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9 JUNE 2000

NEWS OF THE WEEK

PLANETARY SCIENCE: Most-Common Meteorites Find a Home Among the

PLANT GENETICS: From Genome to

BIOTECHNOLOGY: Disease Group Invests

BIOMECHANICS: Geckos Climb by the

NEUROBIOLOGY: Trigger Found for

Functional Genomics

in Do-It-Yourself Drugs

Hairs of Their Toes

Synapse Formation

NUMBER 5472

Path

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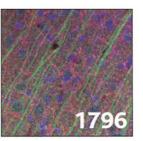
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COVER This immunofluorescent microscopic image of mouse brain section shows the localization of molecular motor KIF17 (green) in the dendrites of nerve cells. KIF17 transports neurotransmitter receptors along microtubules from the cell body to the synapses formed with nerve axons (red), where they likely serve as raw material for the construction of new or enhanced synapses during learning. Nuclei of glia and nerve cells are stained blue. Image width, 300 µm. [Photo: M. Setou and N. Hirokawa]



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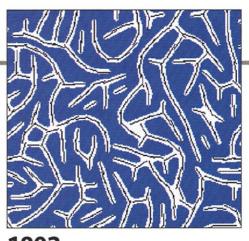
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PATHWAYS OF DISCOVERY

Cloning: Pathways to a Pluripotent Future A. McLaren

In this month's essay, Anne McLaren

traces the winding and pitted pathways that connect the origin of the cell theory of life in the 1830s to the new and unfolding era of cloning science and technology. The possibilities are fantastic—and ethically charged.

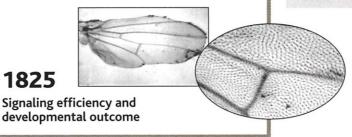
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- Antarctic Ice Sheet During the Last Glaciation S. L. Kanfoush, D. A. Hodell, C. D. Charles, T. P. Guilderson, P. G. Mortyn, U. S. Ninnemann Extinct ¹²⁹I in Halite from a Primitive
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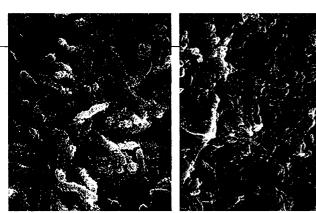
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IMAGES

Bathroom Science

Next time you think about dropping into bed without brushing your teeth or cleaning your contacts, consider what might be growing on them. Shown here are biofilms of bacteria in dental plaque (left) and in the contact lens case of a patient diagnosed with an eye infection. (The tooth bacteria, stacked into corncob shapes, are unidentified, while the lens case contains dried-up rod-shaped bacteria and Acanthamoeba cysts.) Professors seeking photos to spice up their lectures can troll a new American Society for Microbiology educational Web site offering over 150 images, along with a slew of course materials. Check out everything from hot spring-loving algal mats to bacteria lurking in septic systems, the Lyme disease parasite, and a movie of budding yeast at: www.microbelibrary.org

HOT PICKS

Chinese science express. The Bulletin of the Chinese Academy of Sciences, an English-language journal, now has a free Web site offering news updates on science in China. Recent stories covered a meeting on AIDS and an expedition to set up long-term environmental monitoring on a Himalayan peak. www.bulletin.ac.cn

Four seasons. Environmental and earth science students can click on these color animations of global climate data to get a feel for the seasonal shifts in surface temperatures, precipitation, heat flux, winds, and other measurements.

geography.uoregon.edu/envchange/clim_animations/index.html

Nothin' but mammals. Ancient lemurs, rodents, dogs, tapirs, and other fossilized mammal species are cataloged in these two North American fossil mammal databases. The first site offers taxonomic and phylogenetic data on 3200 named species, while the second paleofaunal database includes clickable maps of fossil locations and trivia (such as the 10 smallest mammals and the most productive taxonomists).

www.nceas.ucsb.edu/~alroy/nafmsd.html www.nceas.ucsb.edu/~alroy/nampfd.html







Wild ride. The present best theory of what all matter boils down to, known as the Standard Model, is explained in the remarkably clear and simple pages of The Particle Adventure, a widely praised site aimed at high school students. Replete with animations of decays, guizzes, and a pop-up glossary, the site starts out by discussing quarks, leptons, and other particles, lays out the experimental evidence for them, then explains the workings of giant accelerators and detectors. www.particleadventure.org

edited by JOCELYN KAISER

Genome scorecard. Keep tabs on genome sequencing projects at the Genomes OnLine Database, which tracks the status of over 250 genomes-from Salmonella bacteria to the justcompleted human chromosome 21. The links-packed site, which also includes viruses, phages, and organelles, recently found a new home with a company but will remain free. igweb.integratedgenomics.com/GOLD

SITE VISIT Arsenic Dilemma

Arsenic, a favorite poison in Victorian novels, today poses a vexing global water pollution problem. In the United States, for instance, federal officials last month proposed clamping down on arsenic in drinking water supplies even while acknowledging that many communities can't afford to remove the carcinogen. Meanwhile, in Bangladesh and west Bengal, India, wells heavily tainted with arsenic have led to a massive health catastrophe-the slow poisoning of at least

70 million people.

