14 April 2000

Science

Vol. 288 No. 5464
Pages 217–388 $8

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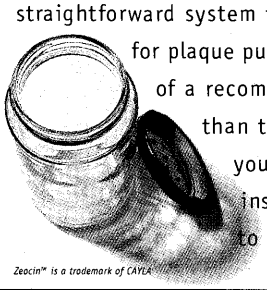

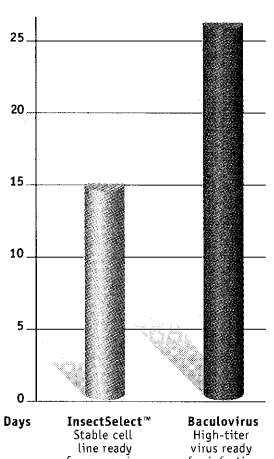

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VOLUME 288 14 APRIL 2000 NUMBER 5464

Science

www.sciencemag.org

COVER This genetically modified mouse lacks the receptor for capsaicin (the pungent ingredient in chili peppers) and no longer avoids the spicy Habanero pepper. These mice also exhibit a reduction in their ability to detect protons or heat under normal or pathophysiological conditions, illustrating a requirement for the capsaicin receptor in detecting diverse modalities of pain-producing stimuli. [Photo: G. Hollopeter and A. DePace]

248
Mice rule

NEWS

NEWS OF THE WEEK

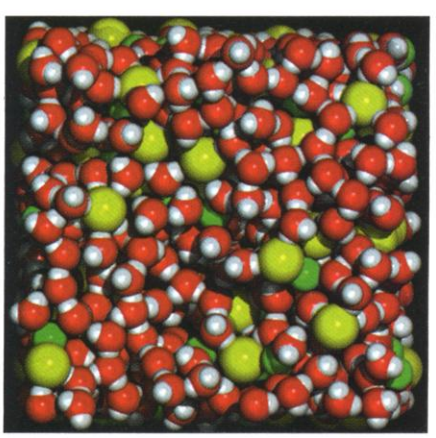
NEWS FOCUS

MOUSE ECONOMY

RESEARCH

RESEARCH ARTICLES

REPORTS



301
Aqueous NaCl aerosol surfaces

DEPARTMENTS

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SCIENCE'S COMPASS

287

PATHWAYS OF DISCOVERY

Infectious History J. Lederberg

In this month's essay, Joshua Lederberg escorts readers on a many-century, transglobal history of the ever intimate and often harrowing cohabitation of humanity and microbes. Ultimate survival, he suggests, may require us humans to embrace a more microbial point of view.

344
Mapping the brain

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SALTY INTERFACE

Reactions between the atmosphere and sea salt aerosols are important for many tropospheric processes. Conventional gas and bulk aqueous phase chemical models have been unable to explain the observed chemistry of these particles, however. Knipping *et al.* (p. 301; see the Perspective by Seinfeld) have now combined experimental observation, computational kinetic modeling, and molecular dynamic and quantum mechanical calculations to show how the production of chlorine gas must occur from NaCl aerosols in the presence of OH^-. Their results demonstrate that the concentration of chloride ions is enhanced at the aerosol surface and that reactions at the air-water interface must dominate.

BURNING QUESTIONS

Carbon monoxide is a pervasive atmospheric pollutant, and identifying its sources is important not only for scientific reasons but for questions related to environmental policy as well. Forest fires are one known source, and anthropogenic fossil fuel burning is another. Wotawa and Trainer (p. 324) have combined ground-based and aircraft measurements with a transport model to identify the origin of an episodic pollution event that affected the southeastern United States in the summer of 1995. By tracing the source of the carbon monoxide to emissions from forest fires in Canada, they show that boreal fires can be important contributors to the pollution budgets of mid-latitude regions.

HISTORY IN TITANIA

The mineral phases within a rock can provide clues to its previous environments. Hwang *et al.* (p. 321) have uncovered a nanometer-sized inclusion of TiO_2 (titania) with an α-PbO_2–type structure sandwiched between two rutile crystals in the diamond-bearing ultrahigh pressure metamorphic rocks of the Erzgebirge in Germany. This phase of titania has not been observed previously in nature, and its recognition provides an important temperature and pressure indicator for the history of deformation in metamorphic rocks (for example, the diamonds in these rocks could have formed over a wider range of pressures and temperatures). This finding indicates that the massif experienced a rapid subduction and burial to depths of greater than 200 kilometers, one of the deepest recorded by any mineral phase, and then was rapidly exhumed.

THE NANOMECHANICS OF RECOGNITION

Intermolecular forces arising from the adsorption of molecules on surfaces are known to induce surface stress. Fritz *et al.* (p. 316) exploit this effect to transduce molecular recognition into nanomechanical responses. Cantilevers were functionalized with biomolecules such as DNA. Molecular recognition of a ligand—such as a complementary DNA strand—was measured as a differential nanomechanical response between differently functionalized cantilevers. This method, which was also demonstrated for protein-protein recognition, does not require labeling, optical excitation, or external probes, is compatible with silicon technology, and may easily be run in parallel.

SELF-CONTAINED OXIDE GROWTH

The layers of silicon dioxide that are used in the gates of MOSFETs (metal-oxide-semiconductor field-effect transistors) cease to be good insulators if they made only a few atomic layers in thickness. Further downsizing of these devices should be possible if other metal oxides with higher permittivity, such as alumina or zirconia, could be used as a dielectric, but if silicon is oxidized during their deposition, the lower capacitance of the silica layer will limit the effectiveness of this approach. Ritala *et al.* (p. 319) modified the method of atom layer deposition so that the reaction chemistry requires no separate oxygen sources. They can deposit thin layers of high-permittivity alumina and other oxides on silicon without forming an intermediate layer of silica.

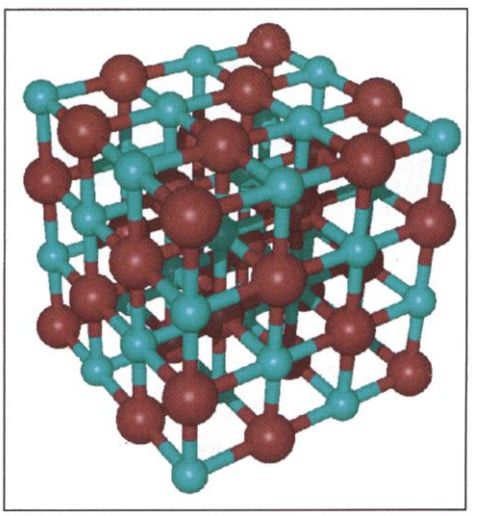
CAN TAKE THE HEAT

The "heat" in hot peppers or from an acid burn turns out to be due to the triggering of one of the same receptors that contributes to the sensation of painful heat. Caterina *et al.* (p. 306; see the cover and the news story by Vogel) have constructed transgenic mice that are lacking the VR1 receptor, a cation channel selectively found in neural ganglia that mediate pain, which opens when activated by capsaicin or protons. These mice can eat chili peppers without painful consequences. The ability of these mice to sense noxious heat is impaired, but not completely eliminated, which suggests that other systems also contribute to heat detection. The VR1 receptor likely integrates stimuli released from tissue damage (such as protons) with the sensation of painful heat to send a rapid danger signal to the brain to remove the animal from the stimulus.

