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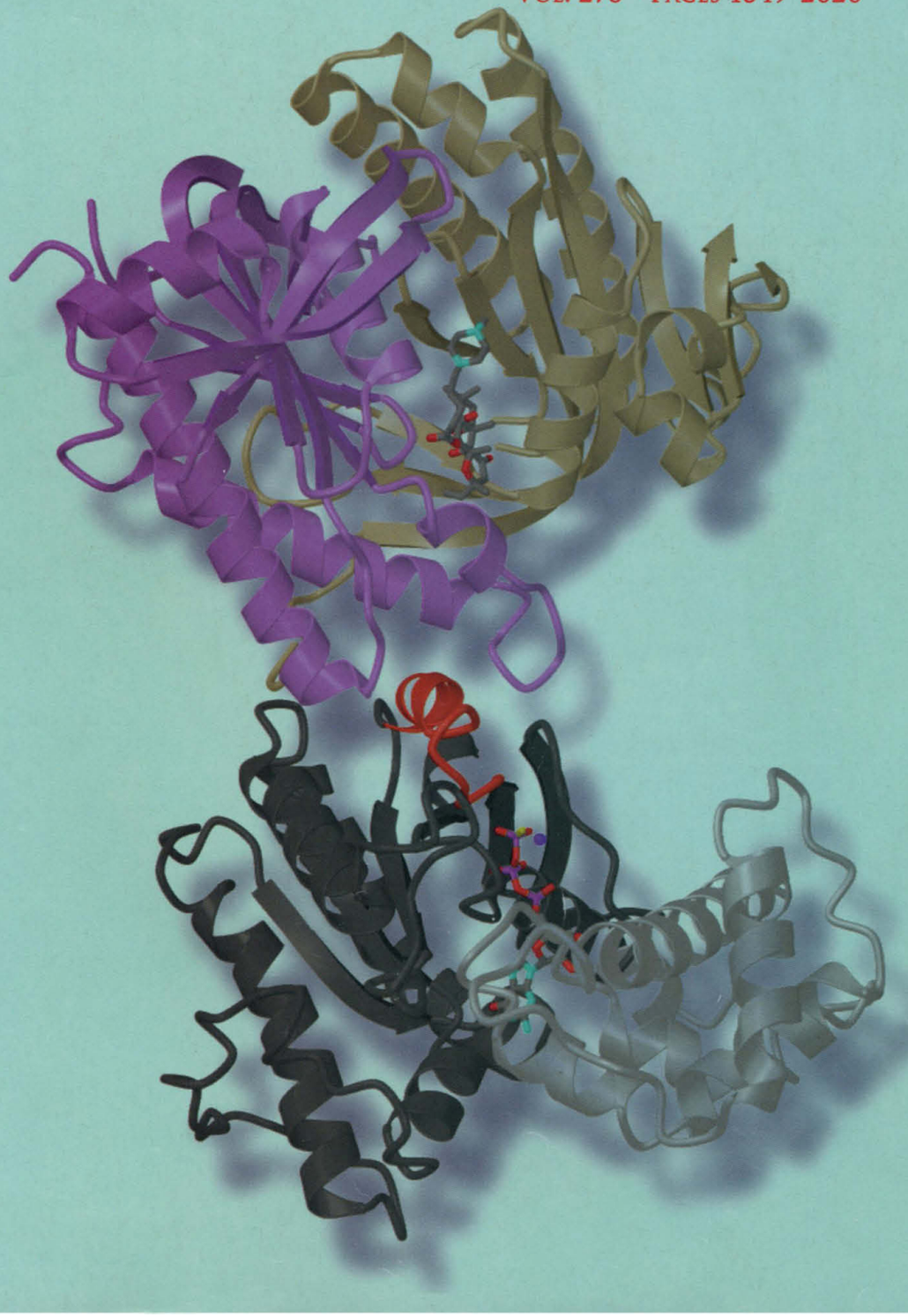

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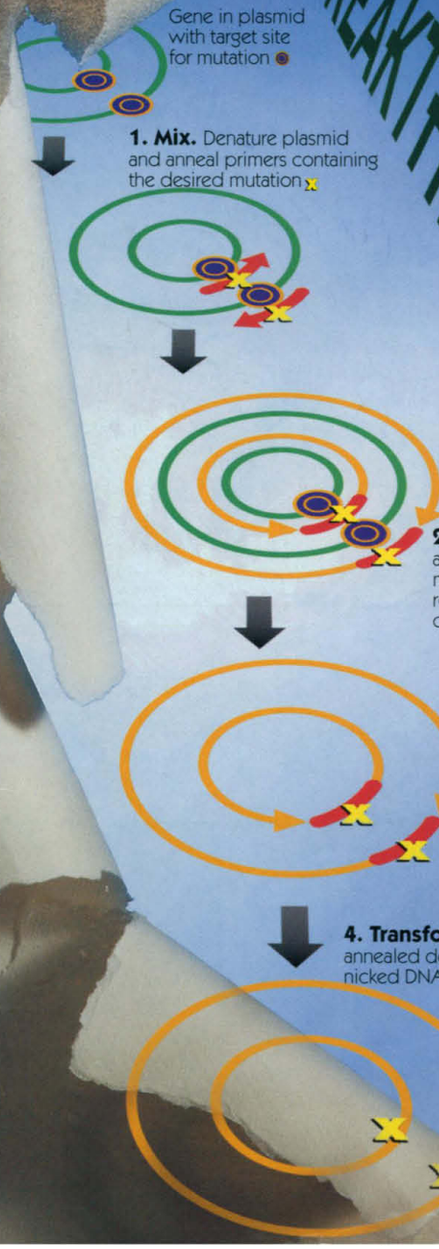

