22 March 2002

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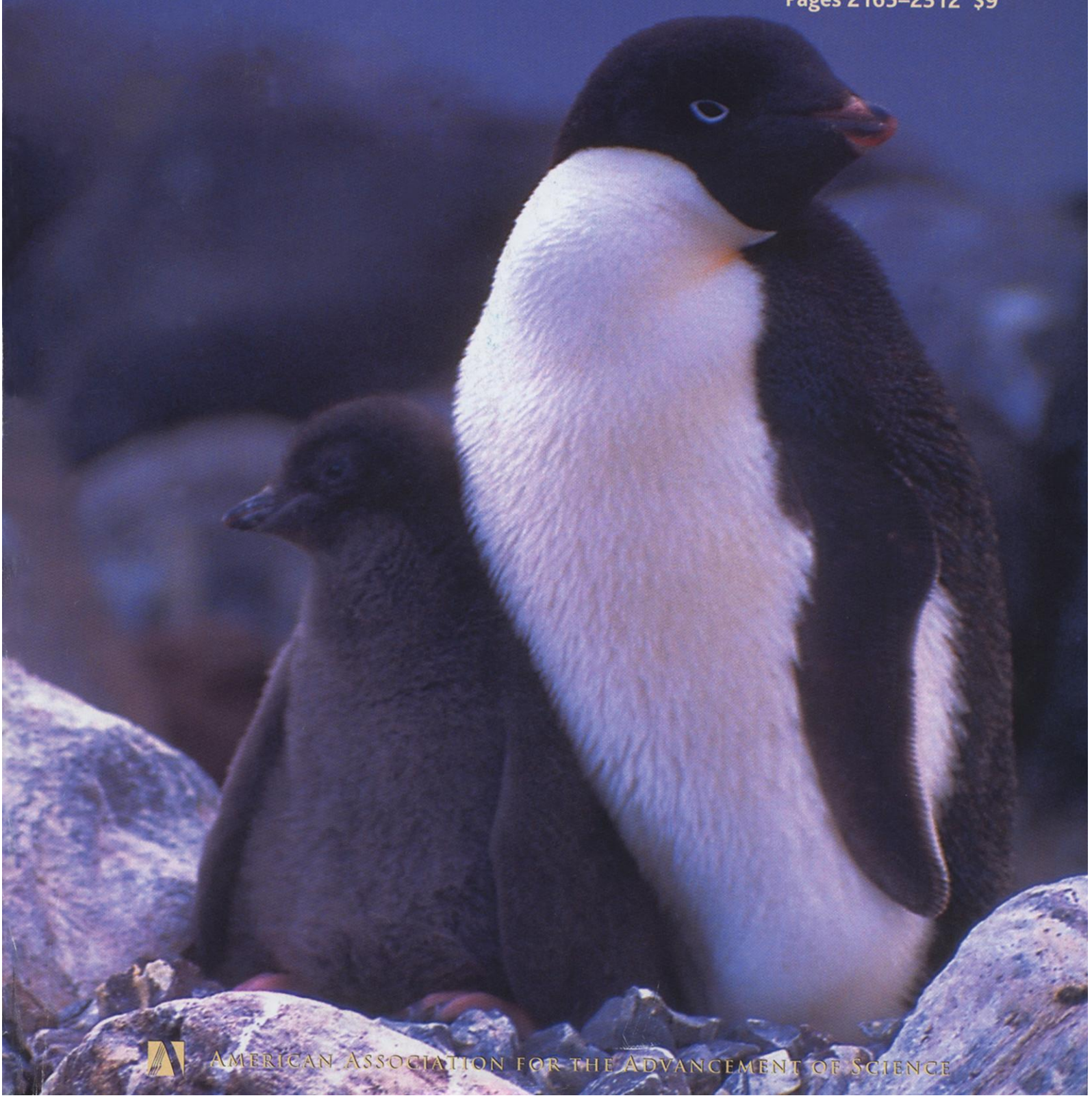
Pages 2165–2312 $9



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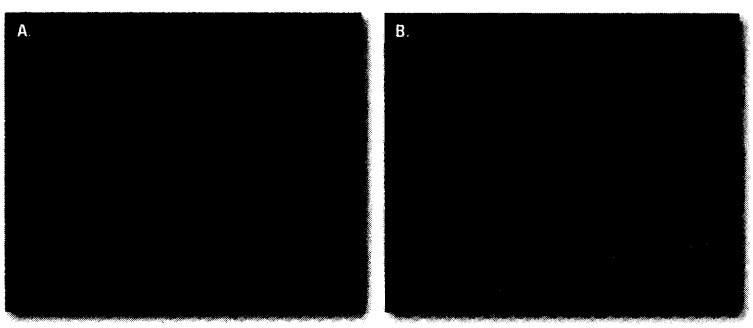

RNAi in *C. elegans*
Fluorescence microscopy of a *C. elegans* adult female with a transgenic GFP reporter gene (green) highly expressed in the pharynx (A). Double-stranded RNA corresponding to the GFP coding region was produced using the HiScribe RNAi Transcription Kit and injected into the syncytial gonad of transgenic adult worms. RNAi is demonstrated by the reduction of GFP expression in the progeny (B).

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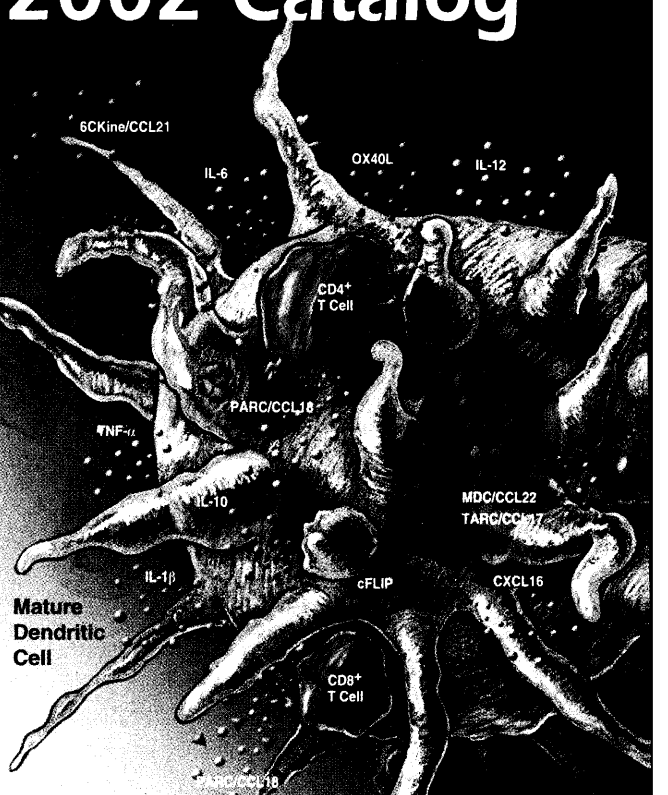