LEAVING TOGETHER

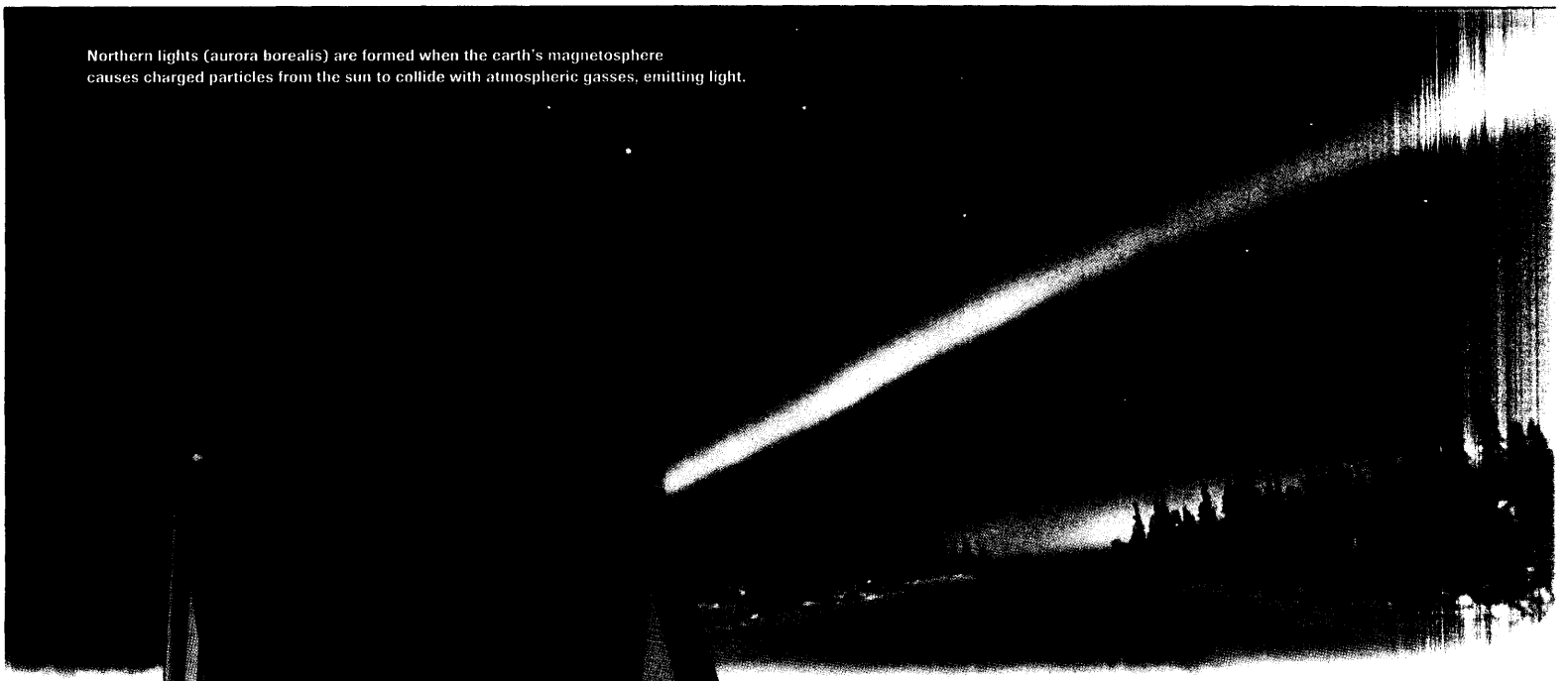
The loss of evolutionary history and biodiversity incurred with the loss of entire genera of threatened animal species is very much worse than if extinction strikes at

STELLAR REMNANTS

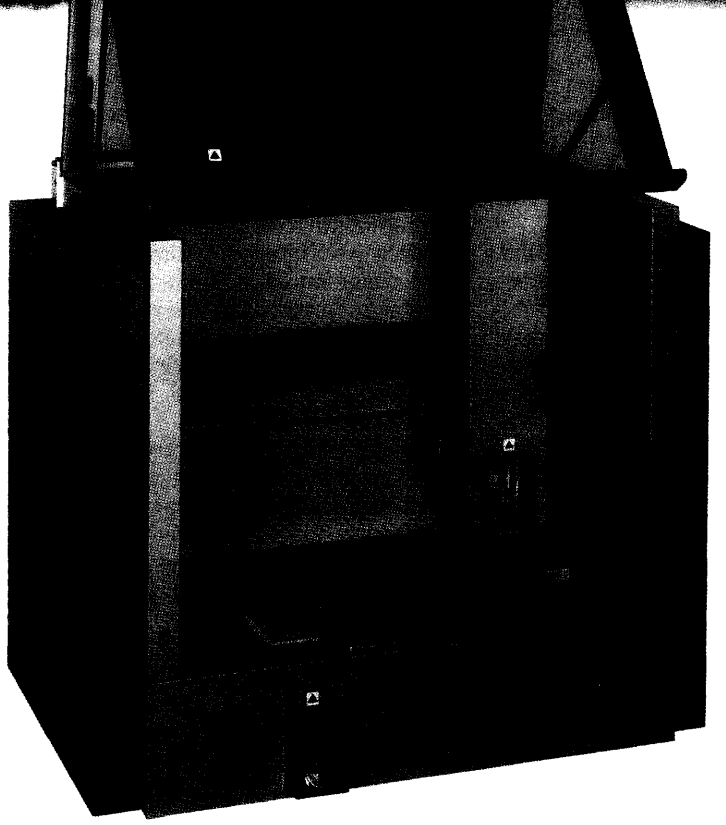


Titanium carbide grains, enclosed in amorphous graphite, have been described in meteorites and inferred to be evolved from asymptotic giant branch (AGB) stars. Von Helden *et al.* (p. 313) now provide a more direct link between these grains and the ejection of a carbon- and titanium-rich superwind from a post-AGB object after the death of the star. They measured the infrared wavelength spectra of TiC clusters in the laboratory and found a 20.1-micrometer peak with a similar width and intensity as the 20.1-micrometer peak that has only been detected in post-AGB objects by the Infrared Space Observatory. Combining meteoritic and spectral observations, they calculate the density and mass loss rate of the superwind coming from these post-AGB objects.

CONTINUED ON PAGE 227



Northern lights (aurora borealis) are formed when the earth's magnetosphere causes charged particles from the sun to collide with atmospheric gasses, emitting light.



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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 225

random, as is commonly assumed. Purvis *et al.* (p. 328) show that extinction risk is, in fact, unusually high for bird and mammal species that have few close relatives, and they also show that closely related species have unusually similar risks of extinction.

CHAPERONE SELECTION

Secretory and plasma membrane proteins begin their life with cotranslational translocation into the endoplasmic reticulum (ER). Inside the ER, the correct folding of newly synthesized proteins is assisted by a group of chaperone molecules including binding protein (BiP) and the lectins calnexin and calreticulin. Molinari and Helenius (p. 331) found that chaperone selection occurs cotranslationally and describe some of the criteria that select for a particular chaperone. The position of carbohydrate chains in the nascent chain of the protein diverted it from an interaction with BiP to an interaction with calnexin and calreticulin.

TOXIN AND PHAGE SECRETION

Cholera toxin is secreted from *Vibrio cholerae* bacteria harboring the filamentous bacteriophage CTXϕ. Davis *et al.* (p. 333) examined the requirements for release of new phages from infected bacteria and discovered that a protein known to be involved in secretion of cholera toxin, EpsD, was also required for phage release. This finding is unexpected given the different size and nature of a protein toxin versus a protein-coated DNA molecule.

EXECUTING THE EXECUTIONER

Amyotrophic lateral sclerosis (ALS) is characterized by rapid death of motor neurons in the brain and spinal cord and results in paralysis and death, usually within 5 years of disease onset. The discovery of mutations in the *SOD1* gene, which encodes a copper zinc superoxide dismutase, in a familial form of the disease enabled the creation of a mouse model of ALS in which the mice overexpress a mutant version of human *SOD1*. Li *et al.* (p. 335; see the Perspective by Gurney *et al.*) now demonstrate that motor neurons in the ALS mice die by apoptosis. By blocking the activity of caspase enzymes, the cell's executioners during apoptosis, with the inhibitor zVAD-fmk, they dramatically prolonged survival of the ALS mice. These findings suggest that caspase inhibitors may be beneficial in the treatment of ALS, particularly if combined with other neuroprotective drugs.

