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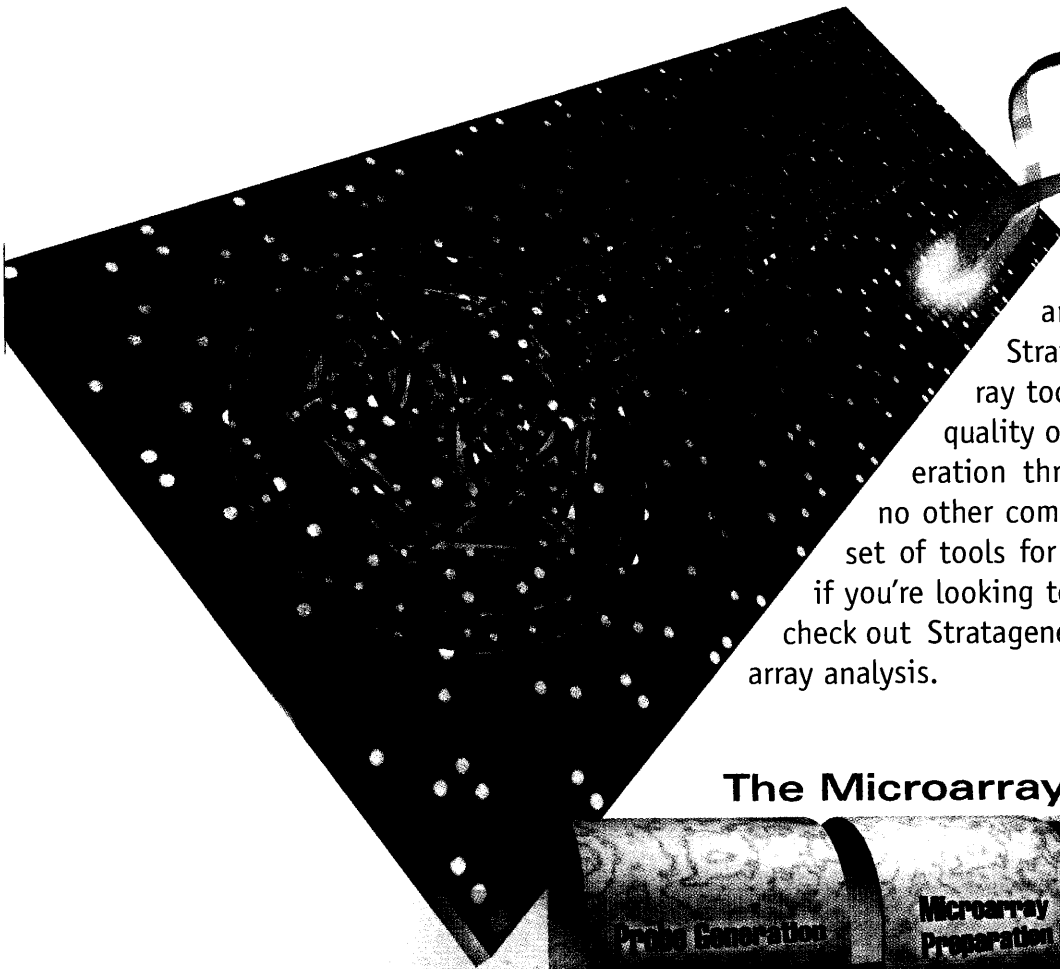
3 May 2002

