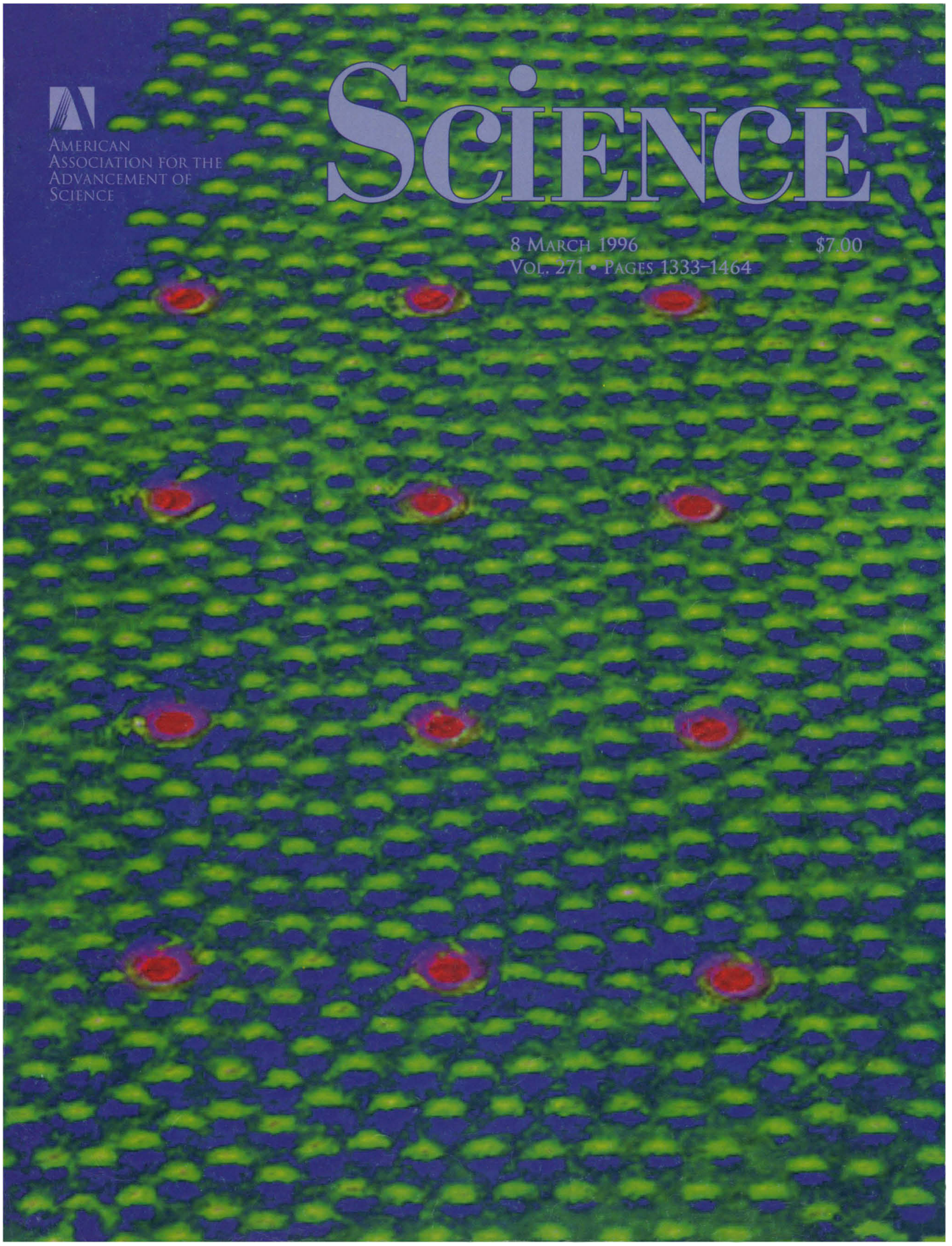

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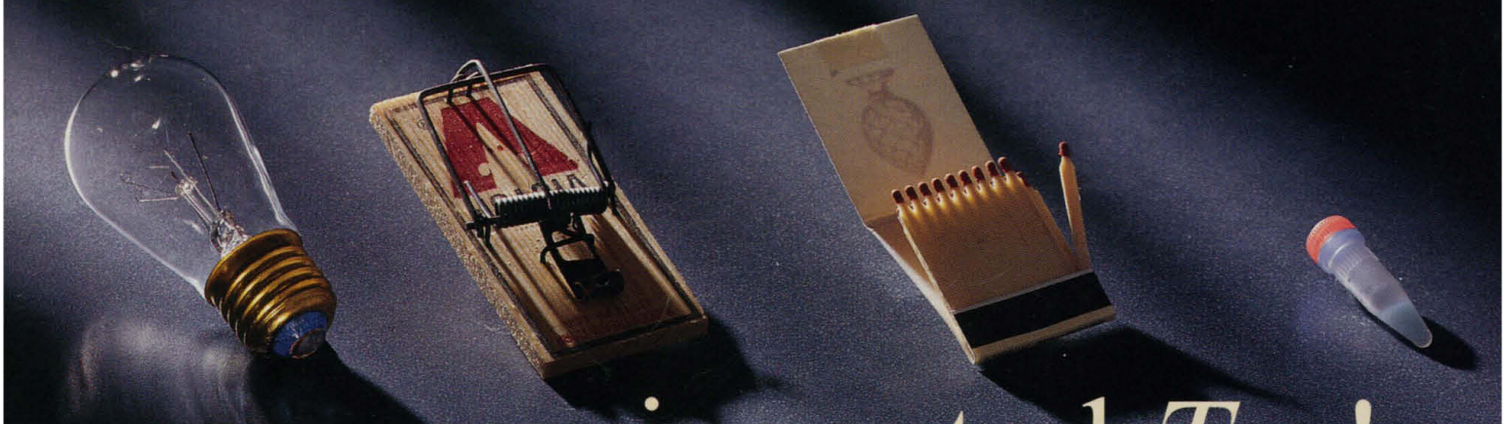
8 MARCH 1996 $7.00
VOL. 271 • PAGES 1333–1464

One of these had room for improvement...



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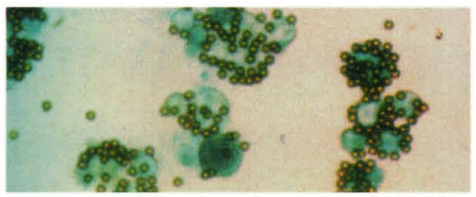

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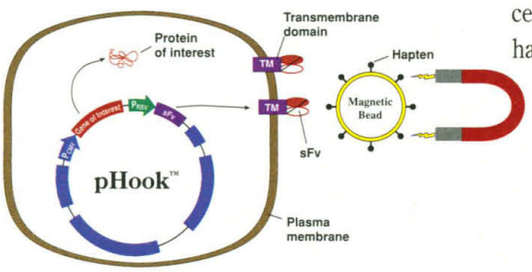

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The prizes will be presented in Stockholm, Sweden, during December 1996.

