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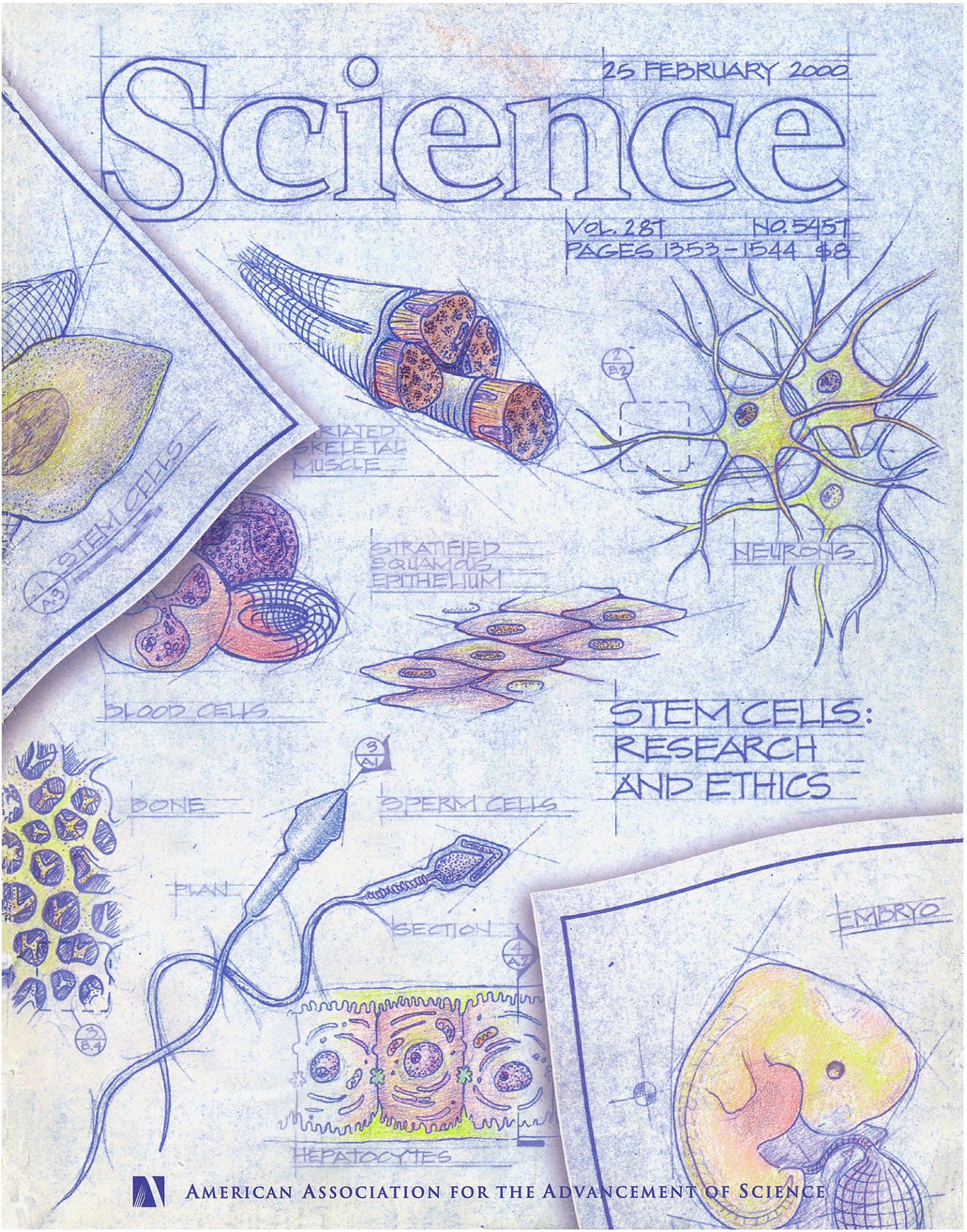

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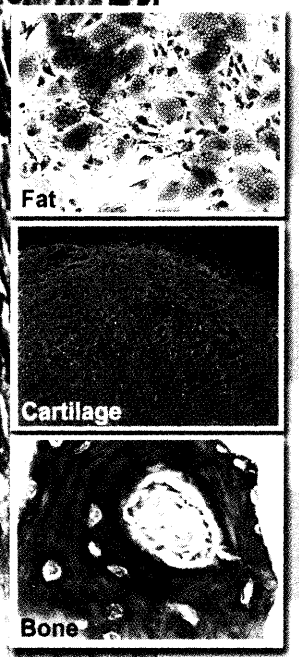

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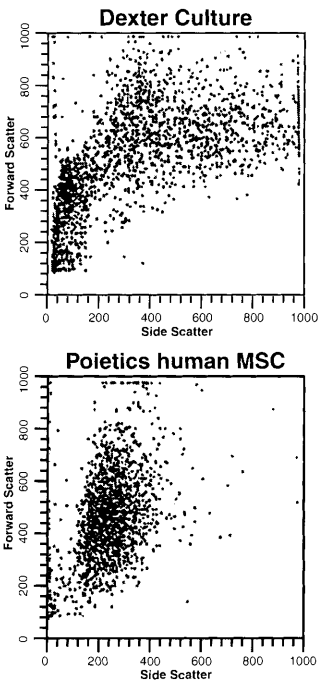

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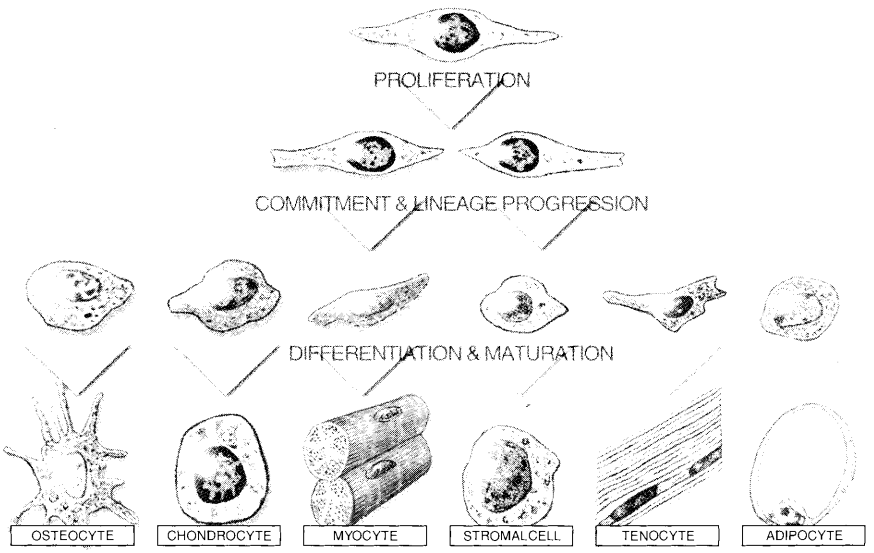

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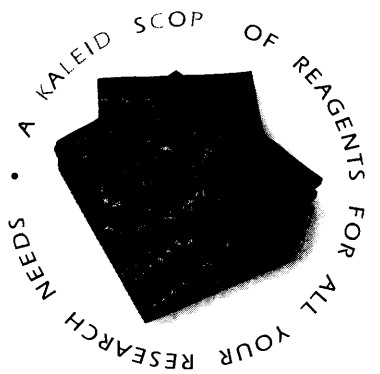

