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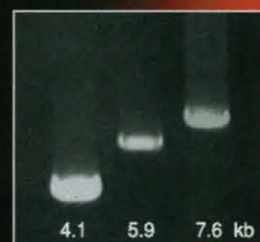
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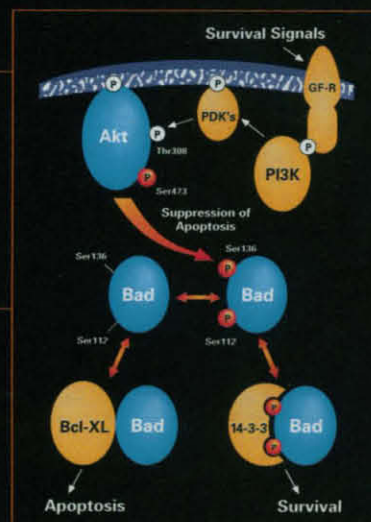
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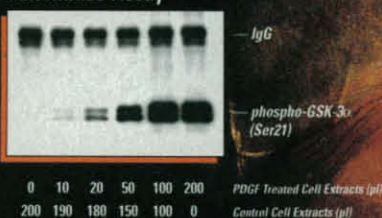
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Cell Death/Survival Signaling

FOR ANALYSIS OF Akt & Bad



Akt Kinase Assay



Akt Kinase activity of PDGF treated NIH3T3 cell extracts was analyzed by IP/Kinase assay. Cell extracts were incubated overnight with Akt Ab and protein A beads. After extensive washing, the kinase reaction was performed in the presence of GSK-3 α substrate. Phosphorylation of GSK-3 α was measured by western blot using Phospho-GSK-3 α (Ser21) Ab.

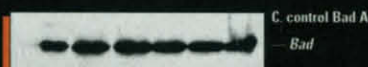
Cell Death/Survival related Phospho-specific Antibodies

Akt (S473)	#9270
Akt (T308)	#9275
Akt Kinase Assay Kit	#9840
Bad (S112, S136)	#9290
c-Myc (T58/S62)	#9401
GSK-3 α (S21)	#9331
p53 (S15)	#9284
pKC β (S660)	#9371
Rb (S249/252, T373, S780, S795, S807/811)	#9300
I κ B- α (S32)	#9240
p38 MAP Kinase (T180/Y182)	#9210
SAPK/JNK G9 monoclonal (T183/Y185)	#9255
p44/42 MAPK E10 monoclonal (T202/Y204)	#9106
p90RSK (S381)	#9341

Bad (Ser112)

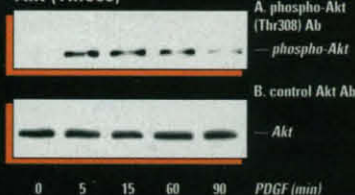


Bad (Ser136)



Western analysis of 293 cell extracts transfected with GST-Bad and treated with TPA using (A) Phospho-Bad (Ser112) Antibody (B) Phospho-Bad (Ser136) Antibody and (C) control Bad Antibody.

Akt (Thr308)



Western analysis of NIH 3T3 cell extracts treated with PDGF (100 ng/ml) using (A) Phospho-Akt (Thr308) Antibodies or (B) control Akt Antibodies.

Akt (Ser473)



Western analysis of NIH 3T3 cell extracts treated with PDGF (50 ng/ml) using (A) Phospho-Akt (Ser473) or (B) control Akt Antibodies.

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COVER The study of animal aggregations such as schools of fish is one of the more surprising areas in which complexity theory is proving useful. It is being applied to understand the evolutionary advantages and drawbacks of group behavior. This is one of many fields of research examined from the point of view of "Complex Systems" in a special section that begins on page 79. [Image: FPG]



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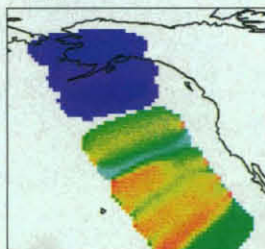
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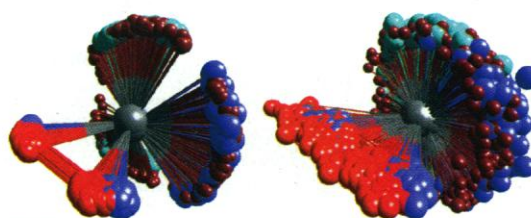
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Navigating the
"maize" of leaf
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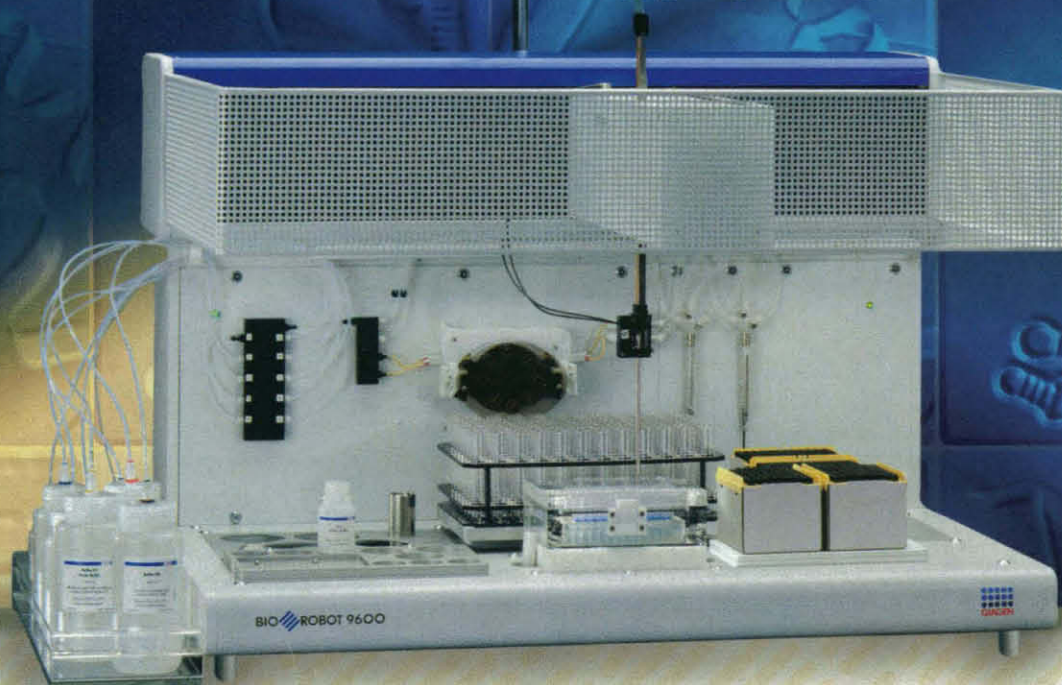
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HUMAN BEGINNINGS

The genus *Homo*, which includes modern humans, seems to have arisen about 2 million years ago, although its origins and the number of species (and which species) included in *Homo* have been debated. Wood and Collard (p. 65) review the status of *Homo* and conclude that two species previously assigned to the genus, *Homo habilis* and *Homo rudolfensis*, do not belong.

A SUPERRADIANT COLLISION

Gamma-ray bursts quickly release an enormous amount of energy, yet the source of this energy remains elusive. Van Putten (p. 115) offers a model involving the coalescence of a neutron star with a black hole that provides such energetic bursts. As the neutron star approaches the massive black hole, its orbit may be circularized and the tidally disrupted star may form a torus of debris with a remnant magnetic field around the black hole. Then the newly formed magnetosphere and the horizon of the black hole can work together to create a resonant waveguide of the plasma waves leading to the formation of a bubble in this cavity that bursts when it becomes unstable. Hence, the superradiance of the plasma waves initiated by the turbulent torus provides a viable explanation for gamma-ray bursts.