Full details and the required entry form can be requested from the administrator, at the address below, or via *Science's* homepage (http://www.aaas.org/science/prize.htm).

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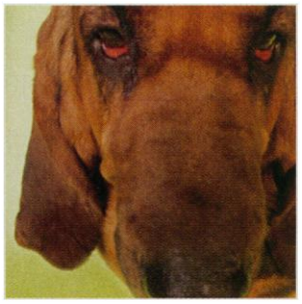

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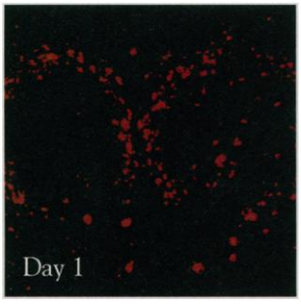

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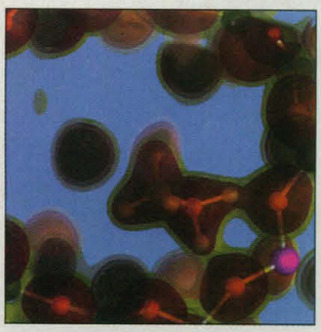
Reaching for complex disease genes



1395
First steps toward gasoline

NEWS & COMMENT

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ARTICLES

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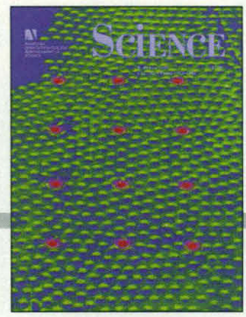
COVER



