21 July 2000

Science

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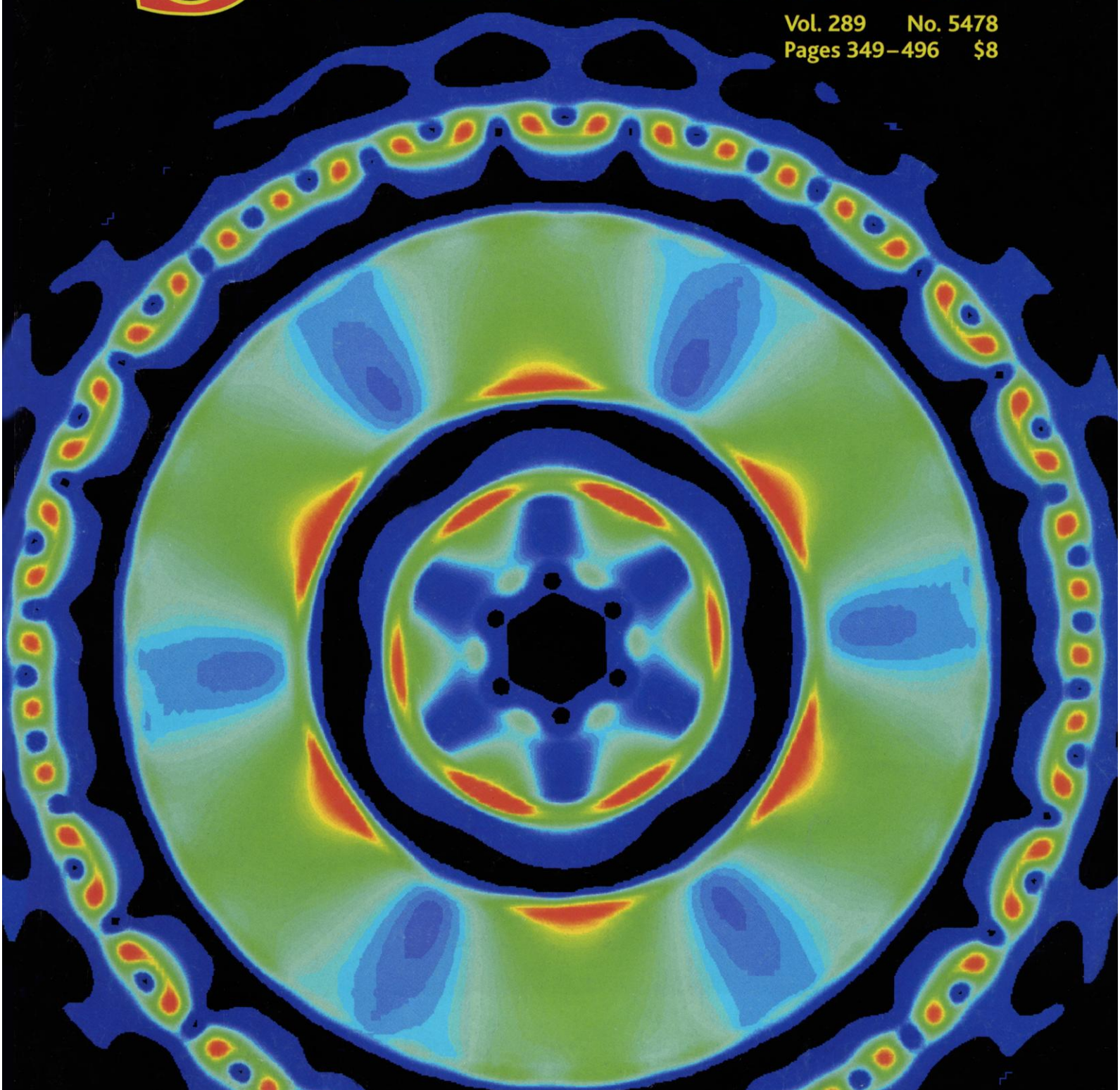

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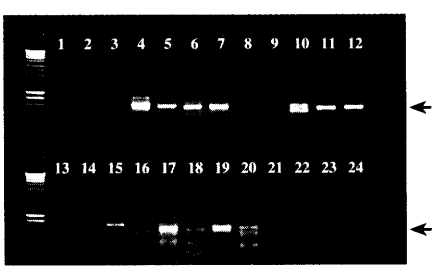
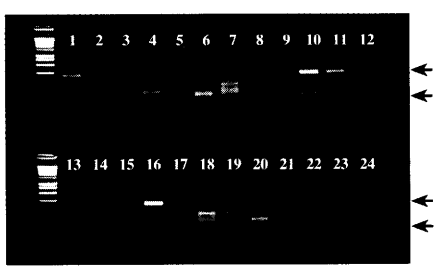


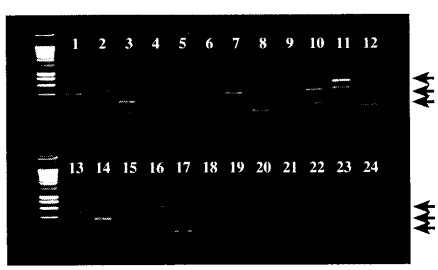
(1) To complete the 5'-end sequences of long and rare transcripts with extensive secondary structures.

The ataxia telangiectasia (ATM) gene encodes an ubiquitous ~12 kb transcript with extensive conformations and heterogeneous 5' ends.



(2) To discover alternate RNA start-sites derived from different tissue-specific transcriptional promoters.

The intercellular adhesion molecule-1 (ICAM-1) gene uses different promoters to initiate transcription.



(3) To identify differentially-spliced transcripts that contain alternate 5' exons that are utilized in different tissues.

The fibroblast growth factor 1 (FGF-1) gene makes use of different 5' exons to regulate its expression.

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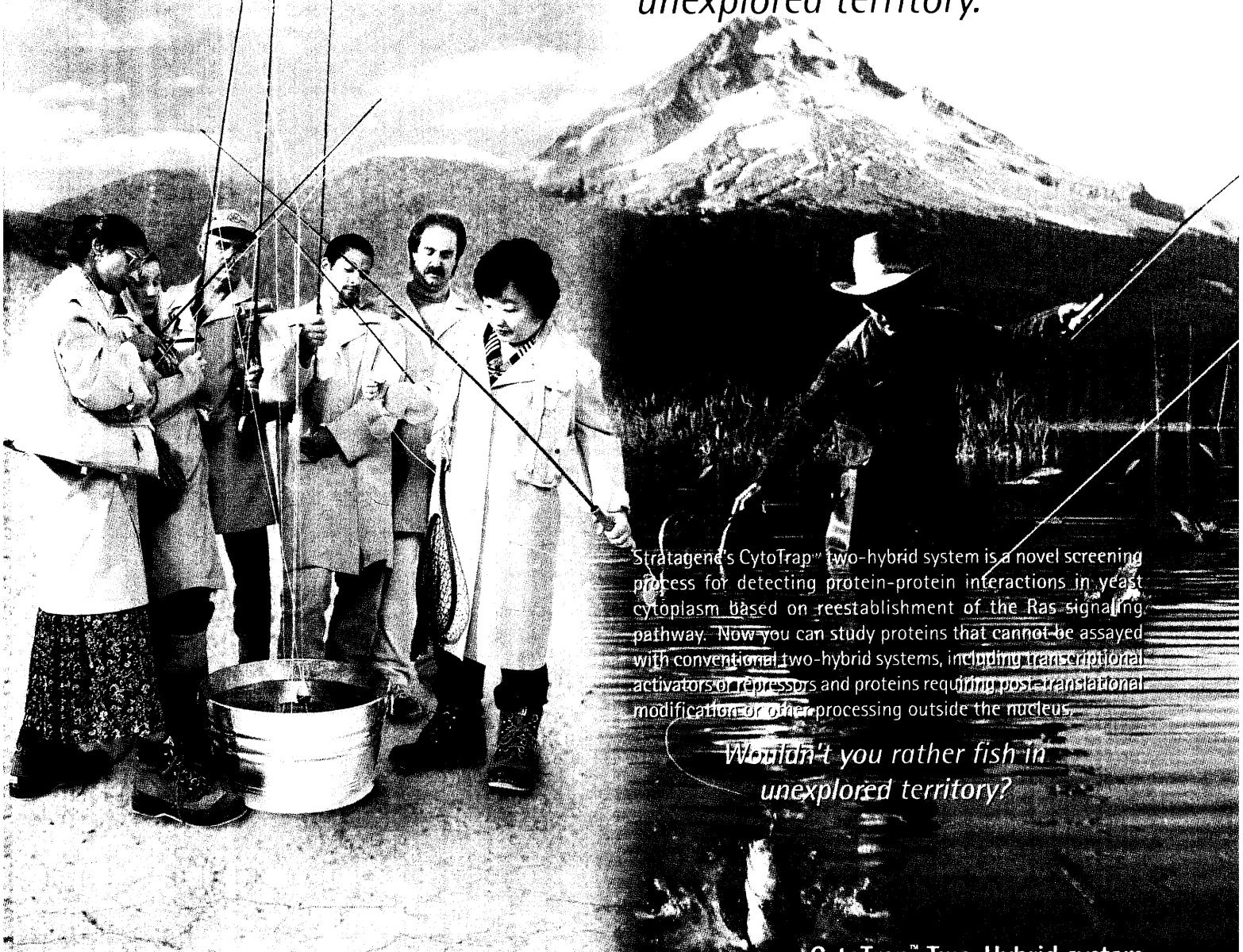