CORAL REEF PERIL

What effect will increasing atmospheric CO₂ concentrations have on marine ecosystems? Kleypas *et al.* (p. 118) predict a severe negative impact on coral reefs: An increase in dissolved CO₂ concentration in seawater will enhance the solubilization of calcium carbonate, decreasing the saturation state of aragonate and therefore reducing calcification. The authors predict that between preindustrial times and the middle of the next century there will have been a drop in reef calcification of 14 to 30%.

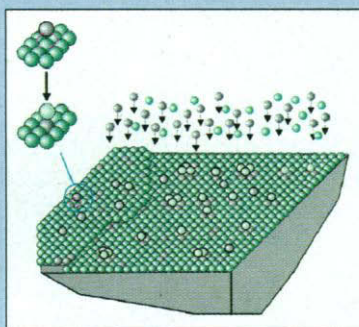
SHIFTING BOUNDARIES

Seismic data reveal a complicated boundary between Earth's core and mantle. Some parts of the boundary layer may be molten; the nature of the boundary varies laterally. Most studies have examined either compressional or shear waves. Wyssession *et al.* (p. 120) analyzed both wave types to infer that part of the boundary layer beneath the mid-Pacific

Ocean is anisotropic. These observations imply that the layer is flowing there or may be recording a relic fabric.

SMOOTHING THE WAY

The growth of thick, atomically flat single-crystal films on a single-crystal substrate usually requires ultrahigh vacuum conditions. Electrochemical deposition, although far simpler, tends to form rough or polycrystalline



films or is limited to thicknesses of ~10 monolayers. Sieradski *et al.* (p. 138) show that flat, thick epitaxial films (~250 monolayers) of silver can be deposited on gold if a mediator such as lead or copper is periodically co-deposited and stripped from the surface. The mediator helps nucleate the growth of two-dimensional islands of silver that promote smooth layer-by-layer growth.

TRANSPORTING ROCK

Subduction during continental collision can bury rocks to great depths, but it can also bring deeply buried rocks to the surface. Erosion and faulting have brought rocks in several mountains to the surface from depths of 100 kilometers or more. Bozhilov *et al.* (p. 128; see the news story by Kerr) describe the presence of clinoenstatite in material from the Alpe Arami peridotite in the Swiss Alps, rock that, previously and controversially, has been proposed to have been exposed from depths of several hundred kilometers. The authors suggest that the clinoenstatite exsolved from another mineral, diopside, at depths greater than 250 kilometers.

MESOSCOPIC MAGNETIC MOLECULAR CLUSTERS

When a magnetic particle is reduced to the extent where its quantum wave function is comparable to its physical dimen-

sions, interference effects for the spin system can be observed similar to those found for electronic charges in quantum dots. Wernsdorfer and Sessoli (p. 133) used highly sensitive detectors to record transitions in the magnetization of single crystals of magnetic clusters that could occur between two stable states only through quantum-mechanical tunneling. The two tunneling paths that the spin states can take interfere, thus providing direct observation for the quantum spin phase in a magnetic system.

SPECTRA OF A MOLECULAR SCRAMBLE

Protonated methane, CH₅⁺, has been known to form under certain plasma conditions, but it has been difficult to study both experimentally and theoretically. Calculations indicate that several structures have nearly the same ground-state energy, and thus the molecule can be viewed as having well-defined C-H bond distances but no well-defined angles between the bonds. Despite this highly fluxional character, White *et al.* (p. 135; see the Perspective by Marx and Parrinello) show that CH₅⁺ has a well-defined C-H stretching band. Tuning of the preparation conditions and elimination of related hydrocarbon species lines were needed to identify CH₅⁺, and further theoretical work will be needed before an actual assignment of lines can be made.

LOCALIZING LIGHT

Materials are generally weakly absorbing to light at frequencies less than their electronic band gap, and making a material porous should make it even more transparent at such frequencies. Schuurmans *et al.* (p. 141) report that macroporous gallium phosphide actually becomes less transparent and scatters more light as it is made more porous. This increased scattering is analogous to that found in electronic systems where charged carriers are scattered from defects and are said to be "Anderson localized" when the density of defects is sufficiently high. Under conditions of extreme disorder, the scattering of the light increases until the propagation ceases to be diffusive and instead adopts a tunneling mode of transport. However, the optical systems are much simpler, in that, unlike charged electrons, photons do not interact with each other. These results give theorists an ideal system in which to model their predictions of light scattering in disordered materials.

CONTINUED ON PAGE 11

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Table 1 - PCR Cloning Efficiencies

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4.8	97%
7.0	80%
10.0	71%

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 9

NEW TRICKS FROM AN OLD ENZYME

Aminoacyl-transfer RNA (tRNA) synthetases link amino acids to the appropriate tRNAs during protein synthesis and play a fundamental role in translational fidelity. Wakasugi and Schimmel (p. 147; see the Perspective by Weiner and Maizels) report that human tyrosyl-tRNA synthetase (TyrRS) harbors two cytokine activities that are unmasked when the native enzyme is proteolytically cleaved. Recombinant forms of a carboxyl-terminal TyrRS fragment induced chemotaxis of leukocytes and monocytes, and an amino-terminal fragment had properties in common with interleukin-8. Native TyrRS was secreted by apoptotic cells in culture and processed into fragments similar in size to the biologically active fragments. The authors hypothesize that TyrRS cleavage may be important in apoptosis, leading both to arrest of protein synthesis and recruitment of cells that engulf apoptotic cell debris.

TURNING OUT A NEW LEAF

Although maize may not much resemble a snapdragon, it seems that the molecules that initiate and direct the pattern of their leaves and floral organs are quite similar. Timmermans *et al.* (p. 151) and Tsiantis *et al.* (p. 154) have both cloned the *rough sheath2* (*rs2*) gene from maize and show that it resembles another gene, *phan*, known from snapdragon. The two genes are similar in sequence and contain features typical of transcription factors; mutations in both generate disturbances in leaf development. The comparison supports intriguing insights into the cascade of regulatory controls, suggesting that the *rs2* gene controls, perhaps epigenetically, the *knox*-type genes that also direct leaf formation.

TUMOR CONTROL

To prevent cancer, an organism will induce the death of cells that are going awry. To determine how p53 is involved in the death of tumor cells, Soengas *et al.* (p. 156) used a system in which cells express the oncogene *Myc* and die in response to conditions that simulate those in tumors (hypoxia, lack of growth factors, or growth in suspension). This p53-dependent cell death was mediated by the apoptosis regulator Apaf-1 and the apoptosis protease caspase-9. Tumors that did not express one or the other of these apoptosis effectors had enhanced tumorigenicity.

Thus, interference with the effectors of apoptosis can contribute to transformation and tumor development.

BONE MARROW STEM CELLS

Stem cells by definition will self-perpetuate but also differentiate along specific lineages to generate fully mature cells. In adults, hematopoietic stem cells are found in greatest number in the bone marrow. Pittenger *et al.* (p. 143) now report that a mesenchymal stem cell can be isolated from human bone marrow that differentiates into adipocytes, chondrocytes, or osteocytes, depending on the in vitro culture conditions. Thus, bone marrow may be a cornucopia of stem cells for many lineages.