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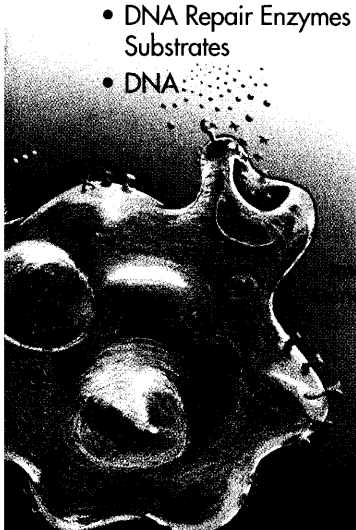

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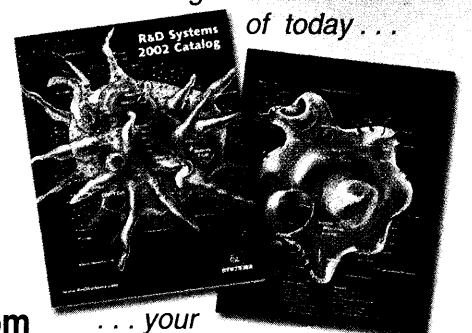

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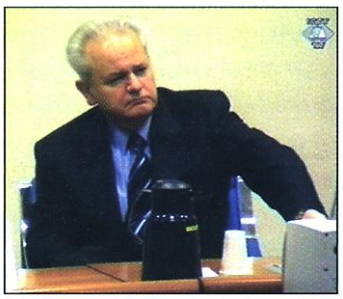

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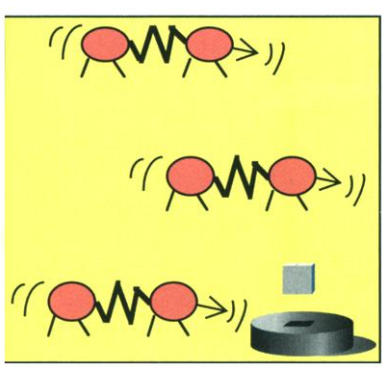
Science and the Milosevic trial

SCIENCE'S COMPASS



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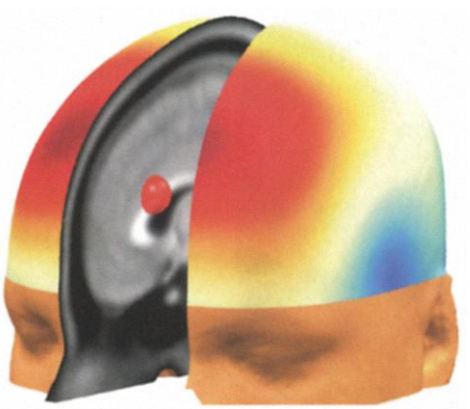
A new paradigm for superconductivity

RESEARCH

COVER 2270

Adélie penguins nest in ice-free areas of Antarctica during summer. Males and females both help to raise one or two chicks. Underlying colonies of these birds are large numbers of ancient bones that contain some of the best preserved ancient DNA yet discovered. [Photo: P. Ritchie]



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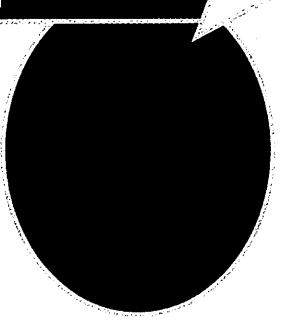
It's not how you play the game...

New on *Science* Express A long-term KO with RNAi



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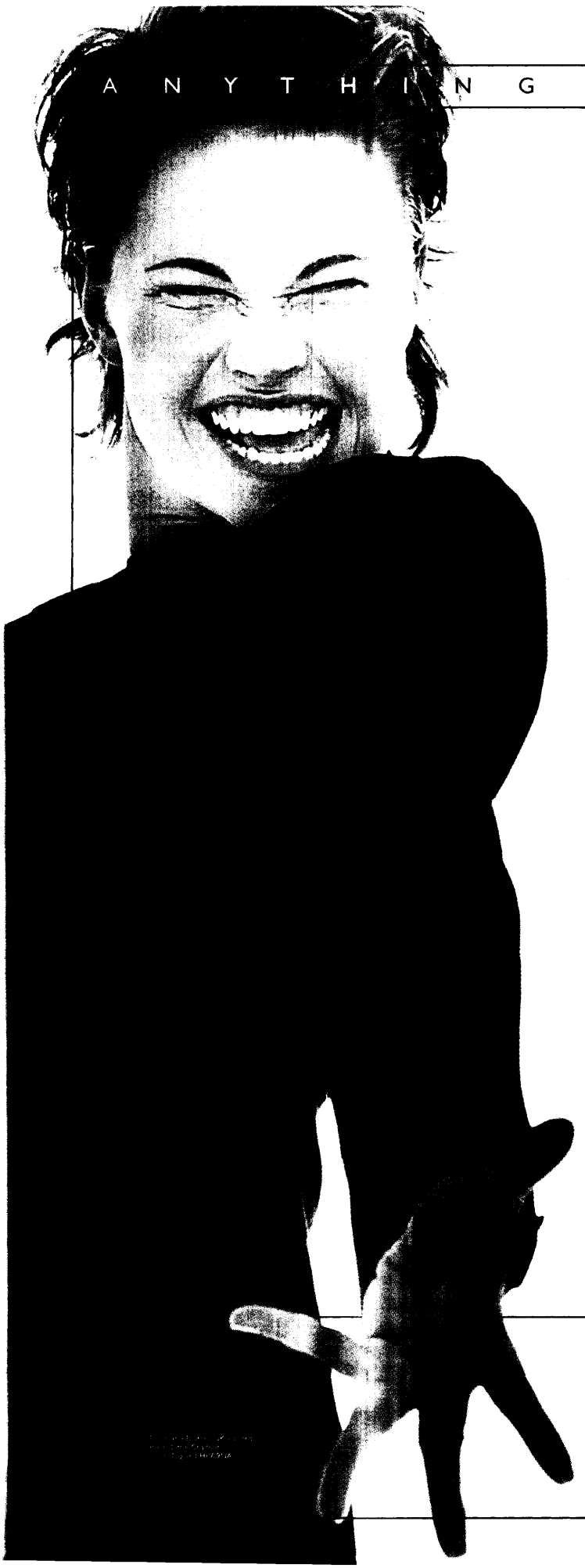

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Ordering in a Fluid Inert Gas Confined by Flat Surfaces S. E. Donnelly *et al.*

PERSPECTIVE: **The Elusive Liquid-Solid Interface** E. Johnson

High-resolution transmission electron microscopy of liquid xenon inclusions in alumina reveals layered ordering at the interface between the liquid and the solid.