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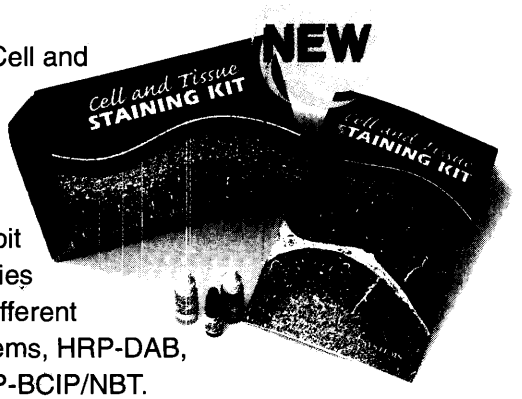

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Science

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COVER Stem cells can follow a variety of blueprints directing cell differentiation. But the final edifice is not built of stone, and differentiated cells show remarkable plasticity. See the special section on stem cells, beginning on page 1417, for information about the research, therapeutic implications, and ethical concerns relating to stem cells. [Illustration: Carin Cain]

1382
The forces that killed Brookhaven's reactor

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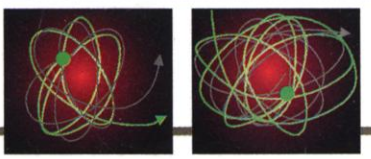
SCIENCE'S COMPASS

1409
In vivo versus in vitro

1406
Isolation and genetic variation

1447
Imaging single atoms in orbit



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How many eggs?

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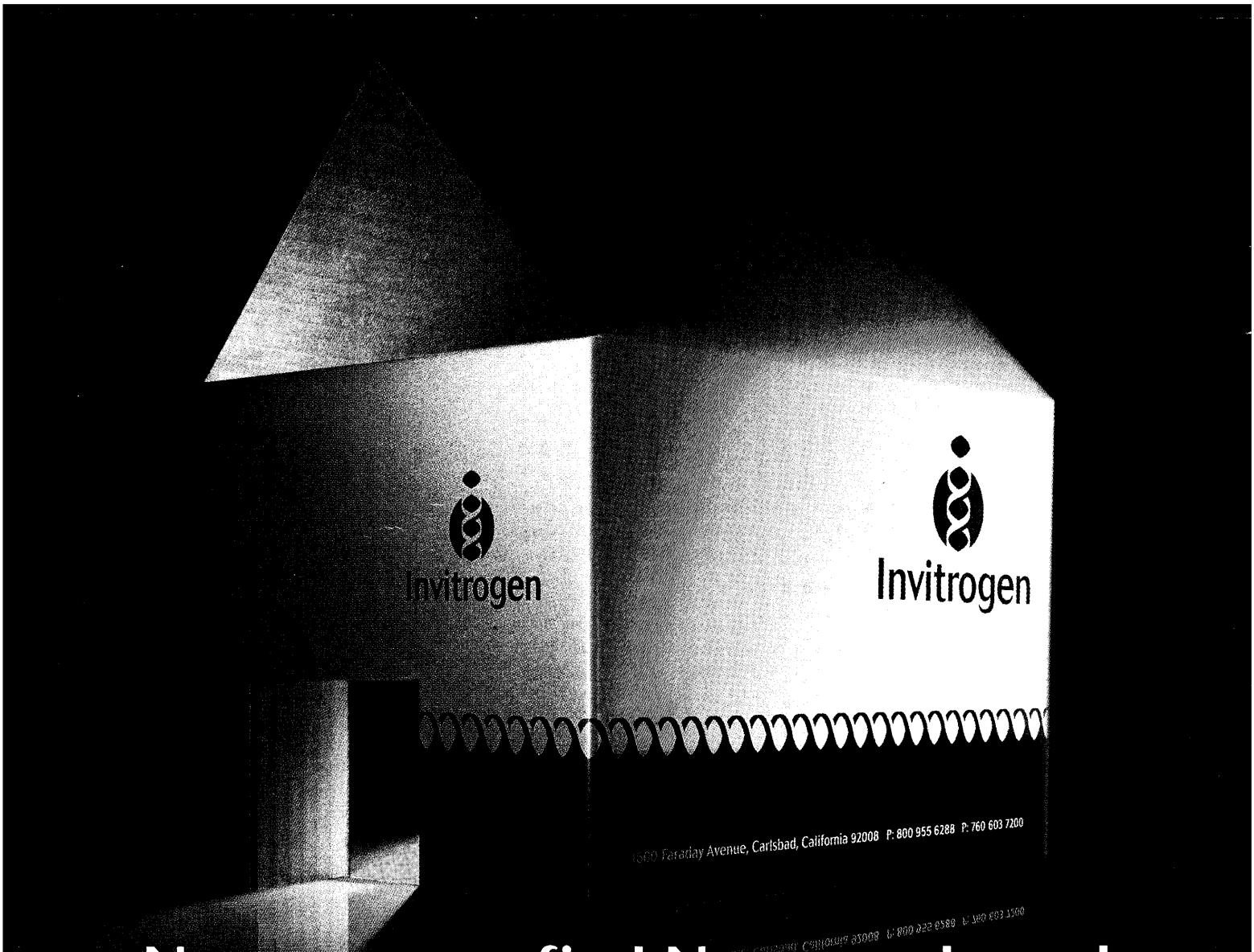

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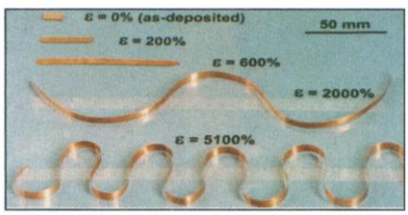
ATOM PATHWAYS

A form of optical microscopy has been developed to visualize the paths of individual cesium atoms in the gas phase. Hood *et al.* (p. 1447) trapped cesium atoms between two mirrored surfaces by using a probe laser beam. The combination of a single atom and a single photon from the laser field created a bound state analogous to the formation of a molecule. Variations in the probe beam's transmission corresponded to changes in the trajectory of the atom; the authors were able to reconstruct most of these atom trajectories with an inversion algorithm.

KEEPS ROLLING AND ROLLING...

If an ordinary metal wire is stretched or rolled many times, it will usually harden (and eventually break) because dislocations of atoms in the crystalline lattice build up at grain boundaries. If these dislocations could be made to diffuse faster, the metal



would remain plastic. Because the diffusion rates increase as grain size decreases, metals with nanometer-scale crystallites should exhibit "superplasticity" and remain ductile even after much processing. Lu *et al.* (p. 1463) describe an electrochemical deposition process for copper that creates such a nanocrystallite material. Samples can be cold-rolled to more than 50 times their original length and still remain ductile.

MAGNETIC LOGIC

Quantum cellular automata (QCA) is a proposed architecture for future microelectronics in which the quantum mechanical characteristics of the switching elements are used to perform the logical operations. However, most implementations to date have been restricted to very low temperatures because they have relied upon the small electrostatic forces between a pair of single electrons. Cowburn and Welland (p. 1466) introduce and demonstrate an architecture based on magnetism (MQCA), in which the magnetization of series of magnetic disks in response to an external field depends on the magnetization of a single control disk. The magnetic switching is not restricted to low temperatures and can operate at room temperature.

CLOSE-UP OF A CATALYST REACTION

Industrial heterogeneous catalytic processes usually proceed at high pressures, whereas laboratory surface science tools often require vacuum conditions. This "pressure gap" is quite significant, because the catalytic activity of a surface often changes significantly with pressure. Over *et al.* (p. 1474; see the Perspective by Knözinger) study one such reaction, the oxidation of carbon monoxide on ruthenium, which proceeds very efficiently at high pressure but not at low pressure. An oxygen-rich overlayer on the surface may be responsible for the catalytic activity, but detailed evidence has been lacking. The authors investigated such an oxygen-rich surface phase using low-energy electron diffraction and scanning tunneling microscopy. These results, along with those from density functional calculations, show that this oxygen-rich overlayer is actually a surface oxide, RuO_2. The binding strengths of CO and O atoms are more comparable on the oxide than on the metal, which facilitates the reaction.

