15 September 2000

Science

Vol. 289 No. 5486
Pages 1829–1992 $8

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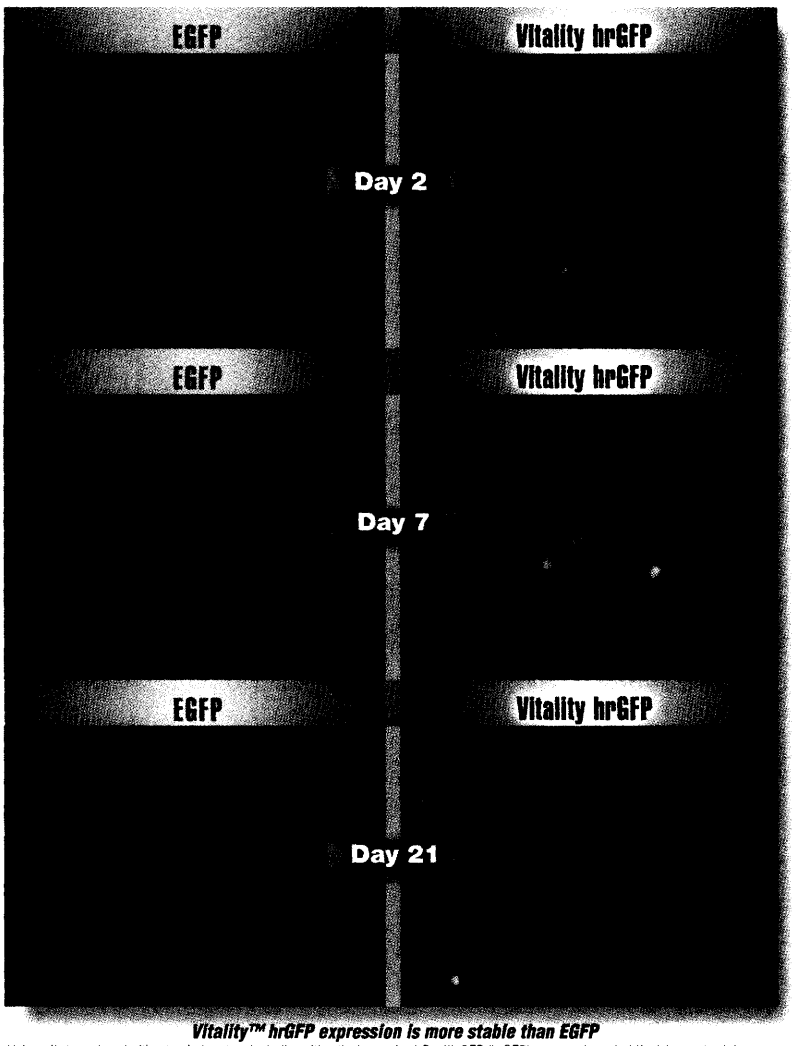

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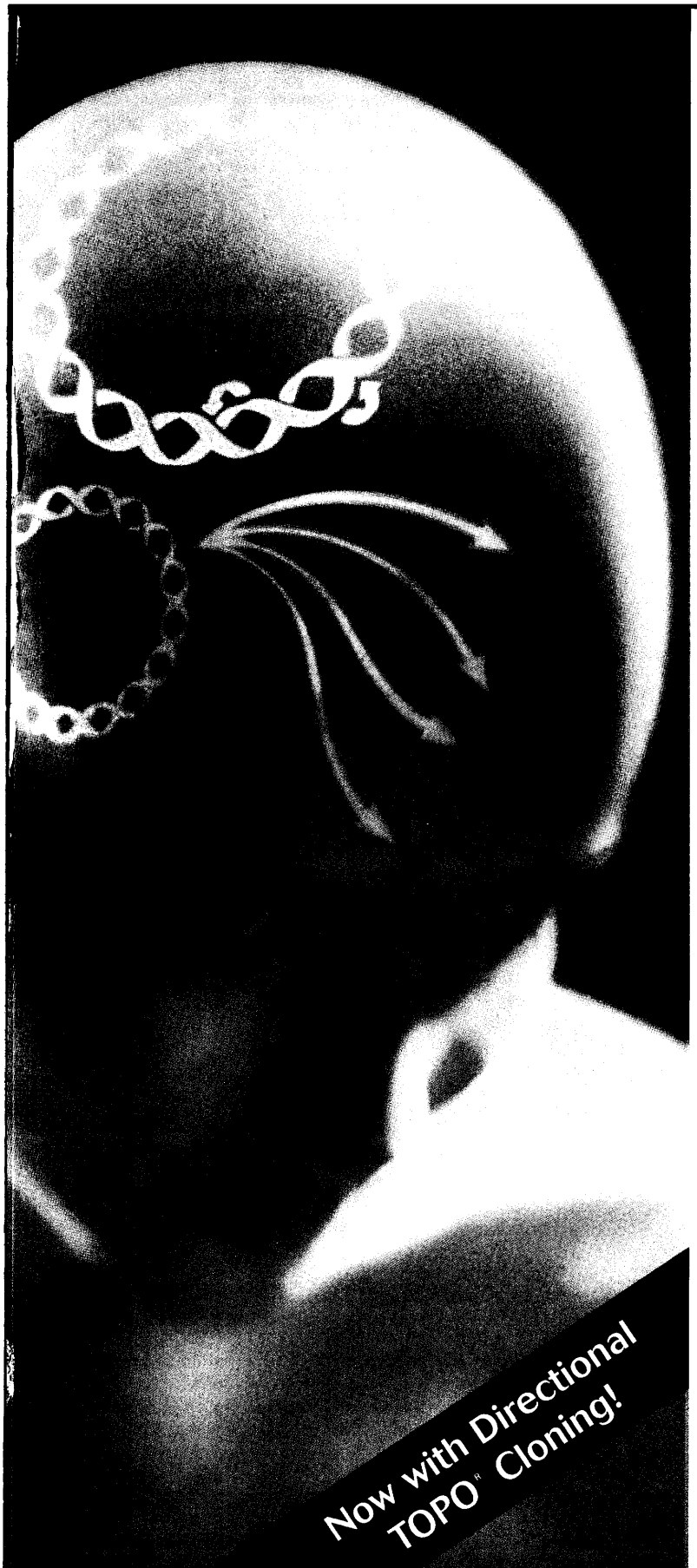

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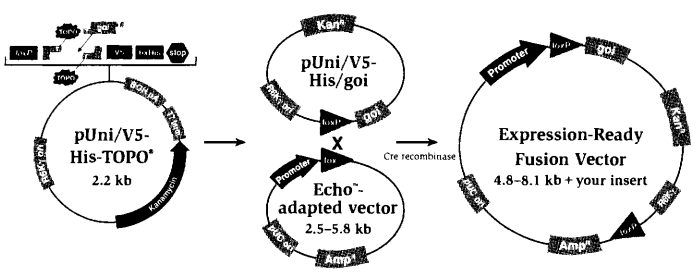

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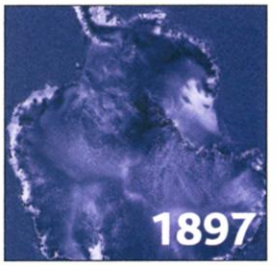

COVER A record of the 100,000-year ice-age cycle is preserved in the oxygen isotopic composition of calcium carbonate made by deep-sea foraminifera. This record is reinterpreted by comparing it to the isotopic composition of atmospheric O_2 extracted from ice cores from Vostok, Antarctica. The comparison suggests that variations of Earth's orbital eccentricity drive the glacial cycles by influencing atmospheric CO_2 levels. [Image: NASA Goddard Space Flight Center/Scientific Visualization Studio]