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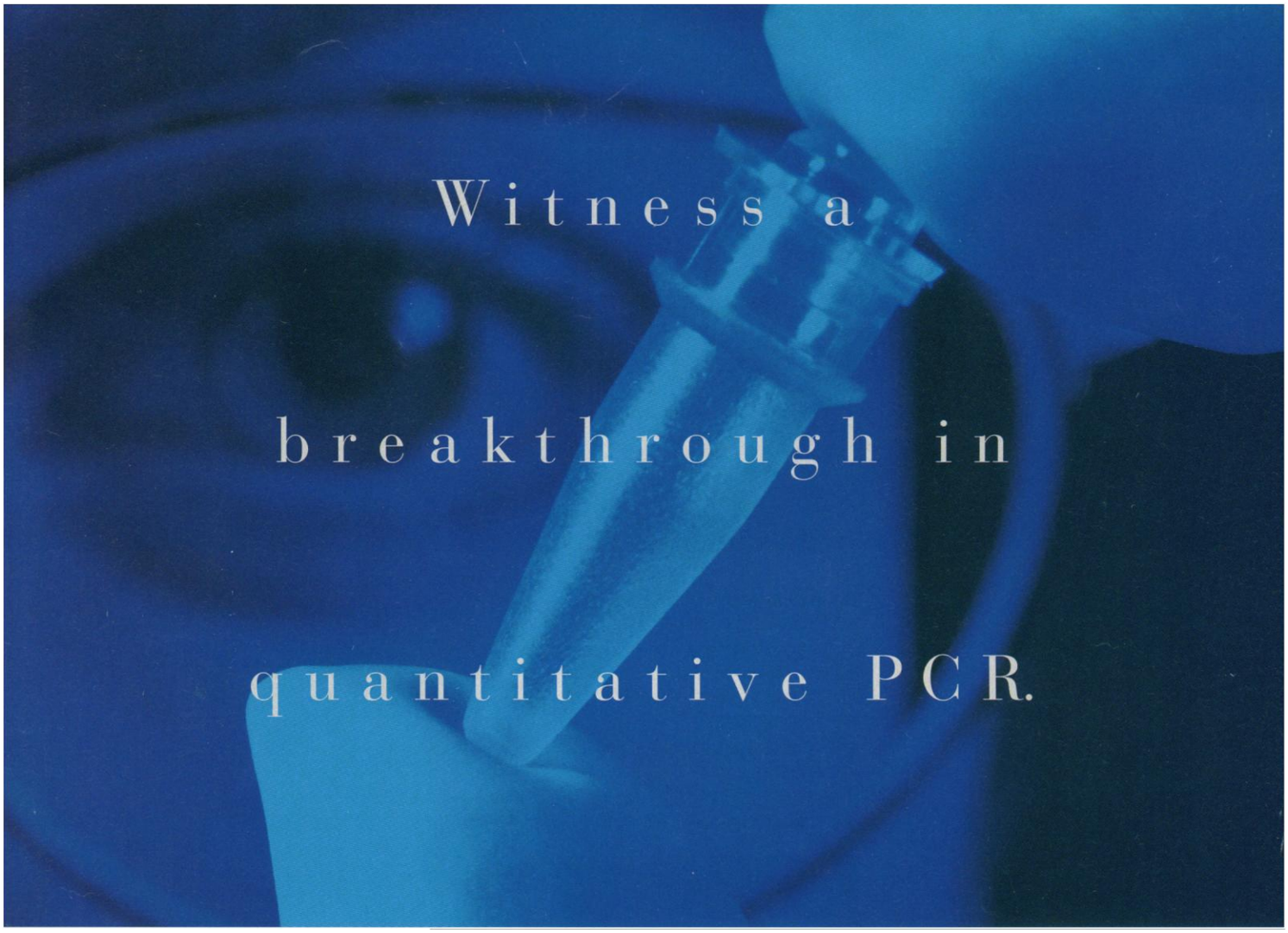

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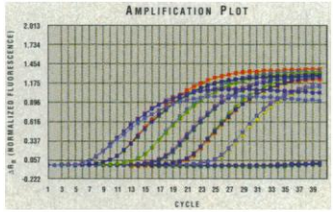

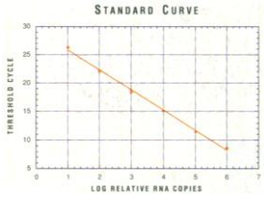

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- Cellular DNA Fragmentation ELISA
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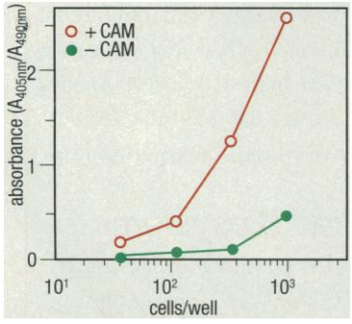

Figure 1. Sensitive detection of nucleosomes in cytoplasmic fractions at different cell concentrations using the Cell Death Detection ELISA. HL-60 cells were cultured at different cell concentrations with or without CAM (camptothecin) at 2 µg/ml for 4 hr at 37°C. Cell lysates were prediluted 1:10 and tested in the immunoassay with a 10 minute substrate reaction.

The most extensive line of products for apoptosis and cell proliferation

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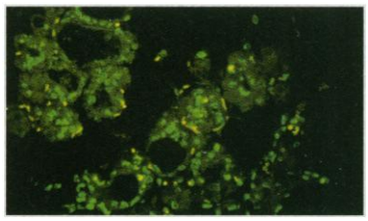

Figure 2. Detection of apoptotic cells (green) in involuting mouse mammary glands by fluorescence microscopy. Formalin-fixed, paraffin-embedded tissue sections were dewaxed and stained using the *In Situ* Cell Death Detection Kit, Fluorescein, to show apoptosis occurring in involuting mouse mammary glands after 3 days. Erythrocytes appear yellow due to autofluorescence (data kindly provided by R. Friis, University of Bern, Switzerland).

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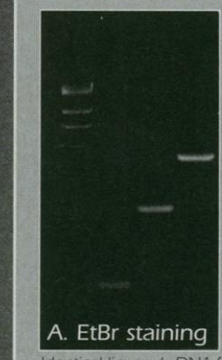
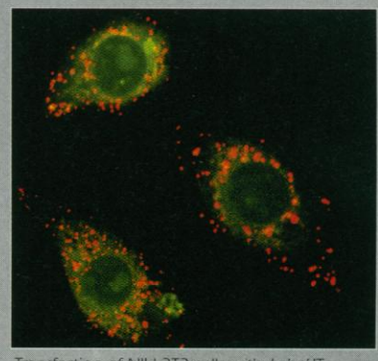


Identical linear ds DNA fragments, either unlabeled (A), or labeled with the *Label* IT™ Rhodamine* Labeling Kit (B), were analyzed by gel electrophoresis and visualized under UV illumination. Gel A was stained with EtBr; the labeled fragments on Gel B were visualized WITHOUT EtBr staining. This demonstrates the high labeling efficiency and non-destructiveness of the *Label* IT method.



Transfection of NIH 3T3 cells with *Label* IT rhodamine labeled DNA. Red spots indicate internalization of labeled DNA.

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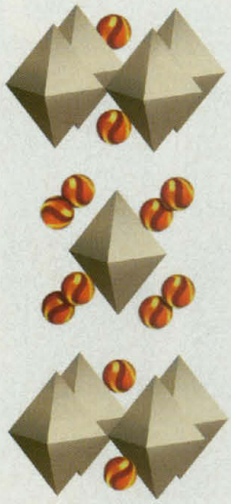
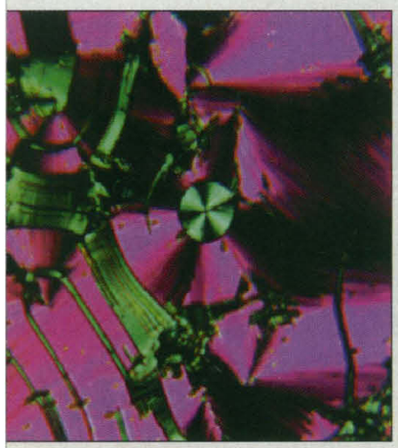


1879

Abnormal normal state of high-T_c superconductors



1924

Chiral liquid crystals from achiral molecules

NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVES

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RESEARCH ARTICLE

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DEPARTMENTS

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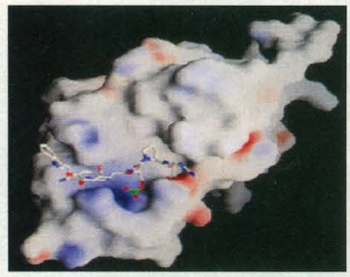
COVER