IMMUNIZATION AGAINST STROKE AND EPILEPSY

The *N*-methyl-D-aspartate (NMDA) receptor is important in brain plasticity and development and may also be involved in the pathology that results from neurological disorders. During *et al.* (p. 1453; see the news story by Helmuth) have found that immunization of mice with a DNA vaccine encoding the NR1 subunit of the NMDA receptor could induce antibody-mediated, but not cellular, immunity in rats. This treatment induced protective effects against kainate-induced seizures (a model for temporal lobe epilepsy) and endothelin-1–induced middle cerebral artery occlusion (a model for stroke). No effects on movement or behavior were observed. Although long-term effects of such immunization are not yet known, it has the potential of having fewer side effects than pharmacological approaches with NMDA receptor antagonists.

HOLDING BACK A DEATH SIGNAL

In the worm *Caenorhabditis elegans*, certain genes are critical for the timed death of a cell during development. How the protein products from these genes regulate one another in vivo is not clear. Chen *et al.* (p. 1485) report that the pro-death protein CED-4 is translocated from the mitochondria (where it colocalizes with the anti-death protein CED-9) to the perinuclear membrane upon receipt of a death signal, such as expression of the pro-death protein EGL-1. The movement of CED-4 to the perinuclear membrane was not dependent upon caspases and was a prerequisite for normal death, which suggests that the role of CED-9 may be to sequester CED-4 at the mitochondria until the appropriate developmental time for cell death.

FOMENTING RESISTANCE

The evolution of antibiotic resistance in bacteria can be costly to the microbe in terms of biological fitness. These fitness costs can determine whether a resistant genotype spreads through a population. However, bacteria also have the capacity for mutation to compensate for these costs, and these compensatory mutations can take a variety of forms. Bjorkman *et al.* (p. 1479; see the Perspective by Bull and Levin) examine the conditions under which such mutations are selected in *Salmonella*. The form and frequency of compensatory mutations differed, depending on the environment of the bacteria, in this case a host organism versus laboratory culture medium. They suggest that the management of antibiotic resistance will be hampered if it relies solely on data gathered in vitro.

PROTECTING THE NEST

Behavioral ecologists studying birds have long been interested in the evolution of patterns of parental care and clutch size. In a large, long-term comparative study of bird species in Argentina and Arizona, Martin *et al.* (p. 1482) provide evidence that nest predation is also an important factor shaping the evolution of parental care difference (measured as nest visiting frequency and food delivery rate) among bird species. Both in North and South American sites, clutch size is positively correlated with food delivery rate. However, they found no relation between nest predation and the pronounced latitudinal gradient in clutch size (small in the South but large in the North), an enigma that still requires a solution.

CONTINUED ON PAGE 1363

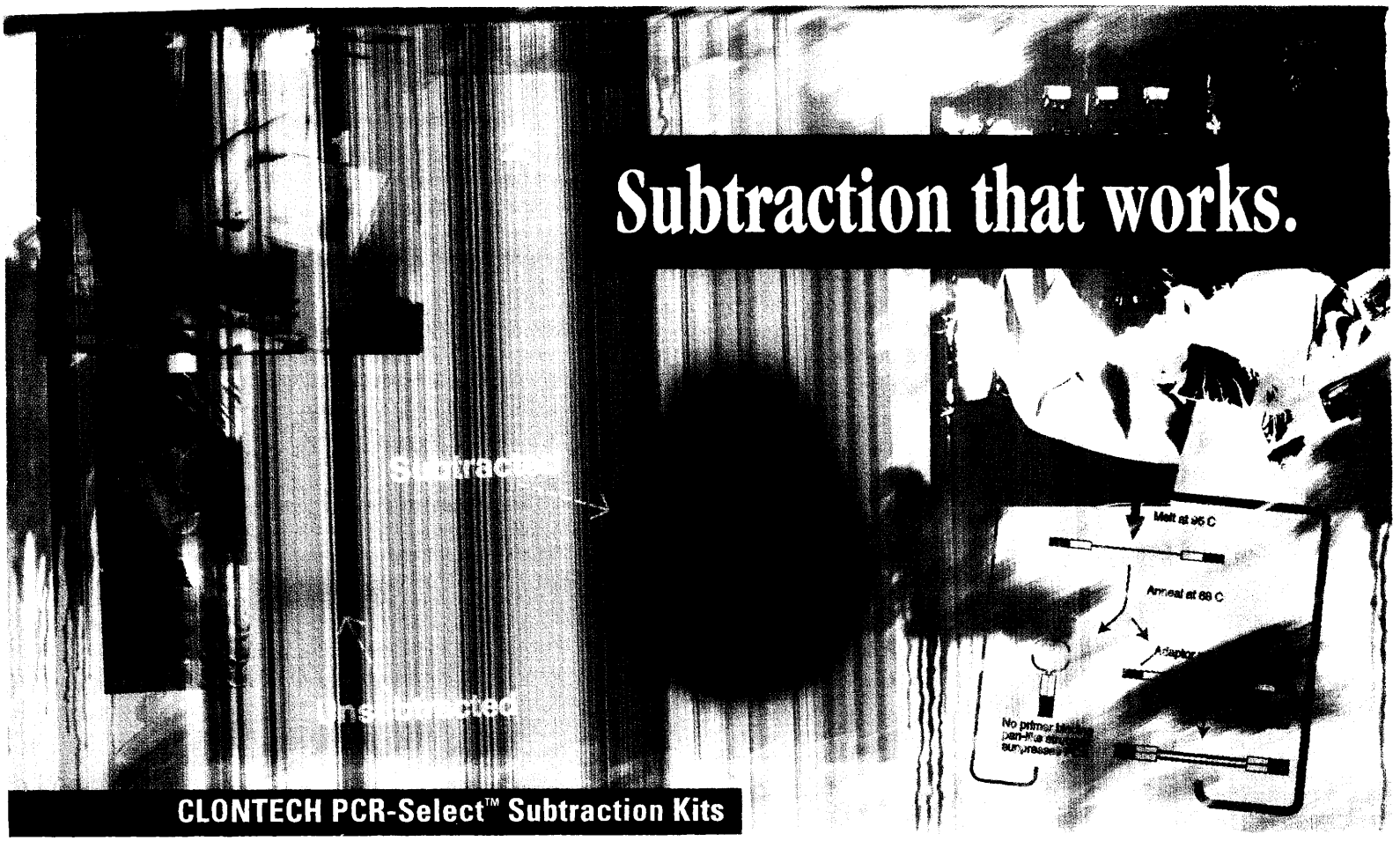
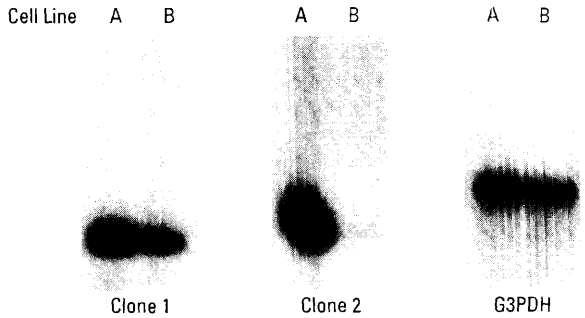


Illustration inspired by the art of Robert Rauschenberg (1925).