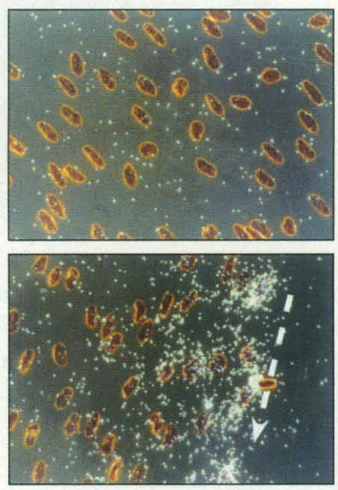
Interaction of magnetic vortices (green spots) with pinning centers (red holes, 3.3 micrometers apart) in a superconductor observed in real time by Lorentz microscopy with a field emission electron microscope. The vortex lattice is disturbed at the pinning centers to form domain structures. "Vortex rivers" flow intermittently like avalanches along the domain boundary. See page 1393 and the Perspective on page 1373. [Image: T. Matsuda, K. Harada, H. Kasai, O. Kamimura, A. Tonomura]

RESEARCH ARTICLE

REPORTS

TECHNICAL COMMENTS

1427
Aortic injury-induced Egr-1



◩ Indicates accompanying feature

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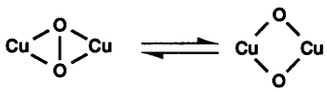
edited by PHIL SZUROMI

A planetary sampler

The discovery of martian and lunar meteorites has caused modelers to reassess the transport efficiencies of impact ejecta from terrestrial planets and the moon to the Earth. Although previous Monte Carlo simulations have shown that lunar meteors could easily reach the Earth, martian meteors seemed to have taken a longer and more torturous path than the cosmic-ray exposure ages of the martian meteorites suggested. Gladman *et al.* (p. 1387) numerically integrated the orbital paths of escaping ejecta in their simulations and show that not only can martian meteors reach the Earth more quickly, but the possibility exists that ejecta can be captured from Mercury or that Earth's ejecta can be recaptured.

Oxygen activation

Numerous biochemical pathways, including those involved in photosynthesis and oxidation, require metalloenzymes that either form or break the bond between oxygen atoms. Halfen *et al.* (p. 1397) have



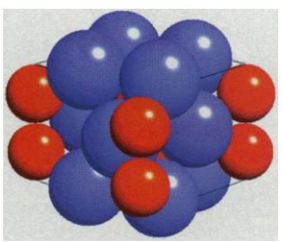
synthetized and characterized copper complexes that reversibly break or form an O–O bond. The equilibrium between these states can be shifted by changing the solvent. Kinetic studies of such models may reveal important details of how enzymes perform this key step.

Methane-hydrogen phases

What do you get if you put methane and hydrogen together? Under ambient conditions, the answer is nothing but a mixture of simple gases. Somayazulu *et al.* (p. 1400) squeezed mixtures of these gases under pressures between 1 to 8 GPa in a diamond-anvil cell, however, and characterized four solid molecular compounds using x-ray diffraction and Raman spectroscopy. The unexpected formation of these solids should provide an interesting avenue of research in fundamental chemistry and material sciences.

Out of Africa: Nuclear DNA evidence

Mitochrondrial DNA evidence has indicated that modern human origins can be traced back through maternal lineages to a single human ancestor who lived in Africa 100,000 to 300,000 years ago. In contrast, the multiregional origin model suggests that several regional populations emerged from *Homo erectus* and evolved in parallel. Tishkoff *et al.* (p. 1380; see the news story by Fischman, p. 1364) have now analyzed two markers [a short tandem repeat polymorphism (STRP) and an Alu deletion] at the CD4 gene locus from more than 1600 individuals from 42 different populations. In Northeast African and non-African populations, the Alu repeat was almost always associated with one STRP allele but was associated with several alleles in sub-Saharan populations. Their analysis suggests emergence from Africa took place approximately 100,000 years ago or even earlier.



Water, CO_2, and climate

Model predictions of the response of the biosphere to an increase in atmospheric CO_2 levels and the resulting effect on temperatures has been uncertain because the effects of both CO_2 uptake and evapotranspiration need to be considered. Sellers *et al.* (p. 1402) present results from simulations with a coupled biosphere-atmosphere model which suggest that the biosphere would act to increase temperatures further because evapotranspiration would be reduced in the tropics.