Vol. 296 No. 5569
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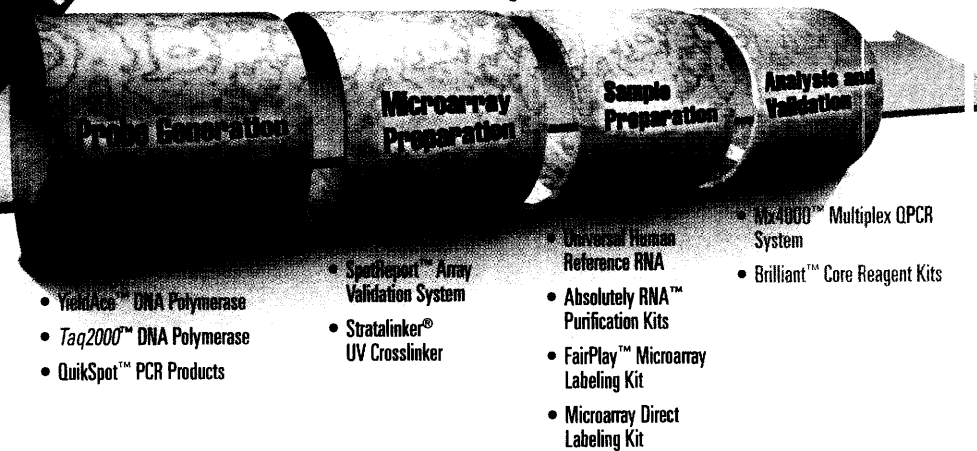
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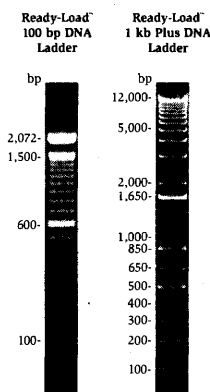
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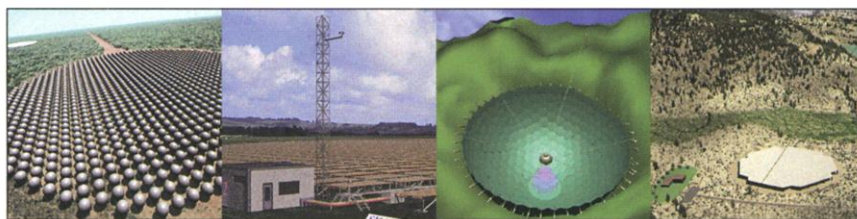
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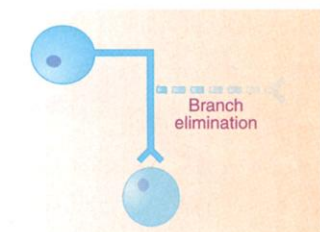
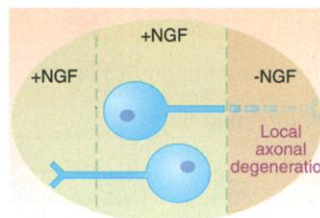
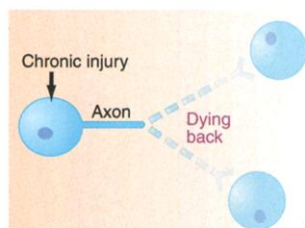
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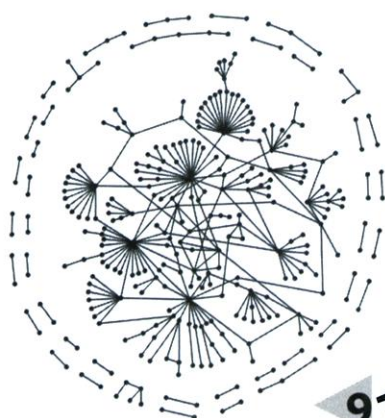
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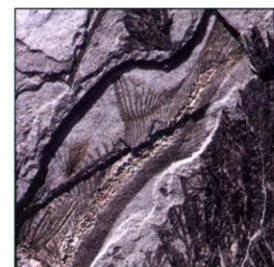
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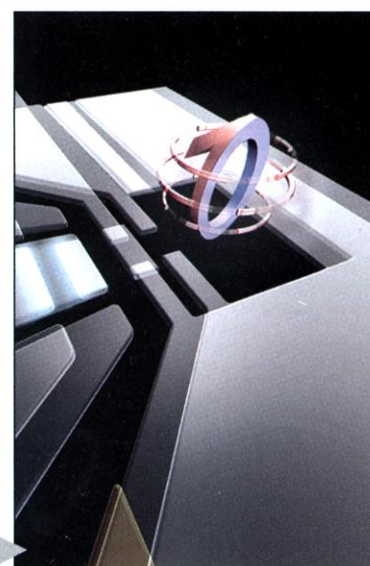
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COVER 899

An early fossil flower, *Archaeofructus sinensis* sp. nov., from the lower Yixian Formation (Upper Jurassic/Lower Cretaceous), Liaoning, China. Morphological and molecular analyses suggest that *Archaeofructus* is a basal angiosperm. Thin stems, dissected leaves, and associated fish (*Lycoperla davidi* Sauvage) indicate that these were aquatic flowering plants. [Photo: David Dilcher, Ge Sun, Qiang Ji]

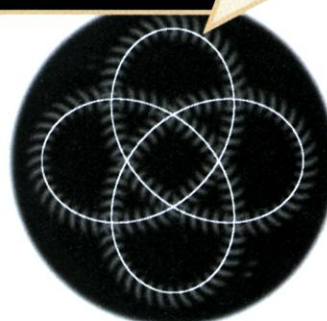


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A macroscopic qubit with long coherence time

New on Science Express

Chemical wave guides



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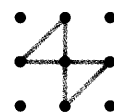
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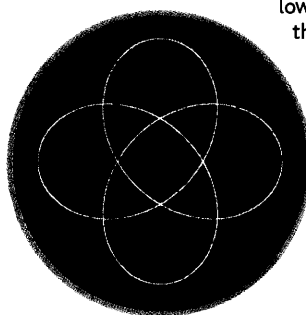
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Design and Control of Patterns of Wave Propagation in Excitable Media T. Sakurai, E. Mihaliuk, F. Chirila, K. Showalter

Feedback control is used to control and guide chemical waves in the photosensitive Belousov-Zhabotinsky reaction.