Complex between a heterotrimeric guanosine triphosphate (GTP)–binding protein α subunit ($G_{s\alpha}$) and the catalytic domains of its effector, adenylyl cyclase. $G_{s\alpha}$ (light and dark gray; switch II helix in red) is activated by the nonhydrolyzable analog of GTP, GTPγS. Forskolin is bound between the C1 (khaki) and C2 (purple) domains of adenylyl cyclase. The structure sheds light on the mechanism by which adenylyl cyclase is activated. See p. 1907, related Report (p. 1943), and Perspective (p. 1898). [Image: J. Tesmer and S. Sprang]

TECHNICAL COMMENTS

1940

Ventralizing signal in *Xenopus* embryo



1883 & 1957

New twist at mitosis

◩ **Indicates accompanying feature**

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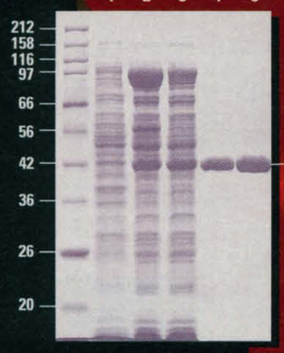

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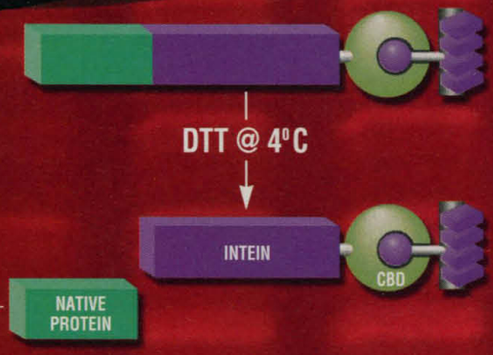

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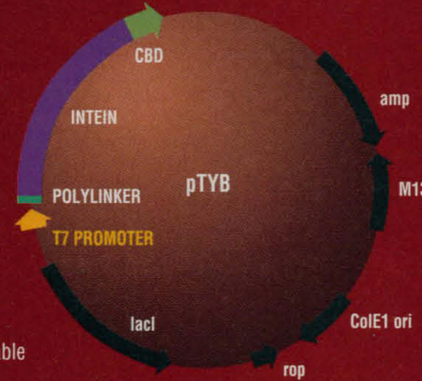

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THIS WEEK IN SCIENCE

edited by DAVID VOSS

Cooler films

Silicon dioxide is the main insulating material used in silicon devices, but more complex architectures will require lower temperature routes for its formation to avoid damaging previously fabricated parts of devices. Klaus *et al.* (p. 1934) show that a two-step reaction that forms single layers of silicon dioxide at temperatures greater than 600 kelvin proceeds readily at room temperature if an organic base, pyridine, is included as a catalyst.

■

A middle road for protein folding

Two extreme views have been invoked for protein folding, one in which the protein folds along a well-defined specific pathway, and one where there is a general bias in the energy surface that guides the protein to the native (folded) state through a variety of routes. Lazaridis and Karplus (p. 1928) have performed extensive simulations of folding pathways and show that the two views can be reconciled; they suggest that while there is considerable diversity between the different trajectories, there are common structural features that define an average folding pathway.

■

Planning and execution

Neurons in the motor cortex change their firing rates during the planning and execution of movements such that a vector summation of the neurons' preferred directions corresponds to the desired movement. Riehle *et al.* (p. 1950; see the Perspective by Fetz, p. 1901) recorded simultaneously from motor cortical neurons in monkeys during preparatory stages and actual movement. They find that the temporal pattern of neuronal spikes becomes synchronized both when the monkey is planning to make a movement and when the movement is made, but that there is no change in overall firing rates during the former stages, only during execution of the plan.

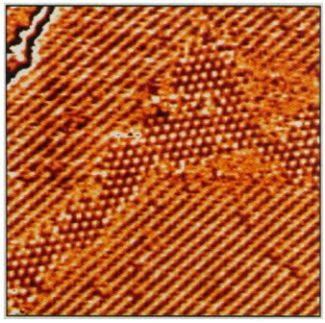
■

Signaling structures

The heterotrimeric guanine nucleotide-binding proteins (G proteins) couple receptors for hormones and other molecules at the cell surface to intracellular signaling pathways that control various cellular responses to their environment. For example, the alpha subunit of the G protein $G_{s\alpha}$ interacts with and activates the enzyme adenylyl cyclase. Adenylyl cyclase passes along a signal by converting adenosine triphosphate to adenosine 3,5-monophosphate, which, in turn, stimulates the activity of the protein kinase PKA. Tesmer *et al.* (p. 1907) and Sunahara *et al.* (p. 1943) present crystal structures of the activated form of $G_{s\alpha}$ alone and in a complex with the catalytic domains of adenylate cyclase (see the Perspective by Bourne, p. 1898). Their data provide insights into the structural basis for the specificity of interaction of various Gα proteins with particular receptors and targets and a potential mechanism by which $G_{s\alpha}$ may activate its primary target, adenylyl cyclase.

Chemical kinetics by counting

Chemical kinetics reflects the sum of enormous numbers of individual reactions, so the thought of examining single reaction events to understand overall kinetics is quite daunting. With the aim of the scanning tunneling microscope, Wintterlin *et al.* (p. 1931) were able to perform an atomic level kinetic study of a simple bimolecular reaction (oxidation of carbon monoxide on platinum). Their kinetic parameters derived from observations of individual reaction events, which take place predominantly at the boundary between domains of CO and O_2, agree with those determined macroscopically.



A cell cycle twist

Pin1 is a peptidyl-prolyl isomerase that plays a critical but poorly understood role in regulation of the cell division cycle. Yaffe *et al.* (p. 1957) examined the peptide-binding specificity of Pin1 and found that it preferentially binds and isomerizes proline (Pro) residues preceded by phosphorylated serine (Ser) or threonine (Thr). The Pro-directed Ser-Thr kinases are important regulators of the cell cycle, and Pin1 binds to a number of proteins that undergo phosphorylation in mitotic cells. Pin1 apparently recognizes phosphorylated Ser-Pro or Thr-Pro sites in proteins phosphorylated at mitosis and facilitates conformational changes in such proteins through its isomerase activity.

■

Grainy echoes in Hyakutake

Comet Hyakutake passed within 0.1 astronomical units of Earth in March 1996 allowing Harmon *et al.* (p. 1921) to image the nucleus and coma by bouncing radio waves off the comet and thus see the cometary structure. They estimate that the nucleus is 2 to 3 kilometers in diameter, consistent with previous estimates and the fact that Hyakutake's brillant activity is not well correlated with its small size. The signature of the echoes also indicates that the high gas production in the coma is the result of porous icy grains in the coma; a cometary mechanism that has not been fully appreciated until Hyakutake's visit.