Copper and Alzheimer's disease

A characteristic symptom of Alzheimer's disease is the deposition of plaques of protein in the brain composed of β-amyloid. β-Amyloid is a breakdown product of a normal brain protein of unknown function, the amyloid precursor protein (APP). Multhaup *et al.* (p. 1406) now show that APP can reduce copper(II) ions to form a protein-copper(I) complex. The accumulation of APP in the neurons of Alzheimer's disease patients might disrupt brain copper metabolism and, together with other oxidative reactions in the brain, produce free radicals that damage the neurons further.

GAA triplet repeats

In certain diseases, regions of repeated nucleotide triplets (either CGC or CAG) that normally contain 20 to 30 repeats expand unstably to hundreds or thousands of repeats and interfere with normal gene expression. These diseases have shown dominant inheritance and exhibit genetic anticipation (the number of repeats increases with each generation, and the severity of symptoms increases with succeeding generations). Friedreich's ataxia (FRDA), an autosomal recessive degenerative disease of the peripheral nervous system and heart that often strikes in adolescence, would not be a strong triplet repeat candidate, but Campuzano *et al.* (p. 1423; see the Perspective by Warren, p. 1374) have identified an expanded GAA repeat associated with the X25 gene. Most of the FRDA patients had an unstable GAA repeat in the first intron of the gene that reduced the RNA expression of its product, frataxin.

Injury response

After blood vessels are injured, a number of growth factor genes are induced that help direct tissue repair, but the molecular signals that initiate this process have yet to be identified. Khachigian *et al.* (p. 1427) show that after injury to the rat aorta, there is a marked increase in the expression of the transcription factor early-growth-response gene product (Egr-1) at the wound edge. They find that Egr-1 interacts with the proximal promoter for the platelet-derived growth factor B-chain (PDGF-B) gene and displaces the transcription factor Sp1, whose site overlaps that for Egr-1. Putative recognition elements for Egr-1 have been identified for other genes that are activated upon injury, which suggests that Egr-1 may be involved generally in the activation of pathophysiological factors after arterial injury.

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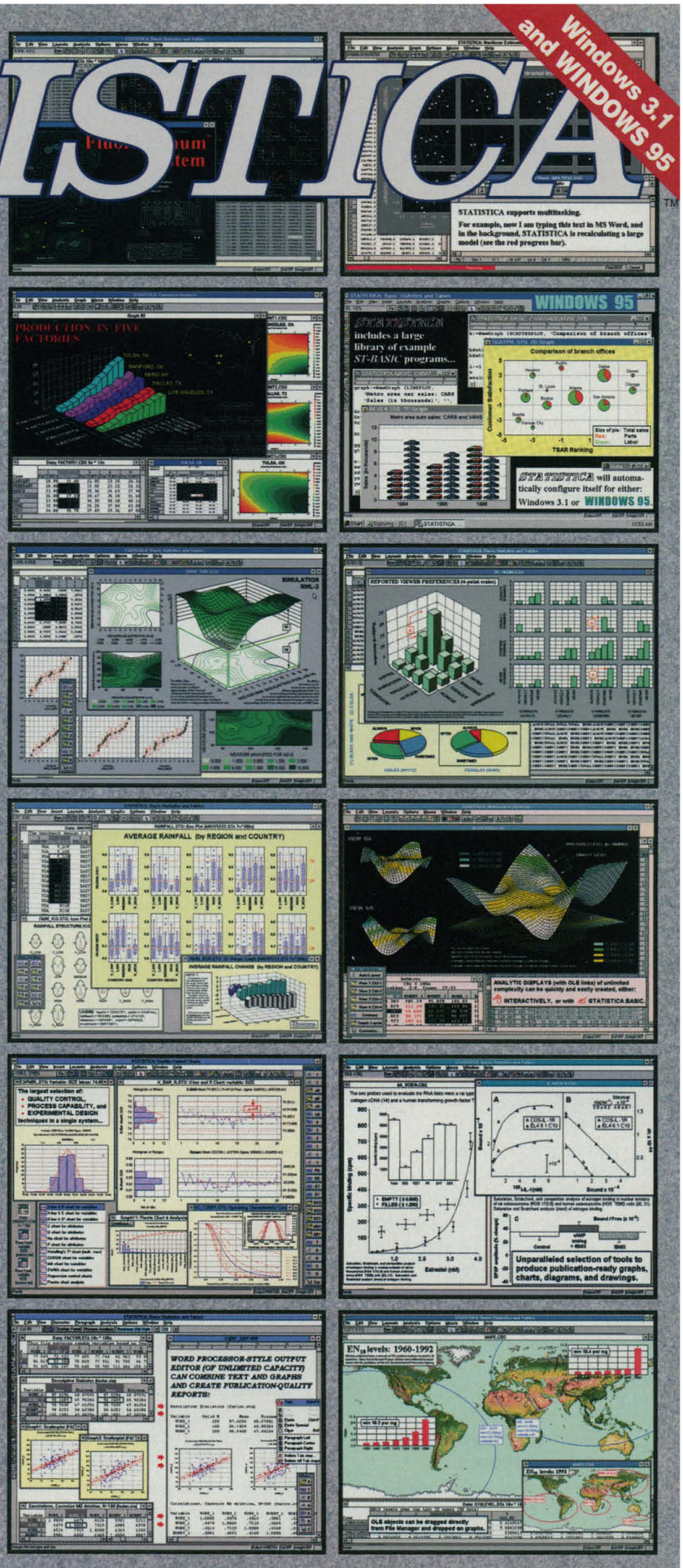

