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Mars Global Surveyor

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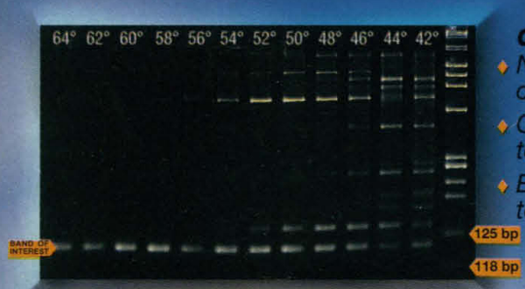

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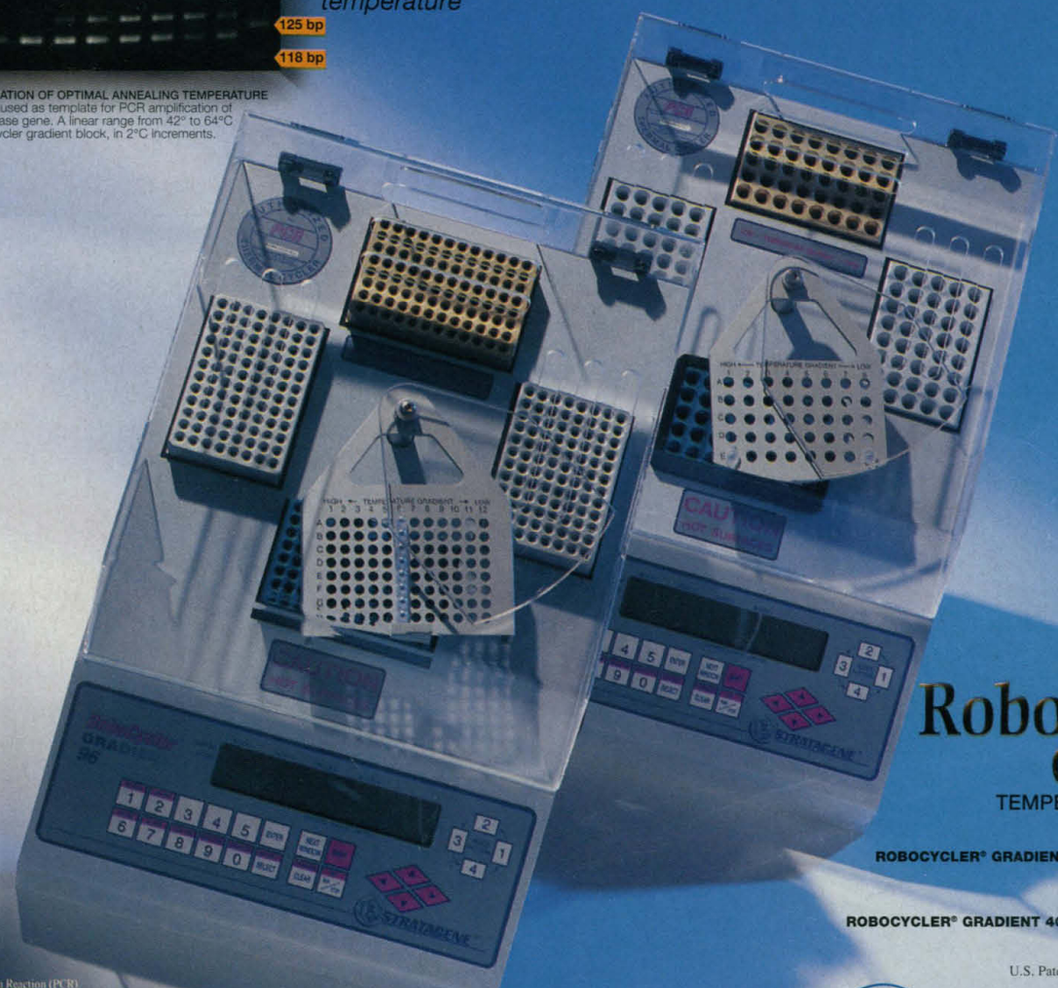

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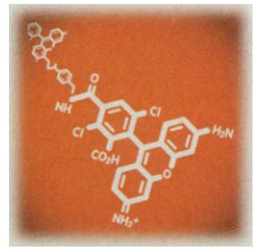

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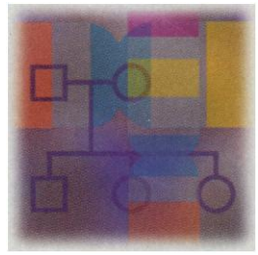

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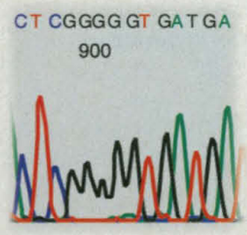

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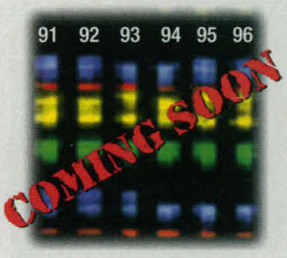

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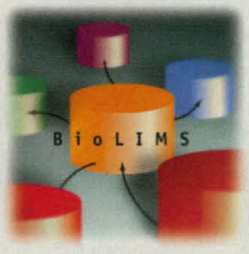

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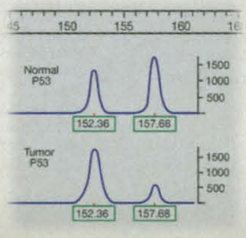

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1626
Fossil-hunters' paradise

1651 & 1661
Organized agricultural origins

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SCIENCE'S COMPASS

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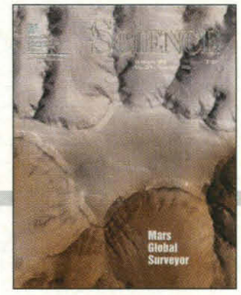
COVER

Mars Orbiter Camera (MOC) image of a 10 km by 12 km area of Coprates Catena (14.7°S, 55.8°W), a ridge with a flat upper surface in the center of Coprates Chasma, which is part of the 6000-km-long Valles Marineris. Rock layers are visible just below the ridge. The gray scale (4.8 m/pixel) MOC image was combined with a Viking Orbiter color view of the same area. The faults of a graben offset beds on the slope to the left. See the Reports on Mars Global Surveyor results beginning on p. 1671 and the News story on p. 1634. [MOC image 8003]



