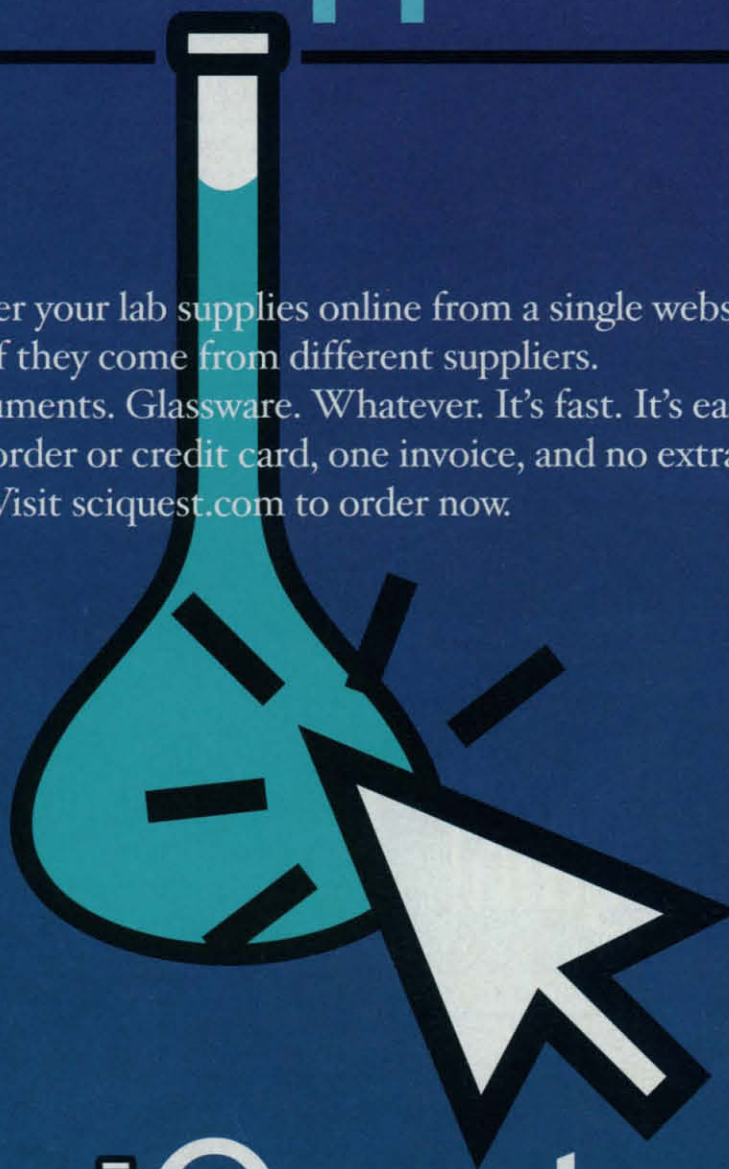
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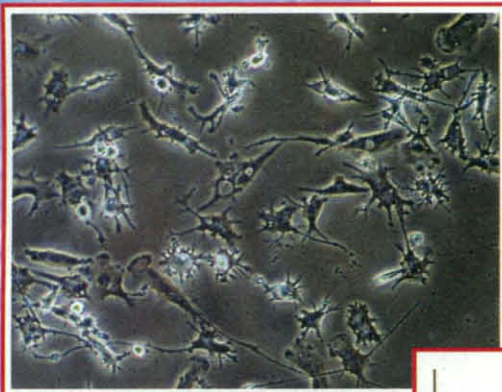
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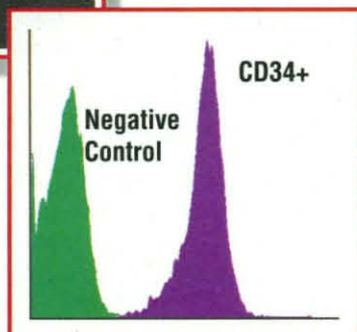
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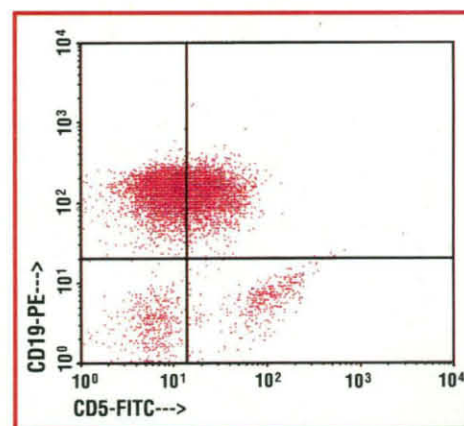
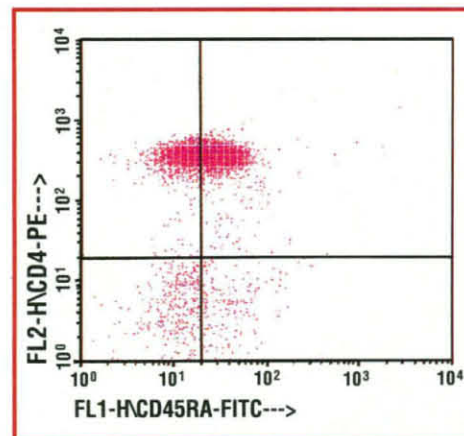