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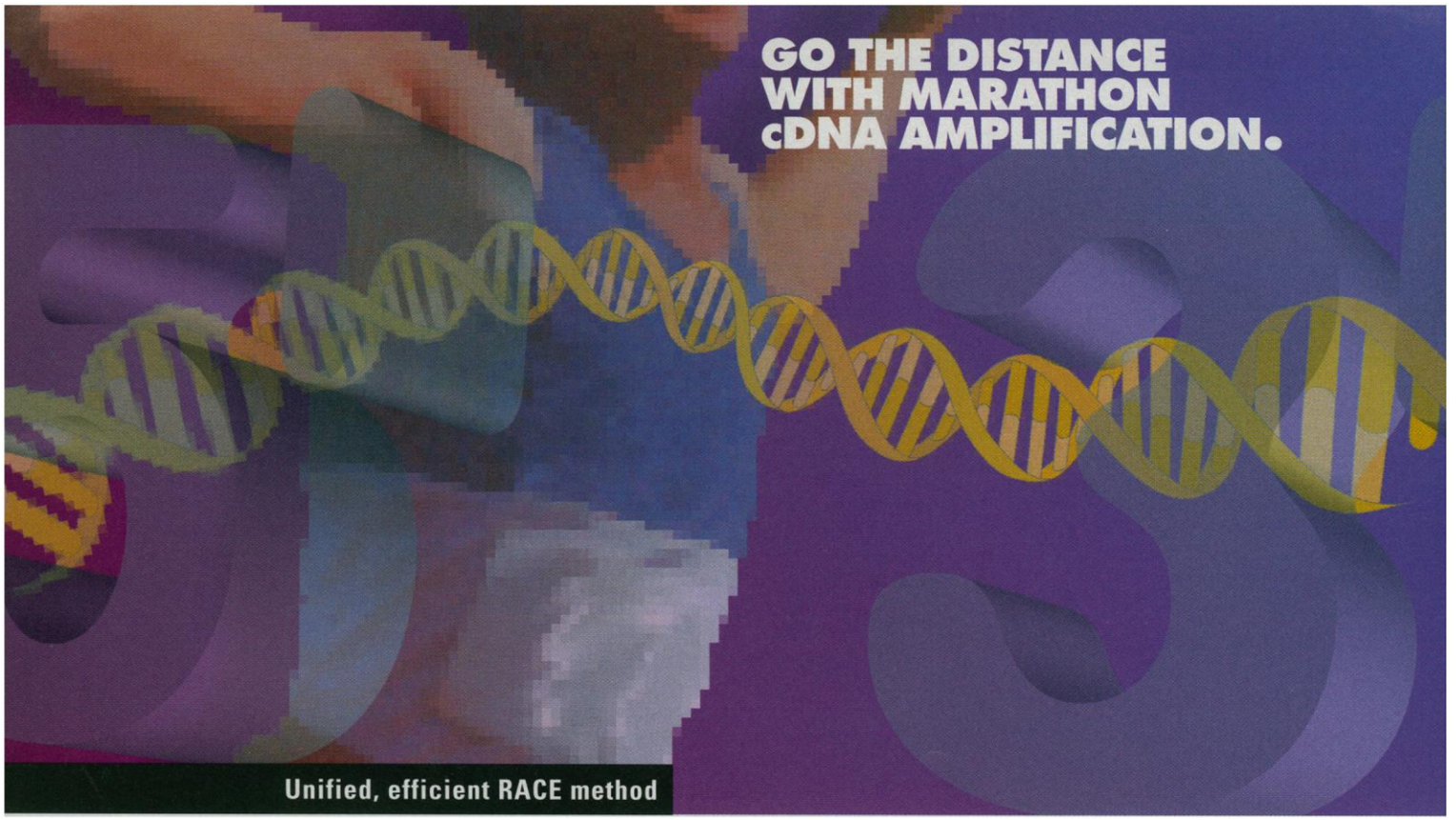