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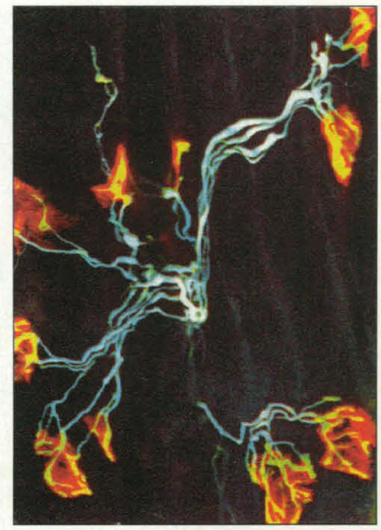
MARS GLOBAL SURVEYOR



1725
Sorting through connections

◩ Indicates accompanying feature

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THE MJ RESEARCH NOTEBOOK

Volume VIII...No. 1 *A Bulletin of Technological Advance in Molecular Biology* *Spring 1998*

BIT OF PROOFREADING ENZYME REALLY HELPS

Difficult Templates Become a Breeze

As experience with PCR has grown, various "tricks" have been learned to facilitate DNA polymerization. These can substantially increase accuracy and yield. They also make possible amplification of very long templates or ones that are difficult because they are GC-rich or have complementary areas. But these tricks are not just applicable to rare protocols – rather, by simply substituting pre-optimized polymerase "cocktails," an investigator can bring the latest innovations to all experiments.

Most single-enzyme reagents (like *Taq*) work reasonably well for PCR. If you try to increase accuracy using a single polymerase that also has 3'→5' proofreading ability, PCR becomes less efficient and requires optimization. But if you combine the two by mixing in just a bit of the proofreading type, you get a synergistic combination that leads to high yield and great accuracy—with little need for optimization with normal templates. DyNAzyme EXT is such a cocktail, and it works incredibly well for PCR.

Finnzymes of Espoo: a Nordic Leader

Winner of Presidential Award

ESPOO, Finland — Finnzymes Oy was founded here in 1987 by three graduates of the Helsinki University of Technology. The three, Pekka Mattila, Kari Pitkänen and Tuomas Tenkanen, had long done research on restriction enzymes and DNA polymerases. With assistance from New England Biolabs of Beverly, Mass., they looked to expand and commercialize their academic work. Thus Finnzymes Oy was born.

Since then, the company has grown steadily, and its products have become well-known in Europe for quality and purity. In 1990, the company took on MJ RESEARCH products as the authorized Finnish distributor. In 1997, Finnzymes obtained license from Hoffmann-La Roche to sell its enzymes licensed for PCR.**

Recently, the President of Finland, Martti Ahtisaari, recognized the company's leadership in enzymology and biotech manufacture, presenting Finnzymes with the first national award for innovation, the "Inno-Suomi palkinto."

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DyNAzyme EXT Polymerase Eases Difficult & Long PCR

Pekka Mattila at a hot spring in Kamchatka

Quest to Kamchatka & Iceland for Better Bacteria

Over the past decade, Finnzyme scientists have traveled to Iceland and the Kamchatka Peninsula of Russia, in pursuit of thermostable enzymes with novel characteristics. Both areas are highly volcanic and have an abundance of hot springs and thermophilic bacteria. In collaboration with Icelandic researchers, Finnzymes collected hundreds of samples from springs with an extraordinary diversity of pH, temperature, and gas/mineral content. The activities of over 190 strains of bacteria have been analyzed, and the best polymerase for PCR was from *T. brockianus*, from a spring in Iceland.

TAQ HARD TO BEAT, BUT *T. BROCKIANUS* HAS THE RIGHT STUFF

Enzymes from Finland Perform

WATERTOWN, Mass. — MJ RESEARCH, INC. proudly announces that it has become the exclusive US distributor for Finnzymes Oy of Finland. Finnzymes specializes in enzyme products for molecular biology, particularly in the DyNAzyme™ line of thermostable DNA polymerases. These enzymes have their origin in *Thermus brockianus*, a thermophile that was isolated from an Iceland hot spring in 1990.

To be sure, *Taq* polymerase is an excellent enzyme and a standard of science. But by almost every measure, DyNAzyme polymerase outperforms *Taq* by at least a whit—and greatly so in some ways. It exhibits higher fidelity, greater thermal stability, and higher efficiency in PCR reactions. In fact, DyNAzyme EXT* cocktail is able to amplify sequences as long as 40kb—and do it with a lower error frequency than *Taq*. In more typical applications, EXT is better able to amplify difficult pieces, creating big bands in gels when *Taq* just squeaks by.

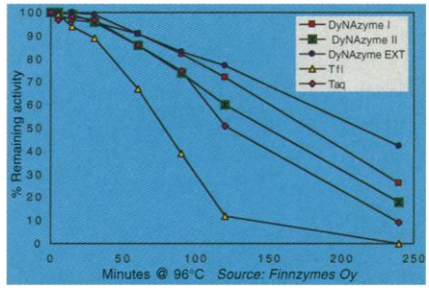
Furthermore, all DyNAzyme enzymes come licensed by Hoffmann-La Roche to perform PCR reactions in research.** And DyNAzyme EXT is priced to give the value of a proofreading cocktail for the price of a single enzyme.

Other Variants of Enzyme Available

Please Call for Free Demo Kit

Three forms of DyNAzyme are available from MJ RESEARCH: 1) native DyNAzyme I DNA polymerase, 2) recombinant DyNAzyme II, and 3) the DyNAzyme EXT cocktail. All are available with various buffers, alone or in kits.

A PCR validation kit for DyNAzyme EXT is available, free of charge *(offer valid through July 1, limitations apply)*. It consists of 50U of DyNAzyme EXT with buffer systems appropriate for short and long templates. Also included are lambda template with primers for 0.5kb & 20kb targets, dNTP's, a wide-range size marker, and gel-loading buffer solution.