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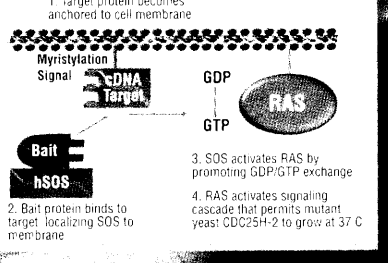

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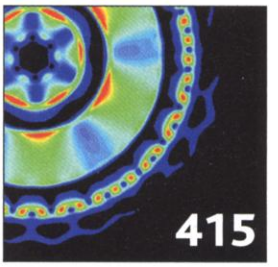
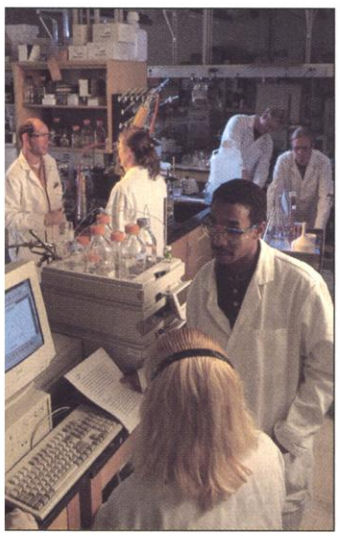


COVER The coaxial cable, long used for demanding electrical applications, has now been used as a model for improving glass optical fibers. A model study demonstrates how light dispersion and polarization shifts that occur in traditional optical fibers can be overcome when light travels through an all-dielectric coaxial cable whose inner and outer walls are made of omnidirectionally reflecting multilayer films, as shown by the model's electromagnetic fields seen here. [Image: M. Ibanescu *et al.*]



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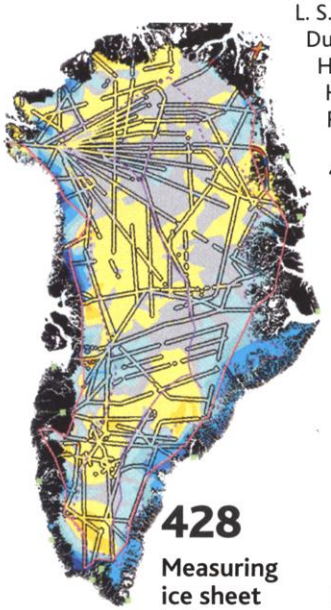

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DEPARTMENTS

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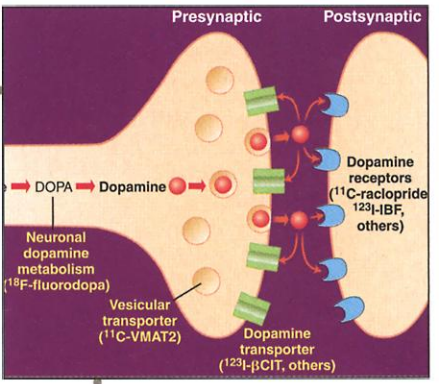

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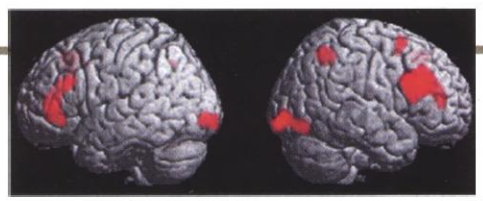
TECH.SIGHT



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What is intelligence?

TECHNICAL COMMENTS

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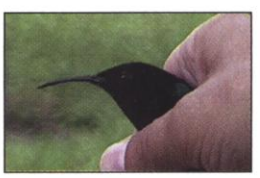

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Vive la différence

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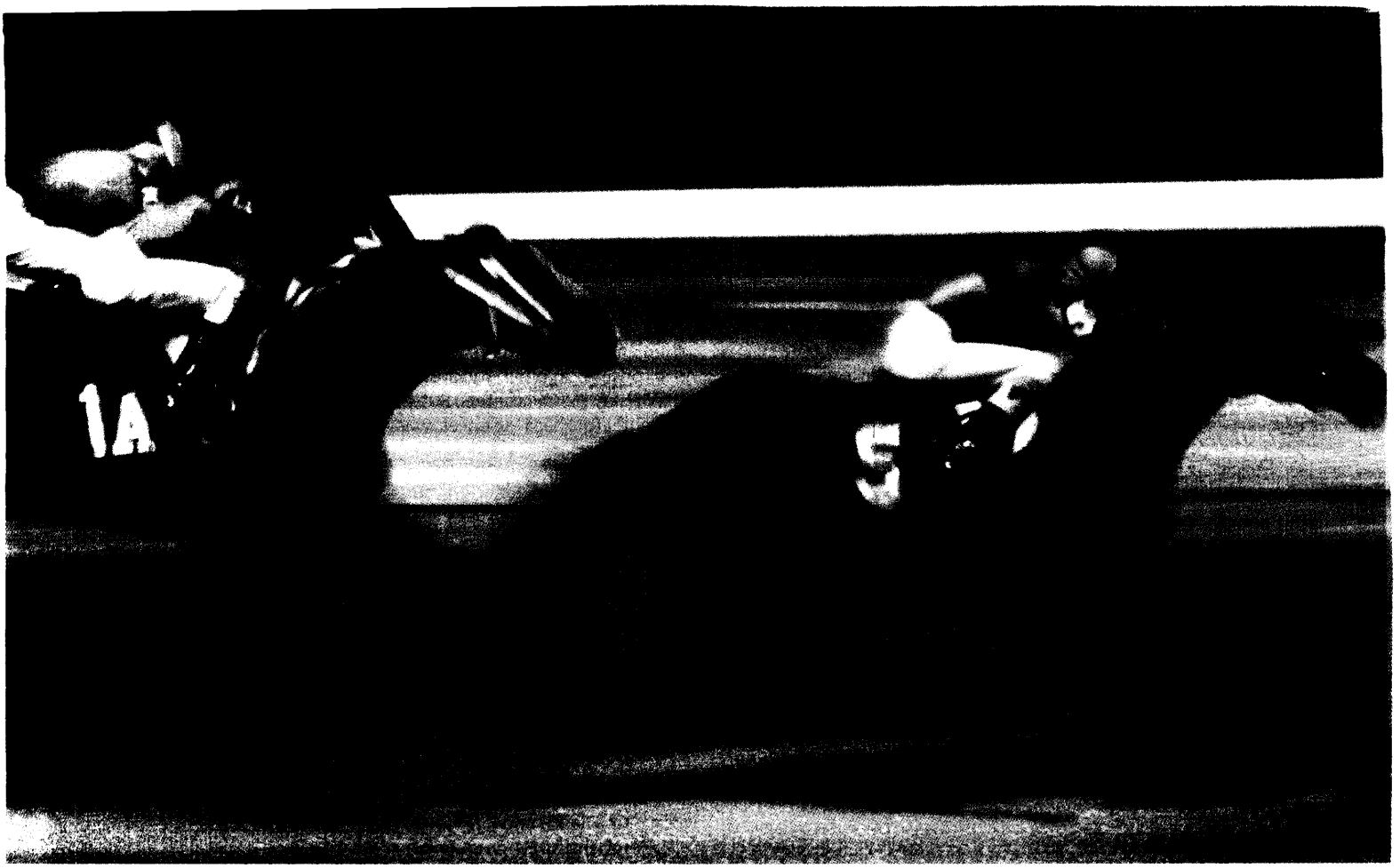