■

Cluster excesses

The Virgo and Coma galaxy clusters emit an excess radiation in the extreme ultraviolet that has not been explained. Theories have suggested exotic mechanisms to produce the excess, such as unusually hot gases or turbulent mixing. Hwang (p. 1917) finds that a more standard mechanism, inverse Compton scattering, can explain the observations. He shows that inverse Compton scattering of photons in the cosmic microwave background produce excess extreme ultraviolet emissions and he supports this model by showing that the same mechanism also explains the diffuse radio emissions observed for the Virgo and Coma clusters.

■

Forming front and back growth

Early in embryonic growth, signaling pathways specify the development pattern. The *Xenopus* signaling proteins Chordin and Noggin function in dorsalization while the bone morphogenic proteins (BMP) function in ventralization. Blader *et al.* (p. 1937) isolated zebrafish *tolloid*, which encodes a protein similar to BMP-1 and is involved in ventralization. *Tolloid* acts as antagonist toward Chordin. Dorsalization of *Xenopus* embryos by the addition of lithium has been thought to function through the polyphosphoinositide cycle, but recent work has implicated glycogen synthase kinase. Kume *et al.* (p. 1940) inhibited the receptor IP_3 by adding an IP_3 antibody to *Xenopus* embryos and found incomplete dorsal differentiation. Thus, the IP_3 signaling system transduces ventral signals, but other factors may also be involved.

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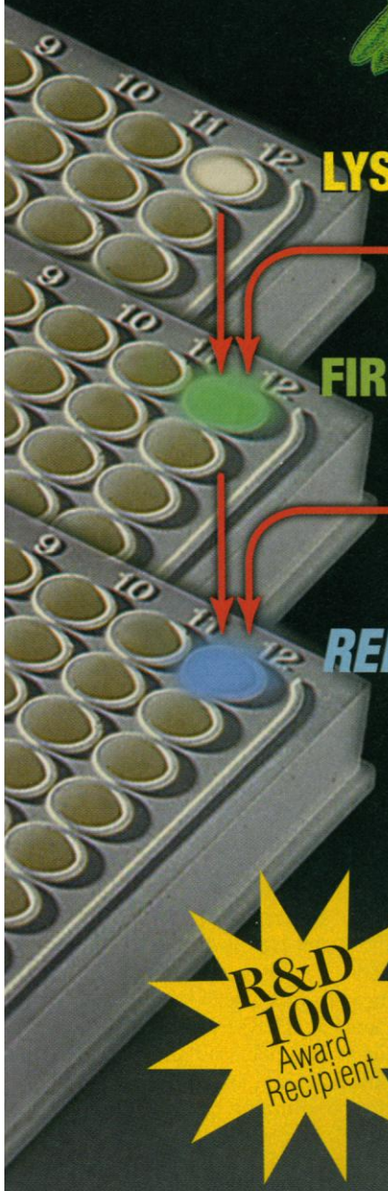

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* U.S. Pat. Nos. 5,283,179, 5,641,641 and 5,650,289 have been issued to Promega Corporation for a firefly luciferase assay method which affords greater light output with improved kinetics as compared to the conventional assay.

** The cDNA encoding luciferase from *Renilla reniformis* is covered by U.S. Pat. No. 5,292,658 assigned to the University of Georgia Research Foundation and sublicensed from SeaLite Sciences, Inc., Norcross GA.

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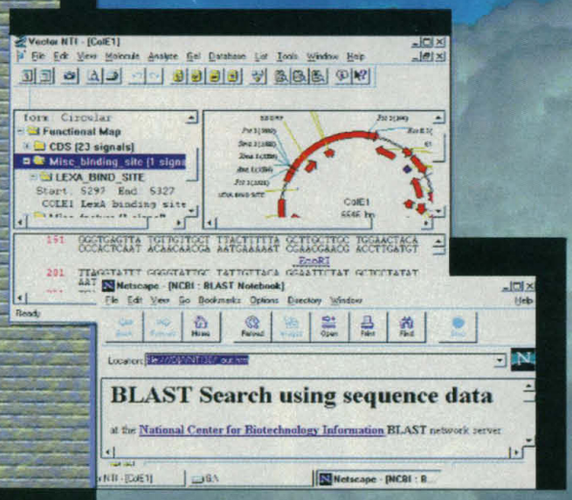

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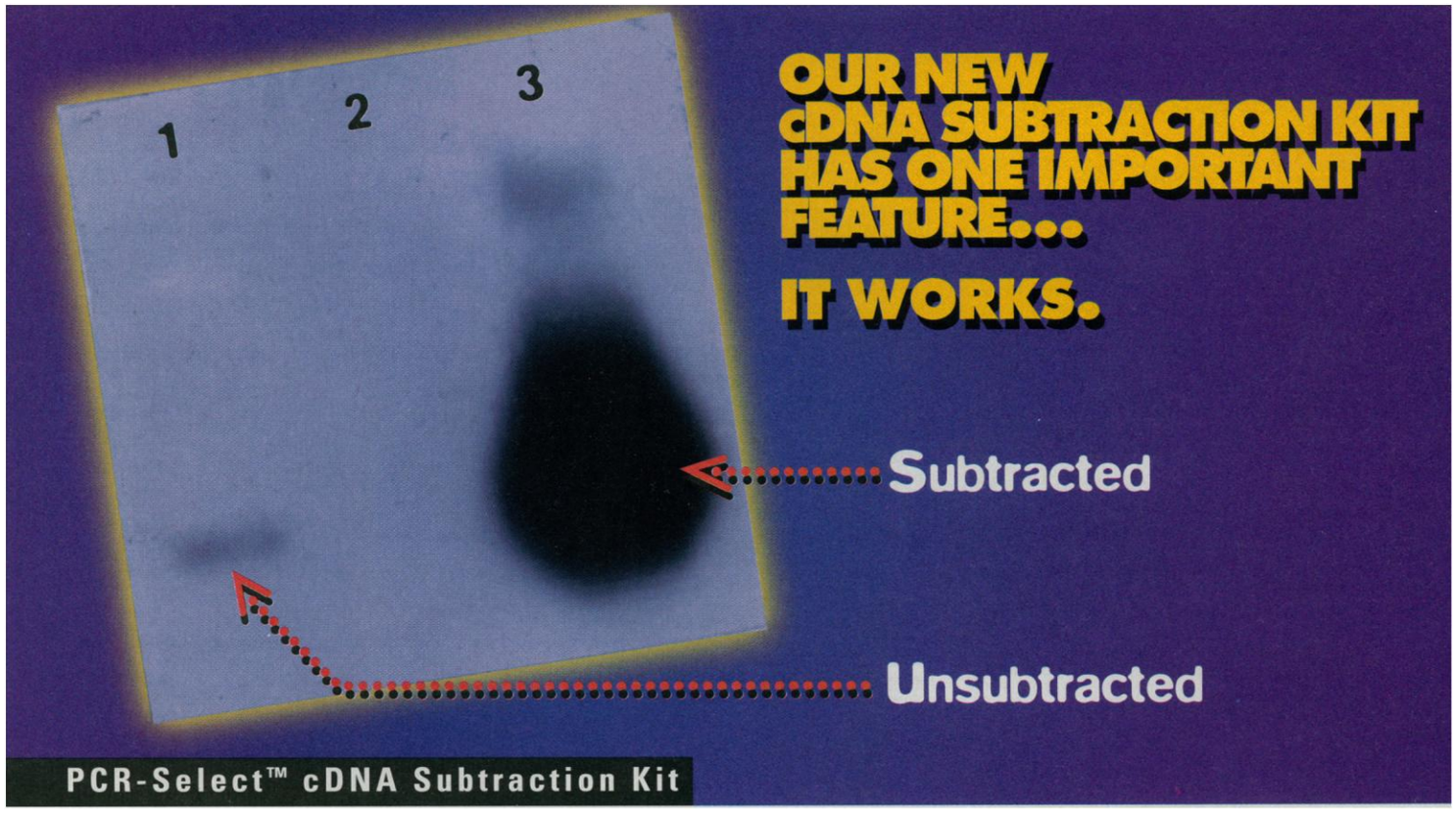
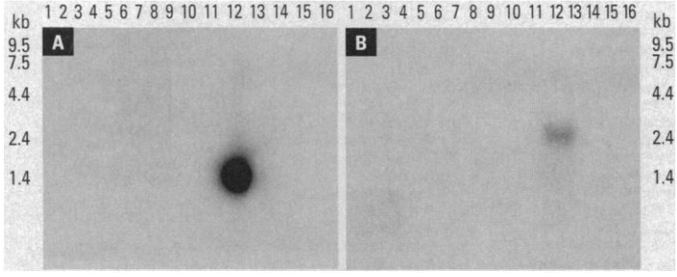


