24 November 2000

Science

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Pages 1453–1640 $8

ISSUES IN NANOTECHNOLOGY

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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2 032 945	10 x 250 units (1250 PCR reactions)	1300.00
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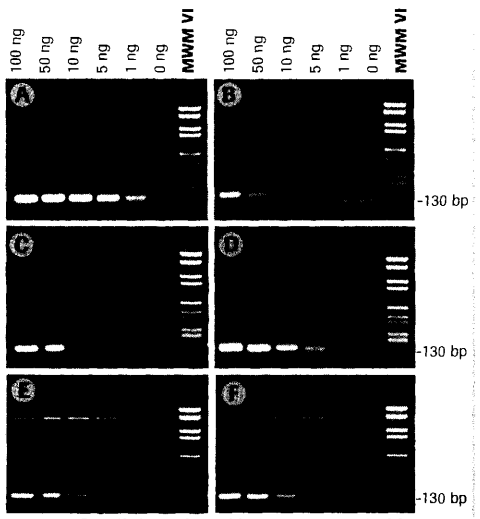


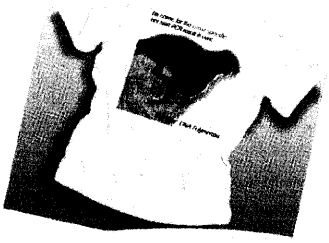
Figure 1: Specificity and sensitivity comparison in PCR using commercially available hot start systems.

Varying amounts of human genomic DNA were used for the amplification of a single 130 bp fragment from the tissue plasminogen activator (tPA) gene. Manufacturers' recommended initial product-activation times were used when applicable. The following cycling conditions were used in all reactions:

35 cycles at 95°C for 30 seconds
60°C for 30 seconds
72°C for 60 seconds
final extension at 72°C for 7 minutes.

A: FastStart Taq DNA Polymerase
B: Taq DNA Polymerase
C: Supplier A, modified hot start polymerase, buffer I
D: Supplier A, modified hot start polymerase, buffer II
E: Taq DNA Polymerase with anti-Taq antibody
F: Supplier B, antibody-modified hot start polymerase

Result: FastStart Taq DNA Polymerase produced the ***best specificity and sensitivity,*** even from little template.



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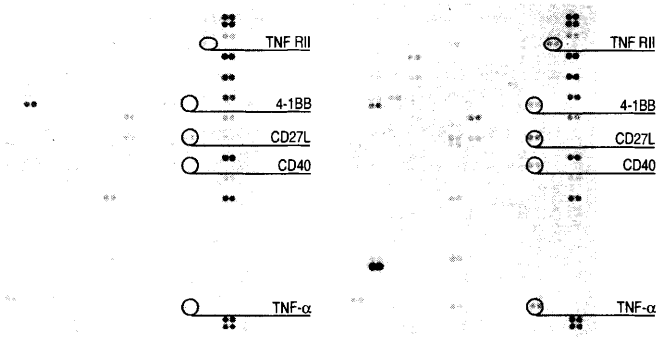
Purchase of this product is accompanied by a limited license to use it in the Polymerase Chain Reaction (PCR) process for life science research in conjunction with a thermal cycler whose use in the automated performance of the PCR process is covered by the up-front license fee, either by payment to Applied Biosystems or as purchased, i.e., an authorized thermal cycler.

Molecular Biology
REAGENTS

DNA ARRAYS • RNA QUANTITATION • PRIMER PAIRS • PROBE COCKTAILS

Expression Arrays

- Semiquantitative analysis of mRNAs using several different housekeeping control cDNAs
- All cloned cDNAs are sequenced and contain no repetitive elements
- Identify differentially expressed mRNAs by comparing expression profiles from different samples



Unstimulated **Stimulated**

The Human Cytokine cDNA Array (Catalog # GA001) shows RNA expression of TNF Superfamily genes in unstimulated and stimulated cells. Stimulated cells show an increase of 3.0, 26, 2.3, 130, and 8.6 fold for TNF RII, 4-1BB, CD27L, CD40 and TNF-α, respectively. Radiolabeled cDNA was made using poly (A)+ RNA, ^{33}P labeled nucleotide and Cytokine-specific Primers (Catalog # GAC11).

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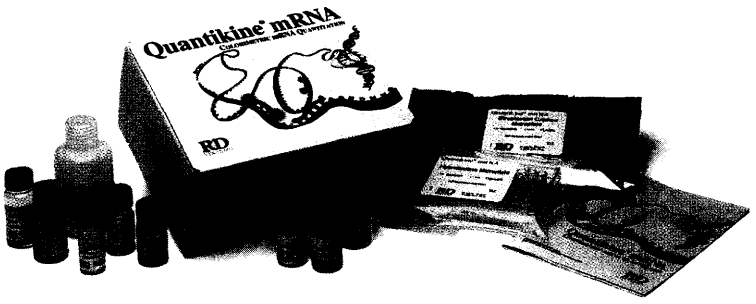
- Less sample RNA than Northern Blot or RPA
- Uses a conventional microplate reader
- Non-radioactive • Non PCR-based



Primer Pairs™ & Probe Cocktails

- R&D Systems' Primer Pairs have been carefully tested to identify optimum amplification conditions so you spend less time optimizing PCR*.
- Probe Cocktails are available labeled with biotin or digoxigenin** or unlabeled with 5'- and 3'-hydroxyl groups.

*PCR is covered by US Patent Numbers 4683195 and 4683202 assigned to Hoffmann-LaRoche.
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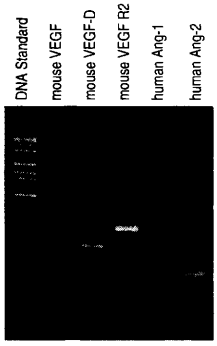
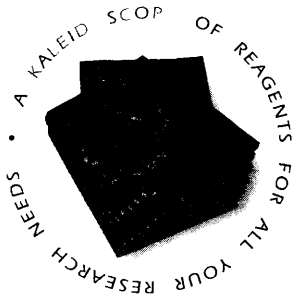


RT-PCR products were amplified from first-strand cDNA samples representing sources known to express the respective mRNA. Products were analyzed on a 2.0% agarose-TAE gel and visualized with ethidium bromide staining.*



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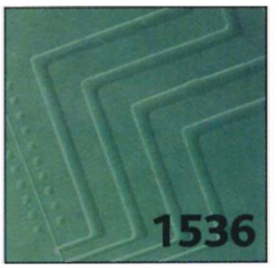
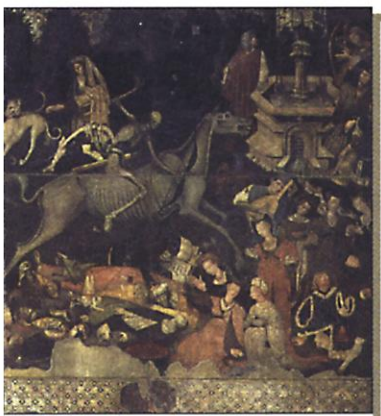


COVER A microfabricated cell sorter, with integrated pumps and valves and channel sizes on the order of 30 μm, was made by molding polydimethylsiloxane. This silicone elastomer is much softer than silicon and allows for low-force pneumatic actuation of the valves. Soft materials and nontraditional fabrication techniques such as molding are promising routes to practical nanomechanical devices, one of the topics of this special issue on nanotechnology, which starts on p. 1523. [Photo: Felice Frankel]



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Yersinia's modus operandi

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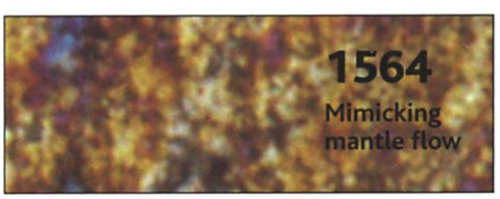

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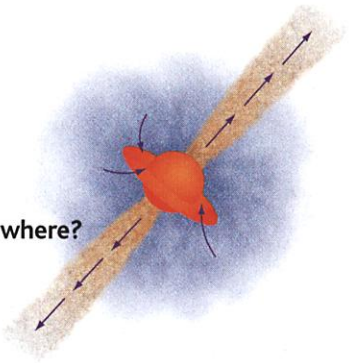

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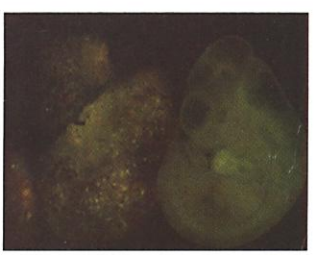