Thermal stability of various polymerases

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** Purchase of DyNAzyme polymerase is accompanied by a limited license to use it in the Polymerase Chain Reaction (PCR) process for research 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.

edited by PHIL SZUROMI

Earlier settlements

Several large central archaeological sites thought to mark the origin of organized agricultural societies in southwestern United States and northern Mexico have been recognized and dated to about 1200 to 600 years ago. These villages, known as cerros de trincheras, typically extend over several hundred meters and are marked by extensive terraces on hills and house rings or other residential structures. Hard and Roney (p. 1661; see the commentary by Smith, p. 1651) describe a large cerros de trincheras in Chihuahua, Mexico, that is dated much earlier, to about 3000 years ago. This age is coeval with the introduction and first use of maize in the region. Thus, large centralized agricultural villages developed rapidly in this region, not gradually over many centuries as had been previously thought.

More deuterium in Hale-Bopp

Deuterium-to-hydrogen (D/H) ratios can be used to estimate the likely origin of such materials as stardust in the laboratory and comets in space by tracing their content of modified versus unmodified (primitive) material. Previous measurements of the D/H ratio in water in comet Hale-Bopp of about 3×10^{-4} were consistent with the only other cometary D/H ratios measured in comets Halley and Hyakutake. Meier *et al.* (p. 1707) have now measured hydrogen cyanide (HCN and DCN) in Hale-Bopp and found a D/H ratio of 2.3×10^{-3}. The different D/H ratios imply that Hale-Bopp has preserved unmodified interstellar material because if the HCN and H_2O species had time to exchange D with the abundant H_2 gas (with an estimated maximum D/H of 4×10^{-5}) in the solar nebula, then both ratios would have been lowered and in closer agreement with each other. These measurements indicate that cometary ices are primitive materials formed in interstellar clouds, probably near the Uranus-Neptune region of the early solar nebula.

Mars Global Surveyor

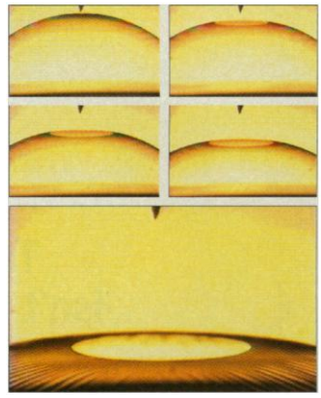
The areally limited but intriguing measurements made during the aerobraking and assessment orbits of Mars Global Surveyor between September 1997 and February 1998 are the subject of an overview (Albee *et al.*, p. 1671) and five reports. The accelerometer (Keating *et al.*, p. 1672) measured the density, temperature, and pressure in the martian thermosphere (the upper atmosphere, between 110 to 170 kilometers). These measurements are essential for planning the aerobraking maneuvers to obtain a circular orbit and also suggest that an observed regional dust storm caused a global thermospheric response and that topographically forced planetary waves may produce the measured thermospheric density anomalies seen at nearly opposite ends of Mars. The magnetometer (Acuña *et al.*, p. 1676) did not find a global-scale magnetic field. However, small-scale magnetic anomalies were seen that appear to be concentrated in the oldest (most heavily cratered) surface deposits of the crust and suggest that Mars may have had a magnetic field early in its evolution. The thermal emission spectrometer (Christensen *et al.*, p. 1692) returned spectra of surface materials, atmospheric dust, clouds, CO_2 gas, and water vapor. Pyroxene is abundant with some plagioclase in the regions where spectra were obtained, whereas carbonates, olivine, clay minerals, and quartz are minor components limited to low albedo surfaces. The laser altimeter (Smith *et al.*, p. 1686) measured the topography along 18 tracks in the northern hemisphere. The Ares Vallis channel is much deeper than previously estimated, implying a much greater water discharge rate and possibly more flowing water. The narrow-angle, high-resolution camera and two wide-angle cameras (Malin *et al.*, p. 1681; see the cover) provided detailed and global views of the planet. Windswept terrains of dunes, sand sheets, and drifts can be seen on the scale of a few meters, whereas the canyons of Valles Marineris reveal layered deposits extending from the top to the bottom of the canyon walls. The complex and in some cases intersecting eolian features provide clues to wind direction, wind intensities, and the possible ages of these landforms that may be related to seasonal changes on Mars.

Mantle boundaries

The abrupt increase in seismic velocities at the boundary between the upper and lower mantle at 660 ± 30 kilometers has been partially attributed to a change in mineral structure of the dominant upper mantle mineral phase, spinel, which is transformed into perovskite and MgO-periclase. Irifune *et al.* (p. 1698), using synchrotron radiation and a high pressure multianvil apparatus, estimated the pressure and temperature at which this mineral phase transformation occurs for the pure magnesium silicate end members. The phase boundary occurs at about 21 gigapascals and 1600°C, which corresponds to a depth of only about 600 kilometers. This depth discrepancy is significant and remains unresolved, although the authors postulate some possible causes. The structure at and above the core-mantle boundary (CMB) is determined from small-amplitude compressional sound waves, which travel through the mantle and the outer core faster and with slightly diffracted paths from the larger amplitude primary mantle–outer core sound wave phase, or PKP. Wen and Helmberger (p. 1701) used complimentary short- and long-period precursors to PKP that sampled the CMB beneath the Western Pacific Ocean. The long-period precursors suggest ultralow velocity zones (ULVZ; a decrease in the velocity of about 7 percent) that have Gaussian shapes with heights of 60 to 80 kilometers from the CMB and widths of 100 to 300 kilometers. The short-period precursors indicate that these ULVZ contain partial melts created by small-scale convection or by a thermal instability at the CMB.

Viscous bubbles

We normally think of foams and bubbles forming in liquid films stabilized by surfactants, but highly viscous fluids can also support bubble formation, at least for awhile. Debrégeas *et al.* (p. 1704) studied drainage and bursting of air bubbles formed in melts of a



silicone rubber and of a borosilicate glass, liquids that are approximately a million times more viscous than water. Although the systems displays very different relaxation behaviors, they can be described with a relatively simple hydrodynamic model.

Selective ceramic membranes

Membranes of amorphous silica supported on more porous alumina hold the potential for separating small molecules of industrial

(*Continued on page 1607*)

Truth is, whatever we say about pcDNA3.1 isn't nearly as important as what researchers say.

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(Continued from page 1605)

importance, as their pore diameters (less than 2 nanometers) can lead to large permeation ratios. Such materials can be impractical, however, in terms of their reproducibility and can contain defects that lower performance. De Vos and Verweij (p. 1710) show that when these membranes, which are made by dip-coating, are produced under clean-room conditions, high reproducibility is achieved in the separation of hydrogen from methane.