AN EVOLVING VIEW OF HCV INFECTION

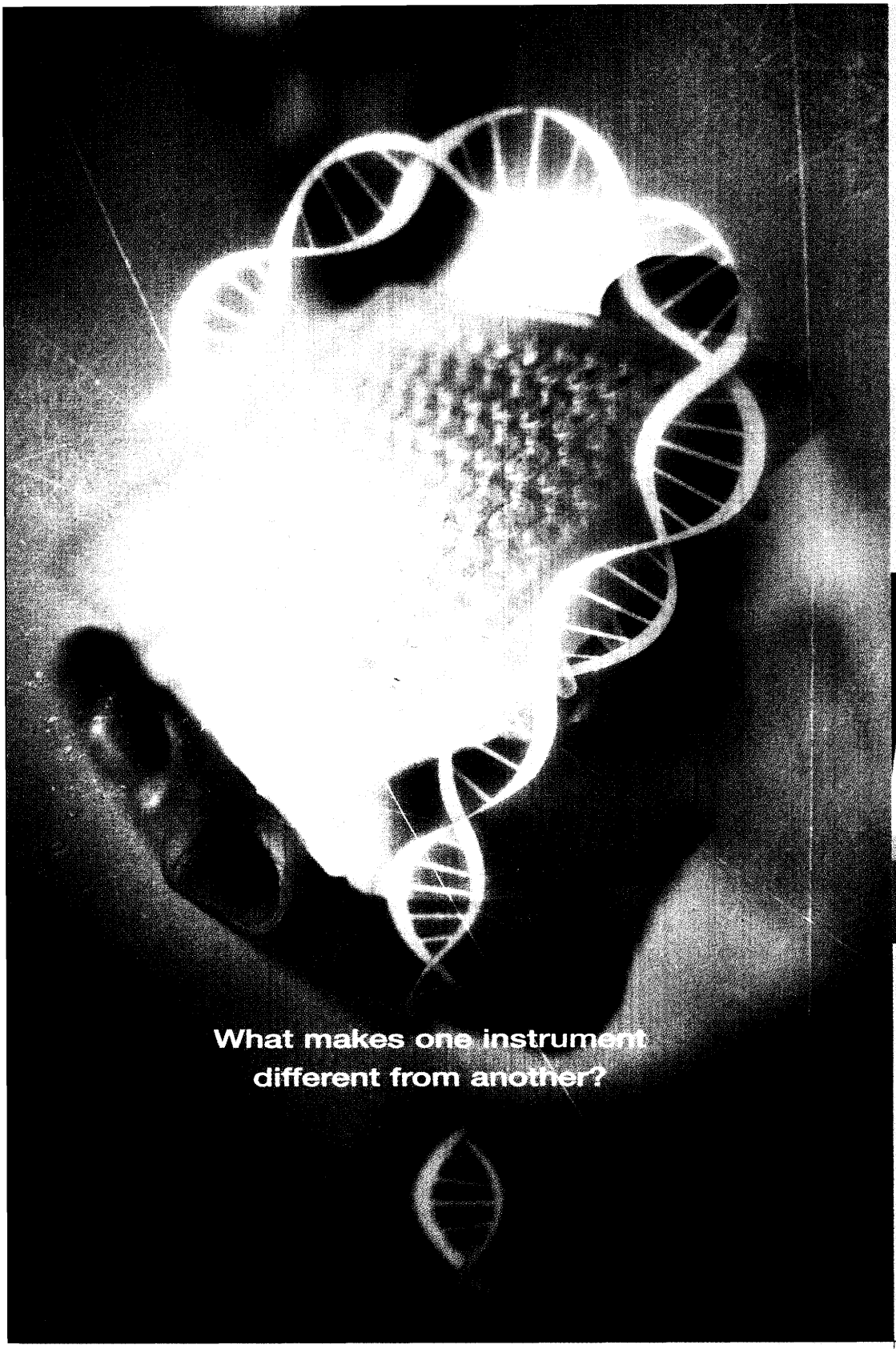
Infection with hepatitis C virus (HCV) is a major public health problem that affects 170 million individuals worldwide. The vast majority of infected individuals develop chronic disease that can remain stable over many decades, whereas others successfully clear the virus soon after infection. To identify factors that might contribute to these diverse clinical outcomes, Farci *et al.* (p. 339) examined the evolution of sequences in the HCV envelope genes at early stages of infection. In patients who developed chronic disease, HCV evolved rapidly and showed a much greater genetic diversity than did HCV from patients who cleared the virus. These results suggest that analysis of viral sequence changes early in infection may be a useful tool for predicting clinical outcome.

DIVIDING UP THE WORK PLACE

During development, areas of the mammalian neocortex acquire specialization and thus different tasks, such as interpreting touch or directing reach, are parceled out to different areas. At least some of the specialization is directed by input from other regions of the brain. Bishop *et al.* (p. 344) now show that the specialization is not entirely dependent on neuronal input—rather, some component of the areal specialization is determined by genes expressed in the cortical cells themselves. Two genes, *Emx2* and *Pax6*, act in opposition to determine the rostral-caudal pattern of neocortical areas, thus establishing the basics of cortical areal specification.

RECOGNIZING LANGUAGE

Although there might be general agreement that language, as commonly understood, is an ability limited to humans, it may nevertheless rely upon component skills that could be present to some extent in nonhuman primates. Ramus *et al.* (p. 349; see the Perspective by Werker and Vouloumanos) provide evidence for at least one of the skills using parallel training and testing paradigms to assess the comparative abilities of human newborns and tamarin monkeys. They find, replicating earlier work, that newborns can discriminate between rhythmically distinct languages when spoken forward but not backward. Surprisingly, the monkeys are equally adept, indicating that they do possess processing skills that help identify a sequence of sounds as language.



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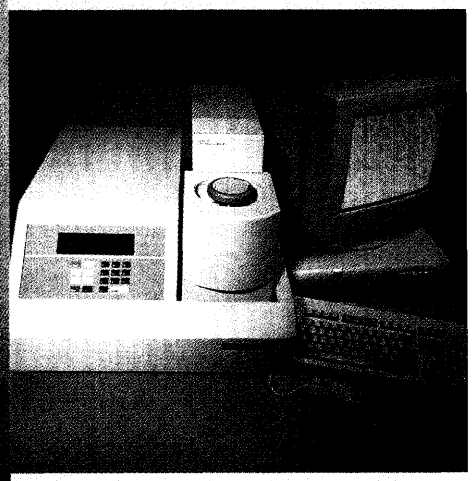

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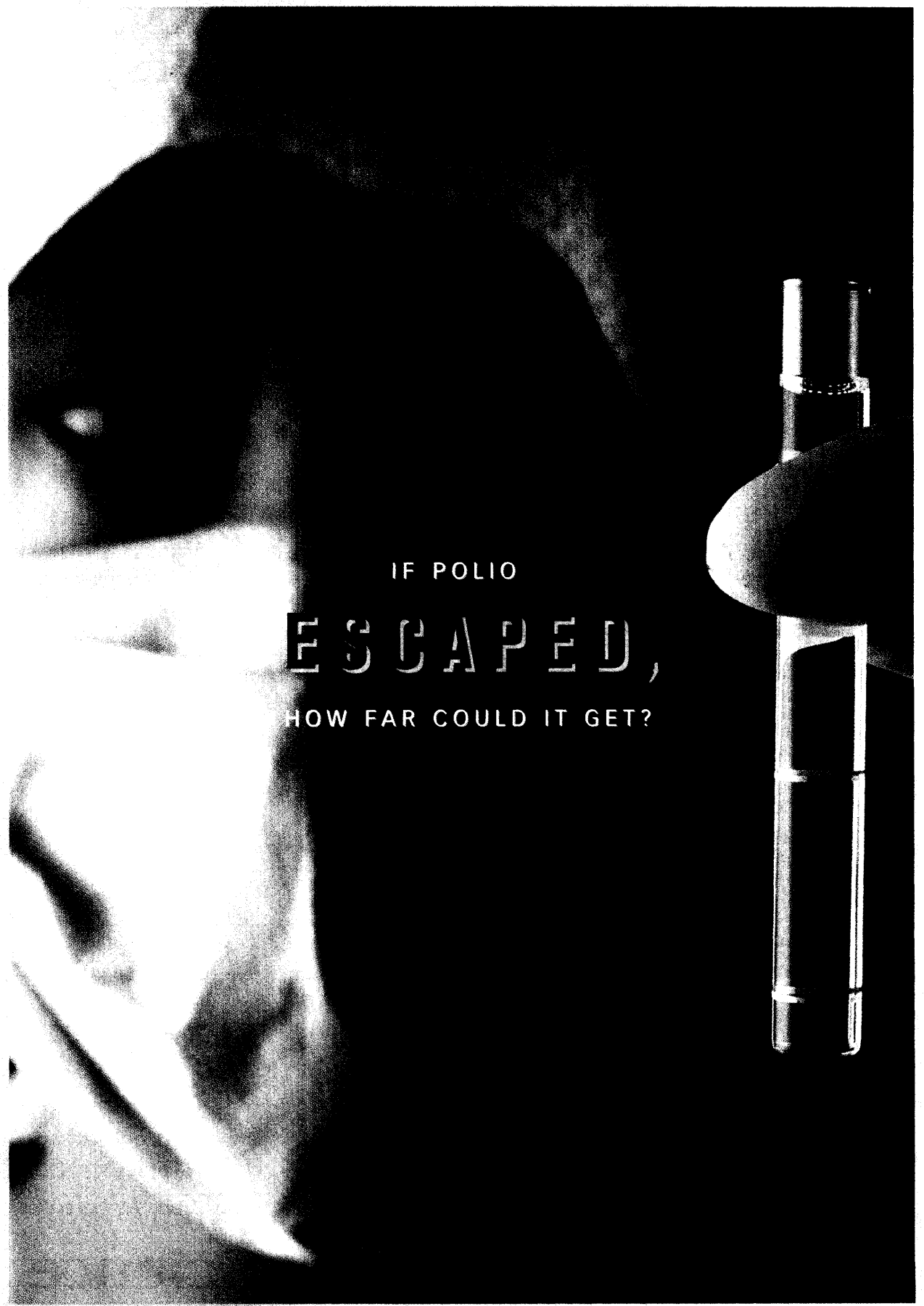
IF POLIO
ESCAPED,
HOW FAR COULD IT GET?

