7 July 2000

Science

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Pages 1–204 $8

CHROMOSOME ORGANIZATION AND GENIC EXPRESSION

BARBARA McCLINTOCK

Institution, Washington, Cold Spring Harbor, N. Y.

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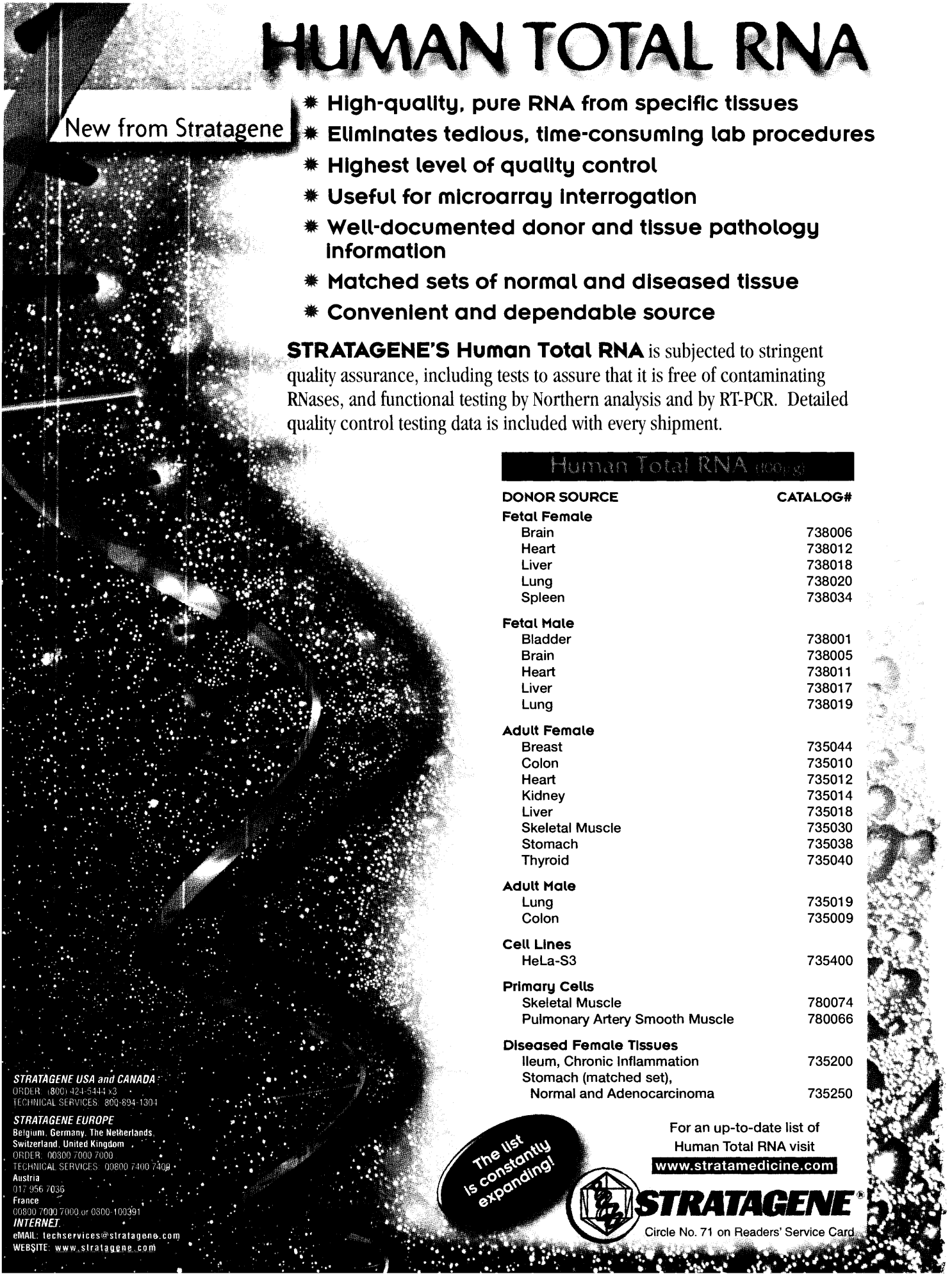

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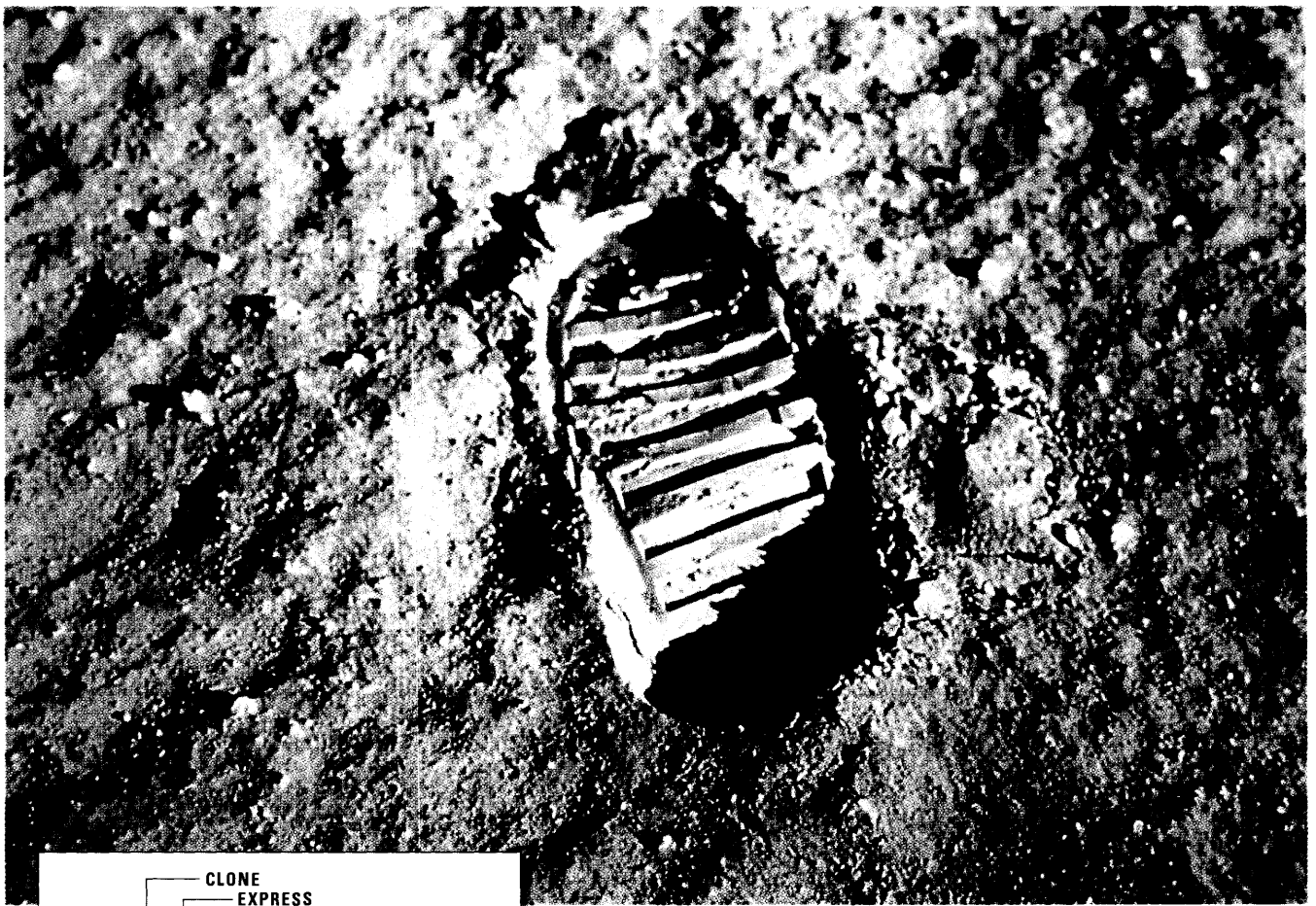

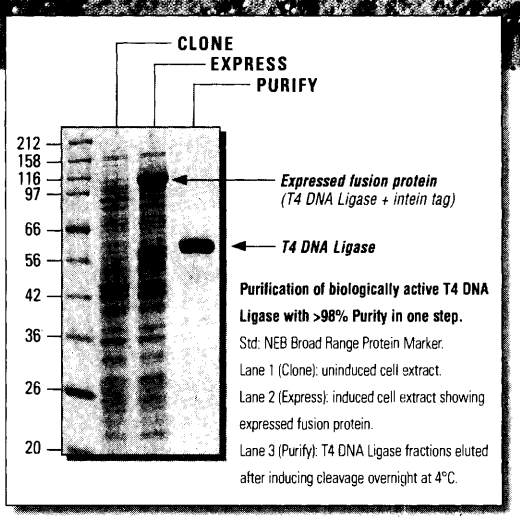

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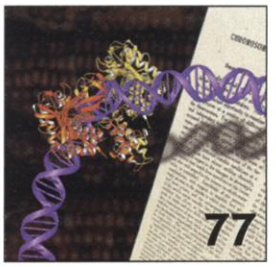

COVER In 1951, Barbara McClintock described mobile genetic elements, now called transposons, that could move from place to place in the chromosomes of maize, producing the variegated pigmentation of kernels (background). The x-ray structure of the key enzyme transposase (orange and yellow), which mediates transpositions such as these, is shown in complex with the two ends of a DNA transposable element (purple).

