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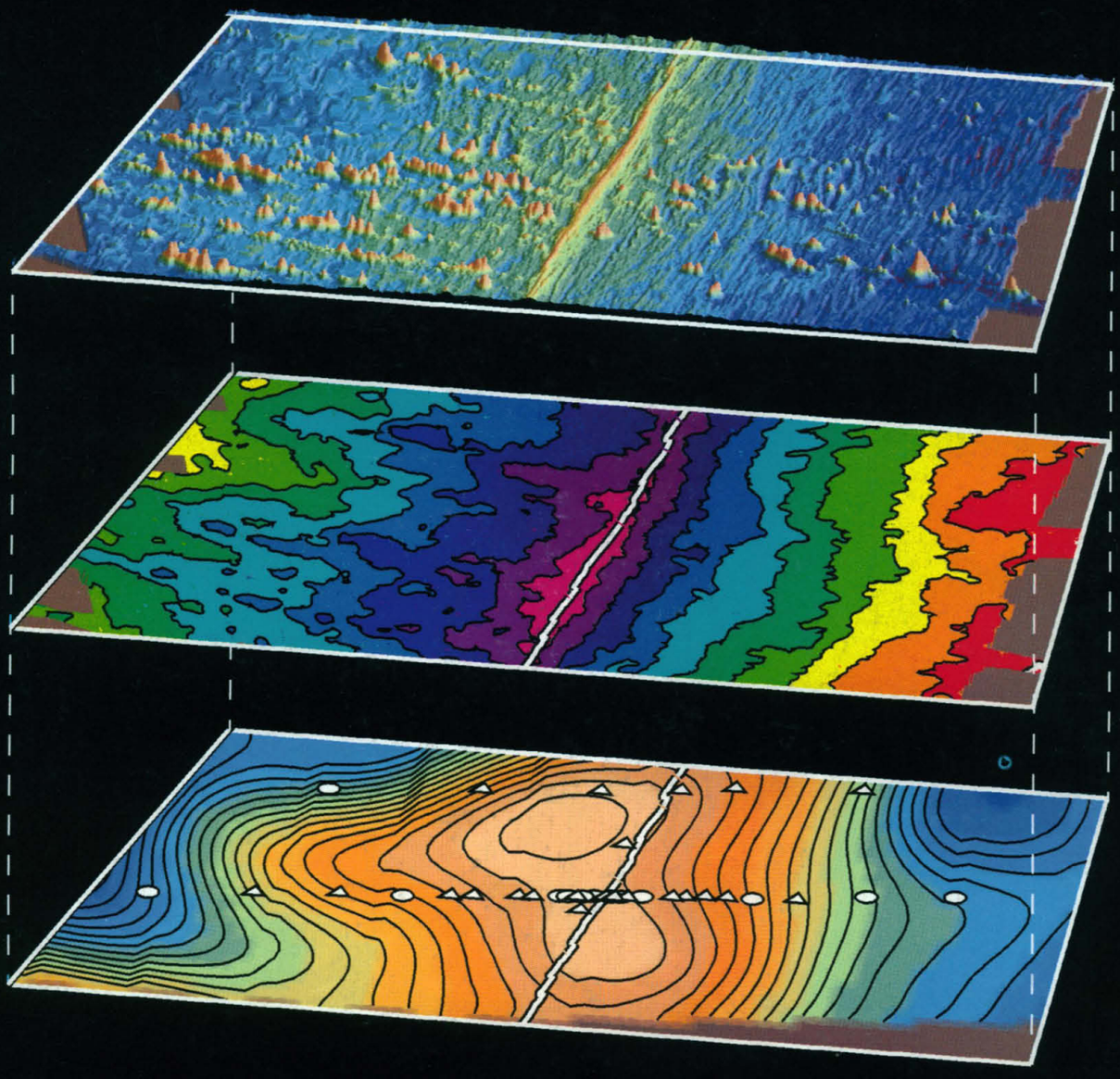

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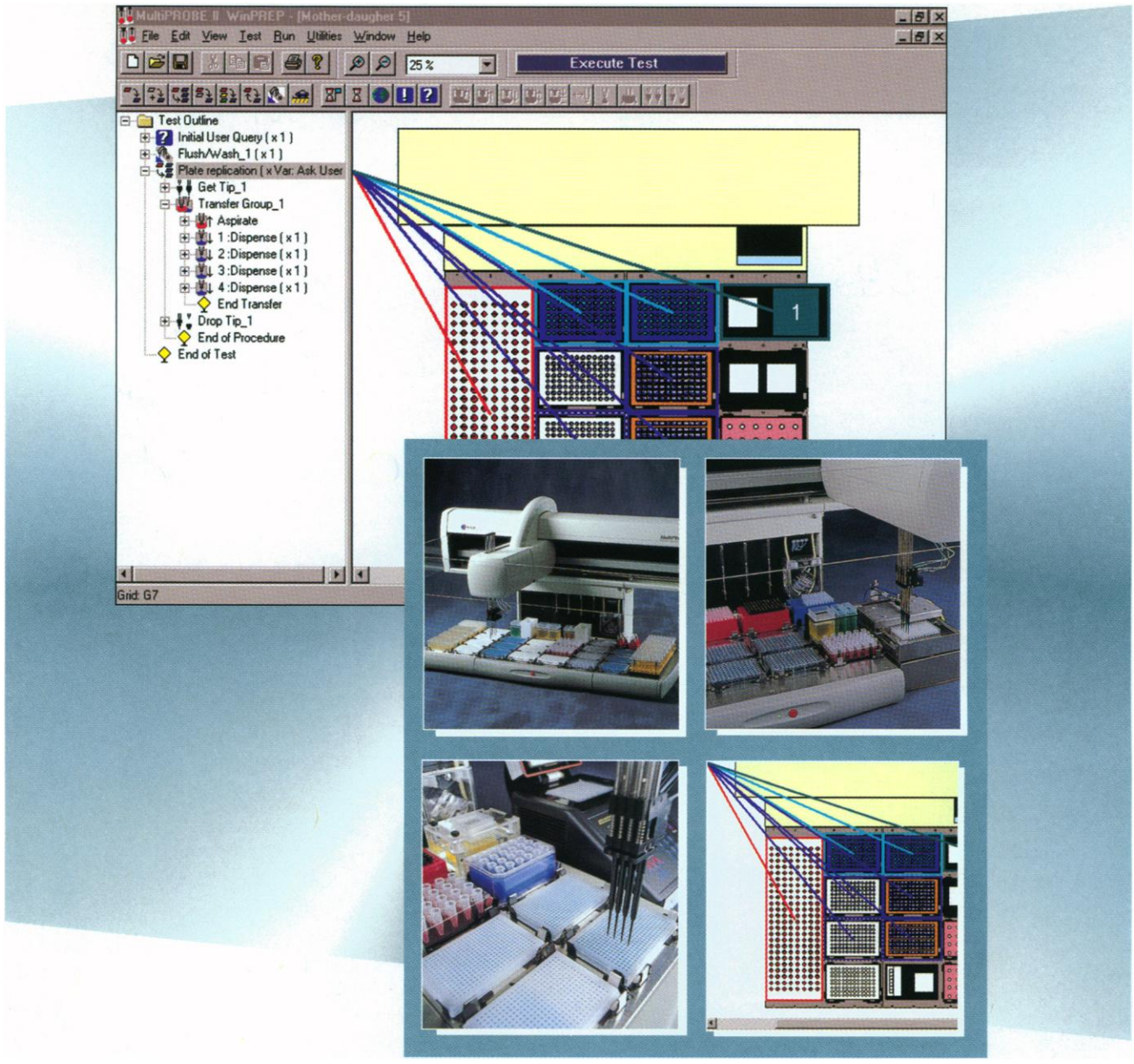