1860
Delta blues

NEWS

NEWS OF THE WEEK

NEWS FOCUS

RESEARCH

RESEARCH ARTICLES

REPORTS

DEPARTMENTS

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SCIENCE'S COMPASS

1882
On the edges of organisms

EDITORIAL

LETTERS

POLICY FORUM

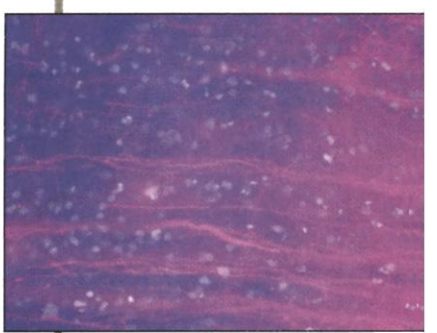
BOOKS *ET AL.*

PERSPECTIVES

TECH.SIGHT

TECHNICAL COMMENTS

Summary appears on page 1839; full text is available online at www.sciencemag.org/cgi/content/full/289/5486/1839a



1946
Specialized brain structures for language processing

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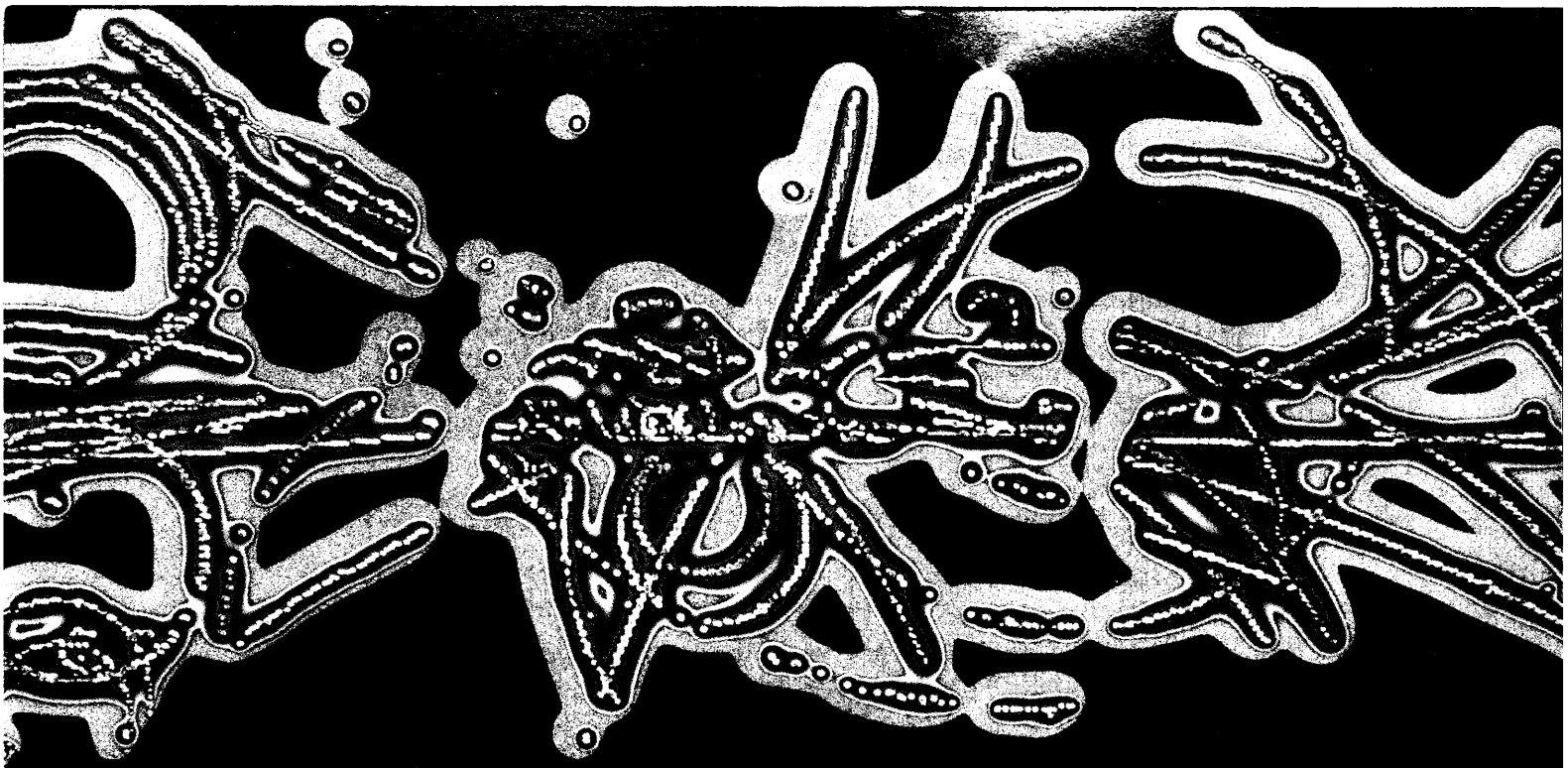

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FARM CREDITS AND DEBITS

Agriculture could play a role in mitigating atmospheric CO_2, but what are its net greenhouse effects? Robertson *et al.* (p. 1922) point out the need for "full-cost-accounting" and show that any carbon storage credits of agriculture must be set against the expenses of increases in other greenhouse gases such as N_2O. In a 10-year study, they compare trace gas fluxes in several different systems: natural communities at different successional stages, conventional field crops, and organically grown field crops. They show a substantive contribution of agriculture to the global N_2O budget and also find little difference between the methane and N_2O fluxes under organic and conventional tillage regimes. The greatest mitigation opportunities are identified in early successional communities and in perennial crops because of their capacity for soil carbon storage.

(EN)TANGLED UP IN DOTS

Quantum information processing requires the formation of entangled states, and much effort is being devoted to producing such states in semiconductor devices. Chen *et al.* (p. 1906) report optically induced and detected entanglement of excitonic states within a gallium arsenide quantum dot. The authors utilized the discrete electronic levels in a quantum dot to create energetically well-defined excited species—an excited electron-hole pair, or exciton—and show that two exciton states can be entangled. The next challenge will be to produce similar entangled states between coupled quantum dots that could form the basis for quantum logic operations.

1000 YEARS IN TIBET

The summertime climate of the Tibetan Plateau is dominated by the South Asian monsoon. The plateau is also high enough that permanent ice, which contains a record of local climate, can be found in some locations despite its low latitude. Thompson *et al.* (p. 1916) present results from a core that they recovered at Dasuopo, Tibet, that provide a record of the monsoon for the past 1000 years. Dust, oxygen isotopes, and anions in the ice show the imprint of episodic droughts caused by monsoon failure, a plateau-wide warming trend during the 19th and 20th centuries, and the regional increase of anthropogenic activity during the past 100 years. The drought of 1790 to 1796 appears to have been the one of the most severe of the last millennium.

MARTIAN SOIL SECRETS

Analyses conducted by the Viking Landers showed that the martian soil is chemically reactive and rapidly decomposed any organic molecules, thus inhibiting their accumulation on the surface. Yen *et al.* (p. 1909) performed laboratory experiments using a martian-like soil in a martian-like atmosphere exposed to simulated solar ultraviolet radiation. Electron paramagnetic resonance spectroscopy indicated that superoxide radicals (O_2^-) were formed under these conditions. These radicals would be sufficiently reactive and mobile to remove any organic molecules.

TUNING IN AND OUT

During the past 1 million years or so, climate has oscillated in a surprising regular fashion. Polar ice and marine sedimentary records show how ice sheets grew and receded, atmospheric CO_2 concentration rose and fell, and the deep oceans warmed and cooled. A reliable way to assign accurate ages to the variations is necessary in order to make sense of when and why these changes occurred. Shackleton (p. 1897; see the cover and the news story by Kerr) used oxygen isotope records of the atmosphere, extracted from Antarctic ice, and records of the deep ocean, derived from benthic foraminiferal tests, to produce precisely orbitally tuned records of these phenomena for the past 400,000 years. By comparing the amplitudes of different climate signals to solar insolation changes, he can separate the factors that have forced the changes and discount the role of orbital precession in the 100,000-year ice-volume cycle.