A Natural Product That Lowers Cholesterol as an Antagonist Ligand for the FXR N. L. Urizar *et al.*

An ancient folk medicine, widely used in India to lower cholesterol, is found to mediate its beneficial effects through the bile acid receptor FXR.

Sp1 and TAFII130 Transcriptional Activity Disrupted in Early Huntington's Disease A. W. Dunah *et al.*

Mutant huntingtin interferes with transcription mediated by the transcriptional activator Sp1 and its coactivator TAFII130.

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The Max-Planck-Institute of Molecular Cellular Biology and Genetics is the newest attraction in Germany's scientific community.

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A career in bilateral collaborations, R&D partnerships, and strategic alliances at the Canadian Embassy is not something that most scientists would consider possible, but they do possess the skills to do it.

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Part 3 of our series on International Research Funding; profiles of two Damon Runyon Cancer Research Foundation awardees; and the latest biomedical funding news.

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Technical issues related to using green fluorescent proteins to study protein interactions.

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THIS WEEK IN Science

edited by Phil Szuromi

Centimeter Nanotubes

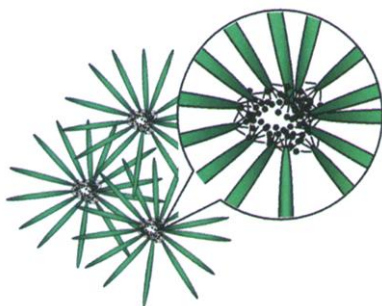
The fabrication of single-walled carbon nanotubes is still somewhat of an art form, and processes that either create the nanotubes at a much faster rate or of much greater length or purity is still needed. Zhu *et al.* (p. 884) use an improved floating catalyst method to create centimeter-long single-walled nanotube ropes that are significantly longer than those obtained from either chemical vapor deposition or laser-ablation methods.

Macroscopic Quantum Systems

Quantum-mechanical effects, such as discrete energy levels and the superposition of energy states, which are normally associated with systems no bigger than the atomic scale, can in fact be observed in certain macroscopic systems. Vion *et al.* (p. 886) and Yu *et al.* (p. 889) present results on the formation of two-level macroscopic quantum systems with superconducting tunnel junctions and show that interference effects between the two states can be observed. The realization of such large-scale quantum systems in more readily manipulated macroscopic systems may prove useful in quantum computation (see the Perspective by Leggett).

Phage Forge Nanoparticle Films

A nanofabrication method is presented that not only forms nanoparticles but also organizes them. Lee *et al.* (p. 892; see the Perspective by Ober) genetically engineered a coat protein of M13 bacteriophage with a specificity for the surfaces of ZnS nanoparticles. The bacteriophage, being long rigid structures, can form liquid-crystalline phases in solution, and thus the attached nanoparticles can assemble into ordered layered structures.



Antarctic Cooling and Ozone Losses

Despite an overall global warming trend, temperatures over large parts in the interior of Antarctica have exhibited a small but distinct cooling trend during the past several decades. Thompson and Solomon (p. 895; see the news story by Kerr) present evidence that high-latitude Southern Hemisphere circulation changes during the past few decades re-

875 Avoiding the Obvious

Chemists usually view elementary chemical reactions as proceeding in a statistical fashion—energy is rapidly redistributed between vibrational and rotational modes, and deep energy minima that lie along the various possible reaction pathways tend to act as a “trap” and dominate product formation. Sun *et al.* (p. 875) present results for dynamical simulations of a nucleophilic substitution reaction, $\text{OH}^- + \text{CH}_3\text{F} \rightarrow \text{CH}_3\text{OH} + \text{F}^-$, which show that despite the presence of a deep minimum in the potential energy surface, more than 90% of the simulation trajectories make their way to products. Product formation appears to occur on a much faster time scale than the competing statistical energy redistribution.

And in Brevia ...

Interactive song playback and microsatellite paternity analysis were used by Mennill *et al.* (p. 873) to test the hypothesis that female songbirds eavesdrop on male territorial song contests in order to make reproductive decisions.

flect a systematic trend in regional atmospheric circulation. Trends in tropospheric circulation trends can be traced to the recent cooling of the lower stratosphere caused by photochemical ozone losses.

Old Family of Flowers

Fossil specimens of a new family, Archaeofractaceae, of herbaceous, aquatic plants from the Upper Jurassic to Late Cretaceous Yixian Formation of western Liaoning, China have been characterized by Sun *et al.* (p. 899; see the cover and the news story by Stokstad). The family consists of a single genus, *Archaeofractus*, with two species, *Archaeofractus liaoningensis* and *Archaeofractus sinensis*. This family, based on

molecular and phylogenetic analysis, is one of the basal angiosperms and provides important information about the origin of reproductive organs in flowering plants.