1578
X inactivation in cloned mice

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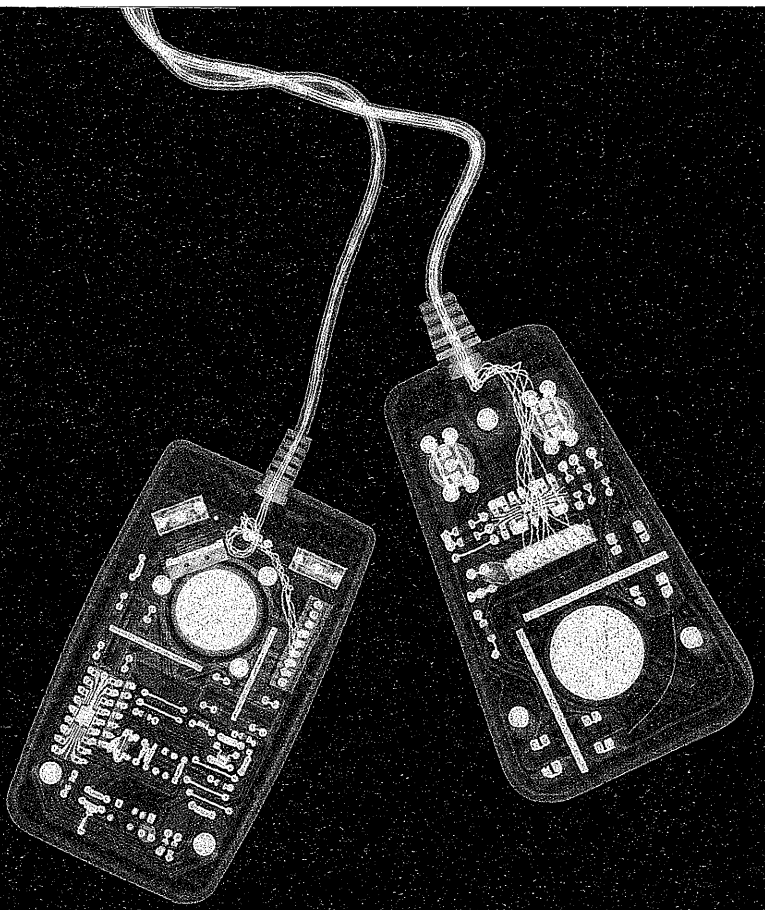

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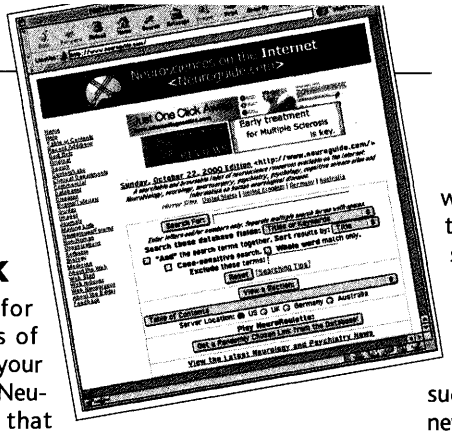
NETWATCH

edited by JOCELYN KAISER



RESOURCES

Neuro Network

Does your Web search for "stroke" turn up hundreds of pages on how to improve your golf game? If so, try visiting Neuroguide, a 6-year-old site that brings order to the Web's tangle of neuroscience resources, from basic science to medical and educational offerings.

Site editor Neil Busis, a neurologist at the University of Pittsburgh, says his goal was "a site that can deal with different parts of the audience and different cognitive styles." So he created three ways of getting around Neuroguide: a key-word search, listings by topic, and Neuroroulette, which launches you to a randomly chosen page. A good starting point is the Best Bets page, a list of what Busis thinks are the most useful links. Under Images you can find scores of sites such as Harvard's Whole Brain Atlas, which offers a series of labeled CT, MRI, and other scans of the human brain. Visit the online tutorials and exams to learn more about topics such as eye function or neuroanatomy. Other links take you to newsgroups and Web forums, neuroscience databases, rosters of labs and professional societies, a calendar of meetings, and electronic journals. Although most of Neuroguide's content comes from elsewhere on the Web, there are also original contributions, ranging from job announcements to peer-reviewed book reviews and papers.

www.neuroguide.com

IMAGES

This critter is the classic antarctic krill, *Euphausia superba*, the 55-millimeter-long copepod that whales trek south from the tropics to feast on. At this krill site,* you can zoom in on details such as the delicately ribbed plankton filter and compound eyes of krill and another specimen, a species of amphipod. The shrimplike creatures were photographed aboard an ice-breaking research vessel journeying through the Southern Ocean.

To see more antarctic sea life, check out this field guide† describing a whole menagerie of cold-loving animals and plants, from sponges to jellyfish to diatoms. Also don't miss a professional photographer's amazing shots of the eerie, blue-green world below the frozen sea surface.

* **krill.rutgers.edu**

† **scilib.ucsd.edu/sio/nsf/fguide/index.html**

HISTORY

Chronicling Physics

The 1600s were heady days for physics, what with such giant advances as the invention of thermometers, the discovery that dumping acid on a metal created a flammable gas (hydrogen), and an experiment showing that if you put two halves of an iron sphere together and suck out the air, even teams of horses can't pull them apart. Those are highlights from a timeline of thermodynamics and statistical mechanics being built by Jeff Biggus, a physics history fan in Boulder, Colorado. Biggus, who's also chronicling electromagnetism and hypercomplex numbers from Greek times to the late 1900s, has created timelines that are concise, readable, and filled with references and links. The site also lists other good science timelines.

history.hyperjeff.net

EDUCATION

Cells and Sleuths

As many baby boomer parents know, children are often light-years ahead of adults in their instincts for using the Web. That's clear from a browse through finalists in ThinkQuest, an annual contest in which middle and high school students create Web sites. This year's crop of science sites, on topics from natural disasters to leukemia, could rival many professional sites with their clean design and technical bells and whistles. NetWatch especially likes Cellupedia, a site created by seniors from three high schools working through cyberspace: Besides providing basic information on cell organelles and processes, gorgeous images, and a multiuser variation of the Game of Life, the Web masters added depth with links to abstracts in MEDLINE. Other top sites are set up entirely as games: You can learn about carbon chemistry by playing a spy named Carbon Bond, for instance, or dig into paleontology by catching a dinosaur bone thief.

www.thinkquest.org/tqic/finalists_2k.html

Science ONLINE

Scientists noticed more than 300 years ago that camphor particles dropped on water will dance across the surface, propelled by surface tension. This week in *Science*, Schmid *et al.* report on p. 1561 that a mechanism similar to the "camphor dance" may be at work in the formation of alloys. In two videos on *Science* Online, you can see this process: amoeba-like blobs of tin sweep across a few hundred nanometers of copper, exchanging atoms with copper to form pockets of bronze, then scamper away to unalloyed areas.

www.sciencemag.org/cgi/content/full/290/5496/1561

Send Internet news and great Web site suggestions to netwatch@aaas.org

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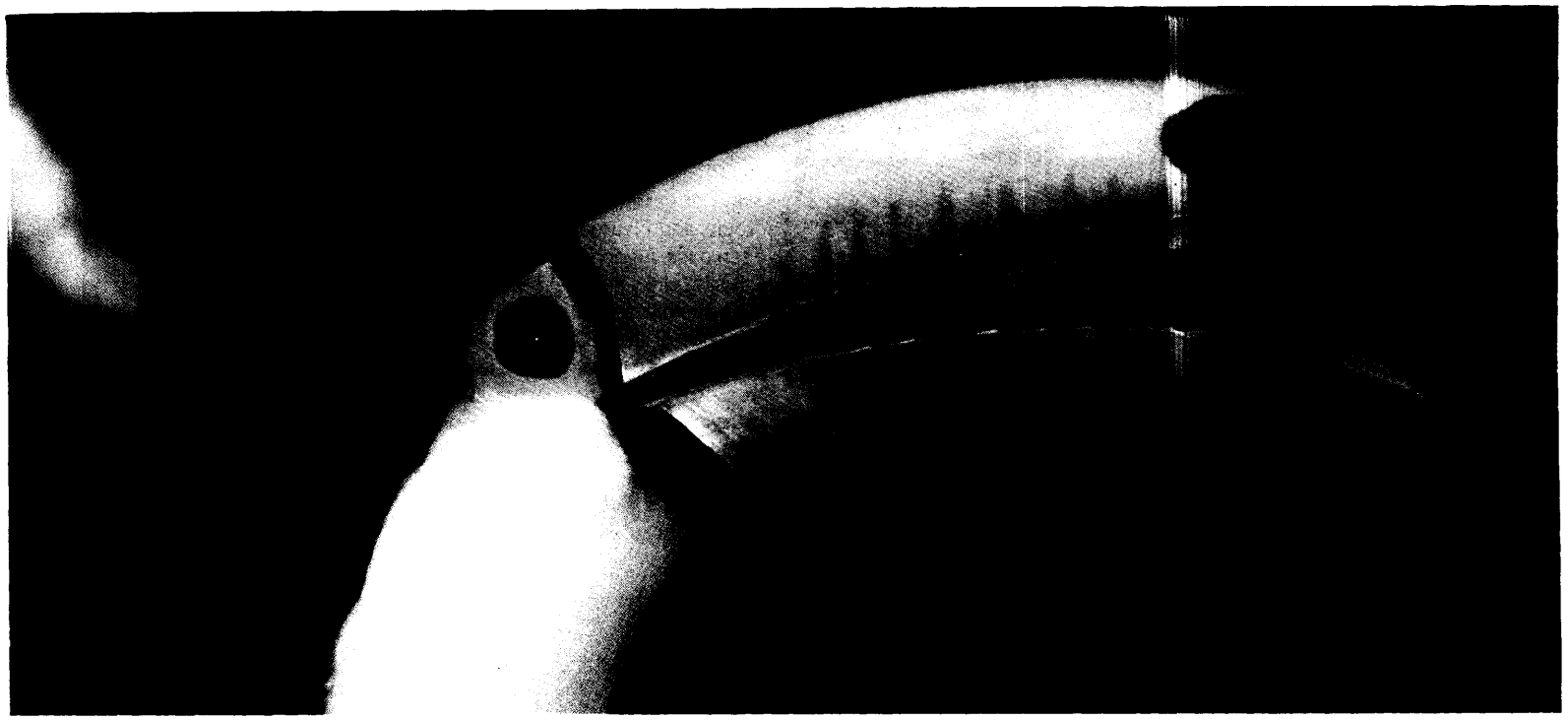

