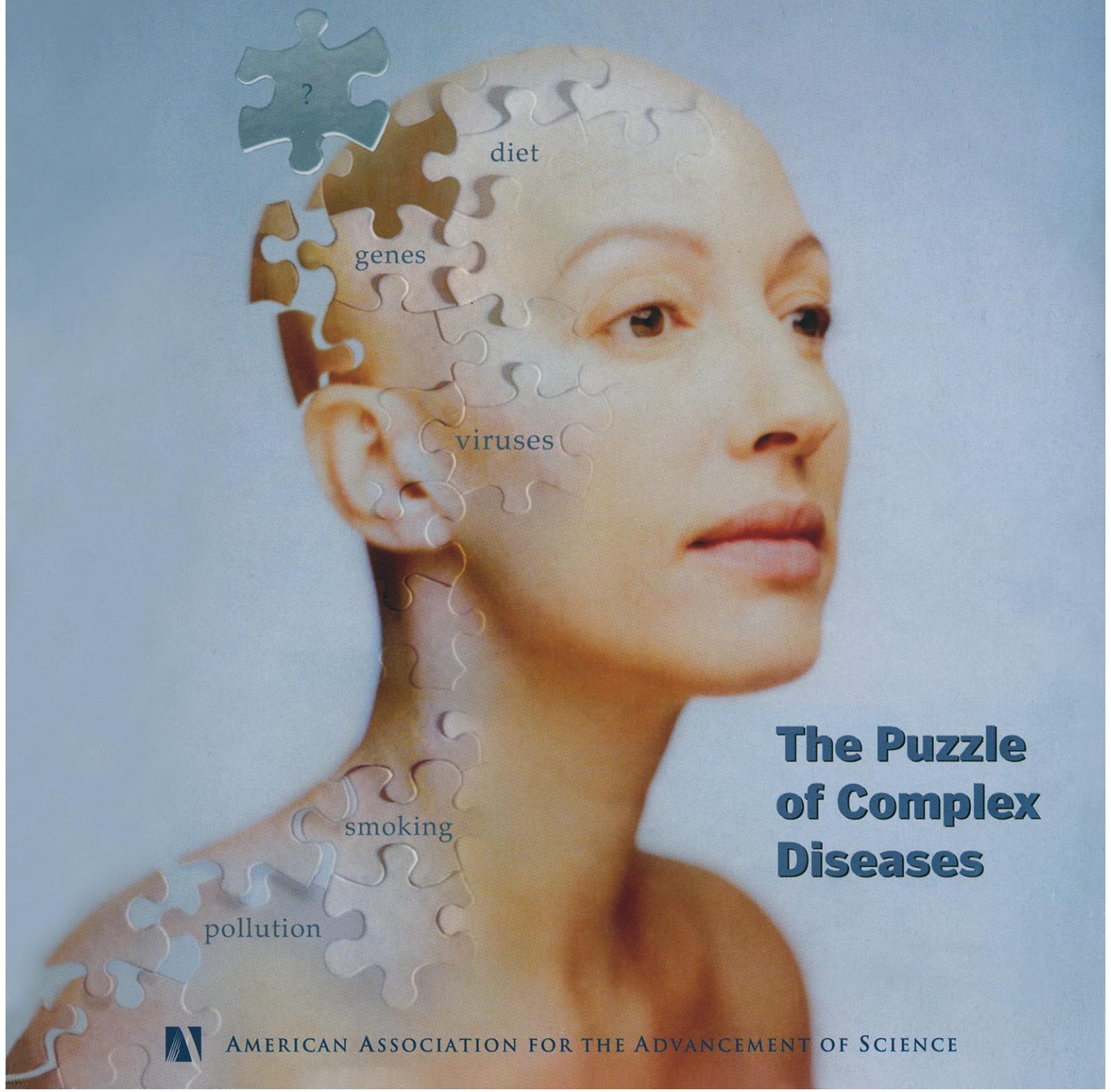
26 April 2002

Science

Vol. 296 No. 5568
Pages 605–792 $9



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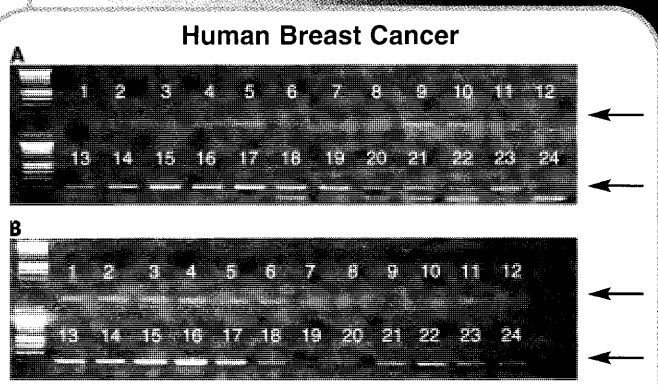

Lanes 1–12 represent normal breast epithelium samples from different individuals. Lanes 13–24 represent breast cancer samples from different individuals.

A and B represent analyses of 2 individual genes whose expression is up regulated in breast cancer samples.

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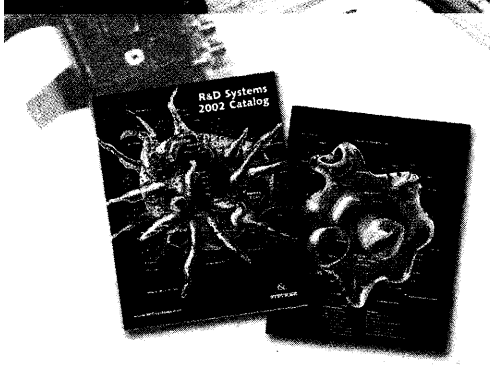

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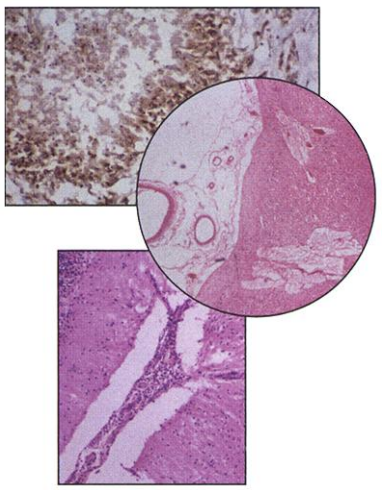
Science

Volume 296 26 April 2002 Number 5568



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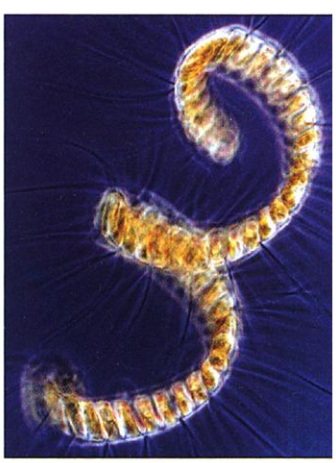
***See also* Science's *STKE* on p. 611, *News* on p. 642, and *Report* on p. 739.**

COVER 685

Complex diseases, such as heart disease, diabetes, and cancer, are among the most common and costly illnesses in Westernized countries. The special section in this issue considers the challenges of sorting out the multiple factors—including lifestyle, diet, infectious agents, and a host of genes—that contribute to disease susceptibility. [Photo illustration: Ann Cutting]



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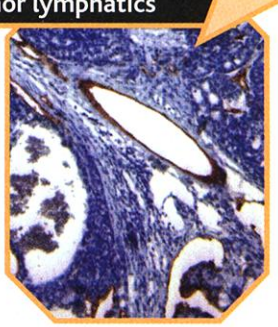
North Atlantic diatoms

New on *Science* Express

Functional defects in tumor lymphatics



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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $120 ($66 allocated to subscription). Domestic institutional subscription (51 issues): $390; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $85. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

Change of address: allow 4 weeks, giving old and new addresses and 8-digit account number. **Postmaster:** Send change of address to *Science*, P.O. Box 1811, Danbury, CT 06813–1811. **Single copy sales:** $9.00 per issue prepaid includes surface postage; bulk rates on request.