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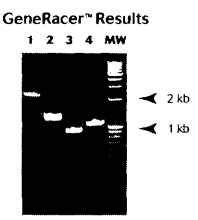

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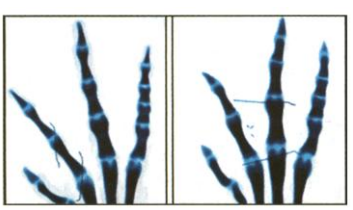
RUNNING LIGHT DOWN COAXIAL CABLES

Although highly successful in communications, present optical fibers are limited in that sharp kinks in the fiber render them useless because the light is guided by total internal reflection from the internal walls of the fiber. Also, as the light passes through the fiber, the polarization is shifted, making it awkward for applications requiring information on the polarization to be transferred. Ibanescu *et al.* (p. 415; see the cover) introduce the concept of a coaxial optical fiber in which the light-guiding region is sandwiched between two omnidirectional (angle- and polarization-independent) mirrors—a dielectric inner core and a cylindrical, all-dielectric multilayer. Their simulations show that such a waveguide should support a single-mode transverse electromagnetic wave similar to those in coaxial cables used in electrical connections.

DIGITAL SIGNALING

Proximal-distal patterning of the developing limb causes the digits to be placed at the end of the limb. What determines the rather useful difference between, for example, the big toe and its little compatriot has remained obscure. Now, in studies in



the chick, Dahn and Fallon (p. 438; see the news story by Hagmann) show that the identity of each digit is specified by the mesoderm that temporarily forms a continuum between digits early in development, not by digital primordia itself. These positional clues may be carried by the bone morphogenic signaling proteins.

RESOLVING SUBATOMIC FEATURES

Despite the name, much effort and care is usually needed to obtain atomic resolution with the atomic force microscope (AFM). Giessibl *et al.* (p. 422) now go one step further. They used a special detection scheme particularly sensitive to short-range forces to resolve subatomic features on the silicon (111)-(7×7) surface with an AFM. Individual adsorbed atoms on this surface show features that can be interpreted in terms of orbital overlap between the tip and the adsorbed atom. The method may provide detailed insights into features such as dangling bonds.

DROP BY DROP

How has polar ice responded to the extraordinary warmth of the 1990s? Two different methods have recently been used to determine the mass balance of the Greenland ice sheet (see the Perspective by Dahl-Jensen). Thomas *et al.* (p. 426) estimated rates of ice discharge for all of Greenland between 1993 and 1997 by using a dense network of global positioning satellite measurements of ice motion. They then compared these data to snow accumulation rates to determine where and how fast the ice sheet is growing or shrinking. Krabill *et al.* (p. 428) made the same type of estimates using aircraft laser-altimeter surveys. These two independent methods reveal an ice sheet that is close to being in balance in the north and in the interior but is thinning rapidly along much of the coast, especially in the southeast. The rapid thinning at the margins appears to be too fast to explain only by melting and probably involves changes in the dynamics of ice flow. The annual net loss from the ice sheet is about 50 cubic kilometers of ice per year, enough to account for 7% of the measured rate of modern sea level rise.

A SUDDEN END TO THE PERMIAN

The largest mass extinction occurred at the end of the Permian, about 250 million years ago, and eliminated more than 90% of all marine species and many land plants and animals. The duration of the extinction (whether it occurred in one episode or in several stages) and the primary cause have been uncertain. Jin *et al.* (p. 432) analyzed in detail fossil occurrences in the Meishan marine section in South China. The data are consistent with a sudden extinction (within a few hundred thousand years) rather than a series of extinction steps. The marine extinction coincides with an abrupt decrease in carbon isotope values, although the specific cause of the extinction remains enigmatic.

SETTING SEED

Intricate networks of signals define the boundaries that develop between groups of developing cells, and later tissues, as they diverge during differentiation. Studying the seed pod of *Arabidopsis*, Ferrándiz *et al.* (p. 436) now identify some of the signals that differentiate valve cells from margin cells. A negative interaction between the *FRUITFULL* and *SHATTERPROOF* genes ensures that cells in a narrow strip along the edge of the valve acquire characteristics such that a particular zone of the seed pod (the dehiscence zone) can break to release seeds. Dehiscence, as well as lignification, which is also regulated by *FRUITFULL*, are important agronomic traits.

PROGRAMMING VESICLE BUDDING

Intracellular membrane traffic involves the sequential budding of vesicles from a donor membrane followed by vesicle fusion with a specific target membrane. Allan *et al.* (p. 444; see the Perspective by Brittle and Waters) examined the molecular mechanisms involved in generating vesicles that "know" what their target membrane should be. They found that a protein designated p115 is specifically recruited to vesicles budding from the endoplasmic reticulum. The presence of p115 then helps the vesicle to recognize when it has reached the correct target Golgi membrane and to allow subsequent fusion.

WHEN MALES AND FEMALES FIT THE BILL

Sexual dimorphism in animals is a common phenomenon. Often it is explained by sexual selection, and only rarely have ecological factors been implicated in morphological differences between males and females. Temeles *et al.* (p. 441; see the news story by Brown) report the case of the purple-throated carib hummingbird on the Caribbean island of St. Lucia. The males are larger than females but have smaller bills. Males feed on the nectar from one *Heliconia* species, while females feed on the flowers of a closely related species. The bill morphology of each sex matches the shape of the flowers of its preferred *Heliconia* species. In habitats where only one *Heliconia* species is present, it occurs in two floral morphs that match the bill shapes and sizes of the two sexes of the hummingbird. Food competition between the sexes is the most likely cause of the sexual differences in resource use.

CONTINUED ON PAGE 359

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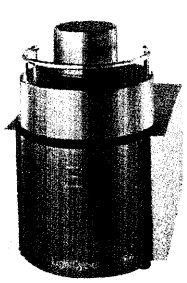

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 357

JEKYLL AND HYDE RNA

The molecular repertoire of RNA continues to impress through its ability to mimic many of the functions of its much more complex molecular cousins, the proteins. Schultes and Bartel (p. 448; see the Perspective by Joyce) have now pulled off an engineering feat unlikely to be equaled by those who work on proteins: a single RNA "enzyme" that can fold into two completely unrelated structures with differing enzymatic functions. The molecule was built by identifying the point in sequence space (or the "neutral network") where two unrelated ribozymes overlap. Thus, from an evolutionary perspective, it would appear that divergence of function in RNA molecules could precede their duplication.