THE ROLE OF PROPERLY FOLDED PRIONS

The role of the pathological form of the prion protein in diseases such as scrapie is now well established, but the function of the normal prion protein in healthy individuals is still unclear. Mouillet-Richard *et al.* (p. 1925) now present evidence that the protein may play a role in signaling at the plasma membrane in neurons through caveolin and the tyrosine kinase Fyn.

BACTERIA PUMP UP

The harvesting of energy by most life on Earth begins with the absorption of sunlight, in its most familiar form, by the process called photosynthesis. There are, however, other avenues for the capture of photons, one of them being the confusingly named bacteriorhodopsin, a light-activated proton pump found in archaea and not previously shown to exist in eubacteria. Béjà *et al.* (p. 1902; see the news story by Pennisi) have isolated a genomic fragment from a library of marine proteobacteria. This fragment encodes a "proteorhodopsin," which the authors have expressed and showed to function as a proton pump with kinetics similar to that of bacteriorhodopsin. These results suggest that this protein supports an unsuspected type of phototrophy in the sea.

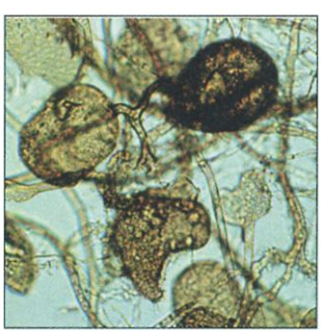
KEEPING AN EYE ON RNA

Cells have a number of ways to detect and deal with defective or inappropriate RNAs. In nonsense-mediated decay, faulty open reading frames in messenger RNA molecules are identified and the RNAs are then destroyed. In RNA interference—possibly an ancestral mechanism for protection against invading viruses or DNA—double-stranded RNA introduced artificially into the cell suppresses the expression of the homologous gene. Domeier *et al.* (p. 1928) now demonstrate that there is a link between these two RNA monitoring systems. They find that particular SMG proteins involved in nonsense-mediated decay are required for the maintenance,

CONTINUED ON PAGE 1839

FUNGI FIRST

The symbiosis of modern plants with certain soil fungi that facilitates nitrogen uptake may have been needed by ancient plants for the early colonization of land. The fossil record has so far recorded that the oldest fungi fossil appeared after the earliest land plants. Redecker *et al.* (p. 1920; see the Perspective by Blackwell) now describe fossil glomalean fungi from Middle Ordovician rocks in Wisconsin deposited about 460 million years ago, before the first vascular plants arose. These findings are in agreement with some molecular evidence for the early diversification of these fungi.



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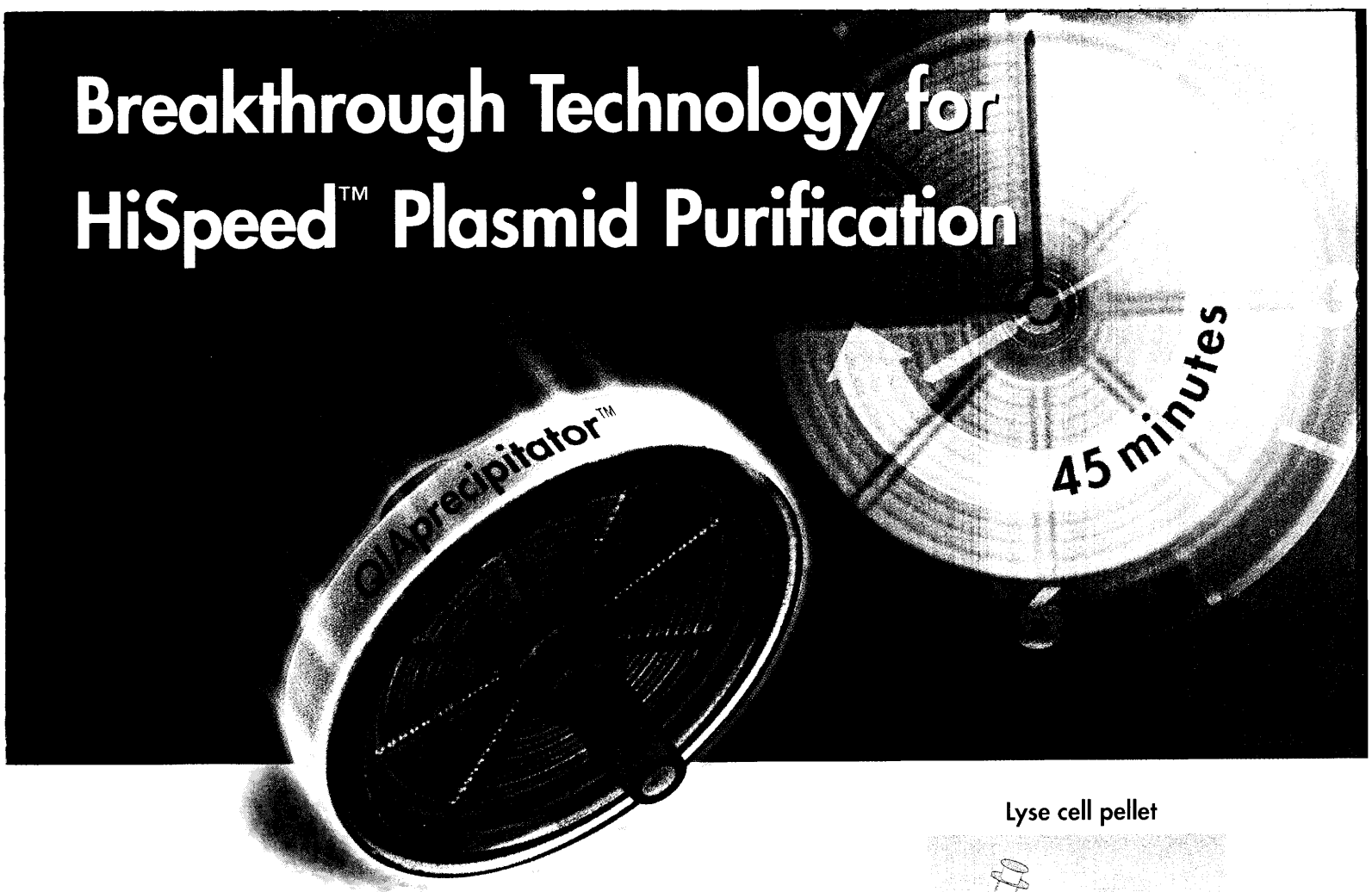

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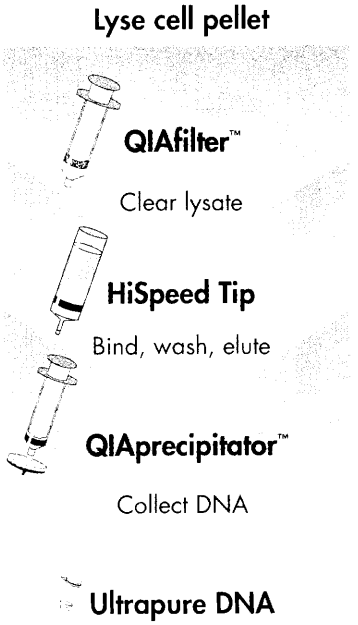

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CONTINUED FROM PAGE 1837

but not the initiation, of the RNA interference effect in the roundworm, *Caenorhabditis elegans*. The authors suggest that these SMG proteins may amplify RNA interference signals.

MENDING MITOCHONDRIA

A number of human diseases are associated with defects in the mitochondria, which have their own small circular genome independent of that in the cell nucleus. Kolesnikova *et al.* (p. 1931) now show that it may be possible to correct these disease-causing defects in mitochondria. First, working in yeast, they demonstrate that modified transfer RNA (tRNA) molecules—part of the machinery that interprets the information in DNA—can be imported from the cytoplasm of the cell into the mitochondria where they can "read" and correct the defective genetic code. They then show that modified tRNAs can be imported into human mitochondria, thus providing a possible route to curing some mitochondrial diseases.