Science is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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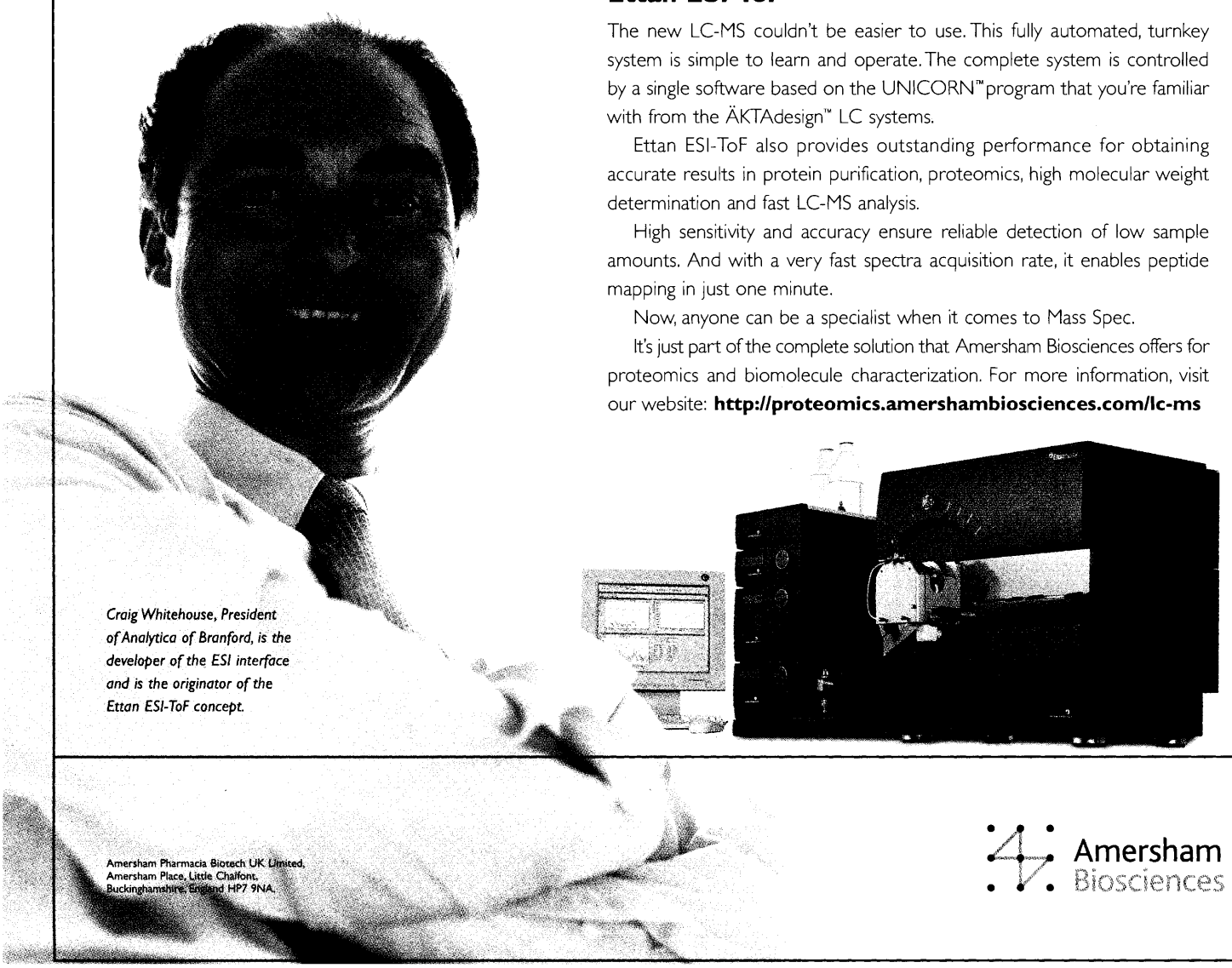

Craig Whitehouse, President of Analytica of Branford, is the developer of the ESI interface and is the originator of the Ettan ESI-ToF concept.

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CONTENT HIGHLIGHTS AS OF 26 APRIL 2002

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SCIENCE EXPRESS

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Lymphatic Metastasis in the Absence of Functional Intratumor Lymphatics T. P. Padera *et al.*

The lymphatic vessels within tumors are shown to be nonfunctional, suggesting that metastatic cancer cells travel to nearby lymph nodes exclusively through vessels located in the tumor margin.

▼ **A Cyclic Model of the Universe** P. J. Steinhardt and N. Turok
639 A different model for the origin of the universe, motivated by string theory and recent evidence for dark energy, proposes cycles of expansion and contraction with no beginning and no end.

Biodegradable, Elastic Shape-Memory Polymers for Potential Biomedical Applications A. Lendlein and R. Langer

A shape-memory, biodegradable polymer has been developed and used to create "self-closing" sutures.

TECHNICAL COMMENTS

Electron Microscopic Characterization of Silver Nanowire Arrays

Hong *et al.* (Reports, 12 October 2001, p. 348) reported that they had synthesized arrays of single-crystal silver nanowires approximately 0.4 nanometers in diameter and up to a micrometer in length, supporting that assertion with high-resolution electron microscope (HREM) images accompanied by selected-area electron diffraction (ED) patterns. In a comment, Ijima and Qin argue that the samples shown "actually represented not arrays of nanowires but highly defected needlelike silver crystals," with the observed array-like geometry due to stacking faults and twinning planes aligned parallel to the needle axis. Hong *et al.* respond that the details of the ED patterns, electron energy loss spectra, and infrared spectra do not support Ijima and Qin's suggestion that the images represented bulk silver, and instead are more consistent with the nanowire interpretation.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/296/5568/611a

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career resources for scientists

MISCINET: Out of Adversity J. Esnayra

This week's Shero describes the overwhelming odds she had to overcome to pursue her career.

US: Meet the Family—The Folks in My Lab M. P. DeWhyse

Picking a lab is like picking a family.

SINGAPORE: The Uncharted Domains of the Mind J. Wong

Singapore's National Neuroscience Institute is a magnet for aspiring neuroscientists.

UK: Book Review—Research Methods for Postgraduates L. Bloodworth

A new book offers helpful hints to students about to embark on postgraduate studies.

NETHERLANDS: Science and the Dutch Election—D66 Fosters Great Expectations M. Scheffer

One Dutch political party plans to create new career avenues for young talent.

GERMANY: Molecular Medicine—New Ph.D./M.D. Opportunities E. von Rusckowski

A new international Ph.D./M.D. program is attracting interest.

CANADA: Industry Research—From Theory to Practical Applications T. Trasler

Benefiting patients: An appealing aspect of the transition from academia to the pharmaceutical industry.

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Insulin-Like Growth Factor 1 (IGF-1) and Mammalian Aging A. Bartke

Genetics and physiology point toward tantalizing connections.

Picture This R. J. Davenport

NMR provides a glimpse of amyloid fibrils.

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signal transduction knowledge environment

Perspective: Do Defects in Ion Channel Glycosylation Set the Stage for Lethal Cardiac Arrhythmias? H. A. Fozzard and J. W. Kyle
685 Sialylation of cardiac ion channels.

Perspective: Opening Pandora's Box—Clinical Data and the Study of Complex Diseases M. N. Liebman
685 Understanding complex phenotypes.

Perspective: Lethal Weight Loss—The Focus Shifts to Signal Transduction K. J. Tracey
685 Molecular mechanisms leading to cachexia.

Protocol: Harvesting Cells under Anchorage-Independent Cell Transformation Conditions for Biochemical Analyses Z. Dong and J. L. Cmarik
685 A simplified procedure for obtaining transformed cells.

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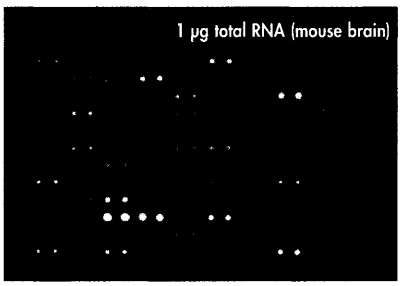

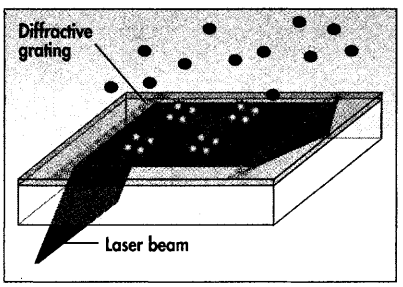

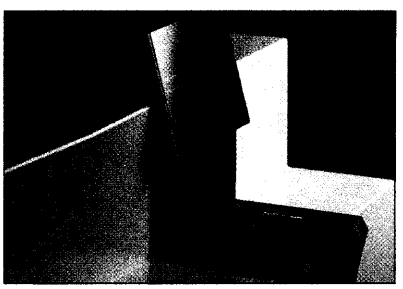

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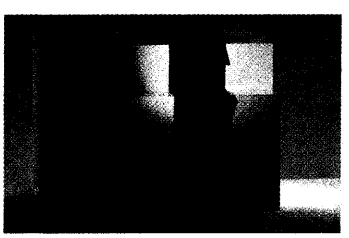

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THIS WEEK IN Science

edited by Phil Szuromi

The Role Not Taken

Although water vapor is the most important greenhouse gas, it is not even agreed whether an increase in its concentration due to global warming will cause more warming or cooling. Warming (a positive feedback) will occur if the biggest effect is to absorb more outgoing long-wave radiation. Cooling (a negative feedback) will occur if the major result is to form more clouds, which would reflect more sunlight. Soden *et al.* (p. 727; see the Perspective by Del Genio) test these two possibilities by using observations of the atmospheric cooling and drying that occurred after the eruption of Mount Pinatubo in 1991 as targets for an atmospheric general circulation model. The cooling that followed the blast is consistent with the measured decrease in water vapor only if the vapor provides positive feedback. These results suggest that current climate models have correctly chosen the role of water vapor.

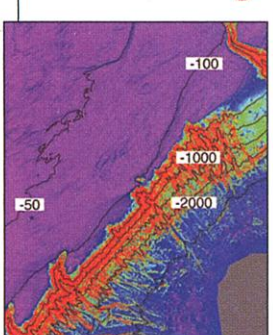
715 Electrons Racing with Nuclei

The Born-Oppenheimer approximation allows theoreticians to treat the motion of the much faster and lighter electrons in molecules separately from nuclear motion. In the reaction of H_2 with the open-shell halogen atoms, F and Cl, three potential energy surfaces (PESs) describe the reaction. If the Born-Oppenheimer approximation holds, only the lowest energy PES should contribute to product formation. Indeed, for F, this is the case to within 10%, and for the heavier Cl species, one would expect an even smaller contribution. Nonetheless, recent experimental results have suggested that for the Cl reaction, the higher energy spin-orbit PESs are the dominant reaction channel. A theoretical analysis by Alexander *et al.* (p. 715; see the Perspective by Manolopoulos) now shows that the spin-orbit PES does not appear to contribute to the reactivity, except at very low energies, and that ineleastic reaction channels open up from the ground state. The origin of the disagreement between theory and experiment is unclear and will warrant further study.

And in Brevia ...

Ajayan *et al.* (p. 705) report that carbon single-walled nanotubes ignite and combust when hit with the light from a photographic flash.