Above photo: Southern blot analysis showing enrichment of IL-2 receptor, known to be activated in human Jurkat T-cells by PHA/PMA treatment. Lane 1: unsubtracted cDNA, treated cells. Lane 2: unsubtracted cDNA, untreated cells. Lane 3: subtracted cDNA, treated cells. A dramatic reduction of the abundant 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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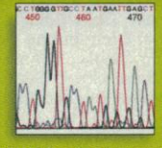

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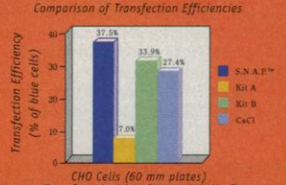

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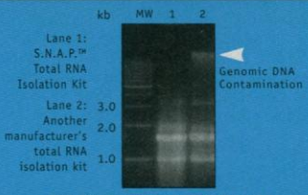

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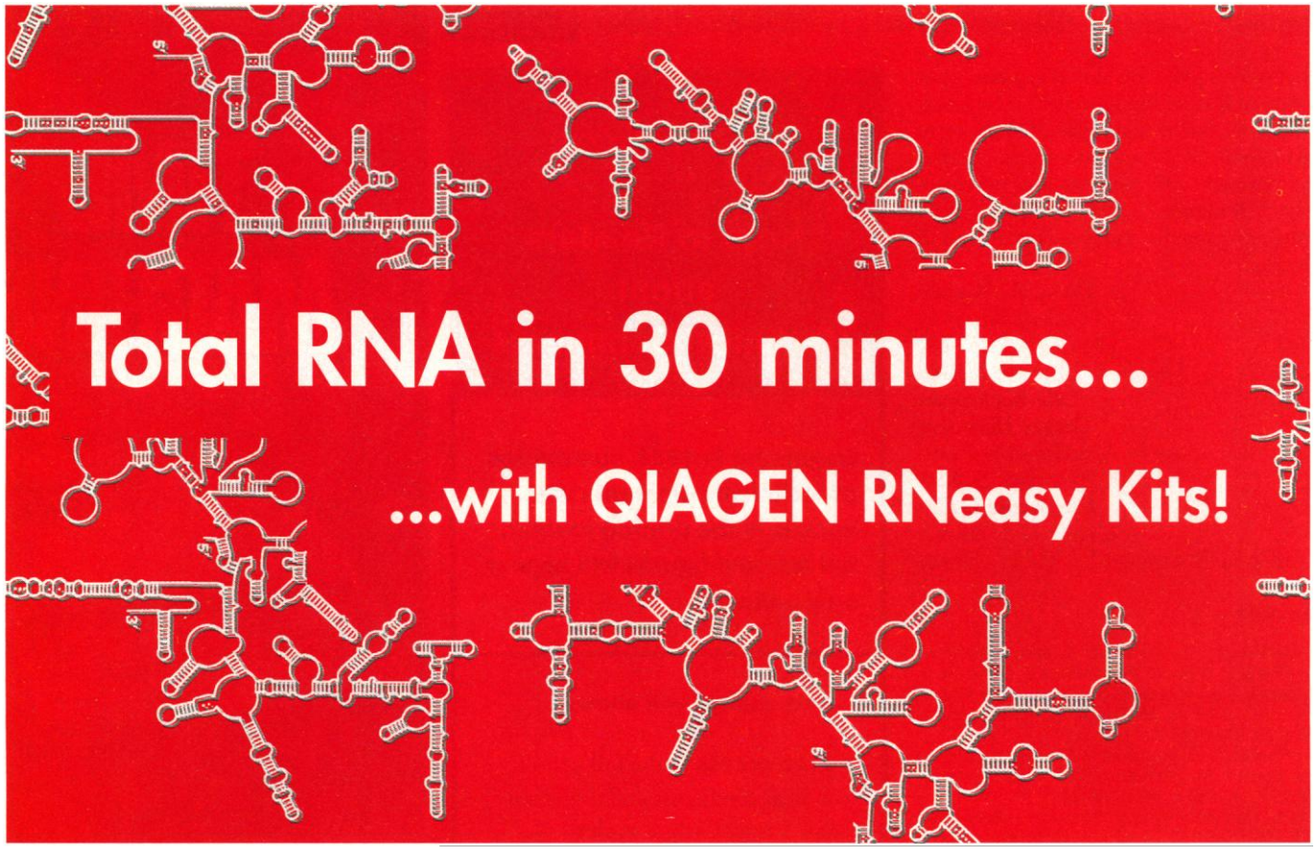

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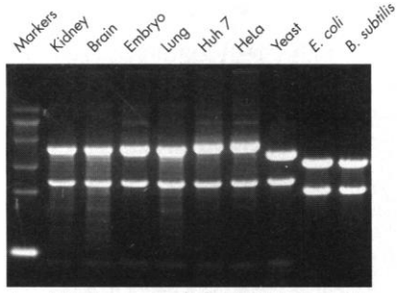

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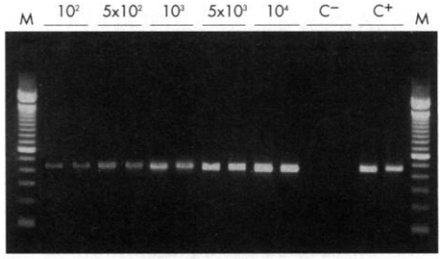