TRANSCRIPTIONAL INFIDELITY

In acting as a template for the synthesis of messenger RNA (mRNA), it is important that the DNA code be transcribed faithfully. Chemicals and ionizing radiation can damage DNA by deaminating the DNA base cytosine to produce uracil. During transcription, RNA polymerase would place guanine opposite cytosine, but when the DNA template contains a deaminated cytosine (uracil), an adenine would be inserted. Viswanathan *et al.* (p. 159; see the Perspective by Bridges) now show that such transcriptional mutagenesis occurs in vivo in nondividing cells, with translation of a mutated mRNA yielding a protein of altered function. Due to the accumulation of DNA damage over time, transcriptional mutagenesis may be involved in diminishing cellular function with increasing age.

IMAGINE THAT

Functional brain imaging has made it possible to observe which areas of the brain become active when a subject receives sensory input, executes a motor behavior, or thinks. For example, previous work revealed activation in the primary visual cortex during imagery even in the absence of any visual input. What has been unclear is whether activity in this first stage of visual processing was required for imagery or was merely a reflection of imagery-producing activity at later stages of the processing pathway. Kosslyn *et al.* (p. 167; see the news story by Barinaga) used transcranial magnetic stimulation to scramble the processing within visual cortex and find that imagery is impaired, arguing in favor of a requirement.

