16 April 1999

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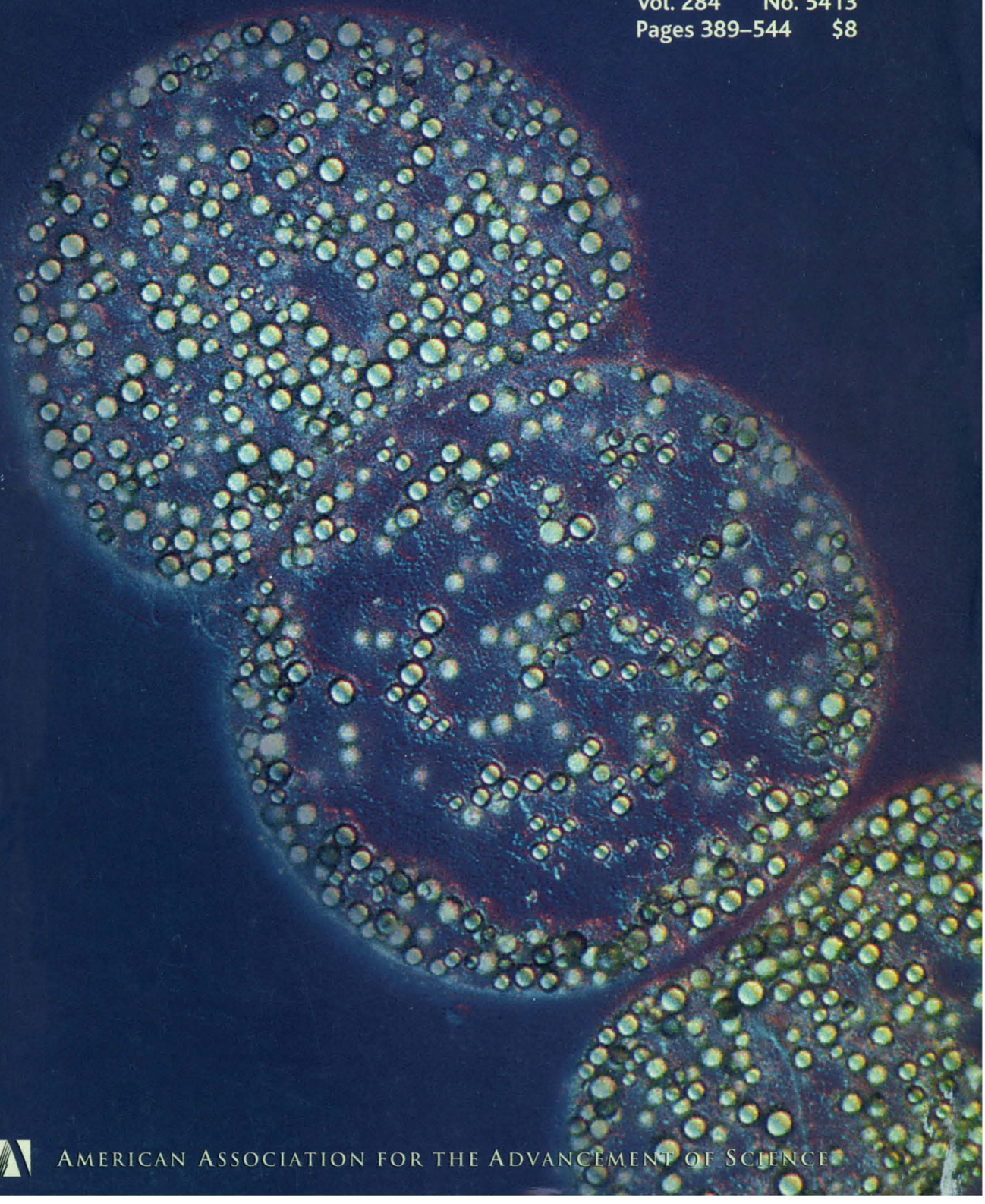

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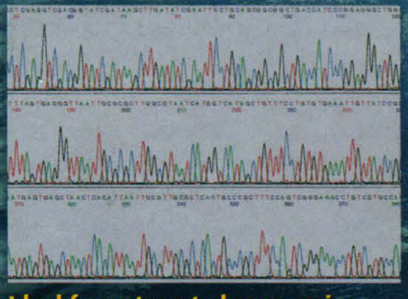

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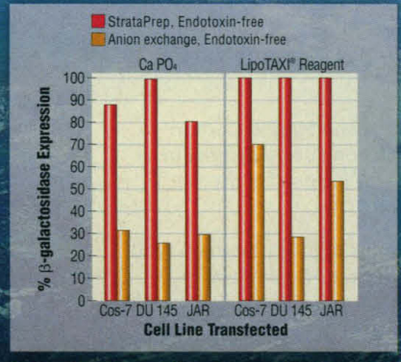

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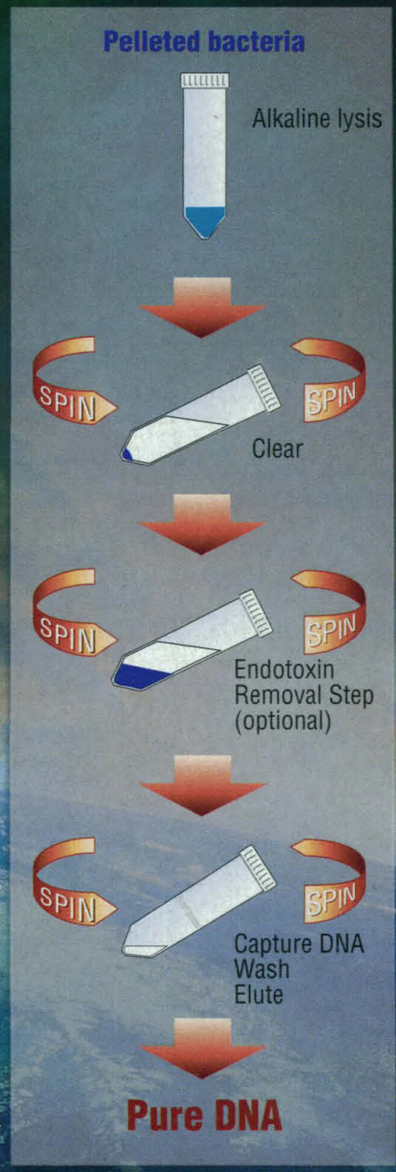