[IMAGE: H. A. STEINBERG, D. R. DAVIES, I. RAYMENT; B. MCCLINTOCK, *COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY* **16**, 13 (1951), USED WITH PERMISSION FROM COLD SPRING HARBOR LABORATORY PRESS]

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Big jobs for small telescopes

DEPARTMENTS

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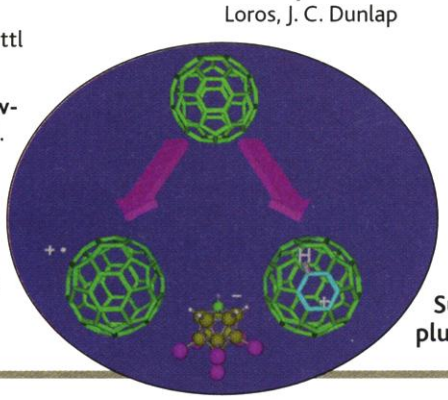

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Superacids are a plus for C_{60}

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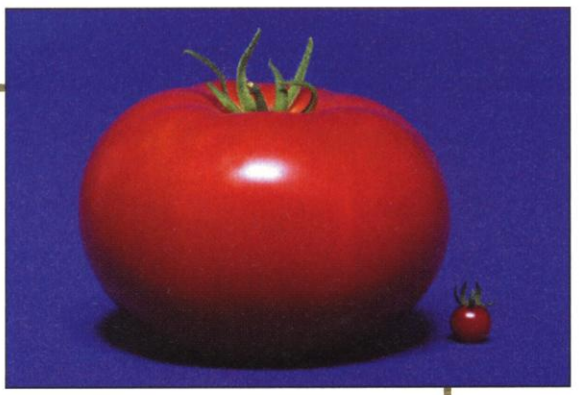

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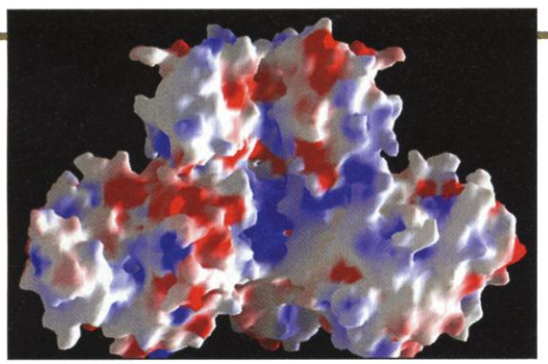
The generation gap



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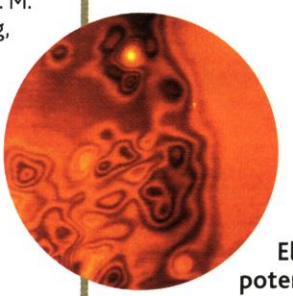
When is a channel not a pore?

www.scencemag.org/cgi/content/full/289/5476/11a



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Electron potential in a 2D landscape

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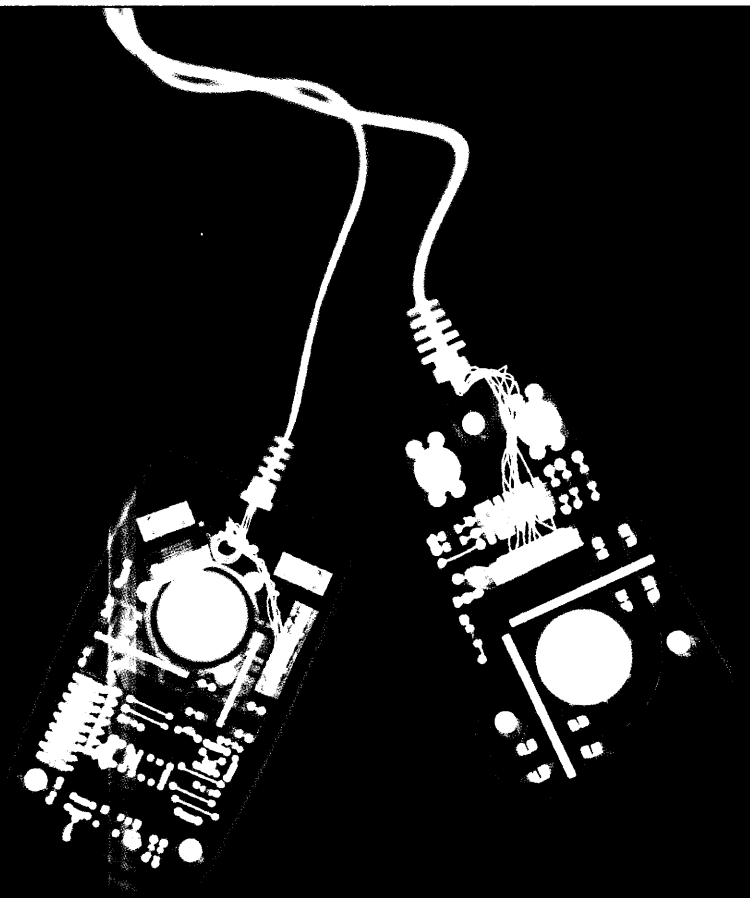

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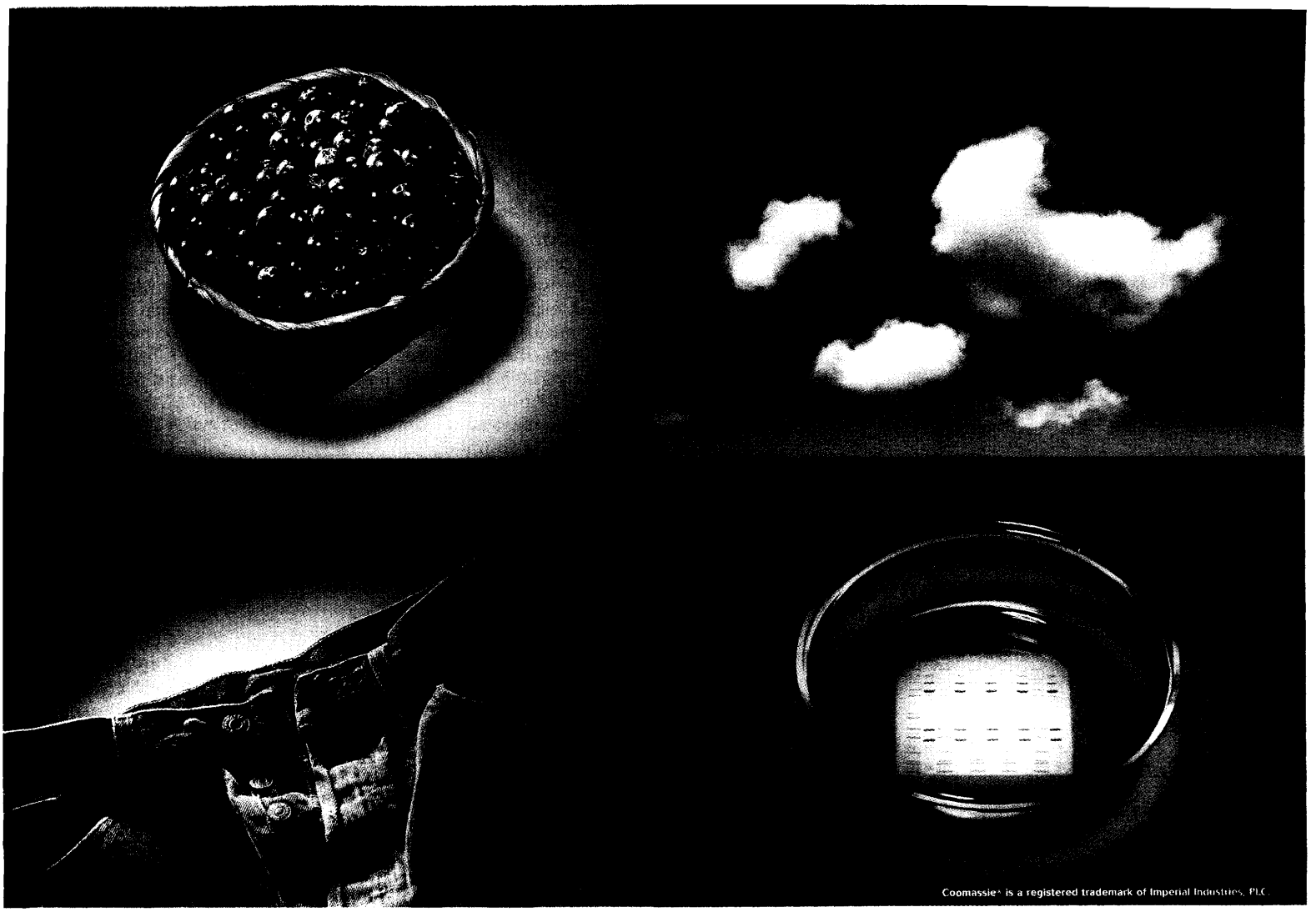

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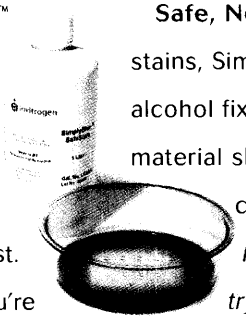

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MAPPING OUT POTENTIAL

The quantum Hall regime in a two-dimensional electron gas is robust against defect densities that decrease the electron mean free path to the order of the electron wavelength. The disorder potential induced by these defects (ionized impurities) is thought to play a crucial role in the quantum Hall effect. Finkelstein *et al.* (p. 90) used a scanning probe to "pull-up" a small bubble of electrons. They then mapped out the electrostatic potential over the two-dimensional plane by scanning the bubble across the sample and looking at the number of electrons that fall out of or into the bubble as it passes regions of high or low potential. The technique offers the ability to investigate and understand a wide variety of submerged electronic structures on nanometer-length scales.

