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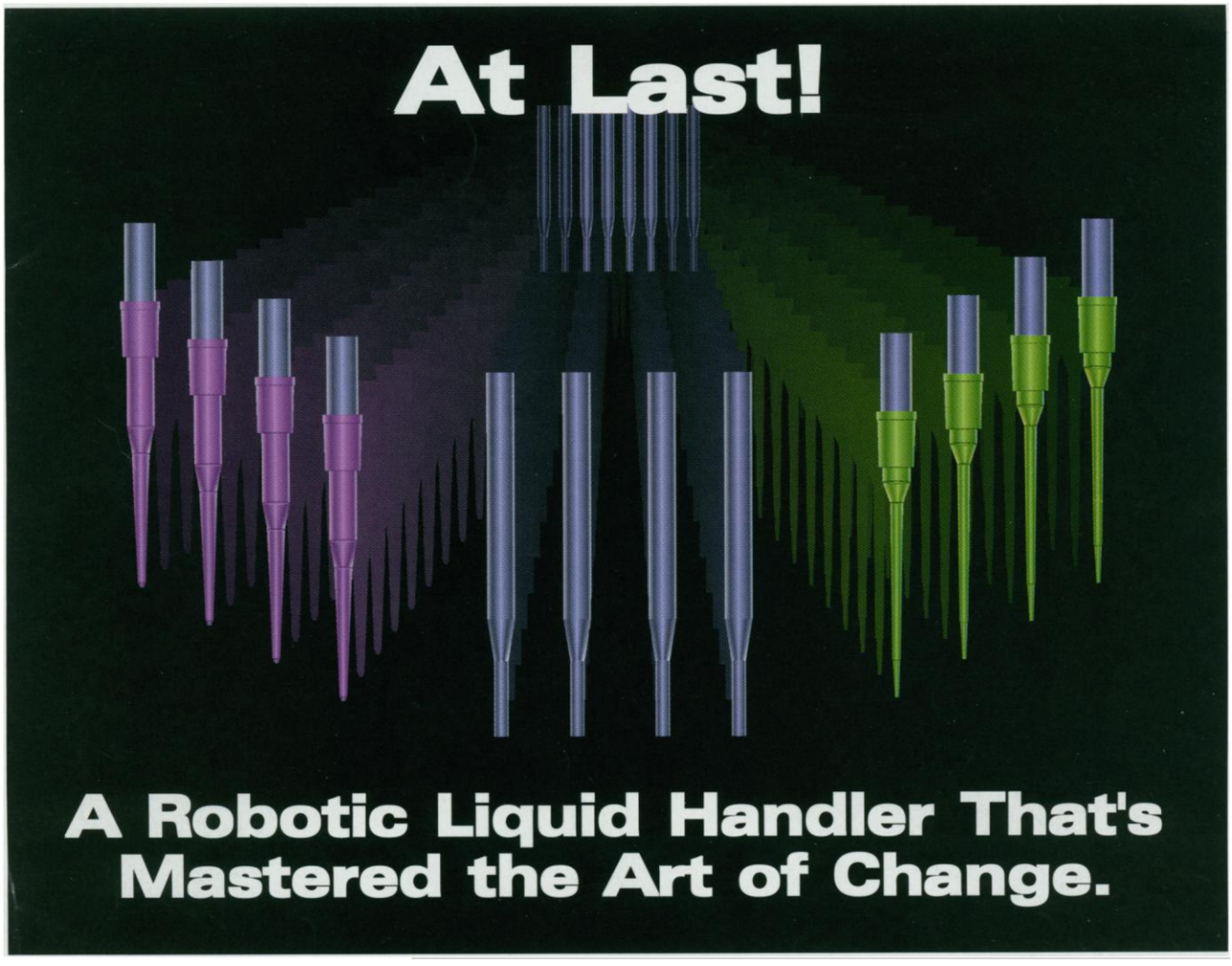

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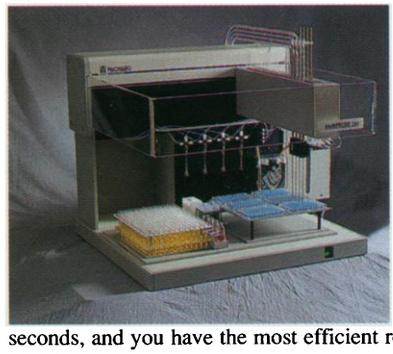

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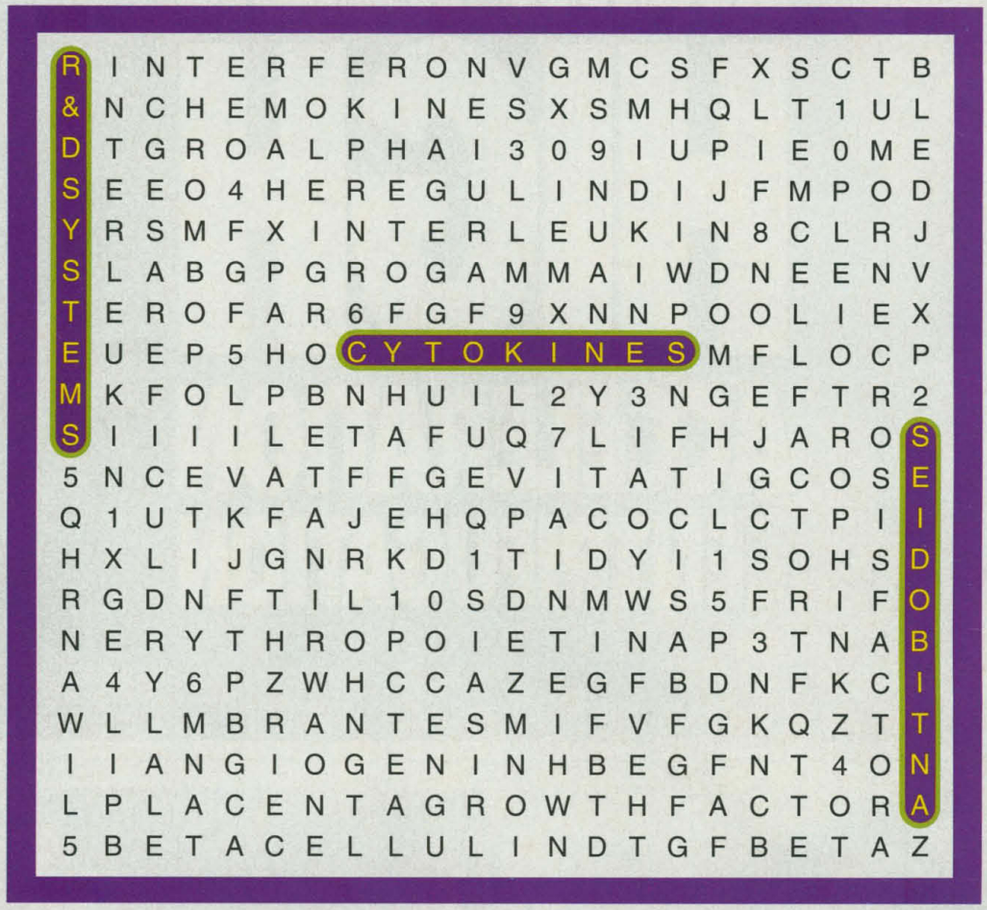