■

Interfacial phosphor

Combinatorial methods that search for new inorganic materials often make use of "inert" substrates for deposition of the elements of interest. Wang *et al.* (p. 1712), in searching for new photoluminescent materials, identified an efficient blue material prepared on a silicon substrate as a gadolinium-gallium oxide. When this material was prepared on $LaAlO_3$, however, no emission was observed. They show that interfacial effects with the silicon substrate contribute to its luminescence.

■

Recruiting tRNAs

Transfer RNA (tRNA) molecules with more than one type of anticodon region that recognizes messenger RNA can have the same identity, that is, accept the same amino acid, and form an isoacceptor group. The classical model of tRNA evolution suggests that all of the tRNAs with the same identity have a common ancestor. An alternative model based on recent experimental evidence suggests that the anticodon interacts sufficiently with the aminoacyl tRNA synthetases so that a point mutation that changes the isoaccepting group could also change identity. Saks *et al.* (p. 1665) inactivated an essential threonine tRNA with a UGU anticodon in an *Escherichia coli* strain and show that an arginine tRNA, with a UCU anticodon, underwent a point mutation to UGU and changed its specificity to threonine.

■

Reducing oxidation

Oxidation can be damaging to cells. In the presence of oxidizing agents, *Escherichia coli* activates antioxidant genes by the action of transcription factors such as OxyR. Zheng *et al.* (p. 1718; see the commentary by Demple, p. 1655) show that OxyR is specifically activated by hydrogen peroxide through the formation of an intramolecular disulfide bond, and the disulfide bond is reduced by glutaredoxin 1. An autoregulatory loop in the defense mechanism occurs through the regulation of glutaredoxin 1 by OxyR.

■

Connecting brain to brawn

Early in development, neuromuscular connections are formed in excess and then pruned as development proceeds. Nguyen *et al.* (p. 1725) show that overexpression of a neurotrophic factor, GDNF, in the target muscle cells slows that pruning process. The transgenic mice show a greater than normal amount of innervation to their muscles in the few weeks after birth and display an unusual sort of tremor. Both features fade as the pruning process continues and the mice mature. The results suggest that GDNF may be the physiologically relevant trophic factor for formation of neuromuscular junctions.

■

ORC complexes and cell replication

The origin recognition complex (ORC) is a complex of six protein subunits that control initiation of DNA replication. Dillin and Rine (p. 1733) present evidence for a role of an ORC subunit in the mitotic phase of the cell division cycle as well as in S phase (when DNA replication actually occurs). They found that yeast cells with mutations in the ORC subunit Orc5p arrest either in early M phase or at the G_1-/S phase boundary. After binding of inactive Orc5 during M phase, arrest of cells at the G_1-/S phase border could not be overcome by introduction of wild-type Orc5 protein. Thus, the ORC complex appears to be irreversibly formed in the M phase before replication occurs. Inactive ORC complexes apparently produce an inhibitory signal within the nucleus that can prevent initiation of replication even at origins at which wild-type ORC is bound.

■

Role of γδ T cells

Recently it has been argued that the limited repertoire of γδ T cells in various anatomical sites is of little significance and is not due to selection. Mallick-Wood *et al.* (p. 1729) have now shown that this may not be the case. They used mice that lacked the $V\gamma5$ gene and an antibody that recognizes the idiotype ("shape") of the $V\gamma5$-$V\delta1$ T cell receptor (TCR). Although no T cells in the skin had the $V\gamma5$-$V\delta1$ receptor, the T cells used other TCRs that made the same shape and were recognized by the antibody. This result strongly suggests that these cells are being selected by some self antigen and serve a physiologic purpose. Human intestinal T cells are largely γδ T cells that express $V\delta1$ as part of their T cell receptor. It has been proposed that the restricted repertoire of these T cells makes them ideal for acting as sentinels for self proteins that are expressed in response to damage or infection of the intestinal epithelium. Their localization is matched by the location of the nonclassical class I major histocompatibility complex molecules MICA and MICB, which contain heat shock promoters and are expressed in response to stress. Groh *et al.* (p. 1737) have isolated intestinal γδ T cells and show that they recognize MICA and MICB, independent of antigen processing. Thus, they may be a primitive T cell "first line of defense" for the gut.

■

Sensory representation

Portions of the brain that encode incoming sensory information are known to be highly plastic; that is, reducing or increasing a particular aspect of the input leads to diminished or expanded representation. Kilgard and Merzenich (p. 1714; see the commentary by Juliano, p. 1653) find that electrical stimulation of the nucleus basalis in conjunction with auditory input remodels the auditory cortex in the rat, leading to increased representation of those areas responding to the specific frequencies used and contraction of other areas. They suggest that output from the cholinergic nucleus basalis mediates this stimulus-induced plasticity and that remodeling apparently can occur in the absence of any behavioral content of the input.

■

Calcium sensor

The metabotropic family of glutamate receptors bind to the neurotransmitter glutamate in the brain and influence synaptic transmission and plasticity. Kubo *et al.* (p. 1722) now show that the receptor also responds to the levels of extracellular calcium ions, which may provide a further way to modulate synaptic plasticity.

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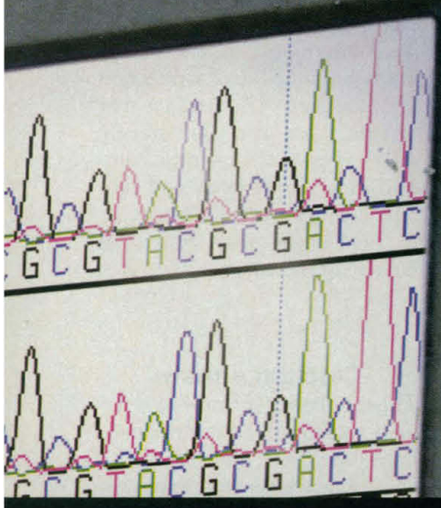

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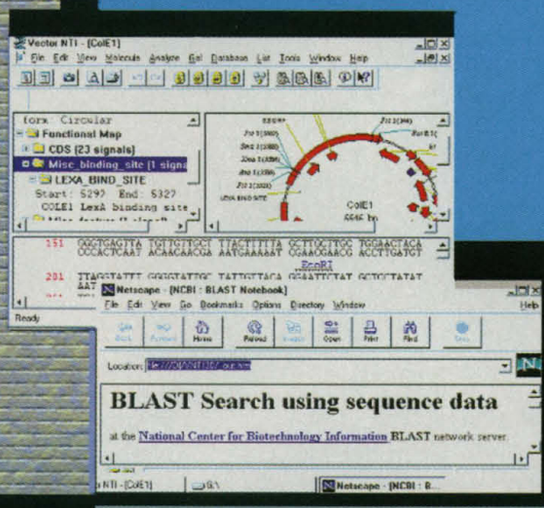