PCR-Select is a powerful method for isolating and cloning differentially expressed genes. cDNA amplified from two cell lines (A & B) was blotted and hybridized to labeled cDNA clones isolated using the PCR-Select Differential Screening Kit (#K1808-1). Results confirm differential expression of both clones. Control hybridization with G3PDH, a housekeeping gene, indicates lanes were equally loaded.

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 1361

STAYING IN THE SWIM

Mammalian spermatogenesis depends on continual replenishment of differentiating spermatids from a pool of spermatogonial stem cells. Meng *et al.* (p. 1489) now show that glial cell line–derived neurotrophic factor (GDNF), known for its importance in directing development of neuronal cells and kidney morphogenesis, also regulates spermatogenesis. In transgenic mice, oversupply of GDNF limits differentiation of spermatogonia, whereas undersupply of GDNF results in early depletion of these stem cells. These results may offer insight into some mechanisms of male infertility.

PREVENTING JEKYLL'S CONVERSION TO HYDE

The transmissible spongiform encephalopathies (BSE in cows and Creutzfeldt-Jakob disease in humans) are fatal, neurodegenerative diseases for which there is no treatment. It is believed that a critical event in pathogenesis is the conversion of the normal form of a cellular prion protein (PrP-sen) into an abnormal protease-resistant form (PrP-res). Transgenic mice that overexpress the hamster version of normal PrP-sen usually die within 80 to 100 days when infected with hamster scrapie. Priola *et al.* (p. 1503) show that treating these infected transgenic mice with tetrapyrrole compounds (effective at preventing the conversion of PrP-sen to PrP-res in vitro) starting on the first day of infection resulted in greatly increased survival times. Certain tetrapyrrole compounds may prove valuable for the prophylactic treatment of the transmissible spongiform encephalopathies.

UNLOCKING VIRAL LATENCY

Herpes simplex virus can maintain itself in a latent state and then become reactivated to start active replication and induce diseases of the eye and genital tract. This process depends on transcription of the viral latency-associated transcript gene *LAT*. Perng *et al.* (p. 1500) have determined that *LAT*-containing viruses block apoptosis in rabbit trigeminal ganglia, and thus promote survival of infected neurons. Similar results were obtained when cultured cells were infected with a plasmid containing *LAT*.

TECHNICAL COMMENT SUMMARIES

Caspase Phosphorylation, Cell Death, and Species Variability

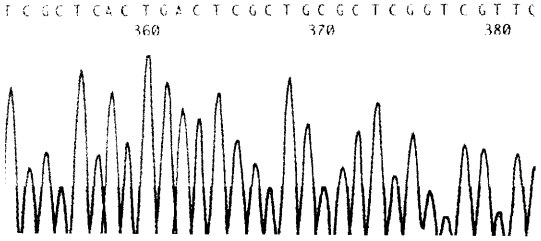
The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/287/5457/1363a

Cardone *et al.* (Reports, 13 November 1998, p. 1318) showed that phosphorylation by the kinase Akt prevents the activation of pro-caspase-9, thereby demonstrating that caspases, which are key players in programmed cell death, can be directly regulated by protein phosphorylation. Rodriguez *et al.*, however, note that "despite the close similarity between human and mouse proteins," mouse caspase-9 has no Akt phosphorylation sites, and that such sites are also absent from dog kidney cells. "Either it must be assumed that Akt regulates apoptosis differently in mice and humans," they conclude, "or the notion that caspase-9 is regulated by Akt phosphorylation has to be reexamined." Reed *et al.* respond that the absence of an Akt phosphorylation site in "shorter-lived lower mammals . . . suggests that this phosphorylation site evolved relatively recently in humans." The original work of Cardone *et al.*, they stress, was performed in human cell lines, and the work thus remains potentially relevant to human disease, especially "pathologies (such as cancer or neurodegenerative diseases) where cell accumulation or cell death occurs."

The Nature of Ant Colony Success

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/287/5457/1363b

Cole and Wiernasz (Reports, 6 Aug. 1999, p. 891) found that harvester-ant colonies with high genetic diversity enjoyed strong survival advantages relative to lower diversity colonies, and tied that fitness advantage to polyandry—multiple matings by a single queen in the colony. Fjerdingstad and Keller observe that polygyny (multiple queens per nest) could also lower within-colony relatedness and "has been shown to be associated with greater colony size and higher productivity in several ant species." Cole and Wiernasz respond that there is little evidence that multiple queens are common in the genus or species studied and that a variety of arguments suggest that polygyny is an unlikely explanation for their results.



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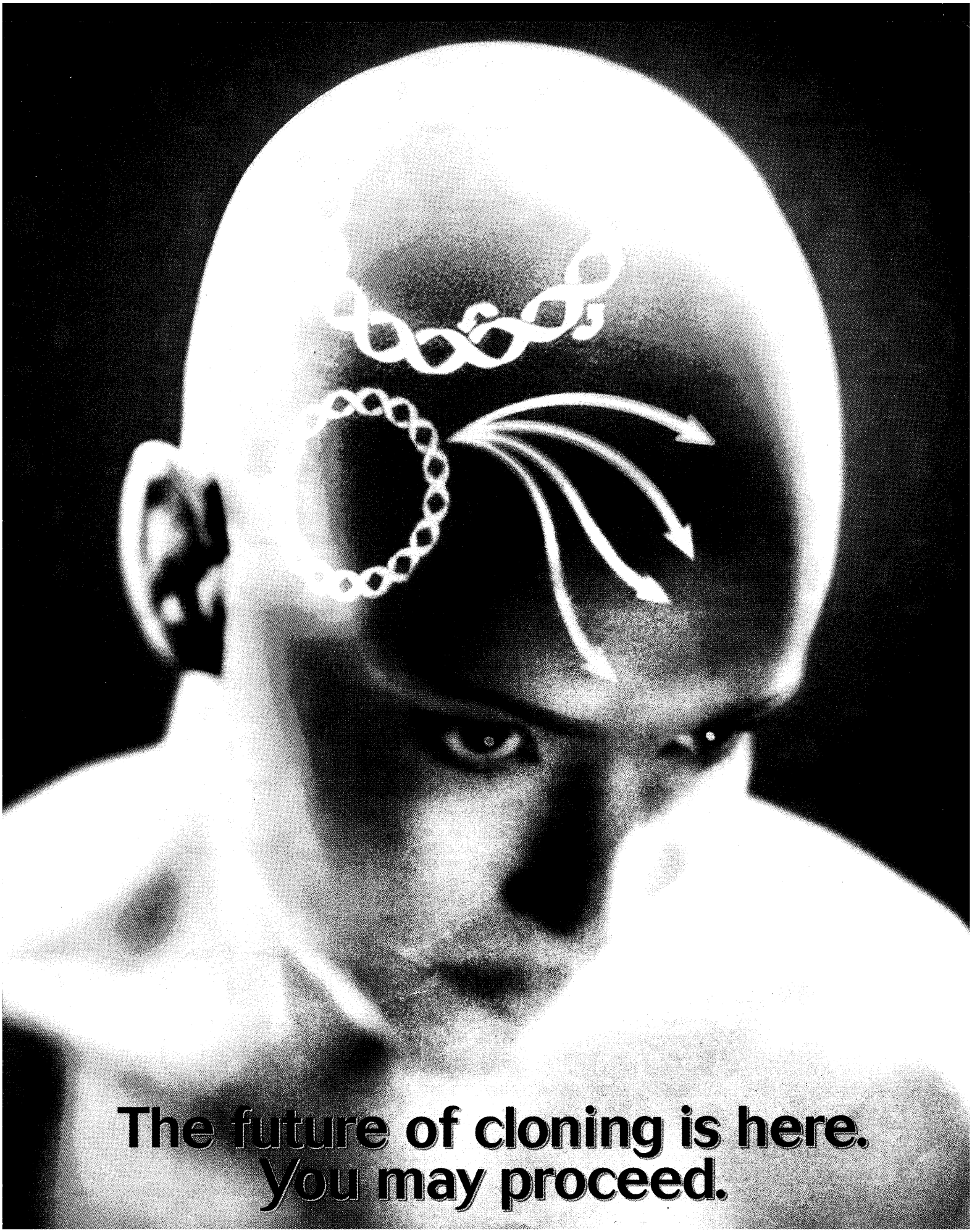
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Figure 1-Rapid Cloning of the Gene of Interest Using the Echo™ Cloning System