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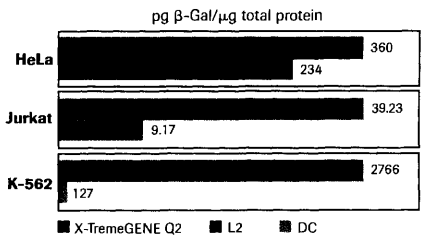

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HOW BRONZE GOT LEFT BEHIND

Metal alloys have been the subject of many structural studies, but the dynamics of their formation has been more difficult to study. Schmid *et al.* (p. 1561; see the Perspective by Besenbacher and Nørskov) have investigated the formation of bronze by placing very low concentrations of tin (hundredths of a monolayer) on an atomically flat copper surface. What they find is an unusual cooperative mechanism. The tin atoms form large islands (hundreds of thousands of atoms) on the surface that exchange with copper atoms to form bronze crystallites. However, the tin islands are repelled by the tin atoms that become trapped in the surface bronze, and thus move rapidly across the surface toward fresh copper and leave trails of smaller bronze islands in their wake. This motion, which is driven by surface free energy, is reminiscent of the "camphor dance" seen on liquid surfaces.

DEFECTS DISAPPEARING IN GROUPS

The interactions between the distinct chemical species of block copolymers result in the tendency of regular lines of each species to evolve as the material is annealed (coarsening). However, topological defects (disclinations and dislocations) will ultimately limit the potential of those nanometer-scale patterns for lithographic processing or self-assembled structure formation, or both. Harrison *et al.* (p. 1558) used time-lapse atomic force microscopy to monitor the evolution of the stripe patterns with annealing time. Defect annihilation proceeded by a dominant mechanism involving three or four disclinations, and the density of those defects played a crucial role in the kinetic evolution of the two-dimensional patterns.

THE SPIN ON CARBON NANOTUBES

Metallic single-walled carbon nanotubes (SWNTs) present almost ideal systems in which to study electronic transport in one dimension. Recent interest has now turned to the spin physics of these systems, in which the local interaction between magnetic atoms and the conduction electrons are studied. Odom *et al.* (p. 1549) used scanning tunneling spectroscopy to show that magnetic clusters produce a peak in the tunneling conductance. The decay with distance from the cluster and with temperature are both consistent with a Kondo resonance. Additionally, discrete energy levels of this resonance emerge when the length of the nanotube available to the clusters is shortened, which is consistent with a "spin-in-a-box" scenario.

GOING AGAINST THE GRAINS

Seismologists use differences in wave speeds in different directions (seismic anisotropy) to estimate the direction of mantle flow. On a microscopic scale, the seismic anisotropy is attributed to strain-induced lattice orientation of olivine and pyroxene grains. Bystricky *et al.* (p. 1564; see the Perspective by Mackwell and Rubie) performed laboratory experiments at high temperature and very high bulk shear strains (conditions similar to those in the mantle) to determine the microscopic deformation of olivine aggregates. At the highest shear strains, olivine recrystallizes along subgrain rotation boundaries to create a somewhat more random texture than was expected. Thus, the slowest speeds will not always be normal to the shear plane, and olivine microstructure may not be a good indicator of mantle motions.

THE DOPE ON NANOTUBE DIODES

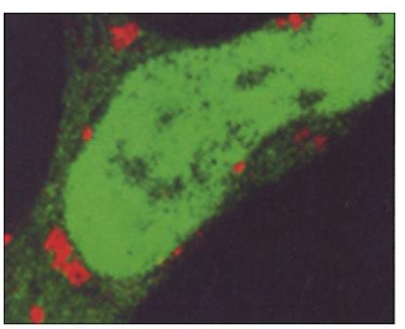
Semiconducting carbon nanotubes are naturally *p*-type conductors—they conduct holes better than electrons. Impurities adsorbed onto the surface can alter the electrical conduction of the tubes and are usually to be avoided. However, Zhou *et al.* (p. 1552) raise the possibility of using adsorbed atoms to good effect. They demonstrate diode behavior for nanotubes where one half of the tube is exposed to potassium atoms, which dopes that region of the tube *n*-type, while the other half remains *p*-type. The subsequent diode behavior may suggest a route toward designer nanoelectronics with carbon nanotubes as the basic building blocks.

HARNESSING BIOMOTORS

The F_1-ATPase enzyme undergoes rotary motion when it uses adenosine triphosphate as an energy source, and previous studies have imaged this motion by attaching actin filaments to the enzyme's central subunit. Soong *et al.* (p. 1555) have now harnessed this enzyme to drive inorganic propellers. Appropriately tagged enzymes were attached to the tops of an array of nanometer-scale nickel posts and, in turn, nickel propellers, 150 nanometers (nm) in diameter and 750 to 1400 nm in length, were attached to the tops of the "motors." Although such assembly is not foolproof (only a small fraction of motors are viable), some can be seen to drive currents in the surrounding solution for more than 2 hours while being fed ATP.

A SCAFFOLD FOR KINASES

The β-arrestins were so named because they function in the desensitization of β_2-adrenergic receptors. However, these proteins play other roles, both in receptor endocytosis and in promoting receptor signaling. McDonald *et al.* (p. 1574; see the Perspective by Pouysségur) now describe yet another function for these versatile proteins—β-arrestin 2 binds to the mitogen-activated protein kinase family member JNK3 (c-Jun NH_2-terminal kinase 3) and to the upstream kinases MKK4 and ASK1 that act in a cascade to activate JNK3. β-Arrestin 2 appears to act as a scaffold that brings the kinases together and helps retain JNK3 in the cytosol. In cells treated with agonists of G protein–coupled receptors, the β-arrestin 2 protein appears to target JNK3 to endosomal vesicles.



RECEPTORS FOLLOW A PARTY LINE

A receptor is normally triggered when, and only when, its ligand binds to the receptor. It's not so simple for the ErbB1 receptor, which responds to stimulation with epidermal growth factor (EGF) by dimerization, cross phosphorylation of the monomers, and triggering of downstream pathways. Verveer *et al.* (p. 1567) have visualized phosphorylated ErbB1 in MCF7 cells with fluoresence lifetime imaging microscopy in conjunction with fluorescence resonance energy transfer, which was used to monitor the binding of an antibody to phosphotyrosine. Focal stimulation of the cell with EGF immobilized on beads resulted in a rapid propagation of

CONTINUED ON PAGE 1463

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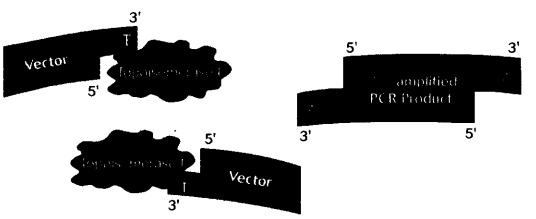

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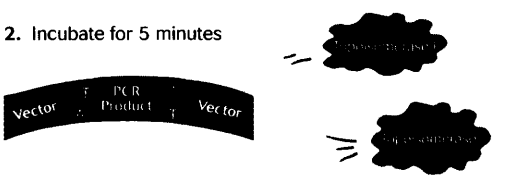

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THIS WEEK IN *SCIENCE*

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receptor phosphorylation over the entire surface of the cell—even those receptors that had not been exposed to EGF.

FOLDINGS FADS

The endoplasmic reticulum (ER) presents an oxidative folding environment to newly synthesized proteins that have been translocated from the cytosol. The formation of disulfide bonds within and between proteins is one of the important reactions that is promoted within the ER, whose faithful performance is crucial for the production of correctly folded secretory and membrane proteins. Tu *et al.* (p. 1571) describe the successful reconstitution of ER-like folding in a cell-free system and find that the cofactor for successful folding is flavin adenine dinucleotide (FAD)—rather than ubiquinone or heme, as may have been expected.

A DELIBLE MARK

Cloning of mammals by nuclear transfer has been thought to require epigenetic reprogramming of the donor cell from a differentiated to an undifferentiated state, but this process has not been demonstrated at the cellular level. One example of an epigenetic mark imposed during differentiation of female somatic cells is X chromosome inactivation. Eggan *et al.* (p. 1578; see the Perspective by Clerc and Avner) used an X-linked reporter gene encoding a fluorescent marker to study X chromosome inactivation in cloned mouse embryos derived from female fibroblast nuclei. Somatically inactivated X chromosomes can be reactivated during early cleavage of the cloned embryos and are then subject to normal random inactivation in embryonic lineages. Thus, the marks that distinguish active and inactive X chromosomes can be erased and re-established during the cloning process. The cloned embryos may be useful tools for studying the precise nature of these epigenetic marks.