Maintaining Continental Slopes



Continental slopes maintain a consistent angle of 2° to 4°, which indicates that some form of steady state is achieved between continental erosion and ocean dynamics. Cacchione *et al.* (p. 724) have determined that semidiurnal internal tides with angles less than the continental slope are reflected toward the sea floor and increase the velocity and shear stresses along the slope and sea floor. This excess energy keeps fine-grain sediment from collecting along the slope and thus maintains the angle. Their model, which is consistent with observations along the northern California and New Jersey coasts, may be used to understand the coupling between continental and oceanic processes.

Seeing Double with Quantum Cloning

The uncertainty inherent in quantum mechanics places constraints on the ability to make perfect copies or "clones" of quantum states. Much theoretical work has focused on how good of copies can be made. Lamas-Linares *et al.* (p. 712) now present an experimental demonstration of the cloning of the polarization state of a photon. The coincidence of a photon with a frequency-doubled photon in a nonlinear crystal results in the production of two photons, one a clone of the input photon. The measurement of fidelity, 0.81, is close to the theoretical limit of 0.83.

When Less Is More

Experimental studies of grassland ecosystems have supported the paradigm of a positive relation between diversity and ecosystem productivity. Paine (p. 736) provides experimental evidence, replicated over several years, from a rocky intertidal community that challenges this paradigm's generality. The intact biotic assemblage containing the natural complement of kelp, herbivores, and predators results in a high-diversity plant assemblage that is maintained in large measure by selective grazing effects of the system's dominant herbivore. However, when this single herbivore species was experimentally removed, a single plant species dominated and overall productivity increased, thus creating a negative relation between plant species diversity and production.

Fickle Finches

Continuous long-term studies of evolution in natural populations of vertebrates are very rare, and we have few insights into the consistency of selection, the frequency of evolutionary responses or hybridization, or the extent to which change is gradual or episodic. Grant and Grant (p. 707; see the news story by Zimmer) have studied Darwin's finches on the Galapagos for more than 30 years, and their data set offers a long-term look at the interplay of predictable and unpredictable components in the evolutionary process.

Still Searching for Schizophrenia Genes

The search for genes involved in schizophrenia has been a long and confusing one. Levinson *et al.* (p. 739) present results of an ongoing effort by a multicenter collaboration to use a sample of about 800 families with schizophrenia to evaluate evidence of genetic linkage in chromosomal regions that have been "nominated" by more than one study. Although previous reports (including one published in *Science*) had strongly implicated region 1q as being involved, this study did not find any evidence of linkage. Nonreplication suggests that the affects of 1q on schizophrenia are, if present, likely to be very small at the population level.

CREDITS: (TOP TO BOTTOM) AJAYAN *ET AL.*; CACCHIONE *ET AL.*

Published online in *Science* Express

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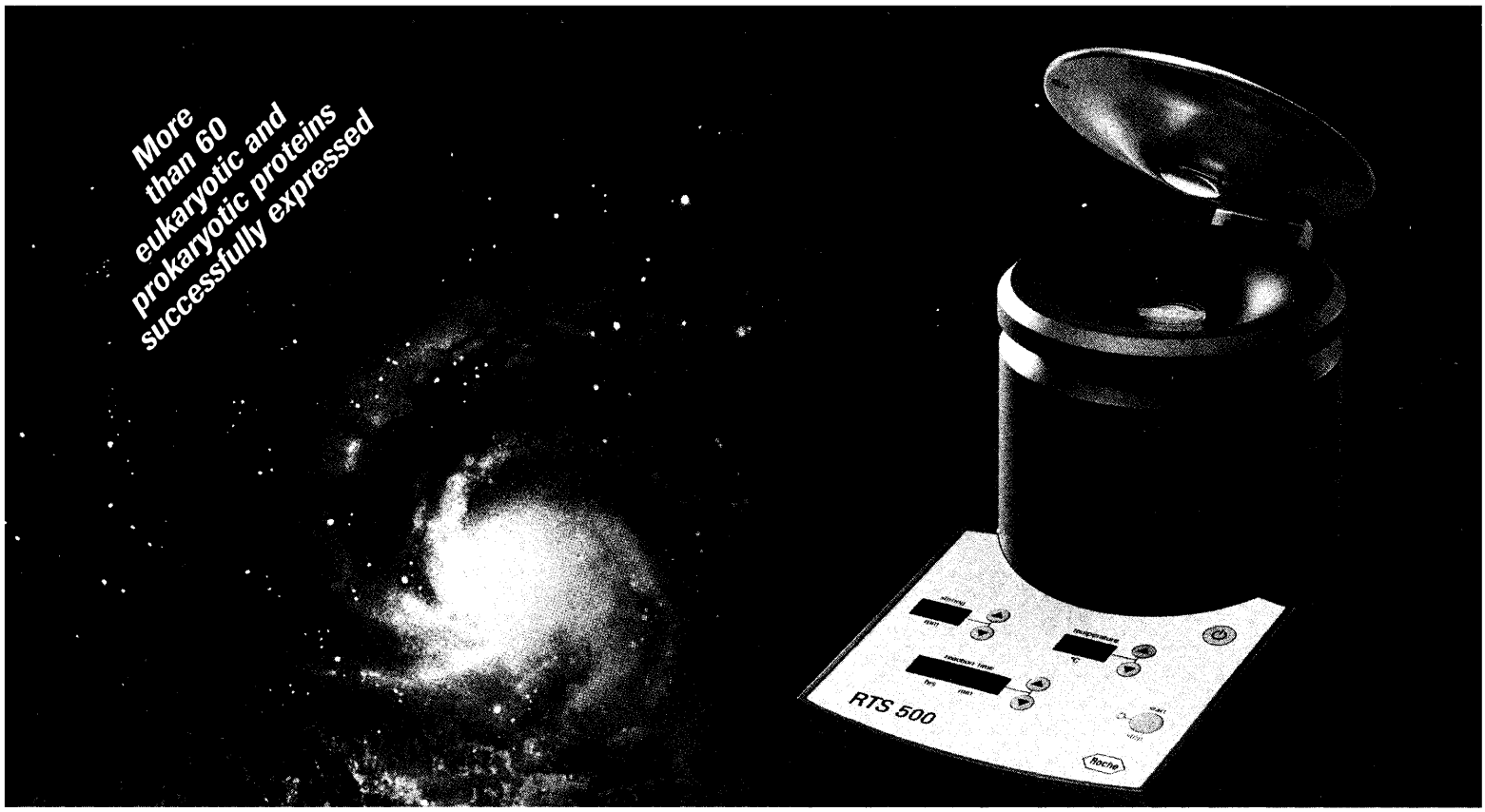

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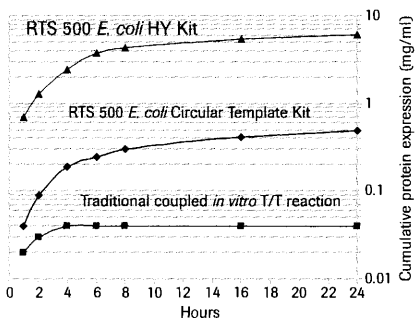

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* The Rapid Translation System currently consists of: RTS 500 Instrument (3.75 kg), the RTS 500 *E. coli* HY Kit, the RTS 500 *E. coli* Circular Template Kit, and the RTS 100 *E. coli* HY Kit (dedicated instrument not required).

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Murine Toxin Misnomer

Plague is caused by the bacterium *Yersinia pestis* and is transmitted via flea bites. Closely related bacteria do not take this tortuous route between human hosts. Hinnebusch *et al.* (p. 733) reveal that the so-called *Yersinia* murine toxin is in fact key to flea transmission. The toxin is in fact an enzyme, phospholipase D, whose activity is important in establishing an infection in the flea gut.

Not All Foraging Is the Same

A comprehensive understanding of how genes and the environment interact to influence behavior is becoming a realistic goal. Ben-Shahar *et al.* (p. 741; see the news story by Pennisi) report that the same gene known to influence foraging behavior in *Drosophila* via genotypic variation also influences foraging in honey bees via regulation of expression during adult behavioral maturation. The gene, *foraging*, encodes a guanosine 3',5'-monophosphate–dependent protein kinase, a key player in many signal transduction pathways. This gene thus influences behavior across strikingly different time scales, both evolutionary and developmental.

Rousing the Resistance in Plants

The "gene-for-gene" hypothesis, long useful in describing how particular plants resist infection by particular pathogens, may now be in for complicating elaboration. An additional plant gene, *Rcr3*, is involved in the interaction between a particular fungal elicitor and its corresponding plant-encoded protein, localized in the plant cell membrane. Krüger *et al.* (p. 744) show that Rcr3 is a protease secreted by the plant cell in response to infection by this fungus. Rcr3 function is required for a robust response to pathogen invasion.

Healing Touch of T cells

Dendritic epidermal γδ T cells (DETCs) are thought to contribute to the integrity of the skin. Jameson *et al.* (p. 747) have extended previous studies which showed that DETCs express growth factors in response to damaged keratinocytes by demonstrating that these cells are involved directly in wound repair. Mice deficient in γδ DETC displayed a twofold lower rate of wound healing relative to mice with normal numbers of DETCs, as well as a marked reduction in keratinocyte proliferation. In a skin organ culture system, reduced wound repair and keratinocyte proliferation in the absence of γδ DETC could be corrected by addition of keratinocyte growth factor. Skin γδ T cells therefore appear to play a prominent role in allowing rapid wound healing.