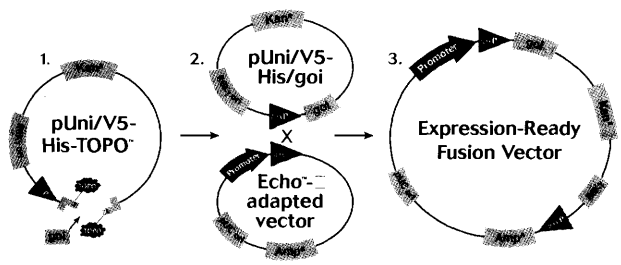

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Table 1-Echo™-Adapted Expression Vectors

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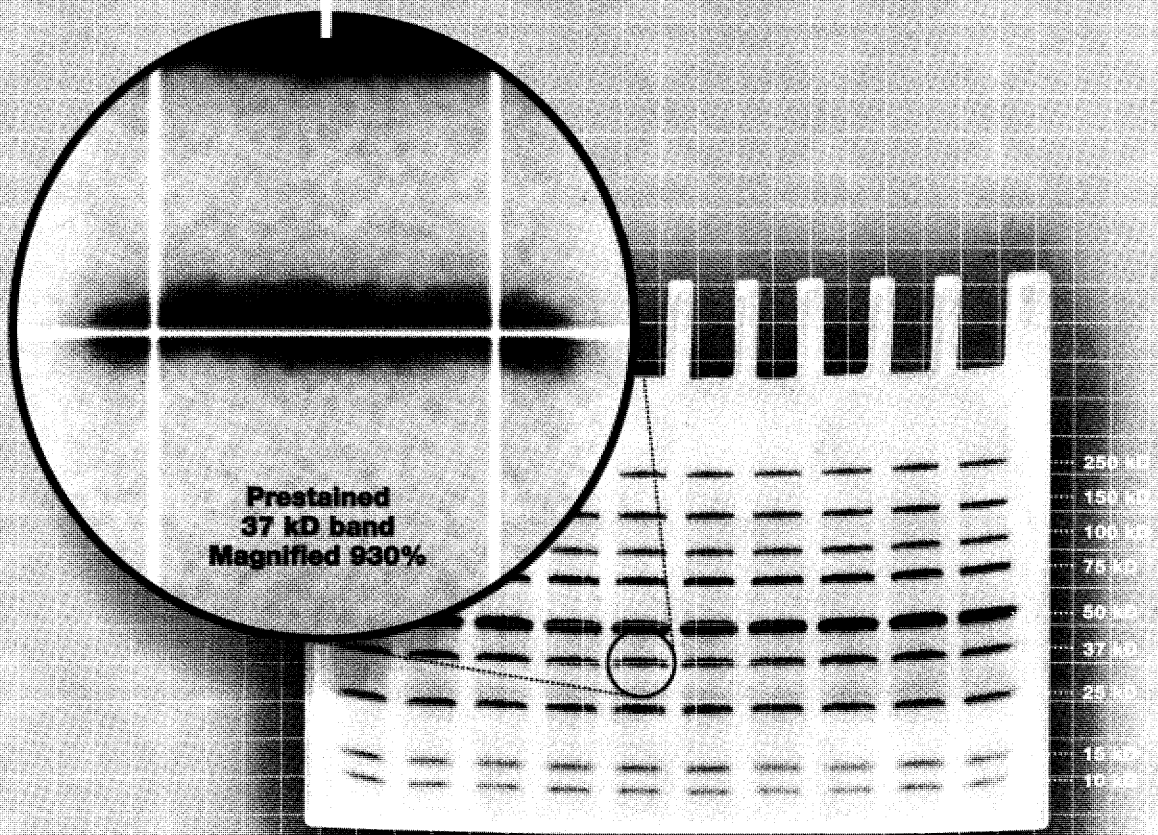

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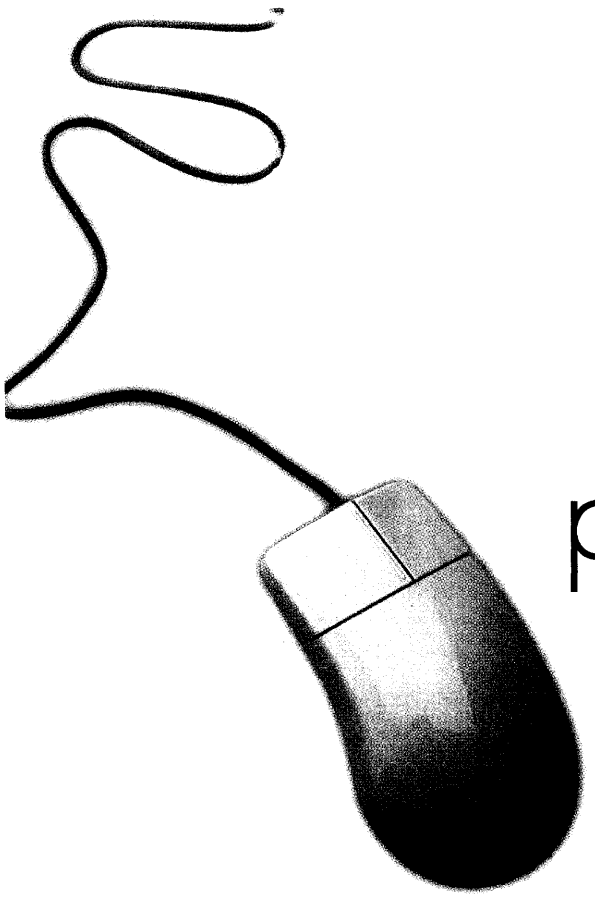