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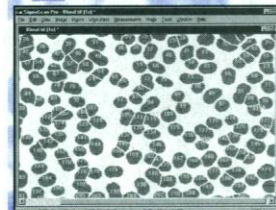
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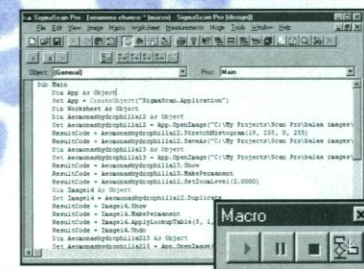
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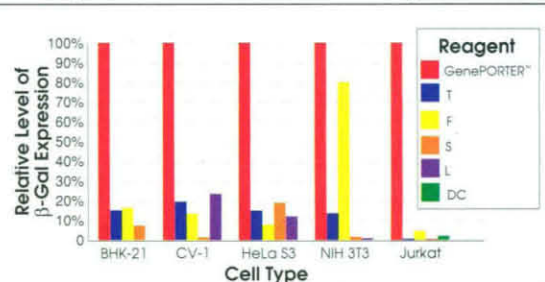
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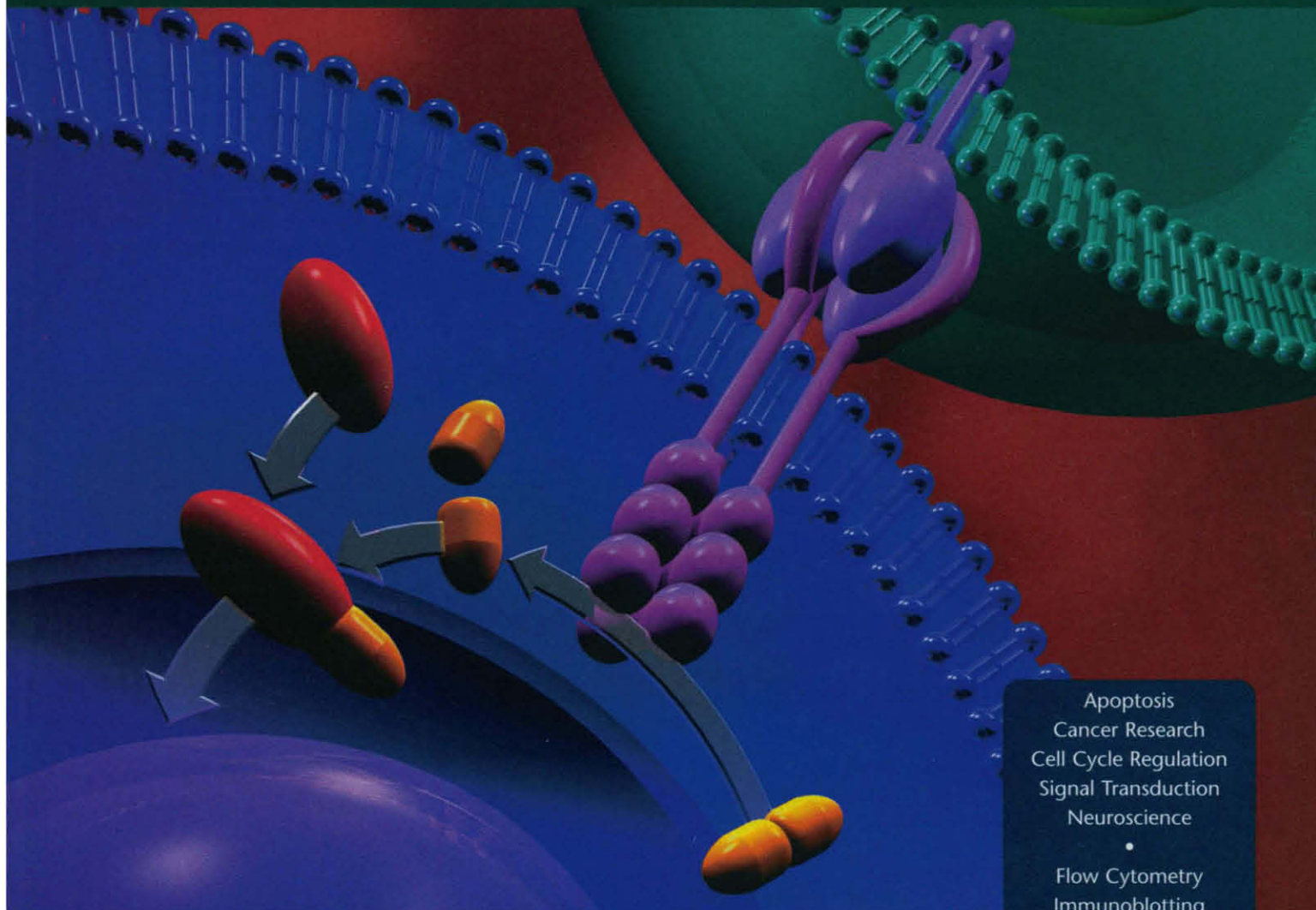
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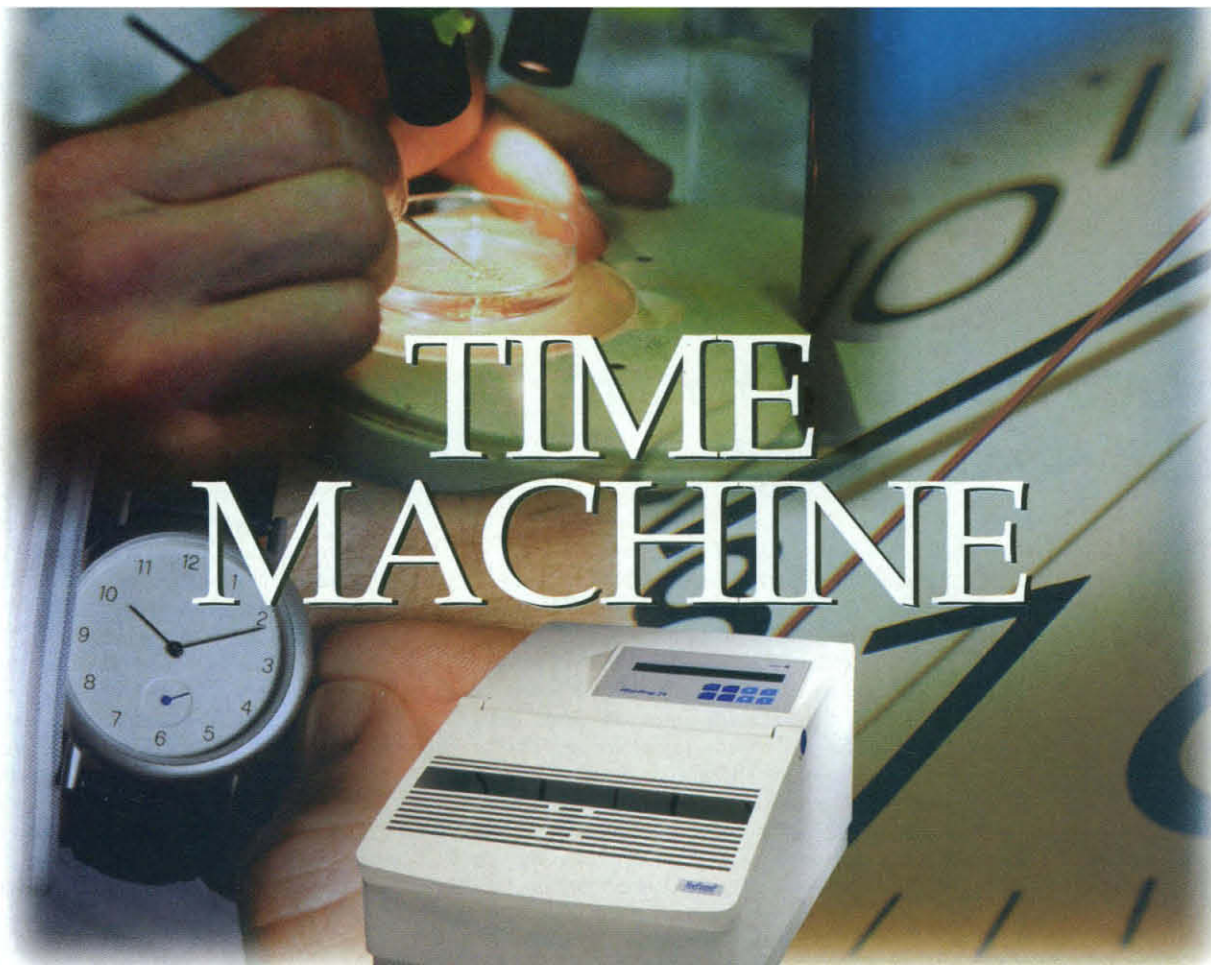