The Arsenic Website Project, run by Harvard University risk expert Richard Wilson, brims with articles and links probing this complex environmental problem. You can learn how the metal leaches into water from both natural and humanmade sources, such as mine tailings and obsolete pesticides. The site also notes arsenic's paradoxical nature: It was



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phys4.harvard.edu/~wilson/arsenic.html

long used in medicines and can reportedly cure a form of leukemia. But long-term exposure can cause cancer and, in Bangladesh, poisoned villagers develop painful skin lesions, depicted here with shocking photos. Click to get arsenic updates for 18 countriés, or pull up maps, reports, and conference proceedings. Another section lays out schemes for providing Bangladeshis with safe drinking water, from filtering well water to switching to other sources.

Science ONLINE

The perpetual balancing act between career and family is among topics addressed this month in Science's Next Wave's feature on women scientists. Log in for advice from role models around the world, thought-provoking essays on women, science, and society, and more. You'll also find articles from the magazine of the Association for Women In Science, the beginning of a partnership through which AWIS members will receive free access to Next Wave.

www.nextwave.org/cgi/content/full/2000/06/01/8

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

CONNECTING RODS

The phase behavior of polymer composite materials is potentially very rich, especially for nanophase-separating systems, and simulations can be used to identify targets that could be realized in experiments. Peng et al. (p. 1802) have studied the behavior of nanoscale rigid rods immersed in an immiscible binary polymer blend in which the minority component wets the rods. The presence of the rods drives the normally isolated minority component domains into an interconnected percolation network. Such an effect could prove useful in designing inorganic-organic composites in which connectivity of nanorods (such as carbon nanotubes) is desired.

WRITE ONCE, COPY MANY TIMES

Scanning probe methods for nanopatterning and fabrication appear to have a huge limitation-they tend to create things one example at a time; that is, in serial fashion, and do not allow the parallel processing that photolithographic methods afford. Hong and Mirkin (p. 1808) now show that parallel processing is possible for "dip pen nanolithography," in which they can draw ultrafine lines and dots of different organic molecules on gold surfaces with an atomic force microscope tip. Up to eight "pens" can now draw the same pattern at one time, with seven tips following a master. They also show that they can "corral" some molecules within patterns formed by lines made of other compounds, thus allowing patterns to be more readily filled in.

PROBING EMPTY STATES

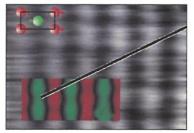
Most of the measurements used to probe high-temperature superconductors or the colossal magnetoresistance materials are limited in that they measure properties only of the occupied states. Although these techniques have provided a vast amount of information on these materials, little remains known about the structure and electronic properties of the unoccupied conduction band. Hasan *et al.* (p. 1811) addressed this problem by using resonant inelastic x-ray scattering to develop a momentum-resolved description of the conduction band of a Mott insulator. These results for Ca₂CuO₂Cl₂ support the Hubbard model of the gap.

ANTARCTIC ICE ARMADAS

The presence of ice-rafted debris in North Atlantic marine sediments shows that flotillas of icebergs were discharged episodically during the last glacial period by Northern Hemisphere ice sheets. Kanfoush *et al.* (p. 1815) provide evidence that analogous periods of Antarctic ice sheet instability occurred as well. Their results, from a trio of deep-sea cores from the Southern Hemisphere, reveal that Antarctica also produced millennialscale pulses of icebergs, although not synchronously with the discharges in the North. These episodes, which occur during cold periods, tend to correlate with warm periods in the Northern Hemisphere and suggest an antiphase relation between Northern and Southern Hemispheric warming and cooling.

IMAGING TWO-DIMENSIONAL ANTIFERROMAGNETISM

The behavior of ultrathin antiferromagnetic films is of interest not only for understanding magnetism in the limit of two dimensions, but also for applications in giant magnetoresistance devices that take advantage of the exchange bias effect. Heinze *et al.* (p. 1805; see the Perspective by Scholl) modified a scanning tunneling microscope by putting a spin-polarized coating on the imaging



tip so that the magnitude of the tunneling current would depend on the relative orientation of the magnetization in the tip and the probed atom. They used this technique to produce a magnetization map of a monolayer of antiferromagnetically coupled manganese atoms on a single-crystal tungsten surface with atomic resolution.