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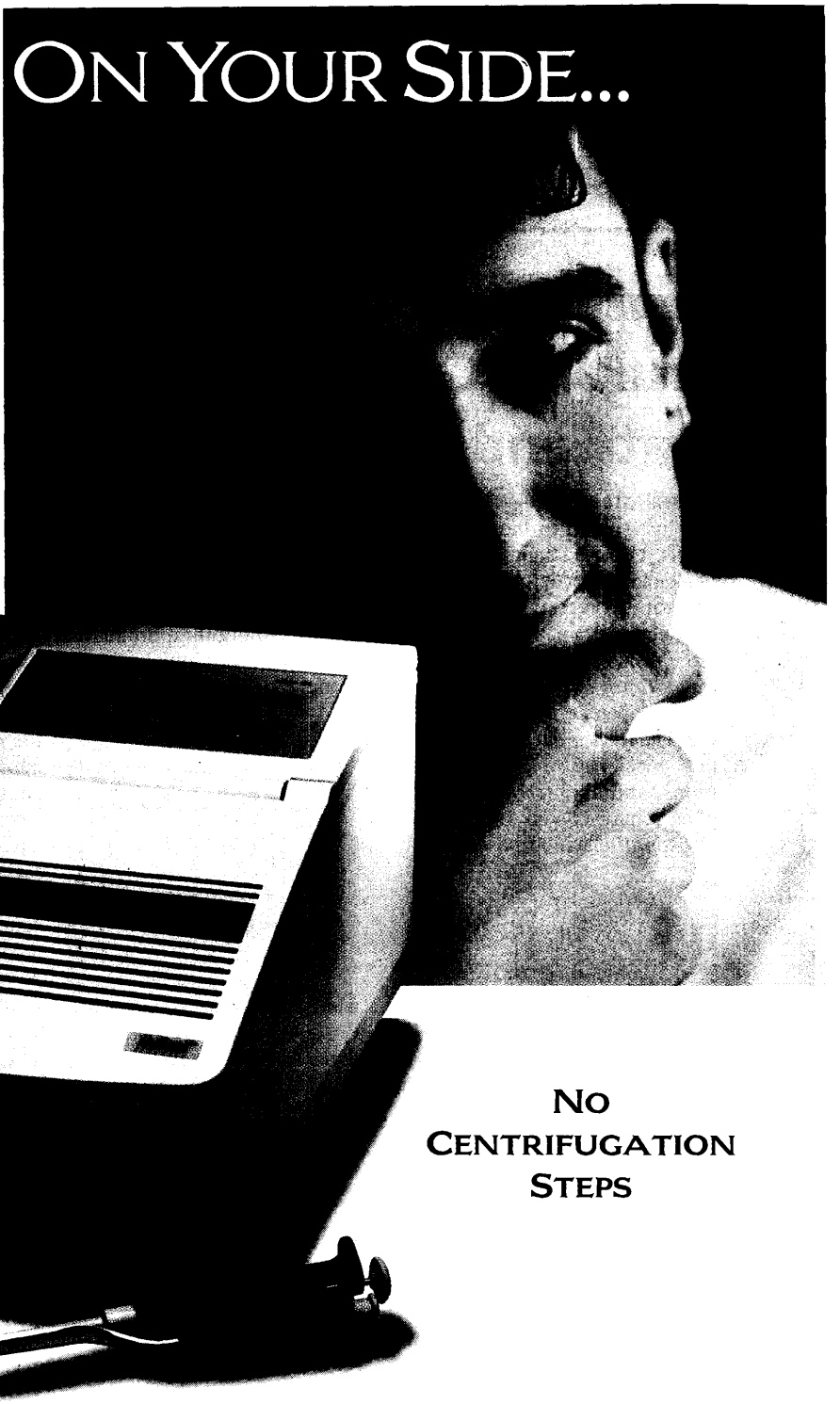

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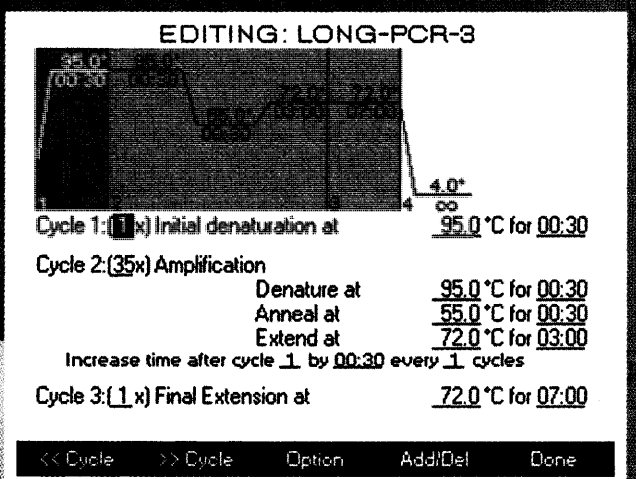

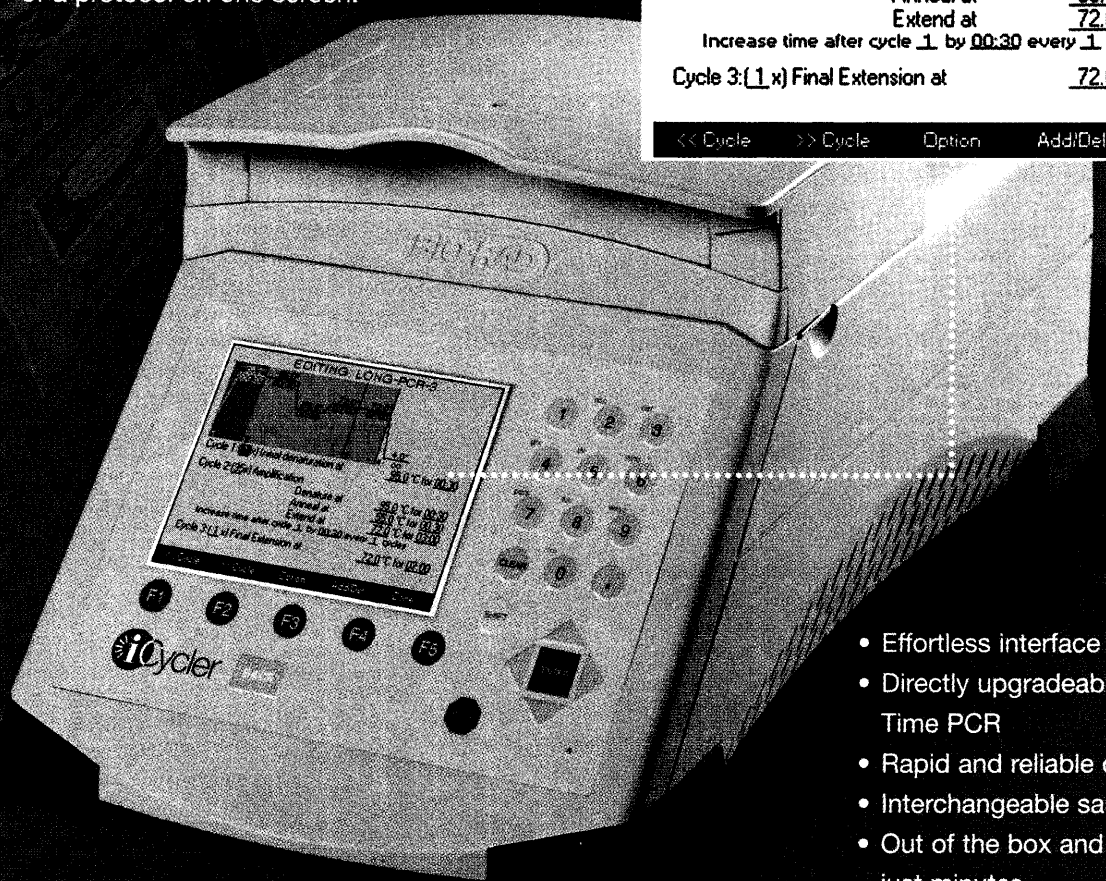

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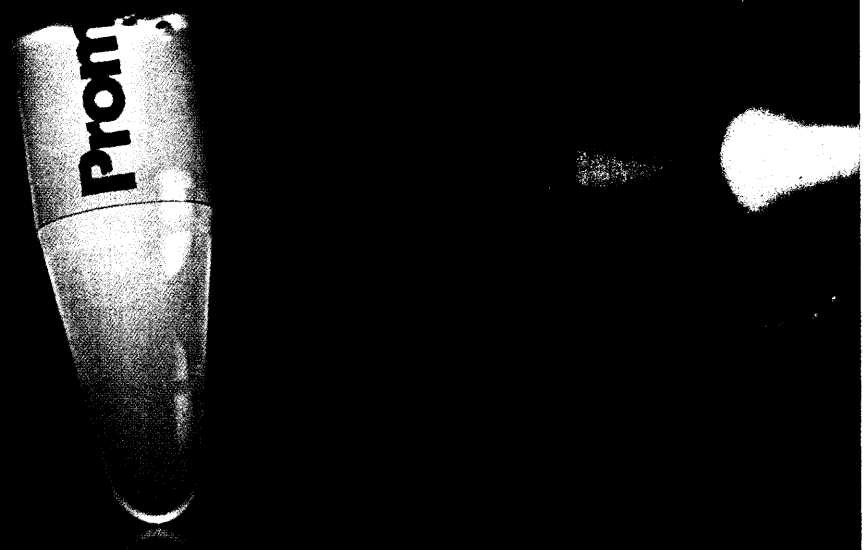