Slowly Changing Partners

A wealth of genomic and proteomic information now makes it possible to analyze fundamental properties and evolution of protein interaction networks. To estimate evolutionary rates, Fraser *et al.* (p. 750) compared putative orthologous proteins in *Saccharomyces cerevisiae* and *Caenorhabditis elegans*. As expected, given that highly interactive proteins are more likely than their less connected counterparts to be required for viability, highly connected proteins also appear to evolve more slowly. However, the authors' analysis indicates that what limits evolutionary rates of interacting proteins is that a greater proportion of the molecules themselves takes part in physical interactions. Changes in interacting partners are expected to only be maintained if a reciprocal change in the other partner also occurs. This requirement appears to require similar evolutionary rates for the interacting partners.

Variations on Some Genes

To identify specific genes that control transcription levels, Brem *et al.* (p. 752) compared gene expression patterns from a laboratory strain of yeast and a natural isolate from the wild that were grown under identical conditions, and found more than 1500 genes that were differentially expressed. The authors analyzed progeny from crosses between the two strains and found that 308 of the differences segregated in a Mendelian fashion and could be mapped. Variation in gene expression typically was controlled by many genes; eight appeared to be trans-acting, with widespread transcriptional effects.

CREDIT: BEN-SHAHAR *ET AL.*

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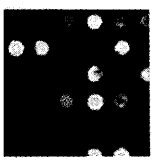

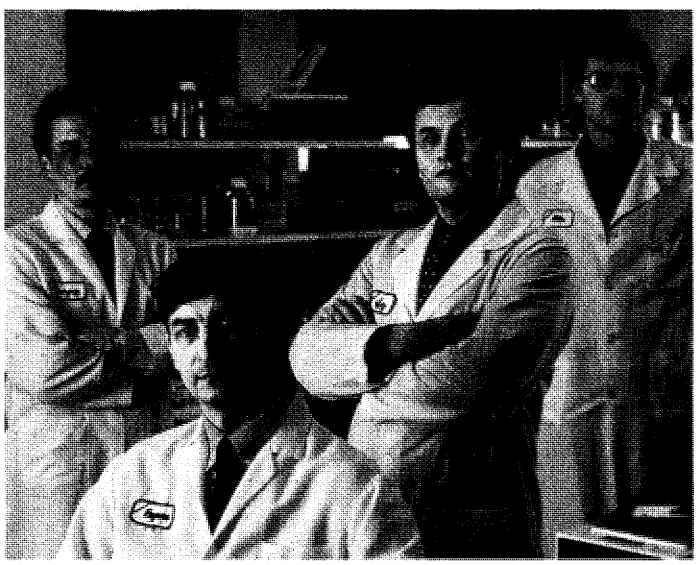

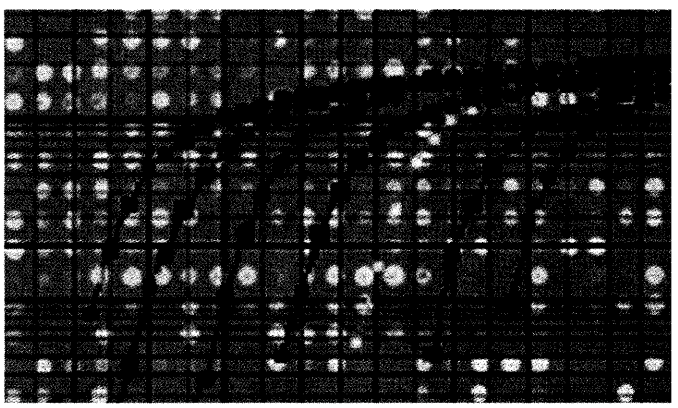

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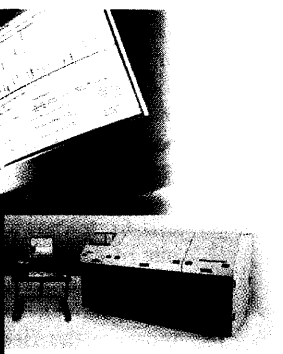

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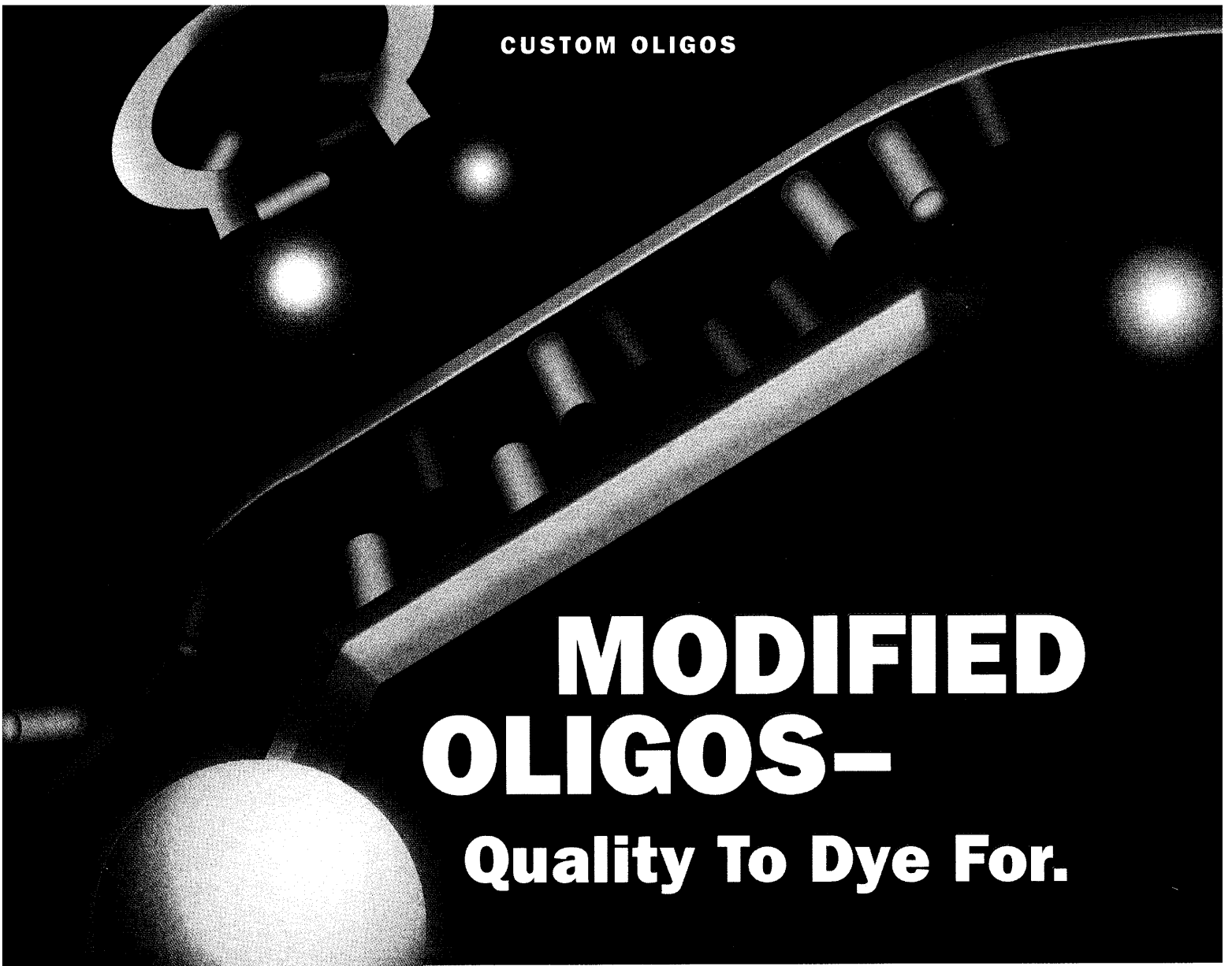

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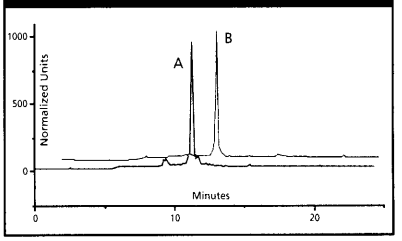

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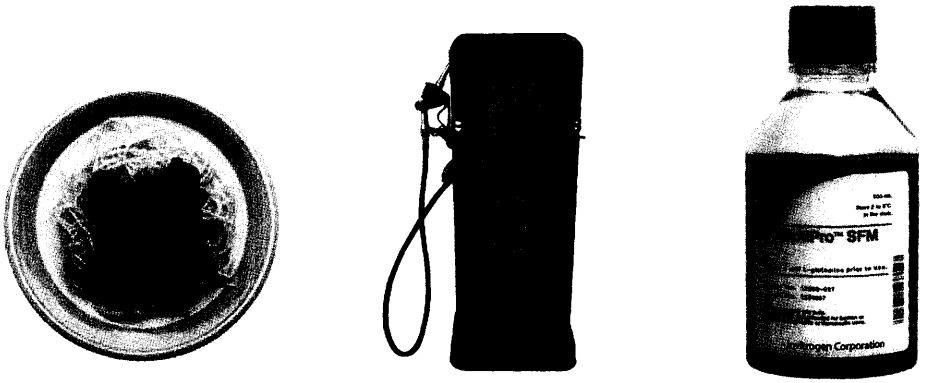