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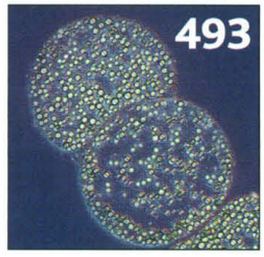

COVER A large sulfur bacterium, *Thiomargarita*, was discovered in sediments off the coast of Namibia that breaks records of size among bacteria. The photomicrograph shows three cells under polarized light (middle cell is ~0.2 mm in diameter), and the small yellow spheres are sulfur globules that are restricted to the thin outer layer of the cell. These bacteria oxidize sulfide using nitrate, coupling the nitrogen and sulfur cycles in the sediment. [Image: Ferran Garcia-Pichel]

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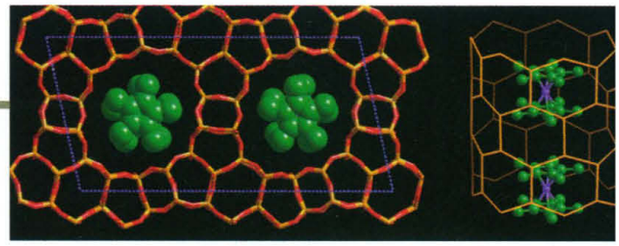
Warheads meet their match?

NEWS

NEWS OF THE WEEK

NEWS FOCUS



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Crystal-clear structures

RESEARCH

RESEARCH ARTICLE

REPORTS

DEPARTMENTS

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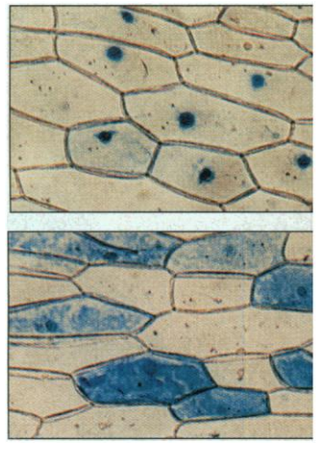

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A CORE FULL OF JELLY

The solid inner core jiggles around within the liquid outer core, and the period of oscillation of some of the modes have been measured with superconducting gravimeters. Smylie (p. 461) estimated the viscosity just above the inner core boundary by assuming that the Coriolis acceleration balances the viscous forces within the boundary layer and that the derived periods of oscillation should match the gravimeter measurements. The estimated viscosity for the boundary layer, 1.22×10^{11} Pascal seconds, is also consistent with a two-phase fluid model of the boundary layer, in which iron-rich liquid and solid iron particles rain down to the inner core.

GLOBAL WARMING FEEDBACKS

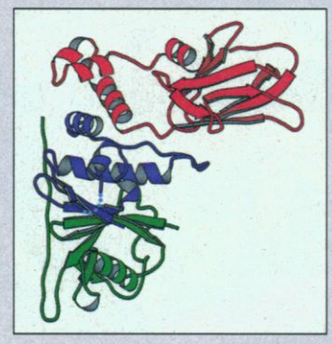
Increasing concentrations of greenhouse gases, particularly carbon dioxide (CO_2), are threatening to increase global surface temperatures. The combination of higher CO_2 and higher temperatures may create positive feedback loops between the atmosphere, the ocean, and the terrestrial biosphere, but our understanding of many of the underlying mechanisms remains limited. Joos *et al.* (p. 464) use a simple model representing oceans, the atmosphere, and the biosphere (both marine and terrestrial). They apply a wide range of scenarios for global CO_2 emissions and atmospheric CO_2 concentrations that have been published by the Intergovernmental Panel for Climate Change and then analyze the role of the ocean circulation and ocean biosphere in oceanic carbon uptake. At high atmospheric CO_2 concentrations, North Atlantic circulation collapse leads to a significant reduction in carbon uptake because of reduced mixing, whereas at lower CO_2 values, the key factor that reduces uptake is sea surface warming.

MINI MAGNETS

The demands for greater computer memory will likely push the size of magnetic storage bits ever smaller; two reports focus on the motion and orientation of nanoscale magnetic domains. A simple method for following the motion of a submicrometer-sized magnetic domain is presented by Ono *et al.* (p. 468). The resistivity of a sandwich of two ferromagnetic layers separated by a nonmagnetic metal layer depends on the relative magnetization directions. As a small domain propagates through one ferromagnetic layer, it switches the magnetization direction and decreases the resistivity on a microsecond time scale. How small can a magnetic domain be and hold a magnetic orientation? Below the superparamagnetic limit (~10 nanometers for cobalt, for example), thermal fluctuations alone will cause switching of the magnetization direction. Majetich and Jin (p. 470) used the Foucault method of Lorentz microscopy to image such direction changes in nanoparticles of $SmCo_5$, magnetite (Fe_3O_4), and carbon-coated iron-cobalt alloys. Such studies allow the effects of surface roughness and modification on the dynamics of magnetization to be measured.

TUMOR SUPPRESSION AND PROTEIN DEGRADATION

Mutations in the von Hippel–Lindau (VHL) tumor suppressor are associated with cancer of the kidney and the central nervous system. Stebbins *et al.* (p. 455) describe the crystal structure of the VHL protein in complex with



ElonginB and ElonginC, two components that together with ElonginA are involved in transcriptional regulation. The VHL protein contains two structural domains, α and β. The former appears to contain a structural motif similar to one known as SOCS (suppressor of cytokine signaling) and binds to ElonginC, and many of the known mutations map to this interface. The β domain also contains a surface hotspot at which many of the other known mutations cluster, which suggests that a functionally important and as yet unidentified partner binds at this site. On the basis of sequence and structural similarities to other components, the authors propose that the VHL protein might also connect to pathways involving protein degradation.

SETTING CO STRAIGHT

Early studies of carbon monoxide (CO) toxicity found that binding of CO to heme proteins, such as myoglobin (Mb), was much weaker than to bare porphyrin complexes, and crystallographic studies offered an explanation—CO adopted a "bent" geometry in the heme proteins caused by steric effects, whereas in bare complexes it could adopt a linear conformation (perpendicular to the porphyrin) and form a stronger bond. However, recent spectroscopic studies have questioned the bent heme geometry. Kachalova *et al.* (p. 473) now report a 1.15 angstrom resolution study at room temperature of deoxy and CO-ligated Mb, which shows that CO indeed adopts a linear geometry in the MbCO complex; concerted protein motions needed to overcome steric inhibition during binding cause the reduced affinity.