PERCEPTIVE MATURATION

The visual process whereby images are decomposed into their component attributes (a line, its orientation, its color, and so forth) imposes the challenge of constructing the perceived world by properly assorting and recombining these characteristics. In particular, the illusory square known as a Kanizsa figure (formed by 90° wedge cutouts in four circles placed at corners of the square) is perceived by 8-month-old infants but not by 6-month-olds, and thus tests the capability for visually "binding" the four isolated objects. Csibra *et al.* (p. 1582) examined the electrophysiological responses in these two groups of infants and found a concomitant appearance of stimulus-induced oscillations in the gamma frequency range (40 hertz) of neural activity. These findings support the idea that this activity represents the correlate of perceptual binding.

HOW GREEN WAS MY PROTEIN

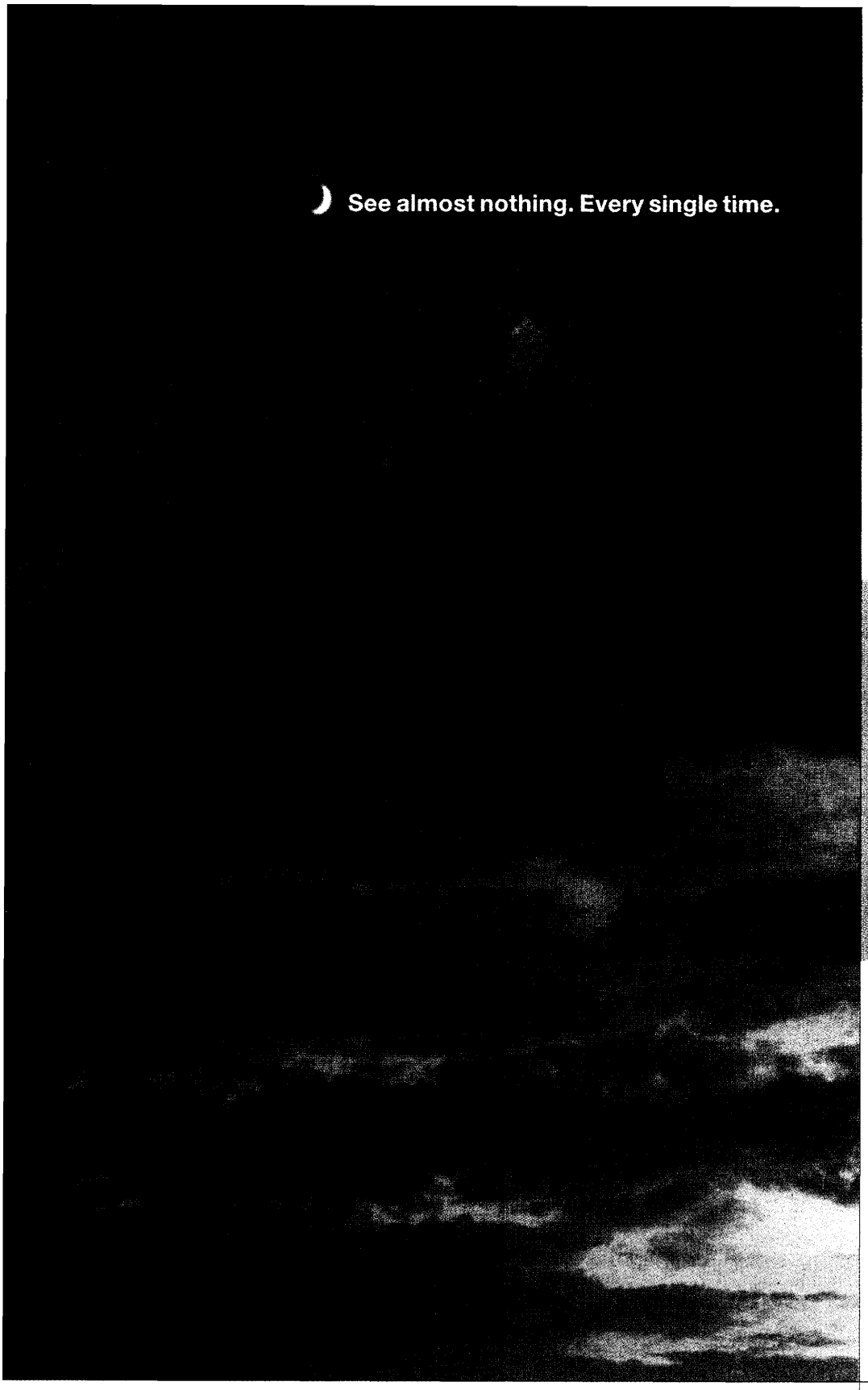
Green fluorescent protein (GFP) is widely used as a non-invasive probe to monitor protein localization or to trace expression. The recently discovered red fluorescent protein is complementary to GFP and allows applications such as fluorescence resonance energy transfer. Terskikh *et al.* (p. 1585; see the news story by Chichurel) have generated a mutant of red fluorescent protein (E5) that changes its fluorescence from green to red over time. Because the rate of color conversion is independent of protein concentration, E5 can be used as a fluorescent clock to monitor the activation and down-regulation of gene expression in whole organisms.

KILLING SIGNALING

Yersinia species are bacterial pathogens responsible for a variety of diseases in animals and plants, including *Y. pestis*, which was responsible for the Black Death. Orth *et al.* (p. 1594; see the news story by Brown) examined the activities of one of the *Yersinia* virulence factors, YopJ. The protein showed homology to cysteine proteases and appeared to act specifically to degrade signaling proteins that had been tagged by the ubiquitin-like molecule known as SUMO-1.

THE ADVANTAGES OF TAKING BREAKS

Reports on AIDS patients undergoing highly active antiretroviral therapies have begun to suggest that structured treatment interruptions (STI) can lead to improved immune response, reduced toxicity, and can favor the appearance of wild-type virus over resistant mutants. If proven, these protocols might be easier for patients to tolerate, and less costly. A randomized, controlled test of the hypothesis that STI is beneficial has been performed by Lori *et al.* (p. 1591), who studied the effects of alternating therapy (3 weeks on and 3 weeks off) on rhesus macaques infected with simian immunodeficiency virus. The protocol resulted in virus-specific immune responses and control of virus replication relative to animals that were treated continuously and then had treatment stopped.



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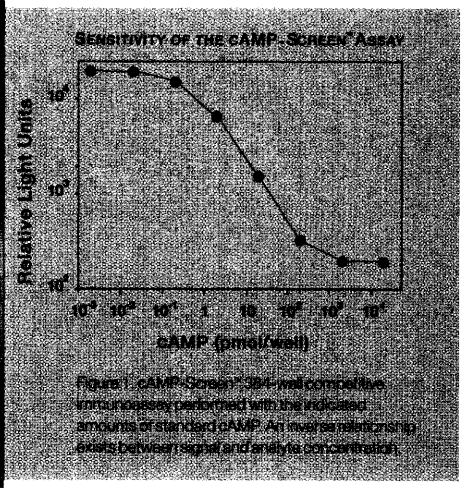