Functional Annotation of a Full-Length *Arabidopsis* cDNA Collection M. Seki *et al.*

A resource useful to plant researchers is made available with the announcement of a library representing transcribed genes of *Arabidopsis*.

A System for Stable Expression of Short Interfering RNAs in Mammalian Cells T. R. Brummelkamp, R. Bernards, R. Agami

A new vector directing the synthesis and stable expression of small interfering RNAs in mammalian cells causes specific and persistent suppression of gene expression.

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career resources for scientists

Singapore: Biotechnology Start-Ups T. Yugarani

We highlight the current status of biotechnology start-ups in Singapore, focusing on some of the challenges they face.

Europe: EU Enlargement—New Opportunities and New Challenges E. von Ruschkowski

Even as the EU enlargement process improves funding schemes for young scientists, the accession states fear that it might also subject them to further brain drain.

UK: A Tale of Two Fellowships C. Pelizon

Your postdoc period can be rewarding and well paid, especially if you take advantage of some of the great mobility fellowships available in Europe.

US: Grad School Adventures, Chapter 3—The Craziness of Comps M. P. DeWhyse

Whatever they are called, comprehensive exams have a way of bringing out the best and the worst in people.

US: MiSciNet Shero J. Bargonetti-Chavarria

This week's "shero" focuses on her career as a molecular biologist and on the racism she has encountered among the academic and African-American communities.

Canada: Japan—A Great Place for Physics Postdocs L. McKarney

A joint NSERC/JSPS fellowship has allowed many Canadian physicists to conduct their research in Japan—and to learn more about the Japanese people and culture.

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Deciphering the Gene Expression Profile of Long-Lived Snell Mice K. G. Becker

A balanced approach helps to determine whether gene expression changes are authentic or artifactual.

Youth Beats Experience M. Leslie

Older parents hatch weaker offspring.

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Perspective: A Herd of Cats, but No Talking Dogs M. Edidin and J. M. McCaffery

A review and commentary on the book *Methods in Cellular Imaging*.

Protocol: Visualizing Cellular Phosphoinositide Pools with GFP-Fused Protein Modules T. Balla and P. Várnai

Methods for monitoring inositol lipids using lipid-binding fluorescent proteins.

Protocol: Confocal Imaging of Subcellular Ca^{2+} Concentrations Using a Dual-Excitation Ratiometric Indicator Based on Green Fluorescent Protein S. Shimozono *et al.*

Detailed methods for imaging changes in calcium concentration.

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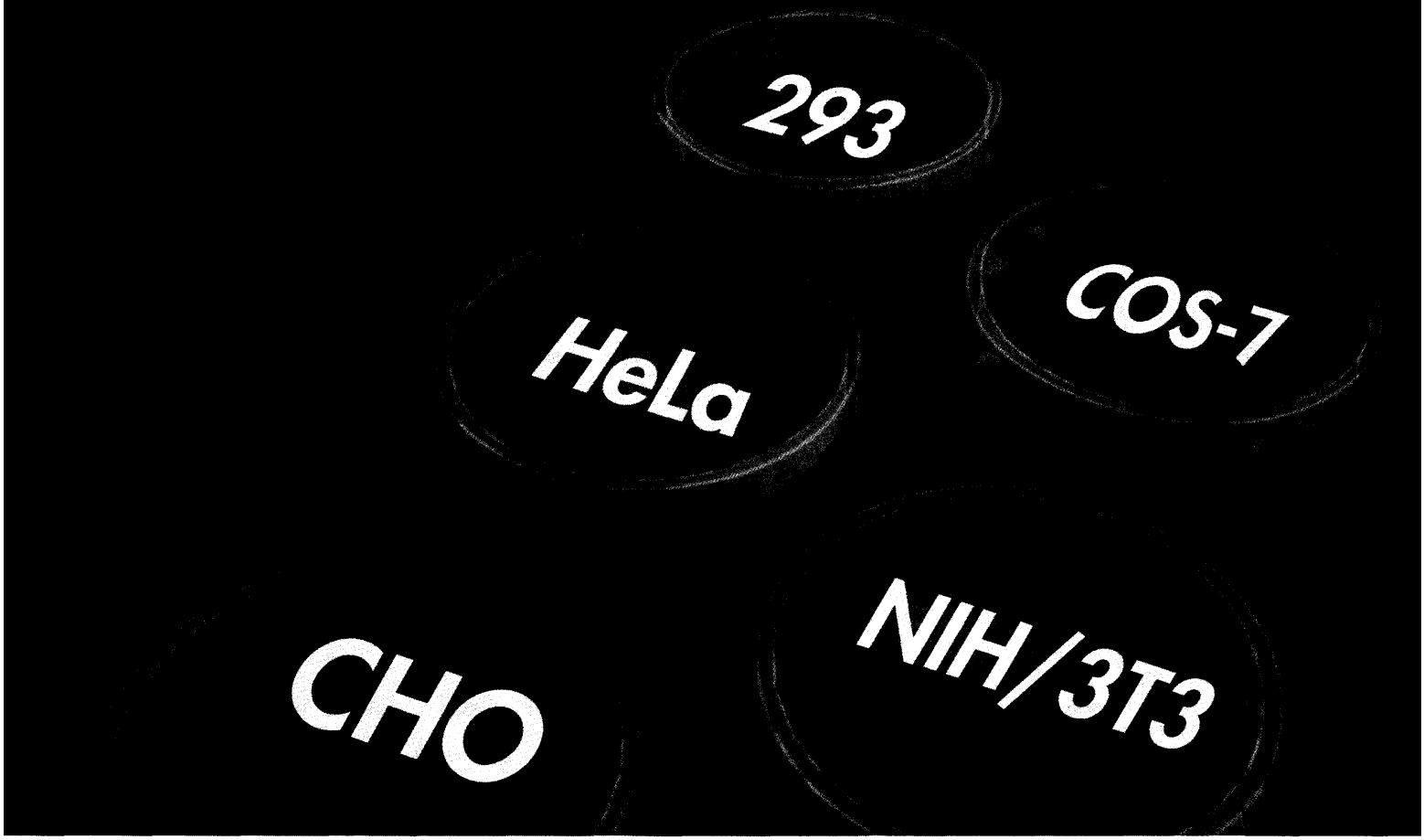