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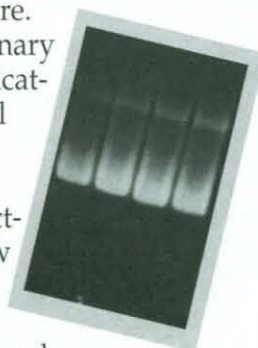
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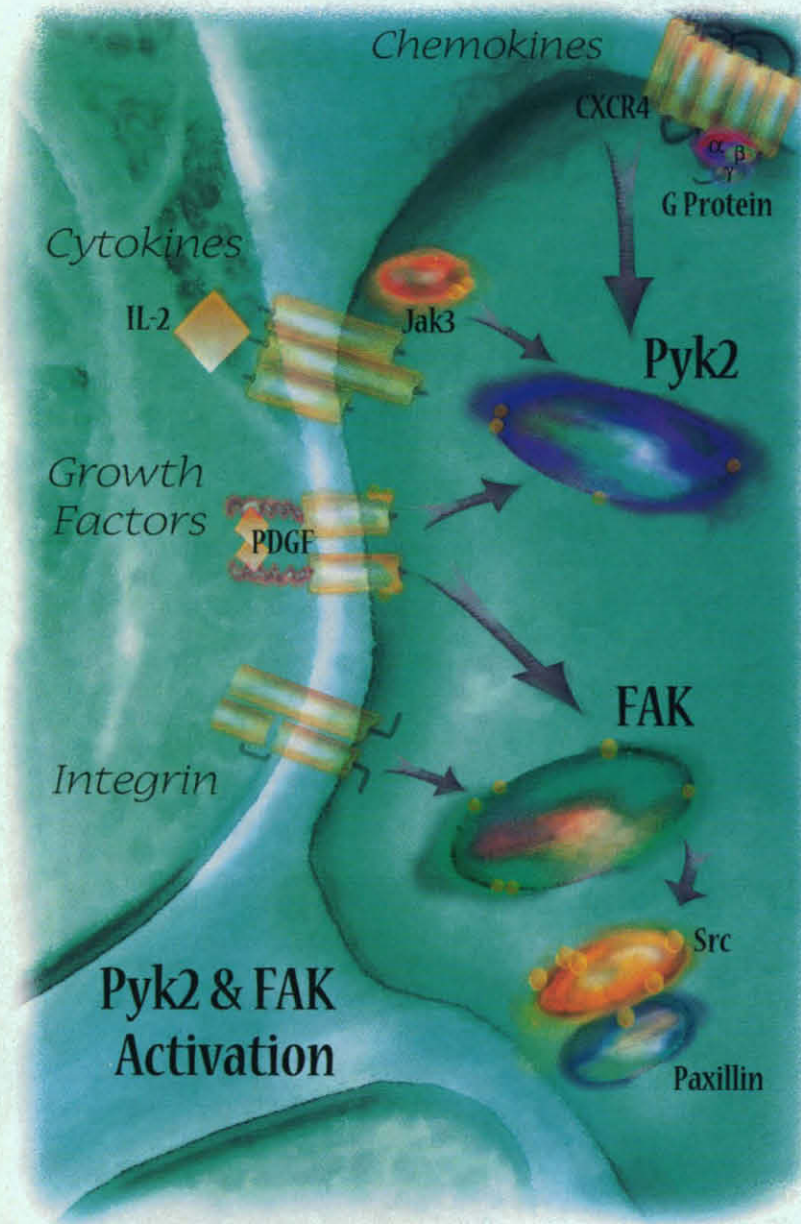
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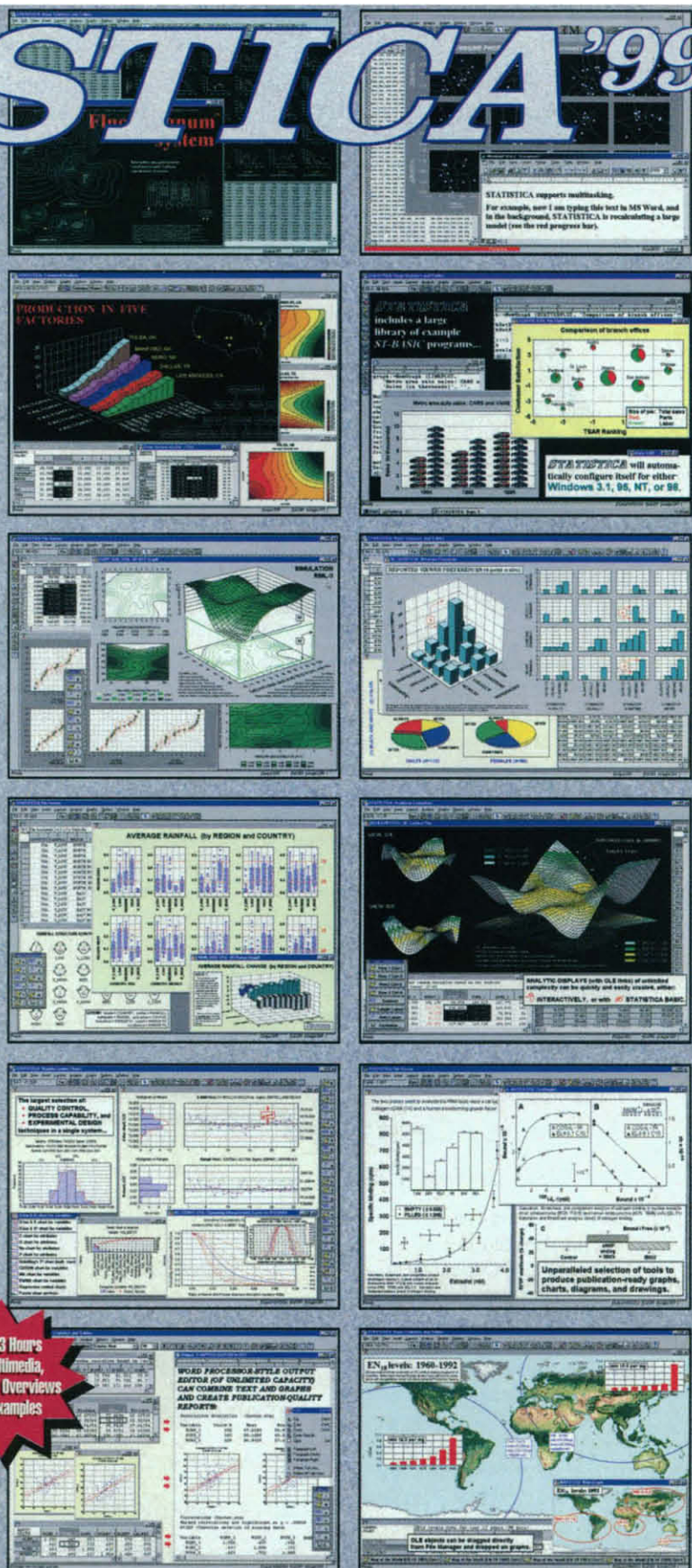
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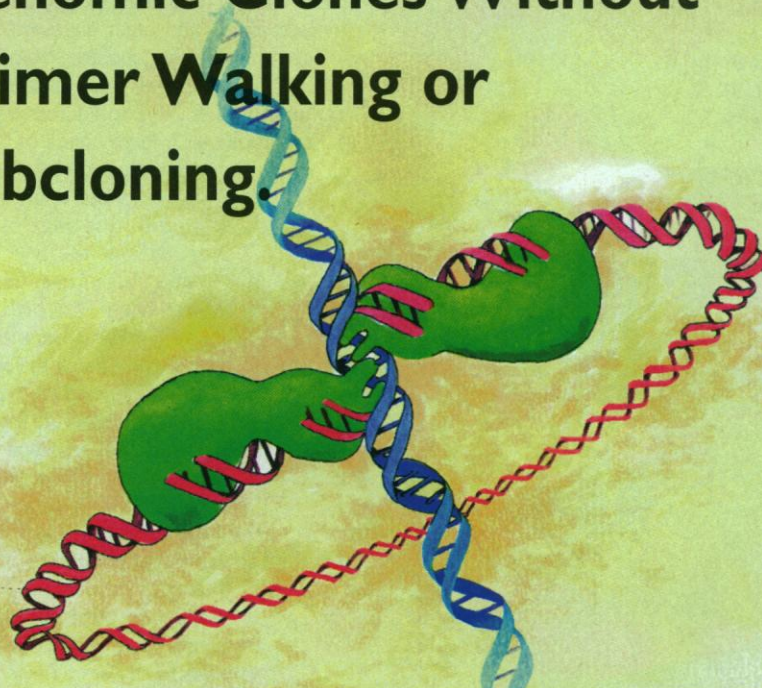