HELP DEFEAT THE SILENT CRIPPLER.

One of the most significant health achievements in history should soon take place. By the end of the year 2005, we should be able to certify that the scourge of polio has been wiped from the face of the earth forever.

Over the last decade, the number of polio cases worldwide has decreased by ninety percent. In 1999, 5,000 cases were identified.

But the world can't celebrate yet. Nor can we be complacent. Polio won't miss any opportunity to escape. If momentum is lost now, if a serious outbreak is allowed to occur, the effort to eradicate the disease could be set back for years, or even lost forever.

Investing in this last battle won't be inexpensive. The World Health Organization estimates it will take an additional $300 million. But the returns on the investment will be enormous. Suffering, paralysis and premature death will be greatly reduced. And billions of dollars in future immunization costs will be saved.

The benefits of this effort extend far beyond the disease itself. A worldwide culture of prevention will be created. Doctors and nurses will have access to vulnerable populations otherwise cut off from health services. And the infrastructure will be in place to target other killer diseases such as AIDS, malaria and tuberculosis.

What remains to be done? Money must be raised. Volunteers have to be recruited. Health professionals need to ensure that every child in every country has been vaccinated. Then, for the next several years, comprehensive worldwide monitoring must take place to watch for any further signs of the disease.

The eradication of polio has to happen only once in the history of the world. The disease is on the verge of extinction. Now is the time to finish the job.

THE POWER AND PROMISE OF VACCINES

No one is safe from an infectious disease unless everyone is safe. Vaccines offer the greatest potential for improved global health. Existing vaccines have become more affordable, and delivery methods increasingly successful. At the same time, efforts are continuing to make vaccines even safer, simpler and available for a wider spectrum of diseases. Aggressive programs to develop vaccines for malaria, tuberculosis and AIDS are underway right now. Success will mean healthier lives for billions of people, and greater opportunities for entire countries.

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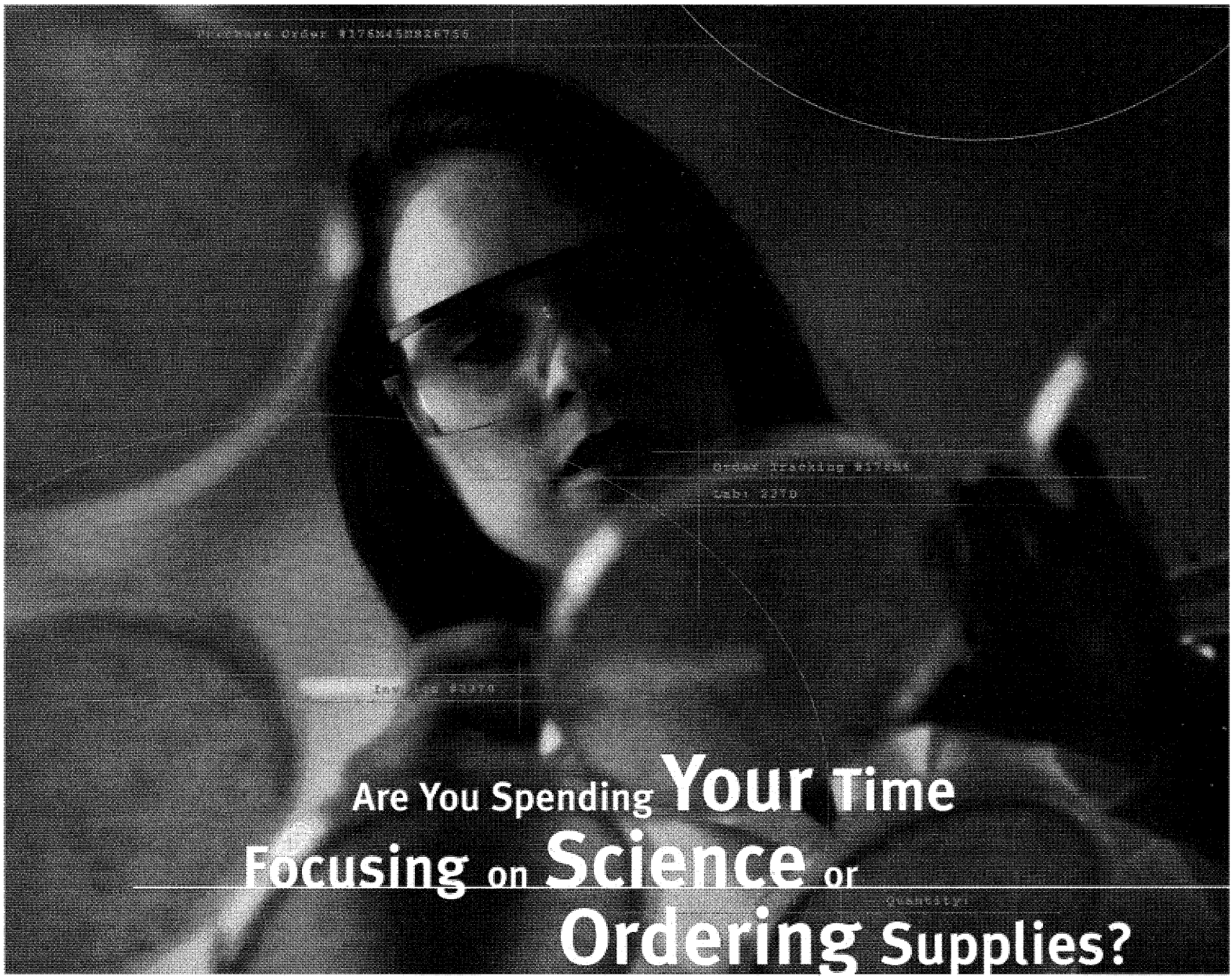

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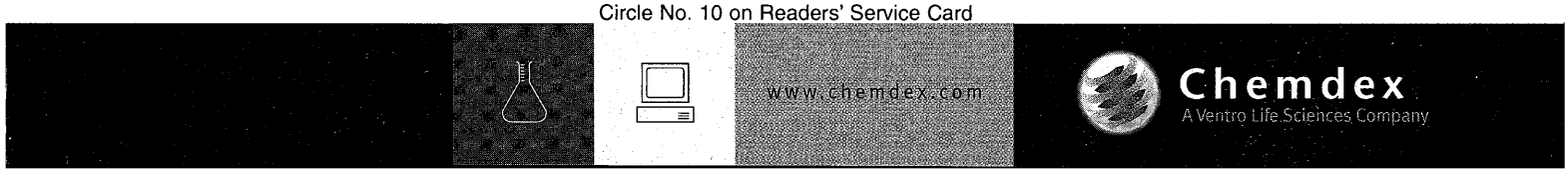

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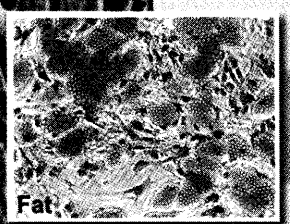