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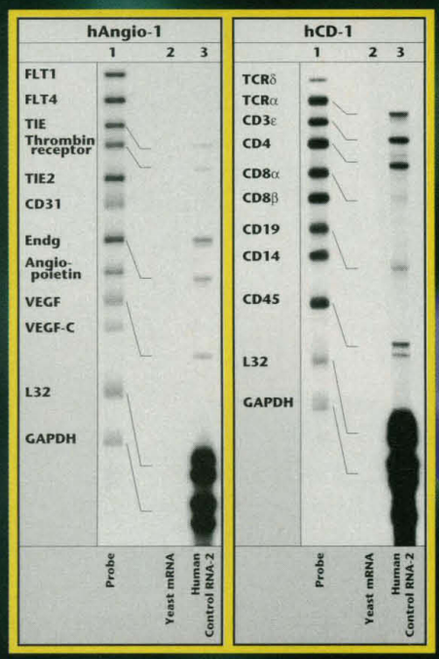

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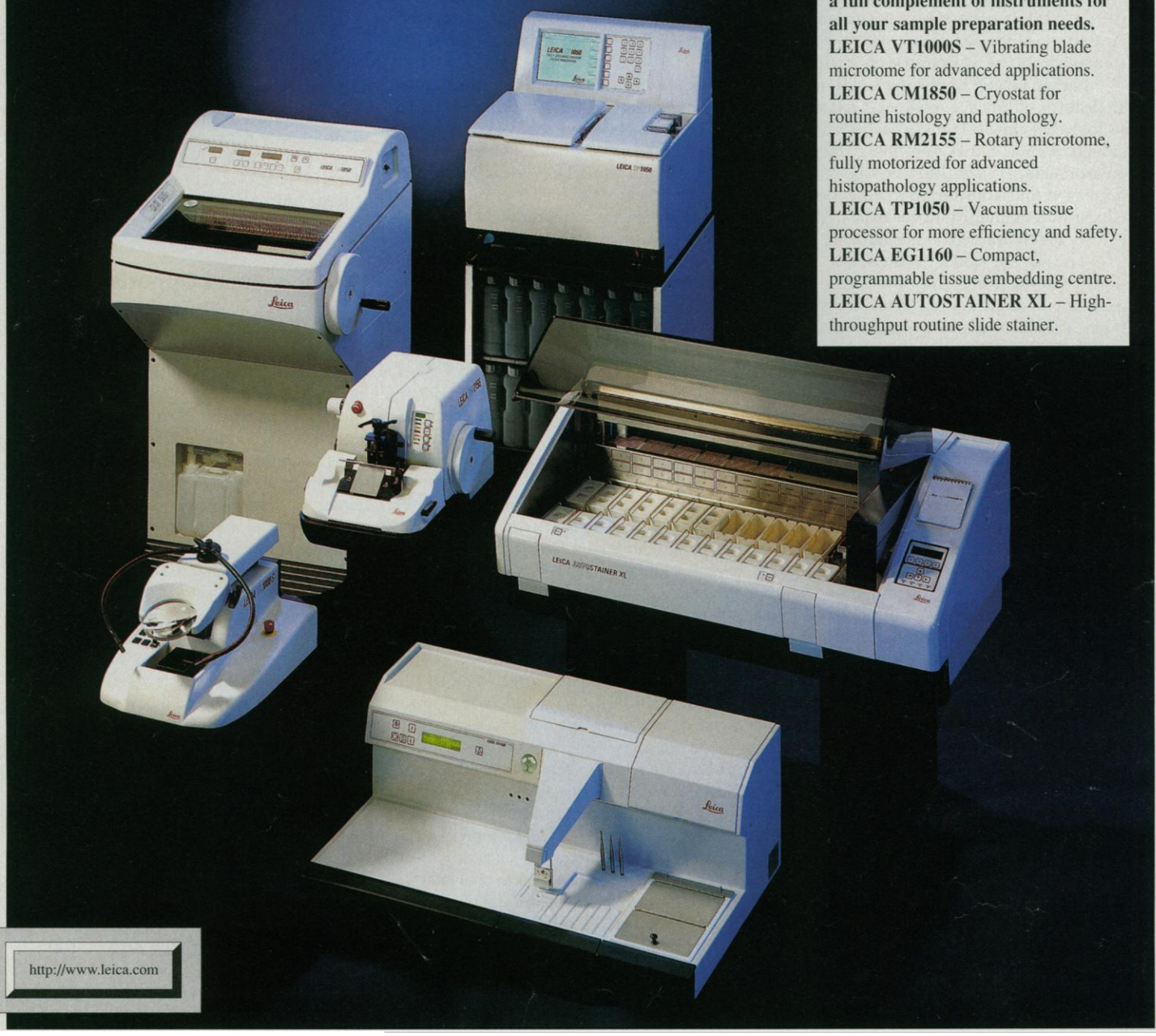