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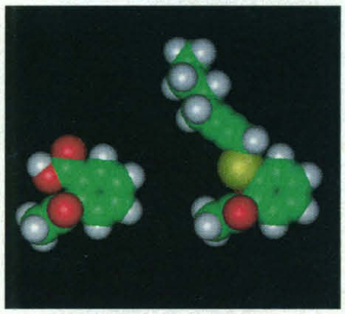

1191 & 1268
Aspirin gets a tail, loses its sting

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Books and New Media

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THE MELT EXPERIMENT

DEPARTMENTS

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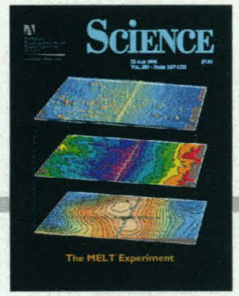
COVER

Sea-floor topography, gravity anomalies, and seismic Rayleigh wave velocities measured in the Mantle Electromagnetic and Tomography (MELT) Experiment on the East Pacific Rise (the center of the image is located at 17°S, 113°W; image width left to right is 640 kilometers). Ocean-bottom seismometers were used to detect partial melting of the mantle and the upwelling of magma, which errupts at mid-ocean ridges. See the eight Reports beginning on page 1215. [Image: D. Scheirer; based on data from D. Scheirer and D. Forsyth]



TECHNICAL COMMENTS

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1256
New clones




1274
Multiple pathways with WNT signals

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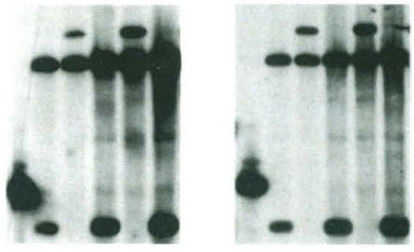
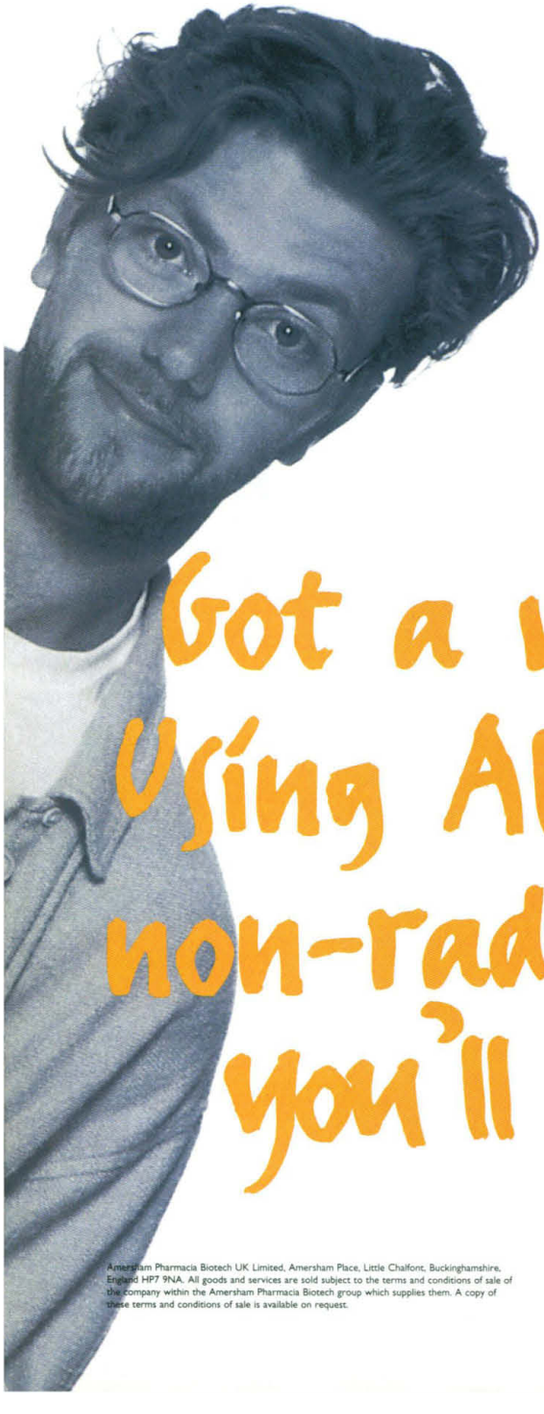


Southern blot: Cosmid DNA digested with *Not* I and *Eco*R I, probed with a 1.1 kb probe labelled with AlkPhos Direct (left) and digoxigenin (right).
(Courtesy of Janet Bartels-Carr, Yale University, USA.)



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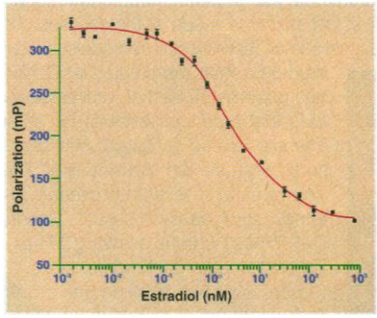

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Lundblad, J. R., *et al.*, Fluorescence polarization analysis of protein-DNA and protein-protein interactions, *Molec. Endocrinol.*, **10**, 607- 612 (1996).
Laurance, M. E., *et al.*, Differential activation of viral and cellular promoters by human T-cell lymphotropic virus-1 Tax and cAMP-responsive element modulator isoforms, *J. Biol. Chem.*, **272**, 2646-2651 (1997).
Lundblad, J. R., *et al.*, Adenoviral E1A-associated protein p300 as a functional homologue of the transcriptional co-activator CBP, *Nature*, **374**, 85-88 (1995).