SUBDUCTED SEAMOUNT

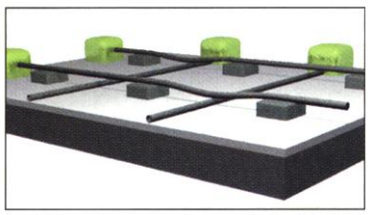
Active subduction in the Philippine Sea Plate beneath the Eurasia Plate has formed the Nankai trough off the coast of southwest Japan and has led to the recurrence of large earthquakes every 100 to 200 years. Of these, the 1946 Nankaido earthquake was unusual because long-period seismic data indicated a large rupture, but short-period data indicated a small rupture. Kodaira *et al.* (p. 104), using ocean-bottom seismometers to image the velocity structure of the Nankai trough, found evidence for the subduction of a large seamount (about 13 kilometers thick by 50 kilometers wide). The presence of this relatively intact seamount would explain the anomalous seismic data from the 1946 earthquake. Quicker and shorter rupture could occur along the plate boundary where the seamount is not coupled to the subducting plate. Slower and longer rupture could occur where the seamount was coupled to the plate, which would cause the rupture to propagate along a new and longer fracture through the seamount structure.

STELLAR CARBON AND OXYGEN PRODUCTION

Carbon and oxygen in the interstellar medium may be produced in the hydrogen- or helium-burning phases of red giant stars when these elements can move up to the surface of the star and be released. Carbon is produced by a three-alpha-particle process and includes secondary production of oxygen during the third alpha-particle interaction. Oberhummer *et al.* (p. 88) found that variations of the nucleon-nucleon strong interaction by more than 0.5% and of the Coulomb interaction by more than 4% would inhibit the formation of carbon-12 and oxygen-16 in models of the hydrogen- and helium-burning phases of low-mass stars (1.3 to 20 solar masses). Thus, there is a narrow range of nuclear forces within which red giant stars can contribute carbon and oxygen to the interstellar medium. Understanding these subtle forces will help to establish more accurate abundances of carbon and oxygen in the universe.

TOWARD MECHANICAL CARBON NANOTUBE MEMORIES

Molecular-based electronics offer the potential of higher integration densities, and much effort has focused on identifying viable molecular units that can be used for switching devices. Rueckes *et al.* (p. 94) propose that junctions of a crossed pair of nanotubes in which the



upper tube is suspended above the lower one could operate as nonvolatile, reversible memory devices. Application of an appropriate bias to each of the wires would produce a stable kink in the upper wire; thus, the separation distance between the tubes and hence the junction resistance could be changed in a manner analogous to a mechanical relay. Preliminary results have been obtained with thicker nanotube ropes. Integration densities approaching 10^{12} bits per square centimeter could be achieved by using many tubes to form a mesh of these junctions.

POSITIVE ABOUT C_{60}

The fullerene C_{60} readily forms anions up to C_{60}^{6-}, and thus, forming positively charged C_{60} species is a particular synthetic challenge. Reed *et al.* (p. 101; see the Perspective by DesMarteau) report a route to C_{60}^{+} via the formation of HC_{60}^{+} through the use of the superacids $H(CB_{11}H_6X_6)$, where X is Cl or Br. Unlike other superacids, their conjugate bases are poor nucleophiles and do not decompose C_{60}. Subsequent reaction of HC_{60}^{+} with a strong oxidant based on a triarylaminium radical cation yields C_{60}^{+}. These results show how the usually interrelated properties of acidity, redox potential, and nucleophilicity can be separated and exploited in separate steps.

THE CORE OF TRANSPOSITION

Transposases catalyze the movement of a double-stranded DNA segment from one location in the genome to another: the sequence of events comprising double-stranded cleavage of both ends of the segment, binding to the target DNA site, and then insertion of the segment into that site. Davies *et al.* (p. 77; see the cover) have solved the structure of a tranposase-DNA complex, which offers insights into the mechanisms of recognition and DNA cleavage as well as how the dimerization of the enzyme leads to initial strand scission and subsequent excision (see the Perspective by Williams and Baker). The similarity of this reaction to retroviral integration signifies an important advance in understanding a fundamental aspect of evolution and of contemporary disease.

BLUEPRINTS FOR BIGGER TOMATOES

Genetic studies of tomato have identified a quantitative trait locus (QTL) responsible for a good portion of the evolutionary change in fruit size that has characterized the domestication of the original wild relatives of the modern tomato into plants that produce large red fruits. Quantitative trait loci characteristically affect morphology in a graded, rather than all-or-none, fashion. Now, Frary *et al.* (p. 85; see the Perspective by Doebley) have cloned and analyzed the tomato fruit size QTL *fw2.2*, which contains several open reading frames. Surprisingly, one gene, *ORFX*, is responsible for the changes in fruit size—cultivated strains expressing the wild species gene exhibited small fruit size. The gene is transcribed early in floral development and may effect fruit size through regulation of cell division.

THE UPS AND DOWNS OF TUMOR CELL GROWTH

Epithelial cells normally have a "top" and a "bottom," but as they become malignant, this important architectural feature is lost. Using the fruit fly *Drosophila* as a model, Bilder *et al.* (p. 113; see the Perspective by Peifer) identify a trio of membrane-associated proteins that act in a common pathway to regulate epithelial

CONTINUED ON PAGE 11

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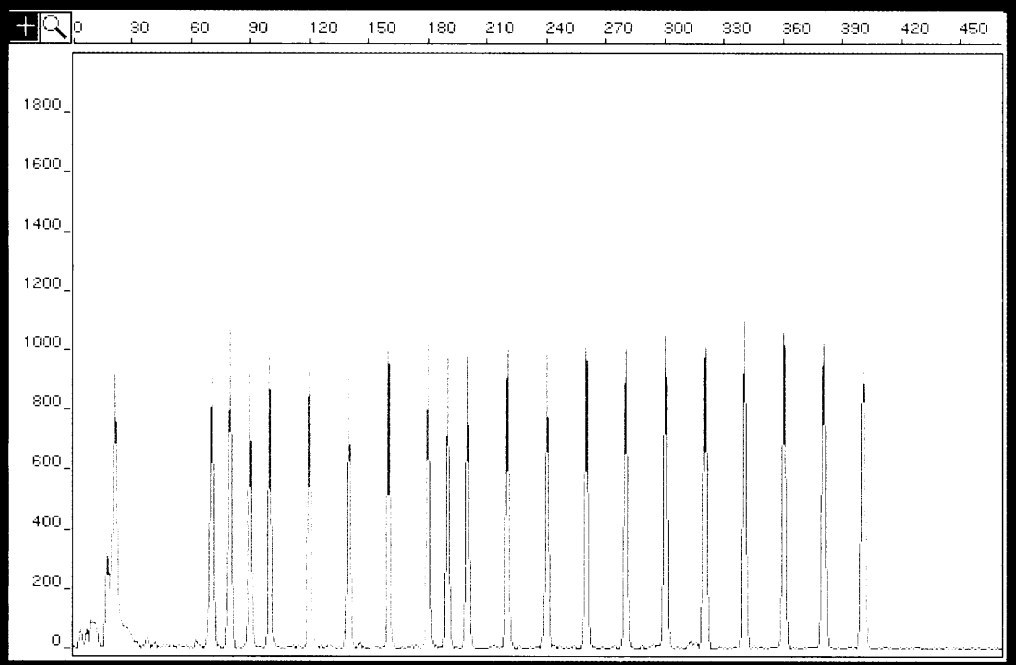

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 9

cell polarity and cell growth. The authors speculate that two of the proteins, Scribble and Discs-large, bind transmembrane proteins that organize the cell surface while the third, Lethal giant larvae, plays a role in the protein targeting system that preserves this cell surface organization.

HOW SWEET IT IS

The receptors in the nose that detect odors are members of an extremely large family of G protein–coupled transmembrane receptors. Ishimoto *et al.* (p. 116) present evidence which suggests that some taste receptors may also be members of this family. In the fruit fly *Drosophila*, the gene *Tre1* specifically controls the sensitivity to the sweet taste of trehalose but not to other sugars; replacement of a mutant *Tre1* gene restores the fly's ability to taste trehalose. The expression of the gene in the cells that sense taste adds to the evidence that this gene may code for a bona fide taste receptor.

HIGH BLOOD PRESSURE AND PREGNANCY

Hypertension is a common complication of pregnancy. An important clue to its underlying cause is provided by Geller *et al.* (p. 119; see the news story by Wickelgren), whose studies take them from patient to molecular causation to a plausible mechanism at atomic resolution. The authors identify a family with inherited early-onset hypertension that is exacerbated in pregnancy and show that the causative mutation lies in the gene encoding the mineralocorticoid receptor (MR), a protein that regulates salt reabsorption in the kidney. The mutation changes one amino acid in the hormone binding domain, which causes MR to become constitutively activated. This aberrant activity is enhanced further by progesterone, a hormone that is produced at high levels in pregnancy and that normally acts as an MR antagonist. The inherited mutation appears to facilitate molecular interactions in MR that normally require binding of its natural ligands.

