Science

28 June 2002
Vol. 296 No. 5577
Pages 2285–2472 $9

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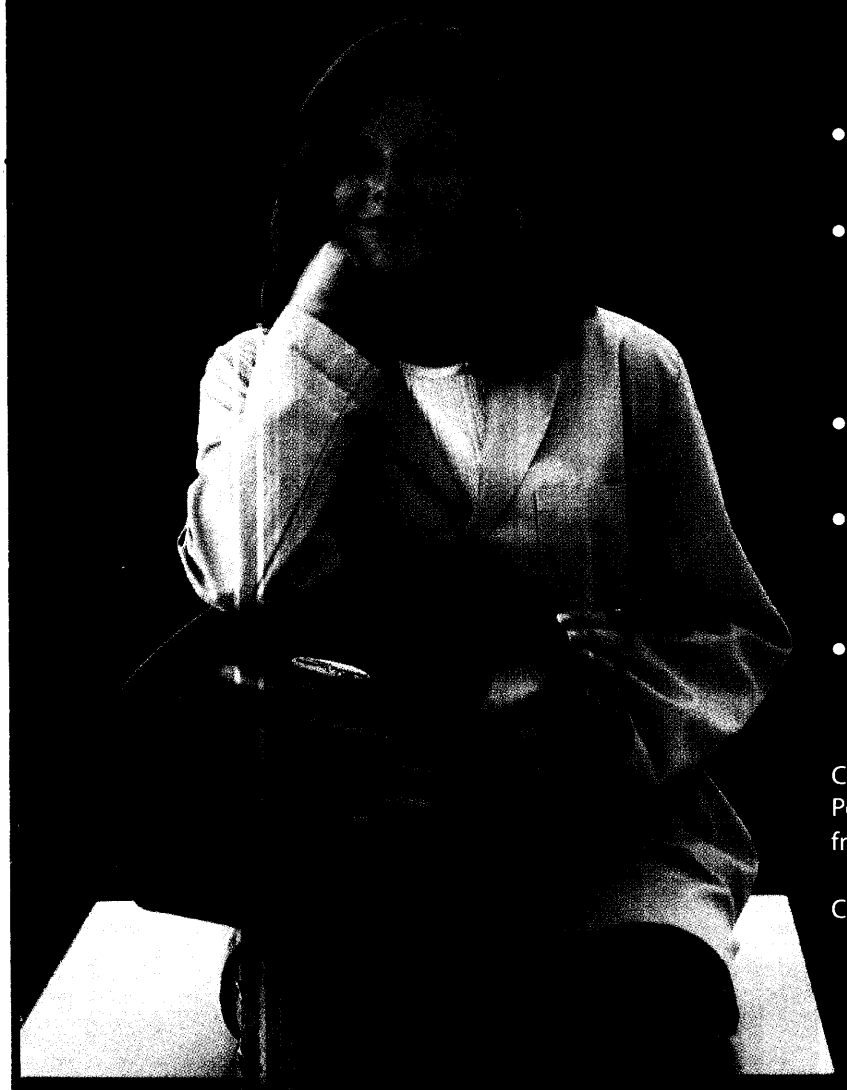

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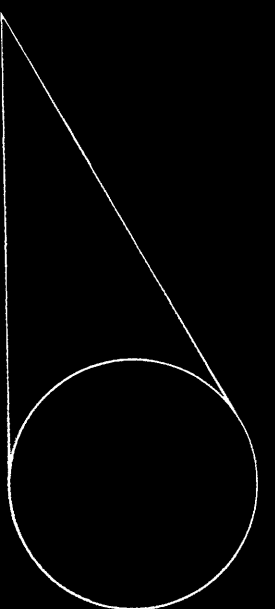

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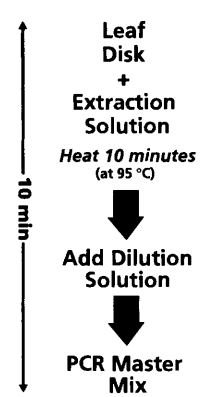

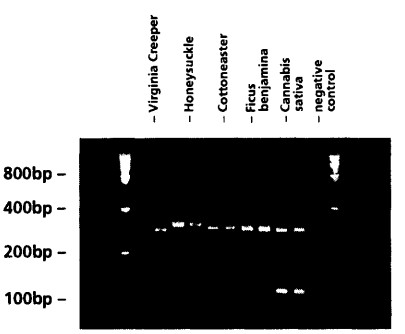

Extract-N-Amp Plant PCR Kit with 5 different plant specimens. *Genomic DNA was extracted from 0.5 cm leaf disks that were cut using standard paper punch. DNA was extracted using the Extract-N-Amp Plant PCR Kit in less than 15 minutes. All samples were then amplified using the specially formulated Hot Start PCR mix. The products were generated from a 30-cycle duplex reaction containing primers specific to plant chloroplast (upper band) and primers specific for Cannabis sativa DNA (lower band).*
Data provided by Andy Hopwood, Forensic Science Service, Birmingham, England.

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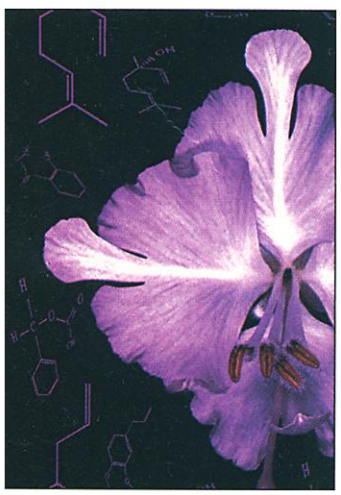
NEWS



2327
Floral fragrance

NEWS OF THE WEEK

NEWS FOCUS

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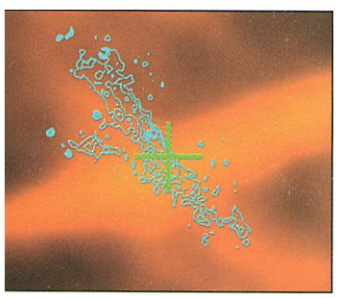