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Detecting the slightest charges

SQUIDs (superconducting quantum interference devices) have revolutionized the measurement of small magnetic fields. Schoelkopf *et al.* (p. 1238; see the news story by Service, p. 1193) have applied the principle underlying a radio-frequency (RF) SQUID, measuring the change in damping of a resonant tank circuit, to quantify charge instead of magnetic flux. They have constructed an RF single-electron transistor that can measure fractions of an electron charge but, unlike other highly sensitive electrometers, can do so even at very high frequencies (100 gigahertz). The sensitivity of the device corresponds to about 250 times Planck's constant.

Salt clues to water on Europa

Recent data from the Galileo satellite has revealed that the icy surface of Europa, a moon of Jupiter, is geologically young, extensively fractured, and may overlie an ocean. McCord *et al.* (p. 1242; see the commentary by Kargel, p. 1211) examined reflectance spectra from the Galileo spectrometer. Hydrated salts, possibly hydrated magnesium sulfates or sodium carbonates, are present predominantly along the cracks in Europa's surface and may represent evaporite deposits that form when water upwelled along the cracks.

Slowly relieving stress

Seismic waves propagate away from the epicenter of an earthquake at the speed of sound of rocks. The stress pulse induced by the local deformation of the rocks in the earthquake moves much more slowly away and depends on the viscosity of the crust or mantle. Several studies of continental seismicity, particularly in Japan, have correlated subsequent earthquakes (years later) with the arrival of a stress pulse from an earlier large earthquake. Pollitz *et al.* (p. 1245; see the news story by Kerr, p. 1194) examine the possible effects of the stress pulse induced by an entire series of large earthquakes along the northern margin of the Pacific Plate that were clustered from 1952 to 1965. They suggest that subsequent seismicity within the Pacific Plate and along the North American margin was increased by the passage of this stress pulse. They use this correlation to estimate the viscosity of the oceanic mantle of the Pacific Plate.

In-depth study of mantle melting

New oceanic crust forms at spreading ridges, and crust is returned to the mantle at subduction zones and oceanic trenches. How melt forms and is extracted from the mantle to form new oceanic crust has been uncertain—in some models, melting occurs in a narrow region beneath the ridge axis, and in others melting extends over a wide region and is focused by flow to the ridge. Resolving the extent and depth of melting is thus a first-order problem for understanding how the mantle is flowing and driving plate tectonics. A series of reports present the initial seismic results from a geophysical study, the MELT (Mantle Electromagnetic and Tomography) Experiment, aimed at resolving this question (beginning with an overview paper on p. 1215; see the cover). Seismic waves move more slowly through regions containing some melt because of its lower density, and so seismometers were placed on the ocean floor across a large region of the East Pacific Rise, where the Pacific and Nazca plates are forming, to image melt generation. The melting region is broad—several hundred kilometers across and extends to depths of 100 kilometers or more—and extends farther to the west of the the East Pacific Rise than it does to the east. Seismic velocities are fastest perpendicular to the ridge axis, perhaps indicating the minerals at depth in the mantle are preferentially oriented by the flow.

A long comet shower

During the late Eocene, the Earth was pelted by an unusual amount of extraterrestrial (ET) material; two large-impact craters evidently formed at about the same time, 35.6 million years ago. To obtain a longer record of the input of ET material, Farley *et al.* (p. 1250) examined the abundance of helium-3, a tracer of the input of ET dust, in Eocene sedimentary rocks. The data imply that the flux of ET material was elevated for a period of 2.5 million years surrounding the time of the two large impacts. All of these events may be explained by a prolonged comet shower triggered by an event in the Oort cloud.

Nanotubes, cut and ready to react

Single-wall carbon nanotubes (SWNTs) can be formed almost free of defects, but their usefulness is limited by how well they can be purified and manipulated. Liu *et al.* (p. 1253) report on a method to purify SWNTs that results in a "bucky paper" material that resembles carbon paper. Resuspension and sonication of this material in strong oxidizing acids (such as

mixtures of sulfuric and nitric acid) cut the tubes to lengths of hundreds of nanometers. The open ends of the tubes are reactive and can be used for derivatization. Thiol-bearing groups were attached to the cut nanotubes, which were then attached to gold particles.