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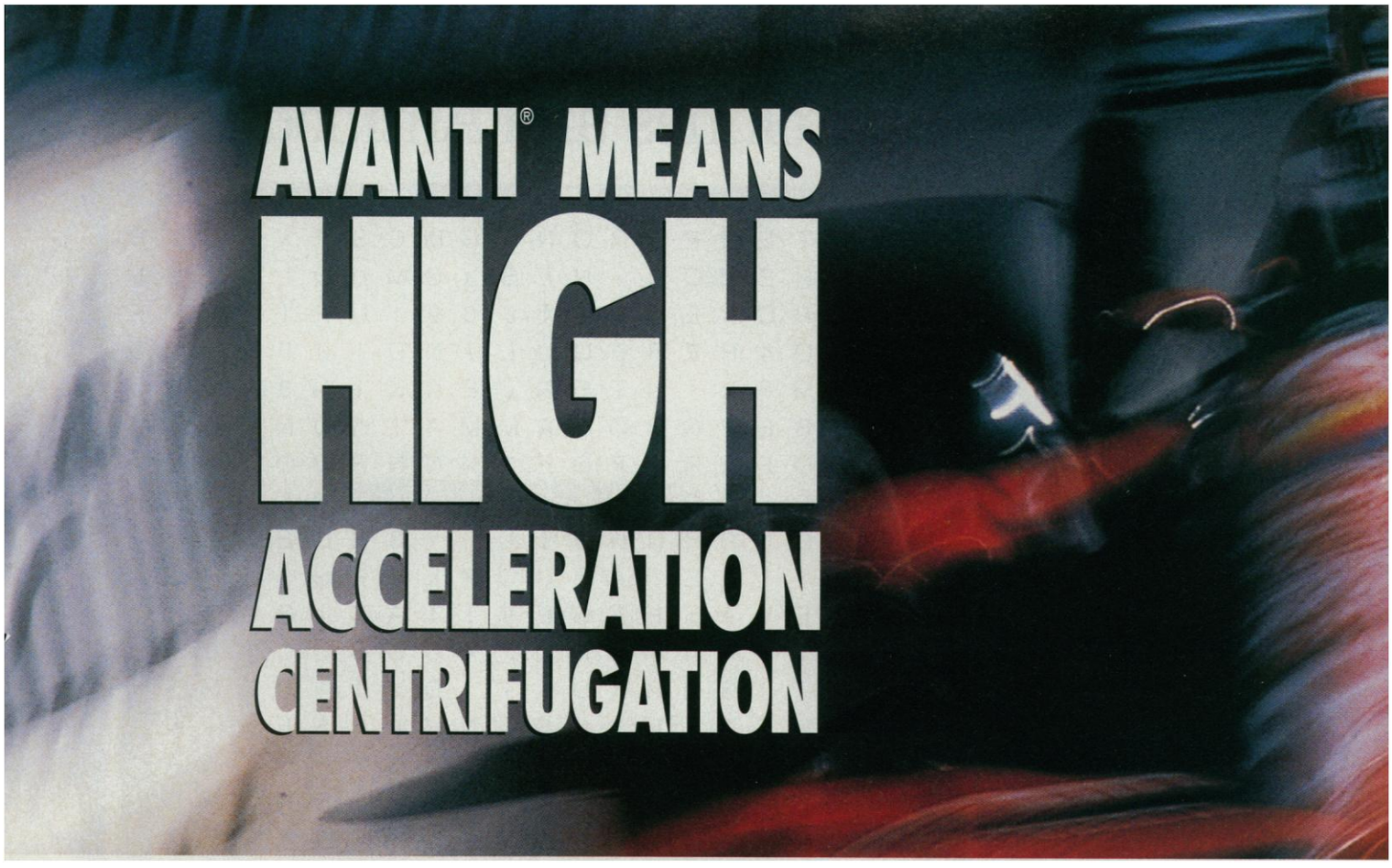
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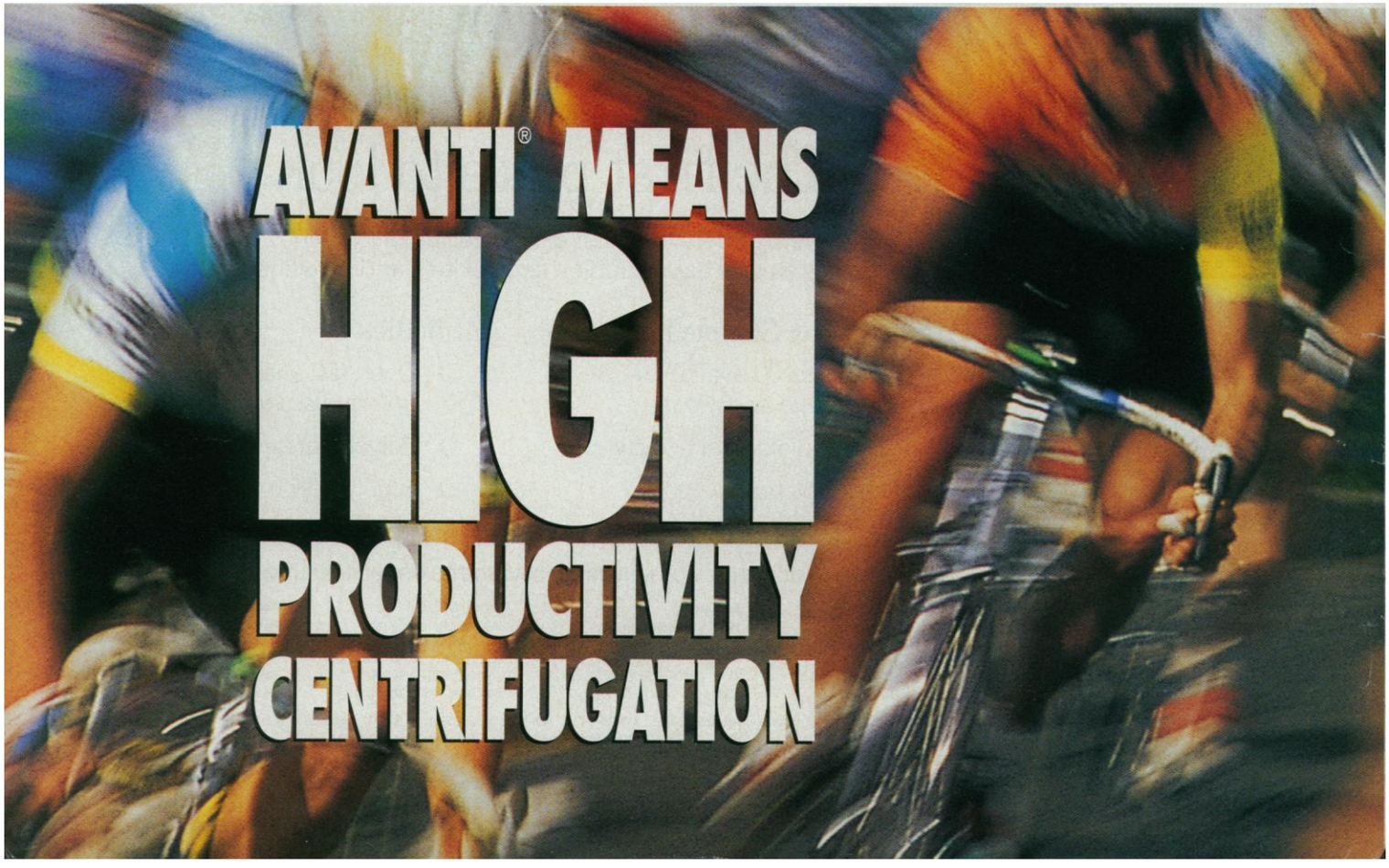
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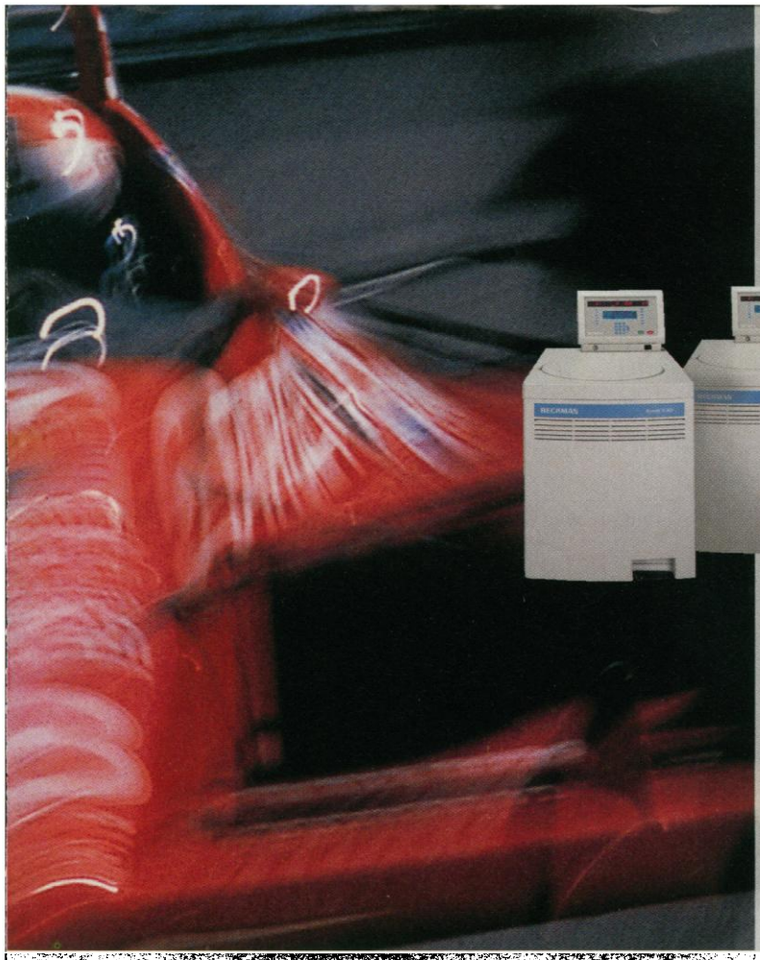