TAKING A NEW LOOK AT INTELLIGENCE TESTING

Intelligence might be categorized as something difficult to describe but easy to recognize. There have been many attempts to develop a test that is predictive of intelligence (with the aim of being explanatory), but the interpretations of these tests and of performance on these tests have been controversial. Duncan *et al.* (p. 457 of functional brain imaging in a study that reveals the patterns of neuronal activation during so-called high-*g* and low-*g* testing. They suggest that these patterns are more supportive of Spearman's hypothesis of a localized general intelligence factor underlying cognitive success on tests, as opposed to Thomson's view that multiple foci of cognitive skills are coordinately recruited (but see the Perspective by Sternberg).

MOBILE RNA TARGETED TO KILL

Group II introns are mobile genetic elements consisting of catalytic RNA that can recognize and insert themselves into a specific target sequence in double-stranded DNA. It is possible, in *Escherichia coli*, and at low efficiency, to modify the introns to insert at new sites in DNA. Guo *et al.* (p. 452; see the news story by Strauss), using a clever in vivo selection method to optimize the sequences that determine the target site, show that the introns can be made to insert with high efficiency into therapeutically relevant genes. The retargeted introns also function in human cells. This proof-of-principle opens the way for developing the group II introns as part of the molecular toolkit of the genetic engineer.

NURTURE CHANGES NATURE

How fixed are the behavioral responses that are inbred in certain strains of mice? Cabib *et al.* (p. 463) analyzed the behavior of two strains of mice after a short period of food restriction. The DBA/2 strain of mice became more sensitive to amphetamine-induced locomotion, and their previously conditioned behavior, place aversion, was replaced by conditioned place preference. A second strain, C57BL/6 mice—selected because they are normally at the opposite end of the behavioral spectrum—showed no change in behavior. A simple environmental manipulation can thus dramatically alter the subsequent behavior of certain inbred strains of animals.

TECHNICAL COMMENT SUMMARIES

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/289/5478/359a

Screening *hCHK2* for Mutations

Bell *et al.* (Reports, 24 December 1999, p. 2528) tied heterozygous germ line mutations in the checkpoint gene *hCHK2* to incidence of Li-Fraumeni syndrome (LFS). Drawing on recently deposited human genome sequence data, Sodha *et al.* point out the presence of six homologous fragments of the gene that include exons 10 through 14, and identify one of the mutations discussed by Bell *et al.*, deletion of T at nucleotide 1422 (1422delT), in one of these homologous fragments in 5% of control individuals screened. They suggest that some of the Bell *et al.* results may thus have stemmed from amplification of this homologous fragment. "The presence of several homologous fragments of the gene," conclude Sodha *et al.*, "has implications for mutation screening in this region of the gene using genomic DNA."

Bell *et al.*, in their response, agree with that statement and acknowledge the presence of the 1422delT mutation in the homologous fragment described by Sodha *et al.* in one of the cases studied. They note, however, that in other cases the mutation in *hCHK2* was identified using both genomic DNA sequencing and reverse transcriptase–polymerase chain reaction (RT–PCR) analysis of the *hCHK2* transcript and that their reexamination confirms that other key mutations discussed in the original study are present in the functional *hCHK2* gene.

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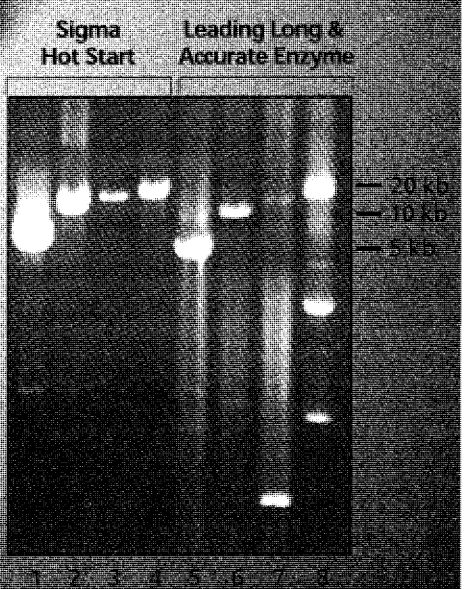

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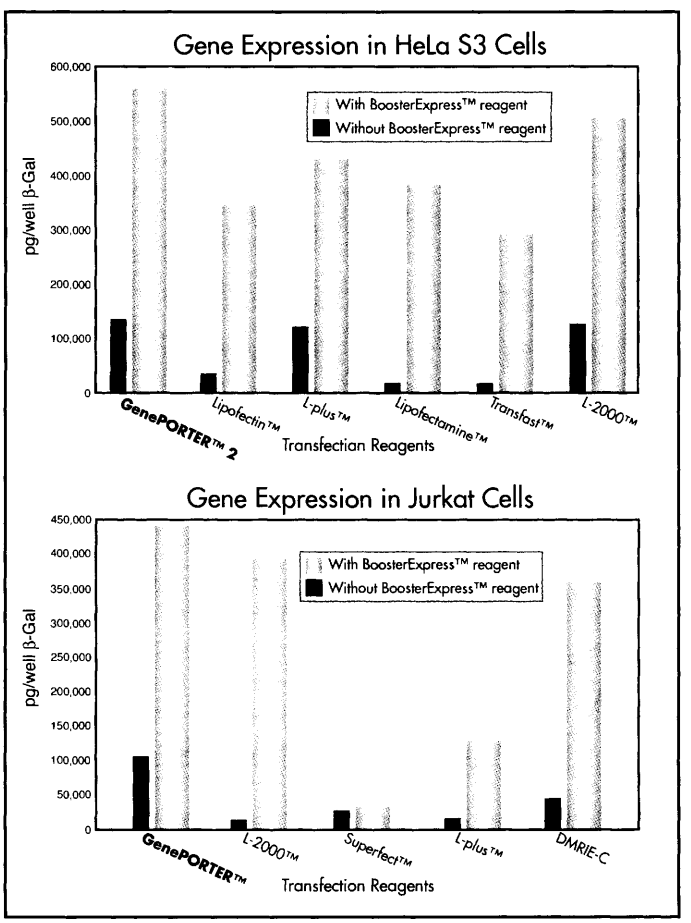

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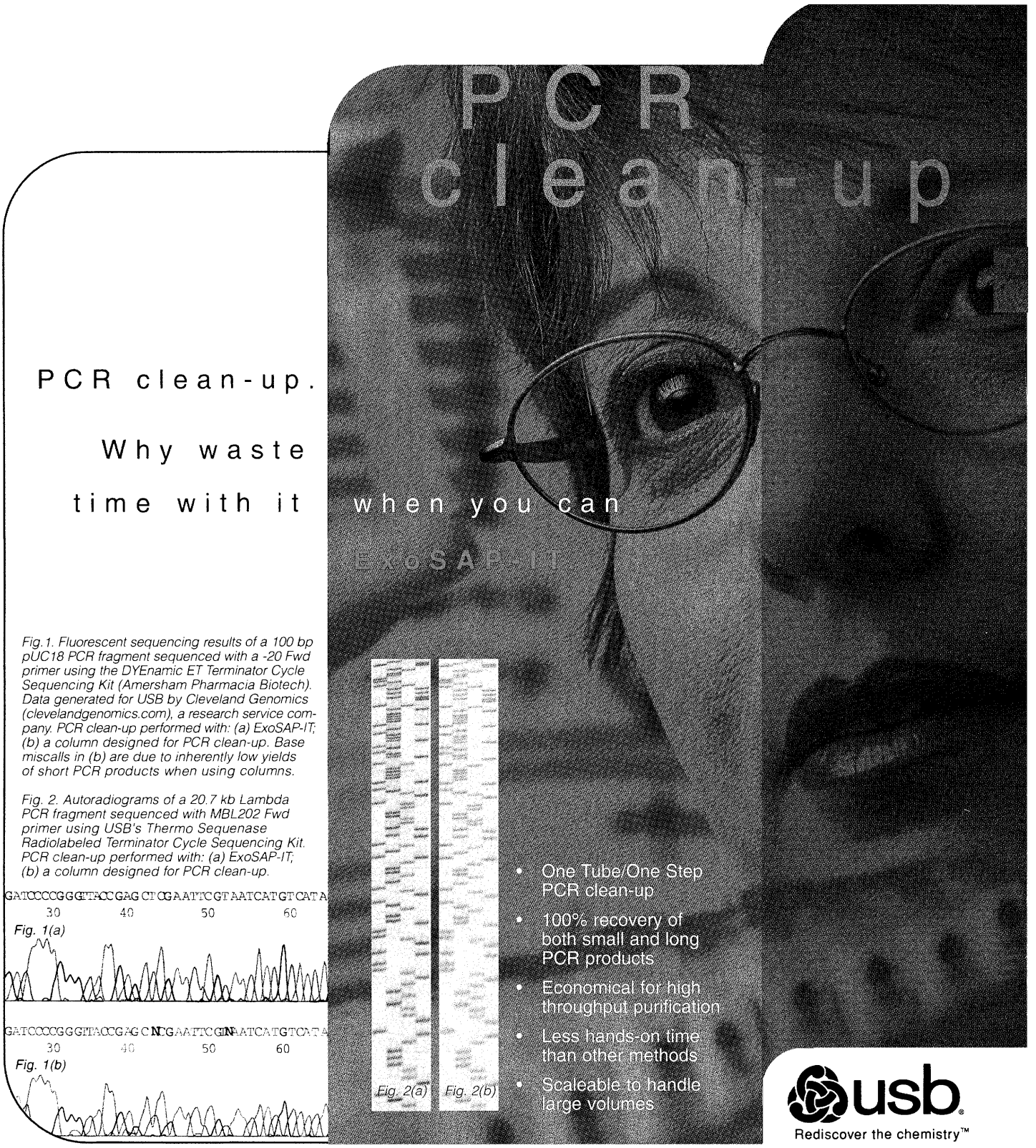