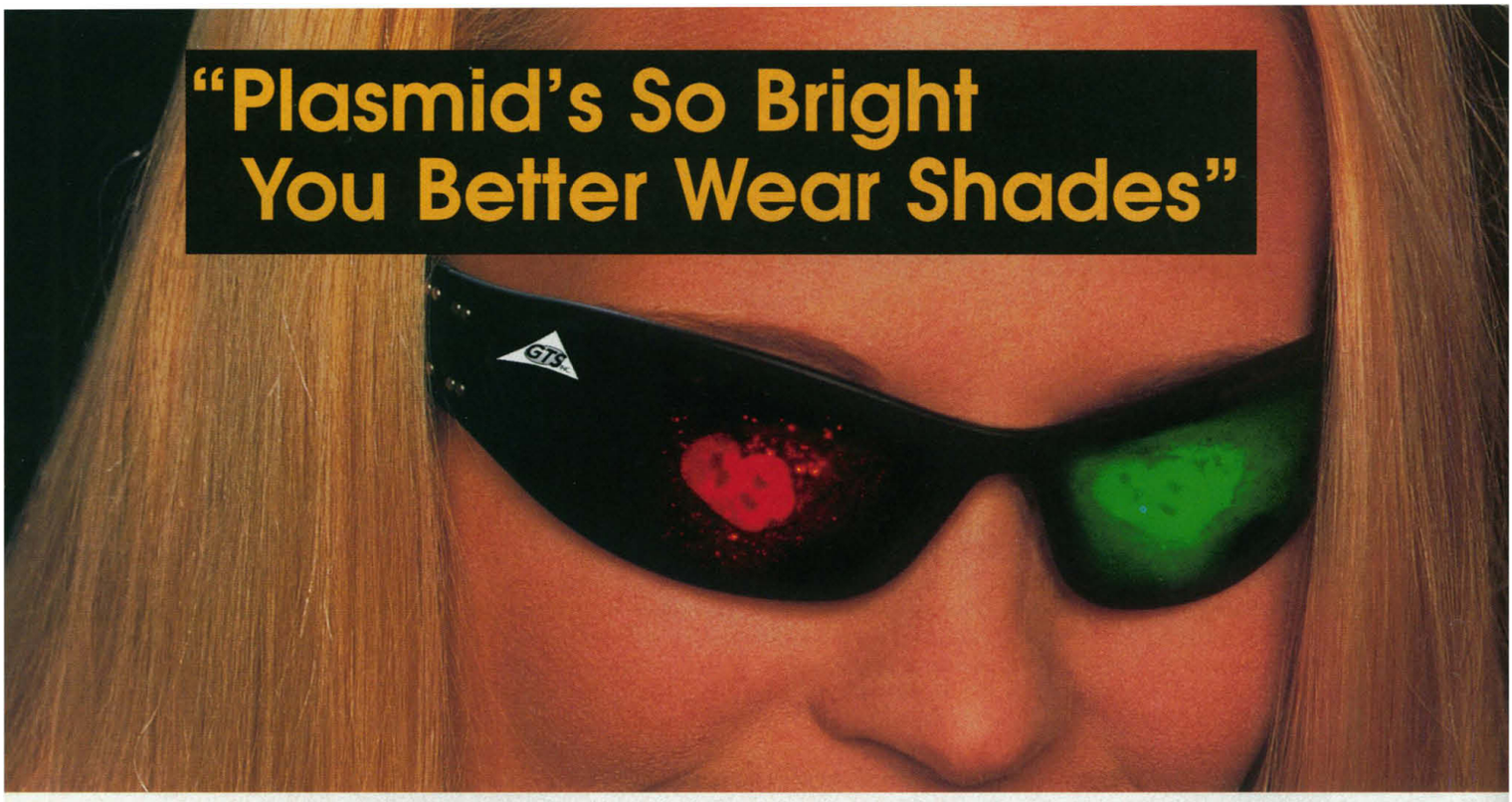
Cloned calves

Fetal fibroblasts have been used by Cibelli *et al.* (p. 1256) as donors for the cloning of three identical transgenic calves. Although this work represents a demonstration that some of the techniques proposed by Wilmut and co-workers for cloning animals from differentiated cells can work in cattle, it also adds new dimensions to the technology. It was not necessary for serum-starved cells to be used, which is helpful given the requirements for rapid cell divisions in developing embryos. Furthermore, it was possible to use cloned cells that were near senescence, which indicates that the process of cloning may reset the biological clock.

Kinase-phosphatase pairs

The importance of tight regulation of cellular signaling pathways is emphasized in two reports that describe association

(Continued on page 1167)



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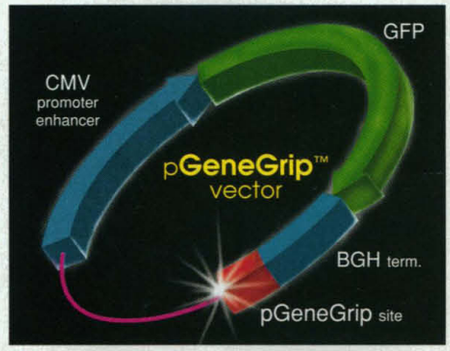

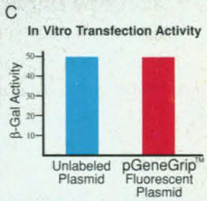

Figures:

A. Fibroblasts transfected with pGeneGrip™ Rhodamine/GFP vector:
1. Rhodamine labeled DNA
2. GFP expression

B. Electrophoresis of pGeneGrip™ Rhodamine/GFP vector fluorescence Lanes: 1. β-gal, 2. GFP, 3. Blank

C. Plasmid expression with and without fluorescent label.

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(Continued from page 1165)

of protein kinases with enzymes capable of inactivating them. Ca^{2+}/calmodulin–dependent kinase IV (CaMKIV) participates in the control of gene expression in T cells. Westphal *et al.* (p. 1258) report that CaMKIV exists in a complex with protein phosphatase 2A (PP2A), an enzyme that dephosphorylates and inactivates it. Inhibition of PP2A activity in cells increased phosphorylation of CaMKIV and increased transcription of a reporter gene regulated in response to CaMKIV-mediated phosphorylation. The authors suggest that such association of PP2A with CaMKIV may help explain why transcription of certain genes that is initiated in a Ca^{2+}-dependent manner in stimulated T cells subsequently decreases in spite of a persistent increase in the intracellular concentration of Ca^{2+}. Camps *et al.* (p. 1262) report association of the mitogen-activated protein (MAP) kinase known as ERK2 with MAP kinase phosphatase-3, an enzyme that specifically dephosphorylates and inactivates ERK2. In this case, binding of ERK2 activates the phosphatase in a manner independent of the kinase activity of ERK2. Lack of such interaction in a mutant *Drosophila* homolog of ERK causes excessive signaling through the MAP kinase signaling pathway. In a commentary, Hafen (p. 1212) discusses the implications of these seemingly unlikely pairings.

■

Complement fragment structure

Before activation, B cells usually need assurance that the antigen that they are binding is foreign. That signal is received through the binding of their complement receptor

type 2 (CR2) to a fragment of complement called C3d, which is deposited on pathogenic microorganisms by the complement cascade. If a B cell antigen receptor binds to a foreign antigen while its CR2 is simultaneously engaged, a strong signal for B cell activation and survival is received. Nagar *et al.* (p. 1277) have determined the x-ray crystal structure of C3d. It is an α–α barrel with two faces, one with a deep acidic pocket that could bind to CR2, and a face on the opposite side where the fragment gets attached to the foreign surface through a thioester bond.

■

Improving the wonder drug?

Aspirin, one of the most widely used drugs in the world, works by acetylating and irreversibly inactivating the cyclooxygenase (COX) enzymes. Aspirin's therapeutic effects, such as acting as an anti-inflammatory, are mediated by its action on COX-2, and its adverse effects, such as ulcers, are mediated by its action on COX-1. Kalgutkar *et al.* (p. 1268, see the news story by Pennisi, p. 1191) have designed aspirin-like compounds that preferentially acetylate and inactivate COX-2 both in vitro and in cell culture assays. This design strategy may lead to the development of aspirin-like drugs that are free of side effects.