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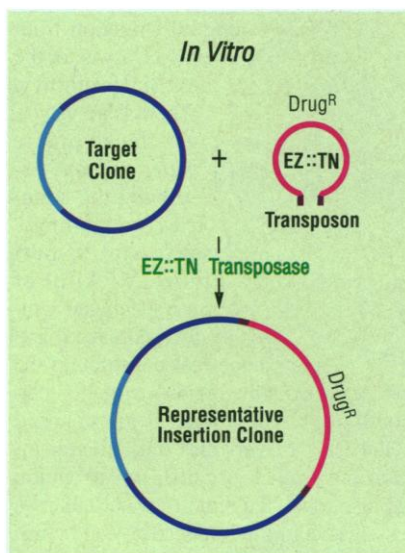
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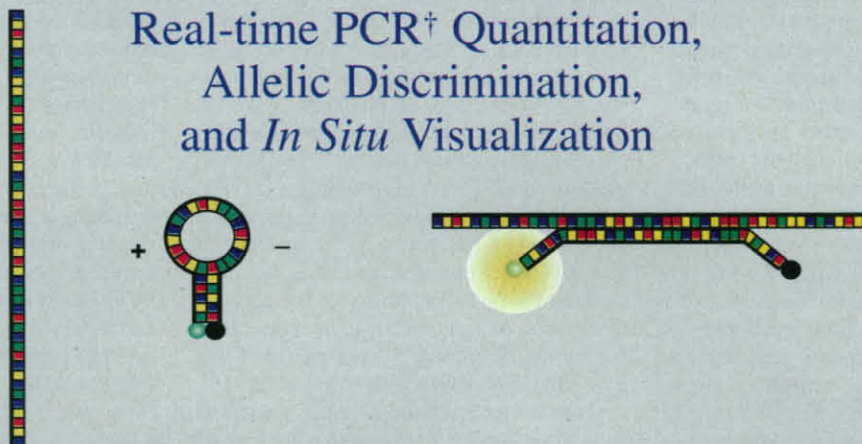
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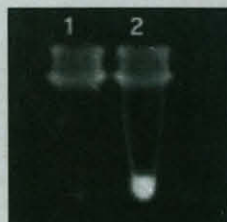


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1. Tyagi, S. and Kramer, F.R. (1996) *Nature Biotech.* 14, 303-8.
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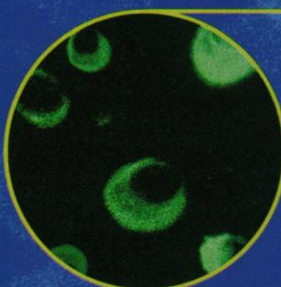
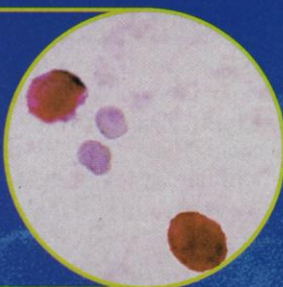
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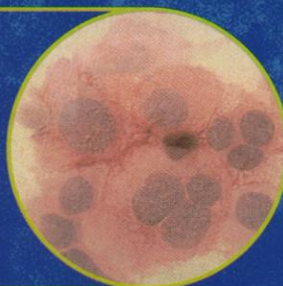


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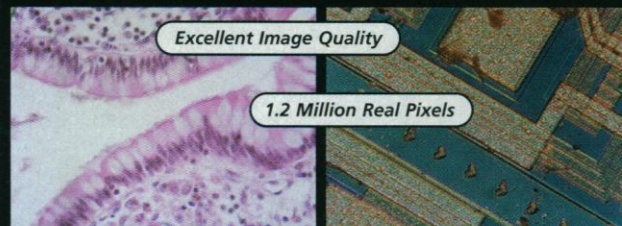