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Fig. 1. Fluorescent sequencing results of a 100 bp pUC18 PCR fragment sequenced with a -20 Fwd primer using the DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech). Data generated for USB by Cleveland Genomics (clevelandgenomics.com), a research service company. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up. Base miscalls in (b) are due to inherently low yields of short PCR products when using columns.

Fig. 2. Autoradiograms of a 20.7 kb Lambda PCR fragment sequenced with MBL202 Fwd primer using USB's Thermo Sequenase Radiolabeled Terminator Cycle Sequencing Kit. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up.

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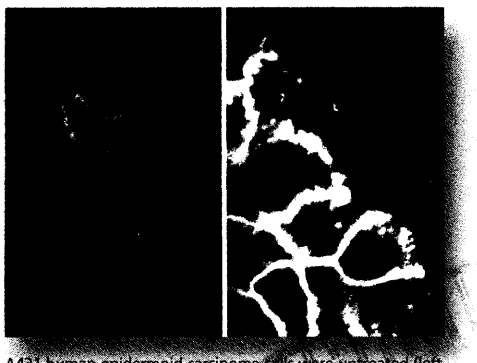
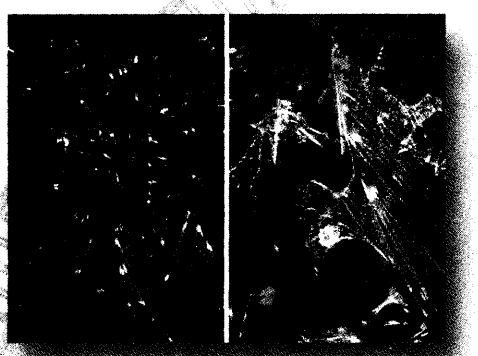
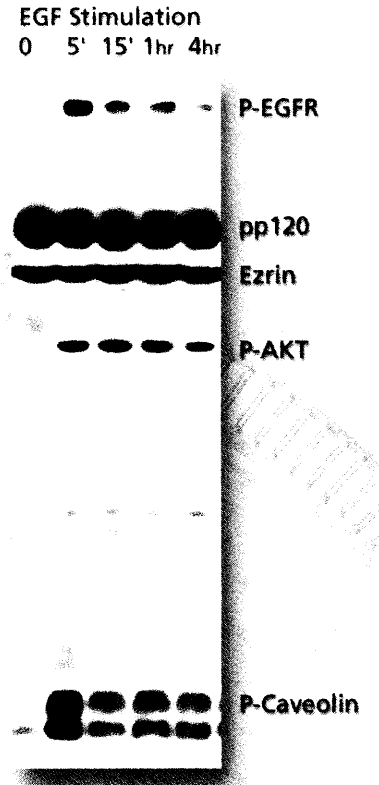


A431 human epidermoid carcinoma cells were untreated (left panel) or stimulated (right panel) with EGF for 5 minutes. Cells were analyzed by immunofluorescence using anti-phospho-EGFR.



NIH-3T3 murine fibroblasts were untreated (left panel) or stimulated (right panel) with pervanadate for 10 minutes. Cells were analyzed by immunofluorescence using anti-Actin (red) and anti-Phospho-Caveolin (green).



A431 human epidermoid carcinoma cells were stimulated with EGF for the indicated time (min. or hr.), lysed, and analyzed by Western blotting with the indicated antibodies. Anti-P-EGFR, anti-P-Akt, and anti-P-Caveolin are specific for the phosphorylated forms of their respective proteins.

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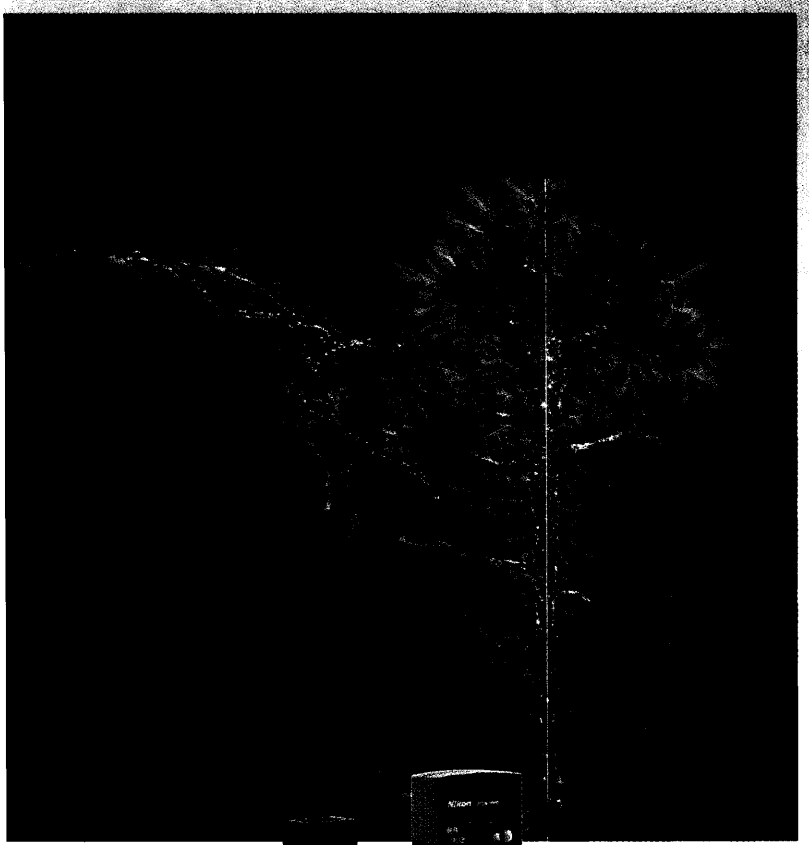