PULLING TWO PATHWAYS TOGETHER

Two growth factors, LIF and BMP2, function together during differentiation of astrocytes. Each growth factor stimulates its own receptor and signaling pathway leading to distinct transcription factors, yet together they support differentiation of neural progenitor cells. Nakashima *et al.* (p. 479; see the Perspective by Janknecht and Hunter) now show that the molecular basis of this cross talk lies in formation of an unexpected complex. The transcription factors from the two pathways, STAT3 and Smad1, bind to opposite ends of the transcriptional coactivator p300 thereby coordinating these two signals.

KILL THE MESSENGER?

Gene expression can be controlled at many different levels. Laroia *et al.* (p. 499) examine the mechanism used by cytokines and proto-oncogenes that limits the usage of their messenger RNA (mRNA) template by degrading them rapidly (within 5 to 30 minutes, compared to hours for other mRNAs). In the mRNA degradation pathway, the protein AUF1 normally binds to a sequence element in the 3′ untranslated region, and this structure is subsequently degraded. However, under the stress of higher temperatures, the heat shock protein prevents AUF1 from recruiting the mRNA to the ubiquitin-proteasome degradation pathway. Hence, a link is made between heat shock, rapid mRNA decay, and the ubiquitin-proteasome pathway.

CONTINUED ON PAGE 399

THIS WEEK IN SCIENCE

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NATURAL DRUG SYNTHESIS

In addition to the well-known machines for making polymeric biomolecules such as proteins and nucleic acids, there are also complex enzymatic machines that synthesize a variety of smaller compounds that are based on a repeating unit. Because two of the classes of these compounds contain widely used and useful antibiotics, such as penicillin and erythromycin, learning how to manipulate and recombine the constituent synthetic modules would offer a pathway to improving existing antibiotics or to new ones. Gokhale *et al.* (p. 482) explore the substrate specificity of the gramicidin synthetase by loading chemically produced aminoacyl–coenzyme A esters onto the free sulfhydryls of the donor and acceptor modules. The donor site can tolerate many different amino acid side chains, whereas the more restrictive acceptor site constrains initiation of the peptide chain to the correct amino acid. Belshaw *et al.* (p. 486) focus on the intermodule connectors within the 6-deoxyerythronolide synthase and find that these are critical for the appropriate progression of intermediates as seven 3-carbon units are polymerized into the cyclic core of erythromycin.

REVAMPING VANCOMYCIN

There is a pressing public health need to develop new antibiotics against bacterial infections. The glycopeptide vancomycin is one of the last efficacious drugs for the treatment of Gram-positive infections, and it acts by inhibiting the cross-linking of amino acids in the formation of the bacterial cell wall. Ge *et al.* (p. 507; see the Perspective by Walsh) show that alterations in the carbohydrate moieties render vancomycin analogs much more active, even against bacterial strains that have developed resistance to vancomycin or methicillin. Their data suggest that the carbohydrate derivatives inhibit a different step in bacterial cell wall synthesis, possibly a transglycosylation reaction, and thus point toward new compounds that may overcome the problem of vancomycin resistance.

OPEN WIDE

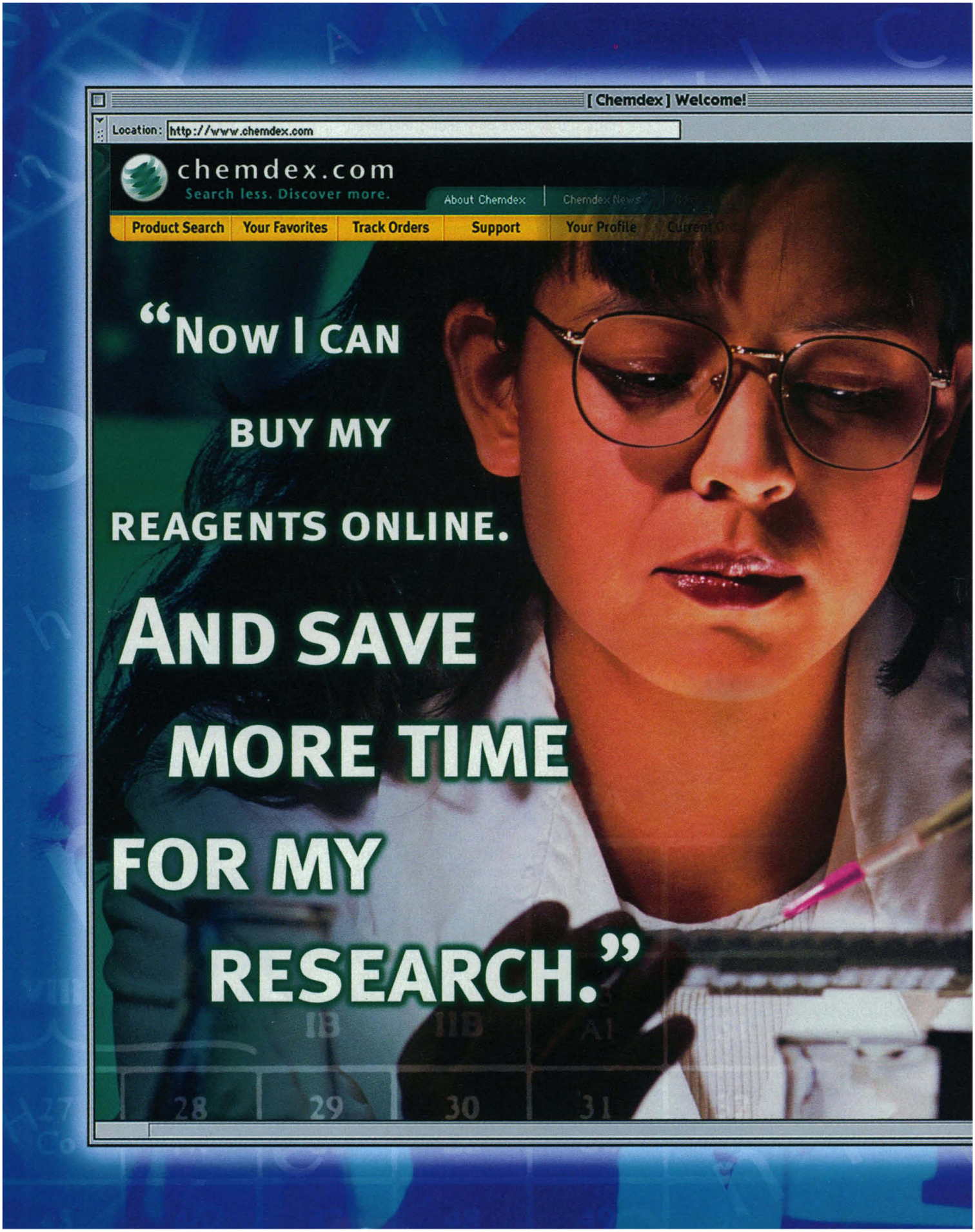
The ability to create small-diameter vascular grafts would have medical implications for treating atherosclerotic vascular disease. Although it is possible to manufacture such vessels from synthetic materials, they have only shown low levels of blood flow. Niklason *et al.* (p. 489; see the news story by Ferber) have generated blood vessels in vitro from bovine or porcine smooth muscle cells that were grown under conditions in which growth medium is pumped through the vessels (providing the type of physical stress they would normally experience during development) on a biodegradable polymer matrix. The pulsatile conditions resulted in vessels that were stronger than those grown without stress, that remained unobstructed longer when transplanted into miniature swine, that had collagen levels which were closer to those of normal vessels, and that showed appropriate contractile responses to prostaglandin.