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Tracing stellar death

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BOOKS *ET AL.*

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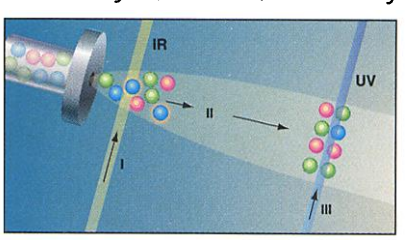

2347
Molecular substates get caught

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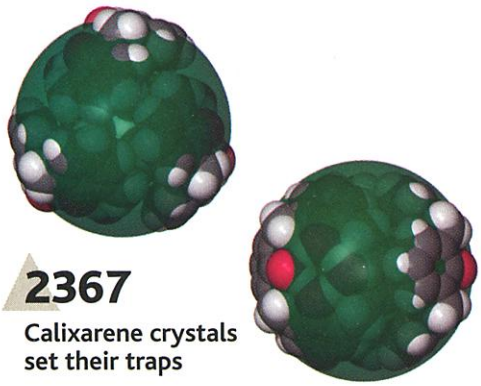
BREVIA



2367
Calixarene crystals set their traps

REPORTS

COVER 2320

A collage depicting two decades of the HIV/AIDS epidemic. Researchers will meet in Barcelona, Spain, next week for the XIV International AIDS Conference. On the agenda: problems limiting the effectiveness and distribution of highly successful therapies, and prospects for vaccines. See also the related Editorial on p. 2297, the Policy Forum on p. 2339, and the Review on p. 2354. (Collage: A. Stonebraker and C. Faber Smith)

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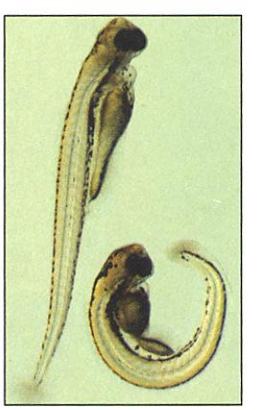
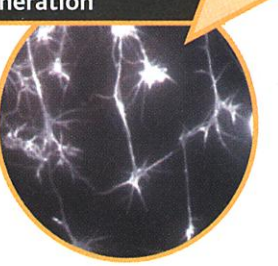


2398
Counting mutant alleles in the wild

New on *Science* Express Another impediment to nerve regeneration



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CONTENT HIGHLIGHTS AS OF 28 JUNE 2002

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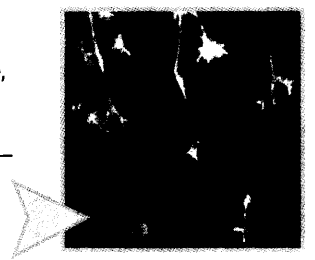
Myelin-Associated Glycoprotein as a Functional Ligand for the Nogo-66 Receptor B. P. Liu, A. Fournier, T. GrandPré, S. M. Strittmatter

Two molecules in the central nervous system that inhibit nerve regeneration—MAG and Nogo—are both shown to act through the Nogo receptor.



Analytic and Algorithmic Solution of Random Satisfiability Problems M. Mézard, G. Parisi, R. Zecchina

Elements of statistical physics and computer science are combined to provide a route to help solve computationally hard problems.

Systematic Identification of Pathways That Couple Cell Growth and Division in Yeast P. Jorgensen, J. L. Nishikawa, B.-J. Breitkreutz, M. Tyers

A comprehensive screen for genes that control cell size reveals unexpected regulatory mechanisms.

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NETHERLANDS: Becoming a Forensic Scientist—A Personal View Z. Geradts

Although he just received a Ph.D. in physics, our feature essayist is on track to become a forensics researcher.

SINGAPORE: Regulating Human Stem Cell Research J. Wong

Singapore's Bioethics Advisory Committee recommends tight regulations on human stem cell research and a complete ban on reproductive cloning.

US: Educated Woman—Cheaters, Betrayal, Denial, and Lies M. P. DeWhyse

A cheating scandal creates turmoil that goes deeper than the grades at risk.

US: Farmer's Hours J. Hall

After years of wandering, an astrobiologist settles in at Arizona State.

US: Dr. Jennie Patrick—An Interview S. Collins

The first African-American woman to earn a Ph.D. in chemical engineering discusses her career and life experiences.

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Odd Couple M. Leslie

Two mechanisms for gene silencing unexpectedly team up.

Hematopoietic Stem Cells and Aging J. Fuller

The cells they are a-changin'.

science's stke

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signal transduction knowledge environment

Perspective: Cytoskeletal Proteins and Gene Regulation—Form, Function, and Signal Transduction in the Nucleus P. de Lanerolle and A. B. Cole

ANGUSTIFOLIA, actin, and myosin I do double duty in the cytosol and the nucleus.

Perspective: Microtubule-Actin Crosstalk at Focal Adhesions A. F. Palazzo and G. G. Gundersen

How microtubules promote focal adhesion disassembly.

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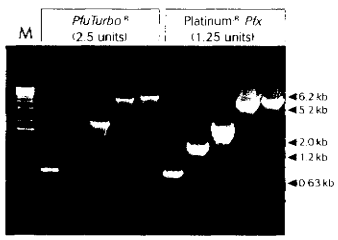

Comparison of enzyme performance on genomic DNA templates from 600 bp to 6.2 kb

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THIS WEEK IN Science

edited by Phil Szuromi

Caught in the Corners

Calixarenes are cyclic molecules designed to capture guest molecules in solution through numerous weak interactions. Atwood *et al.* (p. 2367) report that crystals of calix[4]arene can play an additional host-guest trick—the interstitial sites between the molecules can trap molecules during crystallization with extraordinary thermal stability through nothing more than weak van der Waals interactions. A number of freon molecules as well as methane can be trapped at low pressures and held up to temperatures well in excess of their boiling points.

2383 When Life Got Hard

Biomineralization has been thought to have developed in a series of steps before a great jump in complexity near the base of the Cambrian. Wood *et al.* (p. 2383) now describe a fossil showing complex patterns of biomineralization from rocks dated to 548 million years ago, in the uppermost Precambrian. This organism, named *Namapoikia reitogensis,* may also have helped the formation of early reefs.