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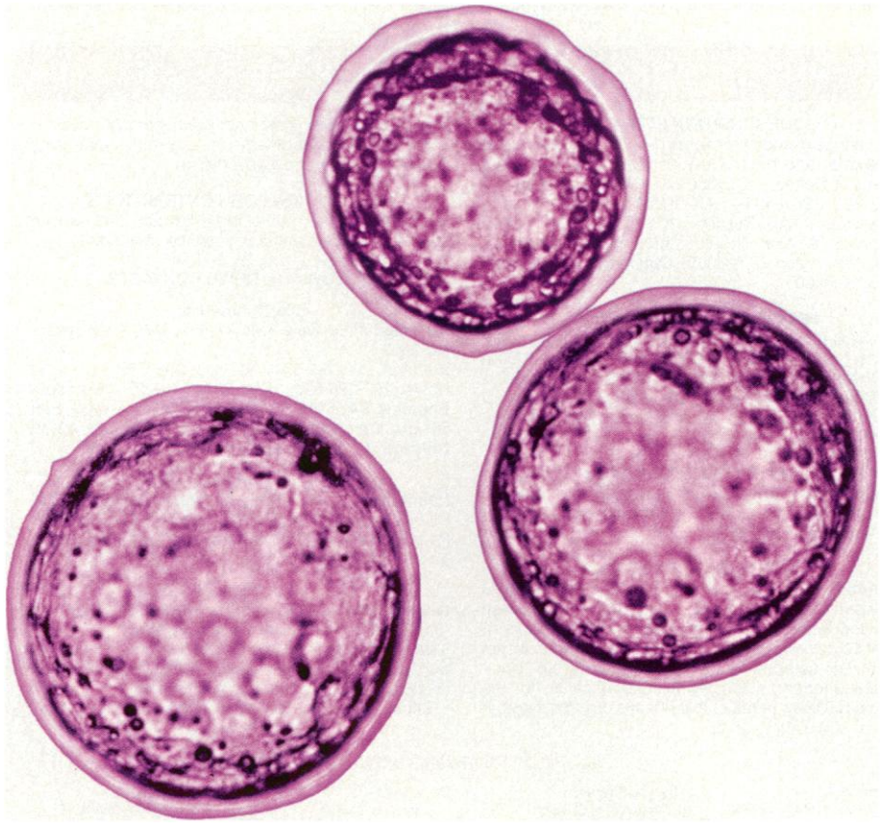

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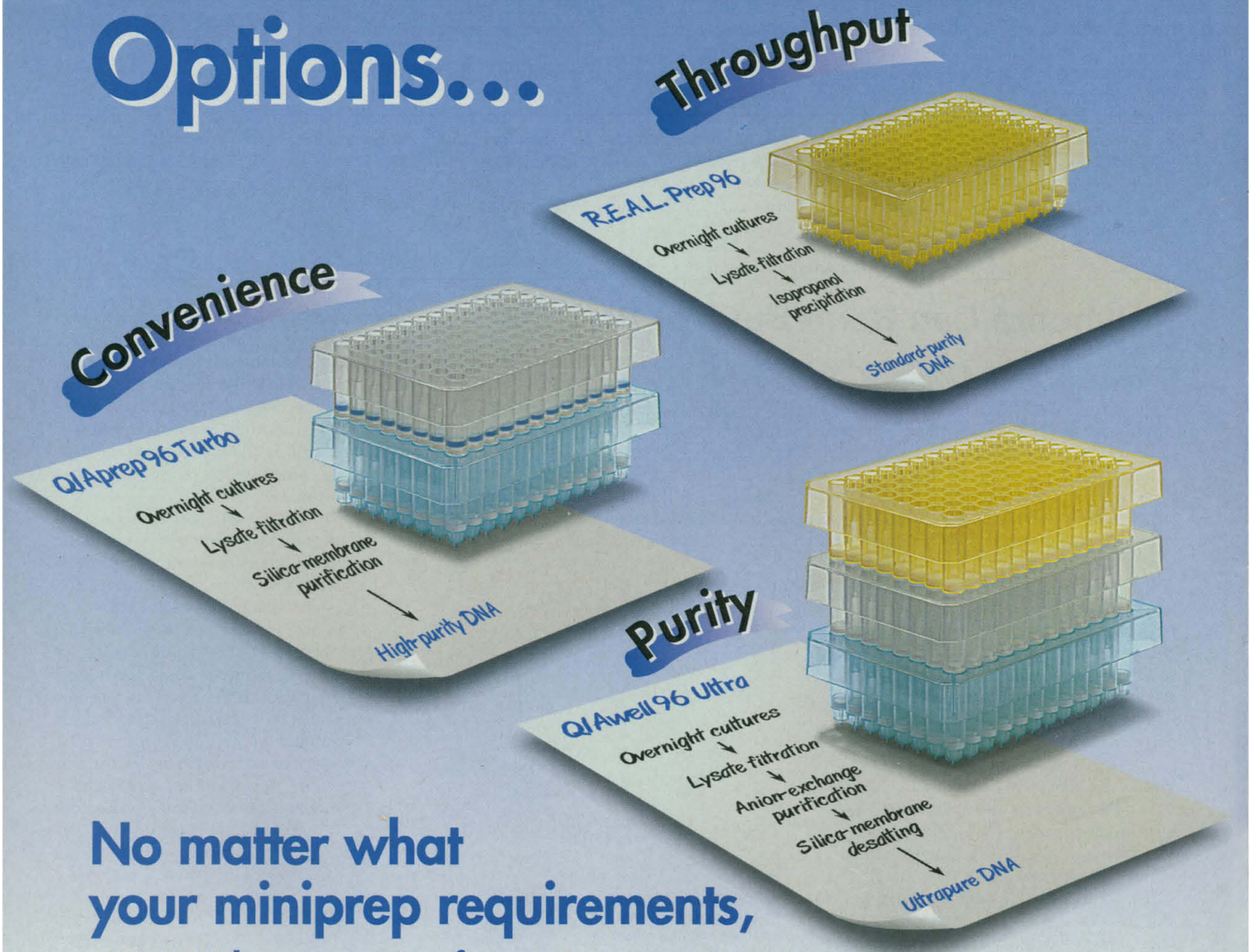

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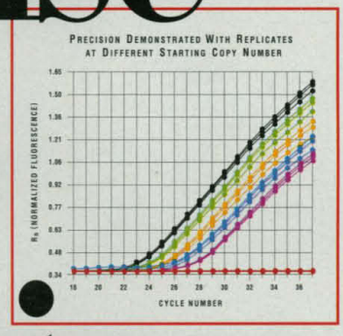