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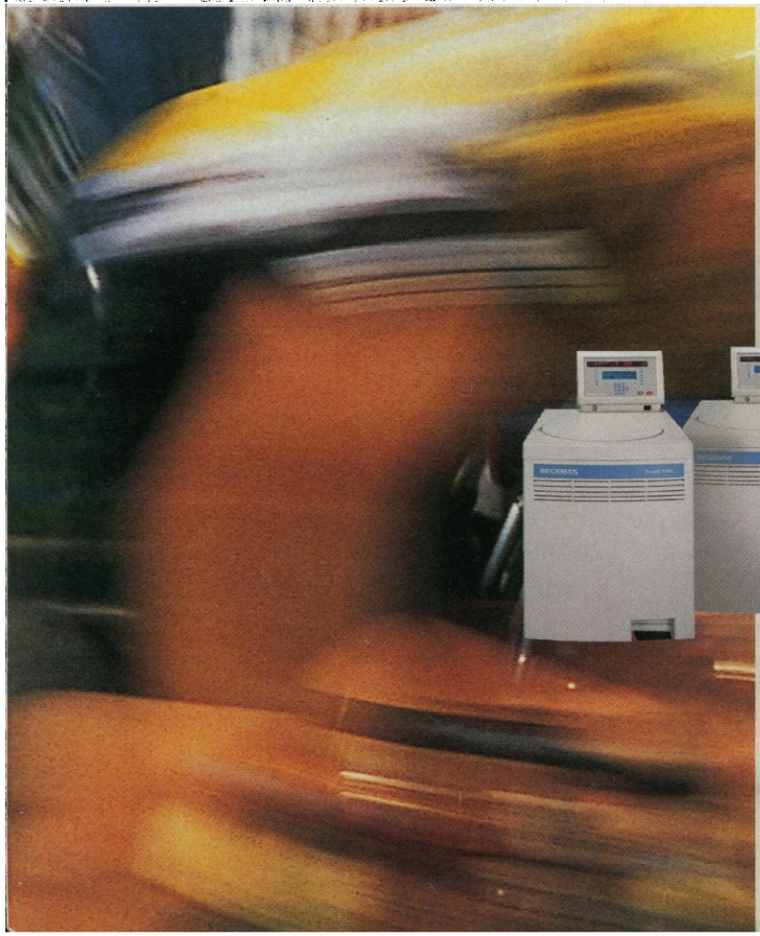

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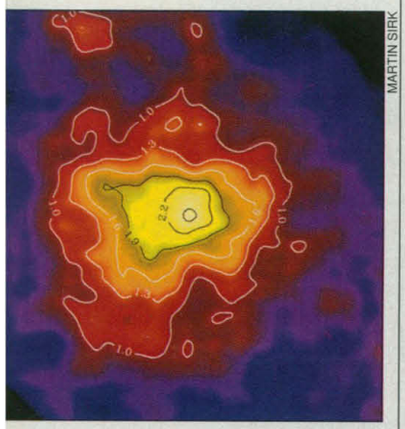

MARTIN SIRK

1338
Cool galaxy clusters

NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVES

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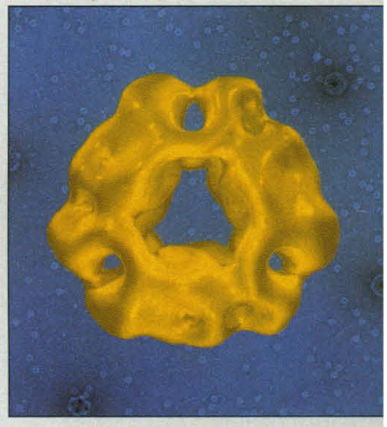
COVER

Cretaceous-Tertiary (K-T) boundary near the town of Zumaya, Spain. The boundary occurs immediately below the ledge (lower center) formed by the erosion-resistant Tertiary strata. The boulders in the foreground lie in the pre–K-T gap. Statistical analysis of the fossil distributions in this and other Bay of Biscay sections reveals a complex of extinction patterns in the latest Cretaceous. See page 1360 and the News story on page 1303. [Photo: Peter D. Ward, University of Washington]

TECHNICAL COMMENTS

1323 & 1385

Tricorn protease



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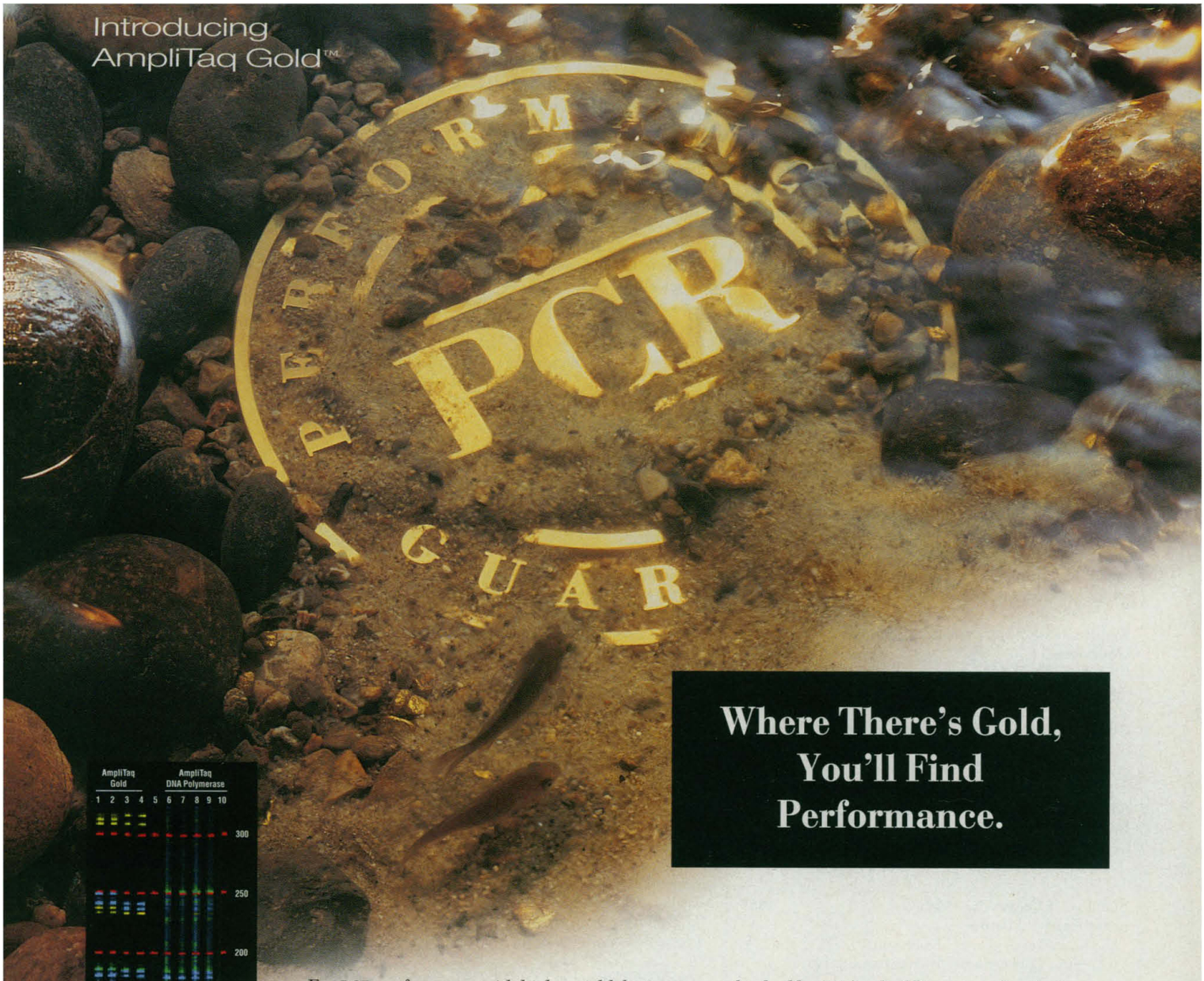

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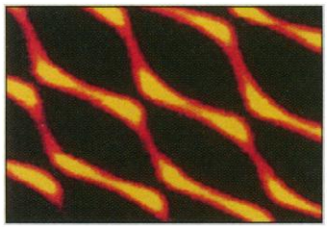
THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Artificial molecules

A quantum dot is a semiconductor structure in which electrons are confined within a small volume and have discrete energy levels resembling those



of atoms. Livermore *et al.* (p. 1332) have constructed coupled quantum dots in which electrons can tunnel between dots, thus creating "artificial molecules." The conductances observed in both the weak and strong tunneling limits agree with predictions from many-body theory.