AN ABL(E) INHIBITOR

Chronic myelogenous leukemia (CML) occurs primarily in adults and is caused by a chromosomal translocation event that produces a persistently activated form of a protein kinase called Abl. A small molecule inhibitor of the Abl kinase, called STI-571, has shown very encouraging results in early clinical trials. To investigate how this inhibitor achieves its high specificity for Abl, Schindler *et al.* (p. 1938; see the news story by Marx) determined the crystal structure of the catalytic domain of Abl in a complex with a variant of STI-571. The ability of the drug to penetrate deeply into the core of the Abl catalytic domain appears to depend on a distinctive inactive conformation adopted by the "activation loop," a protein segment that controls enzyme activity by switching between an inactive and active state. Because the catalytic domains of other protein kinases also adopt characteristic inactive conformations, this finding offers hope that similar inhibitors can be designed for other medically relevant protein kinases.

PROBLEMS IN BREATHING AND DELIVERY

The SK channels are a class of calcium-activated potassium channels that are widely distributed in the organism and that regulate several functions in a number of excitable cells. Several molecular subtypes of these channels have recently been identified, but the physiological roles of the individual subtypes have not yet been determined. Bond *et al.* (p. 1942) identified the function of one of these subtypes (SK3) in mice by using targeted overexpression coupled with an elegant inducible and reversible gene knock-out technique. Although the absence of SK3 did not result in a macroscopically altered phenotype, threefold overexpression of SK3 led to an altered response of the respiratory rhythm to hypoxic challenges (similar to sleep apnea and sudden infant death syndrome) and caused problems during delivery of pups.

TECHNICAL COMMENT SUMMARIES

Temporal Trends in Deep Ocean Redfield Ratios

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/289/5486/1839a

Pahlow and Riebesell (Reports, 4 February, p. 831), studying global data on oceanic nutrients, found "evidence for temporal trends" over the past five decades in the Northern Hemisphere deep ocean Redfield ratio (carbon:nitrogen:phosphorus)—which commonly is assumed not to vary with time at a given location in the modern ocean. Zhang *et al.* raise concerns about the resolution of that temporal signal, arguing that, for oxygen and phosphate concentrations, the magnitude of systematic corrections applied by Pahlow and Riebesell, and uncertainties in those corrections, were comparable to or exceeded the magnitude of the temporal signal itself. They also suggest that a correction for "slope error," rather than the constant-offset correction used by Pahlow and Riebesell, "would eliminate much of the reported temporal signal." Zhang *et al.* conclude that "although Redfield ratios...may indeed change with time, the changes inferred by Pahlow and Riebesell are probably not valid."

Pahlow and Riebesell respond that they applied their systematic corrections "for each set of reoccupied stations individually," and that in almost all cases those individual corrections "were smaller than the respective signals." They also present calculations that suggest that the effect of a correction for slope error in phosphate concentrations would not exceed 5% of the reported temporal trend.

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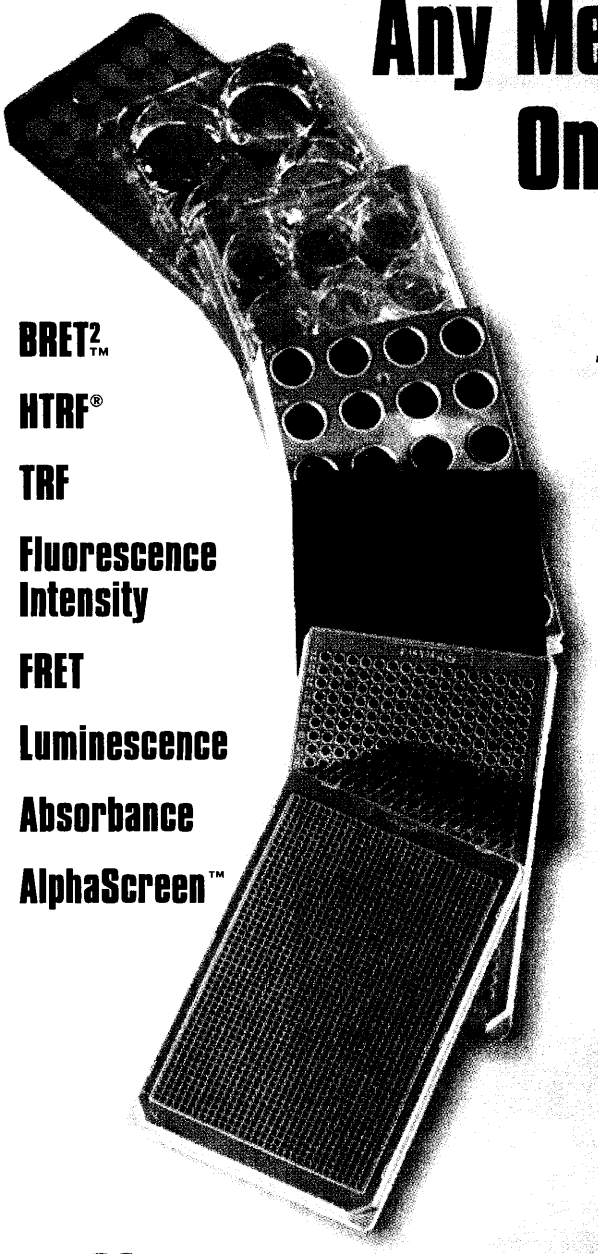

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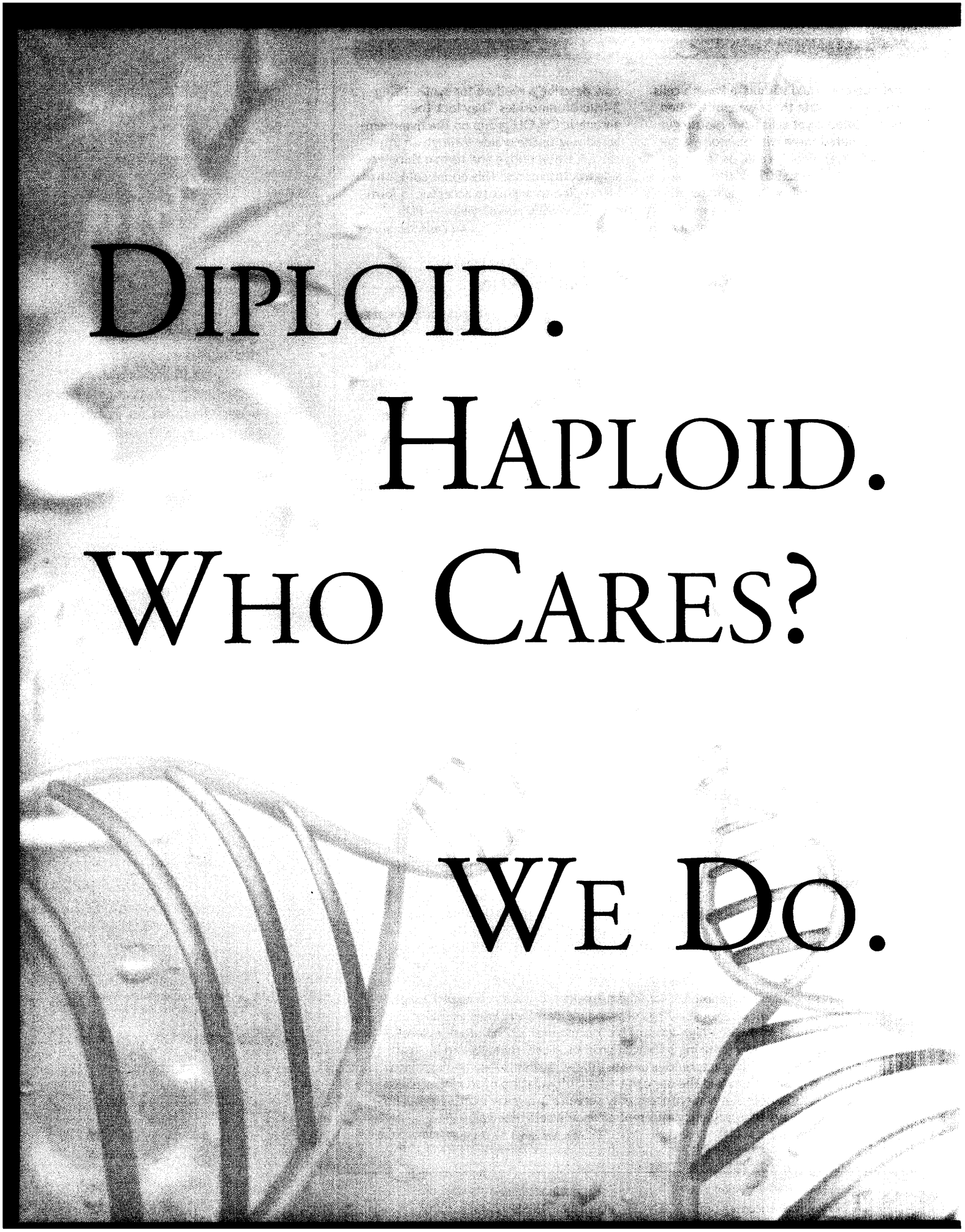
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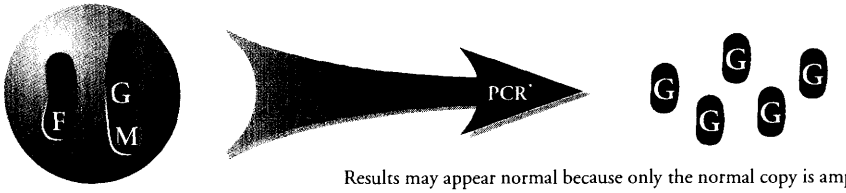
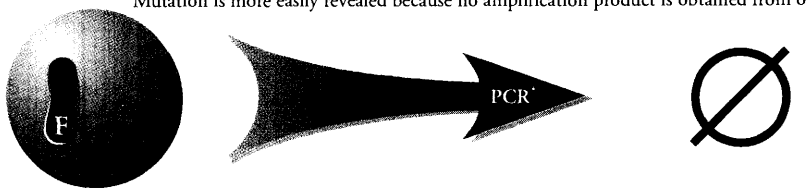