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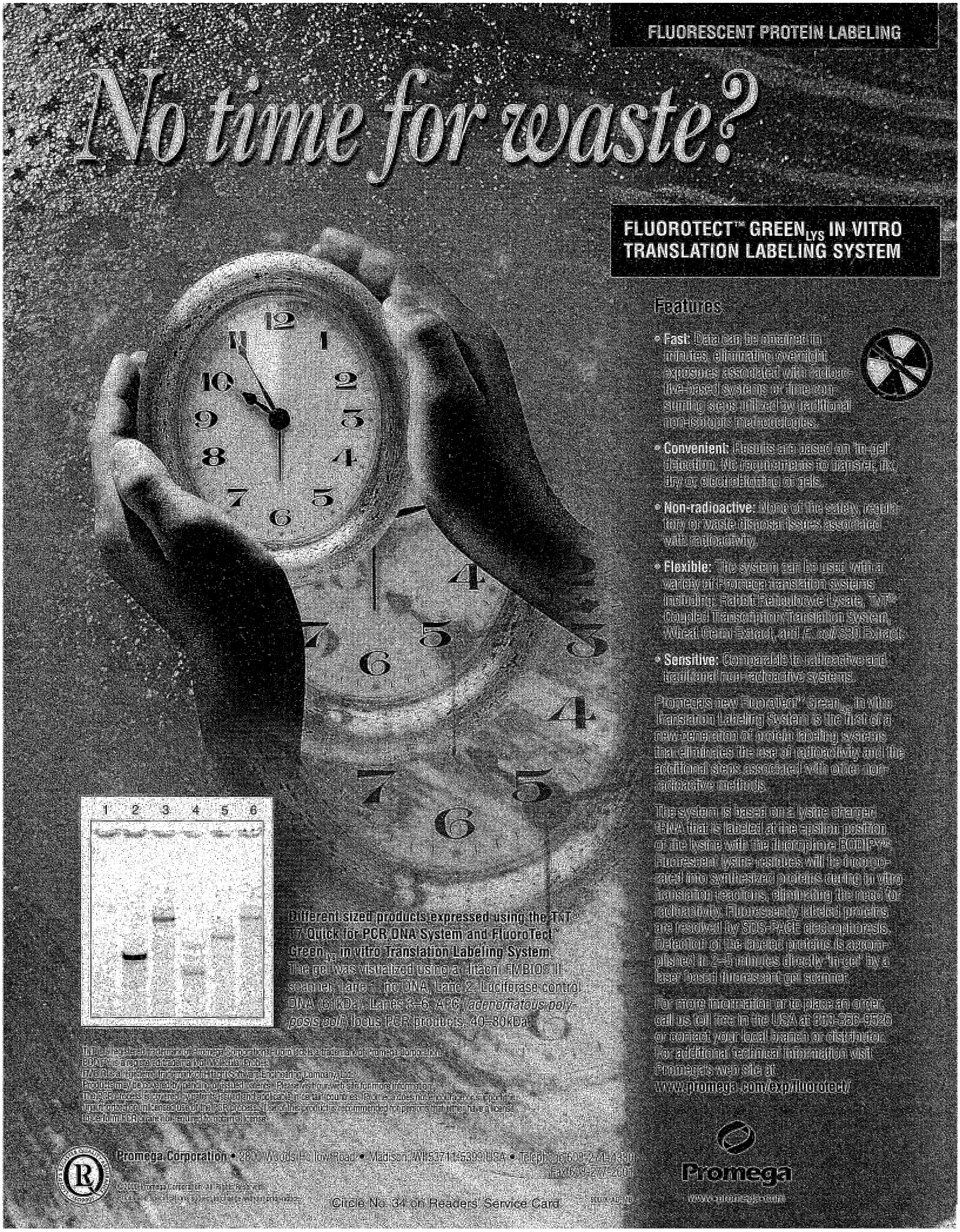
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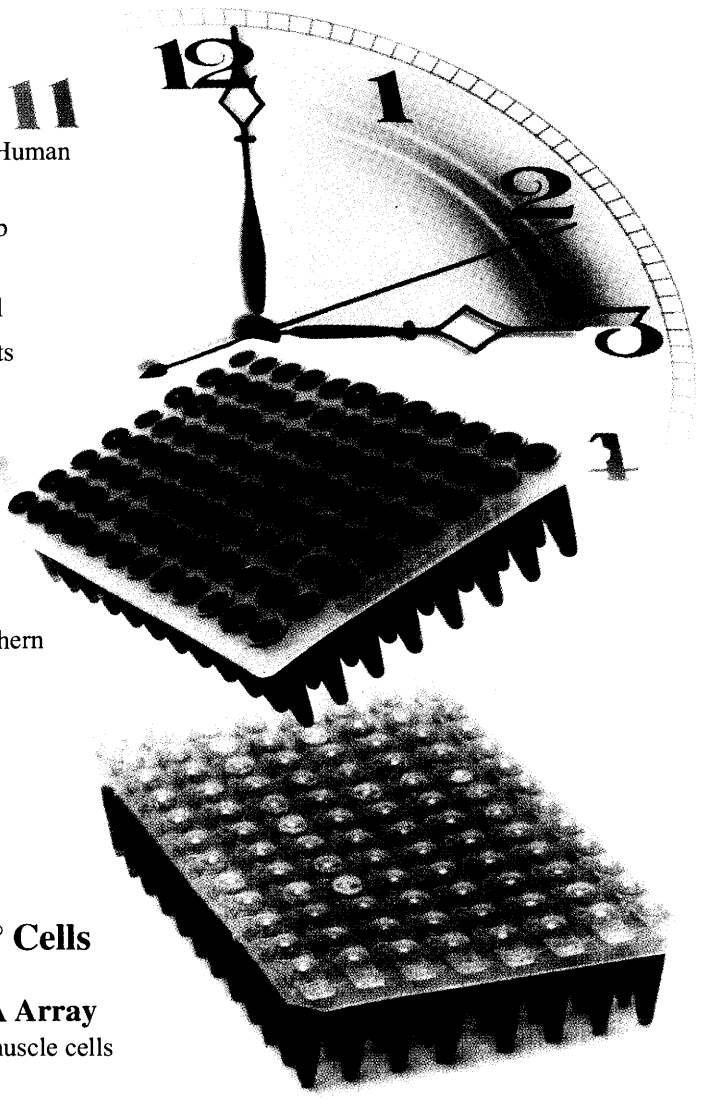

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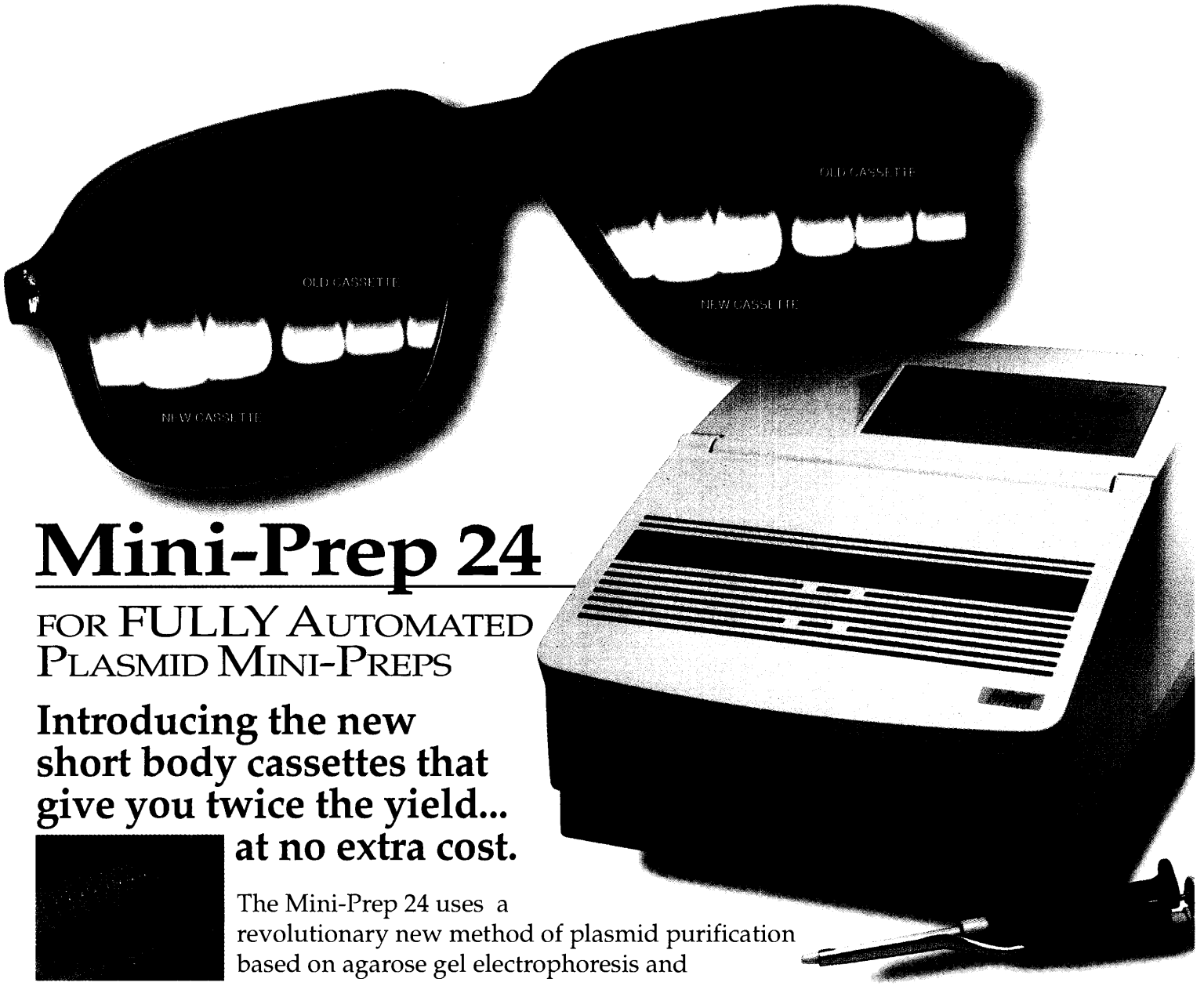