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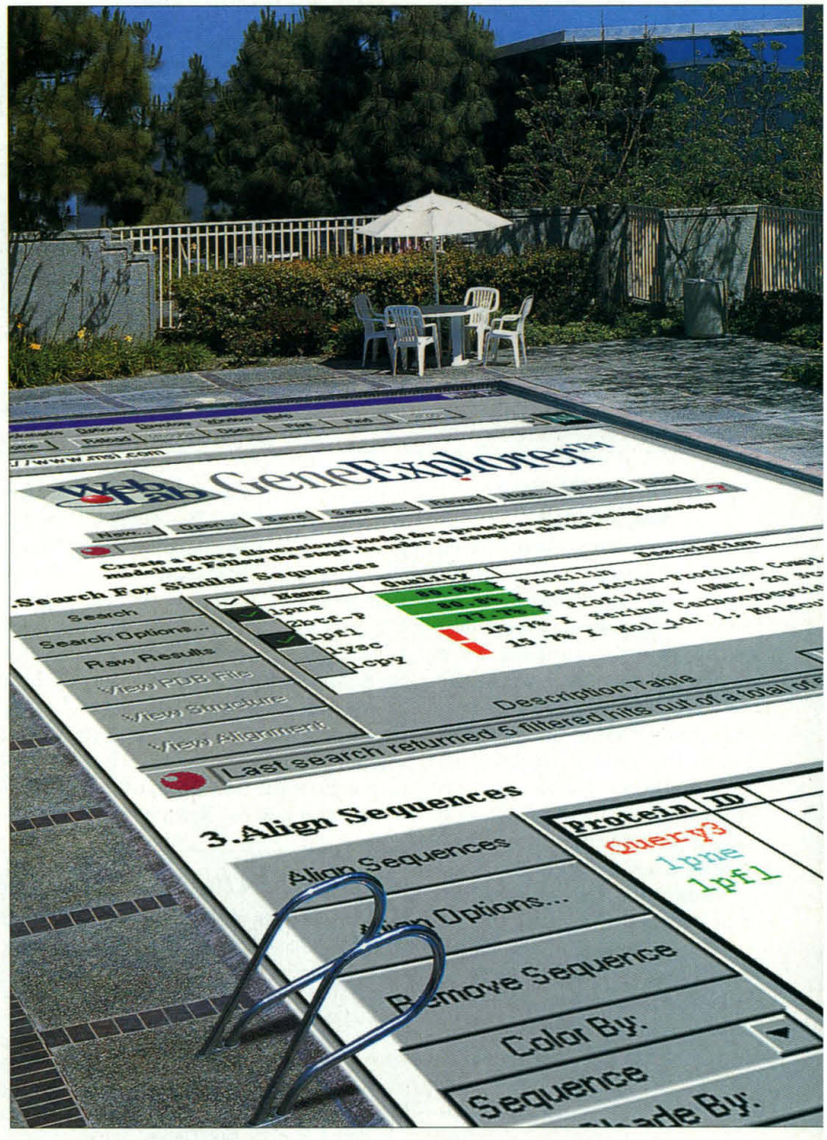

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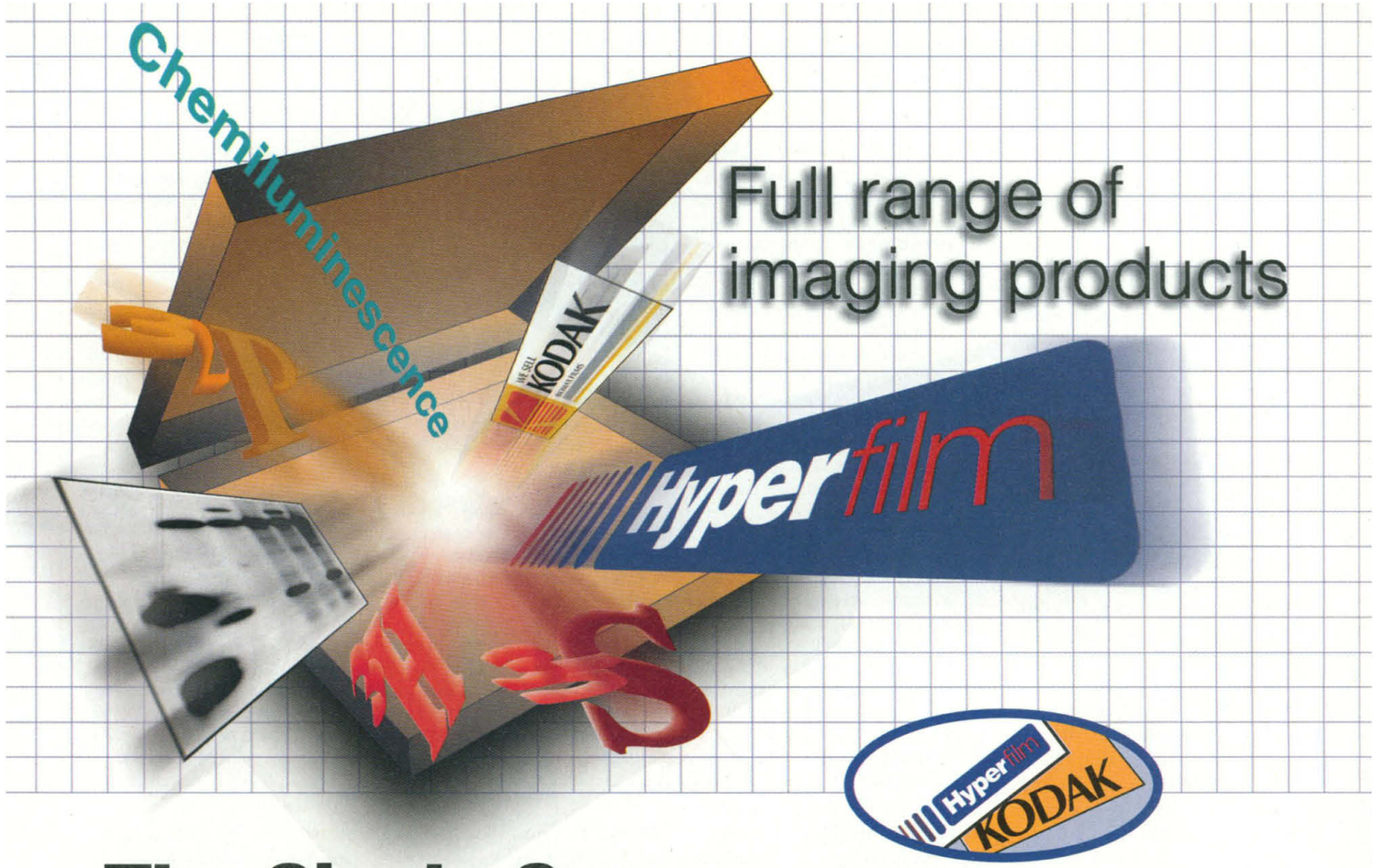