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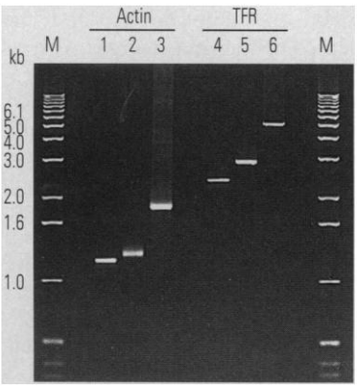

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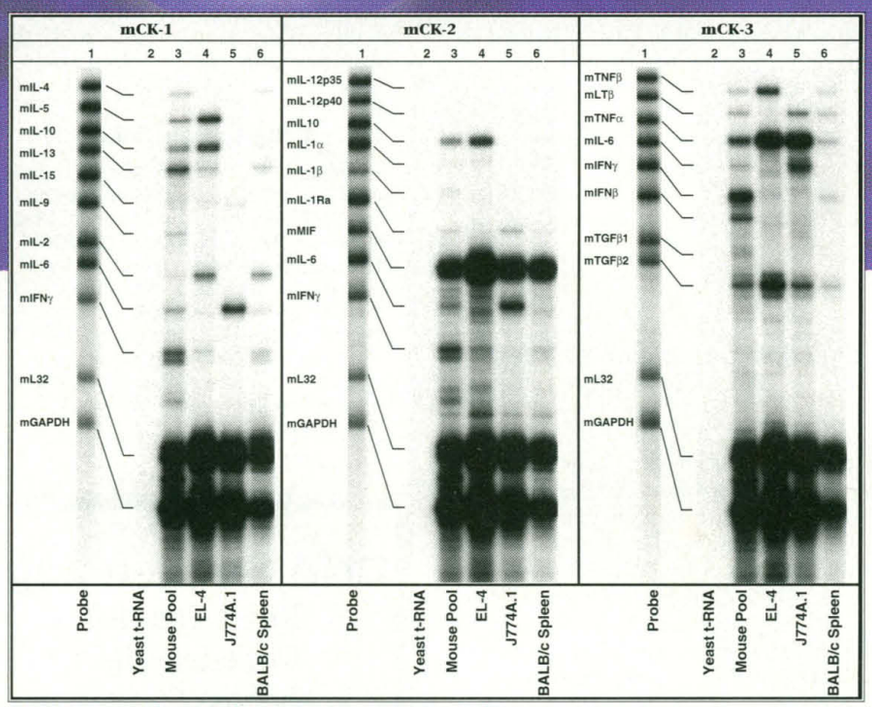

Multi-Probe Analysis of Cytokine mRNA in Mouse RNA Preparations.
Samples of total RNA from various sources were analyzed for distinct mRNA species by using PharMingen's RiboQuant™ Multi-Probe Ribonuclease Protection Assay System with the mCK-1, mCK-2, and mCK-3 probe template sets. The autoradiogram from this analysis shows the mCK-1, mCK-2, and mCK-3 probe sets not treated with RNases (Lane 1). Also shown are the corresponding RNase-protected probes following hybridization with: Lane 2: Yeast tRNA (5 µg). Lane 3: Pooled RNA (5 µg) from a variety of mouse cell types. Lane 4: RNA (5 µg) from mouse EL-4 thymoma cells cultured 4 h with PMA and ionomycin. Lane 5: RNA (5 µg) from mouse J774A.1 cells (macrophage cell line) cultured 4 h with LPS. Lane 6: RNA (5 µg) from mononuclear BALB/c mouse spleen cells stimulated 48 h with plate-bound 145-2C11 mAb (anti-mouse CD3-ε, **cat. # 01080D**). Note that each probe band (Lane 1) migrates slower than its protected band (Lanes 2-6); this is due to flanking sequences in the probe that are not protected by mRNA.