BIG BACTERIA

Bacteria in ocean sediments have been recognized as the important intermediaries in the global cycling of nitrogen and sulfur. Schulz *et al.* (p. 493; see the cover and the news story by Wuethrich) now describe a new species of sulfur bacterium in Namibian sediments that not only is important in the cycling of sulfur and nitrogen but also is 100 times larger than other known bacteria. The huge cell volume and internal vacuole may allow them to store these elements for long periods of time when environmental supplies are limited.

EYEING THE CLOCK

Light can reset the phase of the circadian clock, which is located in the hypothalamus of the mammalian brain and controls the daily periodicity of functions such as sleep, activity, and metabolism. The eyes are necessary for this light-induced resetting, but the identity of the photoreceptor is not known, although transgenic mice that lack rods still show photoentrainment, which excludes rods as the photoreceptor. Now, Freedman *et al.* (p. 502) and Lucas *et al.* (p. 505) construct a line of mice lacking cones and a line lacking both rods and cones (see the news story by Barinaga). Each of these lines is still able to follow a circadian rhythm, as assessed by monitoring the daily activity of the mice and by acute inhibition of melatonin levels. Thus, there must be another type of photoreceptor that relays the light signal to the circadian clock.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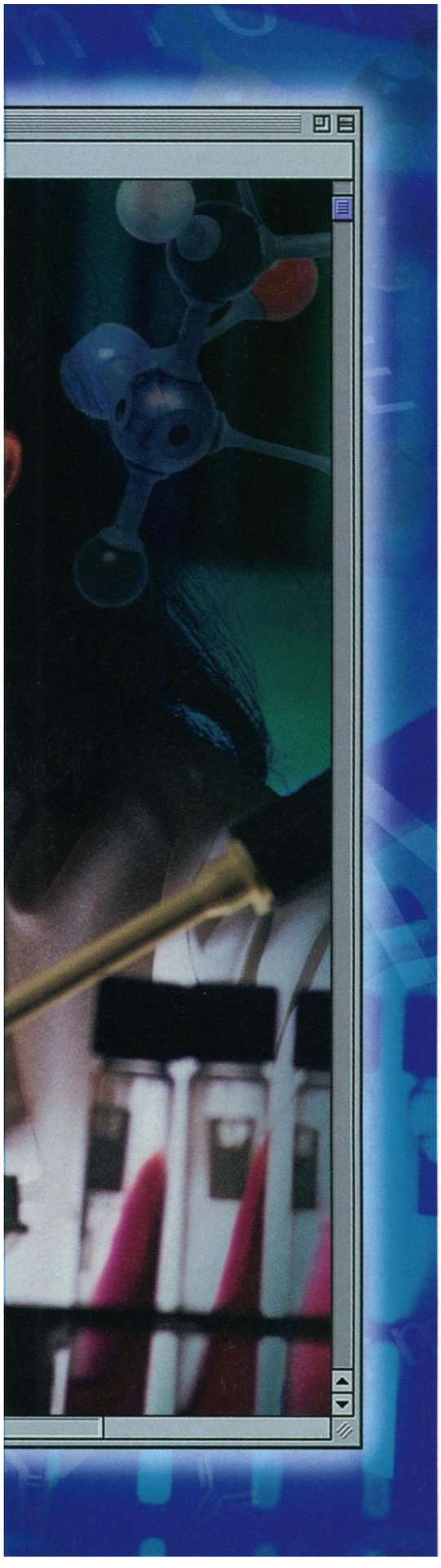

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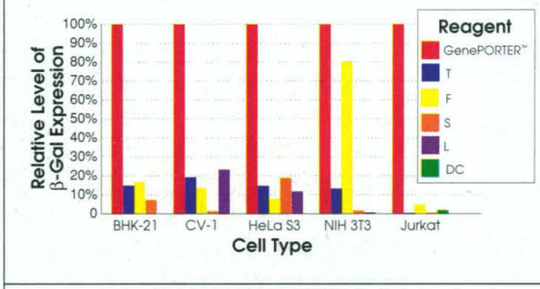