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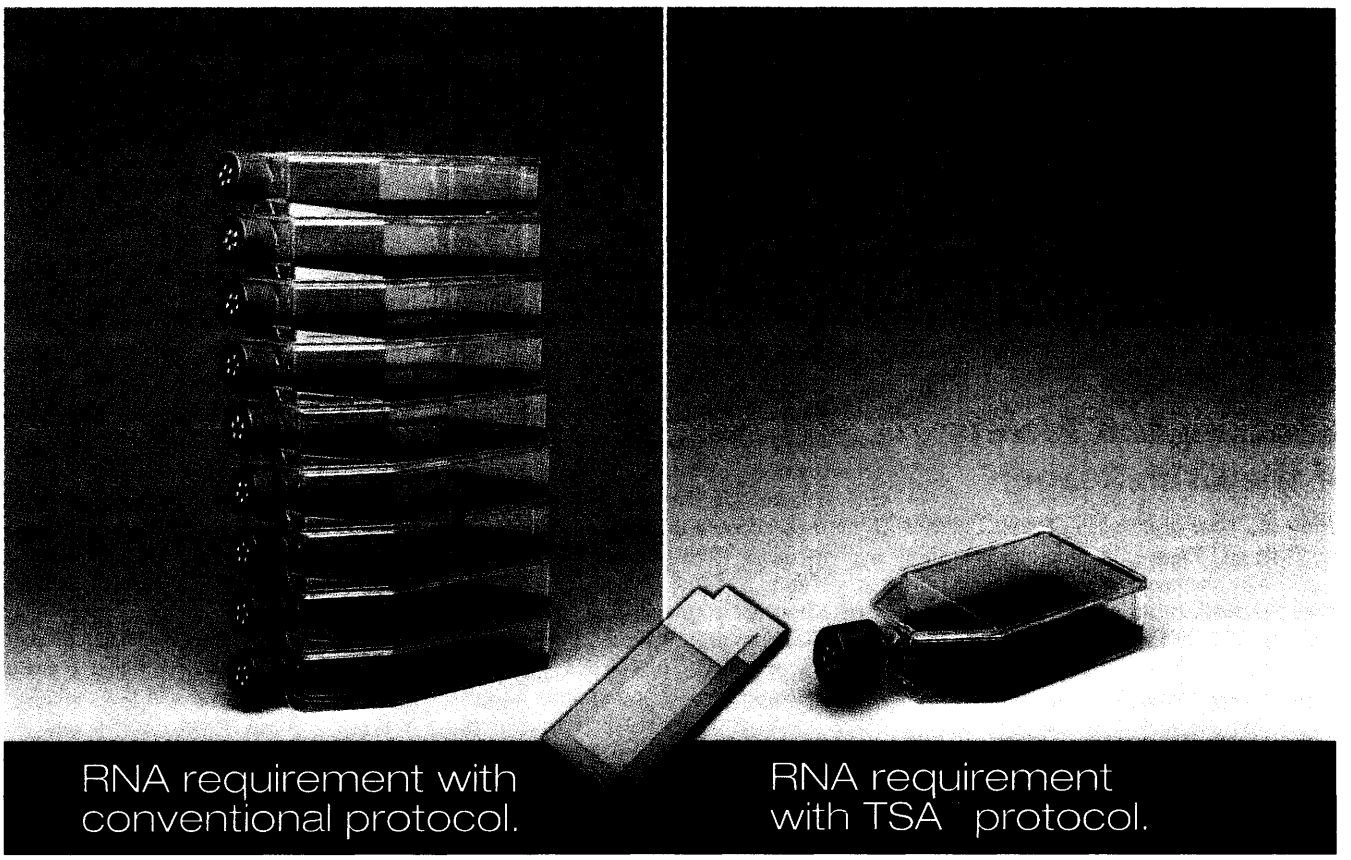

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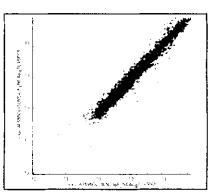

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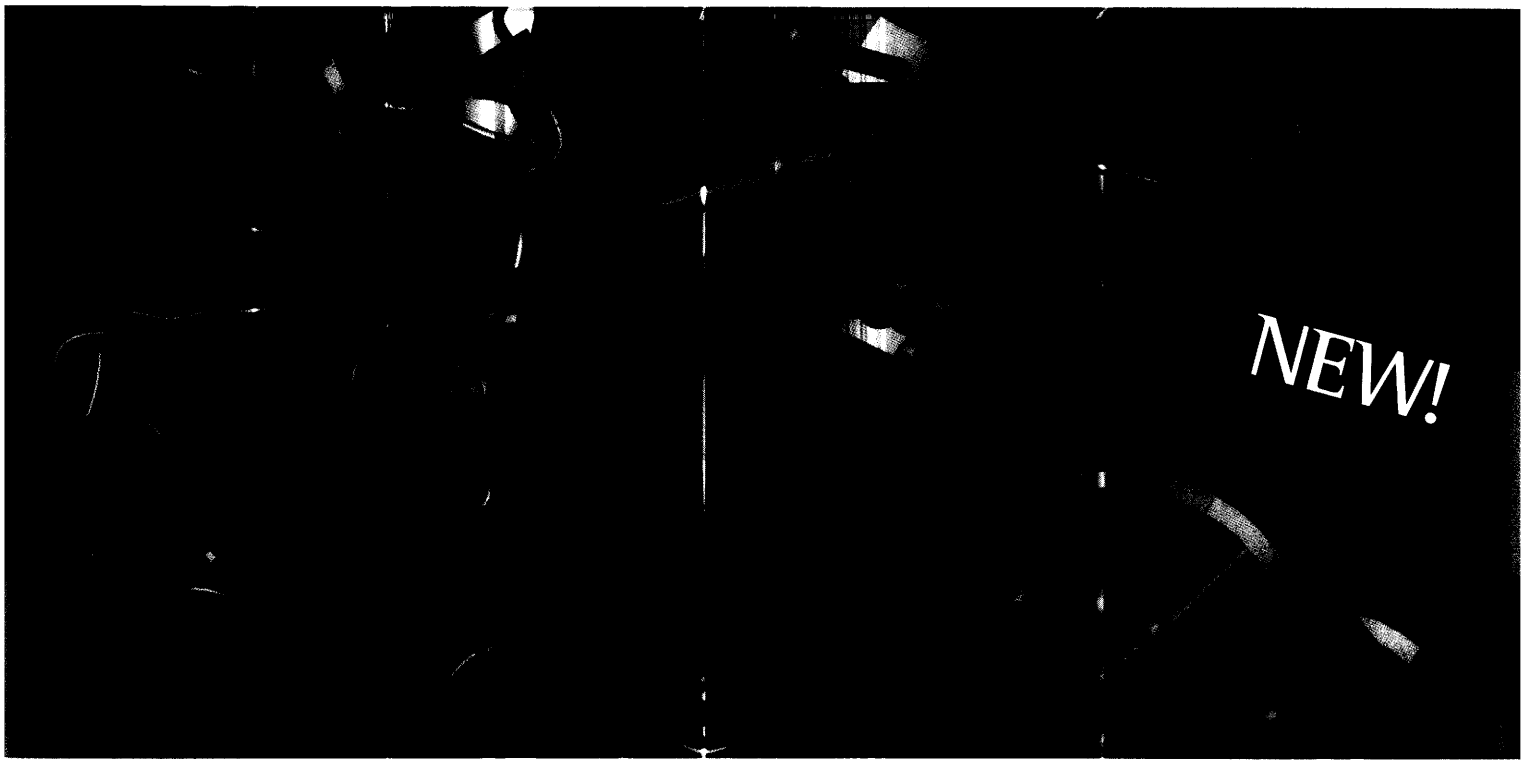

Picture: Model of a Taq DNA Polymerase with a DNA strand.

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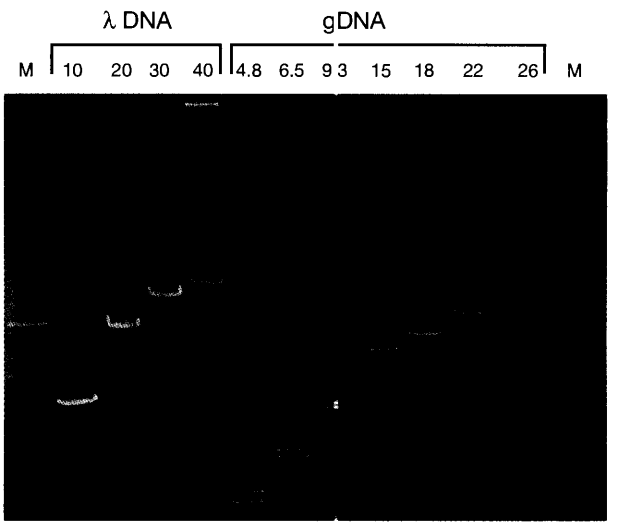

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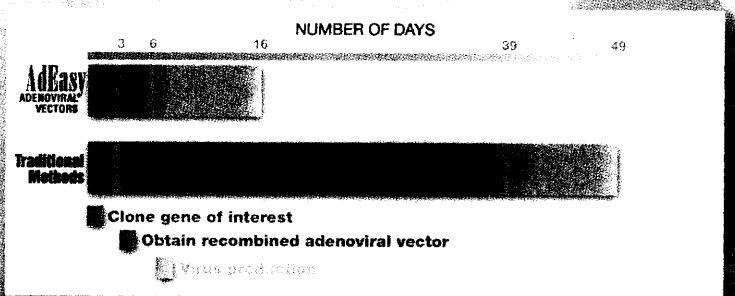