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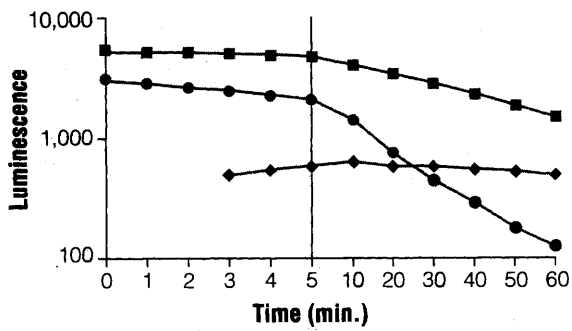

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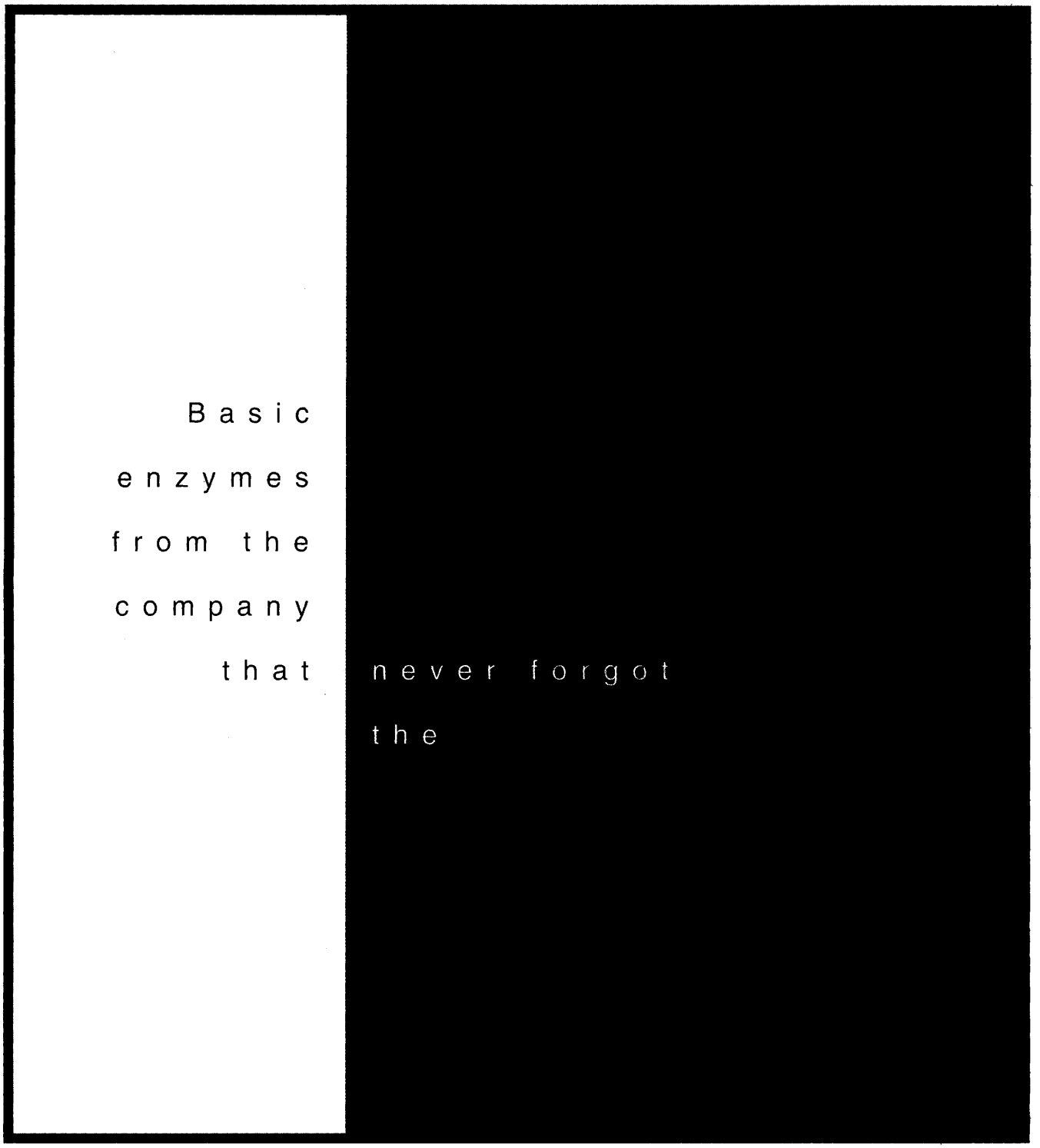

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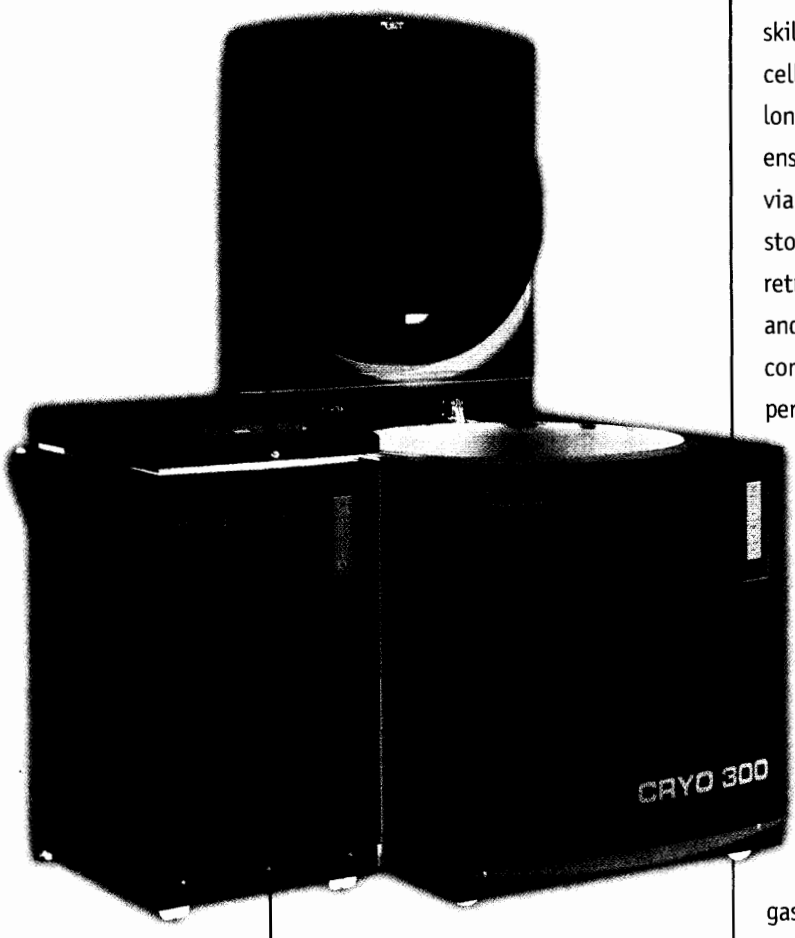