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THIS WEEK IN Science

edited by Phil Szuromi

The Changing Colors of Cuprates

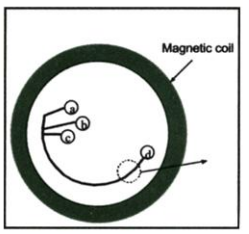
Figuring out just what the "glue" is that binds the electrons into pairs in high temperature superconducting cuprates has been a goal since their appearance nearly 15 years ago. Molegraaf *et al.* (p. 2234; see the Perspective by Hirsch) report on sensitive optical measurements of the in-plane conductivity of the cuprate superconductor BSCCO and reveal that a transfer of the spectral weight from higher energy to lower energy occurs as the temperature is decreased and the sample becomes superconducting. In contrast to conventional superconductors where the pairing mechanism involves a reduction in the potential energy mediated by the electron-phonon interaction, the "glue" in the cuprate case appears to arise from a reduction in the kinetic energy.

2250 Ringing True

Measurements of tree ring widths provide robust records of growing season temperature variations occurring from year to year, but have been criticized as being unreliable over periods of centuries. This concern arises from the fact that some trees experience a trend toward thinner rings with age, an effect which is difficult to distinguish from a cooling trend. Esper *et al.* (p. 2250; see the Perspective by Briffa and Osborn) demonstrate that multicentennial climate variability can be recovered from long tree-ring chronologies if the proper analysis methods are used. The tree-ring record for the past 1200 years from sites distributed across the Northern Hemisphere extratropics was related to Northern Hemisphere temperatures on multidecadal and longer time scales, and it shows strong evidence for a large-scale "Medieval Warm Period" and Little Ice Age in the extratropics, features not readily apparent in some other tree-ring–based chronologies.

And in Brevia ...

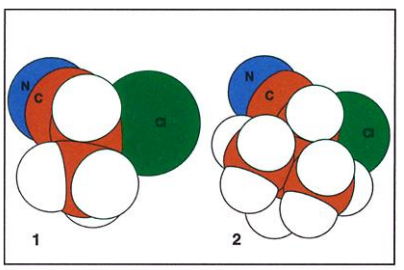
In a magnetic field, a suspension of superparamagnetic particles self-organizes into a quasi-regular array of columns, allowing the rapid electrophoretic separation of long (>10 kilobases) duplex DNA, as shown by Doyle *et al.* (p. 2237).



Uranium-Seeking Noble Gases

Ices of noble gases are often used to trap and isolate highly reactive molecules because they presumably are "inert." Once again, the noble gases show unexpected reactivity. In their investigations of the "insertion" product of the reaction of CO with a uranium atom to form the linear CUO species, Li *et al.* (p. 2242) found that vibrational spectra were much different in the heavier and more reactive noble gases, such as argon (Ar), compared to the spectra for CUO in neon. Theoretical calculations show that Ar can bind to CUO and change the ground state from the singlet state to the triplet, and that multiple Ar atoms may bind to a single CUO.

Solvent Effects in Substitution Reactions



Many common organic reactions are of the S_N2 type—a nucleophile (such as a halide ion) displaces another nucleophile at a carbon atom, leading to a substitution at the tetrahedral carbon. The other three substituents around the carbon atom must "invert" like an umbrella, and it has been argued that bulkier substituents should slow down the reaction. However, many competing effects, such as differing heats of reactions and extent of solvation, make it difficult to examine this question directly. Regan *et al.* (p. 2245; see the Perspective by Farrar) looked at the isotopic substitution reaction of chloride in alkylchloronitriles, which react sufficiently fast to be followed in an ion cyclotron resonance spectrometer. In the gas phase, the difference in barrier height for methyl- versus *tert*-butyl–substituted molecules was less than 2 kilocalories per mole (kcal/mol). These results, along with Monte Carlo simulations, allow the authors to conclude that most of the "steric" effect seen in solution (with barriers of 5 to 7 kcal/mol) is actually caused by differences in solvation.

The Last Wave

When a sound wave travels through a heterogeneous medium, the wave can be scattered multiple times and can generate small wavetrains at the end of its signal, called the coda. Snieder *et al.* (p. 2253) have developed and experimentally tested a coda wave interferometer that would allow seismologists to detect changes in a medium as a function of time. This technique could be used to monitor volcanoes, where the movement of magma, as well as the growth and propagation of fractures, changes the character of the medium on a time scale measurable with a seismic interferometer.

No End to Decay

The information needed to make a protein is contained in messenger RNAs (mRNAs), which are decoded by the macromolecular machine called the ribosome. Termination codons in the mRNA tell the ribosome when to stop adding amino acids, and premature termination codons (PTCs) can lead to truncated proteins that in many instances are deleterious to a cell's health (see the Perspective by Maquat). The quality-control mechanism that deals with PTCs is called nonsense-mediated decay (NMD). Frischmeyer *et al.* (p. 2258) now describe a phenomenon called nonstop decay (NSD) in which mRNAs lacking any termination codons are degraded, and van Hoof *et al.* (p. 2262) provide evidence that this is accomplished by the exosome, a cytoplasmic complex of ribonucleases that is recruited to ribosomes that have stalled at the end of these aberrant mRNAs.