And in Brevia ...

The ortho and para nuclear spin isomers of water have been separated by Tikhonov and Volkov (p. 2363) using a simple adsorption method.

Controlling Molecules Through the Turns

Interactions between functional groups in more complex molecules can lead to numerous conformational minima that are separated by relatively low energetic barriers. Because energy tends to redistribute quickly in larger molecules, even ones as small as dipeptides, one might expect that it would be difficult to excite molecules with infrared radiation and interconvert specific conformations. Nonetheless, Dian *et al.* (p. 2369; see the Perspective by Pratt) used a combination of ultraviolet and infrared spectroscopies to show that in the gas phase, a methyl-capped dipeptide, *N*-acetyl-tryptophan methyl amide, can be interconverted between three distinct conformers, despite the presence of some 60 conformational minima that have similar energies. The selectivity comes from exciting specific vibrations (in this case, N–H stretches) in the dipeptide that then drive the molecules over a specific barrier.

Correlated Superconductors

Electron-electron repulsion should be detrimental to electron pairing in normal metal superconductors. However, some cuprate materials become superconducting near the Mott insulating regime, which brings this intuitive expectation into question. Capone *et al.* (p. 2364), working on a mechanism to explain the recent observation of superconductivity in fullerenes, show that there are similarities between the two materials. Their model calculations suggest that that the pairing is phonon mediated, as in the case of the normal superconductors, but that the correlations between electrons can actually enhance the superconducting transition temperature.

Arsenic Abatement via Nitrate

The problem of high levels of arsenic in surface and ground water is often compounded by a lack of understanding of the abundance, speciation, or even the source of the arsenic. Senn *et al.* (p. 2373), through a detailed study over several years of the chemistry of an urban lake near Boston, Massachusetts, show that nitrate, which is also at high levels from fertilizer use, greatly affects arsenic cycling under anoxic conditions. Nitrate helps oxidize As(III) to As(V), which is less toxic, and oxidizes Fe(II) to create hydrous ferric oxide particles that scavenge arsenic.

Ancient Slime Eaters

The sea floor of the eastern Mediterranean is characterized by stratified sediments. Layers of greenish-brown organic sludge, or sapropels, alternate with carbonate oozes that contain microfossils. The fatty acids found in the sapropels suggest that they have a bacterial origin, but large numbers of dividing cells have also been detected. Coolen *et al.* (p. 2407) have now observed hydrolytic enzyme activity and a slow but significant turnover of glucose in these ancient deposits. These results indicate that sapropel layers more than 200,000 years old are still being modified at a rate that may be relevant to the global carbon cycle. A 16*S* ribosomal RNA analysis shows that most of these microorganisms are green nonsulfur bacteria. These results have implications for the reconstruction of stable isotopic signatures and Mediterranean sea levels from sapropels.

Quicker Recovery

The recovery of forest diversity after the bolide impact at the end of the Cretaceous occurred much more quickly than has been assumed. Johnson and Ellis (p. 2379), report that a tropical rainforest with diversity similar to modern forests existed in Colorado as soon as 1.4 million years after the impact. These findings suggest that diverse plant species survived the impact and that the North American climate was warm during this period.

CREDIT: JOHNSON AND ELLIS

Infection Protection During Inflammation

During microbial infection, neutrophils generate microbicidal agents through the release of myeloperoxidase (MPO). Eiserich *et al.* (p. 2391) report that MPO's actions during inflammation extend beyond generating antimicrobial oxidizing species. MPO permeates the mammalian vasculature and alters blood vessel function during acute inflammation by catabolizing nitric oxide (NO). NO is an endothelial-derived blood vessel relaxant that is produced in response to endotoxin. By reducing NO availability, MPO impairs vascular changes produced by infection. This finding may explain the increased susceptibility of humans deficient in MPO to infection.

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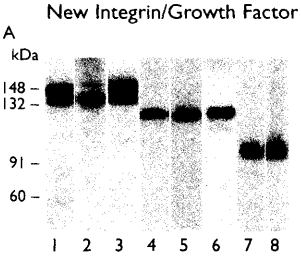

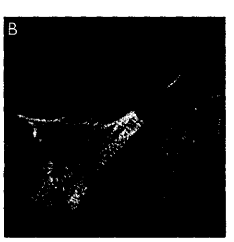

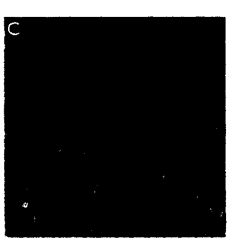

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Gene Flow in the Field

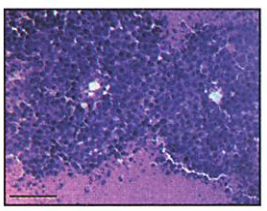
A field study of the extent of gene flow from genetically modified plants into surrounding crops through cross-pollination is presented by Rieger *et al.* (p. 2386; see the news story by Stokstad). A strain of canola (rapeseed oil) modified to be resistant to herbicides was first grown commercially in Australia in 2000. An analysis of surrounding fields across widely dispersed geographical samples revealed a low level of cross-pollination between canola fields. The range of long-distance pollination was more random than expected.

A Light Motif

Green algae move in response to light to find conditions that are optimal for photosynthetic growth, and this movement is mediated by photoreceptor currents. Nagel *et al.* (p. 2395) have identified an opsin-related protein, channelopsin-1, in *Chlamydomonas reinhardtii* that is likely to be the photoreceptor involved in phototaxis. Expression of channelopsin-1 in the presence of all-*trans* retinal in *Xenopus* oocytes produced light-induced proton currents. Characteristics of the conductance suggest that channelopsin-1 forms a light-gated proton channel.

Lethals Equal?

Even a deleterious mutation rarely kills instantly and often persists and accumulates for some generations. McCune *et al.* (p. 2398) have estimated the frequency of such mutations through separate breeding experiments in two phylogenetically divergent teleost fishes, *Lucania goodei* and *Danio rerio*. When the results were compared with *Drosophila* species and with *Xenopus laevis*, it was found that animals with very different genome sizes and gene numbers have roughly the same number of lethal mutations.