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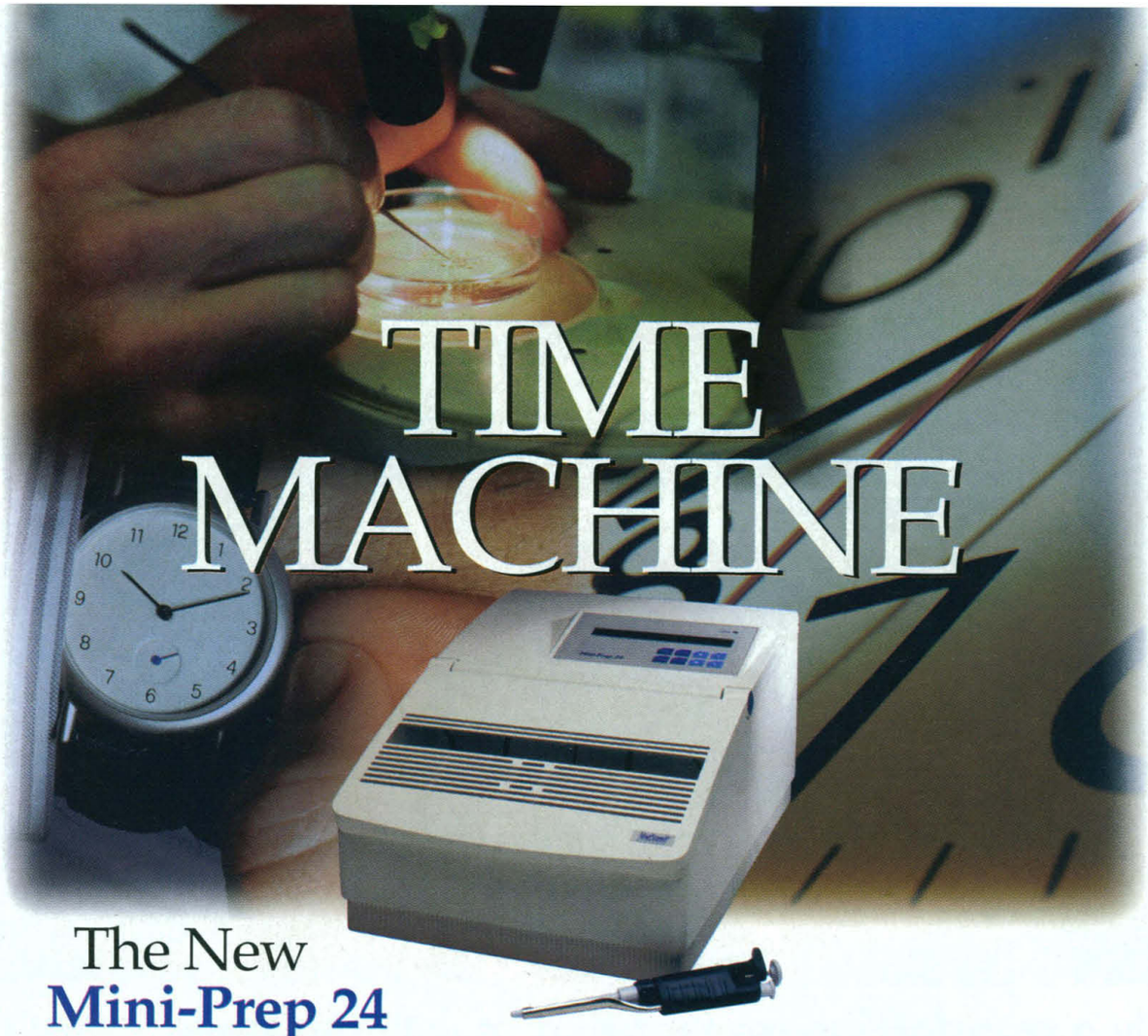

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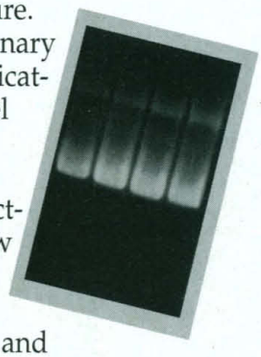

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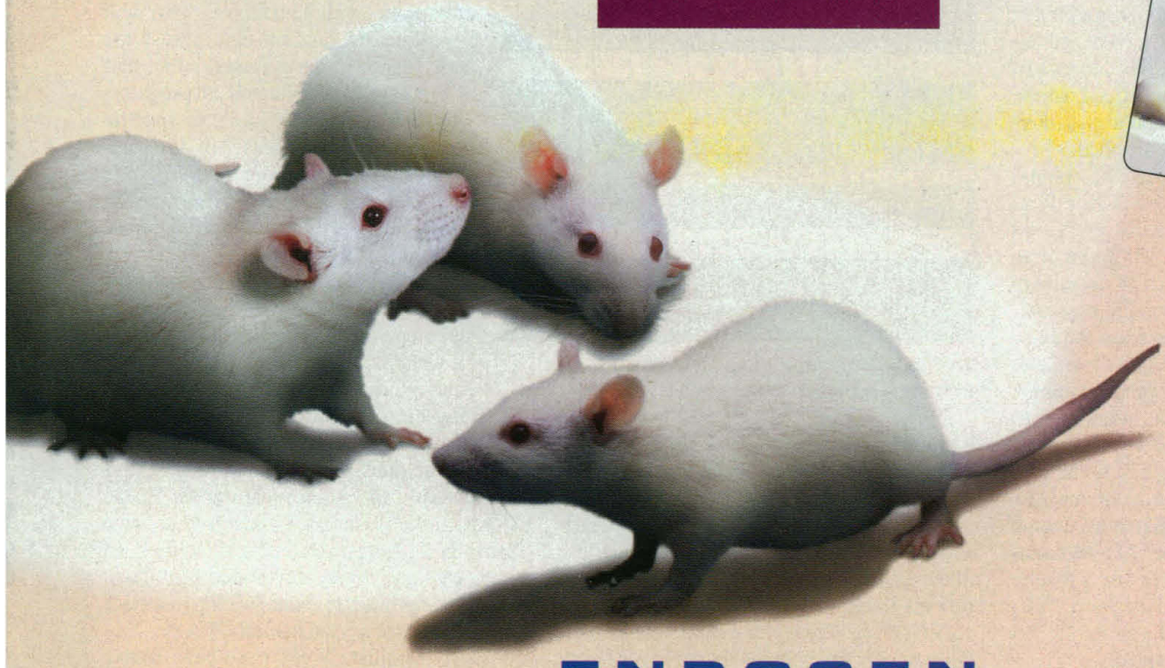