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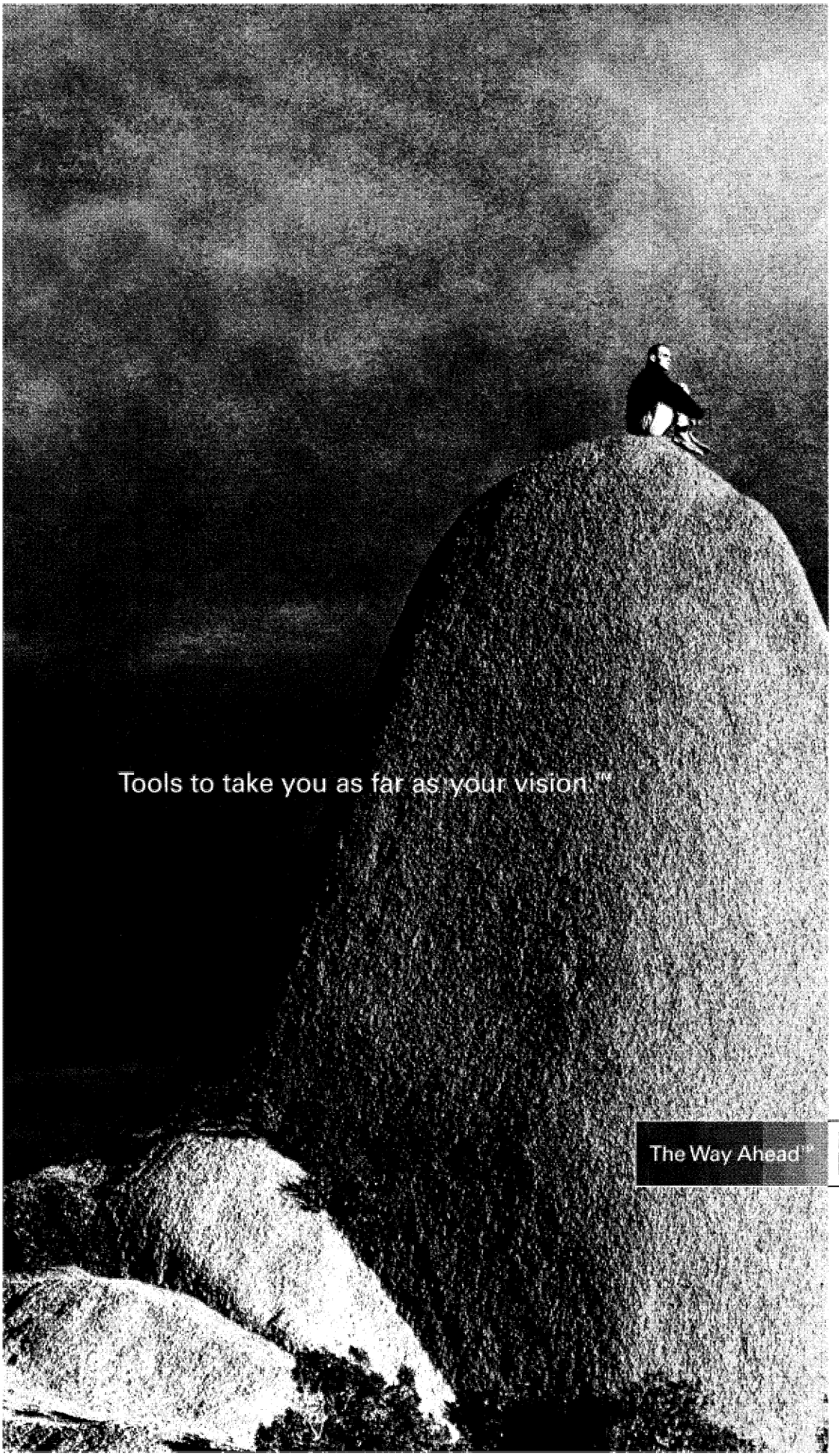

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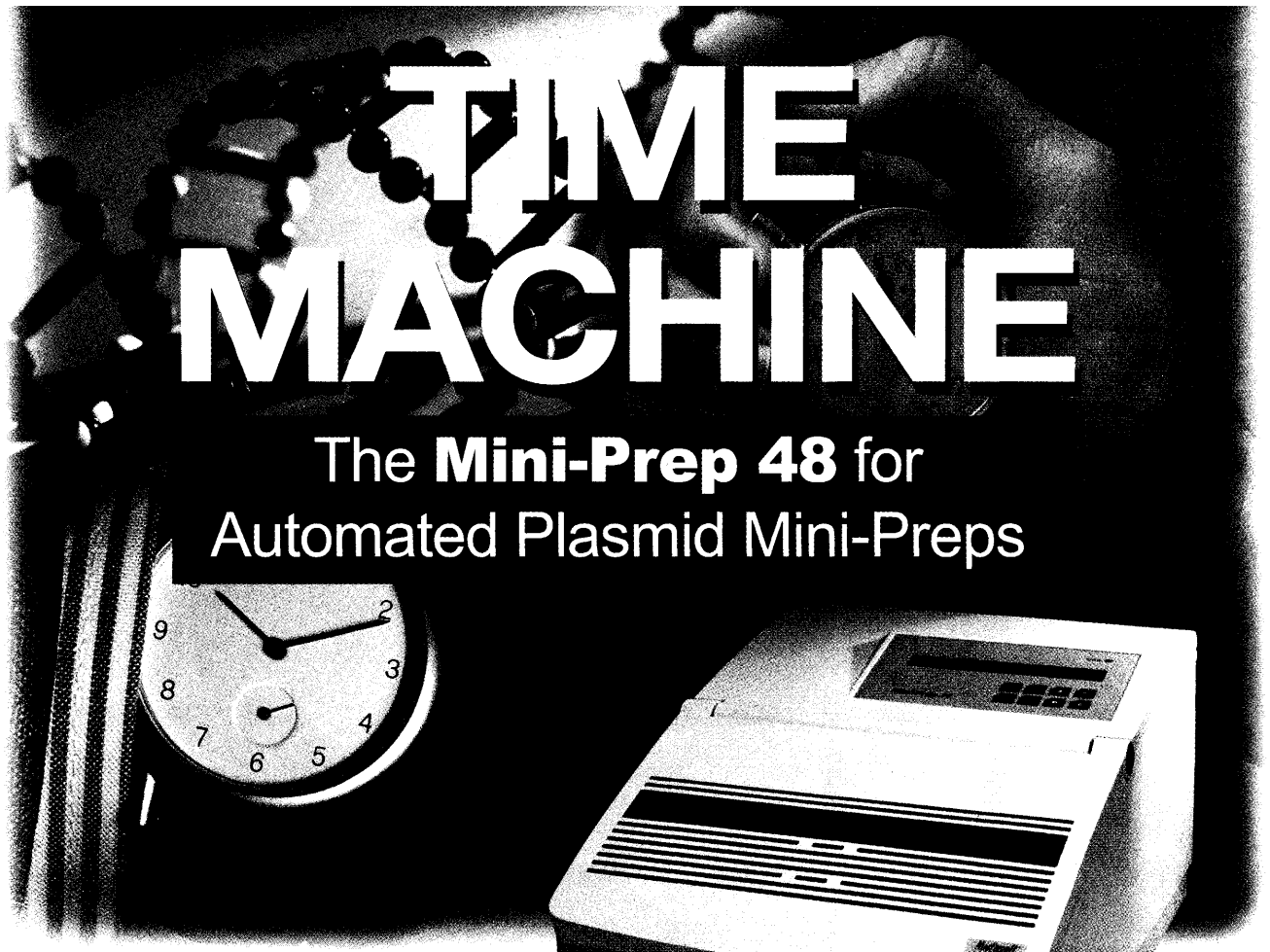

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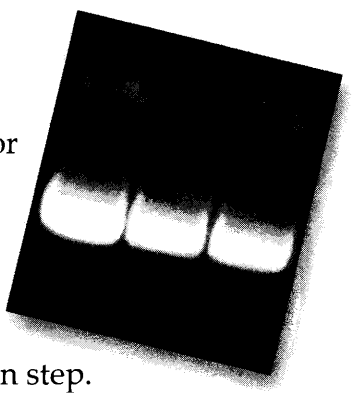

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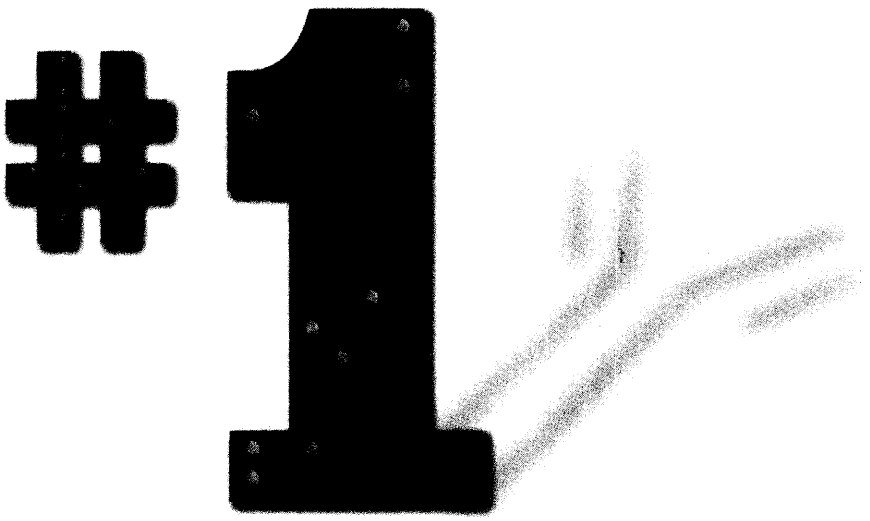