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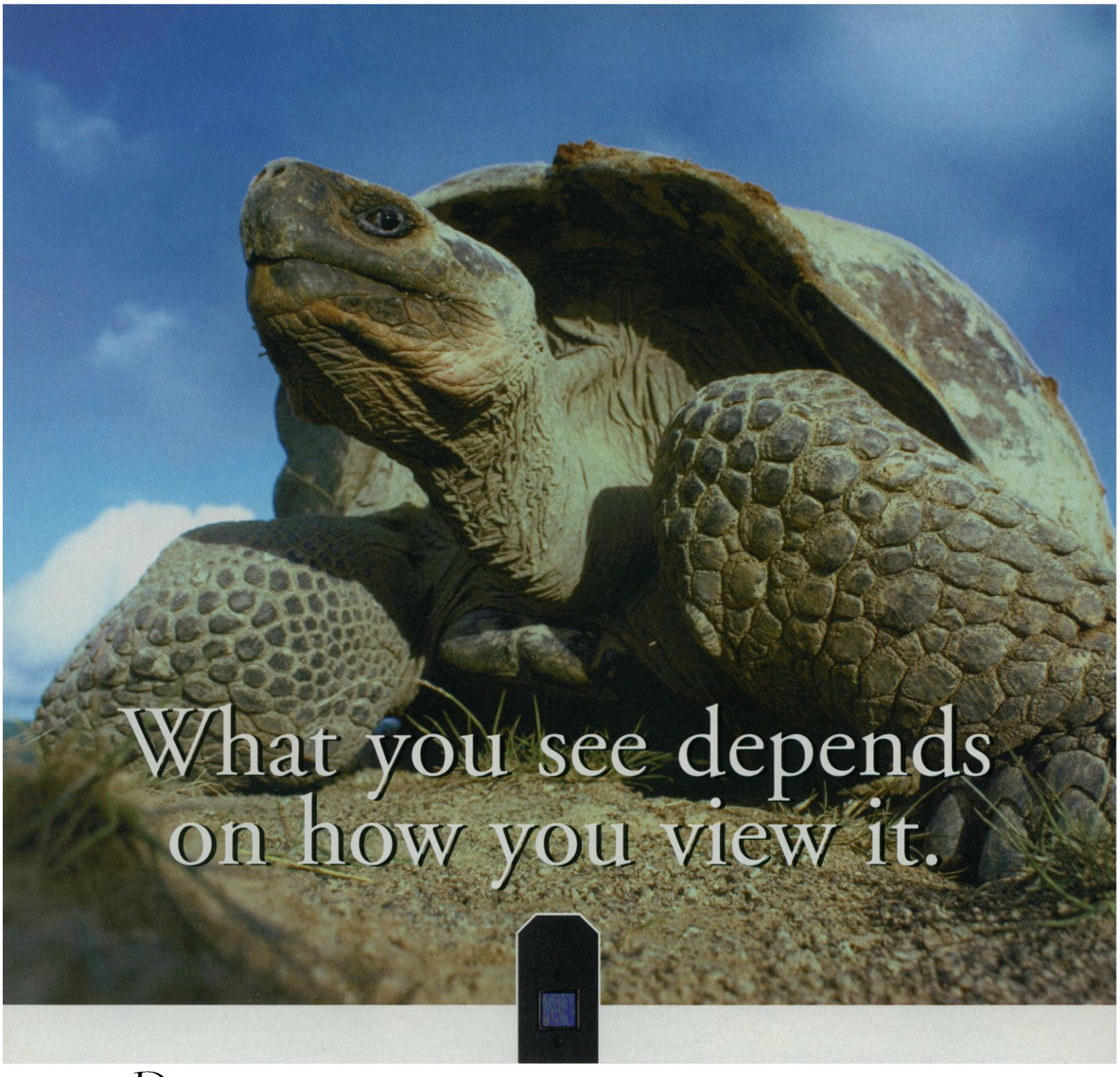

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* *Lennon, G., Auffray, C., Polymeropoulos, M., Soares, M.B. 1996. The I.M.A.G.E. Consortium: An Integrated Molecular Analysis of Genomes and their Expression. Genomics 33, 151-152.*

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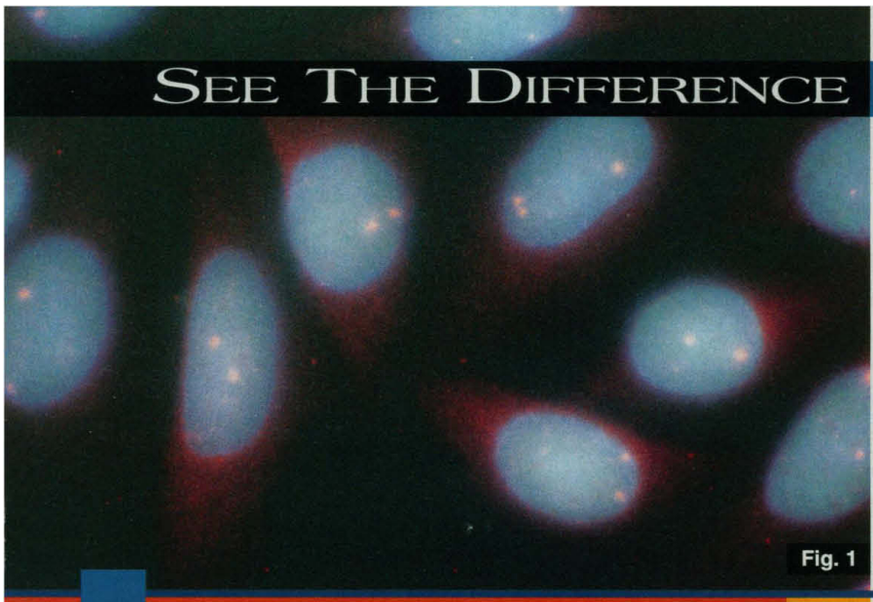

Fig. 1

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Fig. 1. Sensitive detection of integrated HPV in SiHa cells using TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe (1000 bp) hybridized to cultured SiHa cells. TSA fluorescence detection used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slide counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using separate tetramethylrhodamine and DAPI filters. Photo taken on KODAK 1000 speed film with 5 second (Cyanine 3 Tyramide) and 0.5 second (Hoechst 33342) double exposure using a 100X objective.

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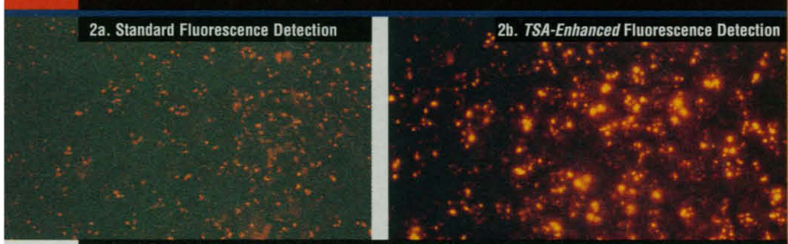
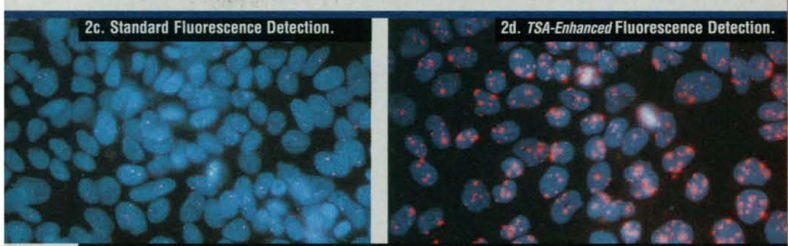


Tetramethylrhodamine filter



Multiband pass filter

Figs. 2a-d. Comparison of HPV fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe hybridized to cultured CaSki cells.