CREDITS: (TOP TO BOTTOM) DOYLE *ET AL.*; REGAN *ET AL.*

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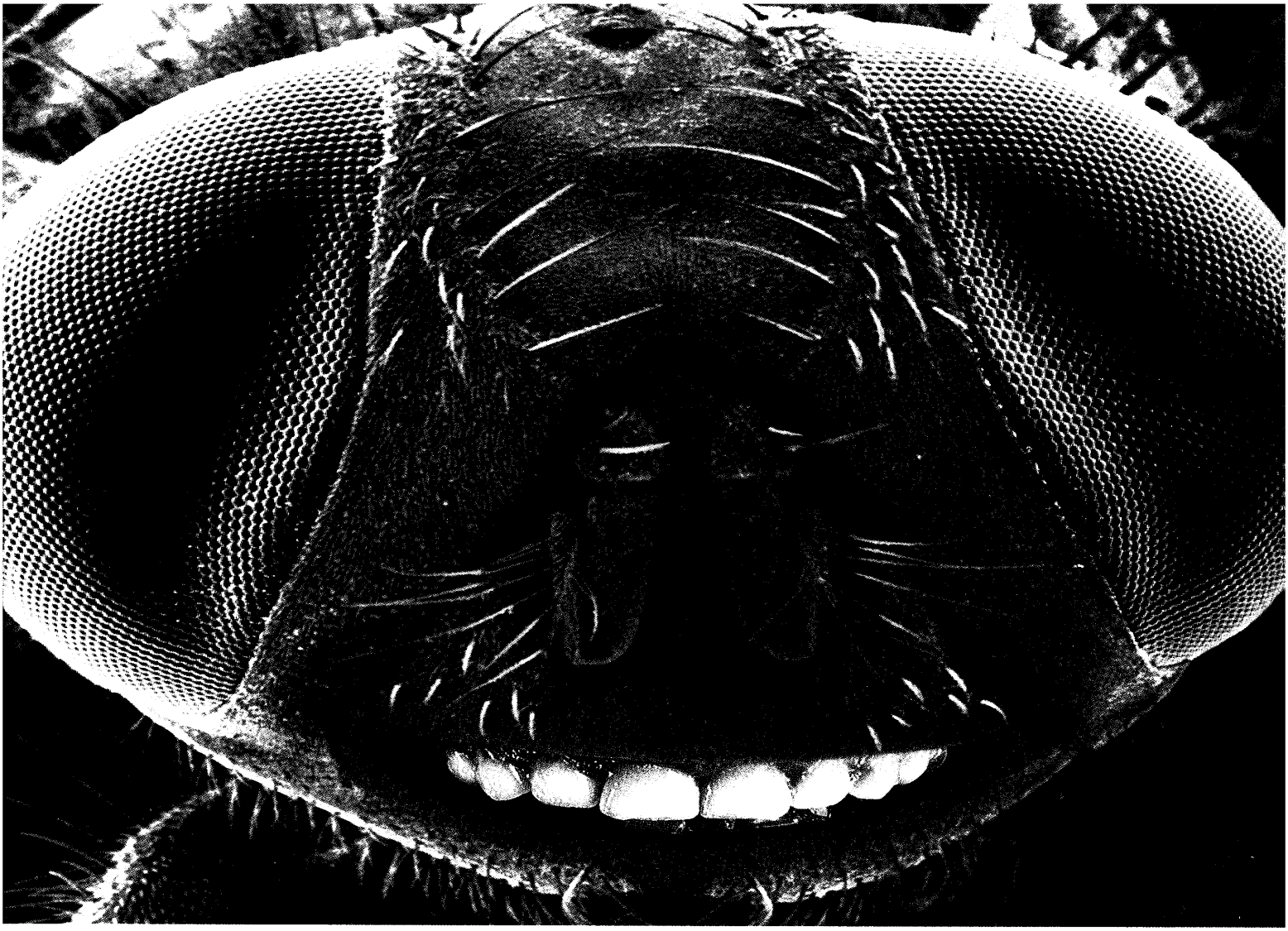

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Taking the Measure of Amyloid

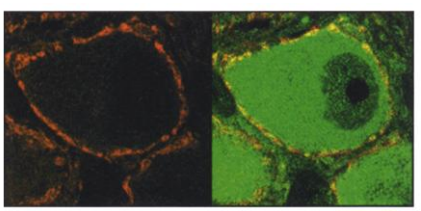
A cardinal feature of Alzheimer's disease (AD) is the deposition in brain tissue of amyloid β (Aβ) peptide. Amyloid plaques seem to appear years before cognitive impairment becomes apparent. A means of measuring amyloid plaque burden in the brain would provide a valuable biomarker and might enable therapeutic intervention prior to neuronal loss. Working in a mouse model of AD, DeMattos *et al.* (p. 2264) demonstrate that administering an Aβ antibody to mice resulted in an efflux of Aβ from the brain into the plasma that was correlated with the amyloid plaque burden in the hippocampus and cortex. Developing a humanized monoclonal antibody may lead to production of a diagnostic test that could quantify amyloid burden in the brains of both preclinical and clinical AD patients.

Dead, But Not Forsaken

DNA from remains of dead organisms, depending on its age, can be used for a variety of investigations from phylogenetic to forensic (see the news story by Pennisi). Techniques for isolating and sequencing ancient DNA offer the opportunity to assess rates of evolution and to map prehistoric population genetic structure, but hitherto a lack of samples of sufficient size, spanning significant periods of time, has precluded such work. Excavations from Arctic and Antarctic ice-bound subfossil remains are opening the door to reconstructions of new levels of complexity and detail. Barnes *et al.* (p. 2267) use sequences from frozen remains of brown bears in Alaska and Siberia to examine patterns of population genetic structure in relation to fluctuating Pleistocene climates. Lambert *et al.* (p. 2270) sequence mitochondrial DNA from Adélie penguin bones in Antarctica, revealing evolutionary rates at least twice as great as those inferred from more conventional phylogenetic analysis.

How Animals Eat

In animals and plants, there is an inverse relationship between body size and population density, but consistent patterns in this relationship are masked by ecological factors such as variation in quantity and type of resources. Carbone and Gittleman (p. 2273; see the Perspective by Marquet) investigate the variation in the size/density relationship within and between species of carnivorous mammal, and reveal an underlying rule: Regardless of body mass or population density, a given mass of prey will support a given mass of predator. They show that scaling laws can predict population density across more than three orders of magnitude in body size.