CREDIT: HOOD *ET AL.*

Destroying Tumors by Special Delivery

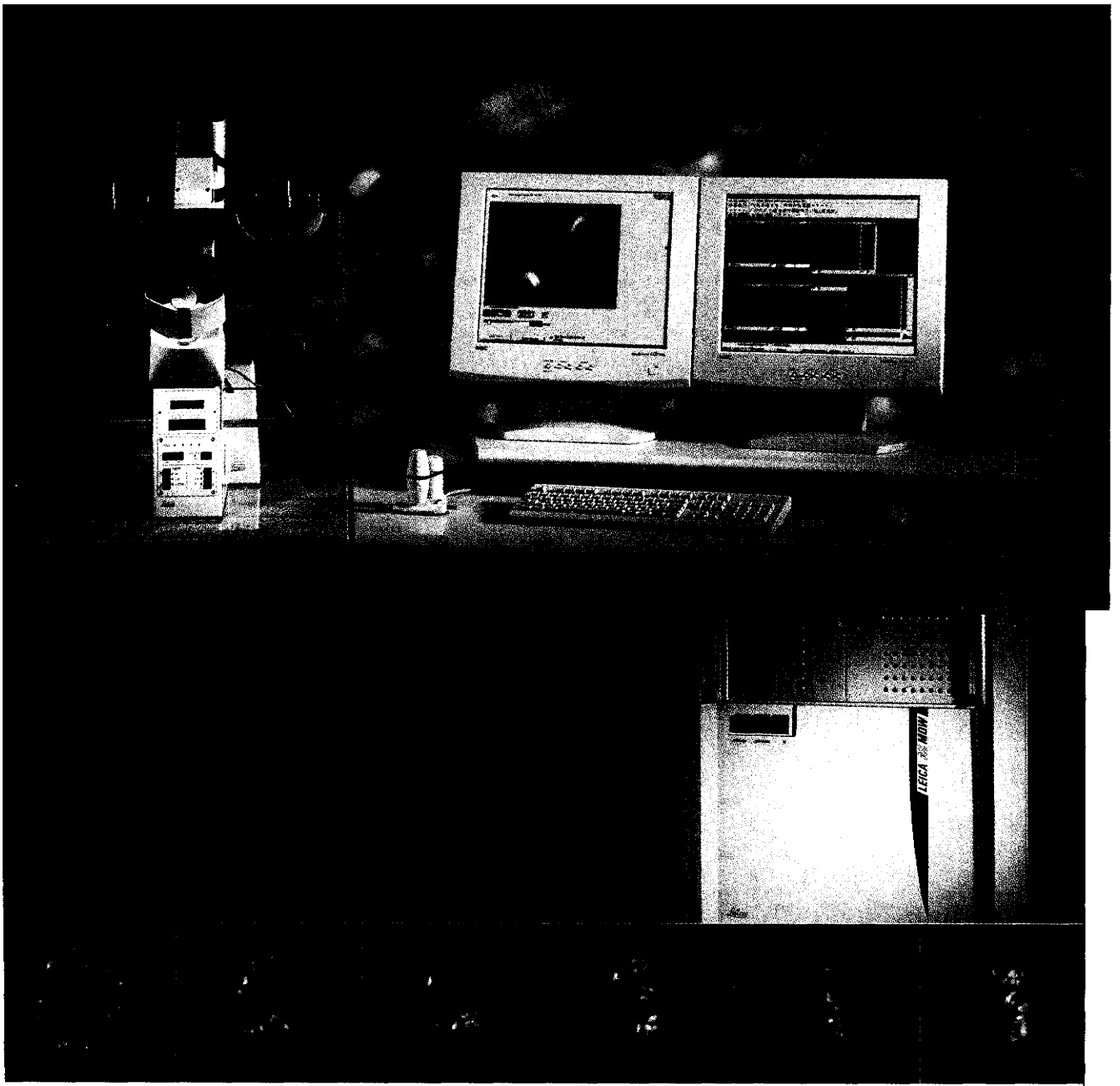
Solid tumors do not grow well without a blood supply, and much effort has been directed toward designing drugs that selectively destroy actively growing blood vessels feeding tumors. Hood *et al.* (p. 2404; see the news story by Couzin) now show that cationic nanoparticles (NPs) can deliver a toxic gene to tumor blood vessels. Vascular targeting and internalization of the NPs was achieved by coupling them to an organic ligand for integrin $\alpha v\beta 3$, and death of the target endothelial cells was achieved by coupling the NPs to a mutant *Raf* gene that blocks cell signaling. Systemic injection of these tailored NPs produced durable regressions of both primary and metastatic tumors in mice.

Genetic Clue to Mental Retardation

One of the receptors for angiotensin II, AGTR1, plays a key role in the regulation of blood pressure and water electrolyte balance. A second receptor, AGTR2, is expressed in a number of tissues including the brain, but its function is poorly understood. Vervoort *et al.* (p. 2401) identify *AGTR2* as the causative gene in a family with X-linked mental retardation and find sequence changes in the gene in several unrelated patients with the disorder. These results suggest that AGTR2 plays a role in brain development, cognitive function, or both. Further study of signaling pathway of AGTR2 may provide insight into the pathogenesis of mental retardation, which affects 2 to 3% of the population.

The Right Conditioning for Gene Therapy

Severe combined immunodeficiency that is caused by a lack of adenosine deaminase has been an attractive target for gene therapy trials in humans. It was hoped that genetically engineered cells would have a growth advantage such that even low levels of correction would be effective in patients. Previous trials showed that low numbers of long-lived genetically corrected cells and low levels of transgene expression were not enough. Aiuti *et al.* (p. 2410) have worked out a conditioning regimen for patients and cells that provided room in the bone marrow for the growth of the transduced cells. High levels of transduced cells and clinical improvements 1 year after treatment were seen in two patients, who now no longer require enzyme replacement therapy. This approach may be useful in treating other congenital diseases involving the hematopoietic system.