GOING IN THE SIDE DOOR

Voltage-dependent potassium (K^+) channels open in response to a depolarization of the membrane potential and conduct K^+ across the plasma membrane. These channels are then inactivated by a peptide that is thought to physically insert into and obstruct the ion-conducting passageway. Gulbis *et al.* (p. 123) have determined the crystal structure of a complex of the cytoplasmic β subunit with the cytoplasmic domain of the integral membrane α subunit. Although the fourfold symmetric β subunit is axially aligned with the channel pore, it appears that ions actually enter through a spacer region between the membrane and cytoplasmic domains of the α subunit, and that the inactivation peptide also penetrates in this lateral fashion.

TECHNICAL COMMENT SUMMARIES

R/M/N Focus Formation and the Presence of Intact BRCA1

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/289/5476/11a

Zhong *et al.* (Reports, 30 July 1999, p. 747) found that formation of irradiation-induced immunoreactive foci related to the Rad50/Mre11/NBS1 (R/M/N) protein complex, which assemble in normal cells after DNA damage, was "dramatically reduced" in the tumor cell line HCC1937, which synthesizes a defective form of the *BRCA1* gene product. Reconstitution of the mutant cells with wild-type *BRCA1* restored normal focus formation. The results, Zhong *et al.* concluded, suggest that BRCA1 is important for the cellular responses to DNA damage mediated by the R/M/N complex. Wu *et al.* present data that "run counter" to these claims. Using two antibodies specific to the NBS1 protein (the monoclonal EE15 and the polyclonal D29), they found no diminution of focus formation after irradiation, and no change in the focus formation pattern after reconstitution with wild-type *BRCA1*. These data, argue Wu *et al.*, "make it difficult to conclude that BRCA1 is responsible for organizing radiation-induced R/M/N foci."

Zhong *et al.* respond that their own experiments using the EE15 and D29 antibodies yielded different results: EE15-immunoreactive foci could be detected in both untreated and irradiated cells, and D29 foci failed to appear in any of the cell lines studied by Zhong *et al.* Experiments with other commercially available antibodies sensitive to NBS1 and Mre11, however, supported the results in the original study, according to Zhong *et al.*: R/M/N irradiation-induced foci were reduced in the *BRCA1*-mutated HCC1937 cells. "Clearly," they conclude, "BRCA1 plays a role in DNA damage repair."

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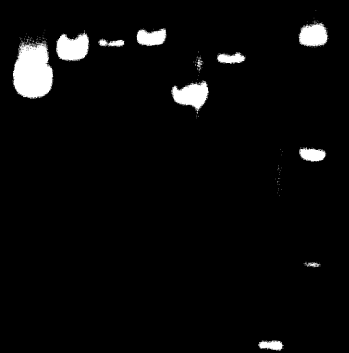

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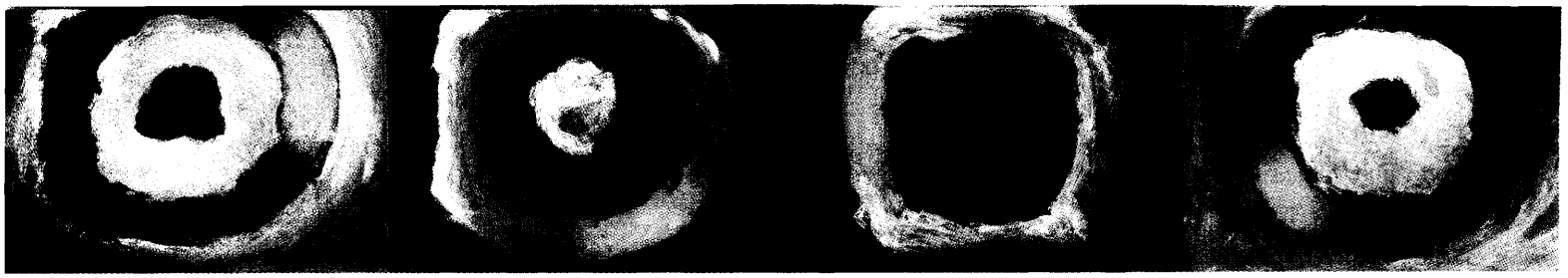

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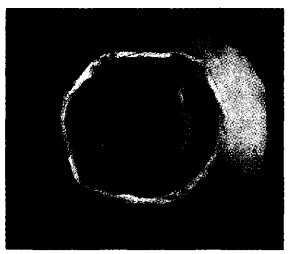

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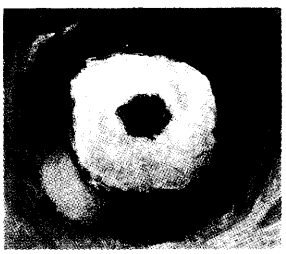

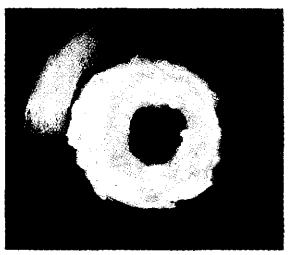

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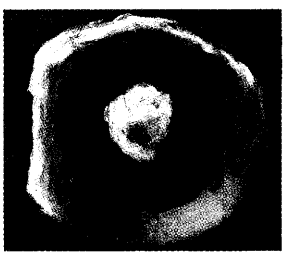

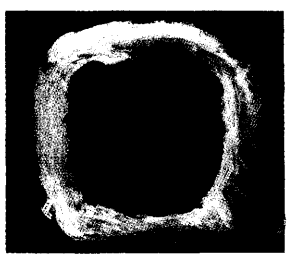

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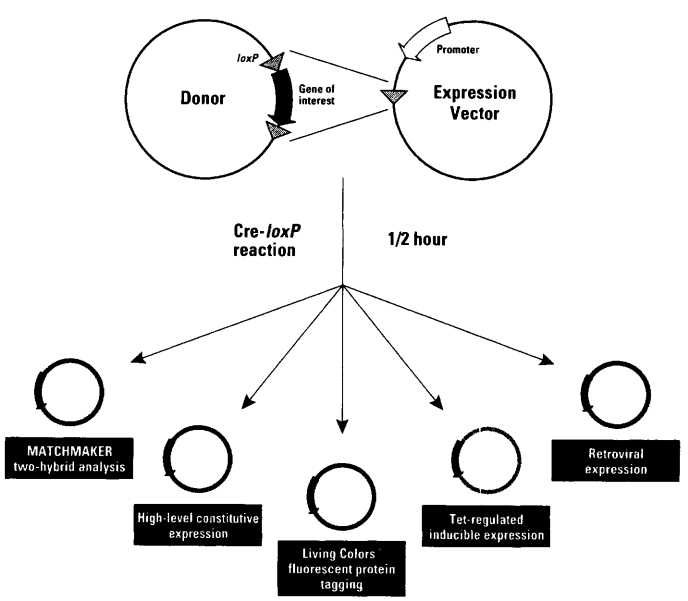

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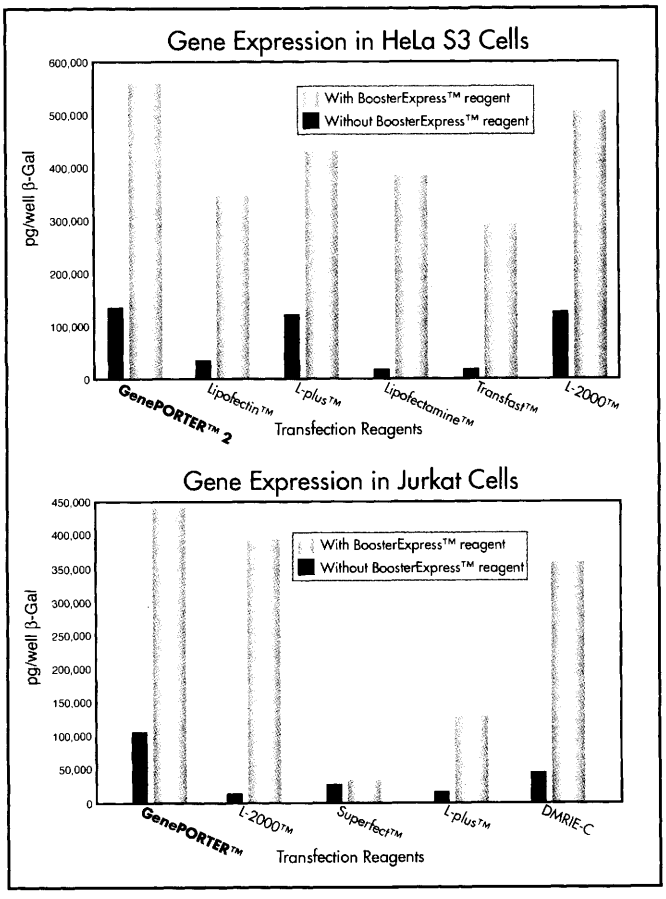