CREDIT: TSUJIMOTO *ET AL.*

Presynaptic Calcium Influx

Neurotransmitter release is triggered by calcium influx through presynaptic voltage-dependent calcium channels. Modulation of presynaptic calcium currents causes a robust alteration in synaptic efficacy. Tsujimoto *et al.* (p. 2276) investigated activity-dependent facilitation of P/Q-type calcium currents at the giant nerve terminals of the calyx of Held and found that calcium current upregulation is mediated by the calcium binding protein NCS-1, a homolog of the *Drosophila* frequenin protein.

Absolute Versus Relative Success

Despite the recent lackluster performance of the U.S. stock markets, some individuals and institutions have claimed relative success by losing less money than the averages. Gehring and Willoughby (p. 2279; see the news story by Miller) report the discovery of a neural processing event that distinguishes between true losses and relative losses. In a gambling task, subjects selected small or large wagers and were then informed of the gain or loss outcomes on all possible wagers. A signal arising from the medial frontal cortex near the anterior cingulate region appeared 200 to 300 milliseconds after results were posted, and this brain potential correlated with losses of all sizes, even in optimal outcomes in which a greater loss had been avoided. Furthermore, the magnitude of this potential increased in trials where the subject had incurred recent losses.

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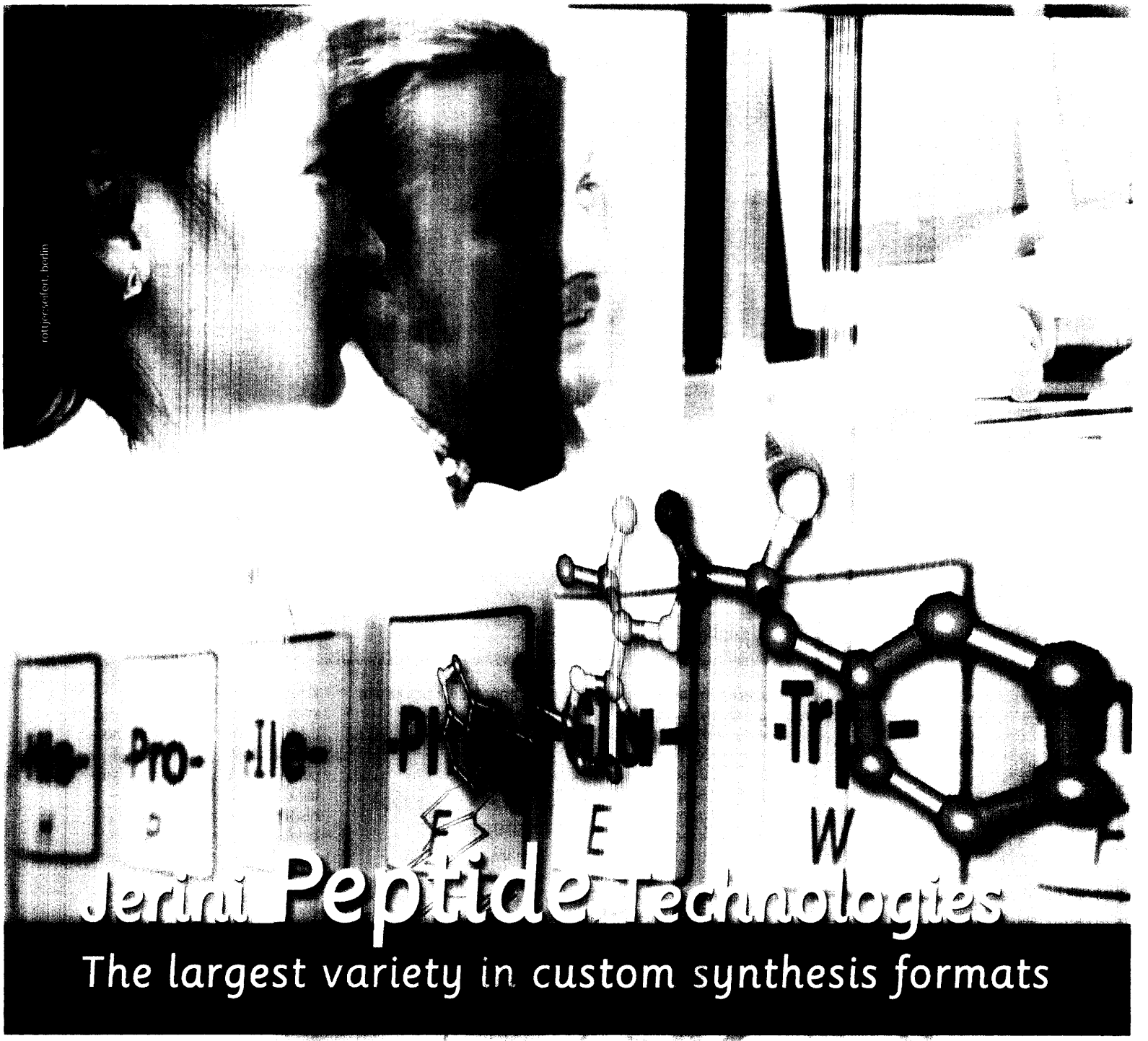