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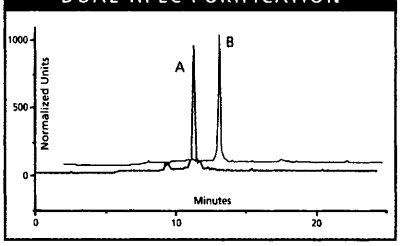

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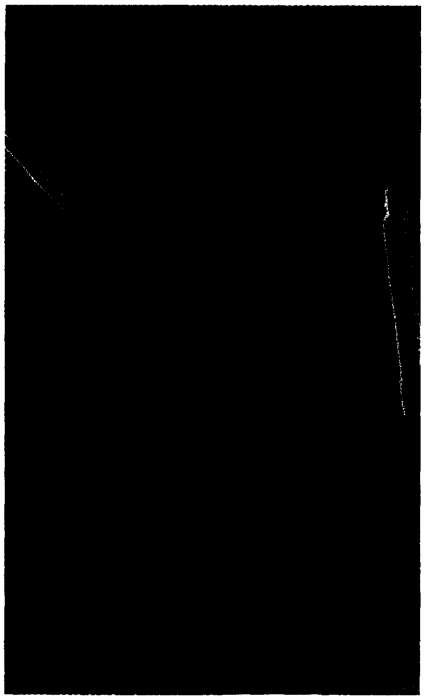

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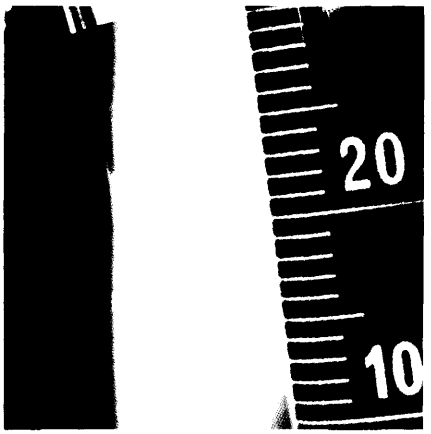

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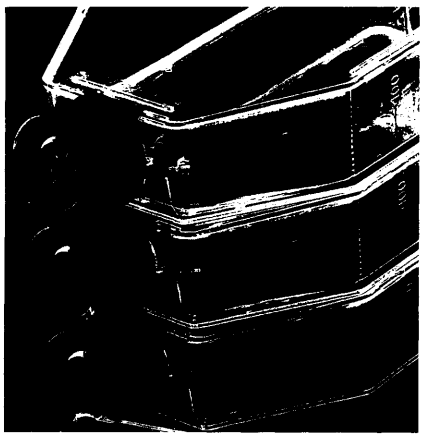

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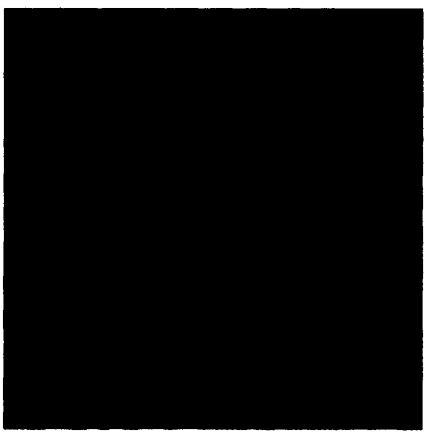

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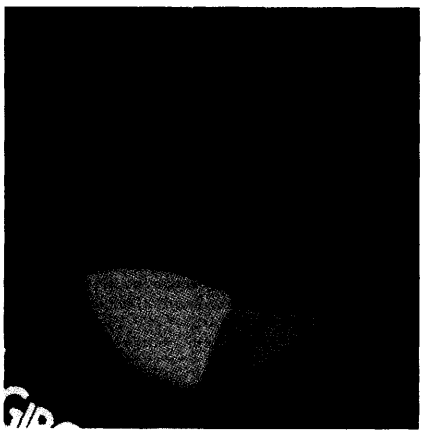

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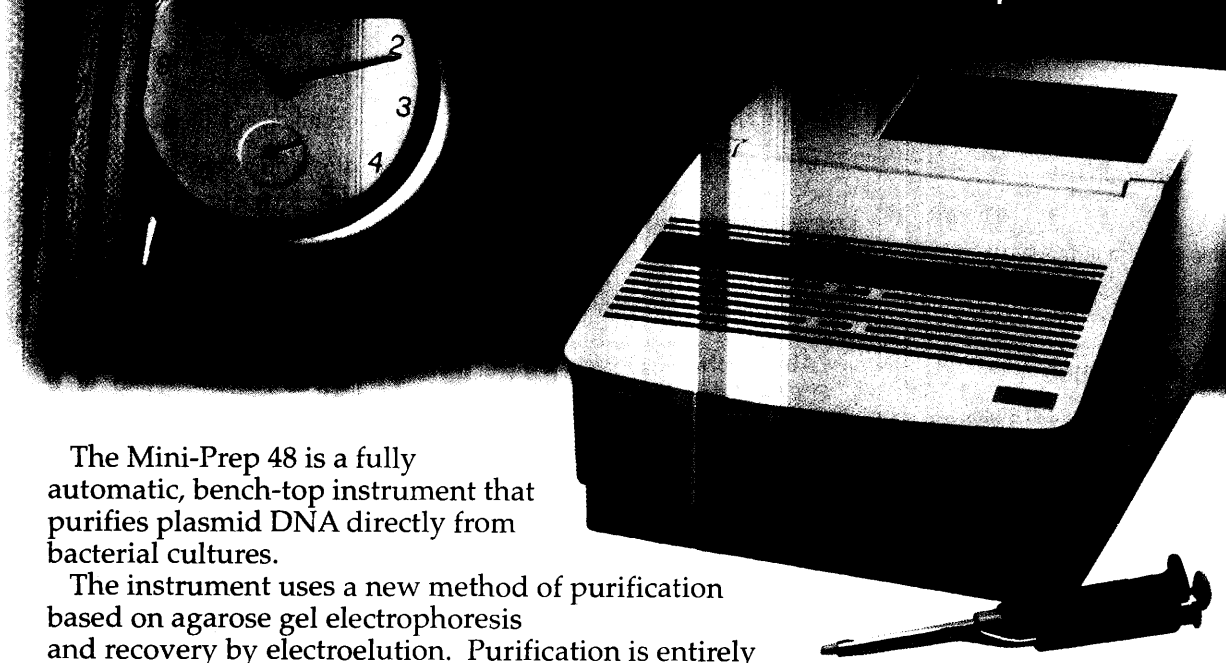