OLD SALTS OF THE SOLAR SYSTEM

Halite and sylvite grains, discovered in primitive meteorites, suggest that water-rich brines dried out and formed evaporite deposits more than 4 billion years ago. Whitby *et al.* (p. 1819; see the Perspective by Ott) used high-precision mass spectrometry to measure the xenon, iodine, and argon isotopic concentrations in halite crystals and matrix material from the Zag H chondritic meteorite. The xenon was isotopically pure xenon-129 generated from the decay of iodine-129 with no component related to solar wind or planetary atmospheric contamination. Thus, the salts in Zag probably formed within 2 million years of the formation of the solar system, which indicates that water loss and evaporite deposition occurred very rapidly and very early.

PROCESSING PAIN

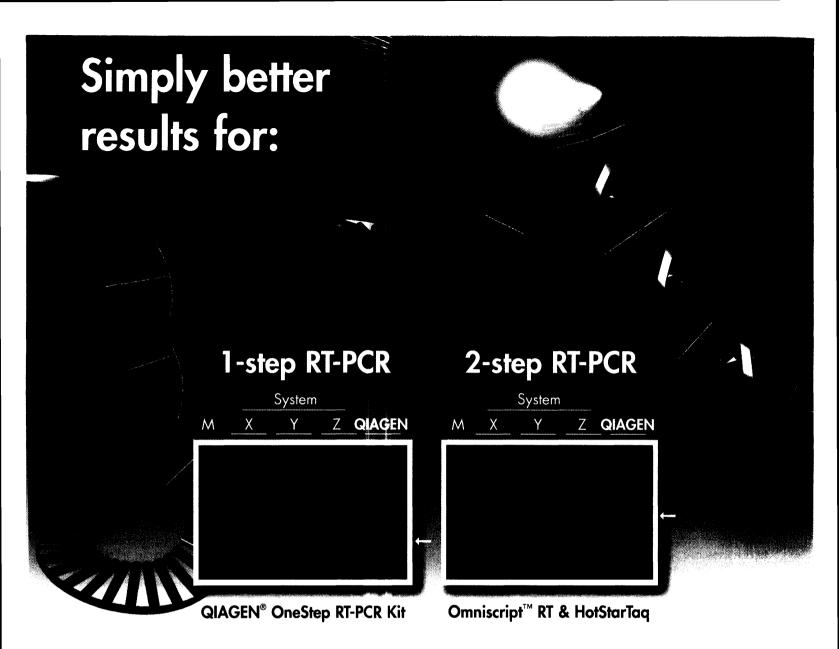
Numerous entities in our nervous system process pain before it reaches the level of consciousness. During the last several years, our understanding of the underlying mechanism has increased on every level of this processing cascade from the stimulation of specialized nerve fibers, so-called nociceptors, all the way up to the highest brain centers where the emotional interpretation of sensations occurs. Woolf and Salter (p. 1765) overview the cellular and molecular mechanisms of pain sensitization as the nerve stimulus moves from the periphery to the spinal cord. Price (p. 1769) describes the integration of painful information in the central nervous system and presents a scheme for the translation of that information into the affective, sensory, and cognitive dimension of the experience of pain.

MOLECULAR SUPPLY LINES

The long processes that characterize neurons reflect their function as processors of information. Signals come in one set of processes, the dendrites, and usually go out in a single long process, the axon. The neuron's complicated shape is convenient for information processing, but presents a difficult housekeeping problem for the cell, which must use motors that run along microtubule tracks to supply the ends of the long processes with appropriate proteins. Setou et al. (p. 1796; see the cover) have now identified a new dendrite-specific motor, KIF17, that binds to a complex of proteins on the surface of small vesicles containing one of the key postsynaptic receptors, the NR2B subunit of the N-methyl-D-aspartate receptor. The authors show that KIF17 binds to a PDZ domain in mLin-10, which is in a complex with CASK, MALS, and NR2B in the membrane of the vesicle. This protein assembly conveys the NR2B receptors to the postsynaptic side of the synapse where they help confer plasticity.