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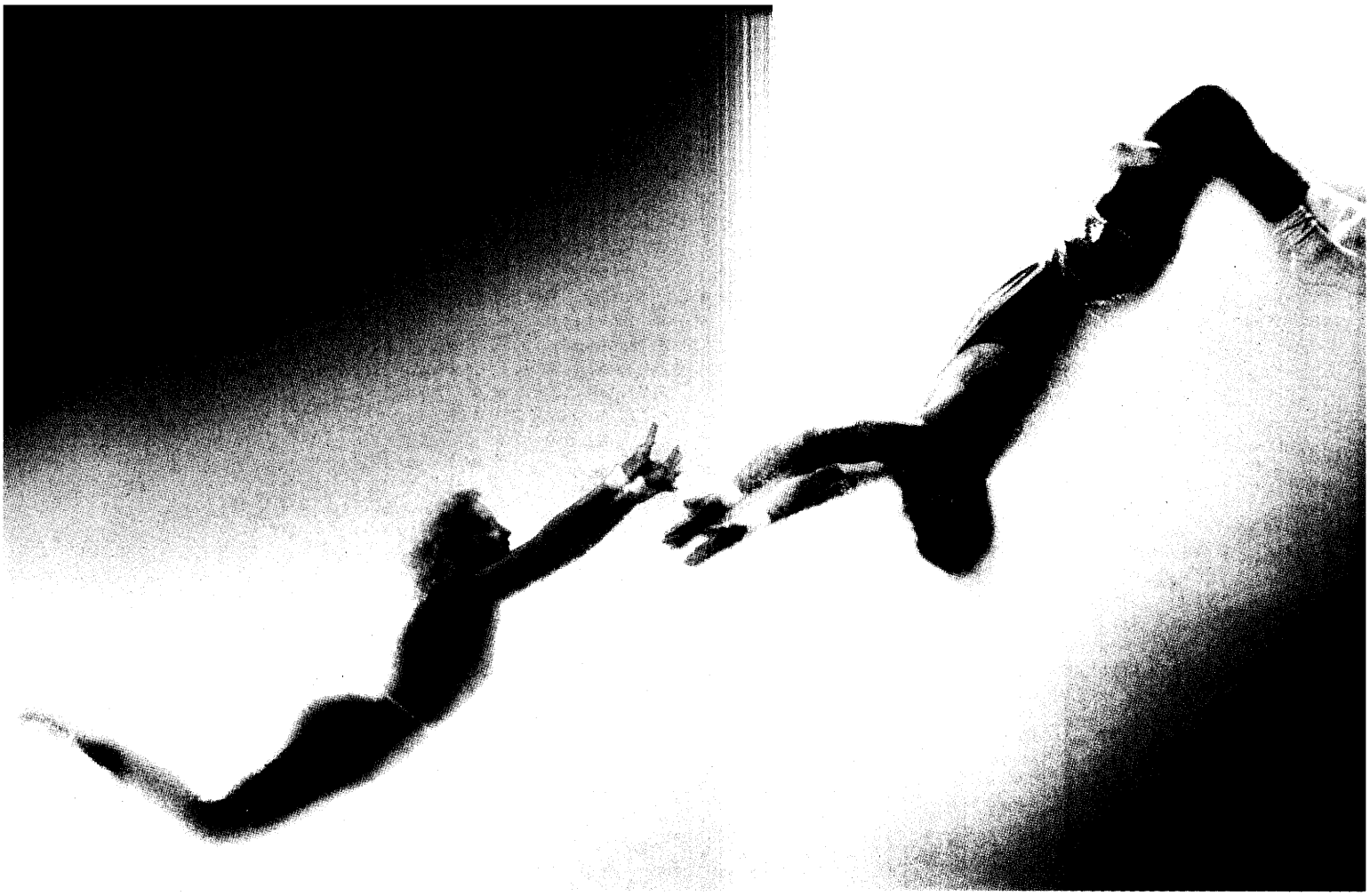

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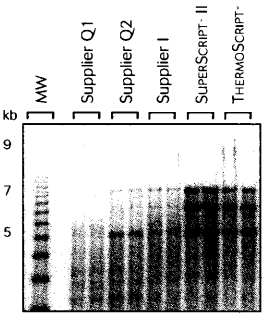

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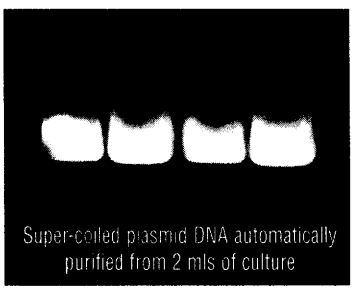

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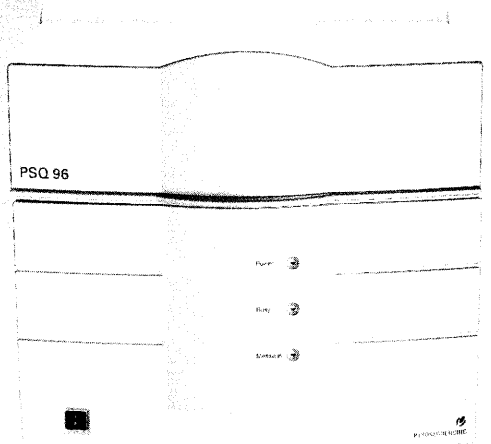

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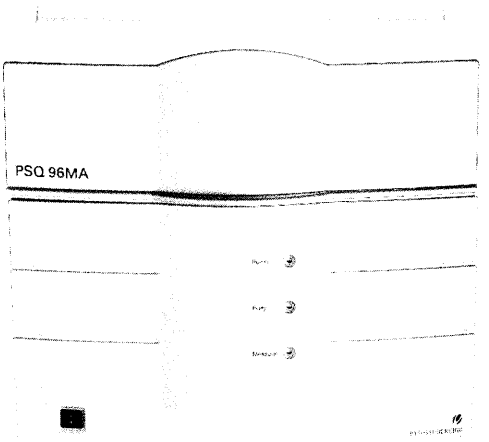