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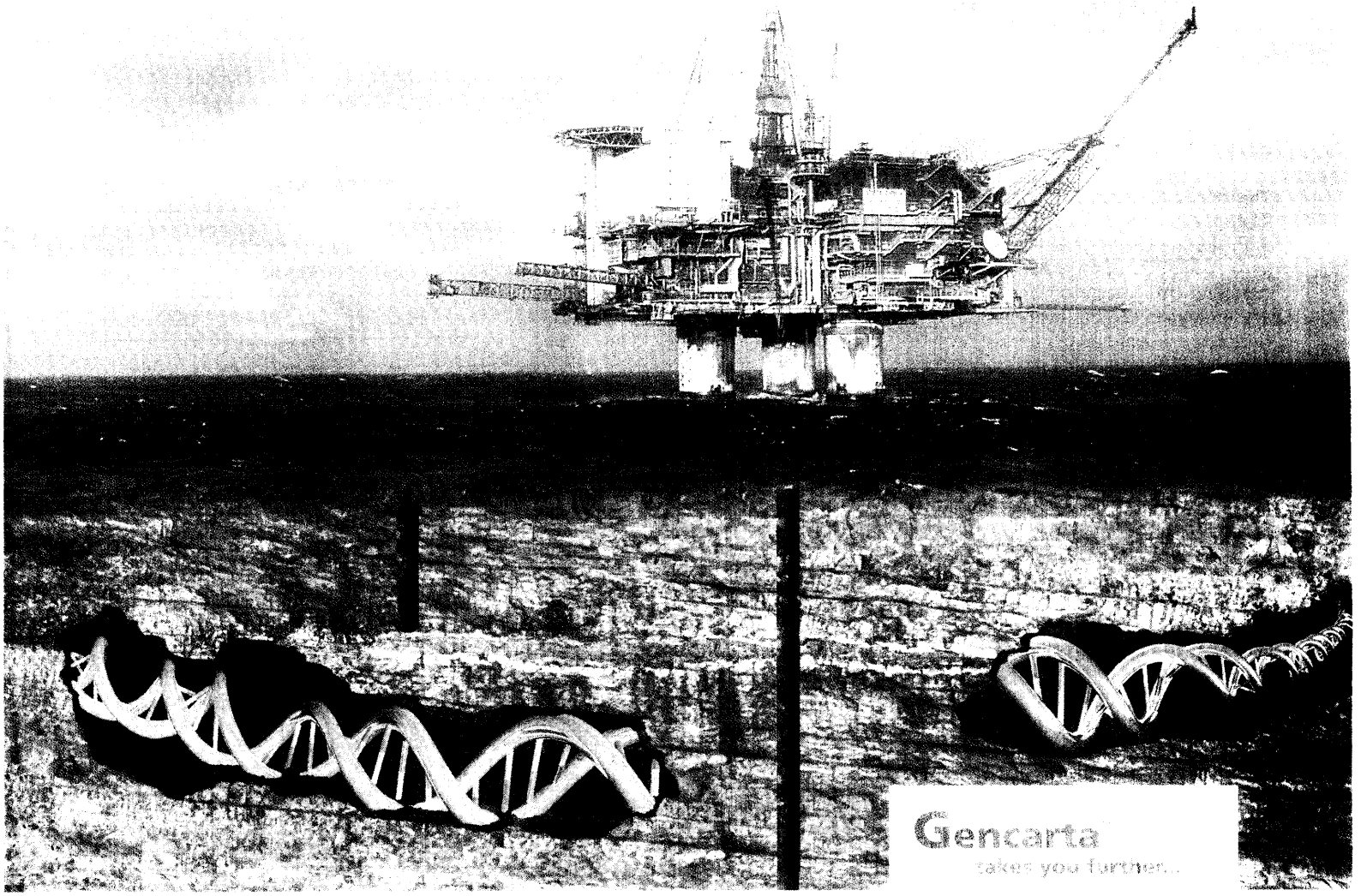

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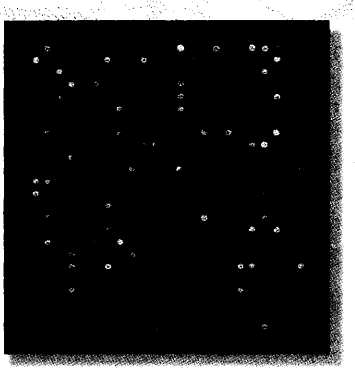

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Stephen Jay Gould...

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Stephen Jay Gould, *Board Chairman, AAAS*
Alexander Agassiz Professor of Zoology, Harvard University

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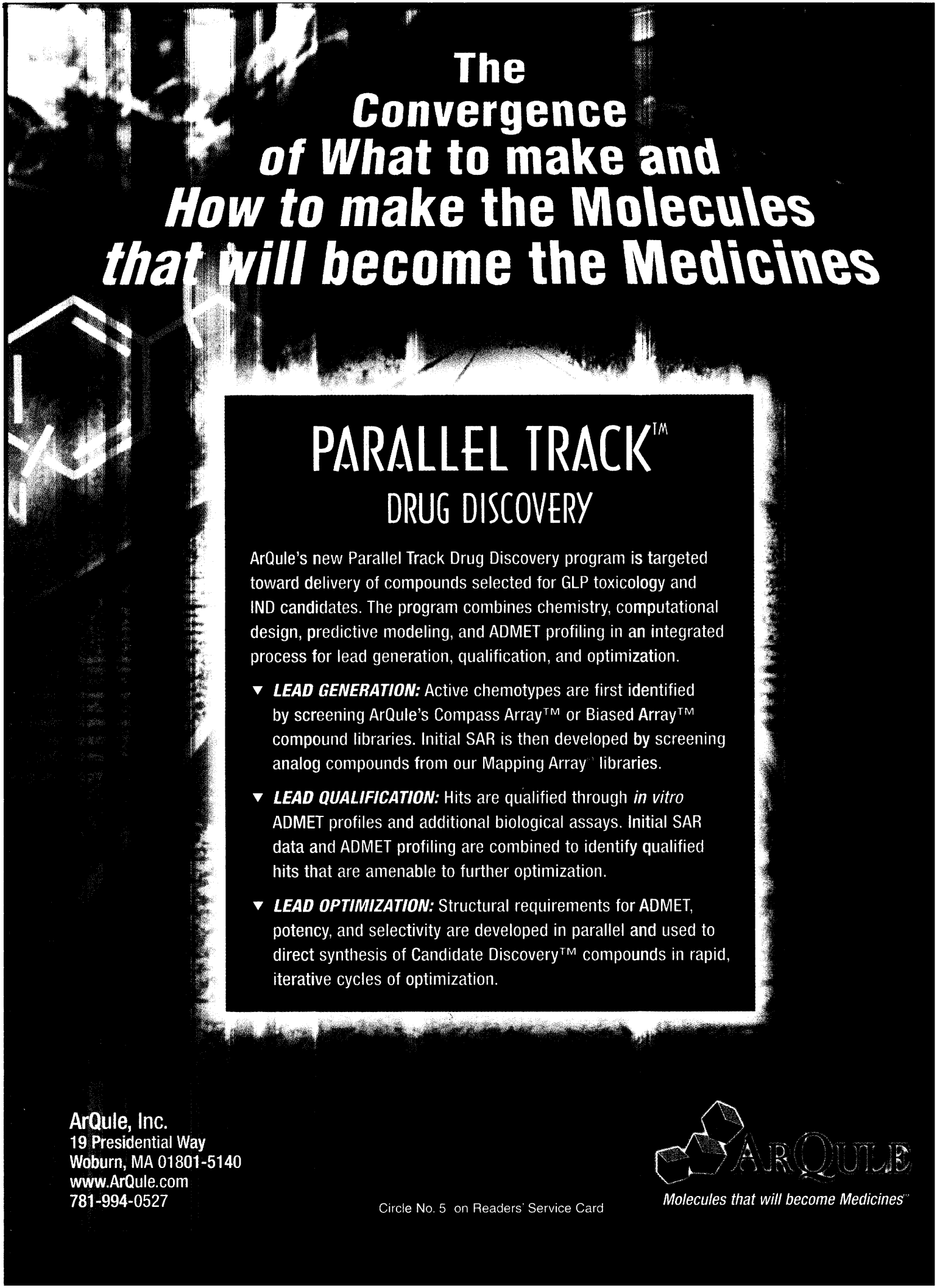
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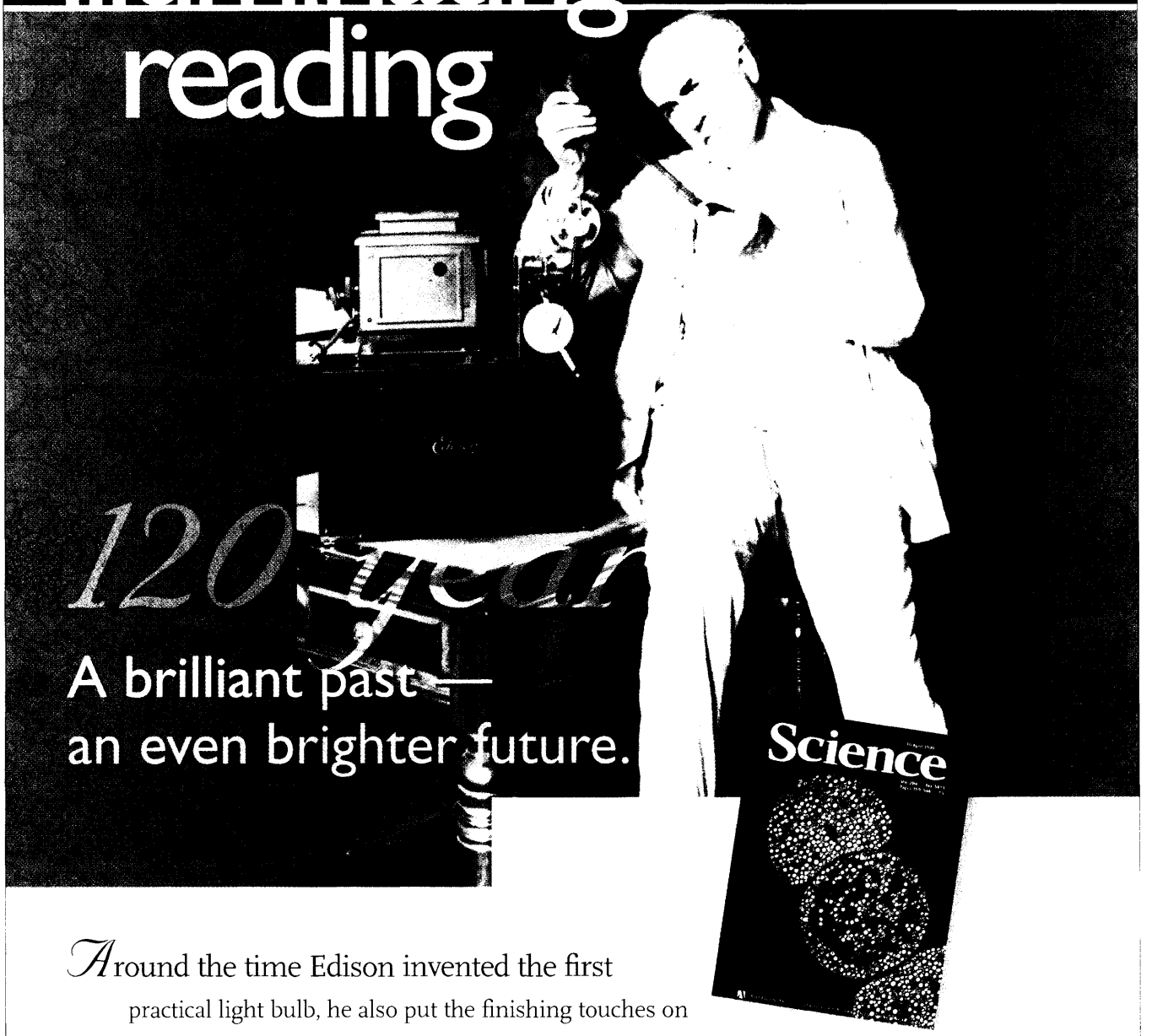