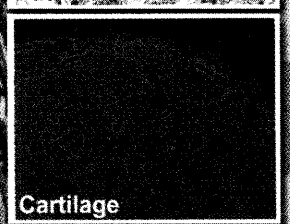

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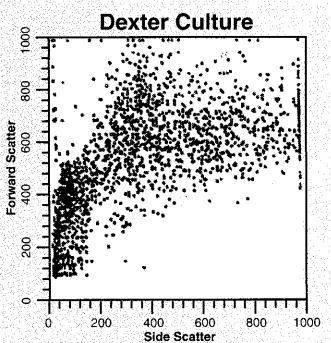

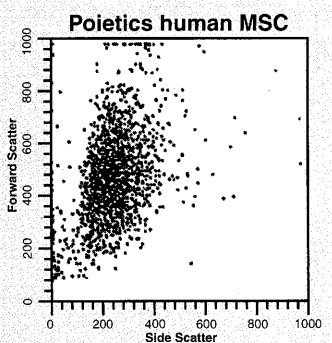

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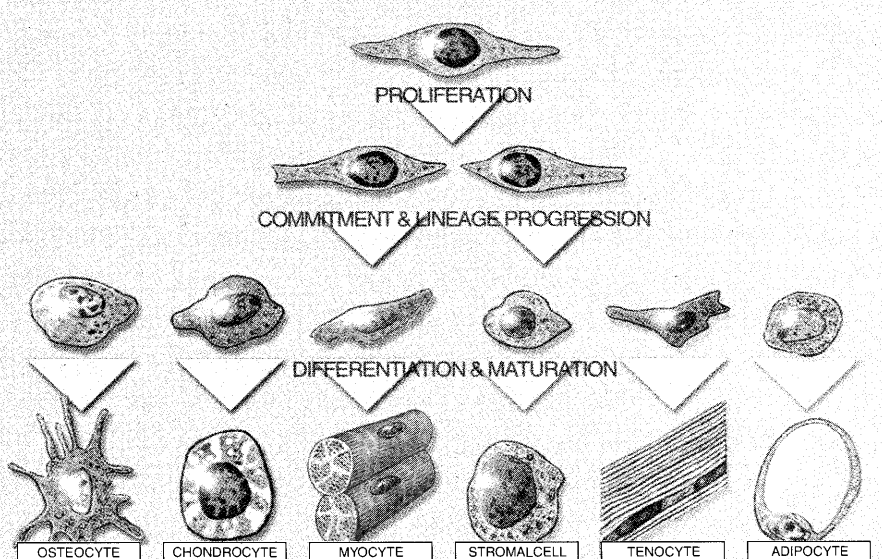

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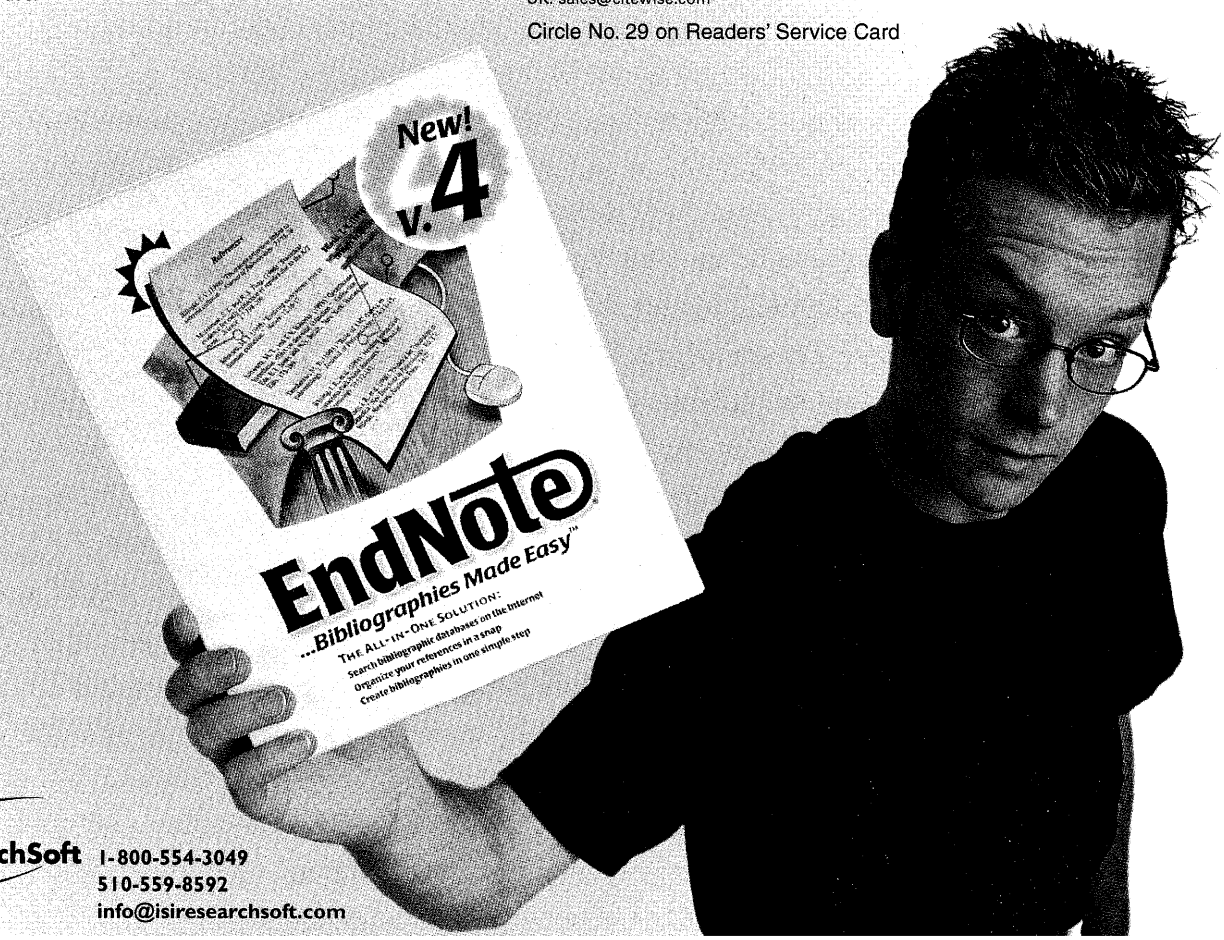

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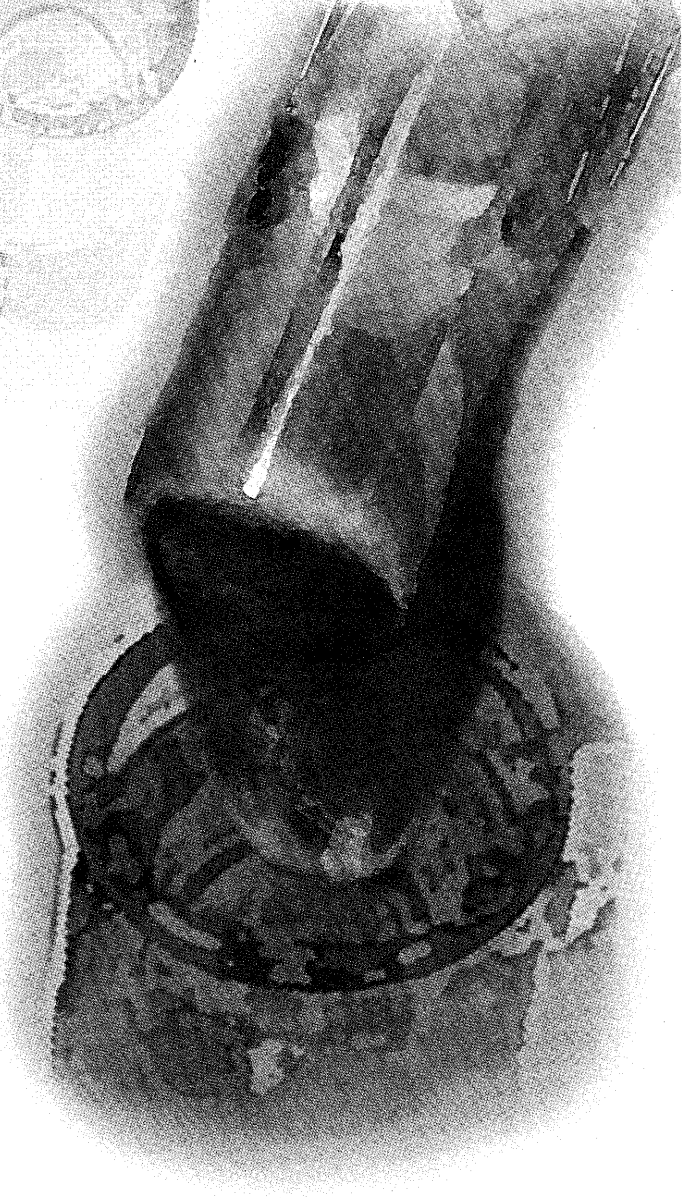