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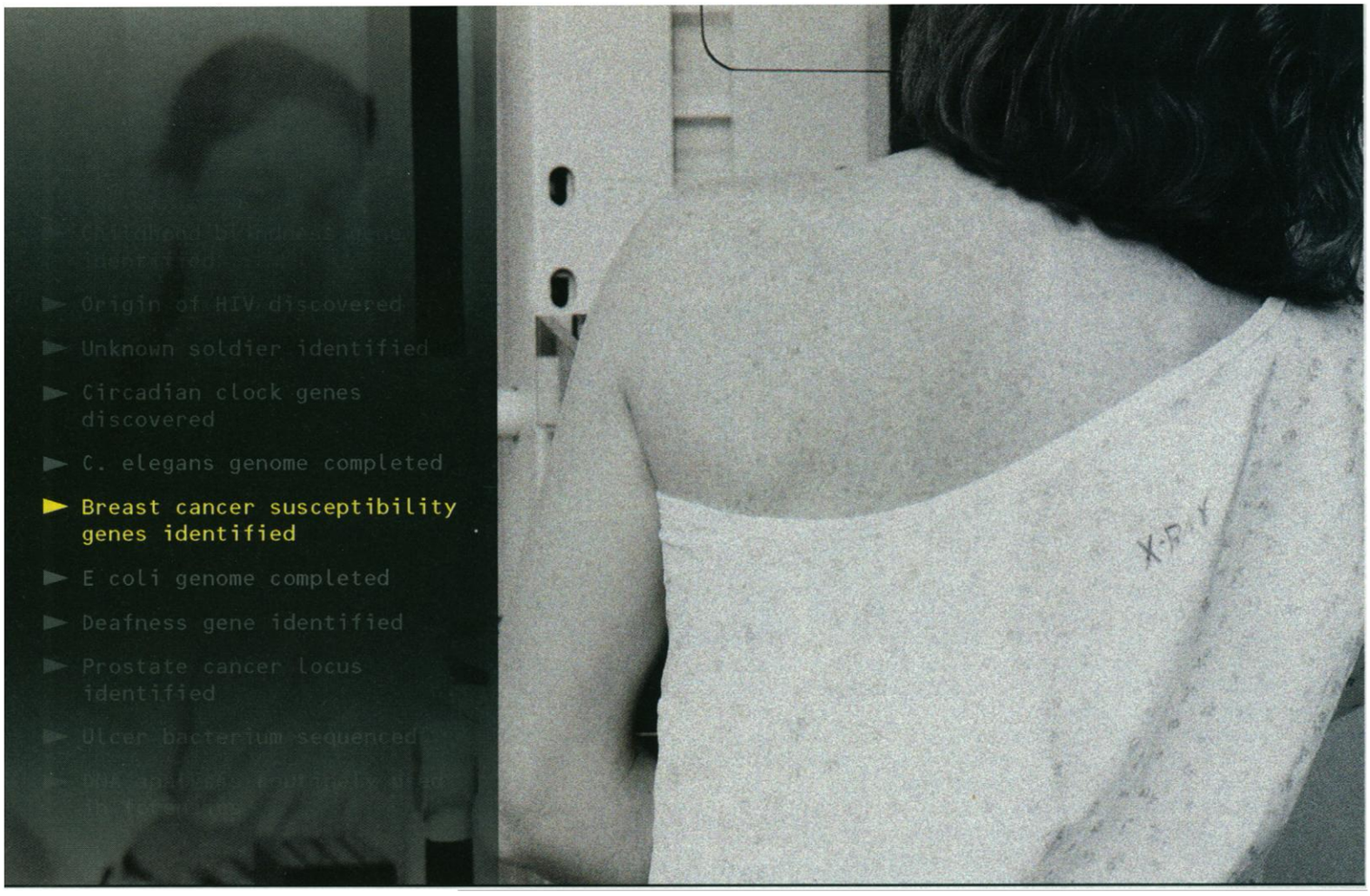

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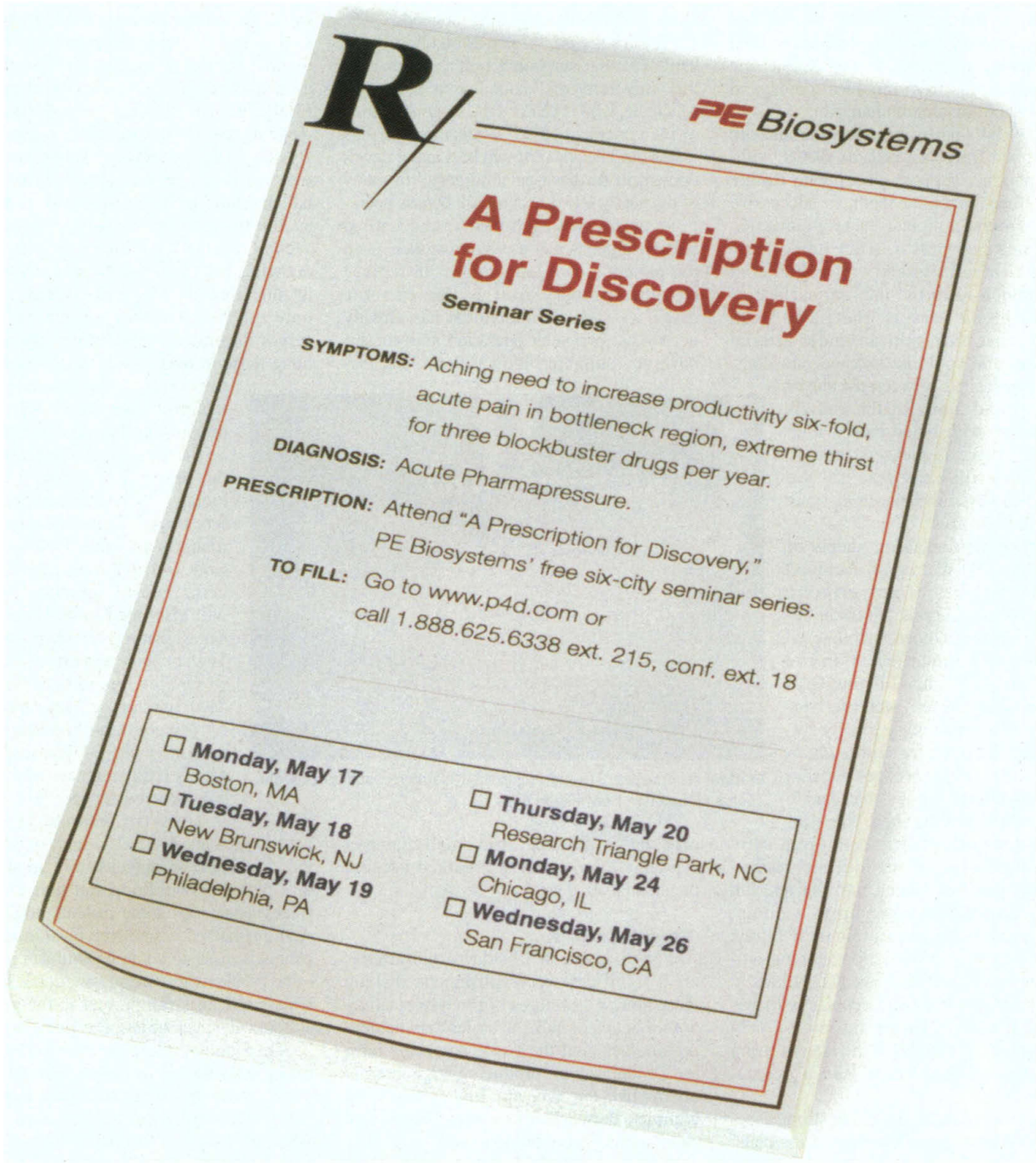