Lung allergies and γδ T cells

Allergic asthma is initiated with the inhalation of an allergen. In a mouse model system in which mice are allergic to the protein ovalbumin, the role of γδ T cells was tested. By comparing mice genetically deficient in γδ T cells to wild-type mice, Zuany-Amorim *et al.* (p. 1265) show that these cells supply the cytokine interleukin-4 (IL-4) during the sensitization process. IL-4 is the component critical for setting up a T helper type 2 (T_H2) response in the lung, which becomes infiltrated by inflammatory cells that produce cytokines and secrete immunoglobulin E (IgE), one of the hallmarks of the response. The identity of the cells that provide the IL-4 to push any immune response in the direction of T_H2 has been elusive; at least in this system, it appears that the γδ T cell, which previously had few definitive responsibilities, is the culprit.

■

Wnt their separate ways

The *Wnt3a* and *Wnt7a* genes are classified in the same Wnt family subgroup; however, the two participate in distinct developmental roles. *Wnt7a* is involved in dorsoventral patterning of the limb, and *Wnt3a* functions in the chick apical ectodermal ridge for limb development. How do these highly related *Wnt* signals play such distinct roles in the same tissue? Kengaku *et al.* (p. 1274) report that the two factors are involved in different signaling pathways, with WNT7A being β–catenin/LEF1-independent and WNT3A being β–catenin/LEF1-dependent.

Technical Comment Summaries

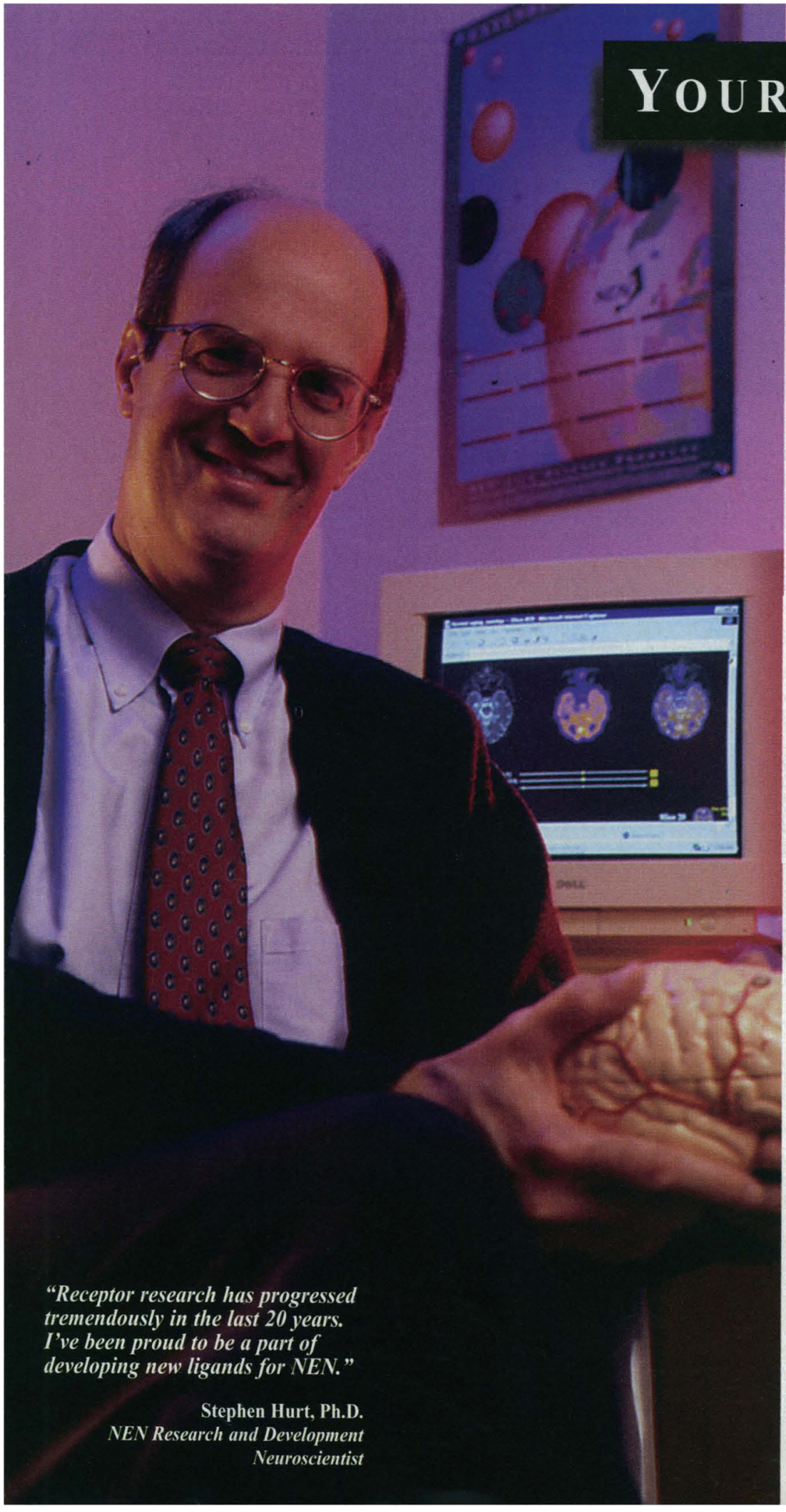
Second Family of Histone Deacetylases

A. Lusser *et al.* identified (Reports, 4 July, p. 88) "a maize complementary DNA encoding the chromatin-bound deacetylase HD2." They stated that the acidic nucleolar phosphoprotein HD2 "might regulate ribosomal chromatin structure and function."

L. Aravind and E. V. Koonin state that sequence analysis detected similarity between HD2 and "insect proteins identified as FKBP peptidyl-prolyl cis-trans isomerases" (PPIases) and also "a trypanosomal RNA-binding protein." Further searches with these sequences "resulted in the characterization of a novel [histone deacetylase] family, which includes proteins from plants, yeast, and two parasitic apicomplexans." They state that experimental characterization of this novel family of histone deacetylases "might open new avenues of research in ... the regulation of eukaryotic gene expression."

In response, M. Dangl *et al.* (Lusser and co-workers) note that "complex formation of nucleolar HD2 with other regulatory proteins, although likely to occur, has not yet been demonstrated." They "favor the idea that HD2-type histone deacetylases and certain PPIases developed from a common ancestor enzyme." They conclude that "the fact that histone deacetylases belong to structurally distinct and rather divergent protein families underlines the importance of histone deacetylation for different cellular functions."