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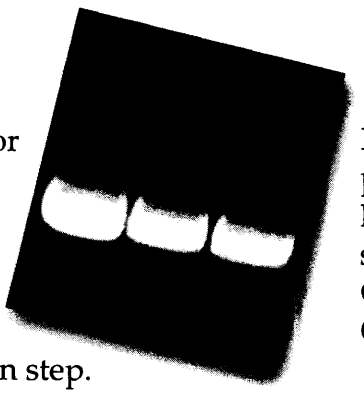

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AD SUPPLEMENT IN THIS ISSUE

East Coast

Along the eastern seaboard biotechnology companies continue to increase the speed at which new innovations turn into applications. This article examines the career opportunities associated with the continued growth in biotechnology on the East Coast.

Look for it on page 2437.

Product News:

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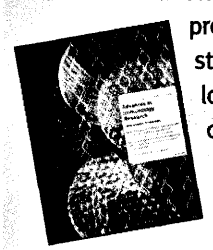
SPECIAL AD SECTION IN THIS ISSUE

Advances in Immunology Research

This section addresses recent advances in technologies and products used in immunology research. Key products used to study the immunological response are covered as well.



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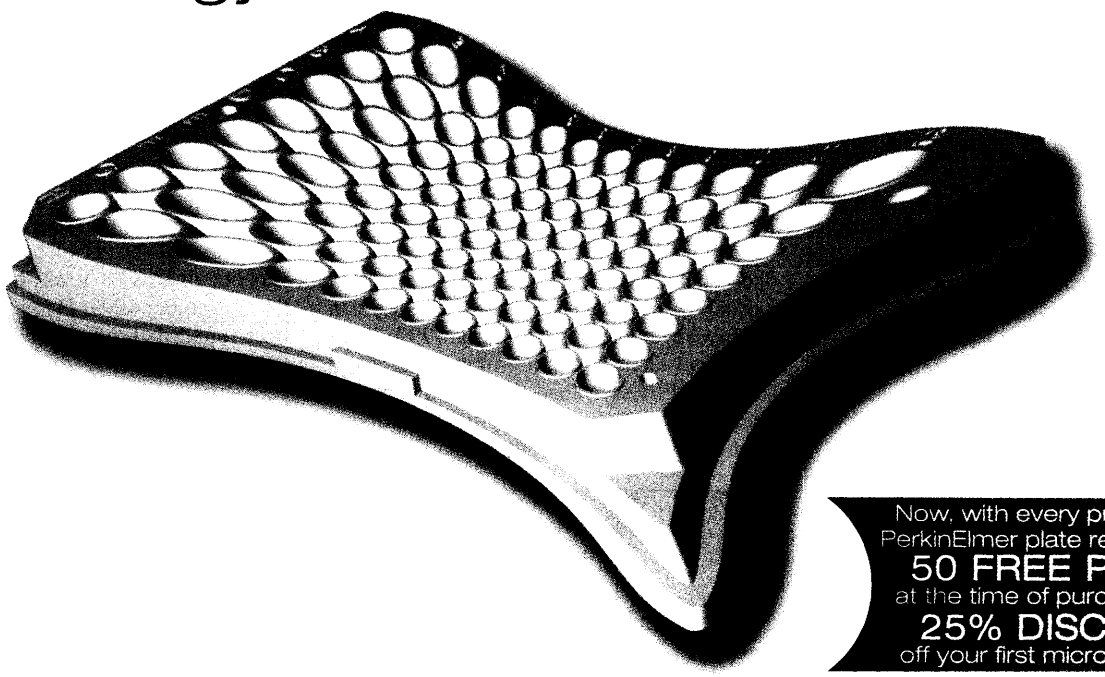

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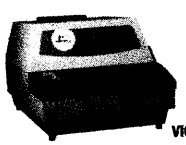

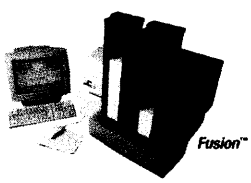

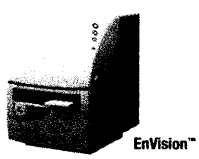

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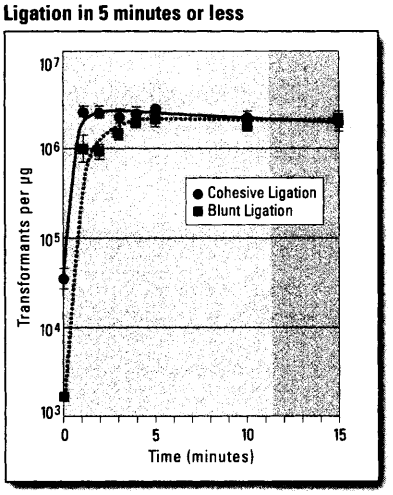

► *Using the Quick Ligation Kit protocol, blunt and cohesive inserts were ligated into LITMUS 28 vector cut with either EcoR V (blunt) or Hind III (cohesive). Ligation products were transformed into chemically competent E. coli DH-5α cells.*