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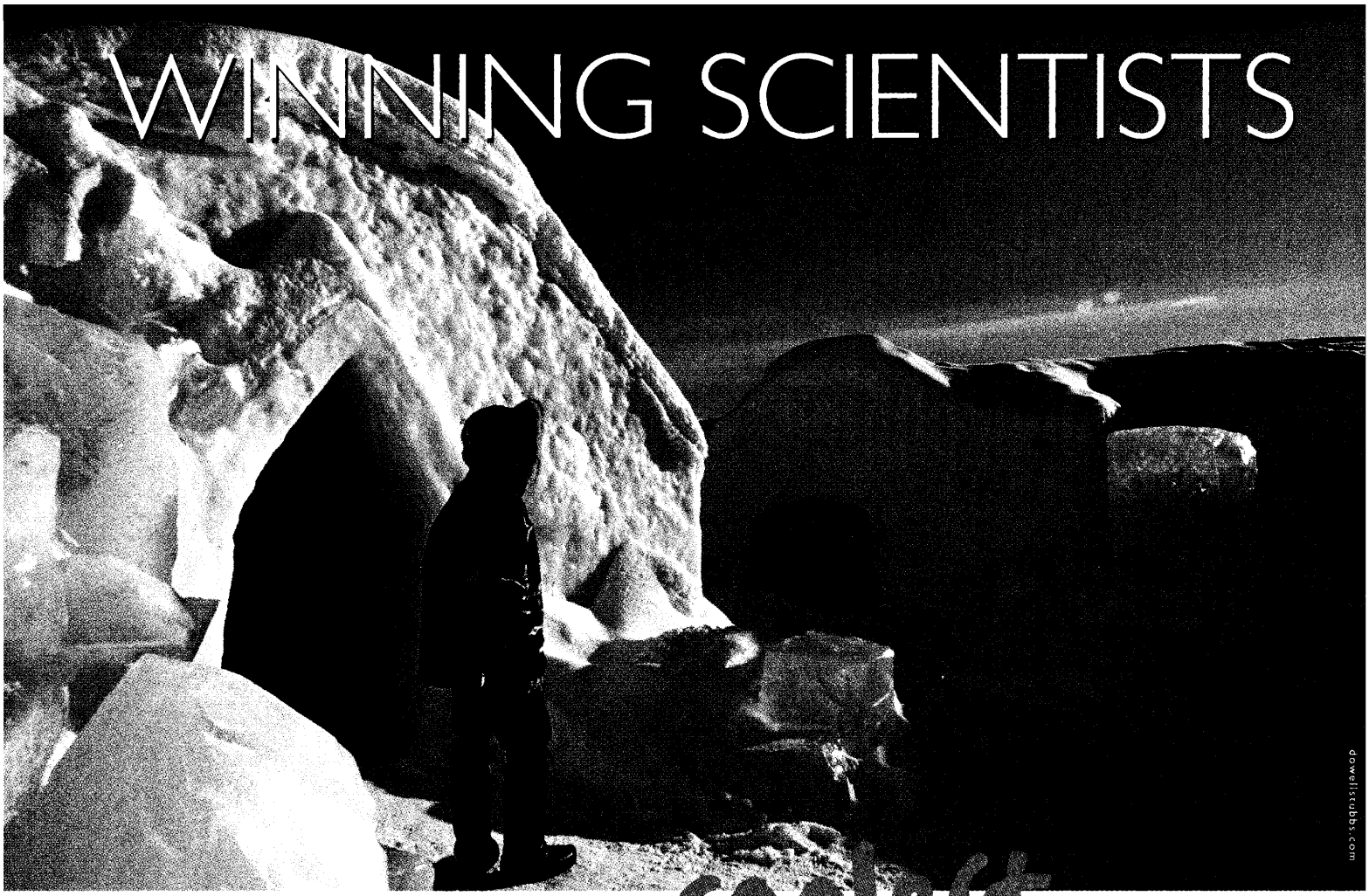

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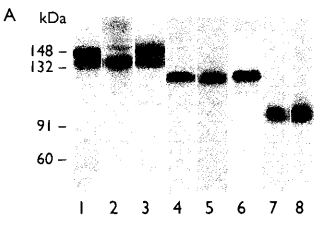

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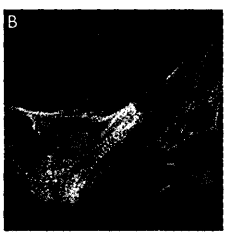

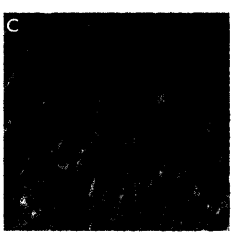

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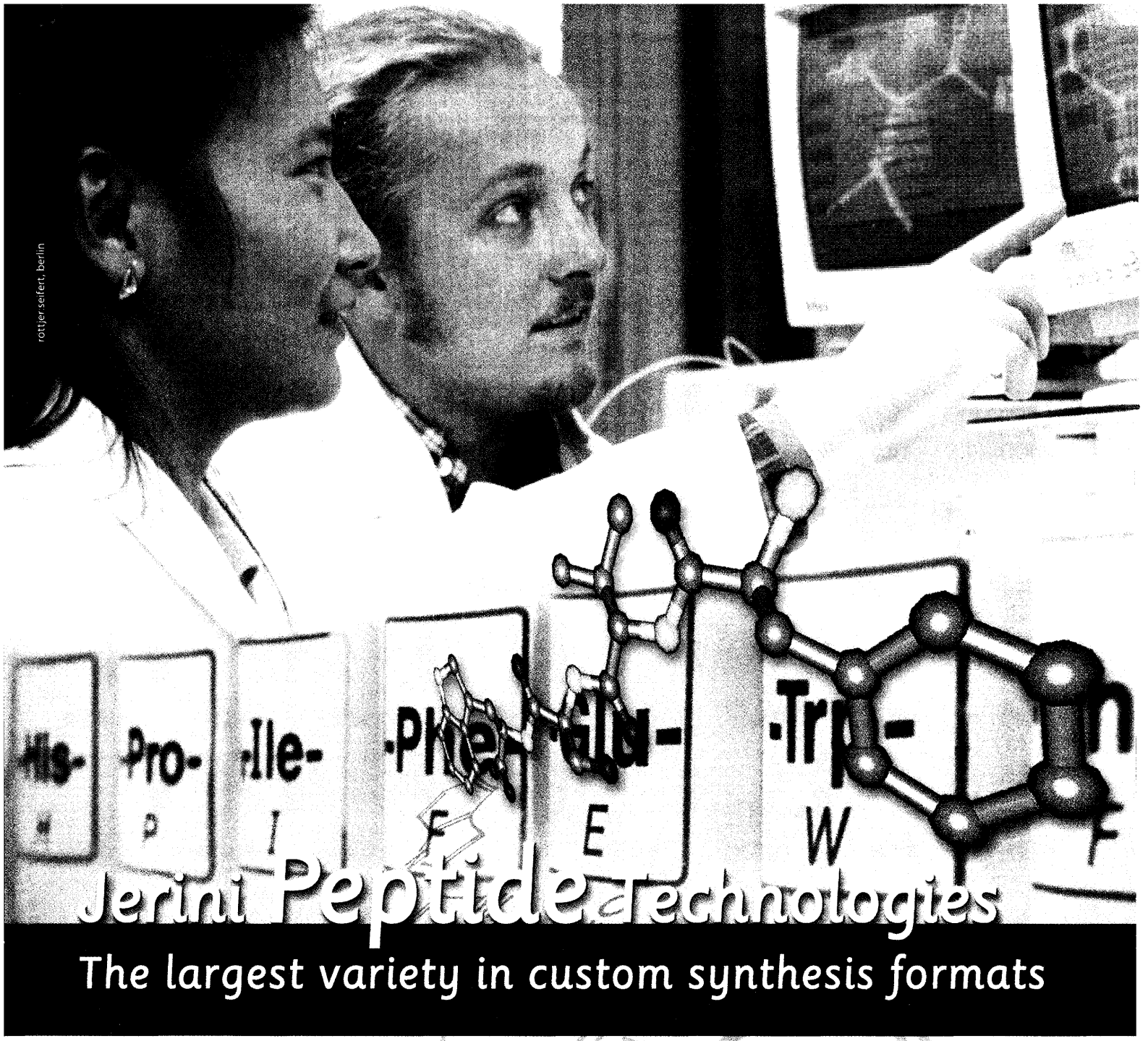

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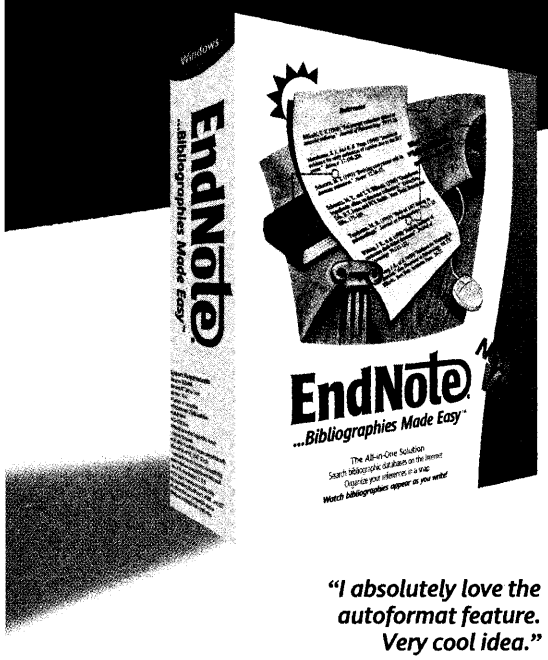