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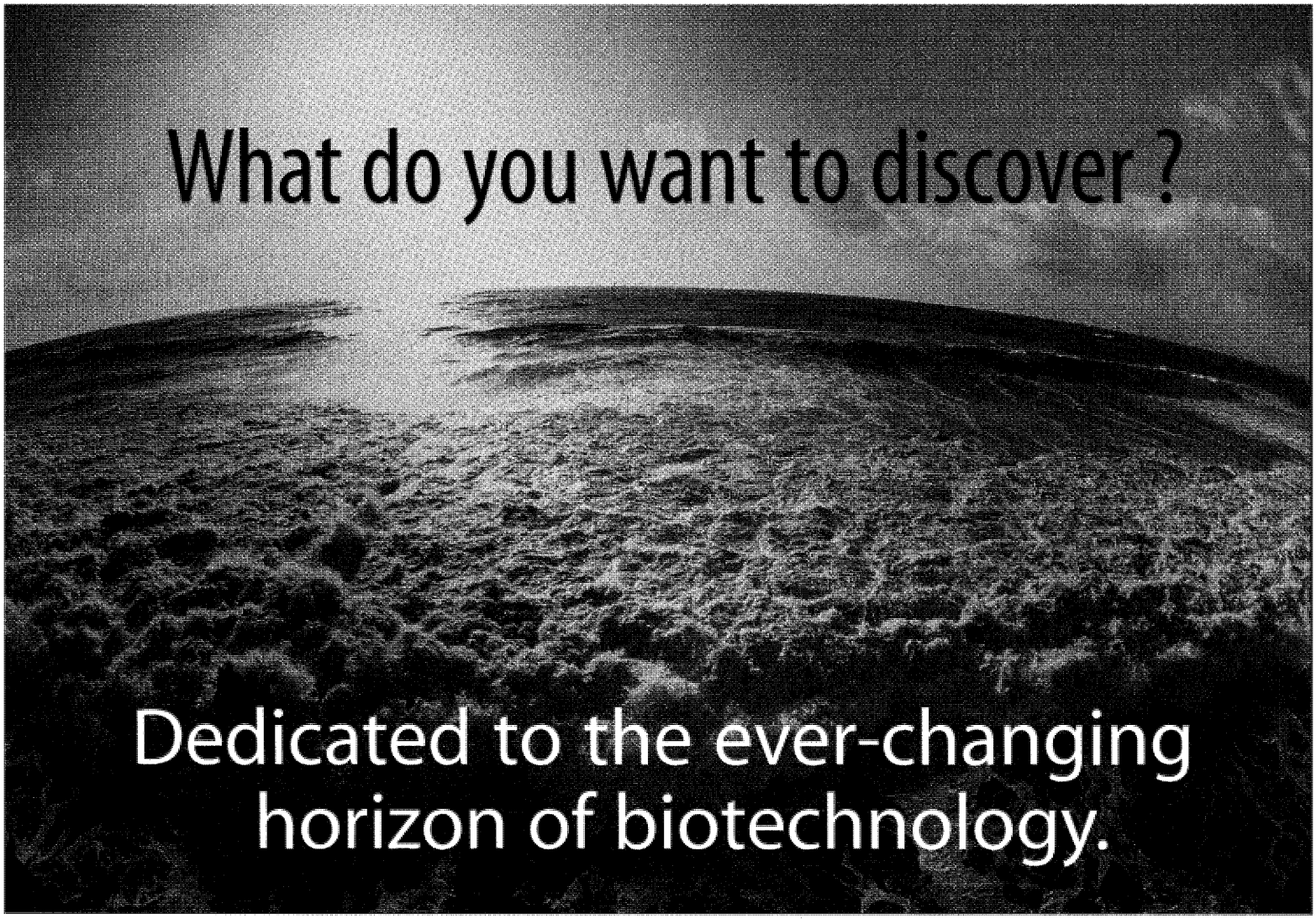

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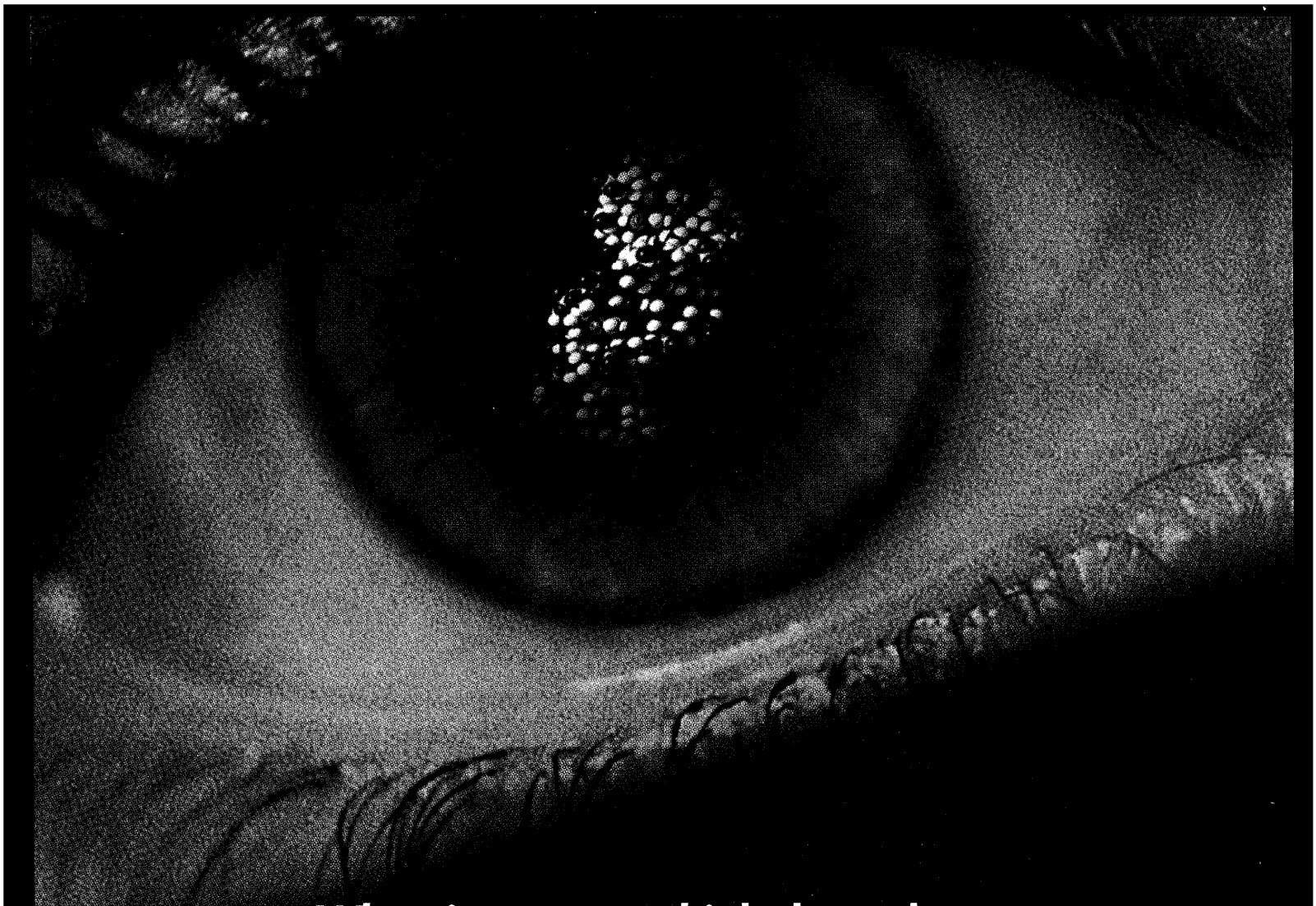