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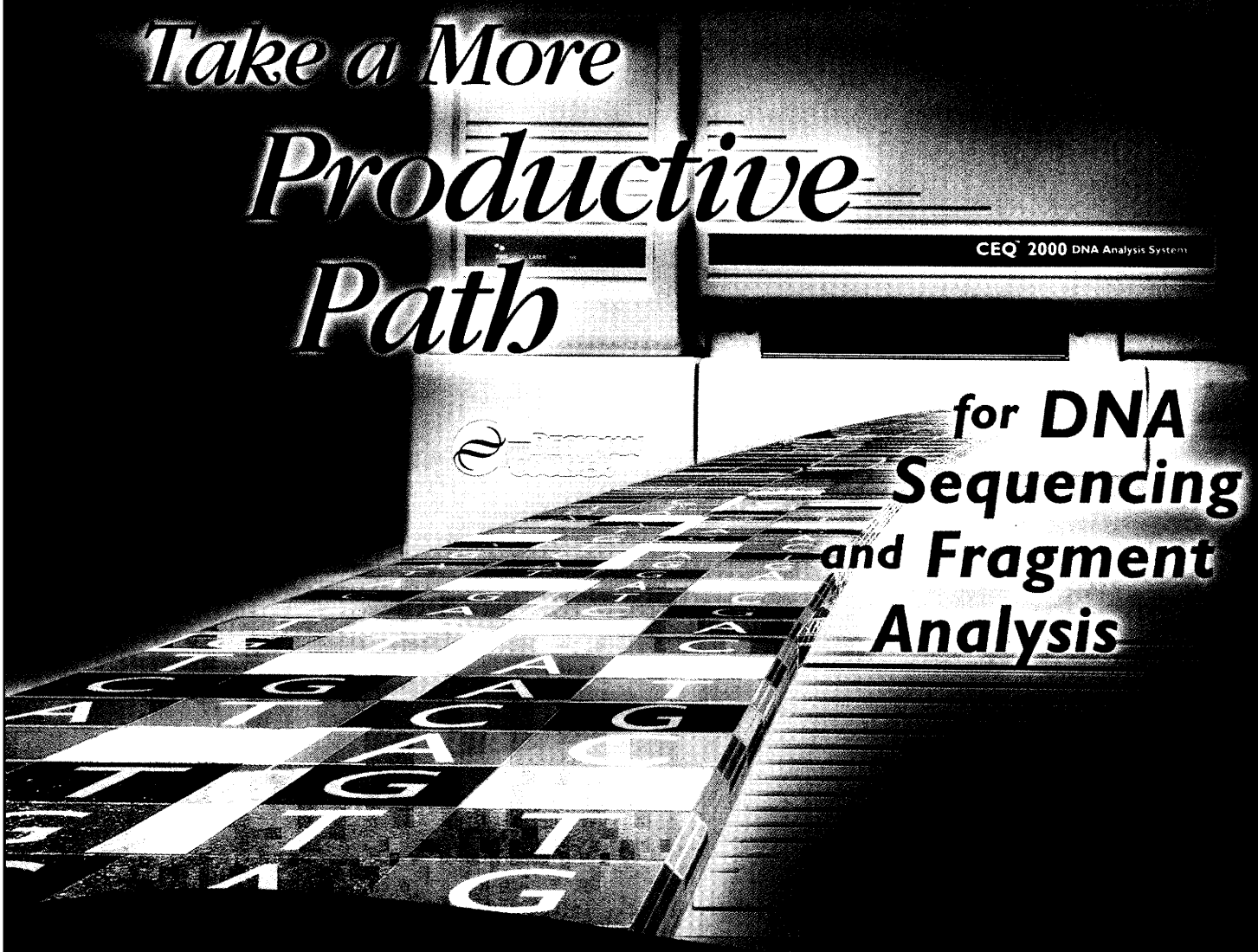

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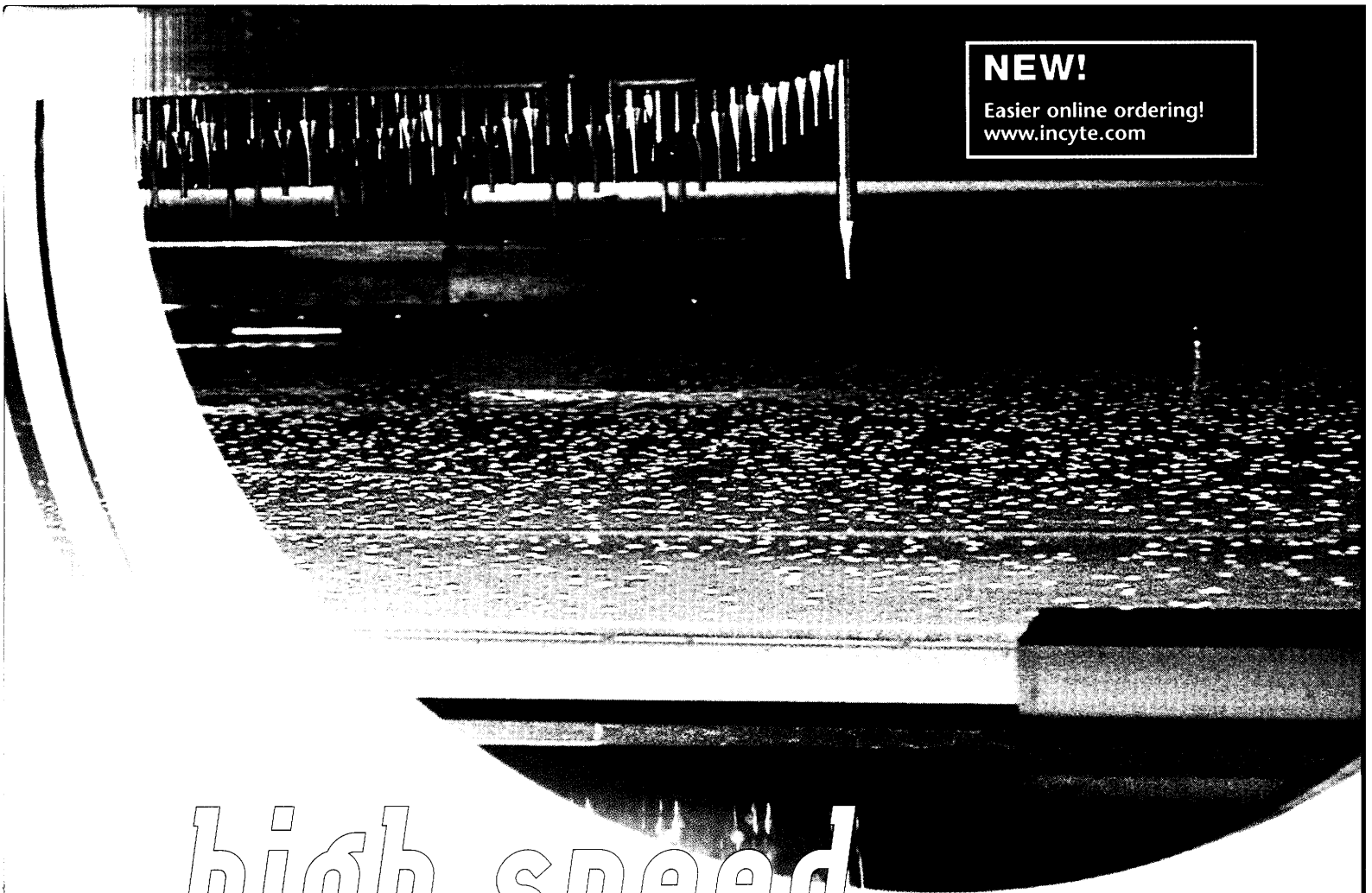

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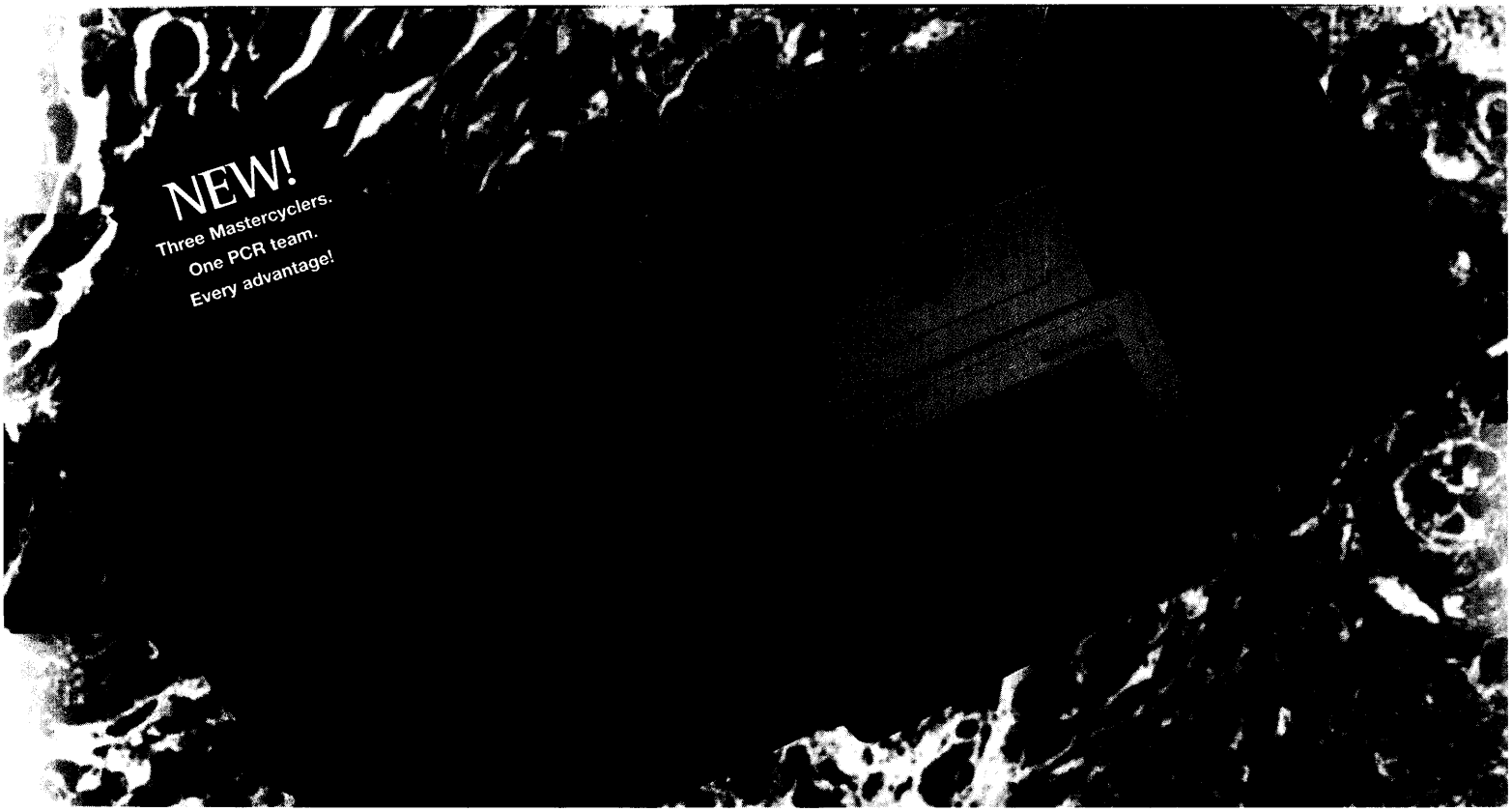