Making Sense of Many Lipids

Homeostatic mechanisms maintain the lipid composition of biological membranes. In mammalian cells, the sterol response element-binding proteins are transcription factors that regulate cellular levels of cholesterol and fatty acids in a signaling and feedback mechanism that responds to these very lipids. Dobrosotskaya *et al.* (p. 879; see the Perspective by Nohturfft and Losick) report that this pathway is conserved in flies but also responds to and regulates synthesis of cellular phospholipids, a major membrane lipid.

The Splice of Life

Although 30 to 50% of human genes produce alternatively spliced transcripts, a much lower percentage is found in yeast. Clark *et al.* (p. 907) developed a microarray-based system to gain a global view of yeast splicing regulation. The authors examine pre-messenger RNA and messenger RNA levels of all yeast intron-containing genes in response to mutation of splicing-related genes to see what happens to splicing, both globally and at the level of individual transcripts. Cluster analysis indicates which introns behave similarly under certain circumstances and which genes affect splicing in similar ways. This method can be applied to more complex genomes for informative expression profiling of those systems.

Protein Raft Trips

Attention has been focused on lipid rafts—microdomains of the plasma membrane enriched in sphingolipid and cholesterol—in part be-



Illustration inspired by the art of Roy Lichtenstein (1923–1997).

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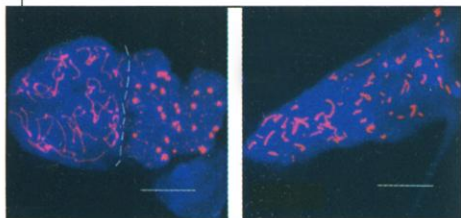


cause many proteins that take part in signaling across the plasma membrane are preferentially located in these structures. Zacharias *et al.* (p. 913; see the Perspective by van Meer) studied targeting of proteins to lipid rafts by monitoring fluorescence resonance energy transfer (FRET) between mutants of cyan fluorescent protein (mCFP) and yellow fluorescent protein molecules (mYFP) that had been engineered to prevent the normal dimerization of these proteins. FRET was detected between a fusion protein of CFP with caveolin, which is known to localize to rafts, and YFP that was acylated on its amino terminus. Prenyl modification of YFP, however, did not target the protein to rafts. Thus, lipid modification of proteins can regulate localization, and hence the function, of various proteins in lipid rafts.

Schwann Cells and Nerve Disorders

The glial cells of the peripheral nervous system, the Schwann cells, play important supporting roles, such as producing myelin, but their generation appears to facilitate two important nervous system disorders. Neurofibromatosis type 1 (NF1) is an inherited disorder characterized by the development of multiple benign tumors in the nervous system (neurofibromas) that occasionally progress to malignancy. Affected individuals have germline mutations in one allele of the tumor suppressor gene *NF1*, and their tumors show loss of expression of the other allele. Neurofibromas contain a complex mixture of cell types and it has been unclear which of these cells gives rise to the tumors. Using a sophisticated mouse model in which *NF1* expression can be selectively ablated in specific cell types, Zhu *et al.* (p. 884) show that the tumors arise specifically from Schwann cell precursors. Interestingly, however, tumor development was greatly accelerated when the surrounding non-neoplastic cells carried only one functional allele of *NF1*, illustrating the importance of tumor-host interactions in tumorigenesis. The causative agent of leprosy, *Mycobacterium leprae*, prefers to infect Schwann cells, and the resulting demyelination of nerve fibers leads to a progressive loss of sensation. It has been assumed that the nerve damage was mediated indirectly by the host's immune responses against the bacteria, but Rambukkana *et al.* (p. 927; see the Perspective by Brophy) show that the *M. leprae* directly causes demyelination via a contact-mediated mechanism. Nerve injury stimulates compensatory Schwann cell proliferation, and in this way *M. leprae* generates more habitable cells to occupy.

Not Keeping Up with Repairs



Replication of DNA or DNA damage processes can result in double-strand breaks, which in turn may lead to chromosomal translocation and an increased risk of malignancy. Celeste *et al.* (p. 922) tested the role of the DNA repair-associated protein, H2AX, in maintaining genomic stability. Cells from H2AX-deficient mice displayed several genetic abnormalities, including elevated sensitivity

to irradiation-induced damage, chromosomal breakage, and an increased incidence of translocations. Male H2AX^{-/-} mice were infertile due to defective spermatogenesis that resulted from failure of synapsis and meiotic arrest. T and B cell development was also diminished, and B cells displayed defects in switch recombination. Recruitment of DNA repair enzymes was severely affected in the absence of H2AX, confirming a central role for this protein in coordinating the response to DNA damage. **X**

Tackling the Link Between Stress and Alcohol

The chances to develop alcoholism throughout one's life are determined by a genetic predisposition and an individual's reaction to lifetime events, such as stress. The corticotropin-releasing hormone (CRH) system regulates endocrine responses to stress and mediates stress-related behavior. To better understand the molecular and cellular mechanism underlying stress-induced alcohol drinking Sillaber *et al.* (p. 931; see the news story by Holden) created knockout mice lacking CRH1 receptors. *Crrh1*^{-/-} mice did not differ from wild-type mice in their basal alcohol intake and preference. However, after repeated stress episodes, the knockout mice gradually increased their alcohol consumption and kept it elevated for the rest of their life. This change in drinking behavior was accompanied by enhanced protein levels of the NR2B subunit of the N-methyl-D-aspartate receptor.