The full text of these comments and figures can be seen at www.sciencemag.org/cgi/content/full/280/5367/1167a



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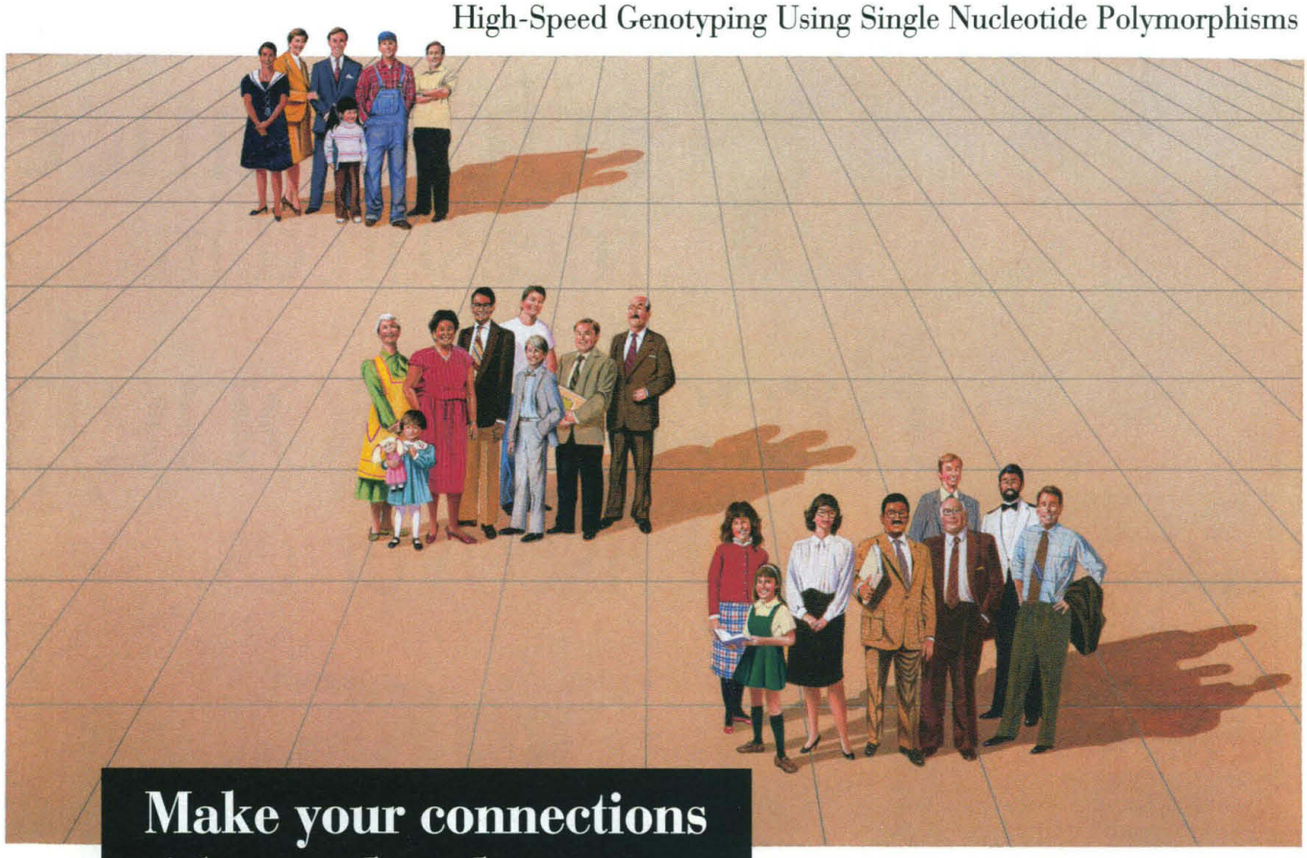

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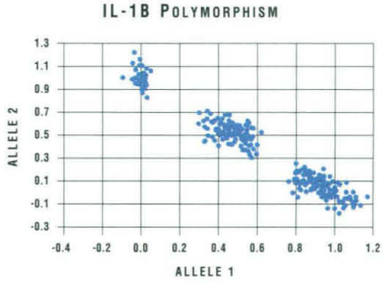

Genotyping of the single nucleotide IL-1B polymorphism: Genotyping of the two alleles of the human Interleukin-1 beta (IL-1B) promoter polymorphism at position −511 was performed using the fluorogenic 5′ nuclease assay. The graph shows genotyping results for 454 individuals. (Results courtesy of Franco di Giovine and Adeel Chaudhray, University of Sheffield, UK.)

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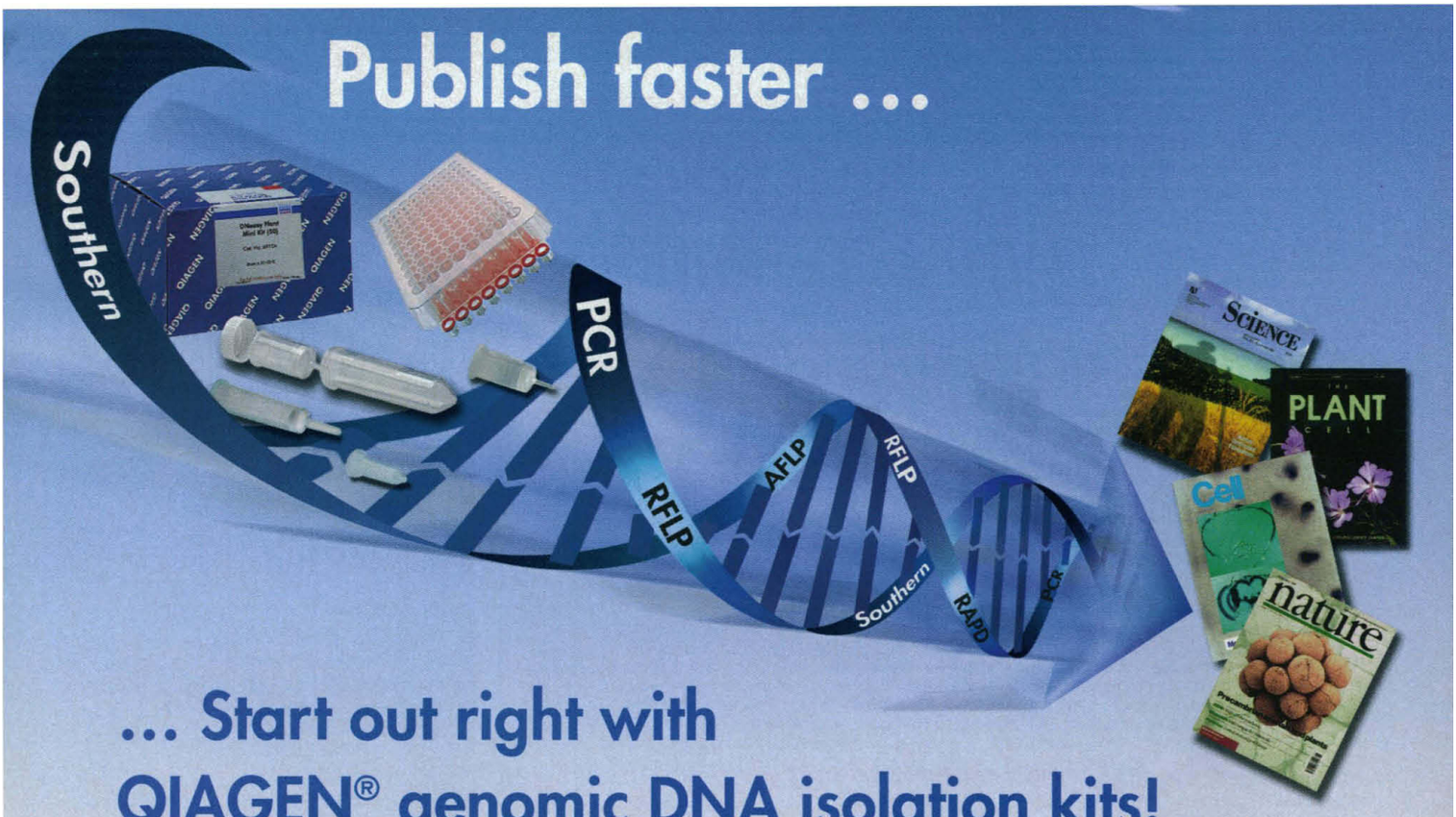