Results may appear normal because only the normal copy is amplified.

GMP CONVERSION TECHNOLOGY™ separates the two DNA sequences so they can be individually analyzed. The result: the mutation or deletion can more easily be detected.

Mutation is more easily revealed because no amplification product is obtained from one of the alleles.



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Our technology, licensed from The Johns Hopkins University School of Medicine, is not a genetic test, nor is it a substitute for the many advanced methods available to search for mutations. Rather, it is a powerful new tool that dramatically increases the accuracy of genetic analysis and testing.

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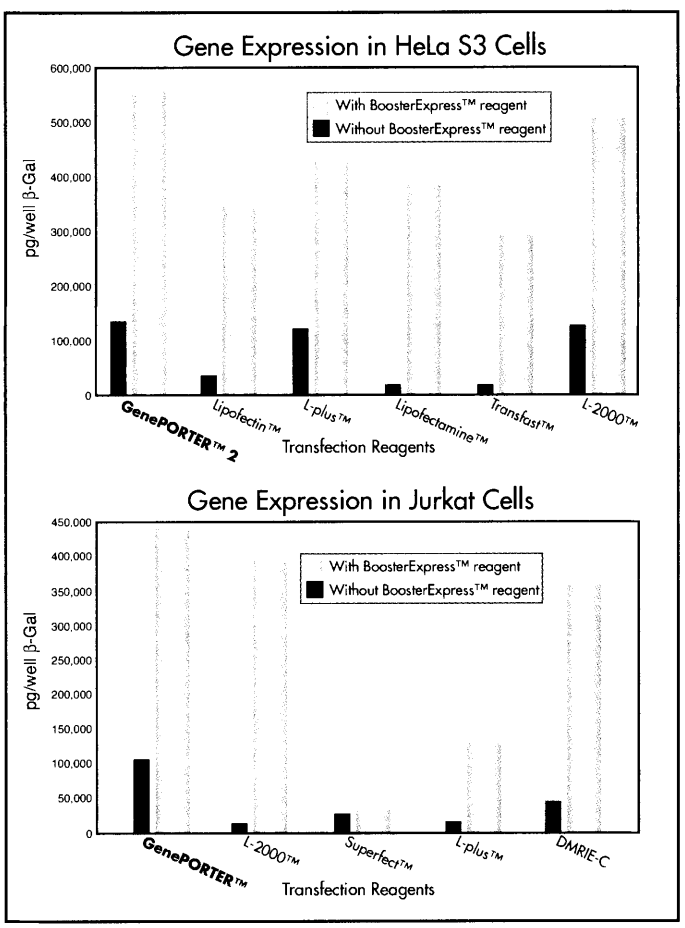

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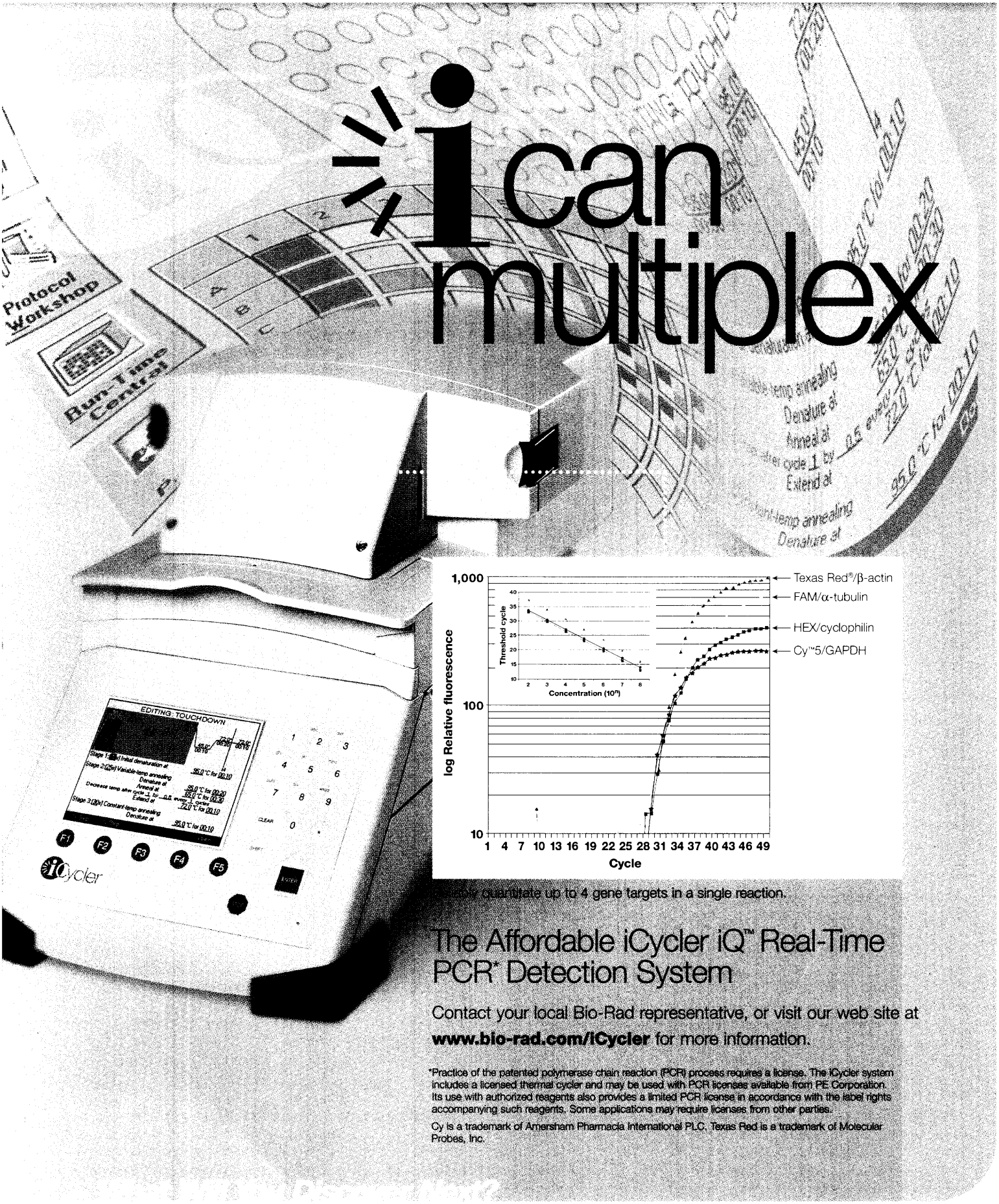