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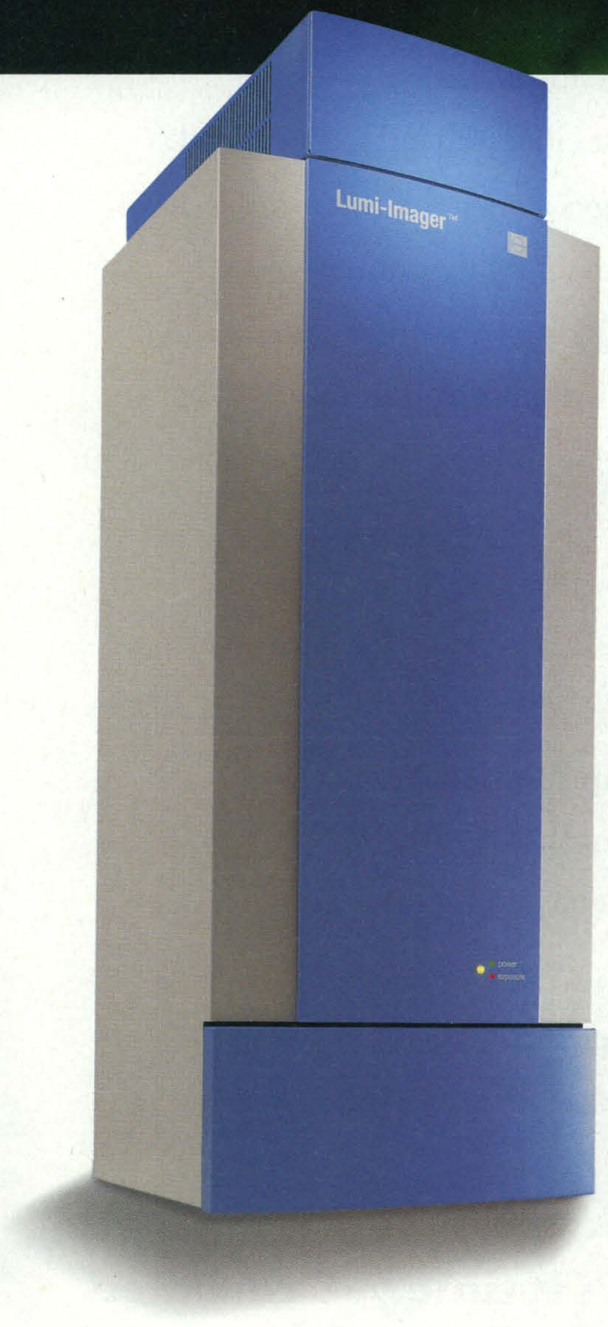

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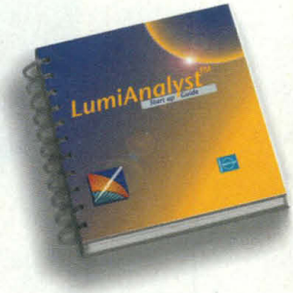

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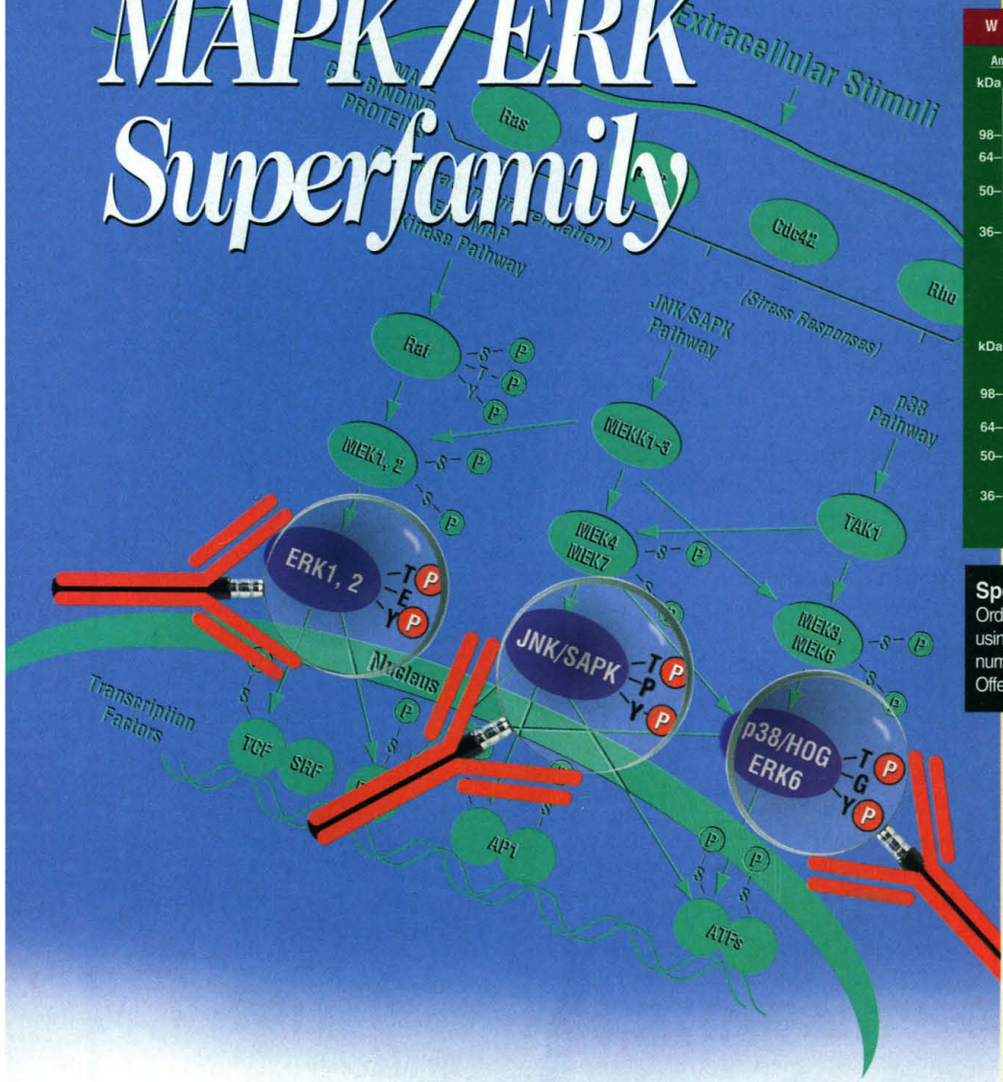