Glowing clusters

Chemical reactions may be accompanied by emission of visible light, or chemiluminescence, if the energy created by the reaction is stored initially in an excited state that later decays. König *et al.* (p. 1353) report that formation of metal clusters can by accompanied by chemiluminescence. During cluster agglomeration in a noble gas matrix, formation of unstable intermediates is proposed to lead to emission of excited fragments, which decay while emitting visible light.

Fresh air?

Transport of air from the troposphere into and out of the stratosphere, and its residence time in the stratosphere, can determine the rates at which ozone-destroying compounds reach the ozone layer and the effects of aircraft emissions. However, details of the global transport of air are difficult to obtain. Boering *et al.* (p. 1340) measured various gases on board the NASA ER-2 aircraft at tropospheric and stratospheric altitudes between 1992 and 1996 and showed that air enters the stratosphere continuously throughout the year and is distributed rapidly. The measurement allowed the determination of the mean age of stratospheric air, which is related to the residence time of pollutants in the stratosphere.

Not so stable

Earth's lower mantle has generally been thought to be composed mostly of perovskite [$(Mg,Fe)SiO_3$], and many geophysical models of the lower mantle are based on this assumption. Some earlier work had indicated, however, that perovskite containing some iron might not be stable throughout the pressure range of the lower mantle. Saxena *et al.* (p. 1357) performed synchrotron x-ray studies on high-pressure, high-temperature samples of the end-member $MgSiO_3$. The results suggest that the perovskite broke down to MgO (periclase) and SiO_2 (stishovite) at pressures of about 60 gigapascals.

Insulin resistance, diabetes, and obesity

Obesity can lead to insulin resistance and diabetes, and the two appeared inseparable in animal models. Hotamisligil *et al.* (p. 1377) now report that in mice lacking the gene encoding AP2, the fatty acid–binding protein from adipocytes, dietary obesity fails to cause insulin resistance or diabetes. Somehow, AP2 must be critical for the metabolic pathway that leads from obesity to insulin resistance. The results provide a focus possibly intervening in the process that causes abnormal glucose homeostasis and symptoms of diabetes as a consequence of obesity.

Aspirin and glutamate

The neurotransmitter glutamate can actually be toxic to neurons if its levels are elevated for too long—as may occur during stroke. Grilli *et al.* (p. 1383) describe how aspirin, at doses already in frequent use for the treatment of arthritis, can help to protect rat neurons in primary culture and in hippocampal slices from glutamate-induced neurotoxicity.

Tumor evasion

Activated T cells are normally eliminated after an immune response is completed by expression of the Fas ligand (FasL, also called Apo-1 or CD95 ligand), and immune-privileged sites in the body such as the eye also express FasL. Hahne *et al.* (p. 1363; see the news story by Williams, p. 1302) show that unlike normal skin cells, malignant melanoma cells express FasL to avoid the immune response. Injection of mouse melanoma cells expressing FasL led to rapid tumorigenesis in normal mice but not in mice deficient in Fas.

Restoring the liver

Adult liver cells (hepatocytes) can replicate rapidly, thus allowing the liver to recover from toxic-induced damage and to regenerate in a few days after surgical procedures that remove most of its mass. Cressman *et al.* (p. 1379) have shown that interleukin-6 (IL-6) is a critical cytokine in this recovery. Mice lacking the gene for IL-6 were unable to regenerate liver tissue unless IL-6 was administered exogenously after tissue removal. The necessity of IL-6 is an important consideration in strategies that produce decreases in cytokine activity in order to control liver damage, such as those used in treating cirrhosis.

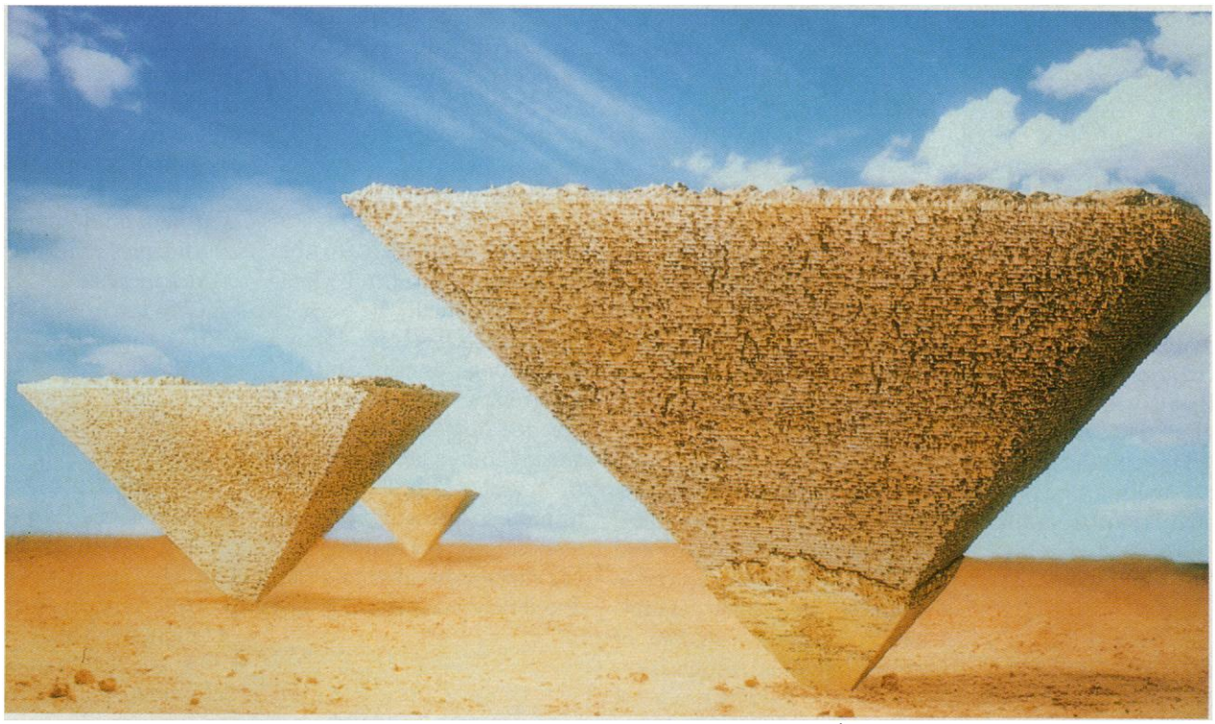
Hats off

There has been a recent explosion in knowledge about how the cell uses selective proteolysis to control a variety of functions. Tamura *et al.* (p. 1385; see the Perspective by Schneider, p. 1323) describe the discovery of a protease complex likely to form part of a multicatalytic complex. The protease subunits have a distinctive structure in electron micrographs and resemble a three-cornered (tricorn) hat.

Stress signal

When the nematode *Caenorhabditis elegans* finds its environment inhospitable, it develops into a dauer larva adapted for survival in adverse conditions. Ren *et al.* (p. 1389) show that response to the pheromone that induces the dauer phase includes alterations in transcription of a growth factor related to transforming growth factor–β. The transcriptional modulation occurs within certain chemosensory neurons of the larva.

Leave No Stone Unturned.



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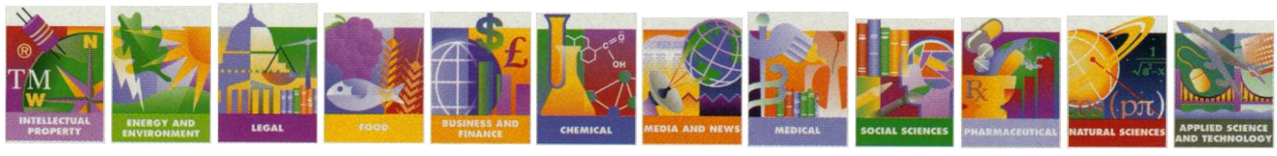

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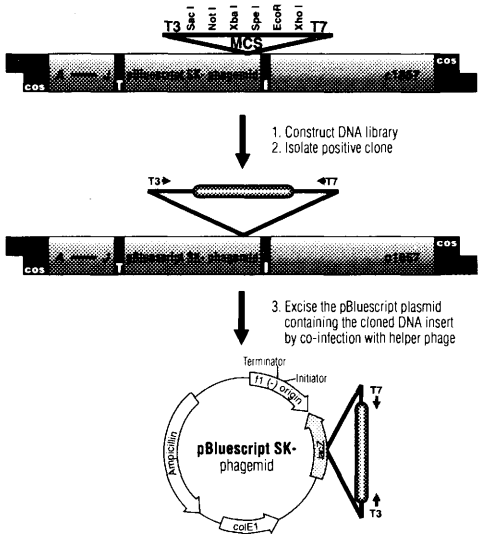
1. Short, J.M., Fernandez, J.M., Sorge, J.A., and Huse, W.D. (1988) *Nucl. Acids Res.* 16: 7583-7600.