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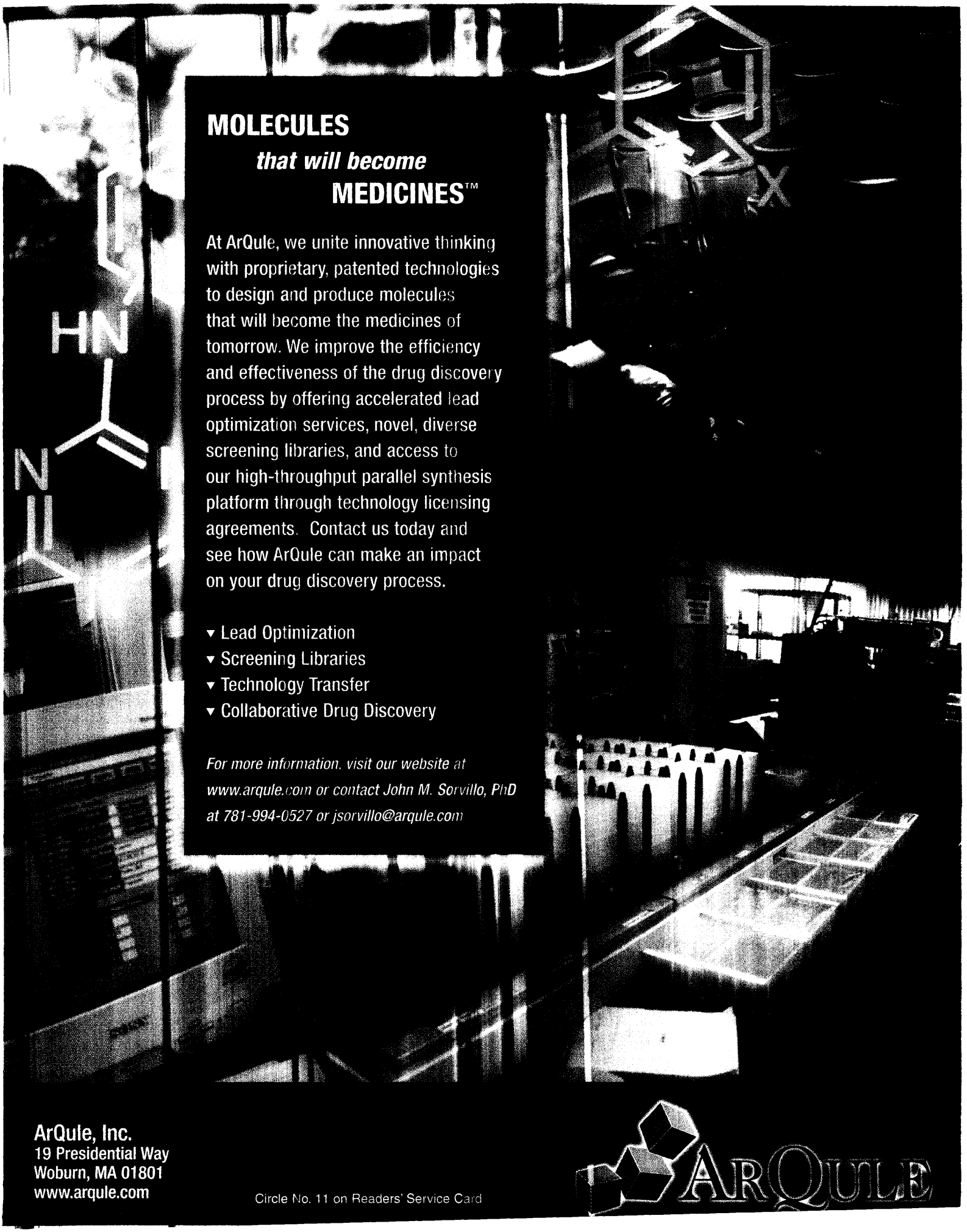

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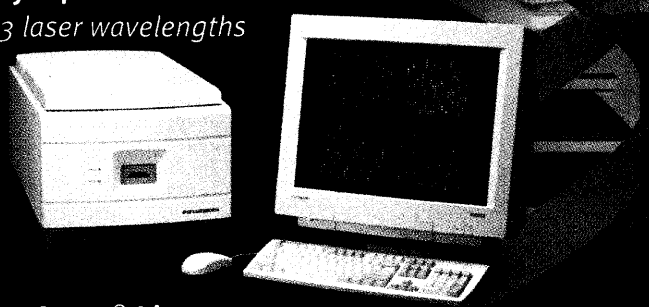

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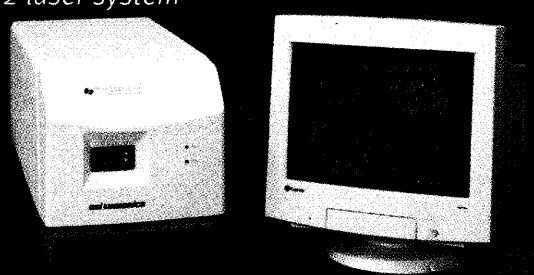

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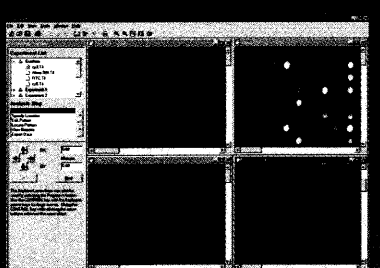

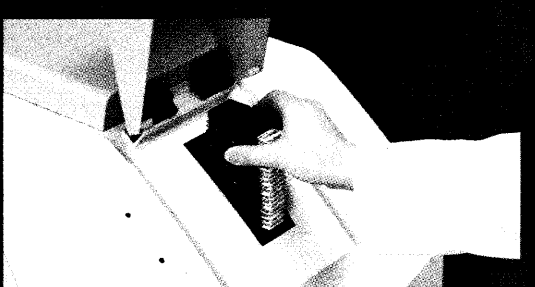

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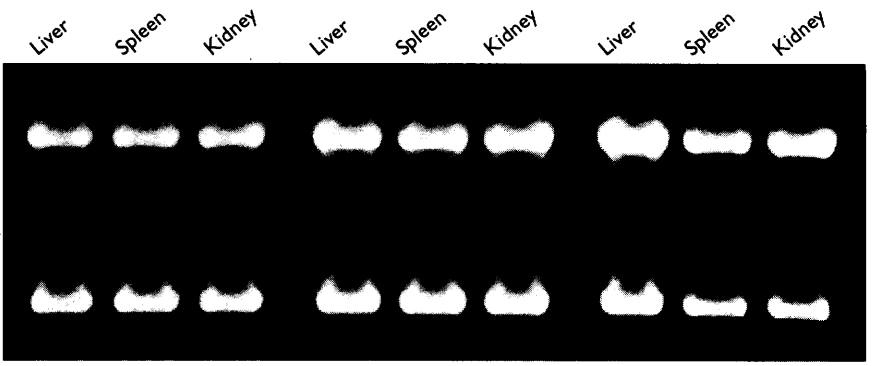

Figure 1a. Quality of RNA isolated from Tissue Stored in RNA*later*™ Solution. Fresh mouse tissues were dissected and stored in RNA*later*™ at 37°C for 1 day, room temperature for 1 week, or 4°C for 1 month. RNA was isolated using TRI Reagent® (MRC) and analyzed using denaturing agarose gel electrophoresis.

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