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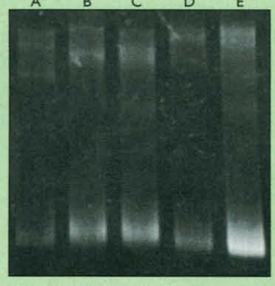
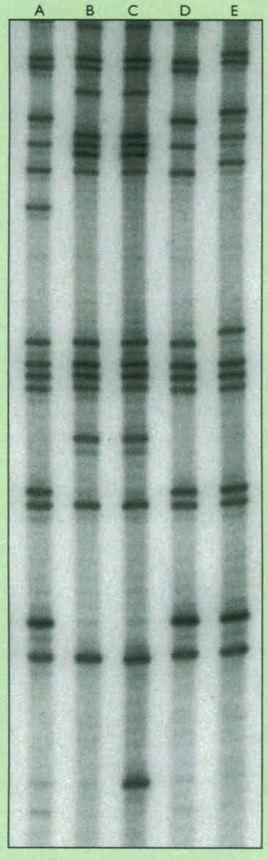


SSCP Method: 1. PCR. 2. Denature 10-15 min. 3. Quick reannealing. 4. Optimize gel conditions. 5. Analyze samples on optimized gels. 6. Sequence to confirm.

BESS

A B C D E



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[1]Hawkins, G. A. and Hoffman, L. M.(1997) *Nature BioTechnology* **15, 803**.

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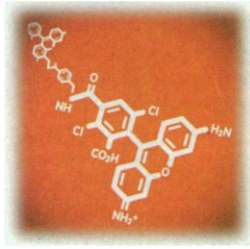

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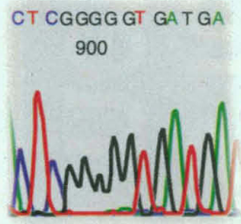

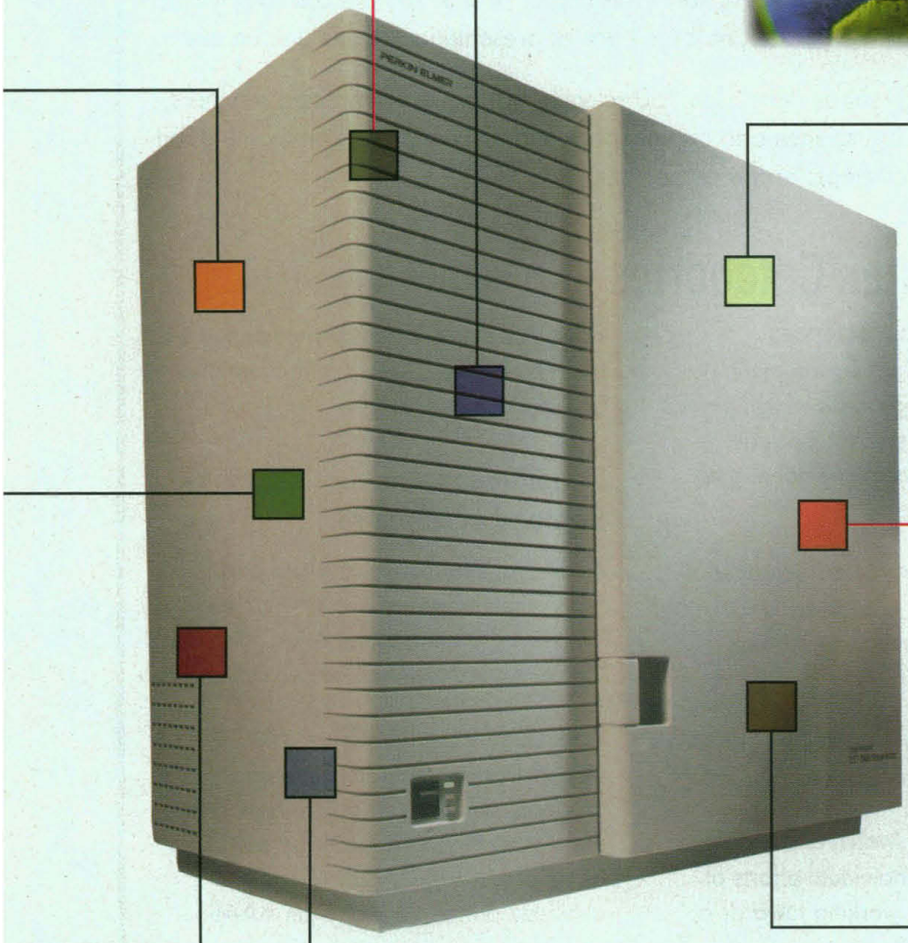

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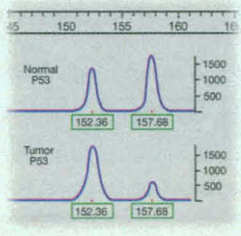