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*U.S. Patent Nos. 5,128,256 and 5,286,636. and European Patent No. 286200B1
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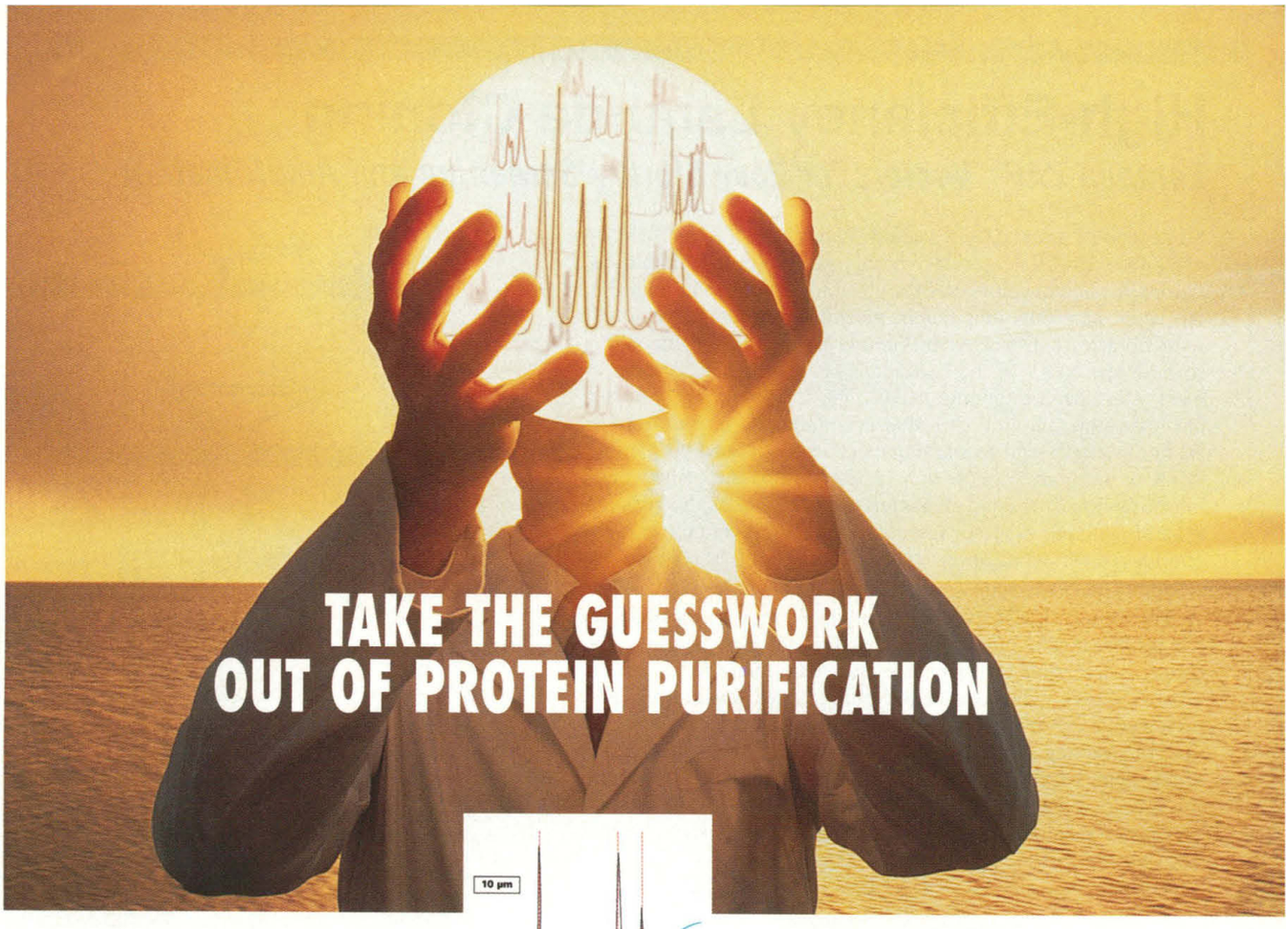

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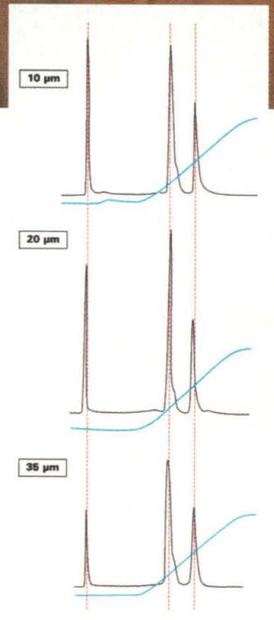

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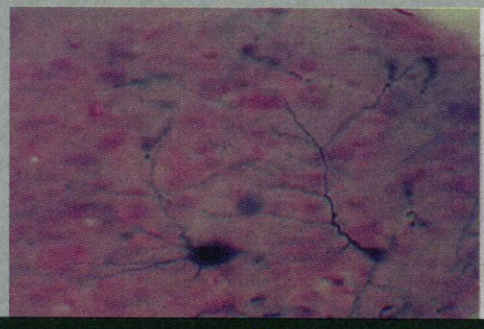
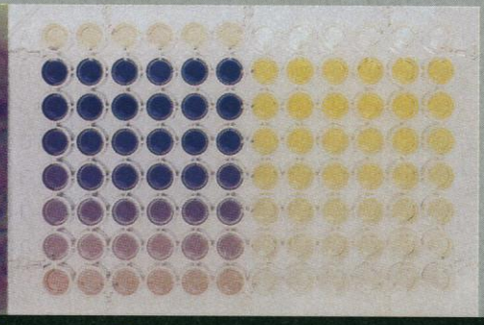
Biotinylated dextran injected iontophoretically into the auditory cortex of rat brain to label somata and neuronal profiles. Tissue treated with KPL's Streptavidin-Peroxidase, followed with TrueBlue™ Peroxidase Substrate. Counterstained with Contrast RED. Photographed using a 3-dimensional light microscope.



Microplate wells coated with 1.5 µg/ml of rabbit IgG excepting row A, then blocked. Alkaline phosphatase-labeled goat anti-rabbit IgG (H+L) added to row A at a concentration of 50 ng/ml, with a dilution series of conjugate ending in row H at a concentration of 2.5 ng/ml. Incubated for 20 minutes with KPL's BluePhos™ Substrate (left side) and *p*NPP Phosphatase Substrate (right side).



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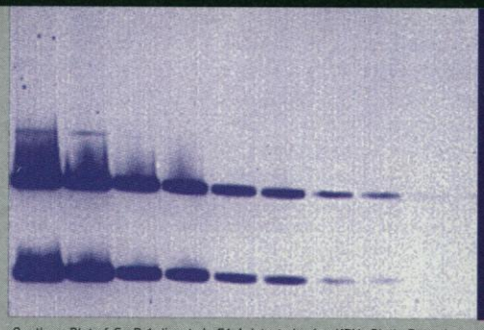
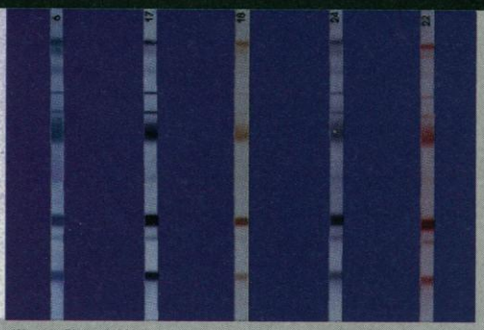


Southern Blot of *Eco*R 1 digested pE1.4 detected using KPL's Biotin Detection Kit. Lane 1: 10 ng pE1.4 Lanes 2-6: 5 ng, 1 ng, 500 pg, 100 pg, 50 pg. Lanes 7-11: 10 pg, 5 pg, 1 pg, 0.5 pg, 0.1 pg.



Western Blots of HIV-1 viral lysate electroblotted onto nitrocellulose membrane. Immunodetection with HIV-positive human serum followed by enzyme-labeled antibody. Immunodetected with appropriate KPL substrate.