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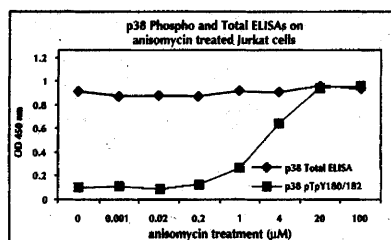
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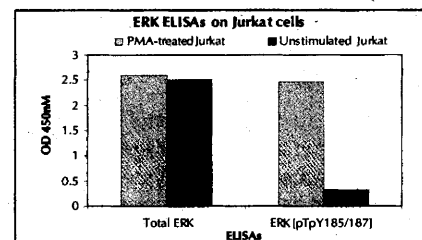
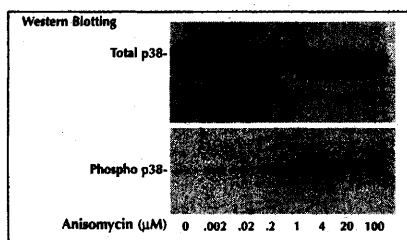
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Cell lysates from Jurkat cells treated with various concentrations of anisomycin were tested with Total p38 MAPK ELISA (Cat.#KHO0061), phospho p38 MAPK ELISA (Cat.#KHO0071) and Western blotting. The data show excellent correlation between ELISA and Western blotting.