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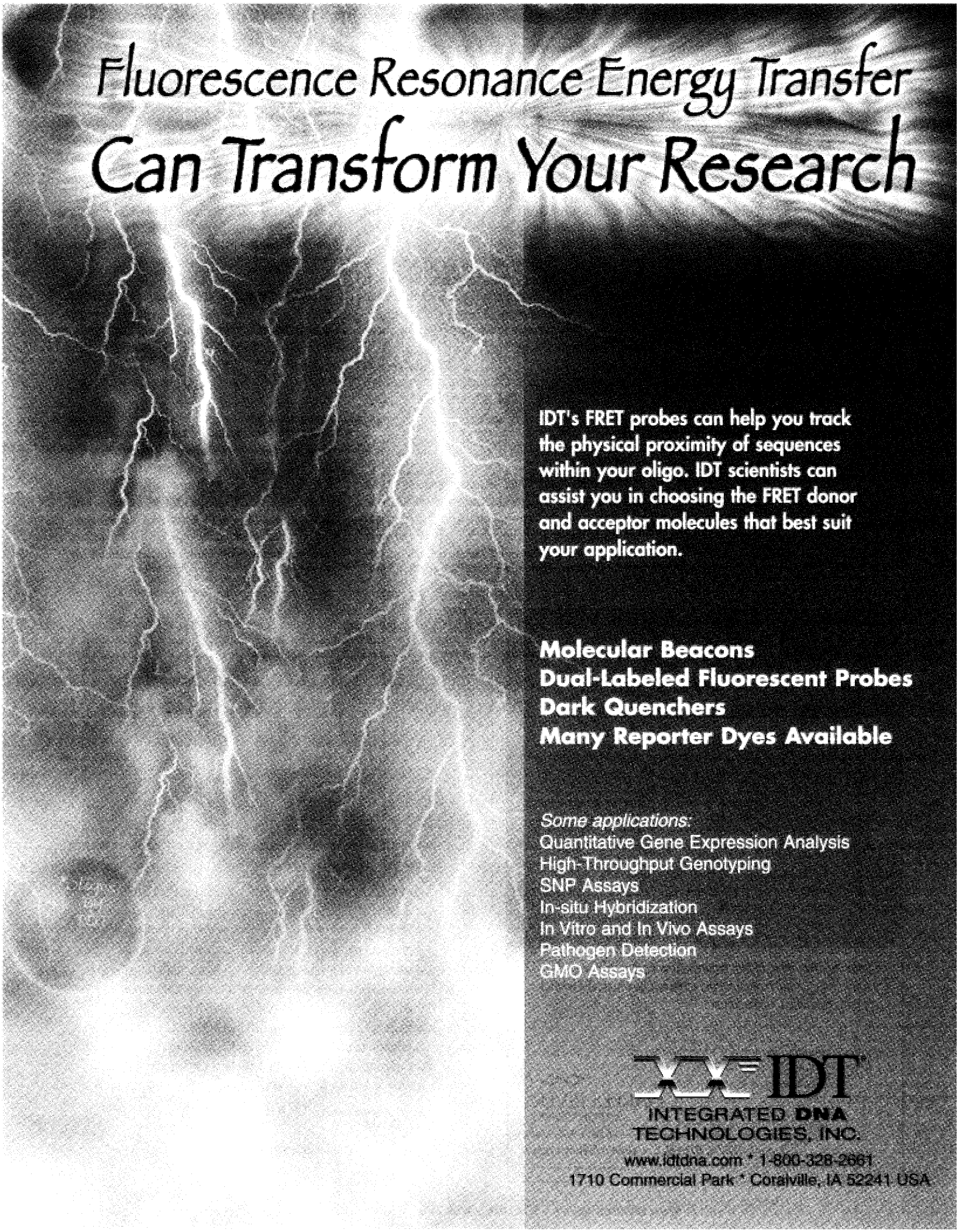
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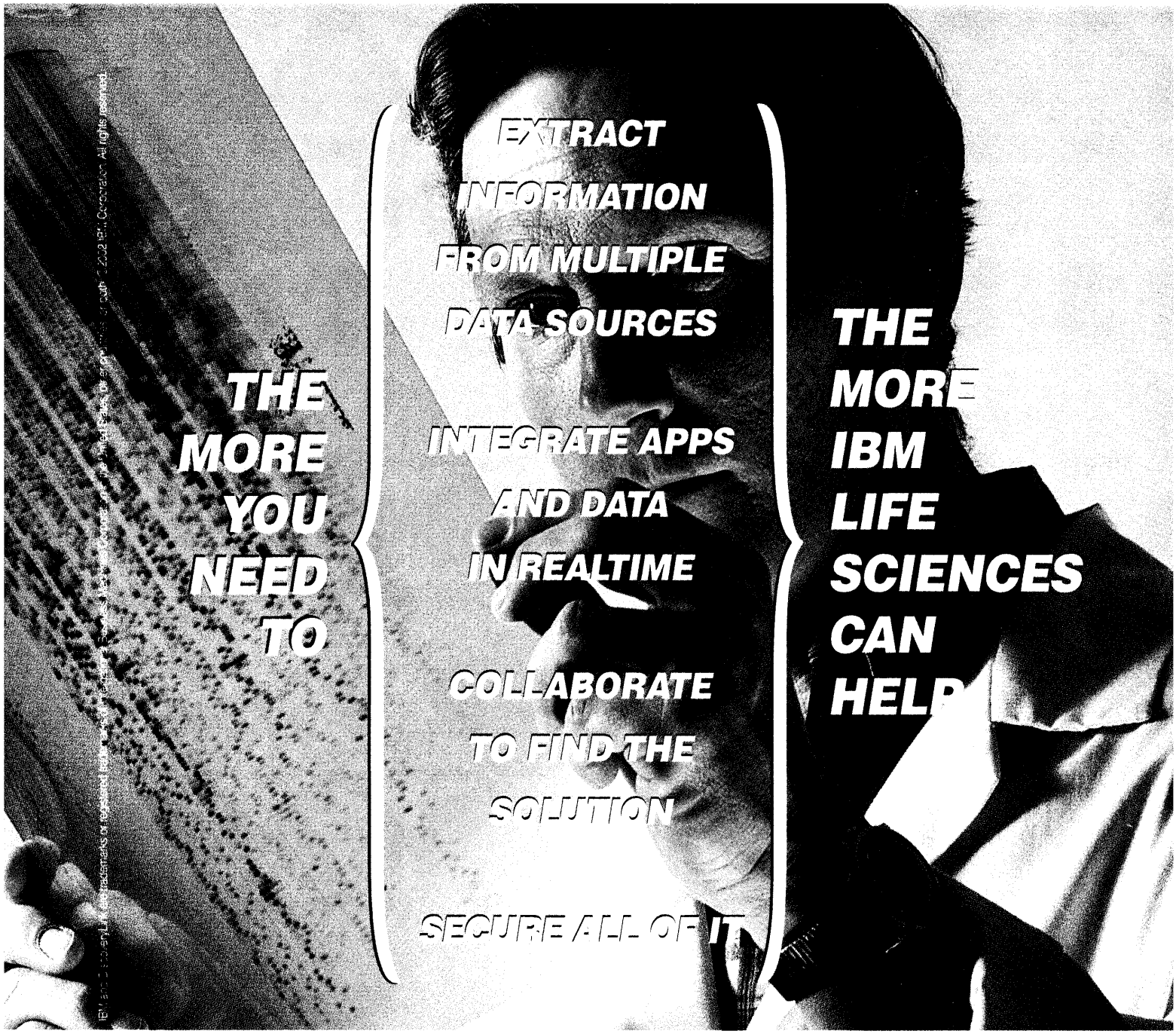

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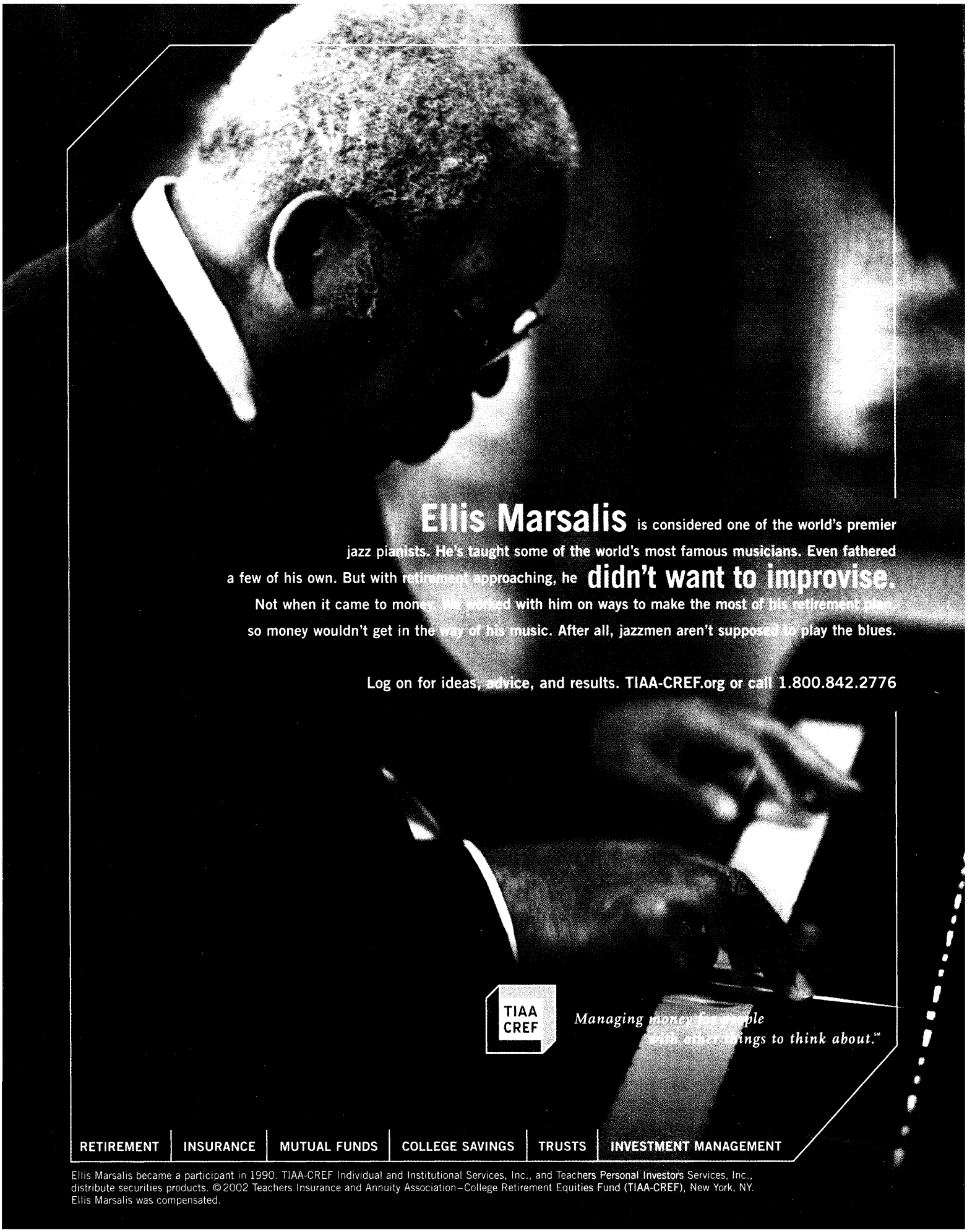