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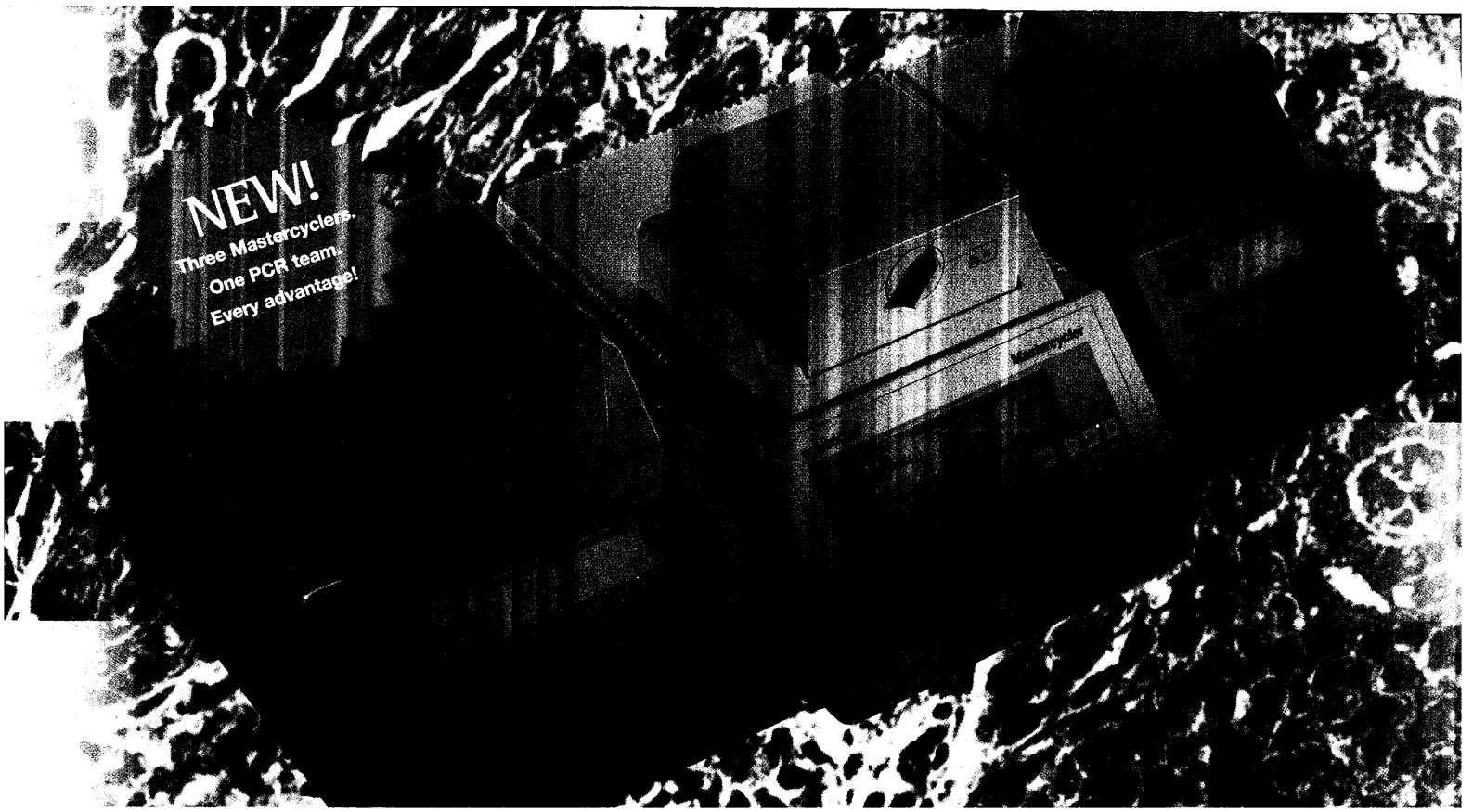

Background picture: PE squamous epithelium-CA of oral cavity, actin-in situ RT-PCR.

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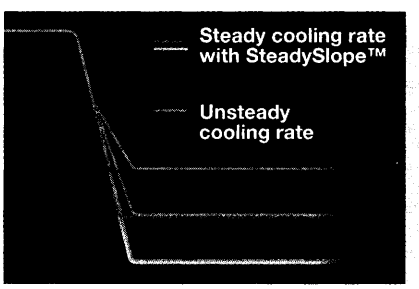

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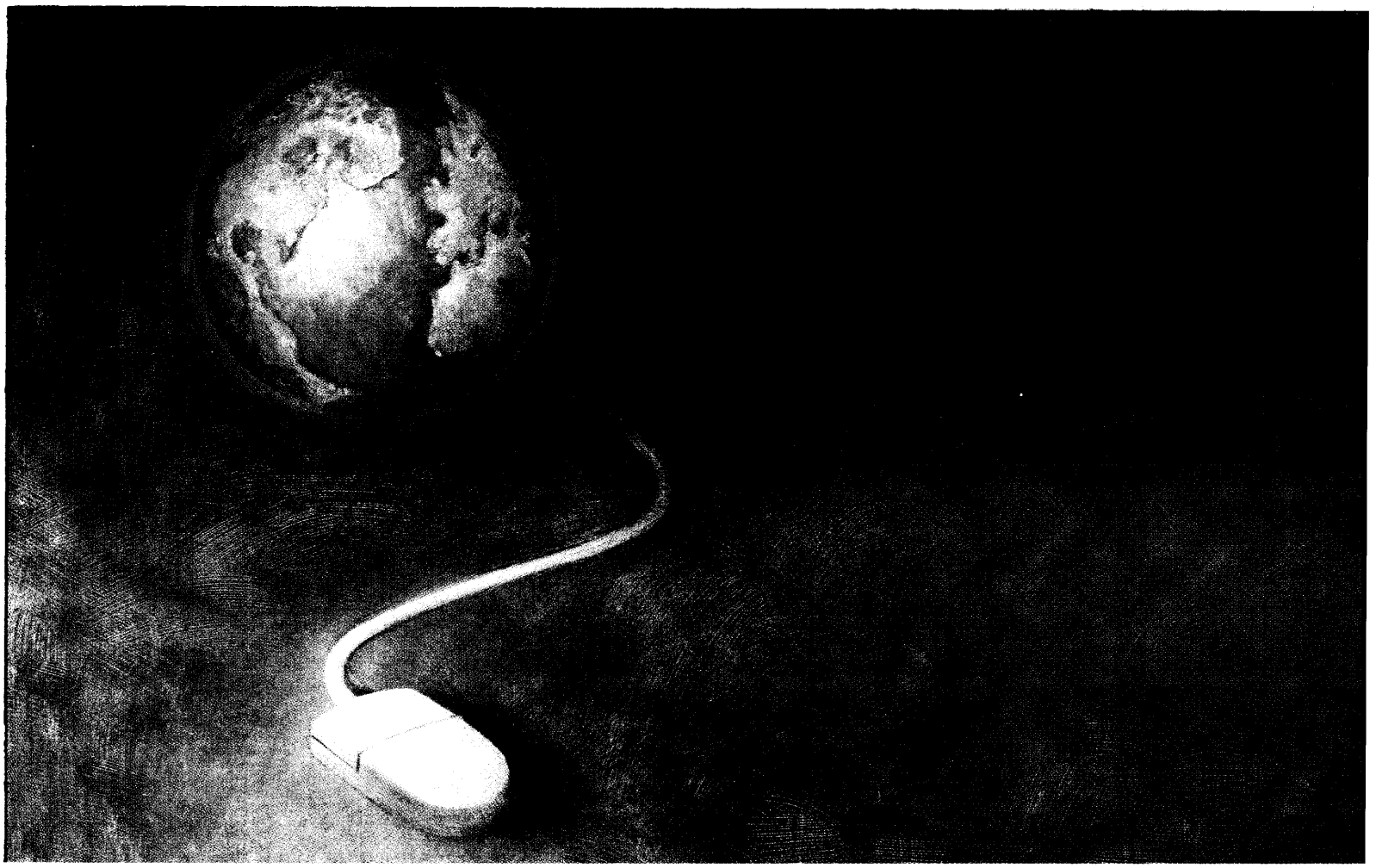