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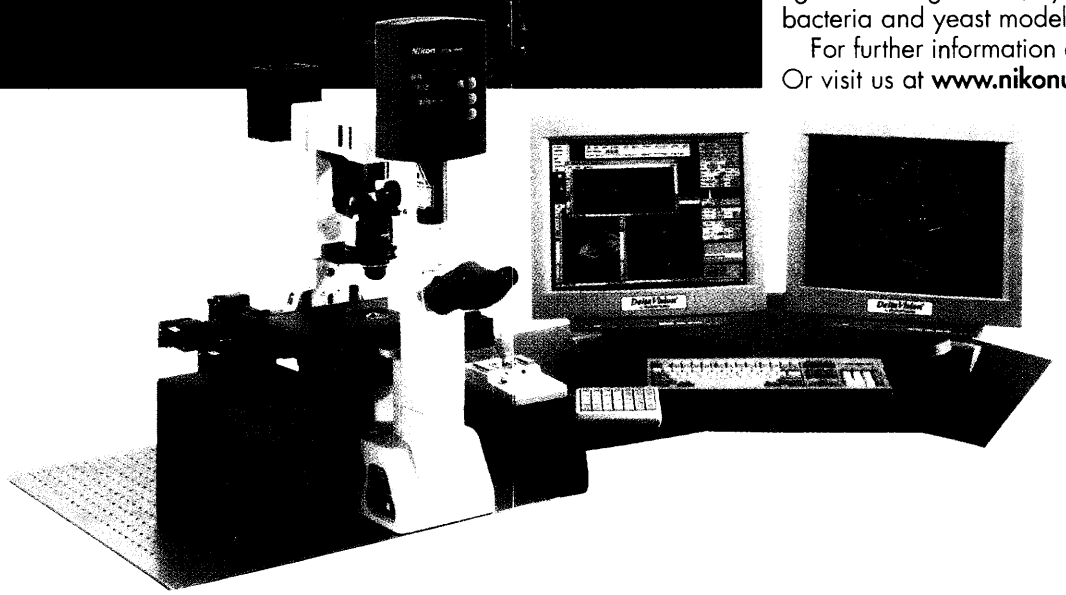

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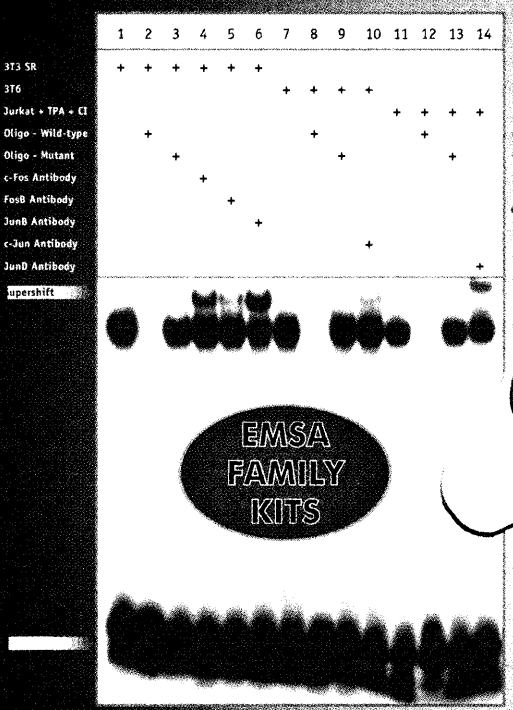

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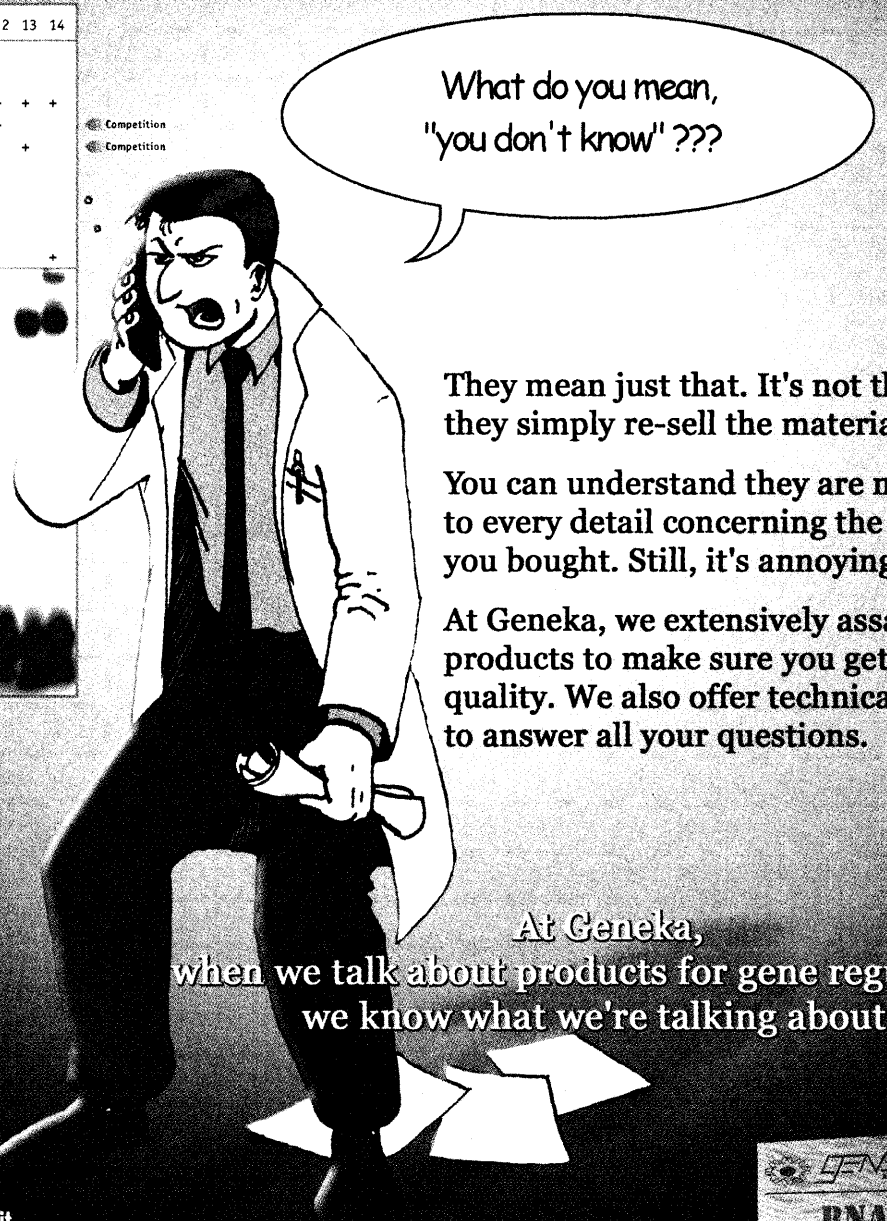

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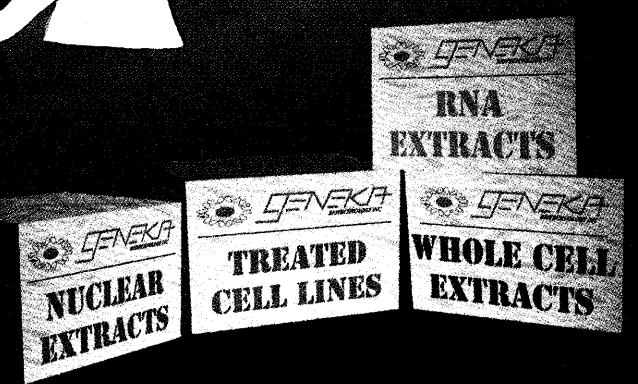