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To further its goal of offering the broadest range of enabling systems and services for life sciences research and related applications, Perkin-Elmer has merged with PerSeptive Biosystems and created the PE Biosystems Division. PE Biosystems consists of the Applied Biosystems, PerSeptive Biosystems, PE Informatics, and Tropix Centers of Excellence. PE SCIEX is a joint venture between The Perkin-Elmer Corporation and SCIEX, the instrumentation technology division of MDS Inc.

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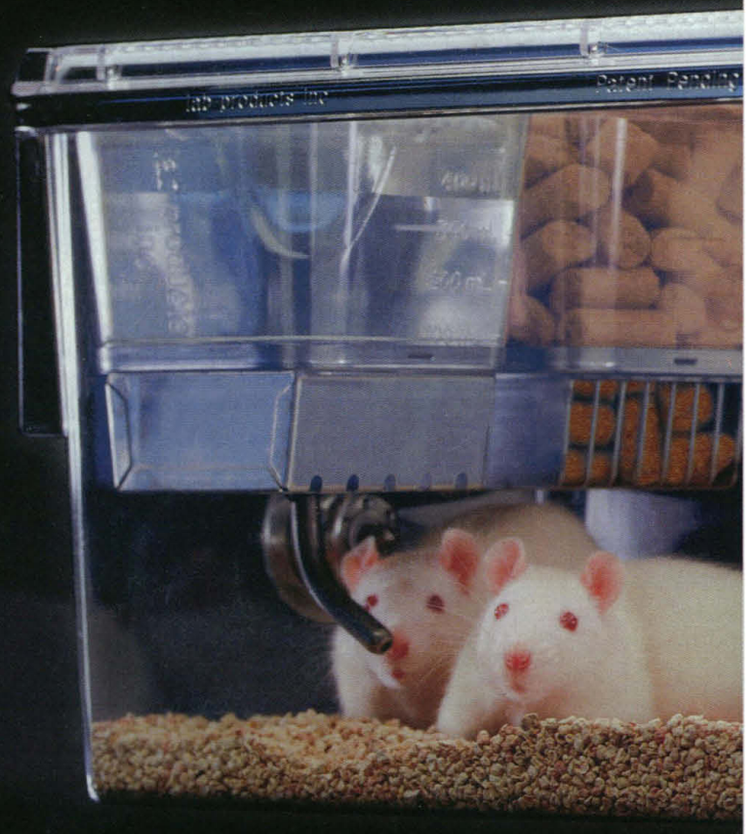
Introducing The Only One Cage

At last: The first cost-efficient, space-efficient, time-efficient answer to universal housing for all species of rodents.

Now you can house more animals per square foot, maximize available space, streamline animal care, and greatly reduce costs. At the same time, you can insure all-critical compliance with both the Animal Welfare Act and the ILAR Guide* recommendations.

One Cage makes it possible to house all your rodents in one system. The revolutionary design features one cage with one feeder, one water bottle, one filter top (no wire bar lid required), and only One Rack™ that will accommodate 112 complete units.



Examples of how THE GUIDE* recommendations apply to the One Cage™ System

Number of animals recommended per cage based on 80 sq. inches of usable floor area, 7-3/4" interior cage height:

MICE (>25g.)	
HAMSTERS (>100g.)	
RATS (200-400g.)	
GUINEA PIGS (≤350g.)	