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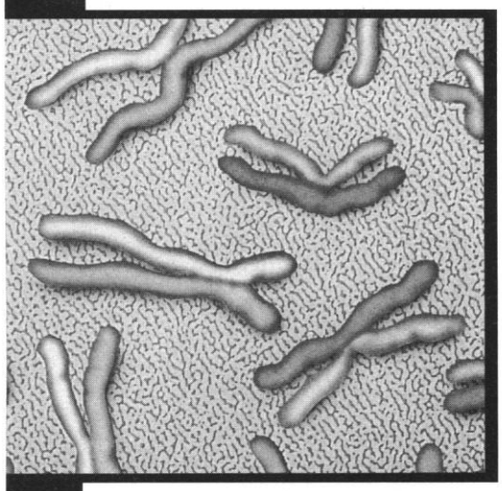

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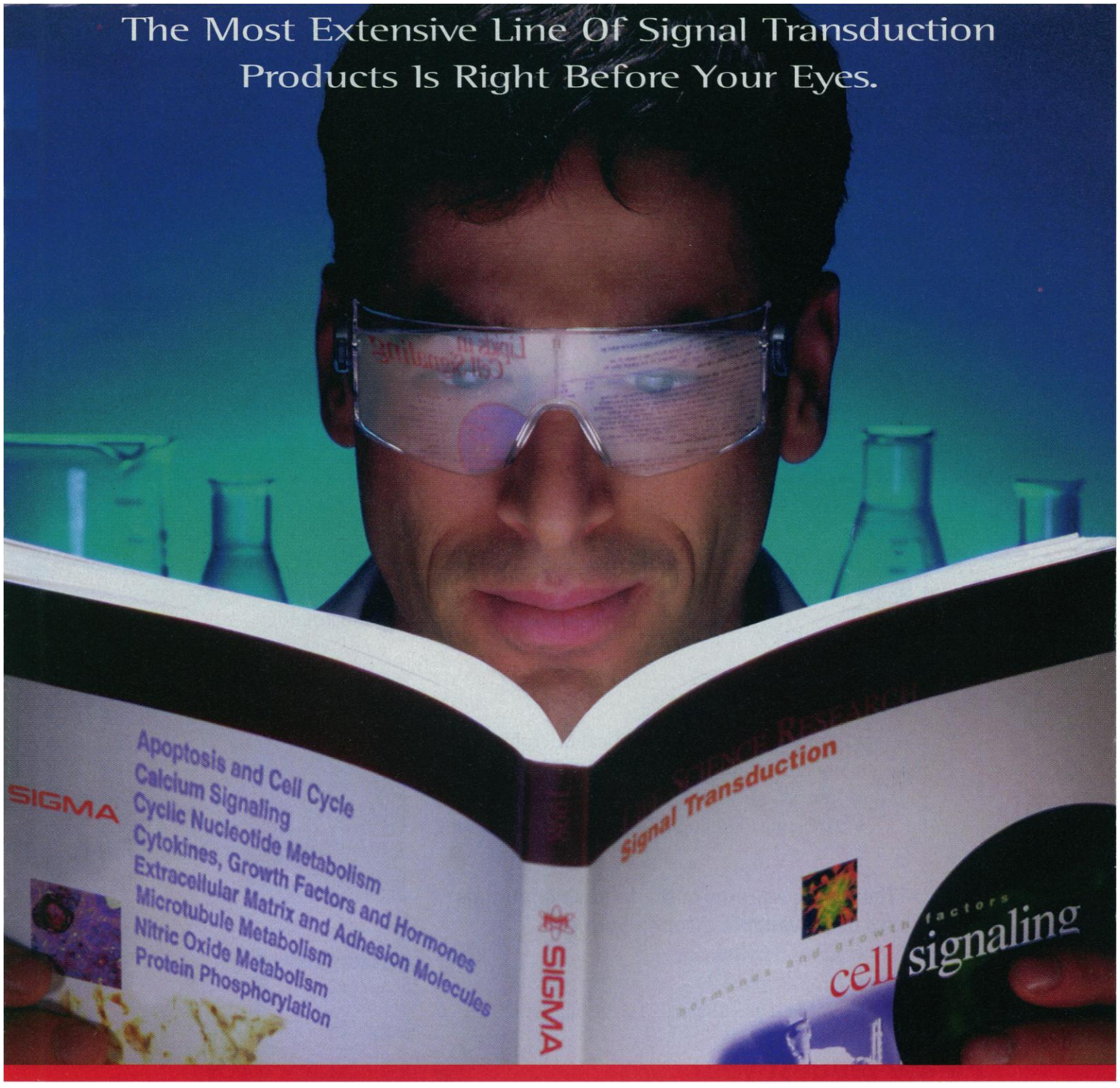

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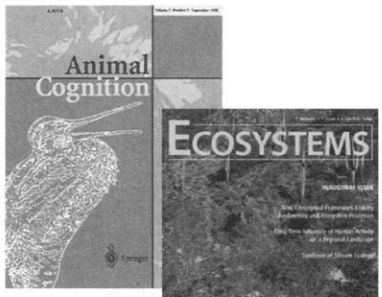

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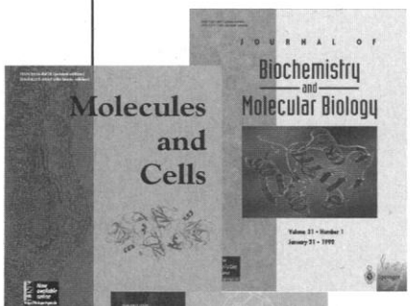

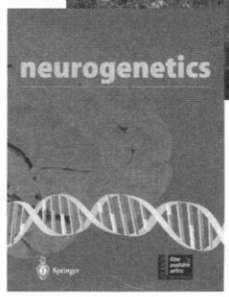

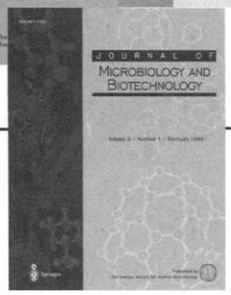

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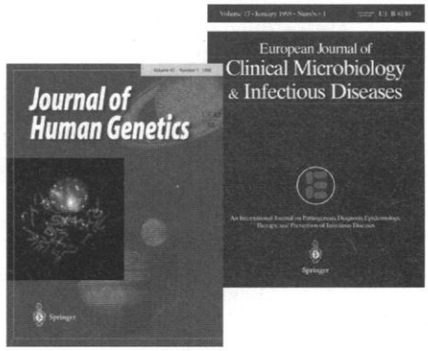

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