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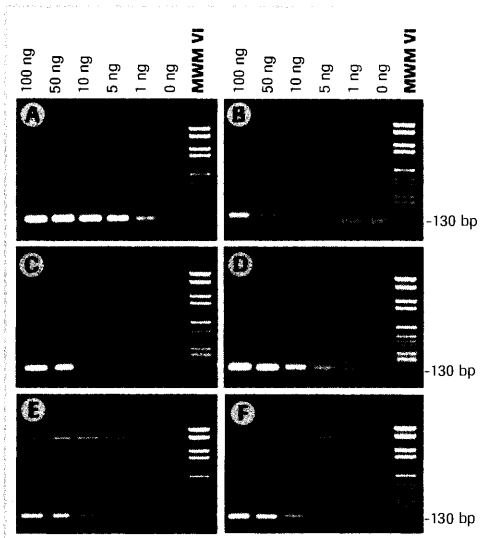

Figure 1: Specificity and sensitivity comparison in PCR using commercially available hot start systems.

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.

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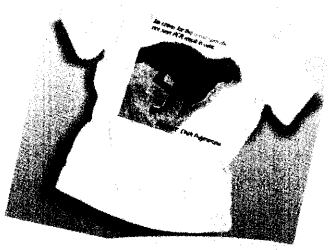

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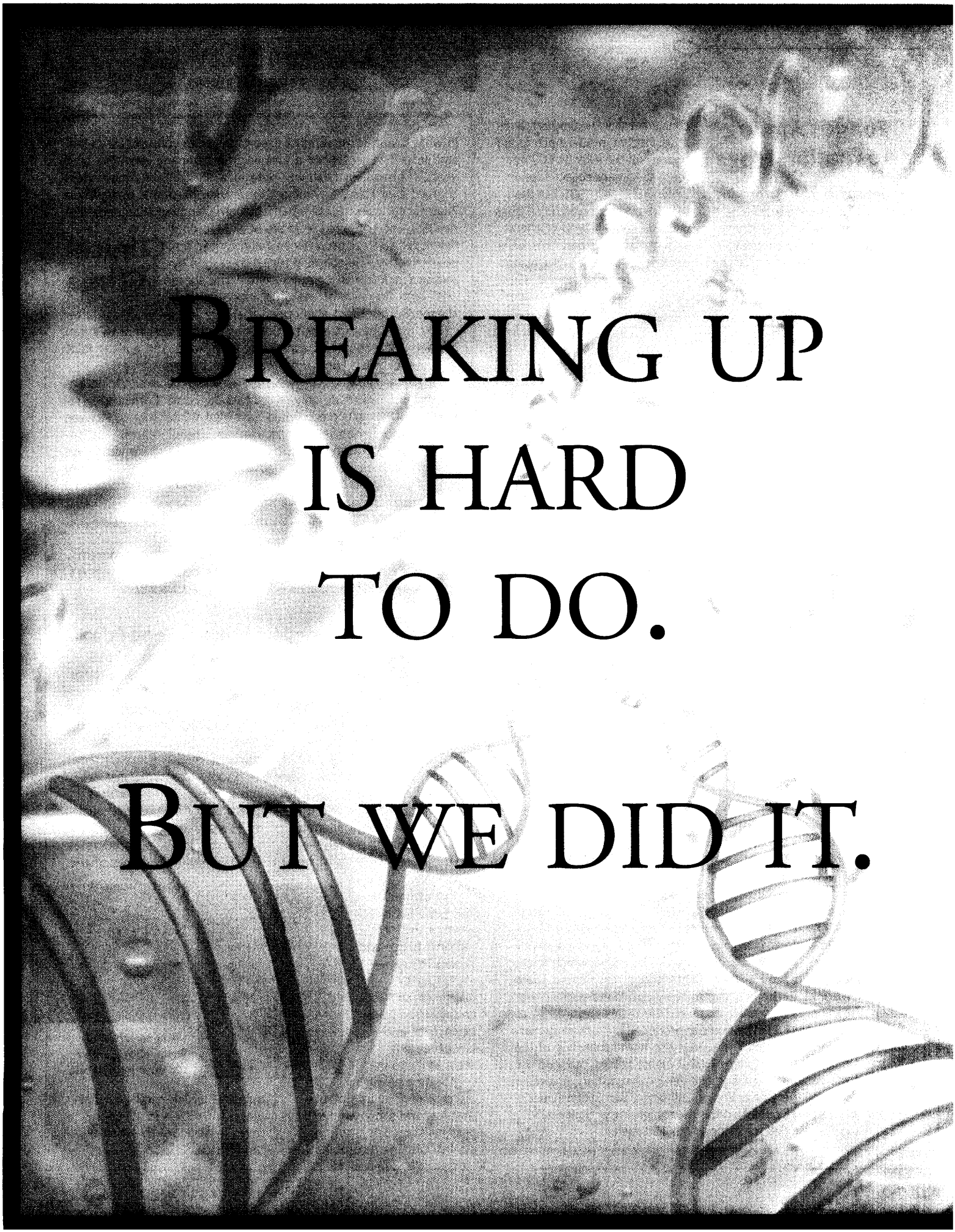
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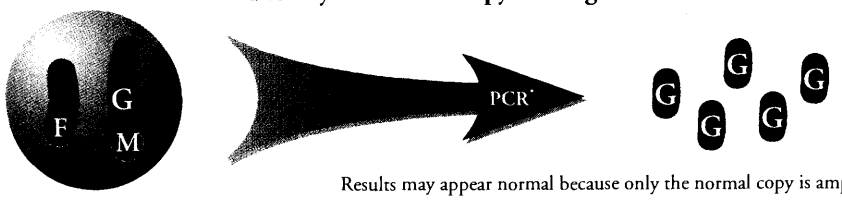

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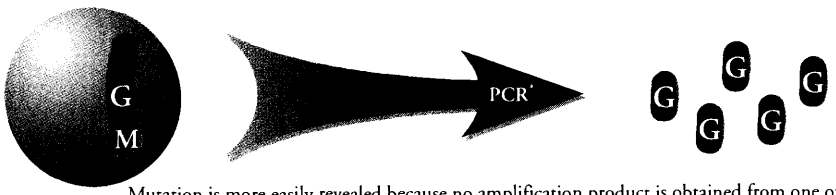
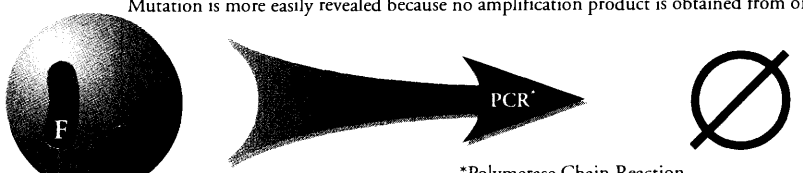


Mutation is more easily revealed because no amplification product is obtained from one of the alleles.