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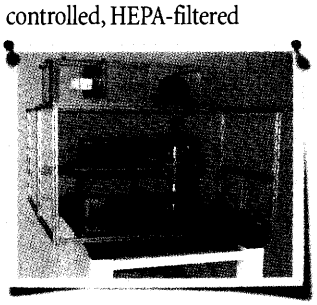

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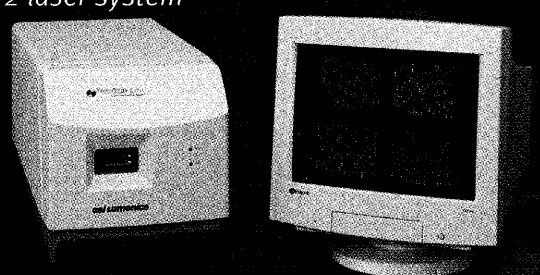

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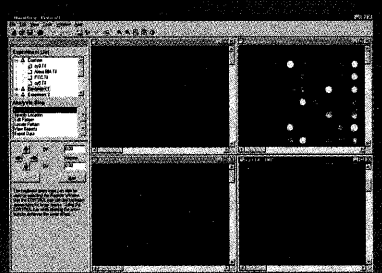

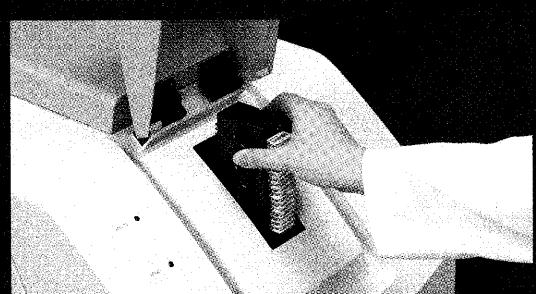

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2000 Tyler Prize

John P. Holdren, Ph.D.

Harvard University

The Tyler Prize Medallion

The Tyler Prize Executive Committee announces the award of the Tyler Prize for Environmental Achievement to John P. Holdren, Ph.D. of Harvard University. Dr. Holdren is an authority on energy technology and policy, global climate change, and nuclear nonproliferation, whose research and leadership have mobilized the international community of scientists and policymakers to take action on these and other critical environmental issues.

Dr. Holden is the Teresa and John Heinz Professor of Environmental Policy at the John F. Kennedy School of Government and Professor of Environmental Science and Public Policy Department of Earth and Planetary Sciences at Harvard University.

As a researcher, analyst, educator, and member of the President's Committee of Advisors on Science and Technology, Dr. Holdren has helped shape the global energy debate. He co-founded and co-directed for more than 20 years the Energy and Resources Group, a pioneering graduate program at the University of California, Berkeley, whose graduates hold leadership positions around the world in the fields of energy, environment, development, and international security.

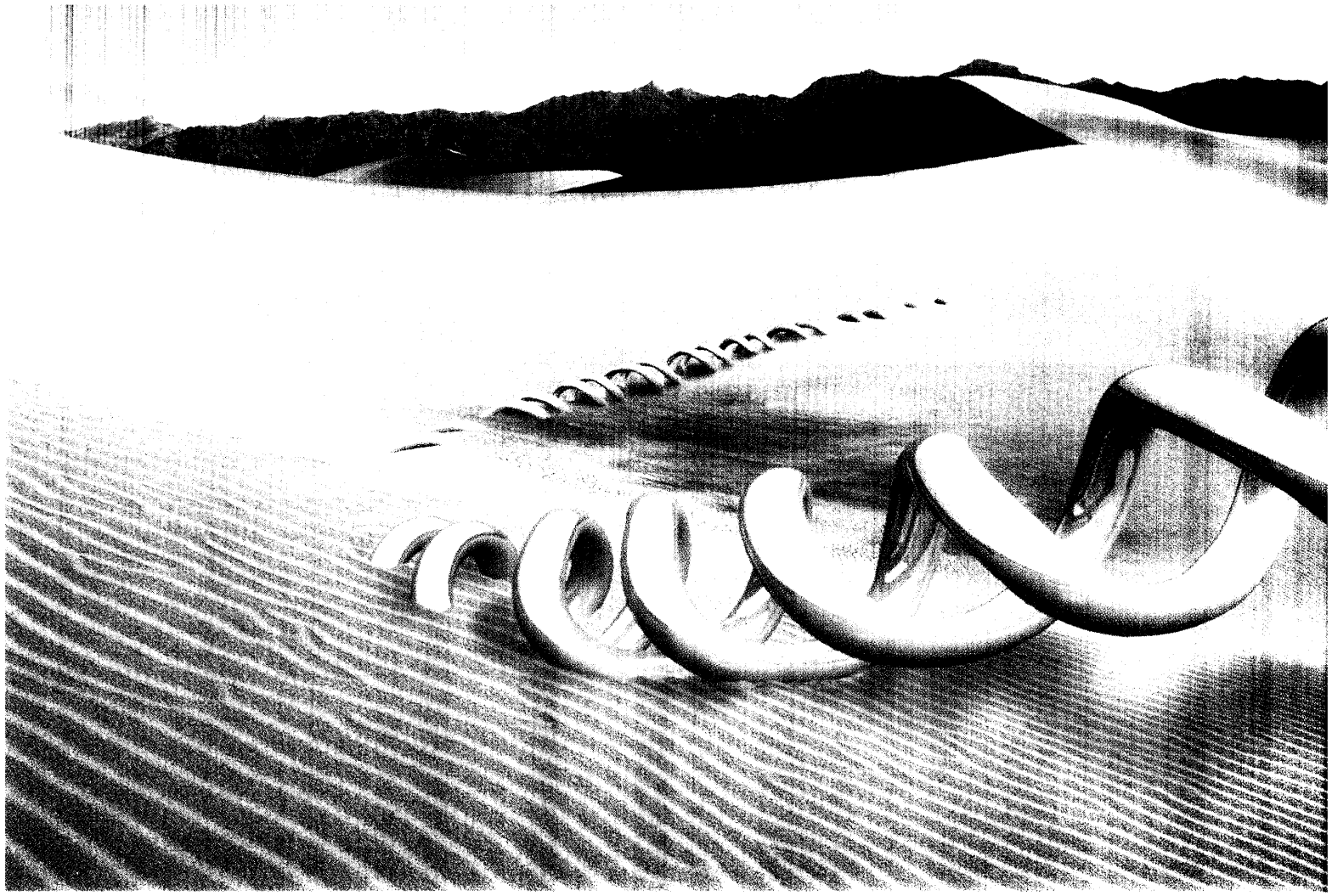
Dr. Holdren's capacity to analyze the most demanding problems at the intersection of science and the human condition, illuminate the connections between problems and solutions, and carry these insights to the highest levels of decision making have made a significant and lasting contribution toward improving and safeguarding environmental conditions for us all.

Tyler Prize

The Tyler Prize was established in 1973 by the late John and Alice Tyler as an international award honoring achievements in environmental science, energy, and medical discoveries of worldwide importance conferring great benefit on humanity. The Tyler Prize consists of a cash award of $200,000 and the Tyler Prize gold medallion.