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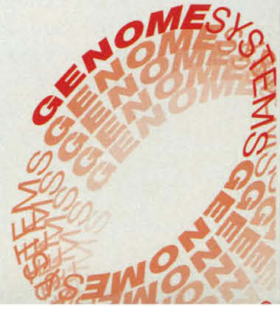
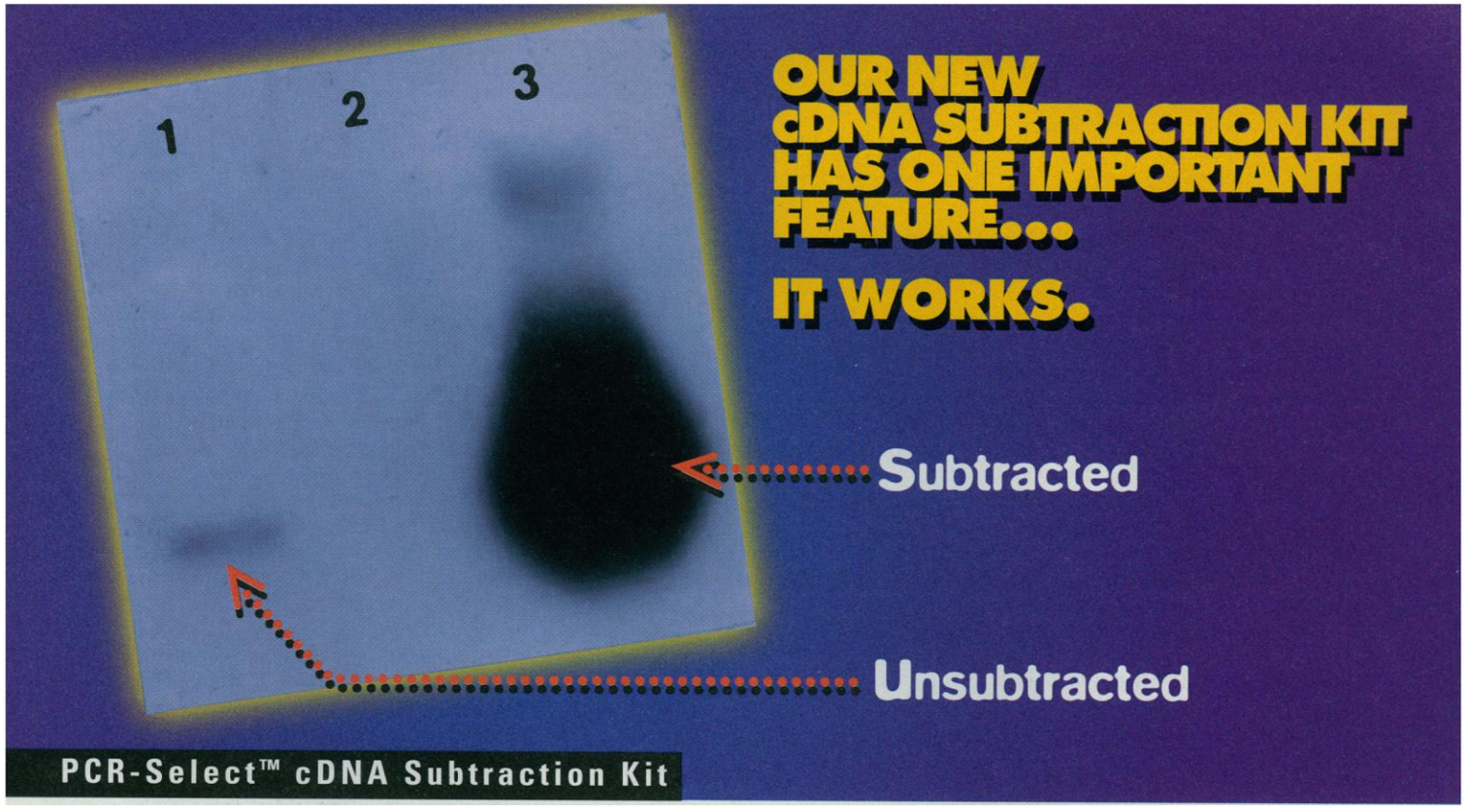
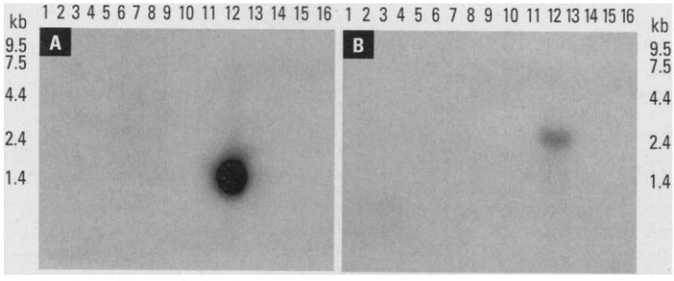




Above photo: Southern blot analysis showing enrichment of IL-2 receptor, known to be activated in human Jurkat T-cells by PHA/PMA treatment. Lane 1: unsubtracted cDNA, treated cells. Lane 2: unsubtracted cDNA, untreated cells. Lane 3: subtracted cDNA, treated cells. A dramatic reduction of the abundant housekeeping gene, G3PDH, was also seen (data not shown).



Northern blot analysis of two selected representative cDNA clones from a testis-specific library. Testis cDNA was subtracted against a mixture of cDNAs from 10 different tissues. The subtracted testis-specific cDNA was cloned into a plasmid vector, and 10 randomly selected clones were used to probe Human Multiple Tissue Northern Blots containing 2 µg of poly A^+ RNA from the indicated tissues. All 10 clones hybridized only to testis RNA. The exposure times needed to generate signal ranged from 5 hr (Panel A) to 7 days (Panel B), indicating that abundant and relatively rare cDNAs were obtained. Lanes 1-16: heart (1), brain (2), placenta (3), lung (4), liver (5), skeletal muscle (6), kidney (7), pancreas (8), spleen (9), thymus (10), prostate (11), testis (12), ovary (13), small intestine (14), colon (15), peripheral blood leukocyte (16).

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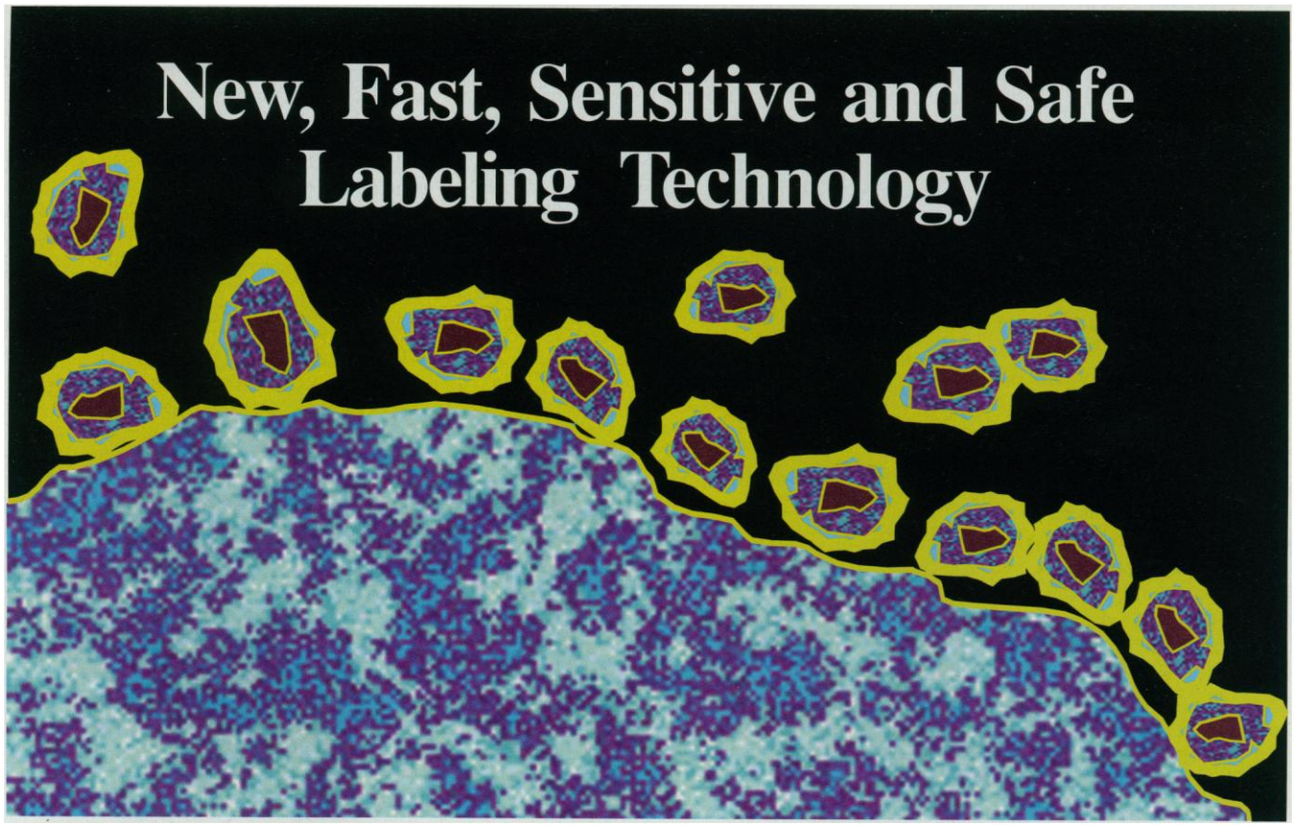