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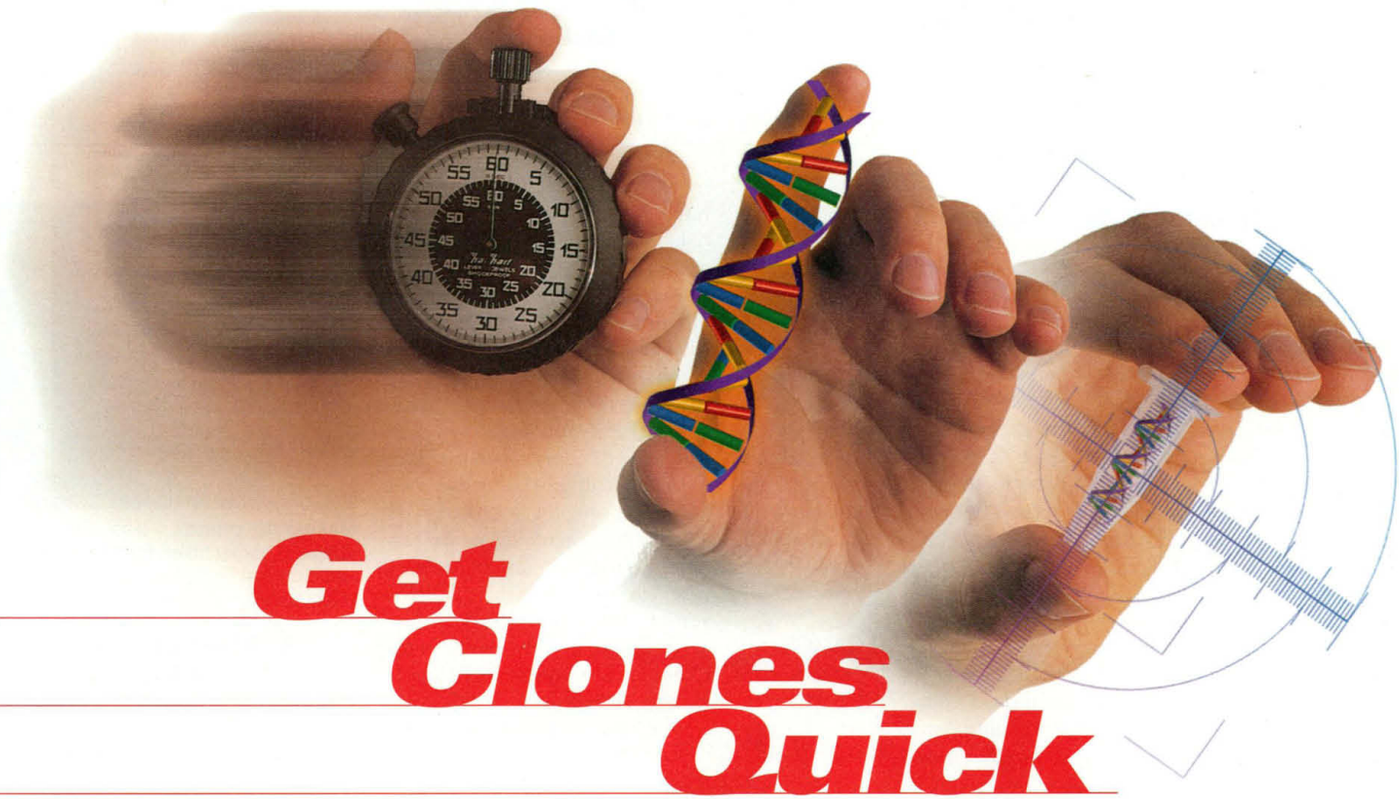

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