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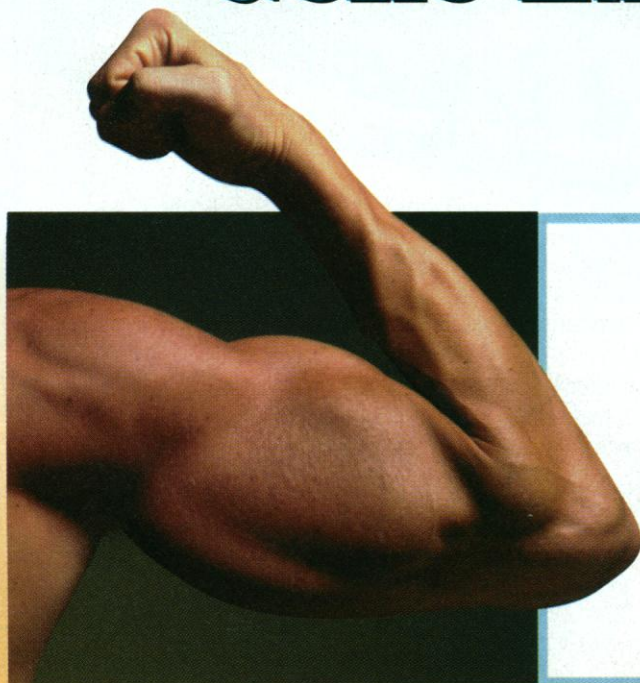
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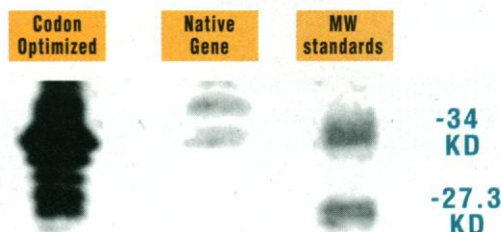
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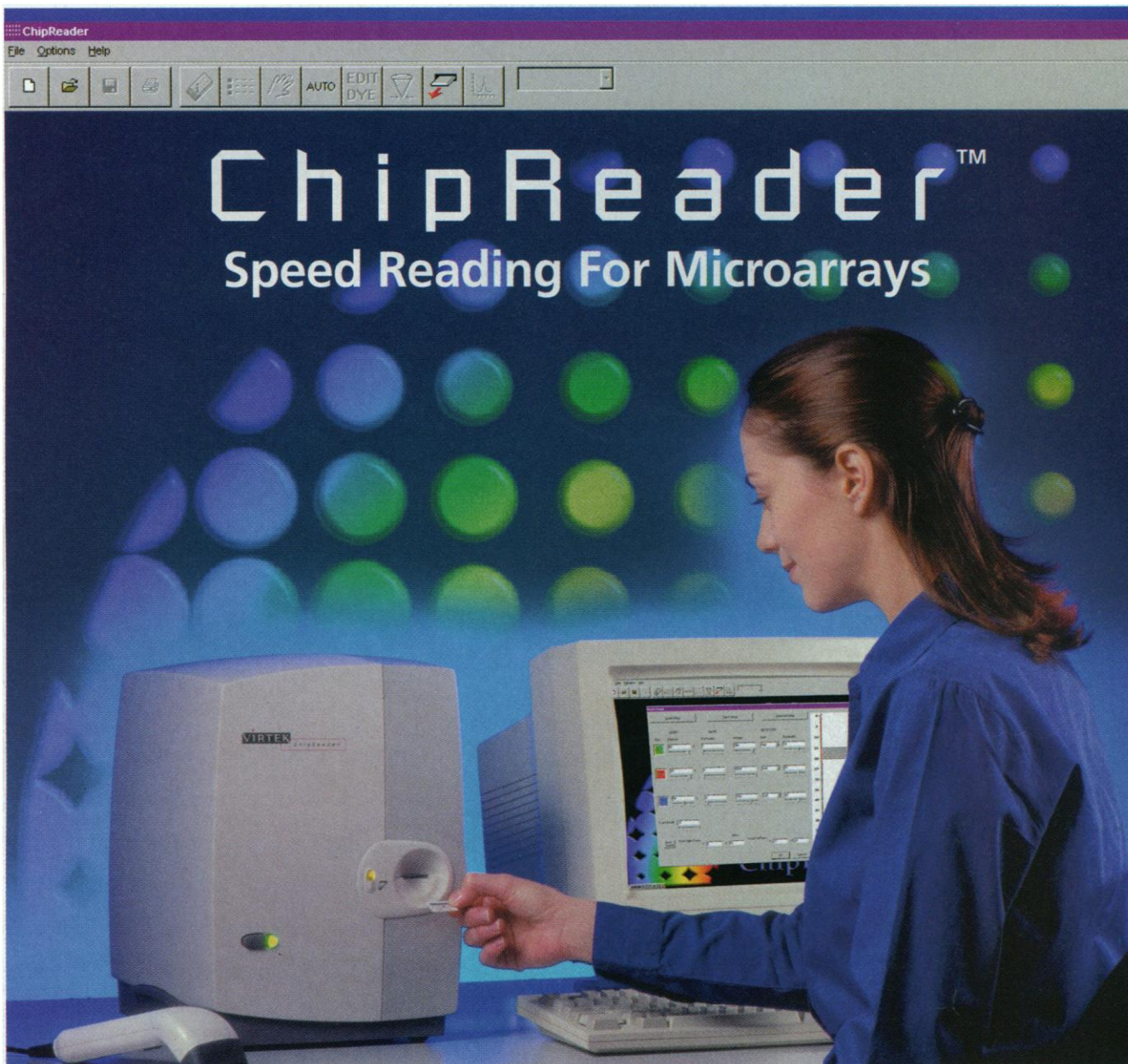
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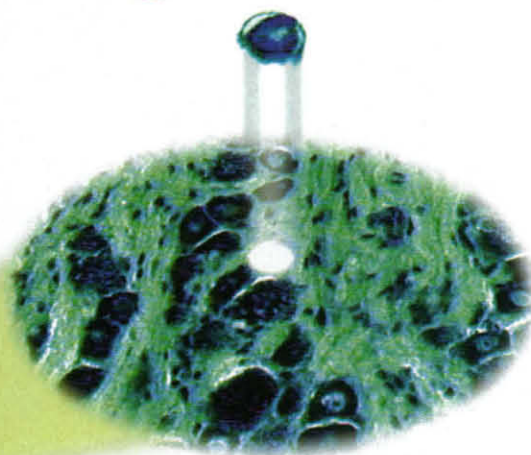
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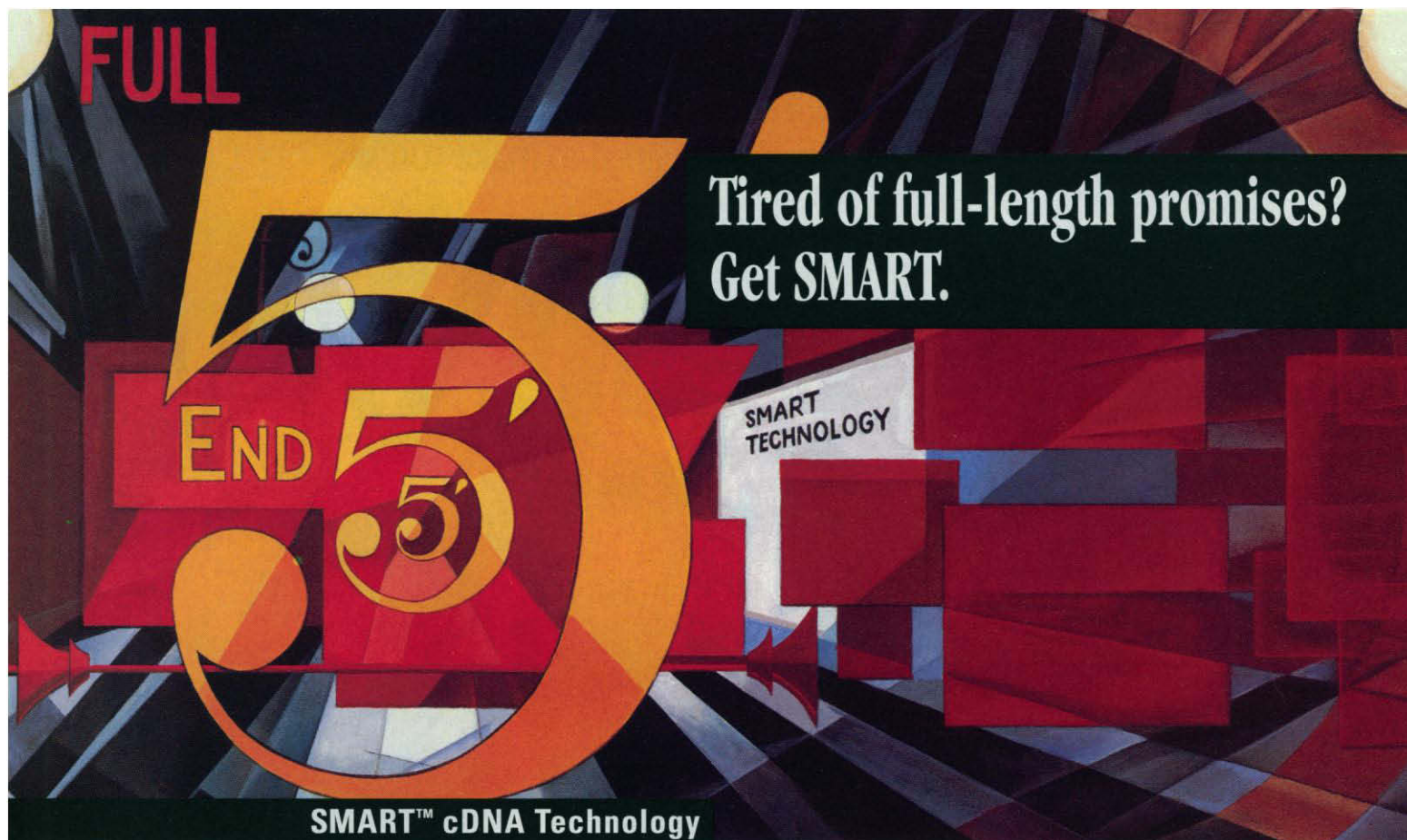
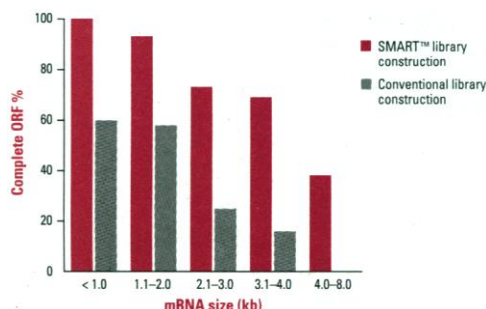