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[1]Patent pending

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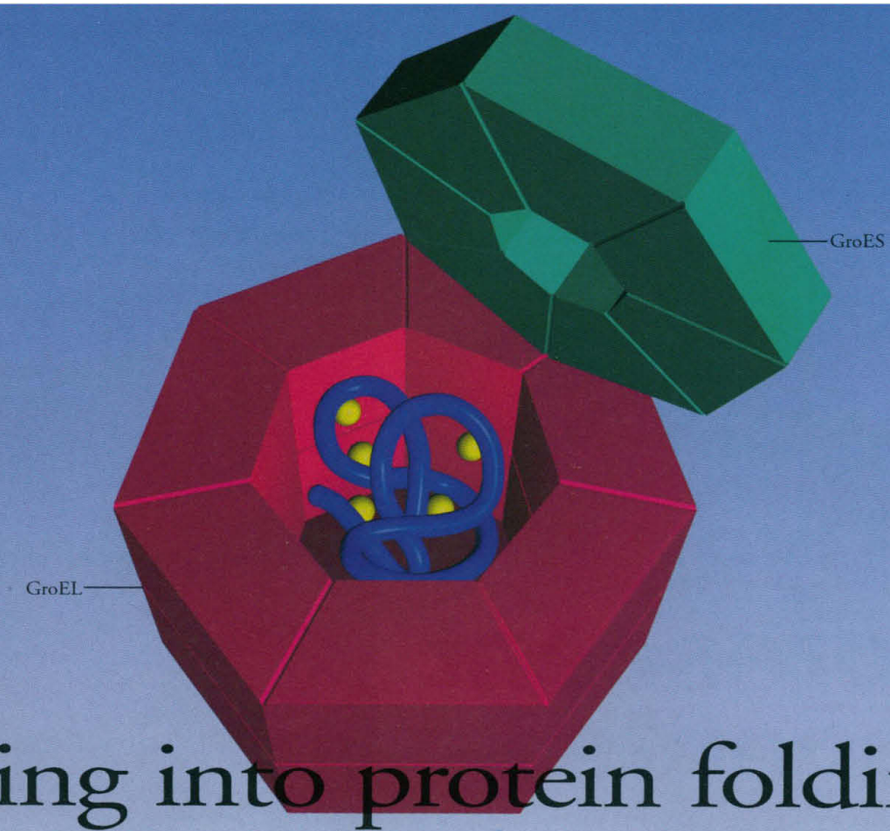

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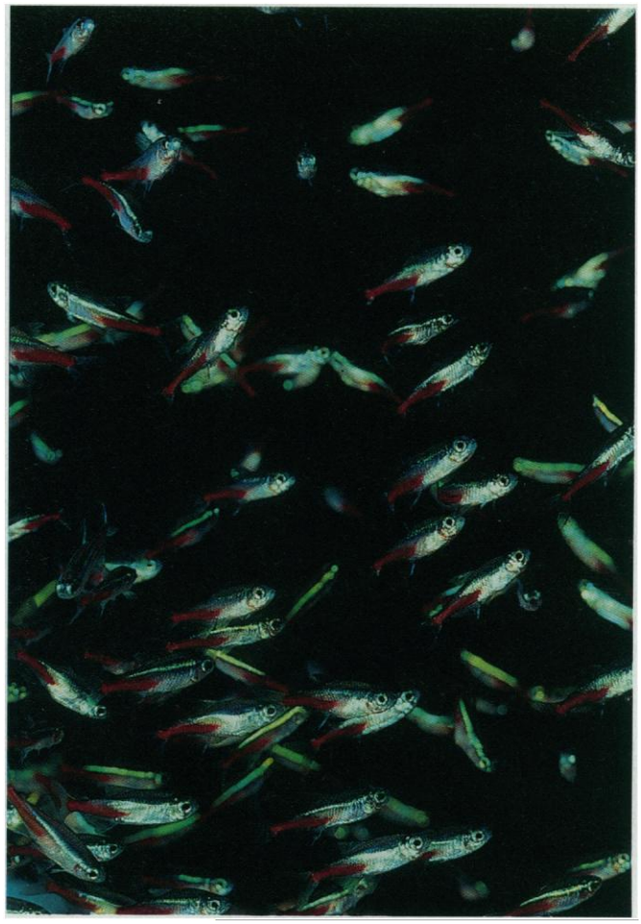

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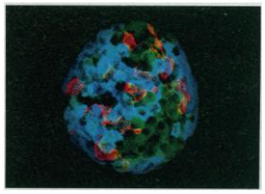
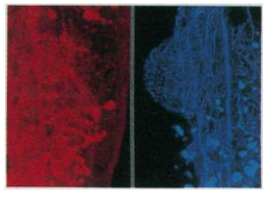


Three colour confocal laser scanning microscope analysis of islet from neonatal rat pancreas. FITC anti-insulin (green), Cy™3 anti-somatostatin (red), and Cy5 anti-glucagon (blue).



Whole insect embryos directly labelled with Cy3 dye (red) and Cy5 dye (blue). Image courtesy of Dr. T.C. Brelje, University of Minnesota Medical School.

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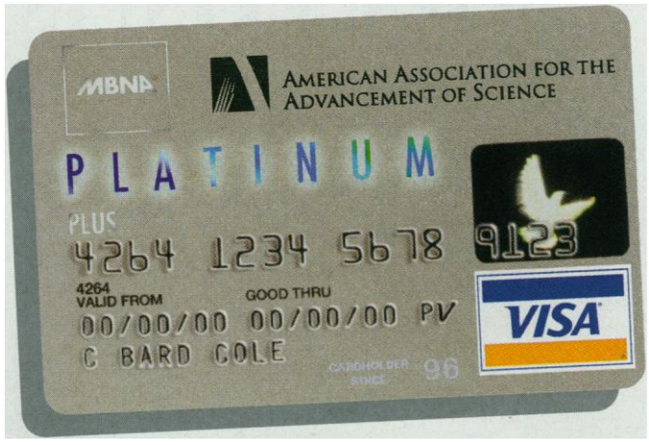

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New Telomerase PCR ELISA Offers Simplified, Nonradioactive TRAP Assay for Measuring Telomerase, A Potential Marker for Cancer Research

Boehringer Mannheim is now offering a Telomerase PCR ELISA for the highly sensitive, nonradioactive detection of telomerase activity in extracts from cell cultures and tissue samples.

Telomerase as an important parameter in cancer research

Telomeres, the specialized DNA/protein structures at the end of eukaryotic chromosomes, contain tandemly repeated DNA sequences that are believed to protect genomic DNA from degradation and deleterious recombination events. During normal somatic cell proliferation, telomeric ends are progressively shortened with each replication cycle, which may play a role in limiting the proliferative capacity of normal cells. Germline cells, many tumor cells, and "immortalized" cell lines are believed to circumvent this telomere shortening using telomerase, a ribonucleoprotein that adds new repeats to the ends of chromosomes. Telomerase activity has recently been identified in many cancers (e.g., prostate cancers [1], advanced-stage breast cancers [2], neuroblastomas [3], and primary lung cancer tissues [4]) that have been confirmed by other methods (*e.g.*, histochemical staining). Thus, telomerase reactivation may allow cells to escape from the proliferative limitations of cellular senescence and could be further investigated as a potential marker for the development of malignant tumor cells.

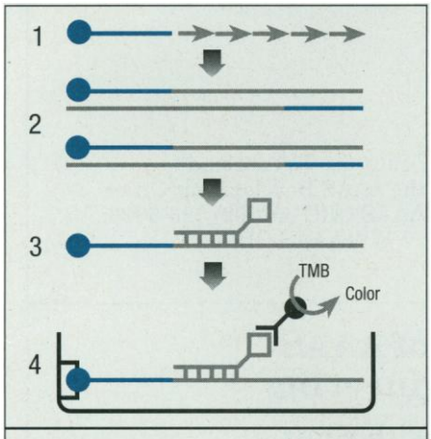

Figure 1. Detection of telomerase activity with the Telomerase PCR ELISA.