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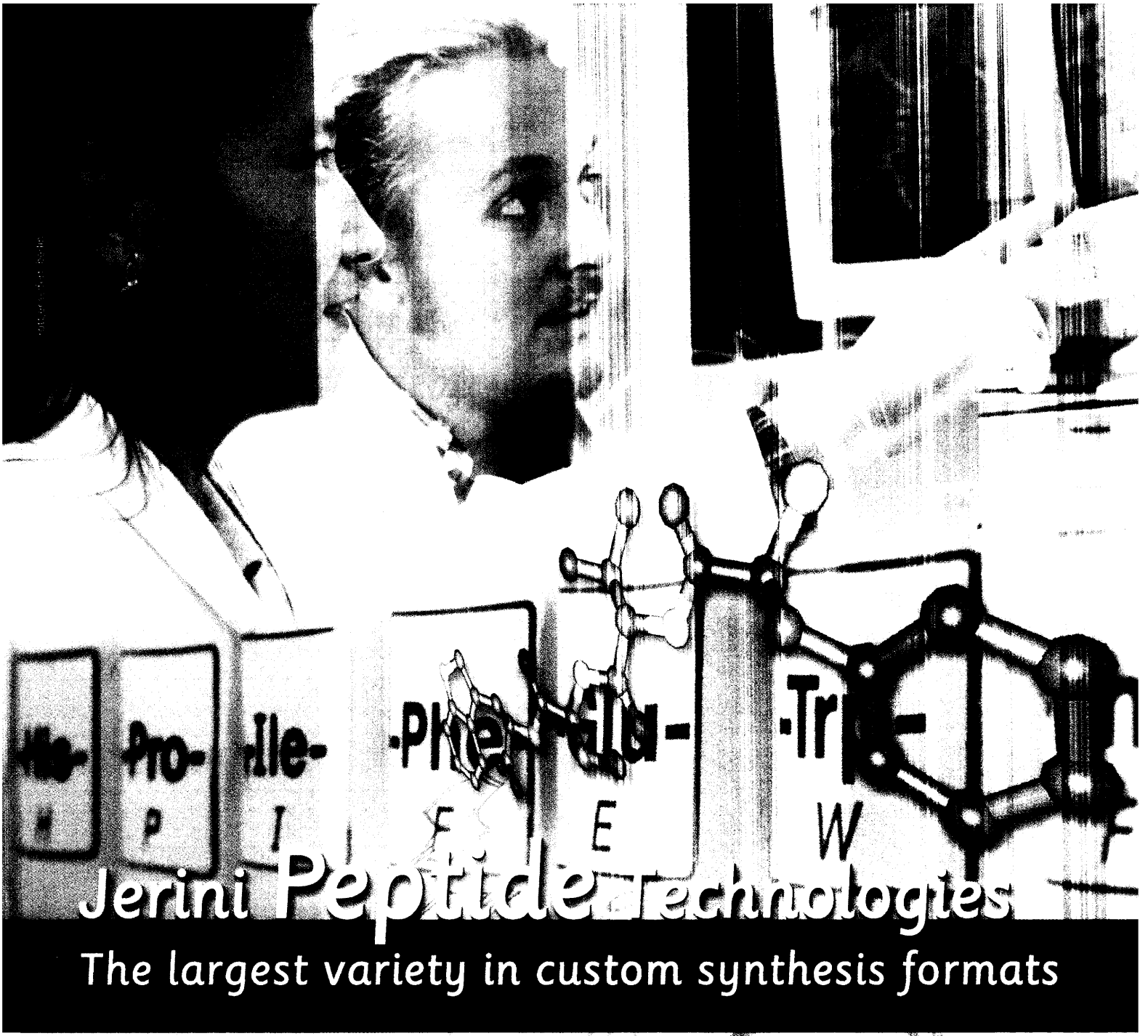

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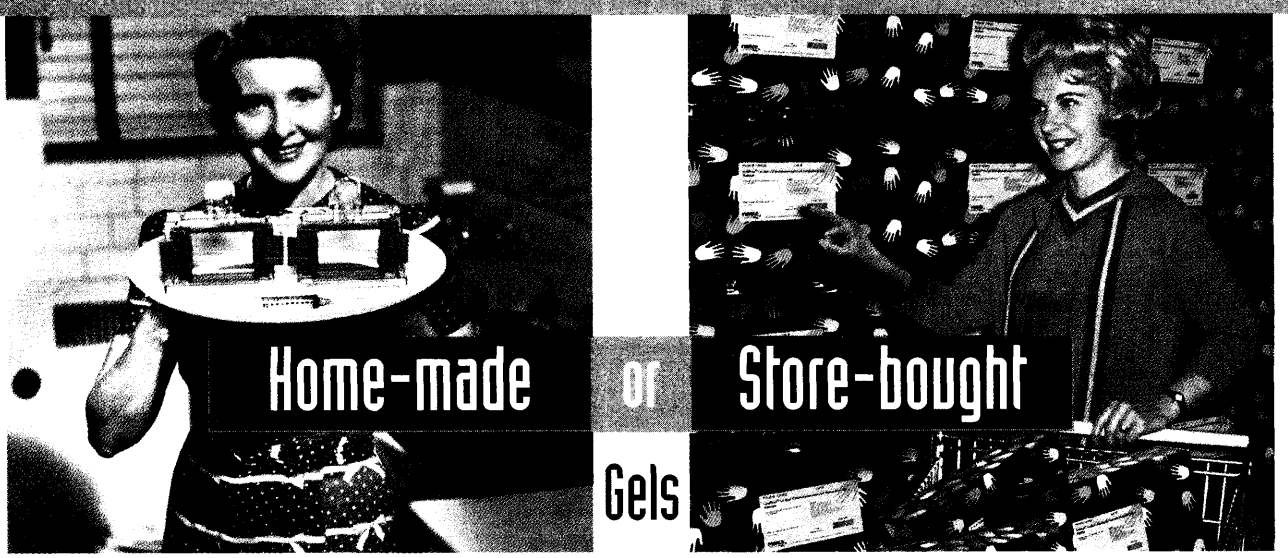

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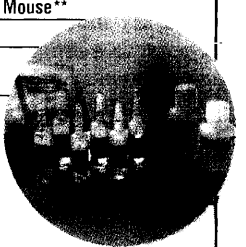