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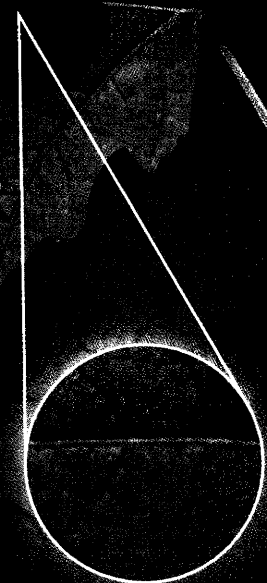
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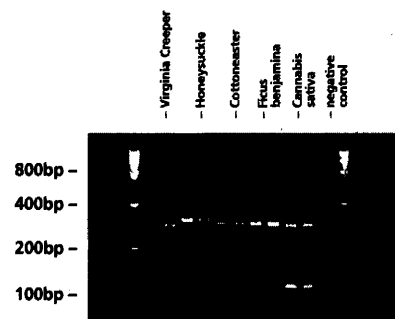
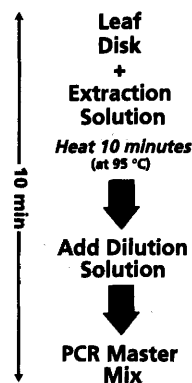
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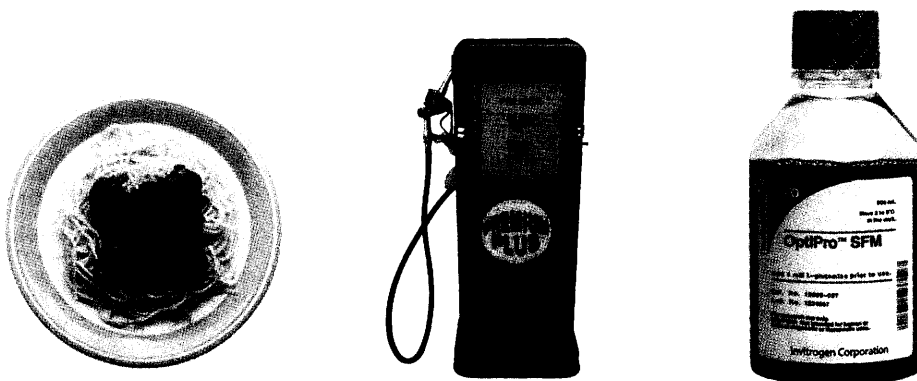
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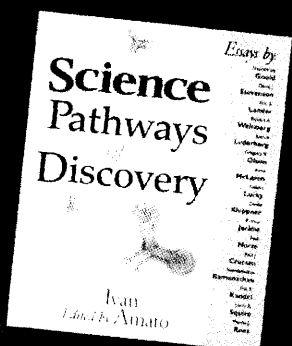
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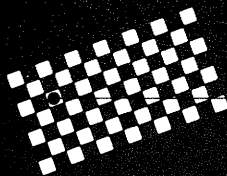