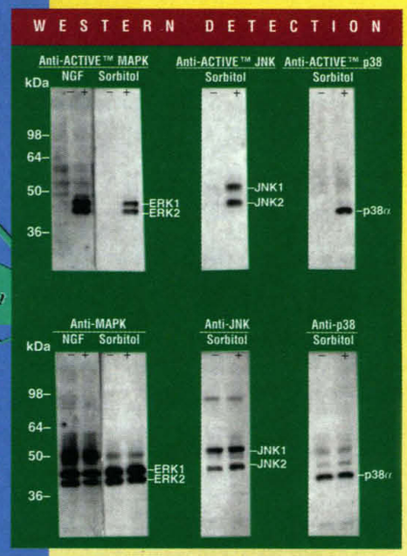

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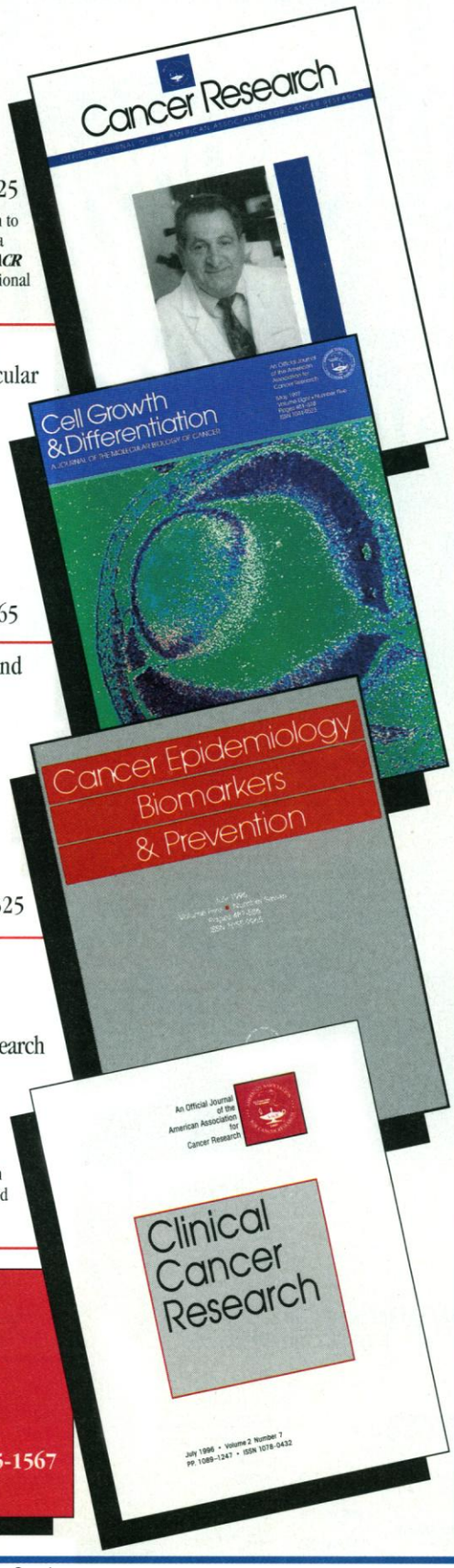

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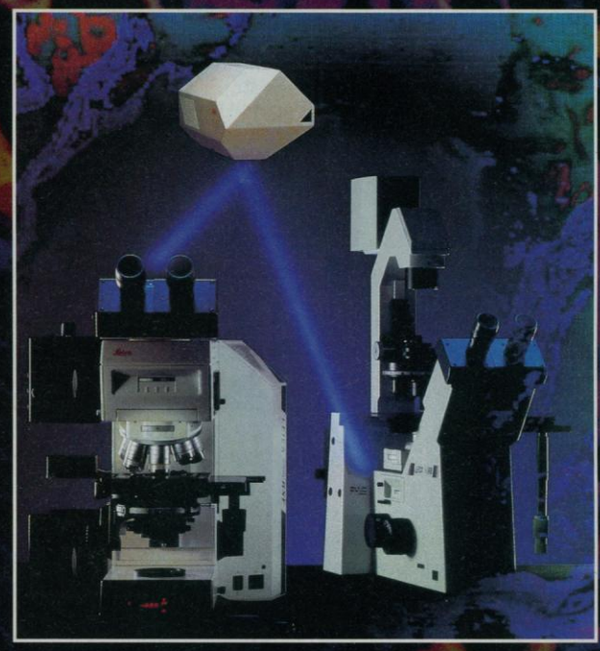

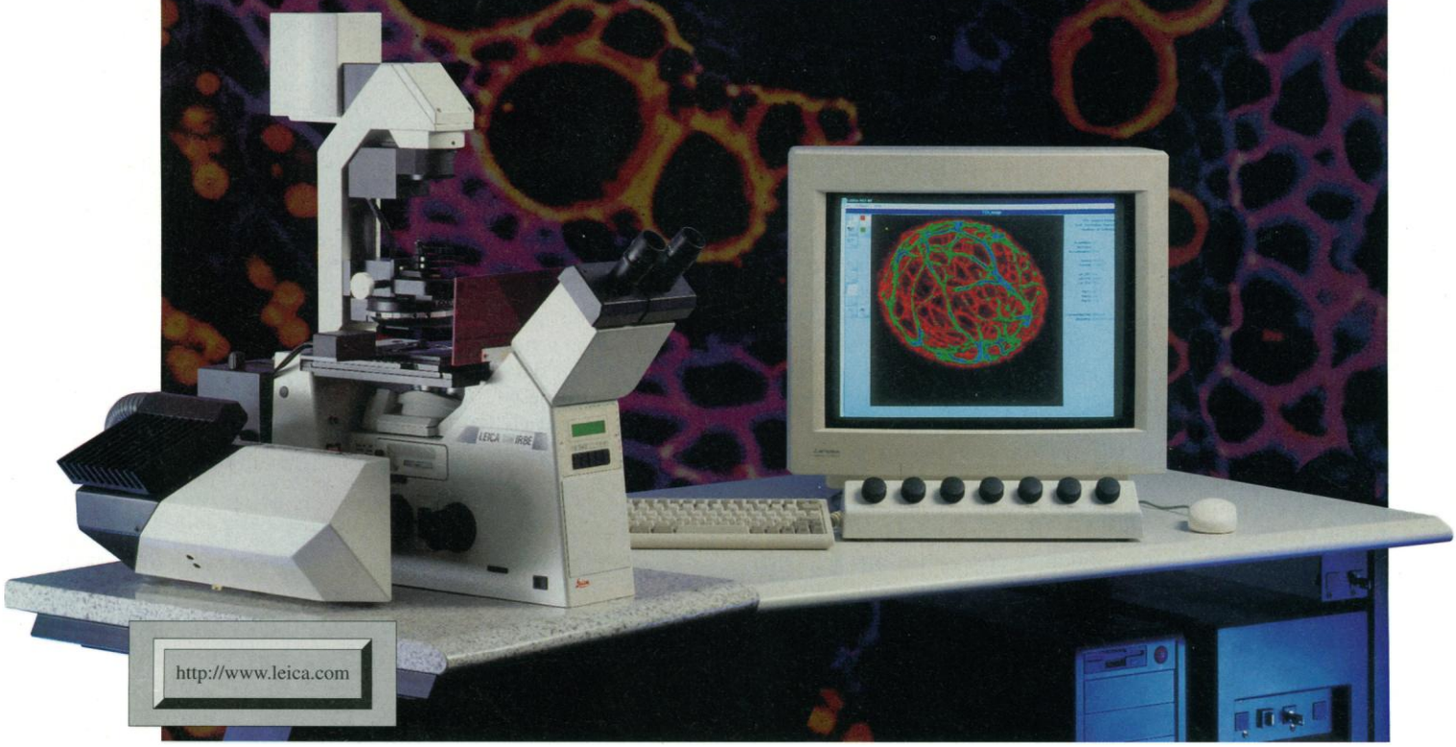

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