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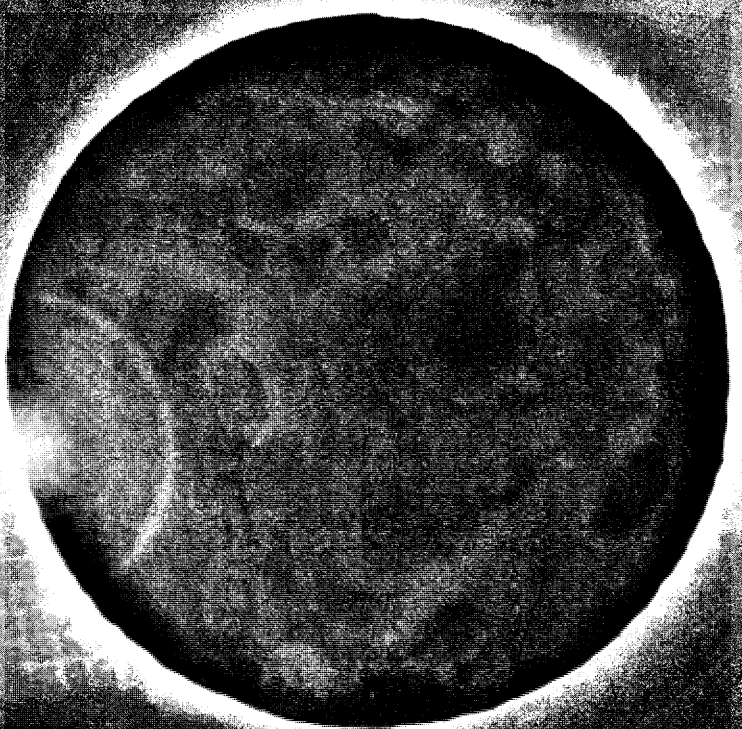

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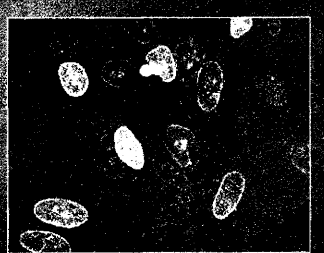
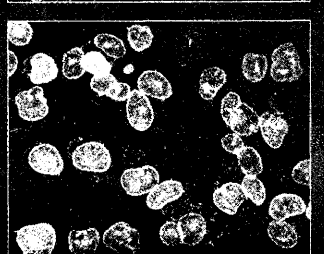
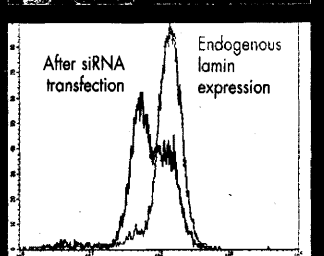


a



b



c

Silencing of endogenous nuclear envelope protein lamin A/C in mammalian cells. Immunofluorescence staining of HeLa cells transfected with lamin A/C siRNA duplex after 72 hours using **jetSI**™ (a) and control (b), visualized by fluorescence microscopy (a,b) or cytometry (c).

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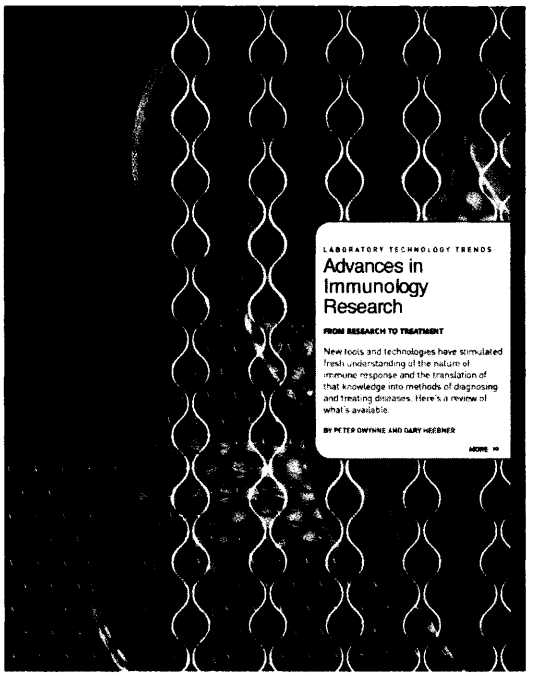

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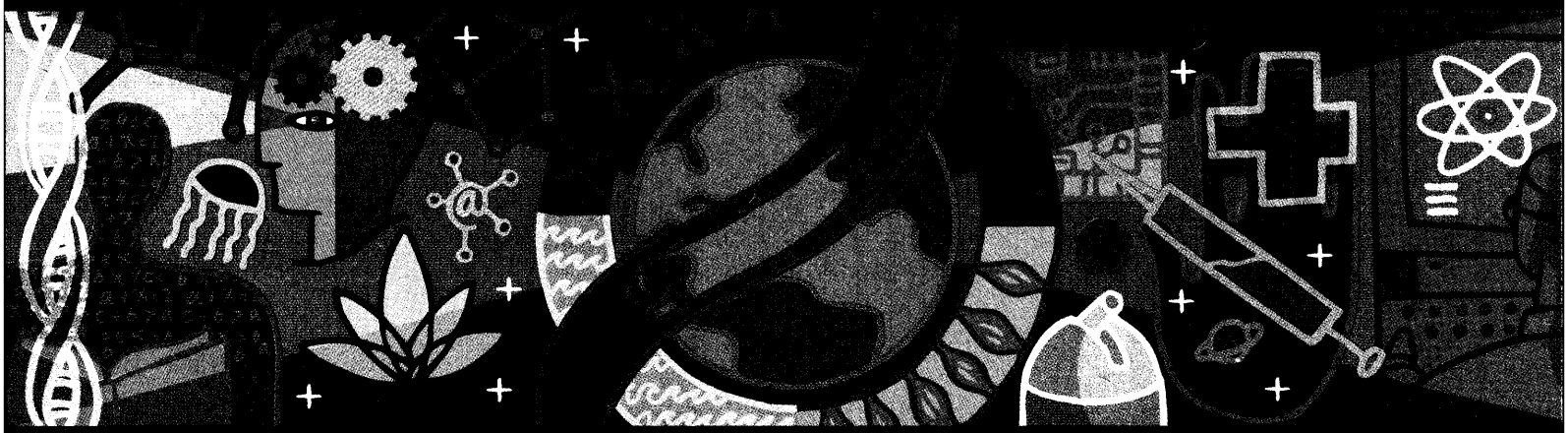

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