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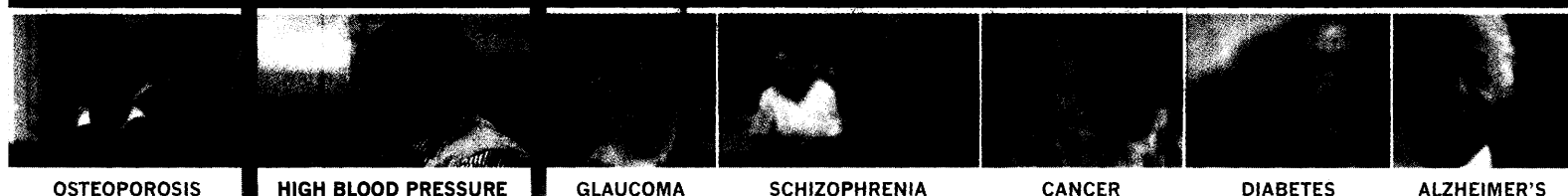
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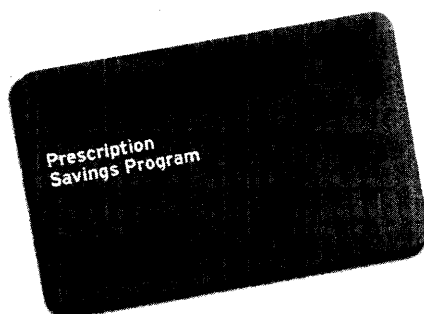
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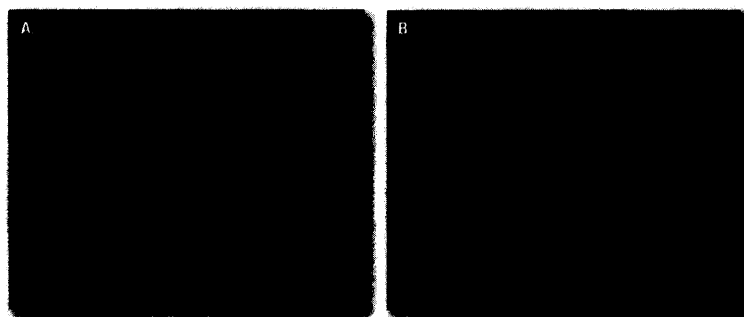
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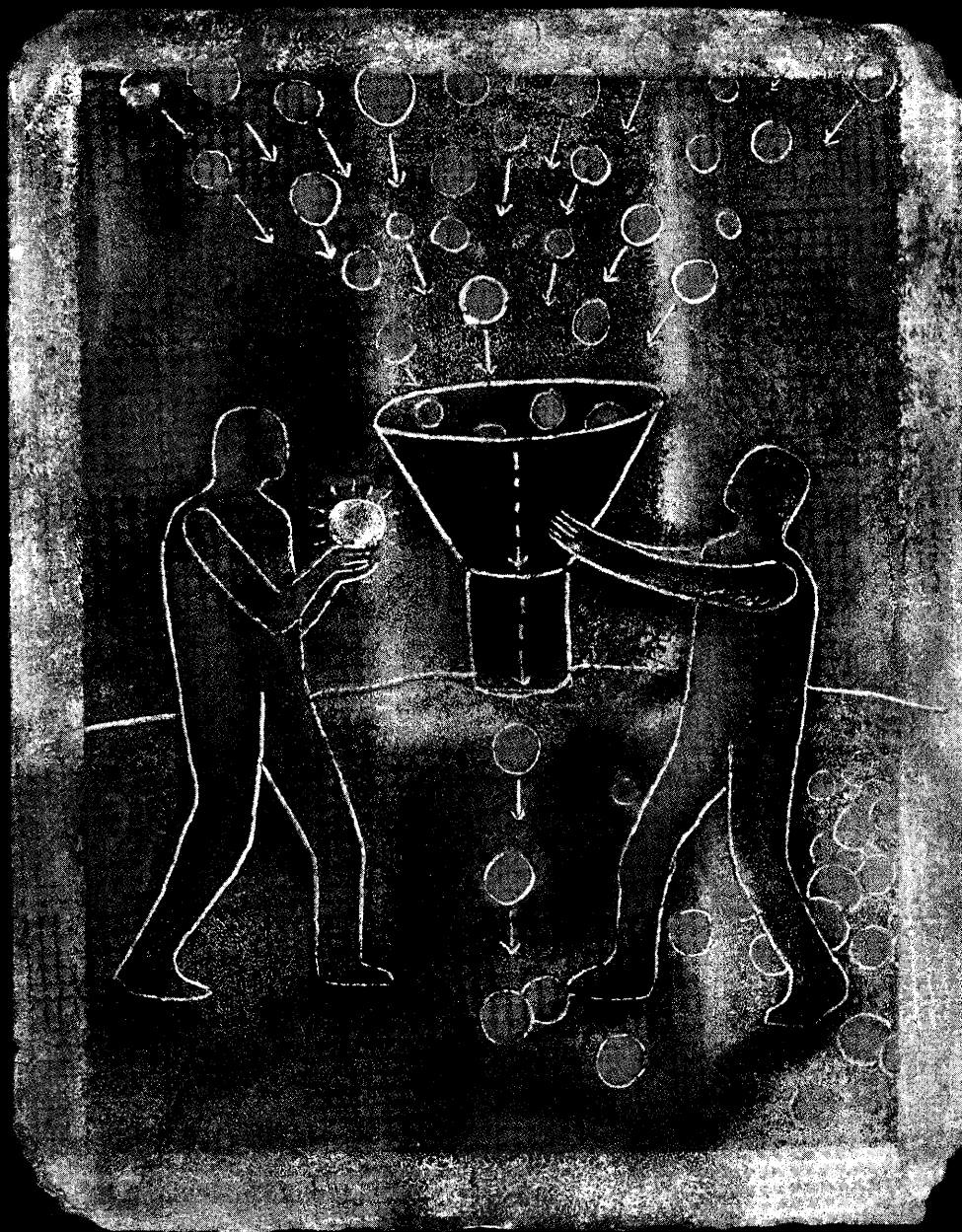
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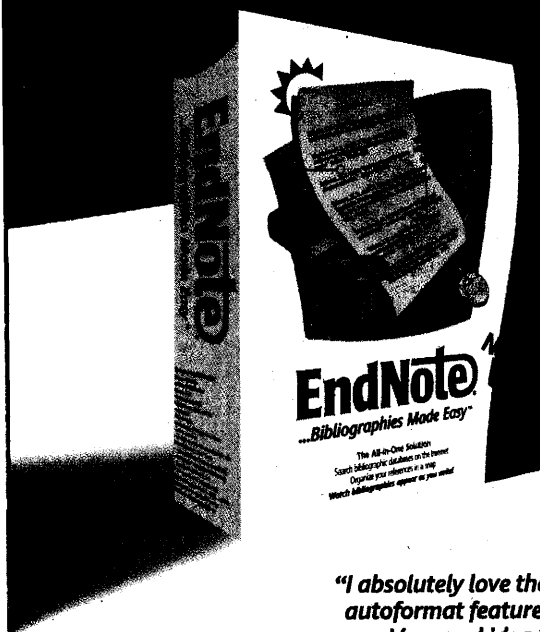