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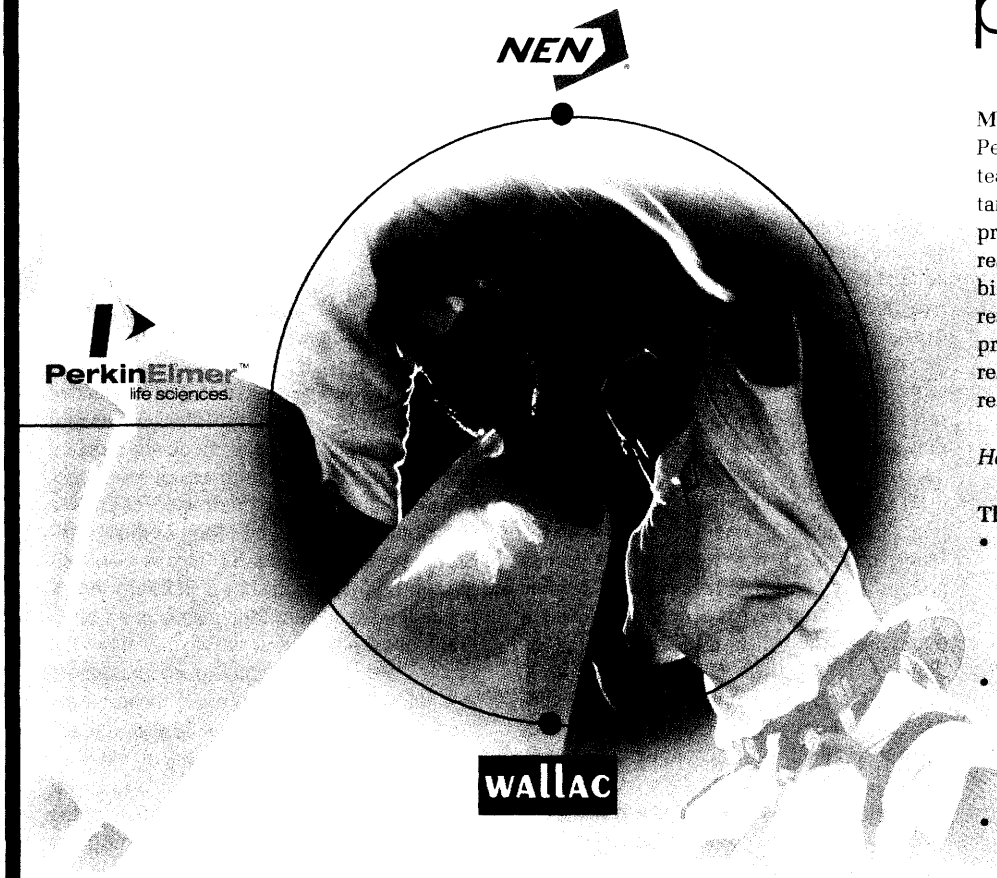

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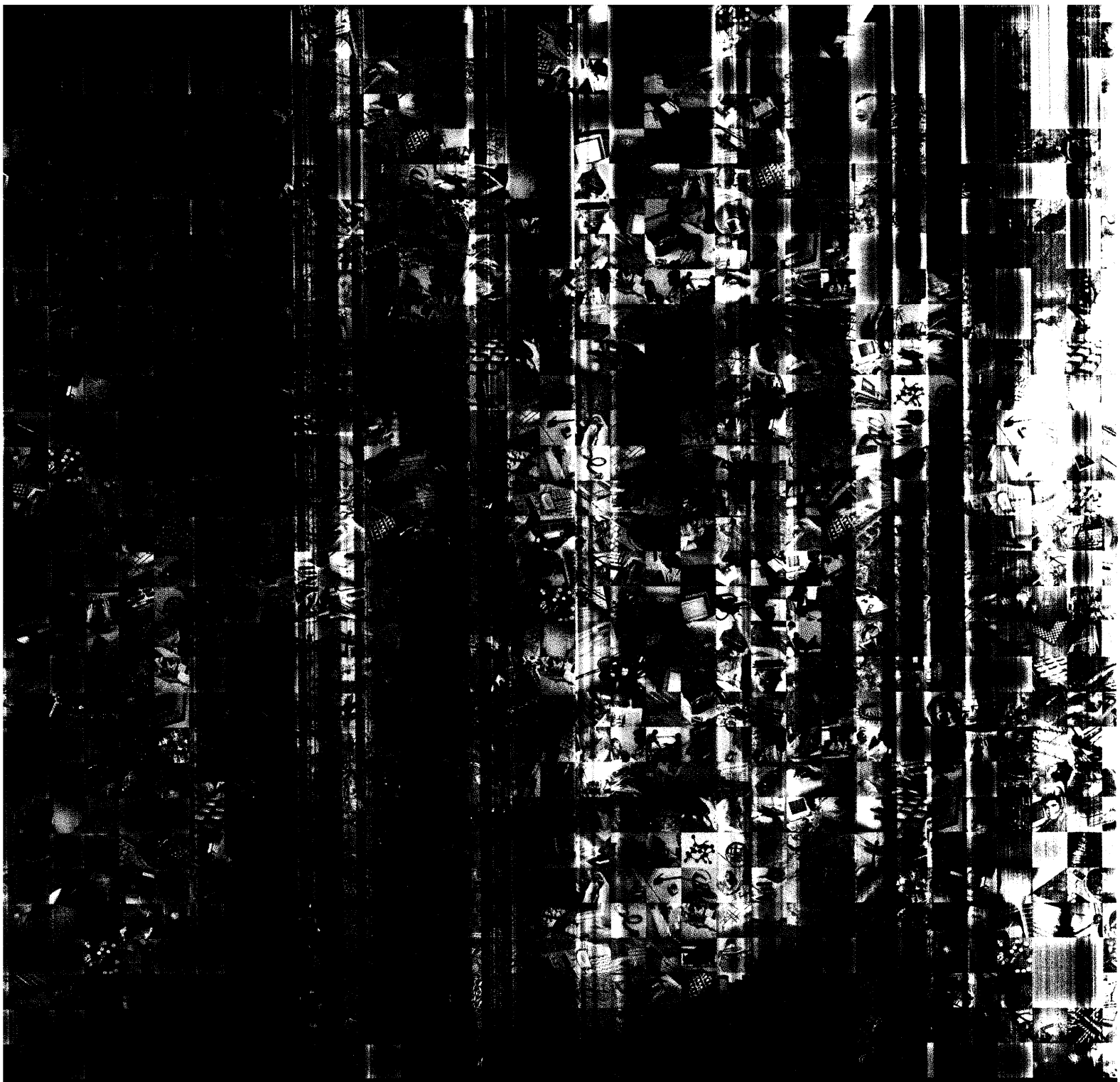

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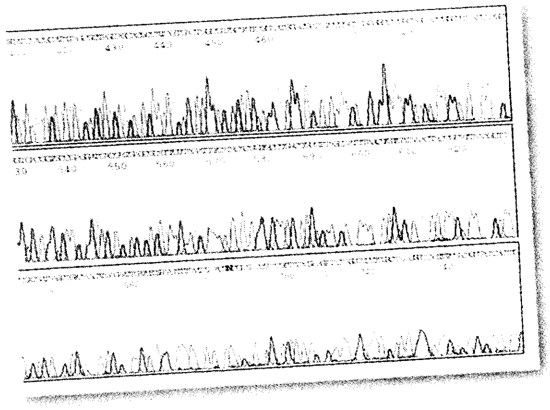

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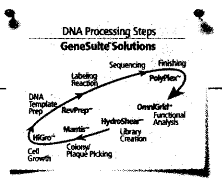

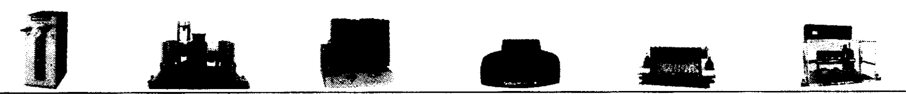

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