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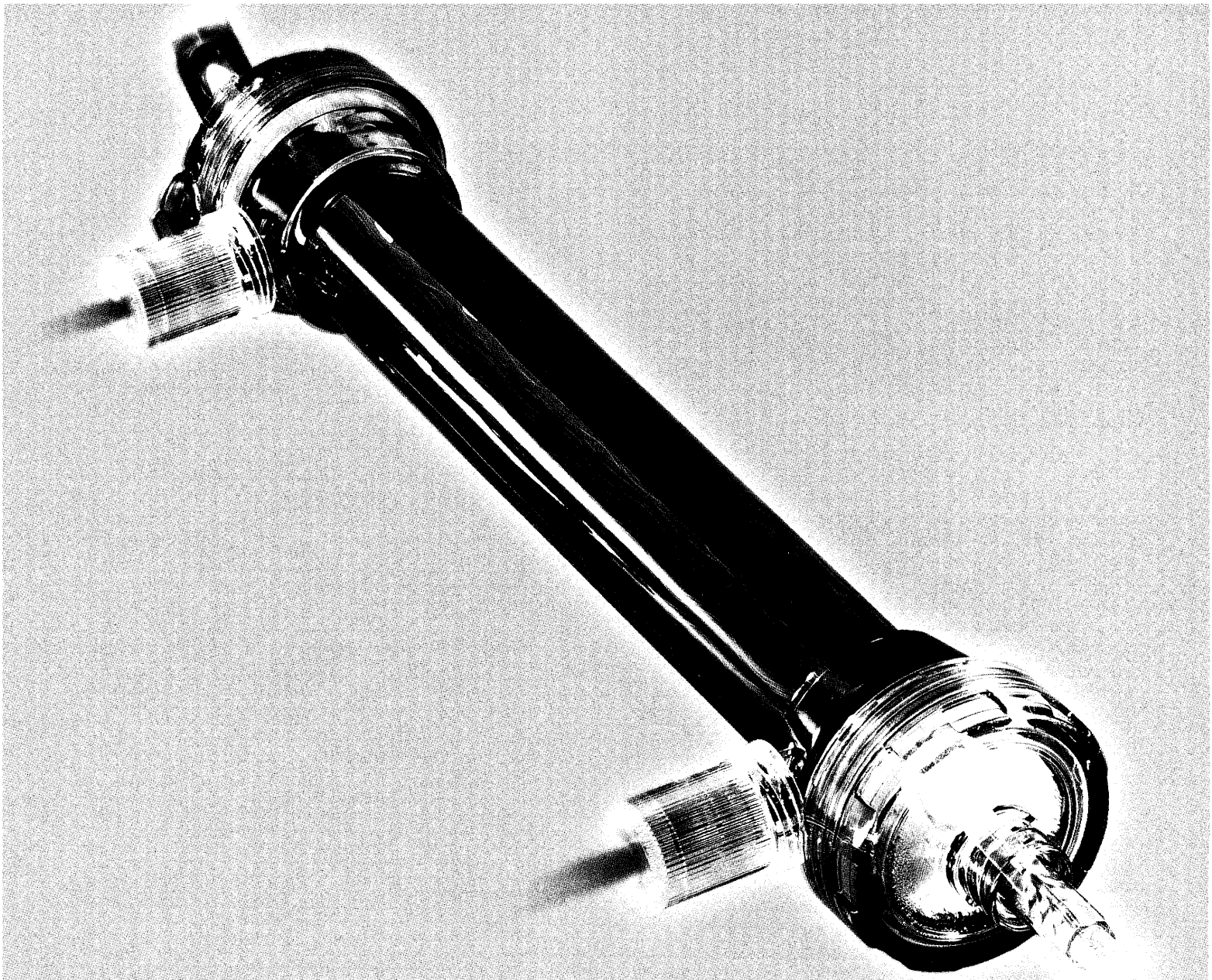

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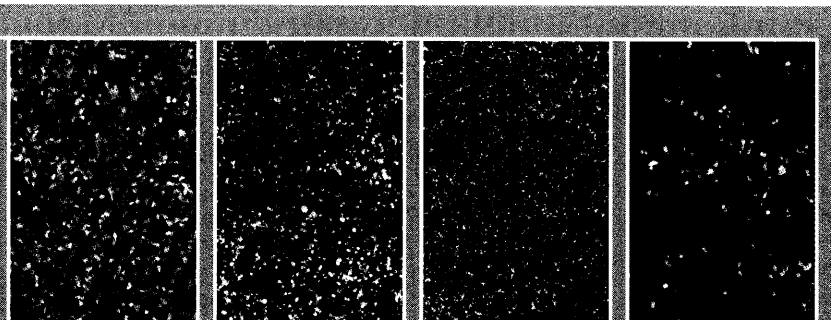

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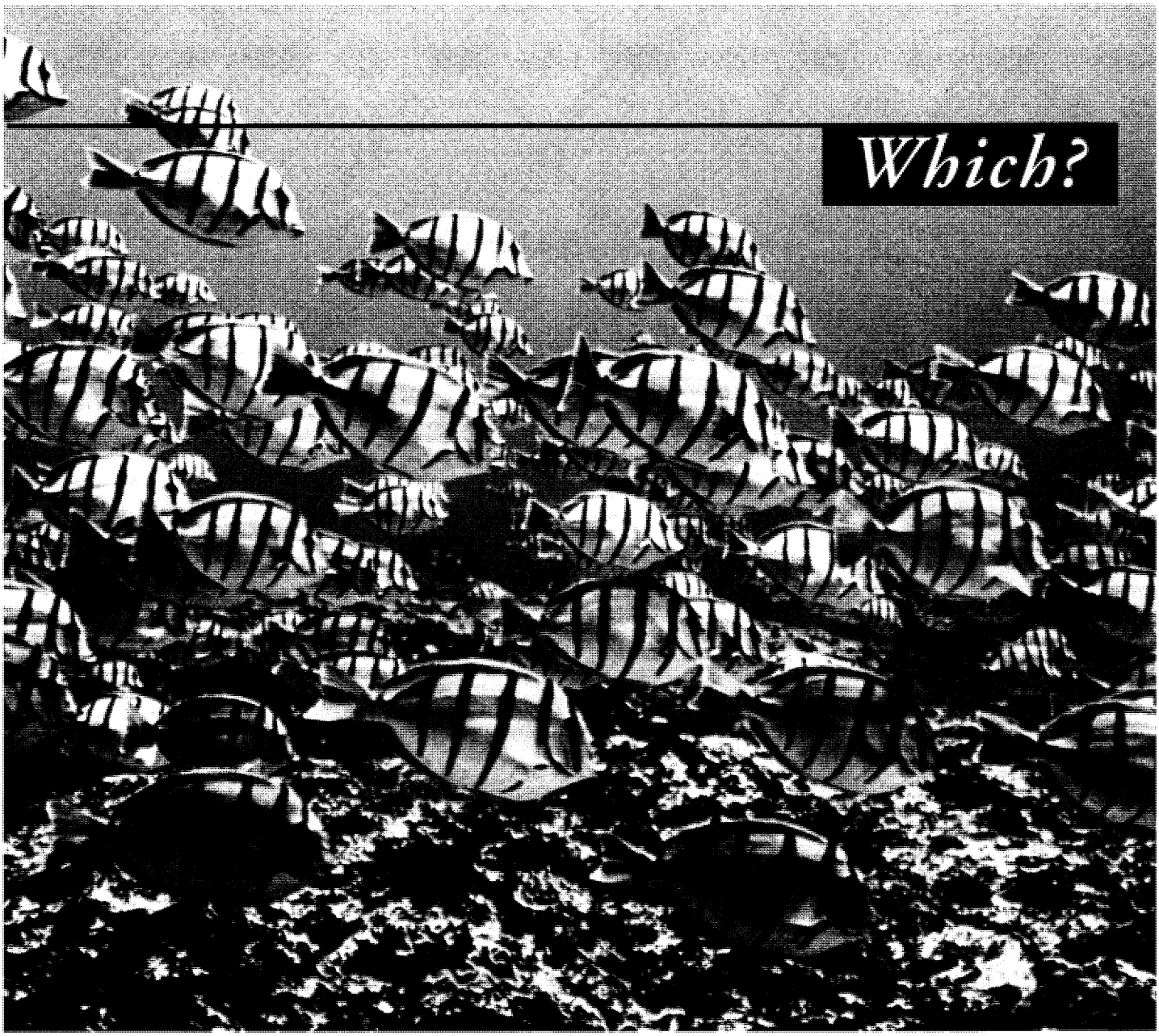

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