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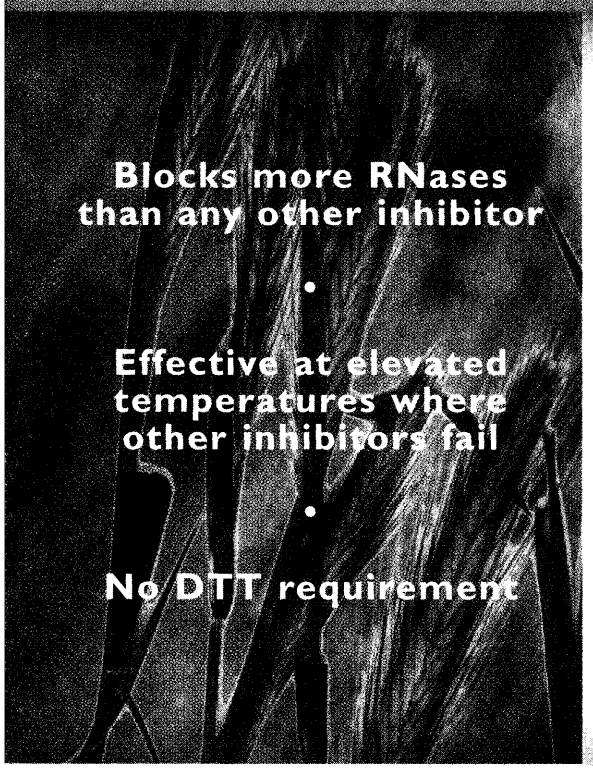

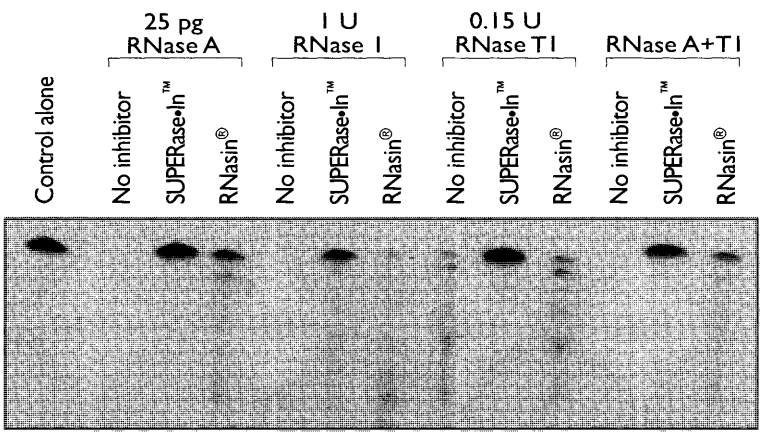

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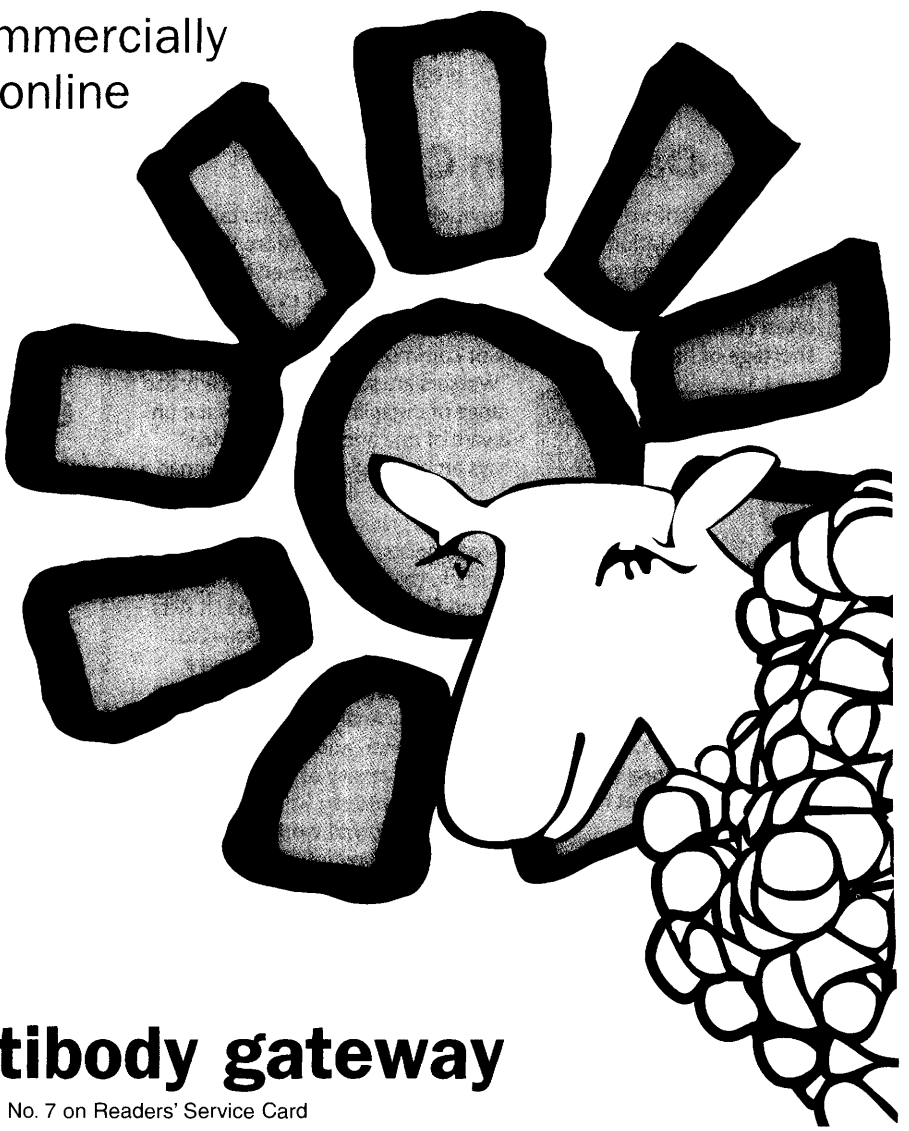

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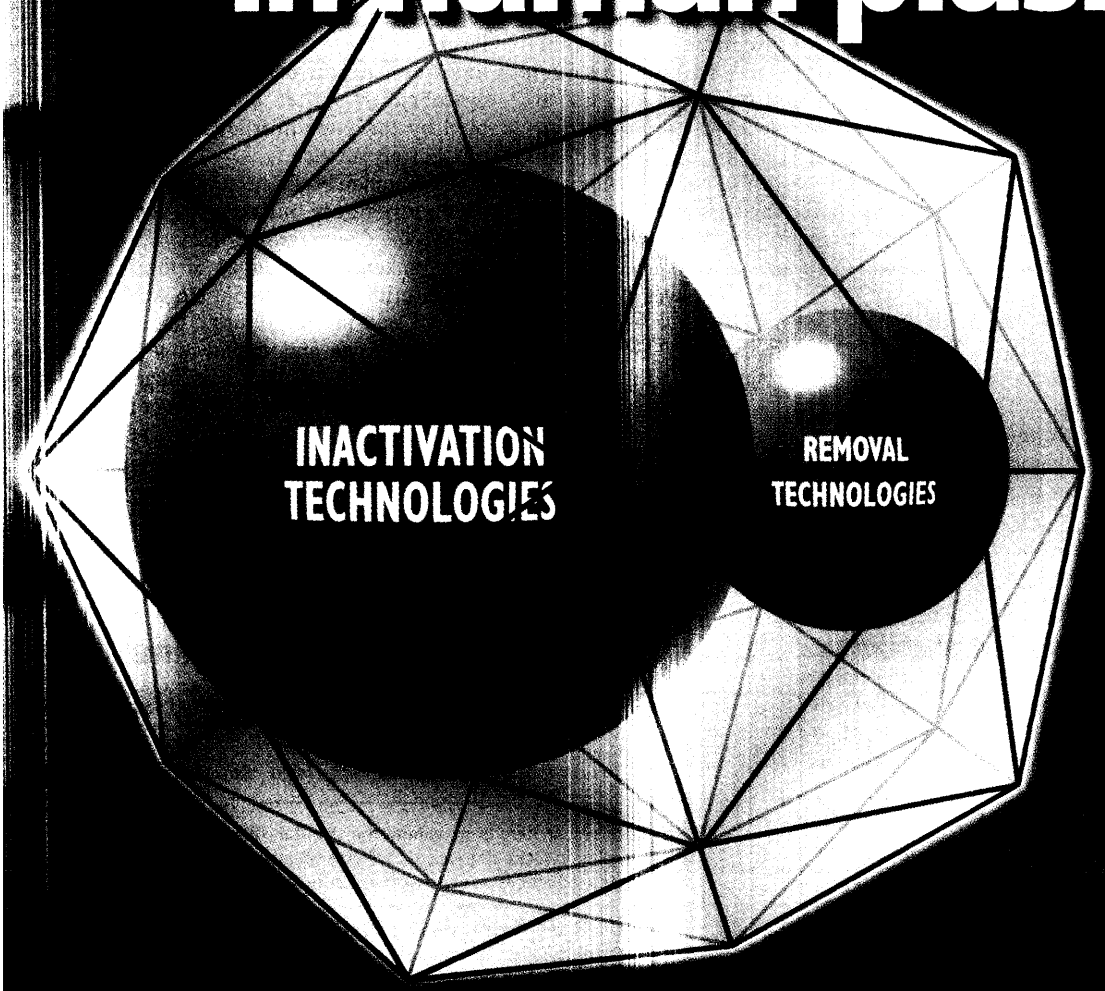