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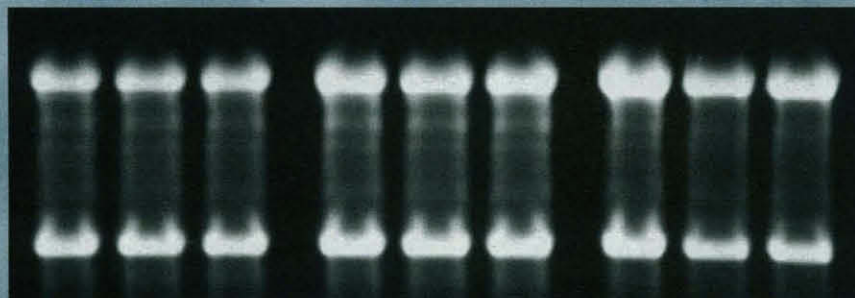
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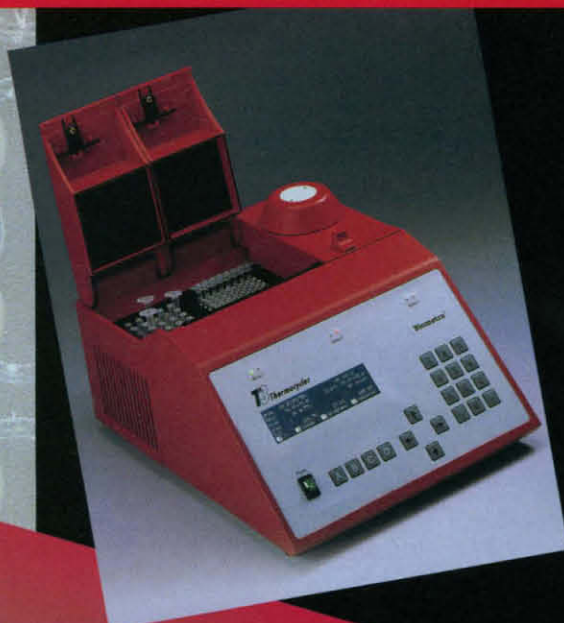
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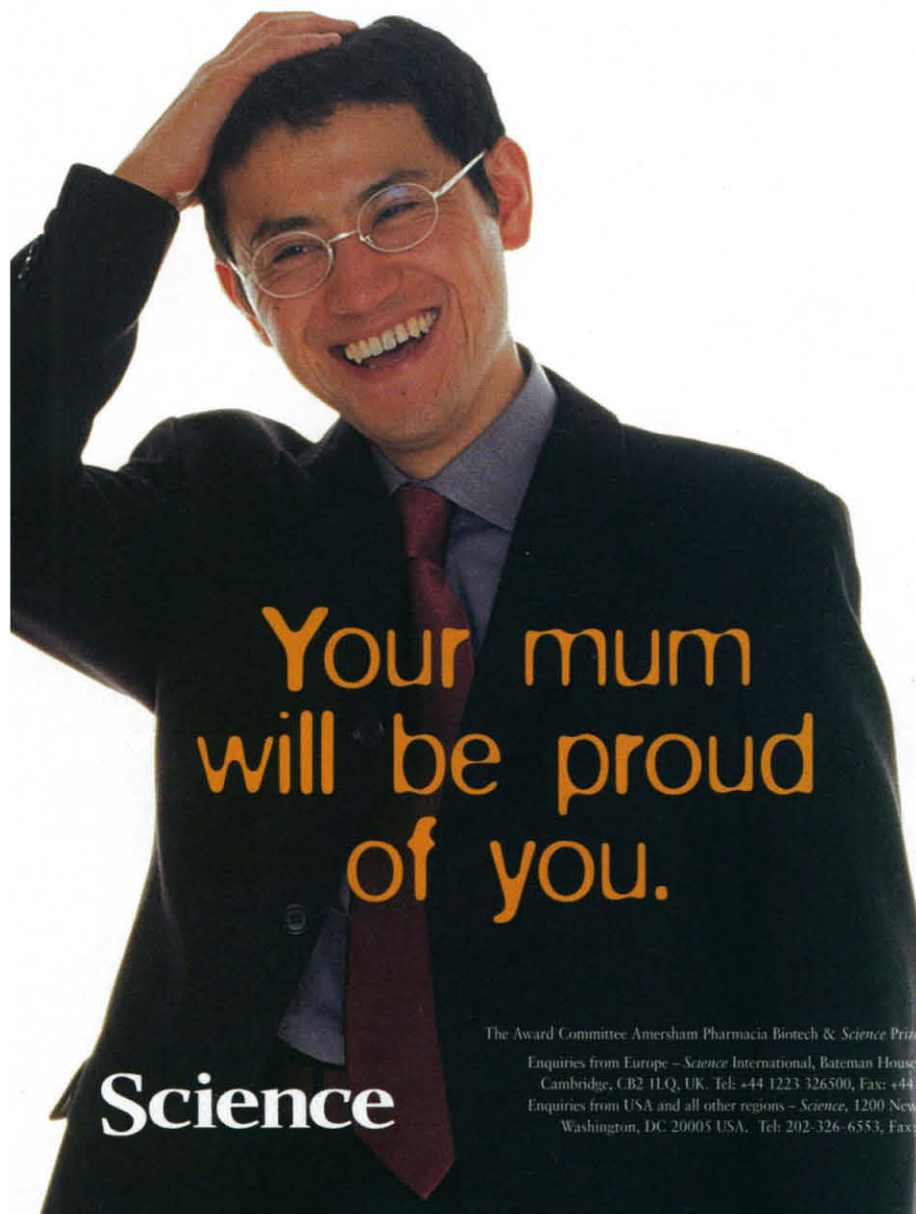
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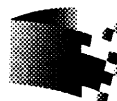
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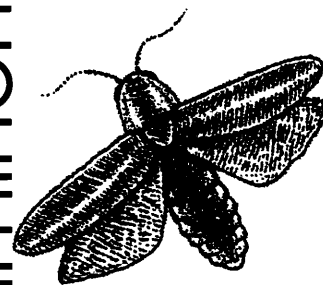
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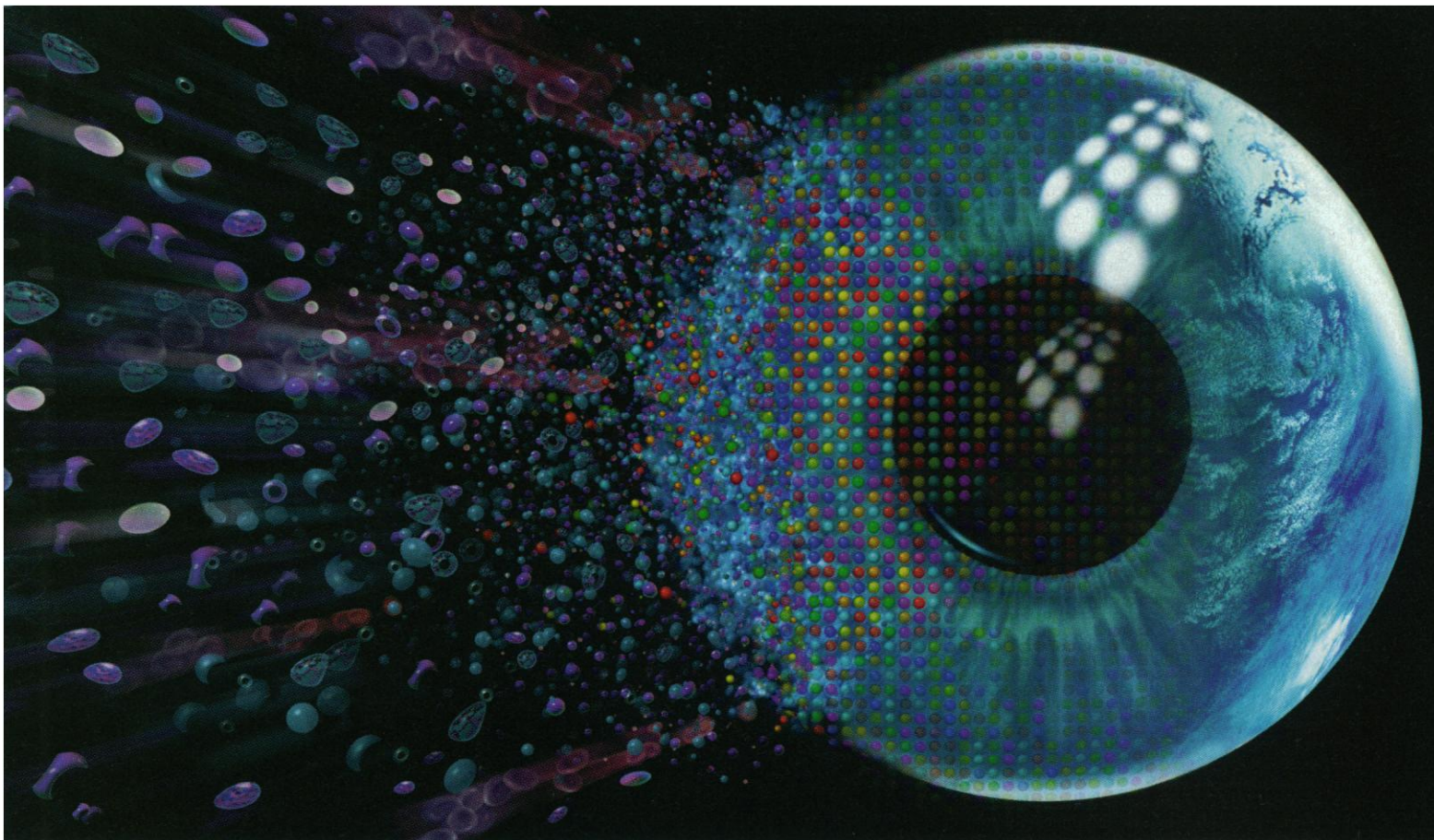
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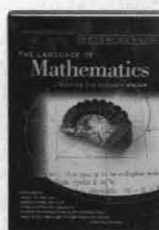
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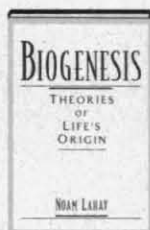
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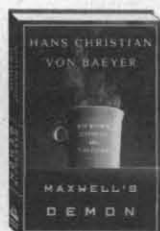
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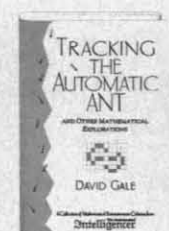
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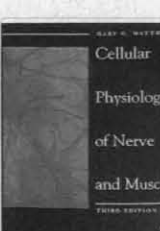
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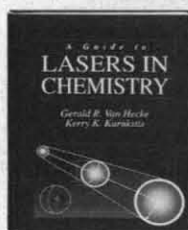
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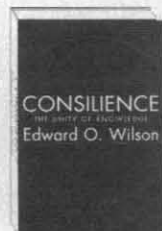
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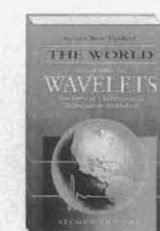
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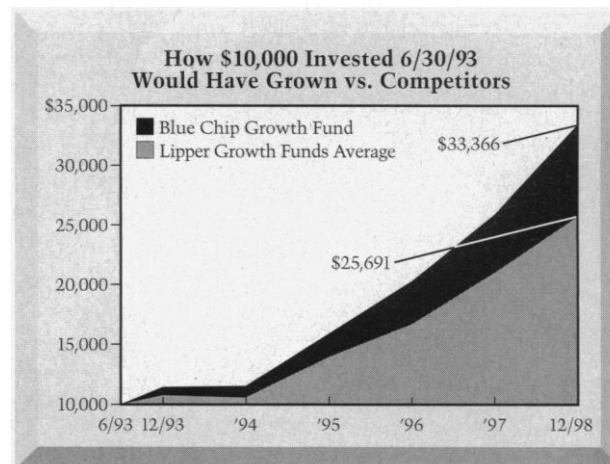
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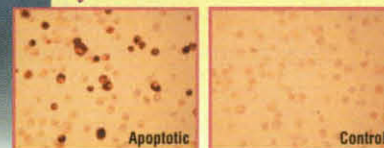


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