For additional information contact Dr. Jerome Walker, Executive Director, The Tyler Prize
Phone 213-740-9760, Fax 213-740-1313, Email tylerprz@usc.edu
Home page www.usc.edu/tylerprize

The Tyler Prize is administered by the University of Southern California



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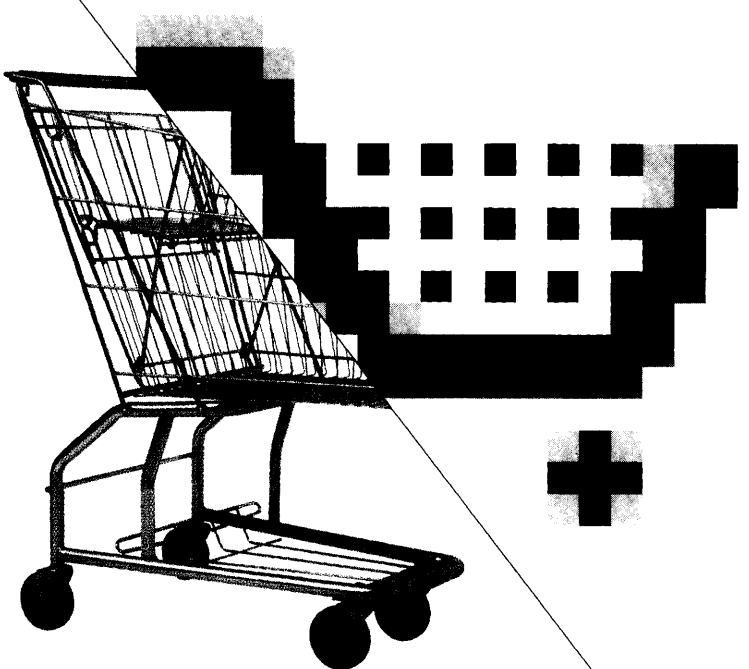

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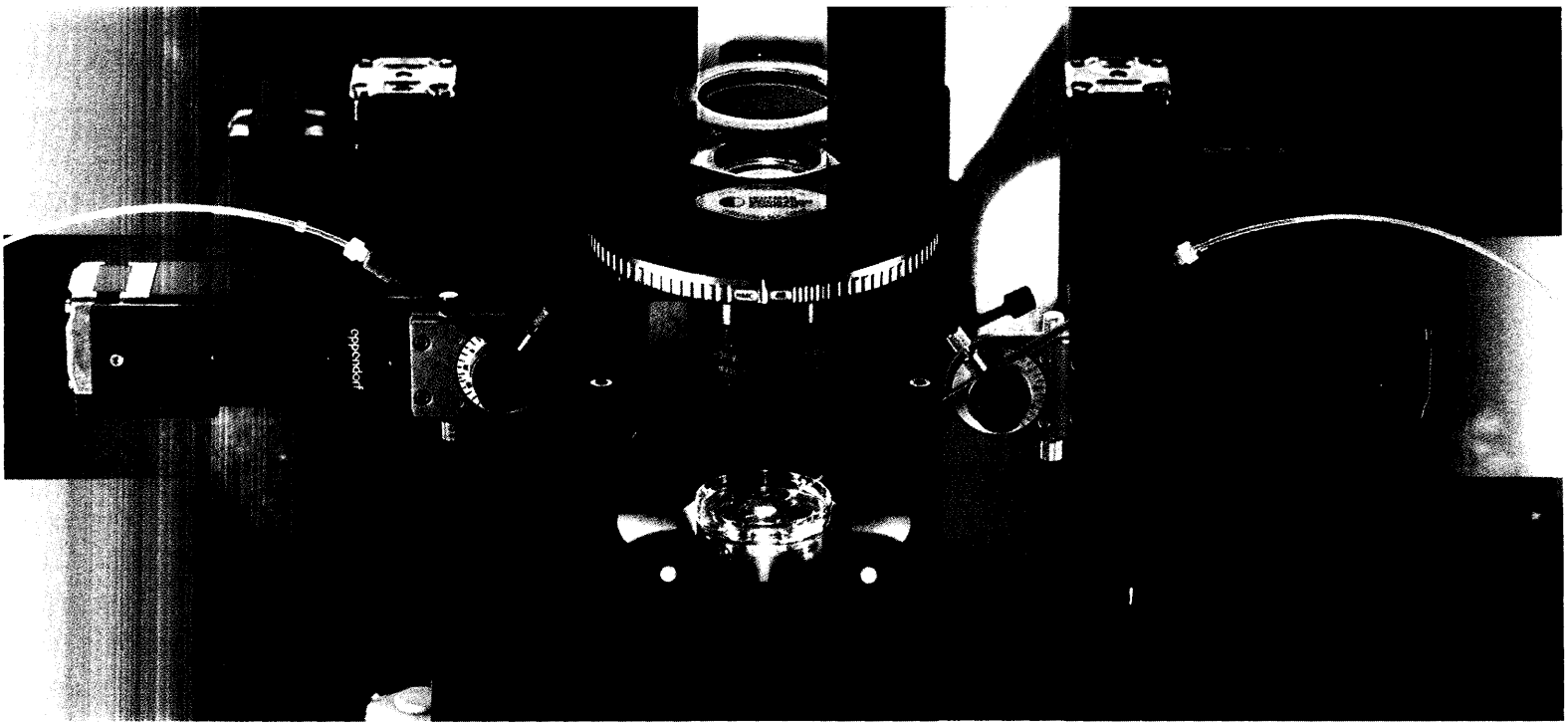

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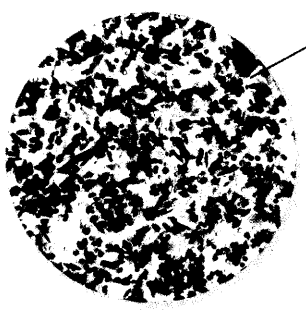

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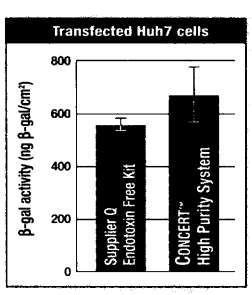

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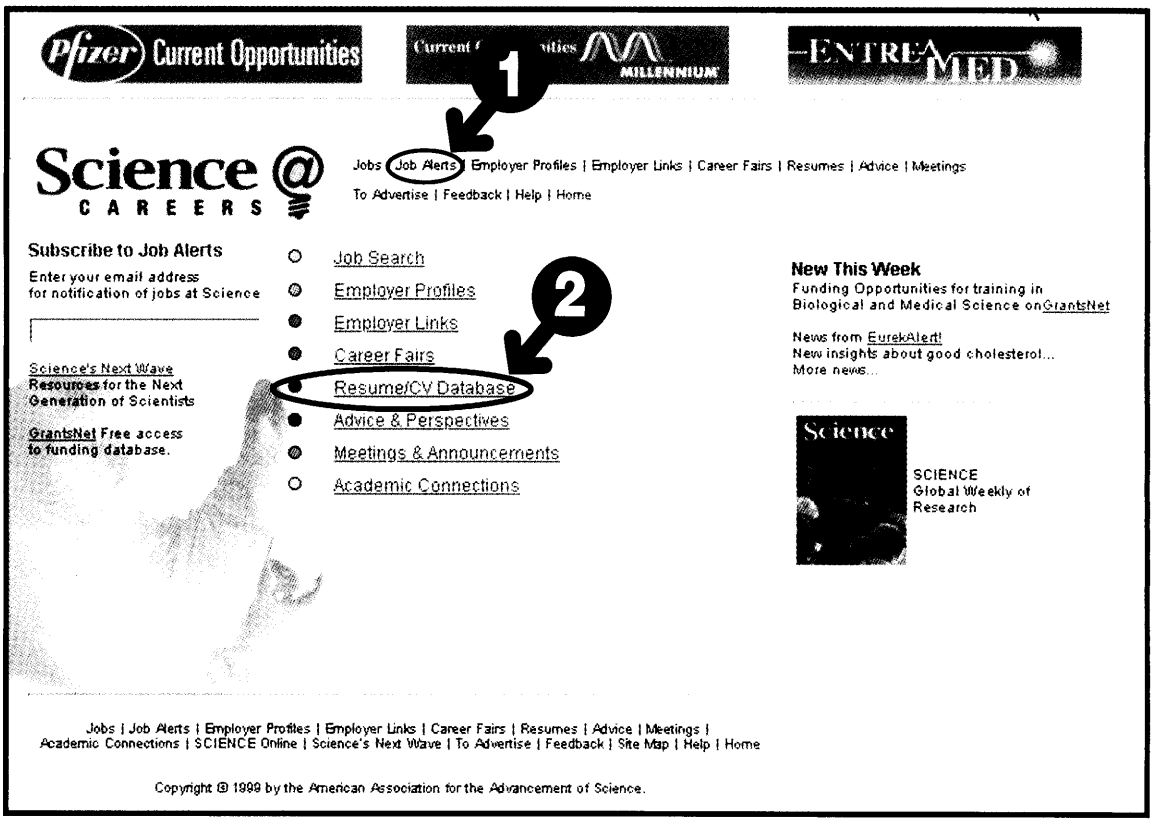

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