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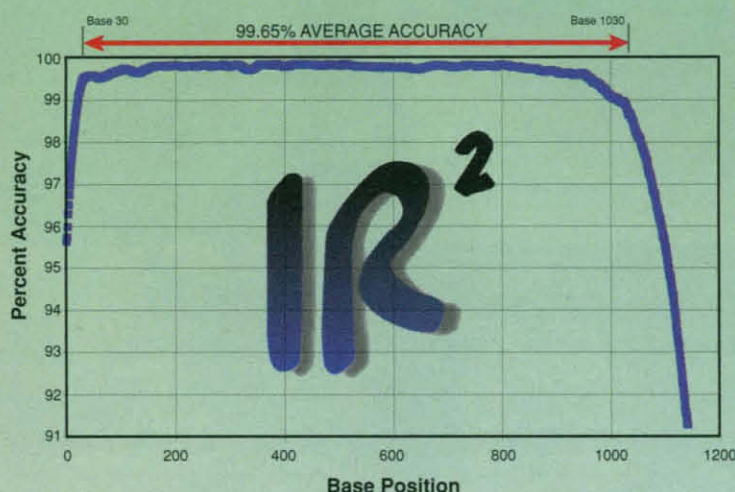
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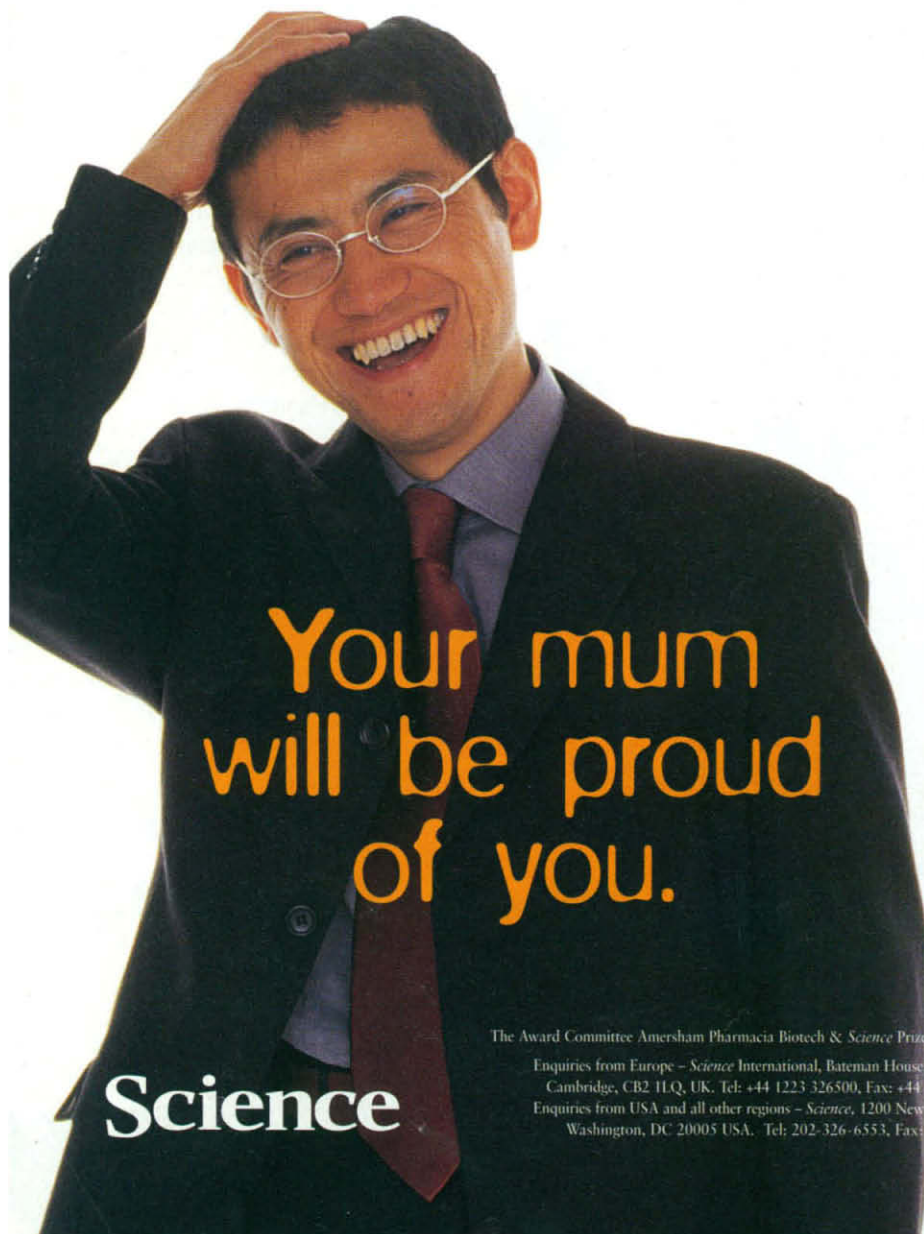
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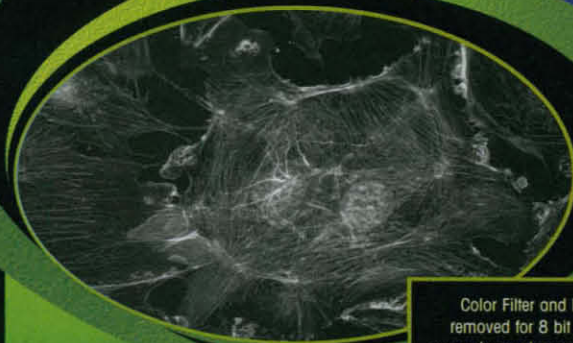
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