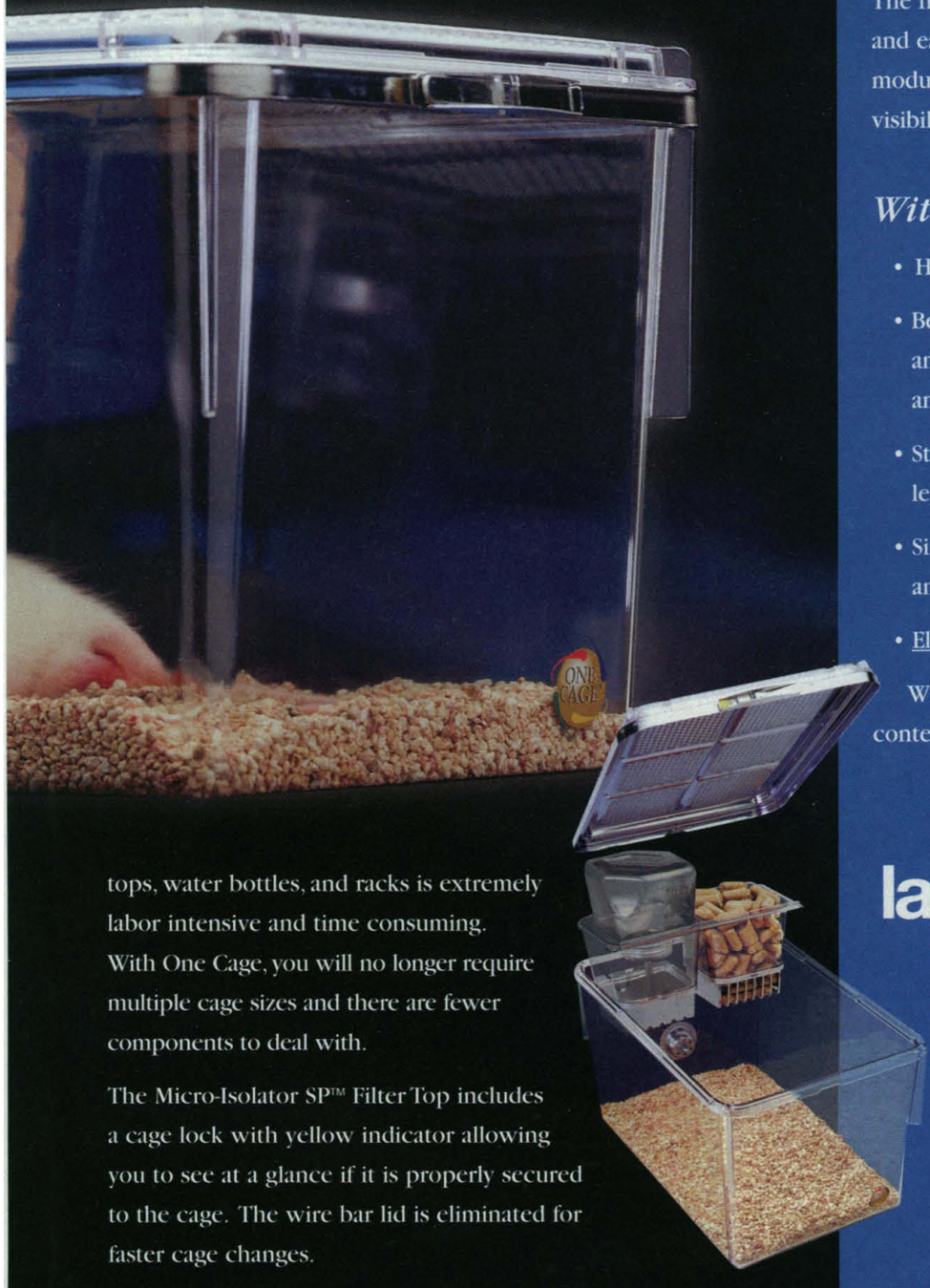
*Based on the Animal Welfare Act of 1966 as ammended 1985 and the Guide for the Care and Use of Laboratory Animals. Institute of Laboratory Animal Resources, Commission of Life Sciences, National Research Council, National Academy Press, 1996.

With One Cage, 560 mice, 448 hamsters, 224 rats, or 112 guinea pigs can be housed in a single rack. This represents up to a 273% increase in animal populations. (A facility housing 2,200 rats would require 37 racks housing 30 cages with 60 rats per rack *(based on old-style racks).* Compare this to 10 One Cage racks housing 224 rats per rack.)

You can house more rodents in less space while meeting interior cage height and floor space requirements.

Cleaning and handling multiple cage sizes, wire bar lids, filter

e™ System



The filter replacement device provides quick and easy exchange of filters. The clear plastic modular delivery system provides greater visibility of food and water for easy inspection.

With One Cage, you can:

- House more animals in less space at less cost.
- Be in full compliance with The Guide* and prepared for the arrival of new animal care policies.
- Streamline your work while improving your level of care.
- Simplify purchasing, cut down on inventory and reduce the number of turnaround units.
- Eliminate wire bar lids.

When you look at the options, there's no contest. It's One Cage.

tops, water bottles, and racks is extremely labor intensive and time consuming. With One Cage, you will no longer require multiple cage sizes and there are fewer components to deal with.

The Micro-Isolator SP™ Filter Top includes a cage lock with yellow indicator allowing you to see at a glance if it is properly secured to the cage. The wire bar lid is eliminated for faster cage changes.

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1999 Tyler Prize

for Environmental Achievement

The Tyler Prize Medallion

Tyler Prize

The Tyler Prize was established in 1973 by the late John and Alice Tyler as an international award honoring one or more individuals for outstanding scientific and/or educational achievements in the understanding of ecological and environmental conditions anywhere in the world; the discovery or further development of known and new sources of energy; and medical discoveries or achievements of worldwide importance.

Dr. Te-Tzu (T.T.) Chang

Principal Geneticist (Retired)
International Rice Research Institute, The Philippines

Dr. Joel E. Cohen

Professor of Populations
Rockefeller and Columbia Universities, New York

Dr. Chang is the world authority on the conservation and utilization of rice. As a principal geneticist of the International Rice Research Institute, he made major advances in rice plant breeding, productivity, and disease resistance. These contributions initiated the 1960s "Green Revolution" that continues to feed hundreds of millions of people today. Dr. Chang is also the driving force behind international efforts to collect tens of thousands of wild rice varieties—many on the brink of extinction—and return native species of rice back to countries where they have been lost.

Dr. Cohen has greatly advanced the understanding of human population dynamics. He developed the quantitative models that laid the foundation for food web ecology over the last 20 years. Dr. Cohen also studies the interactions of neglected human diseases (such as malaria, schistosomiasis, and Chagas disease) with demography, economics, and the environment, in order to help tens of millions of people in tropical climates prevent these killers.

Call For Nominations
by the Tyler Prize Executive Commitee

The Tyler Prize is administered by the University of Southern California
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Nominations for the 2000 Tyler Prize will be accepted until September 15, 1999
Visit the Tyler Prize Home Page to download a nomination form at www.usc.edu/tylerprize

For additional information contact Dr. Jerome Walker, Executive Director, The Tyler Prize, USC
Phone 213-740-6559, Fax 213-740-1313, Email tylerprz@usc.edu

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PORTABLE . . . The RAPID is designed to be air, land, and sea transportable; able to withstand unrestrained collisions with the bed and sides of military and commercial transport vehicles in packaged configurations and operate after exposure to loose cargo vibrations while in transport mode. The instrument and all accessories weigh a total of 50 lbs., and may be manually transported with the included backpack.

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