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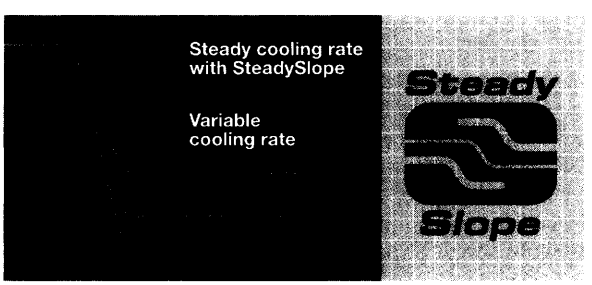

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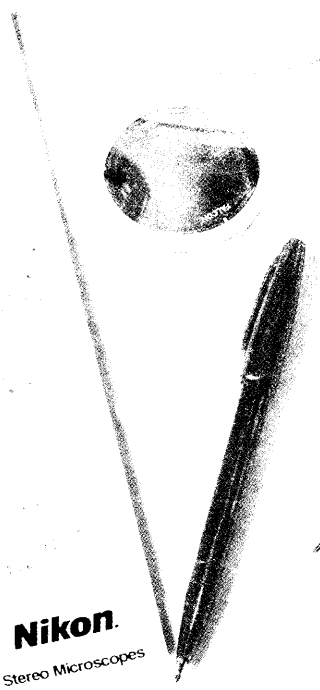

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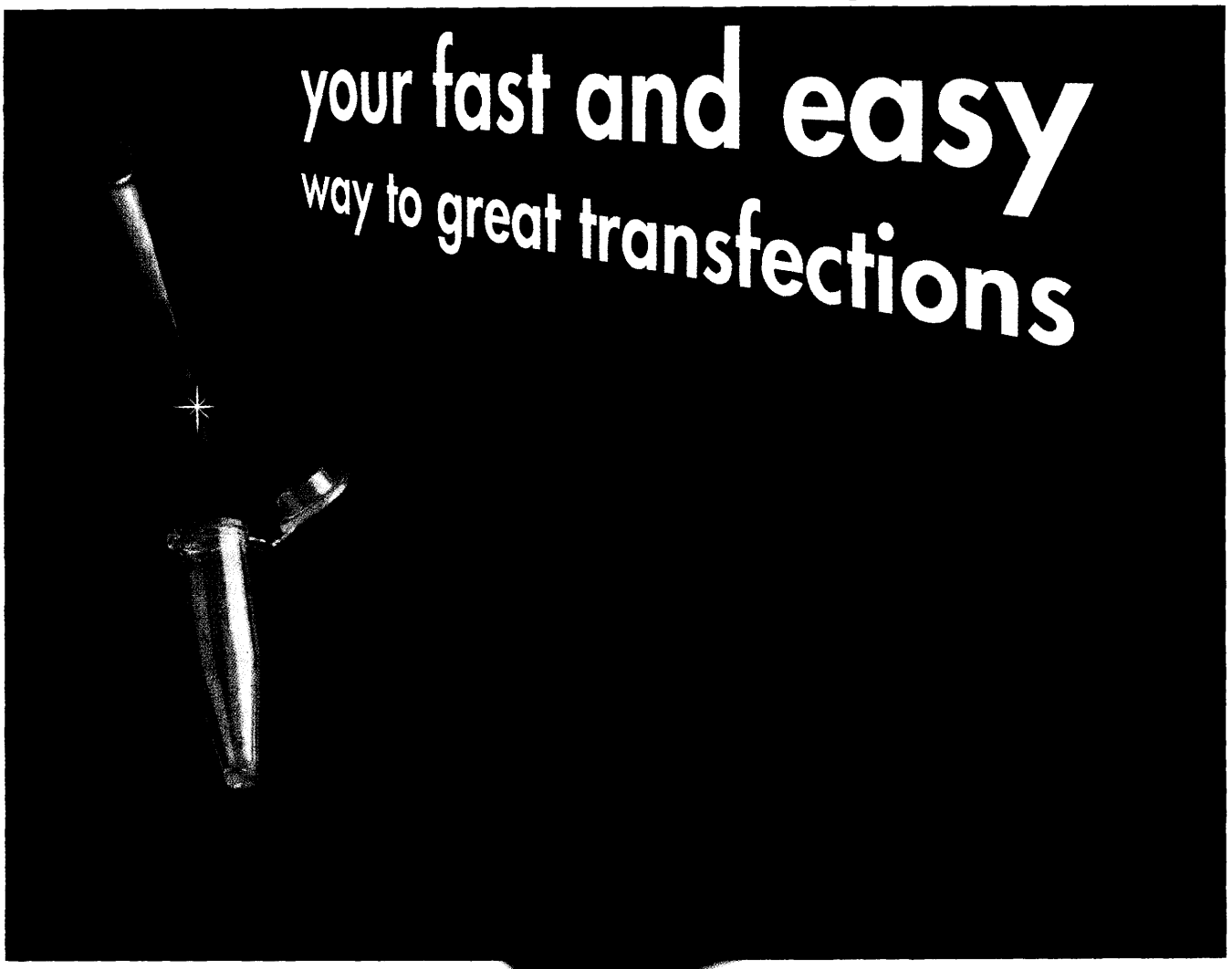

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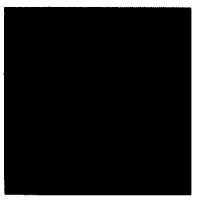

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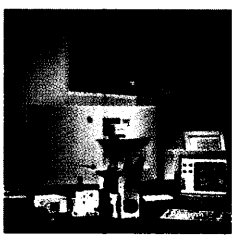

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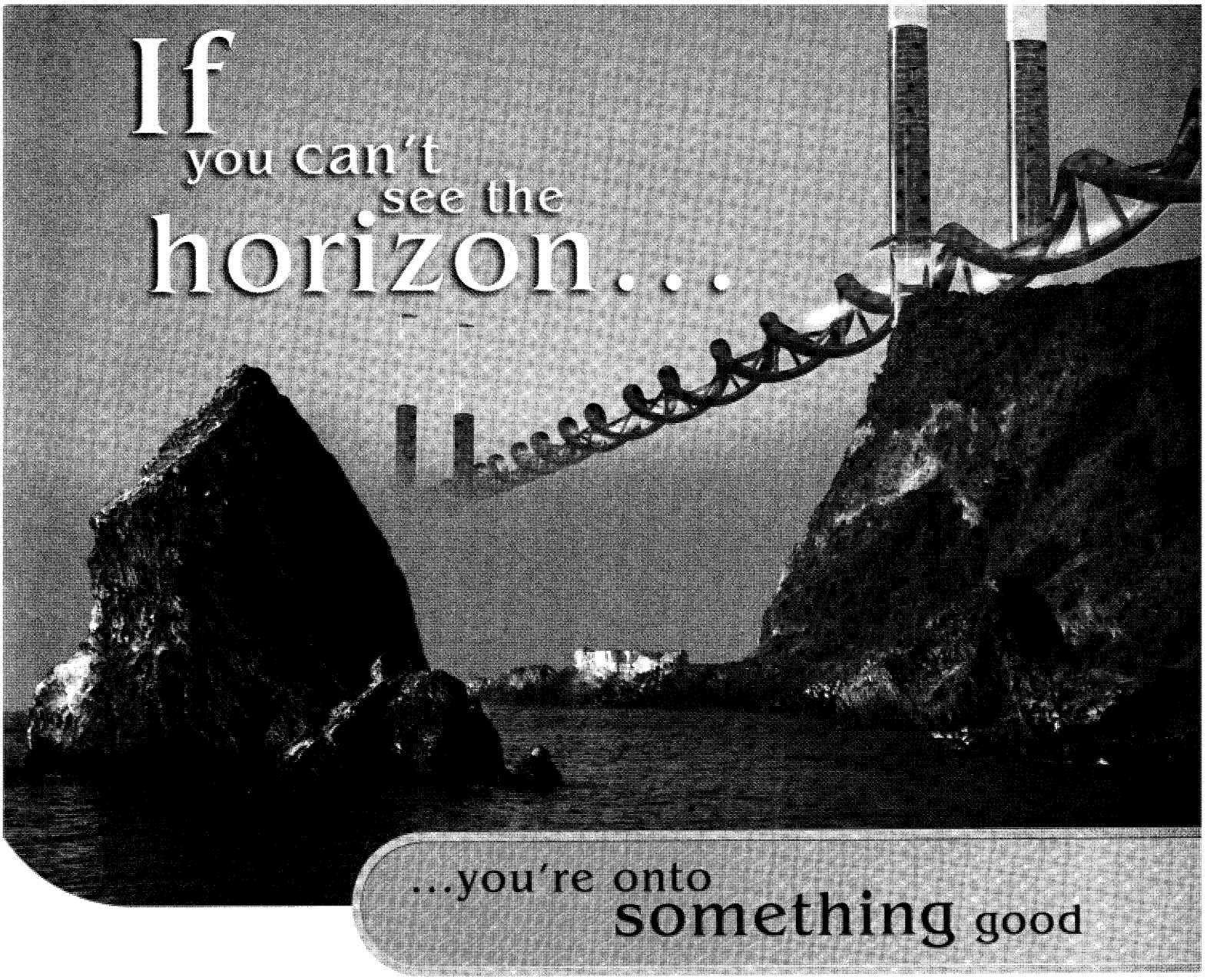