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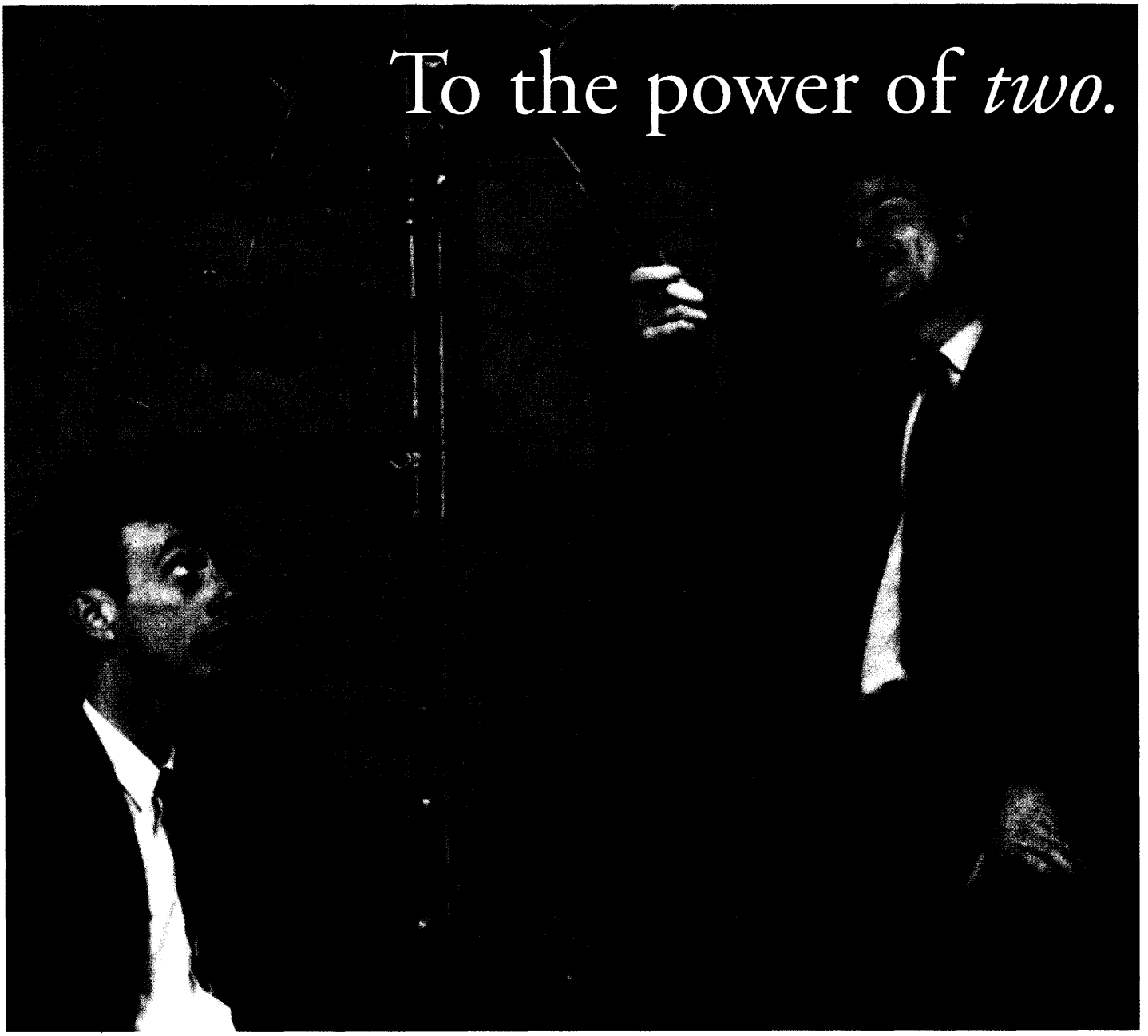

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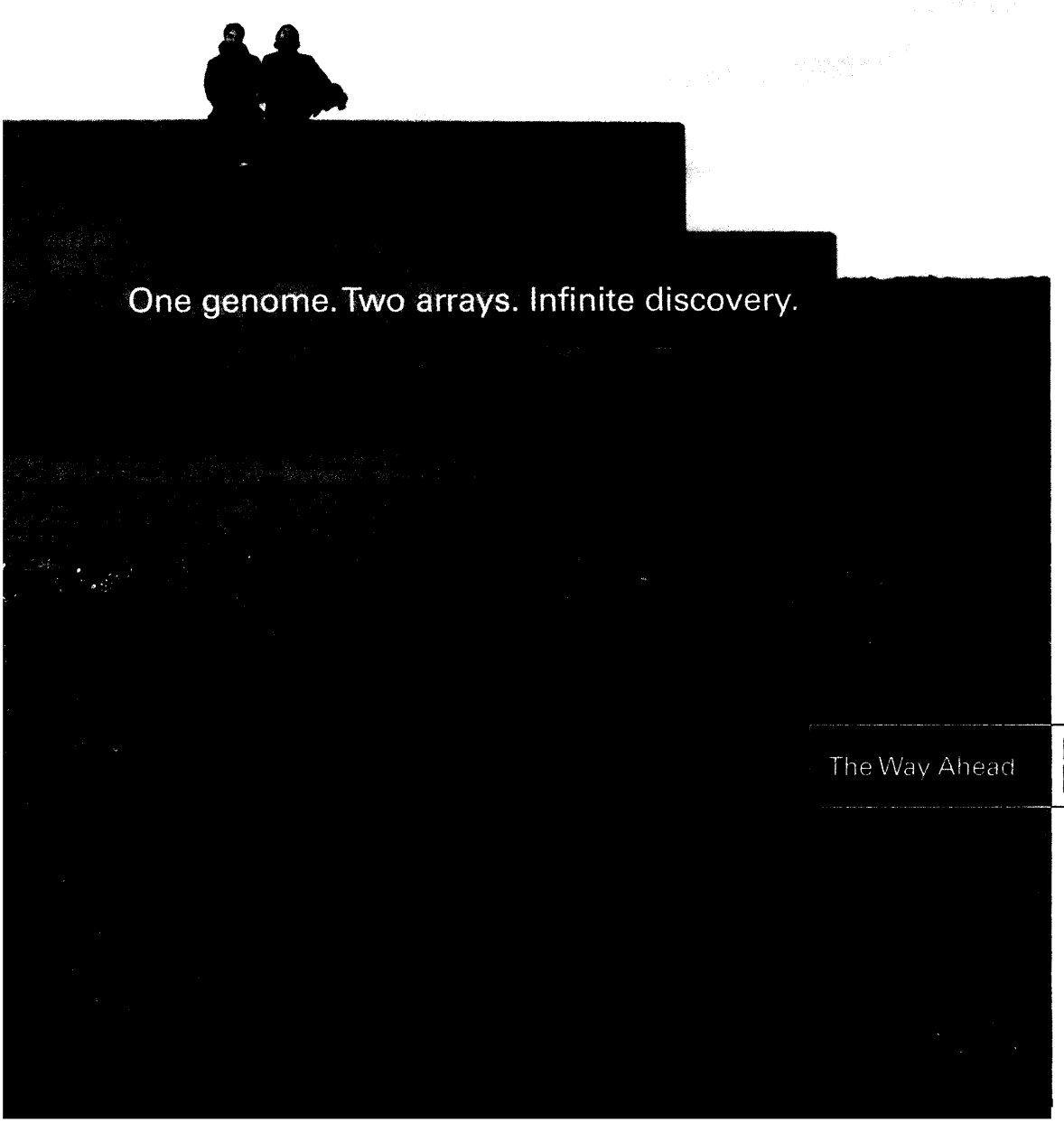

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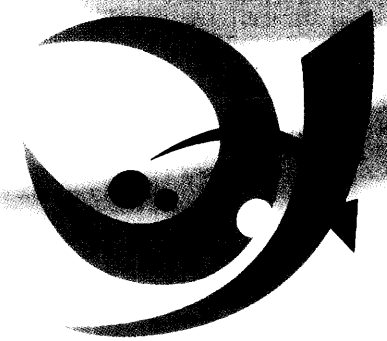

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