2a-b. Standard fluorescence detection carried out with Cy™3-conjugated Streptavidin (Jackson ImmunoResearch Laboratories, Inc.). TSA-enhanced fluorescence used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slides counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using a tetramethylrhodamine filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

2c-d. Protocol same as above but counterstained slides evaluated using a multiband pass filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

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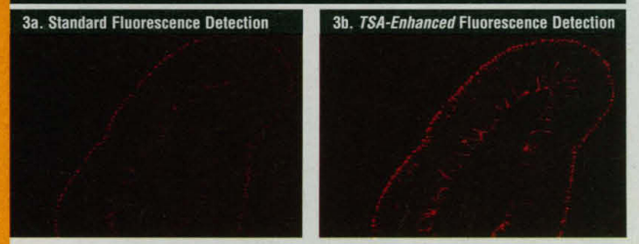

Fig. 3a-b. Comparison of standard fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3). Courtesy of *Kevin Roth, M.D., Ph.D., Washington University School of Medicine, St. Louis, MO.* Bouin's fixed, paraffin embedded mouse intestinal tissue, deparaffinized and incubated with biotinylated wheat germ agglutinin. Sections incubated with Cy3-conjugated Streptavidin (3a) or with Streptavidin-HRP followed by Cyanine 3 Tyramide (3b). Wheat Germ Agglutinin labels intestinal epithelial cells at the base of the crypts.

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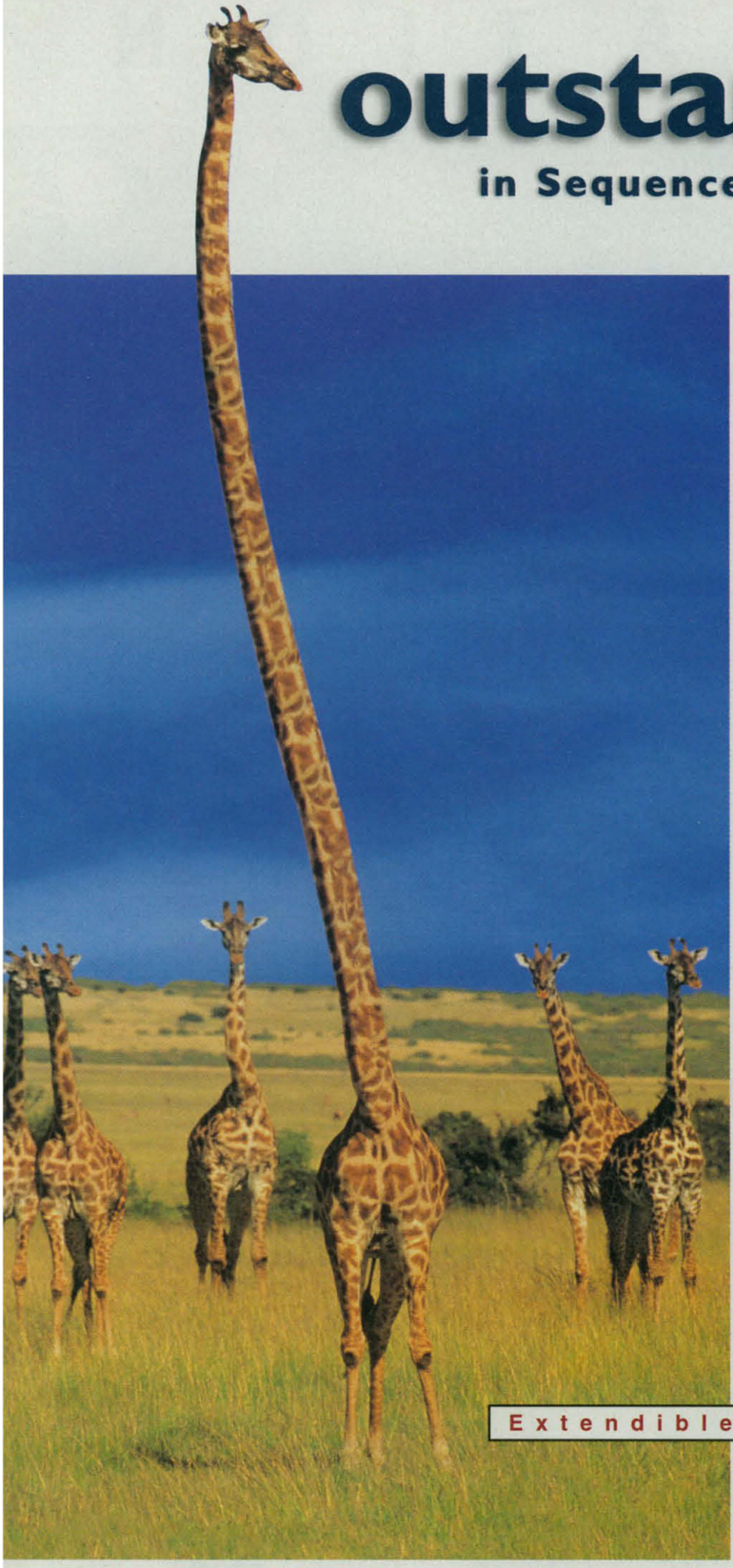

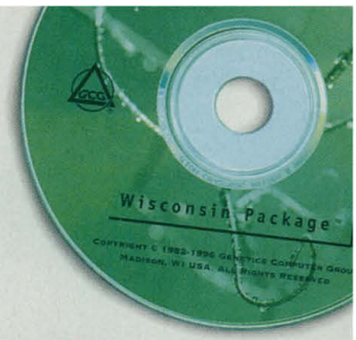

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