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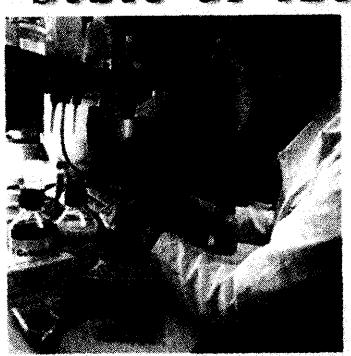

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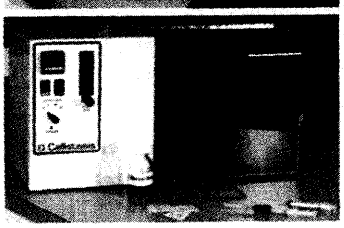

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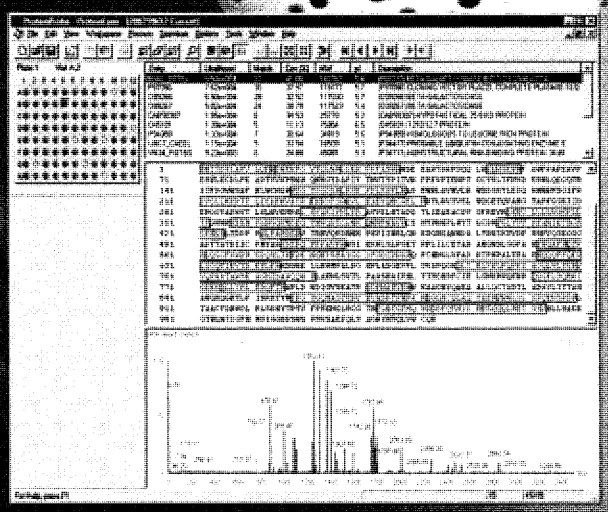

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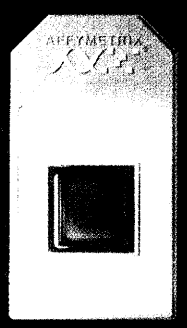

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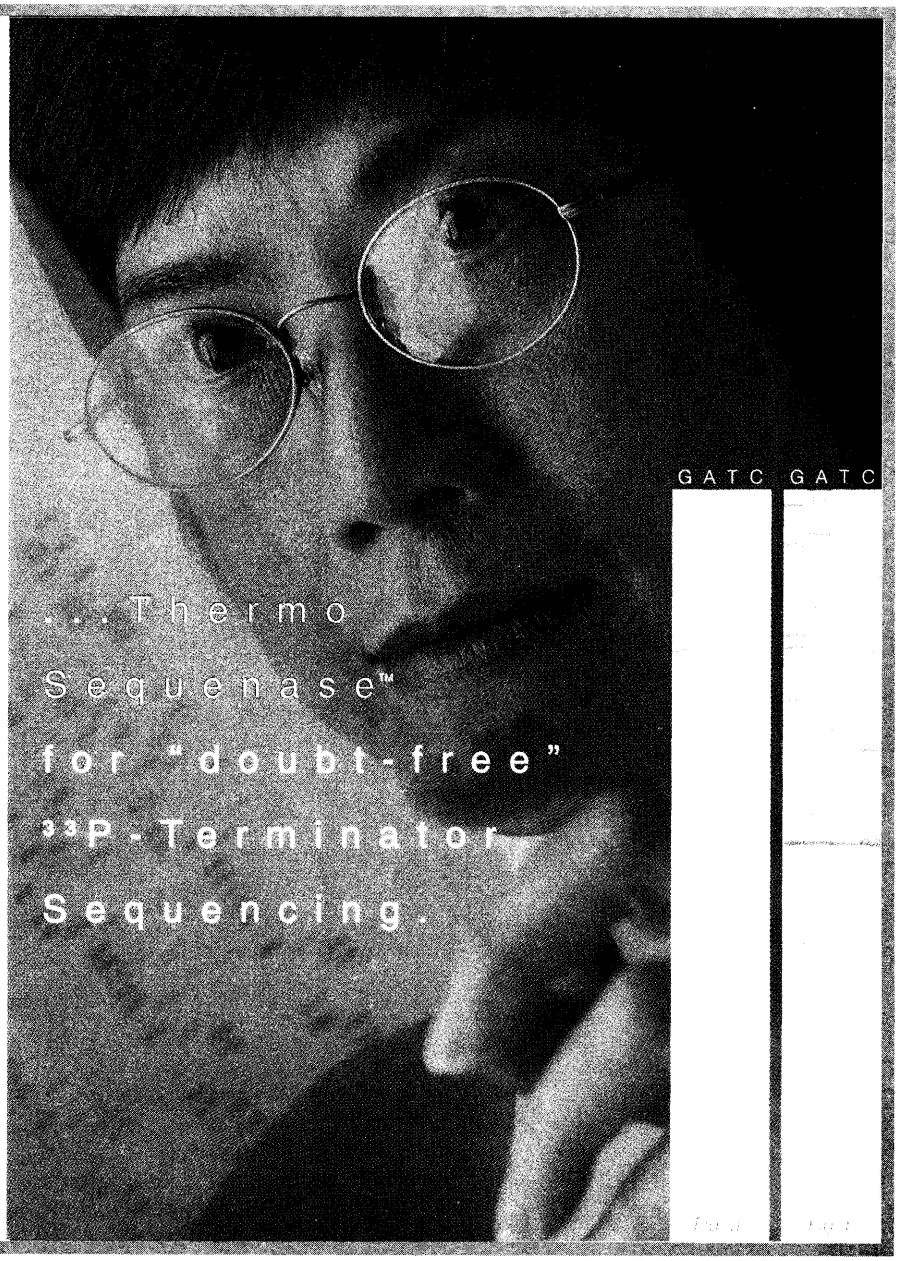

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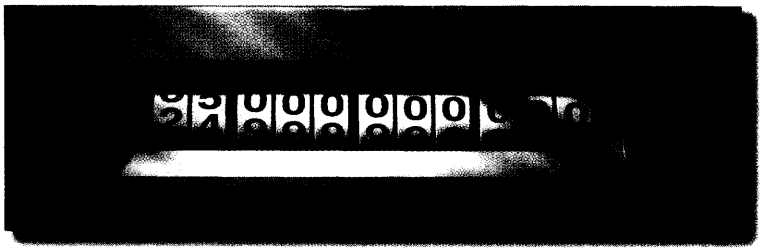

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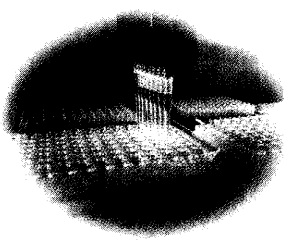