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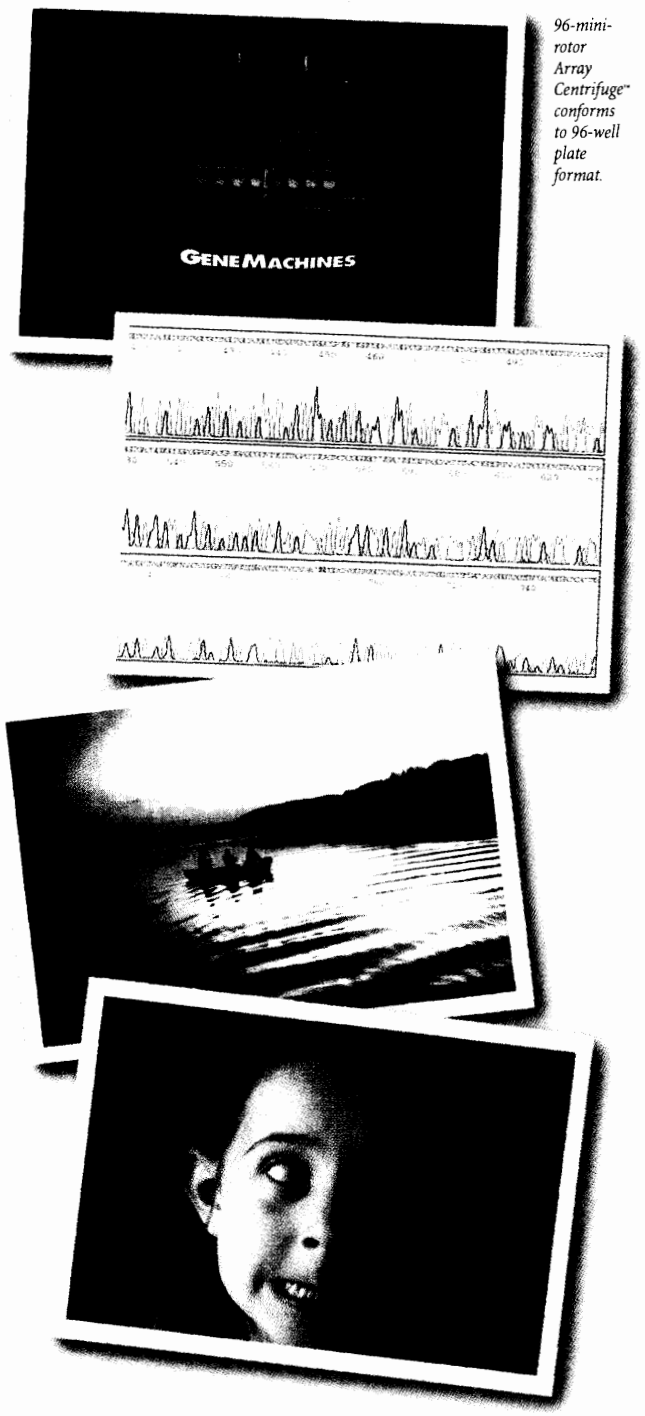

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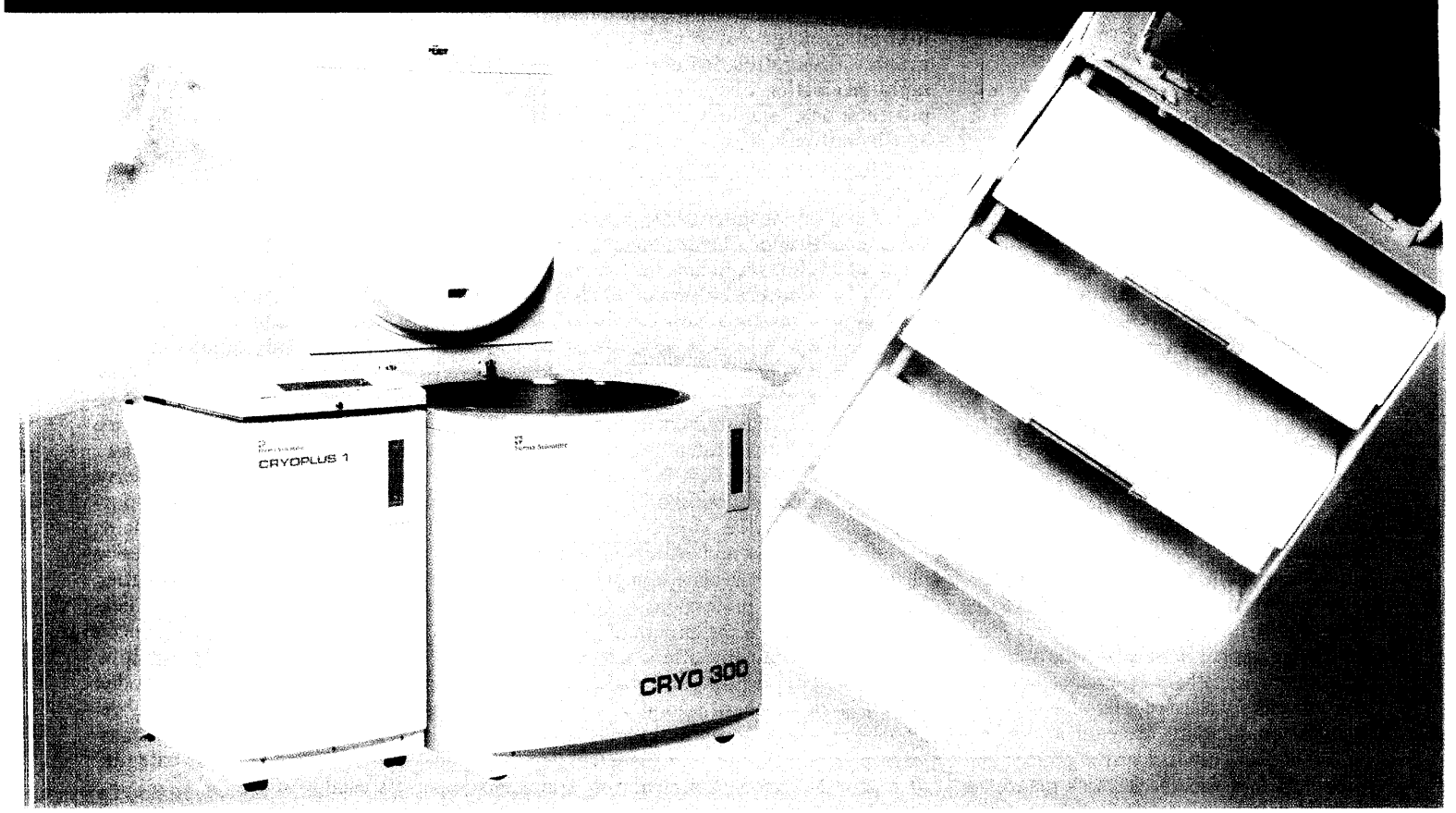

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