Step 1. Telomerase, if present, adds multiple 6-nucleotide telomeric repeats to a biotinylated synthetic primer.

Step 2. The telomerase reaction product is amplified by PCR, using a biotinylated primer.

Step 3. After denaturation, the PCR product hybridizes to a digoxigenin-labeled probe specific for the telomeric repeat.

Step 4. The DNA hybrid binds to a streptavidin-coated microtiter plate, and anti-digoxigenin-peroxidase and TMB substrate generate a colored product measurable with a microplate reader.

Note: If desired, the TRAP reaction product from Step 2 can also be detected by the traditional gel electrophoresis method.

Telomerase PCR ELISA improves upon previous TRAP assays

Telomerase activity is most frequently detected by the Telomeric Repeat Amplification Protocol (TRAP) of Kim *et al.* (5), in which the telomerase-reaction product is amplified by PCR. However, the conventional TRAP assay achieves full sensitivity only when performed with a hazardous radioactive label, and visualization of results requires time-consuming gel electrophoresis and autoradiography. The new Telomerase PCR ELISA*,† combines a one-step/one-tube TRAP assay with nonradioactive detection in a highly sensitive photometric ELISA (Figure 1).

Easy-to-use ELISA delivers results in less time

The Telomerase PCR ELISA delivers results within 6 hours, eliminating the need for laborious, time-consuming gel electrophoresis and autoradiography techniques. Its ready-to-use TRAP reaction mix (telomerase substrate, amplification primers, nucleotides, *Taq* DNA polymerase, reaction buffer) eliminates the need to prepare multiple solutions and minimizes the risk of assay failure caused by contamination. Up to 96 TRAP reactions can be simultaneously analyzed with an ELISA plate reader.

Sensitive results correspond closely with those of radioactive TRAP assays

Besides avoiding the use of hazardous radioisotopes, the Telomerase PCR ELISA produces sensitive results comparable to those of the radioisotopic TRAP assay (Figure 2). The kit's optimized detection probe and hybridization conditions maximize both specificity and sensitivity. Additionally, optimized primer sequences eliminate the need for "hot start" PCR while avoiding amplification artifacts (*e.g.*, primer dimers).

The Telomerase PCR ELISA is currently available

The Telomerase PCR ELISA (96 tests; Cat. No. 1 854 666) is now available from Boehringer Mannheim Biochemicals representatives. Additional information can also be found at http://biochem.boehringer-mannheim.com.

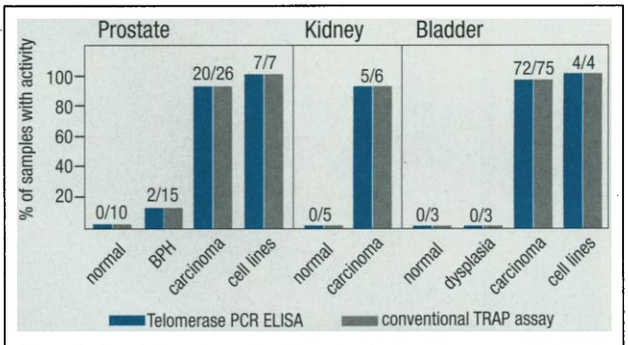

Figure 2. Correlation of results obtained with the Telomerase PCR ELISA and conventional, radioisotopic TRAP assays. Samples from known carcinomas, normal specimens (negative control), benign prostatic hyperplasia (BPH) specimens, and immortalized cell lines were tested with the Telomerase PCR ELISA and conventional, radioisotopic TRAP assays. In all sample types, the methods were able to identify the same number of samples featuring telomerase activity. Data provided by M. Müller and R. Heicappell (6) and by H. J. Sommerfeld.

References:

1. Sommerfeld, H. J. *et al.* (1996) *Cancer Research* **56**:218-222.
2. Hiyama, E. *et al.* (1996) *J. National Cancer Institute* **88**:116-122.
3. Hiyama, E. *et al.* (1995) *Nature Medicine* **1**:249-255.
4. Hiyama, K. *et al.* (1995) *J. National Cancer Institute* **87**:895-902.
5. Kim, N. W. *et al.* (1994) *Science* **266**:2011-2015.
6. Müller, M. *et al.* (1996) *Int. J. Oncology* **9**: *in press.*

†Licensed from Geron Corporation. Patents pending.

*Purchase of this product is accompanied by a limited license to use it in the Polymerase Chain Reaction (PCR) process 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 Perkin-Elmer or as purchased, i.e., an authorized thermal cycler.

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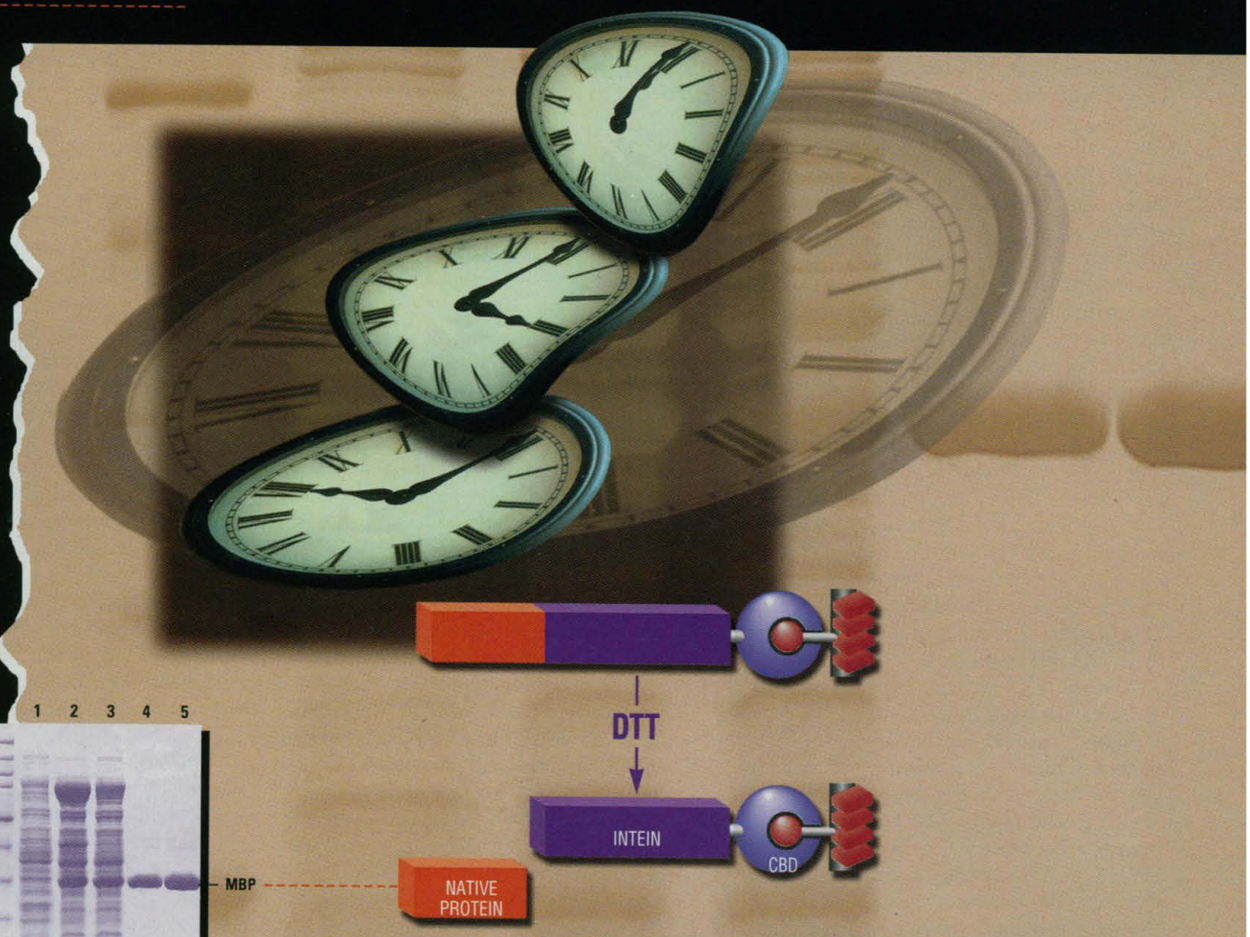

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