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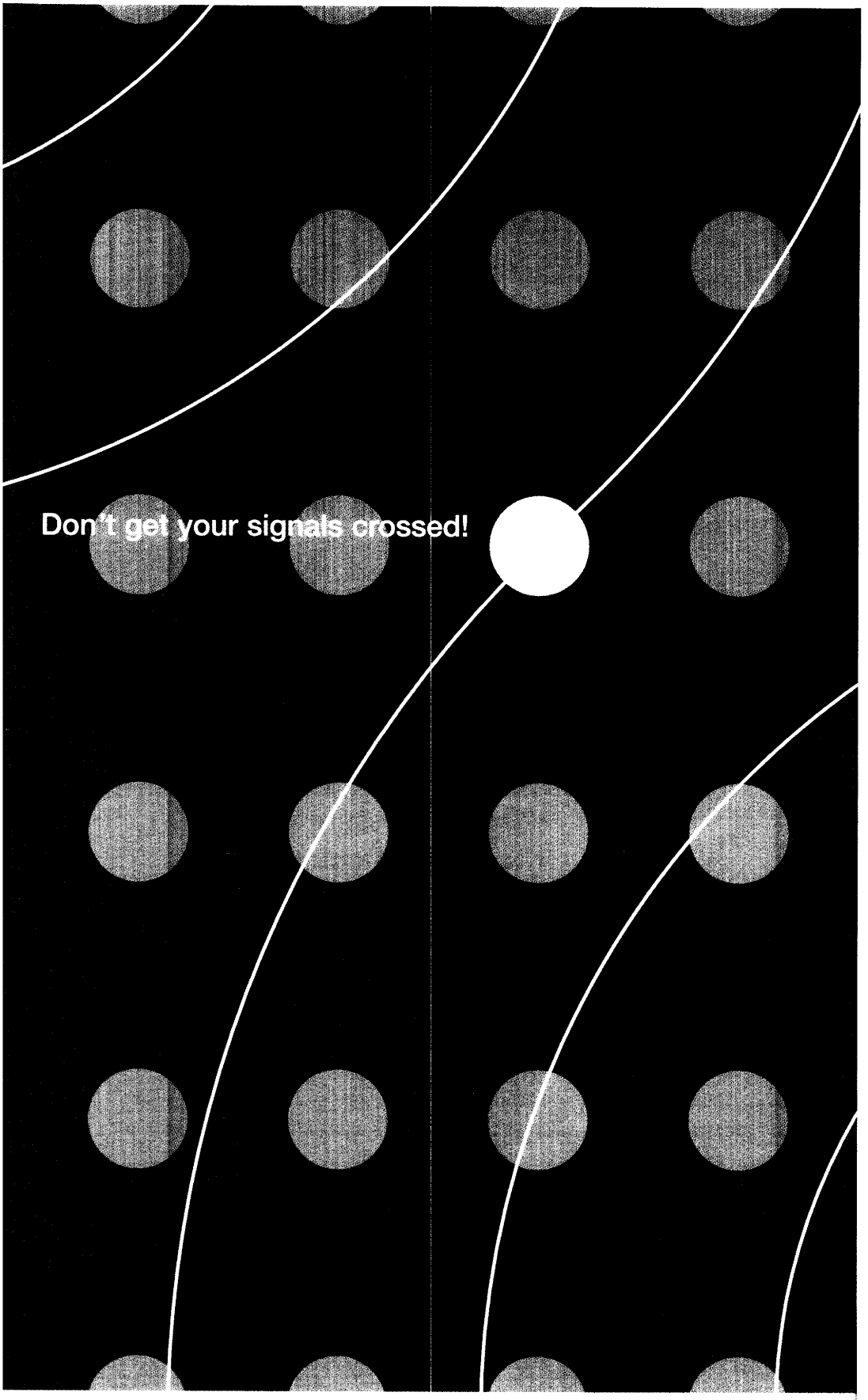

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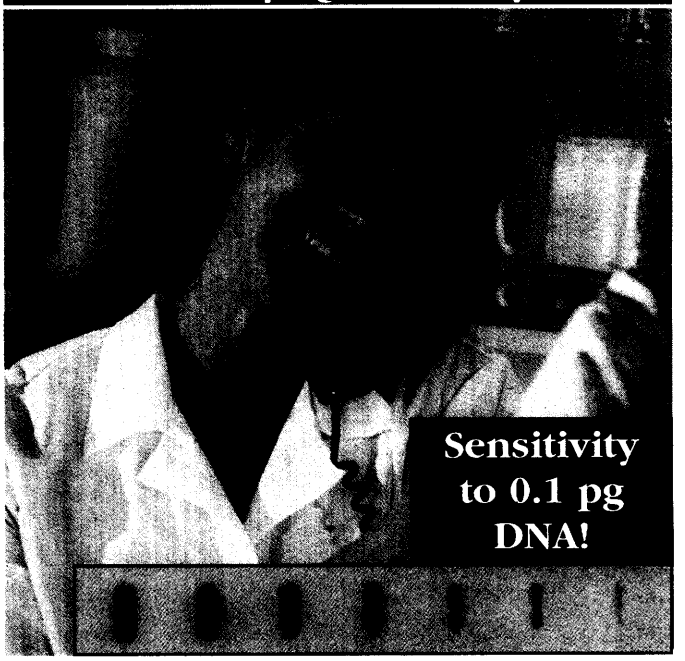

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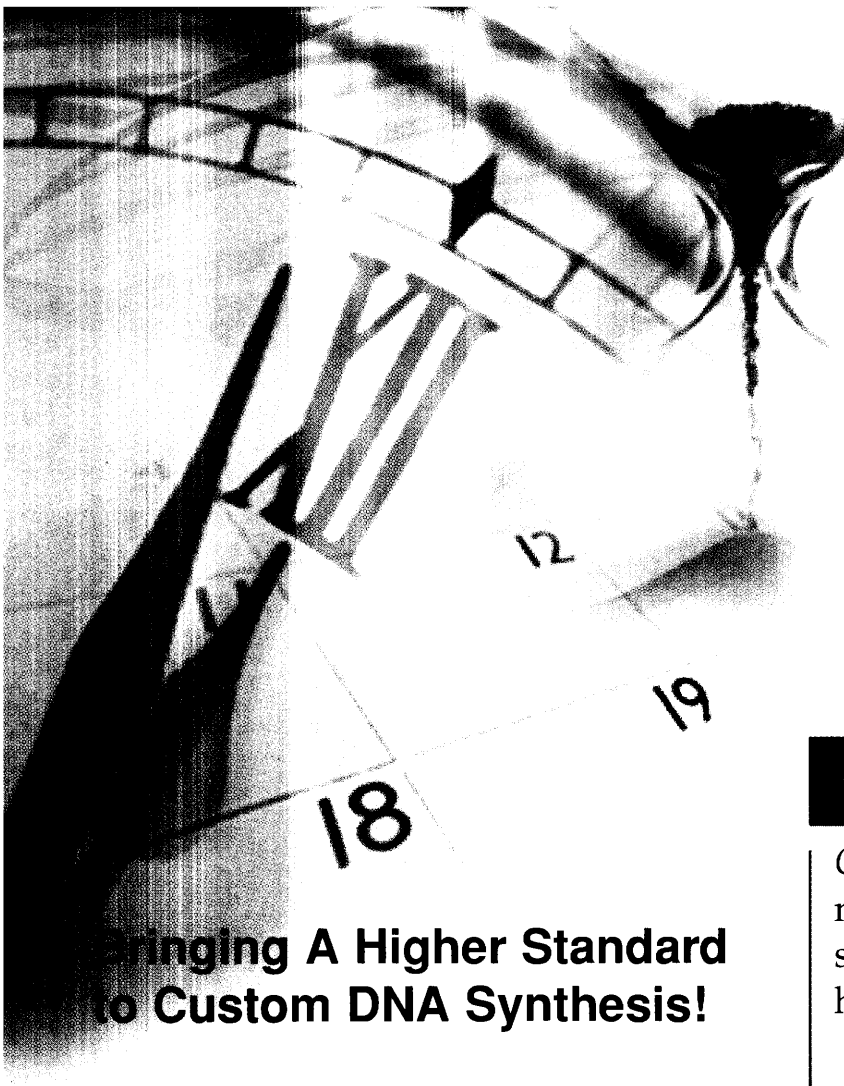

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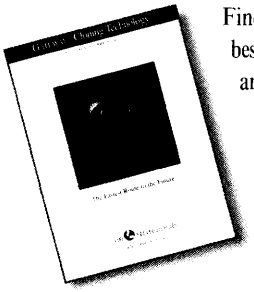

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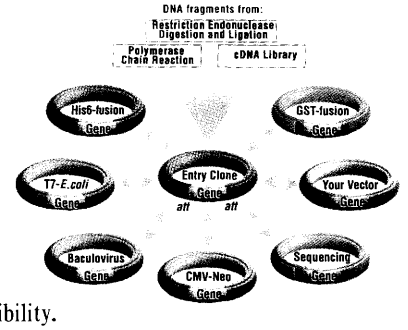

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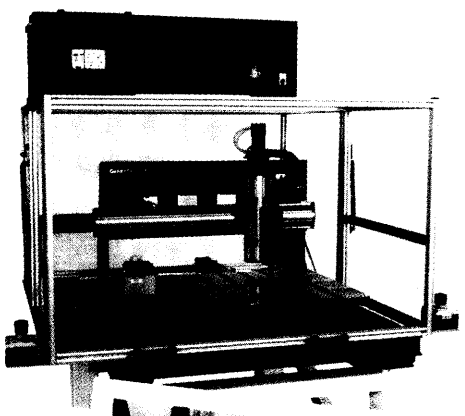

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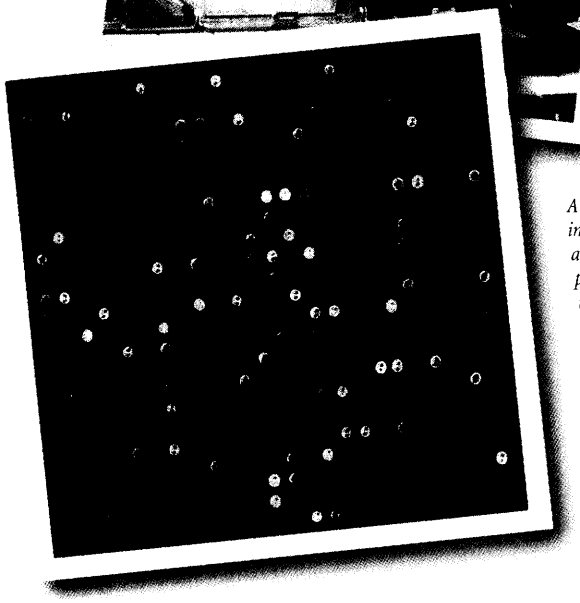

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