*Polymerase Chain Reaction

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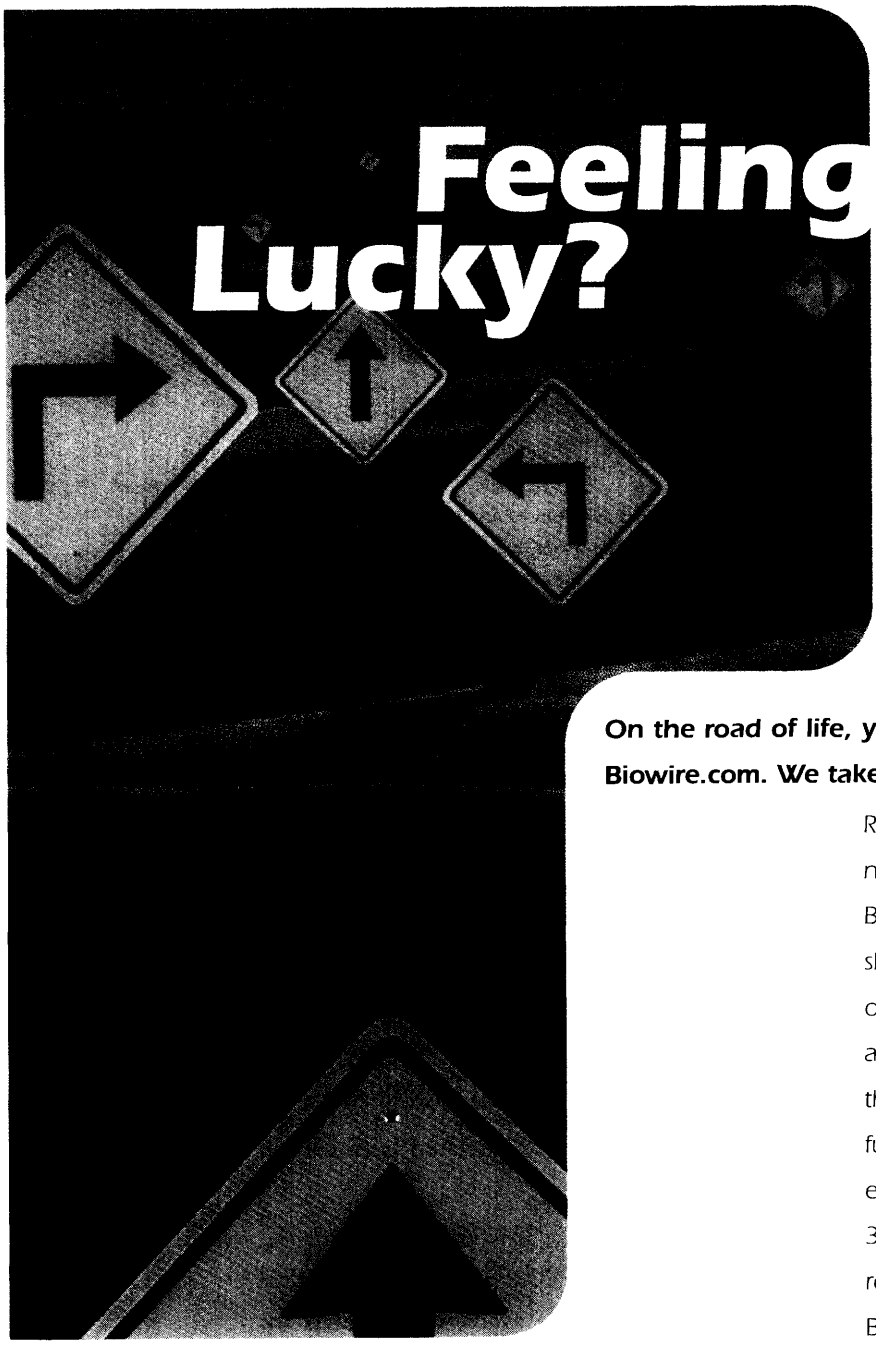

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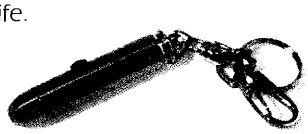

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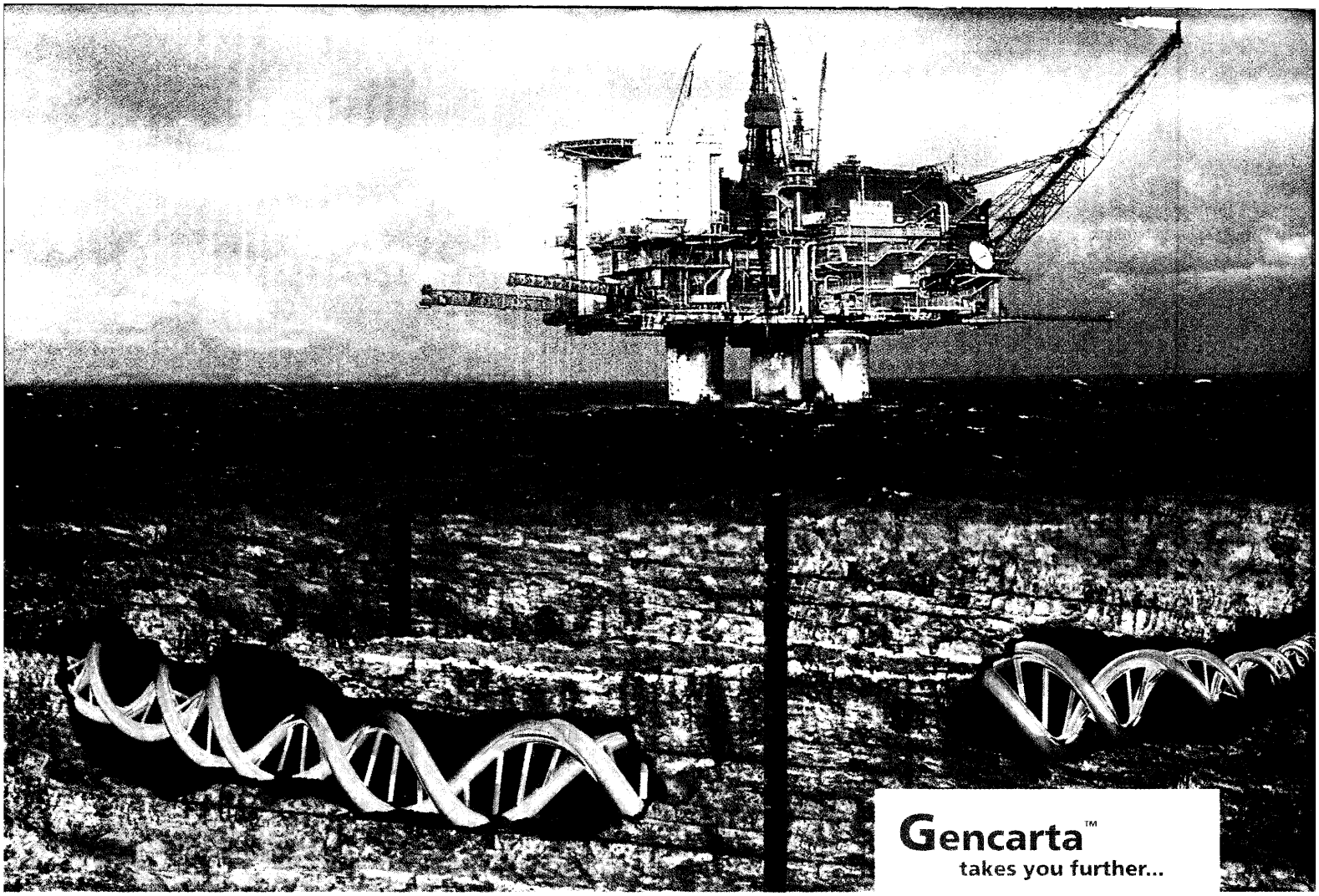

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