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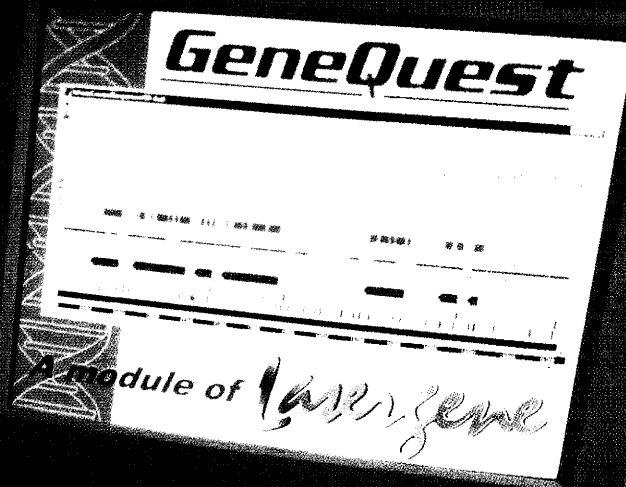
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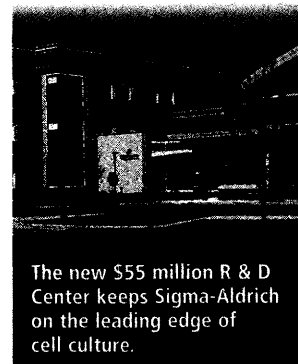
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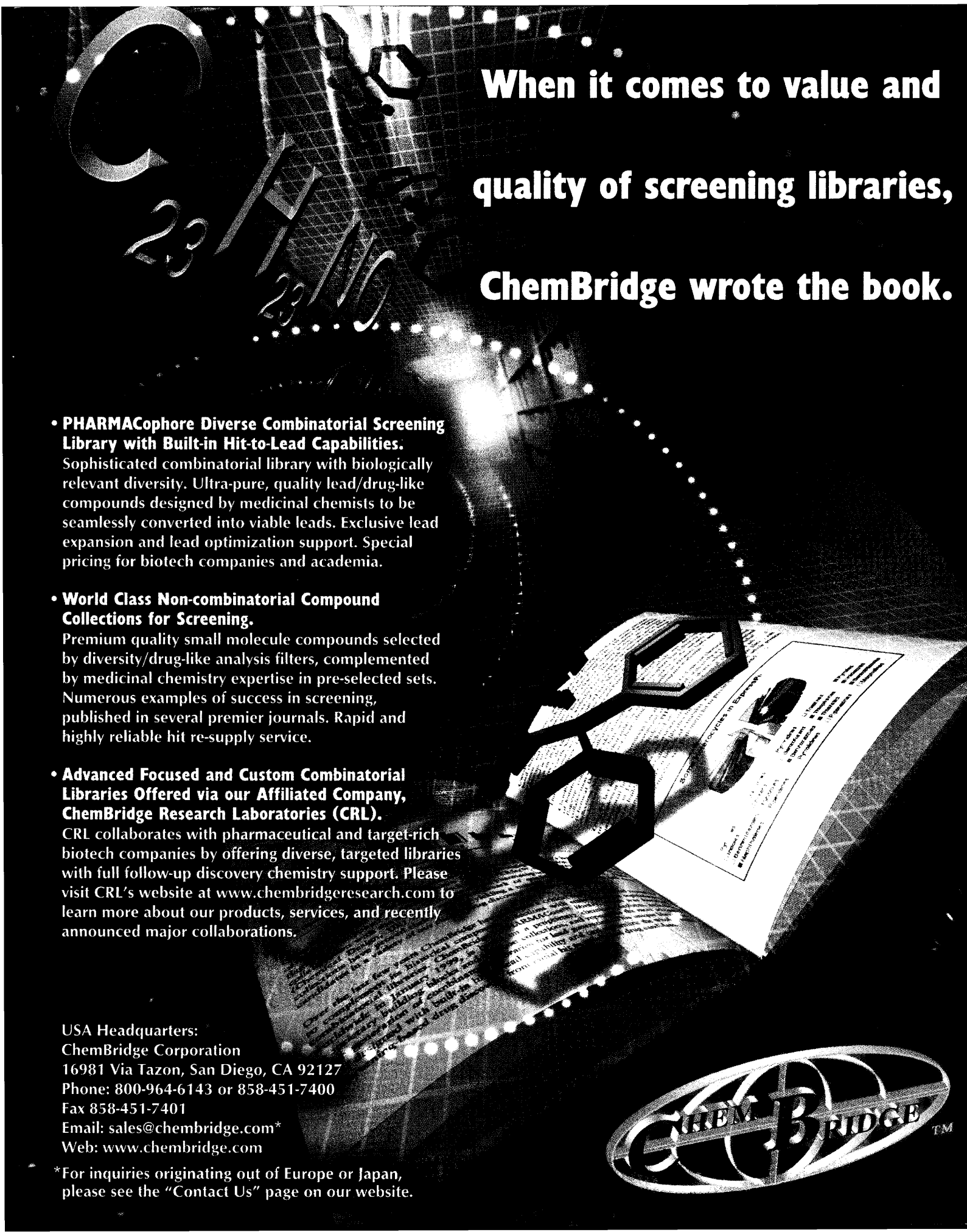
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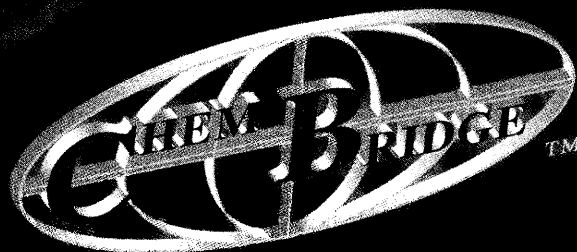
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The first Purdue Pharma Prize for Pain Research has been awarded to William D. Willis, Jr., MD, PhD. This \$50,000 prize is awarded bi-annually by the Purdue Pharma Fund to recognize outstanding contributions to pain research.

Dr. Willis was selected on the basis of his pioneering research into the mechanisms of acute and chronic pain. The author of more than 350 peer-reviewed publications and presentations, his work on the neuroanatomy, physiology, and neurochemistry of pain has been critical to the development and direction of research in this field. A past president of both the American Pain Society and the Society for Neuroscience, Dr. Willis is currently Chairman of the Department of Anatomy and Neuroscience at the University of Texas, Galveston.

The selection committee for the 2002 prize included **Dr. Norman Bowery**, University of Birmingham, England; **Dr. Frank Porreca**, University of Arizona; **Dr. Gary Bennett**, McGill University, Montreal; **Dr. Anthony Dickenson**, University College, London, England; and **Dr. Ken Hargreaves**, University of Texas.

For more information about the Purdue Pharma Prize for Pain Research, please visit www.purduepharma.com.



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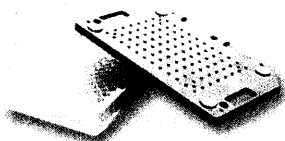
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Pub. No. 070-2001-002A