WHEN HIV-1 AROSE

Although discoveries of dinosaurs and ancient relics have captured the public's imagination, analysis of nucleic acids can also reveal when an organism first appeared. Many evolutionary biologists have relied on the assumptions of a molecular clock (that sequence changes accumulate as a function of CONTINUED ON PAGE 1703



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THIS WEEK IN SCIENCE CONTINUED FROM PAGE 1701

time) but there are questions regarding some of the underlying assumptions, such as whether the rate of evolution is constant. Korber et al. (p. 1789; see the Perspective by Hillis) tackle these issues and compare different evolutionary models to provide improved estimates for the origin of the human immunodeficiency virus-type 1 (HIV-1) epidemic in the human population. Their analysis of errors and confidence limits should be useful in a broad range of studies, but is particularly timely because of recent suggestions that the AIDS epidemic may have originated in the 1950s from contaminated lots of oral polio vaccine. Their estimates place the origin of the AIDS epidemic in the 1930s and make that hypothesis highly unlikely.

KNOWING WHAT YOU'VE DONE

Cognition and the prefrontal cortex is one of the meeting places of psychology and neuroscience. The approach of choice in cognitive neuroscience has been to develop behavioral tasks that dissociate aspects of elements of working memory and then image the brain regions of activity during their execution. Using a modified version of a classical test known as the Stroop task, MacDonald et al. (p. 1835) now describe a double dissociation of dorsolateral prefrontal cortex (Brodmann area 9) and the anterior cingulate (Brodmann areas 24 and 32) where the former region underlies memory of items and response and the latter region monitors conflict and assesses performance.

A MATTER OF EFFICIENCY

The Wnt family of signaling proteins plays key roles in a variety of embryonic inductive events in vertebrates and invertebrates. This diversity appears to be mediated by differences in Frizzled (Fz) proteins, the cell surface receptors for Wnt. Boutros *et al.* (p. 1825) examined two *Drosophila* Fz proteins and found that while they both activate the same signaling pathways, they do so with different efficiencies. The cytoplasmic domains of the receptors are largely accountable for this difference. Factored with differences in receptor-ligand affinities, this domain may be important in determining specific signaling outcomes.

CONSERVATION COSTS

When does it pay to conserve tropical forests? In a detailed economic case study of Masoala National Park in Madagascar, Kremen *et al.* (p. 1828; see the Perspective by Bonnie *et al.*) show that the conservation and sustainable-use approach can provide significant economic benefits at both

local and global levels—the former from sustainable community-managed forestry and ecotourism, and the latter from storage of carbon that would otherwise be released as greenhouse gas. At the national level, however, these benefits are outweighed by those of large-scale logging, and it is at this level that policy decisions are generally made. The Kyoto protocol could nevertheless secure benefits at all levels by recompensing nations for the national costs of conservation.

KEEPING CYCLIC NUCLEOTIDES IN CHECK

Cyclic nucleotides are second messengers that are essential in many physiological processes including vision, cell growth, and differentiation. Their concentration must be tightly regulated, and the key players here are a family of therapeutically important enzymes known as phosphodiesterases (PDEs) that catalyze the hydrolysis of cyclic nucleotides. Xu et al. (p. 1822) have determined the structure of the catalytic domain of the PDE 4B2B to 1.77 angstroms. A deep pocket, identified as the active site, contains most of the residues conserved across PDE families, and two metal ions at the bottom of the pocket are likely to play a role in catalysis. Modeling the cyclic adenosine 3',5'-monophosphate substrate into the active site provided insight into the mechanism of catalysis and nucleotide specificity within the PDE family. This structure provides a framework for designing drugs against PDEs that are clinical targets for diseases, such as congestive heart failure, asthma. and inflammation.

WINNING WITH A PARTIAL KNOCKOUT

Gene knockout experiments have indicated that the metabotropic glutamate receptor subunit mGluR1 plays an important role in a number of phenomena, from the elimination of surplus climbing fiber synapses in the developing cerebellum to the induction of long-term depression. However, because of the generalized nature of these knockout studies, it was unclear whether the observed deficits could be attributed to the missing mGluR1 receptor in cerebellar Purkinje cells or other neurons in the brain. Ichise et al. (p. 1832) report that mice in which mGluR1 is specifically rescued in Purkinje cells show none of the deficits reported in knockout animals. The technique of inducible conditional gene rescue should allow resolution of similar questions about gene knockouts in other types of tissues.

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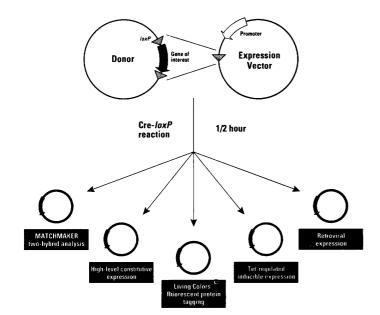




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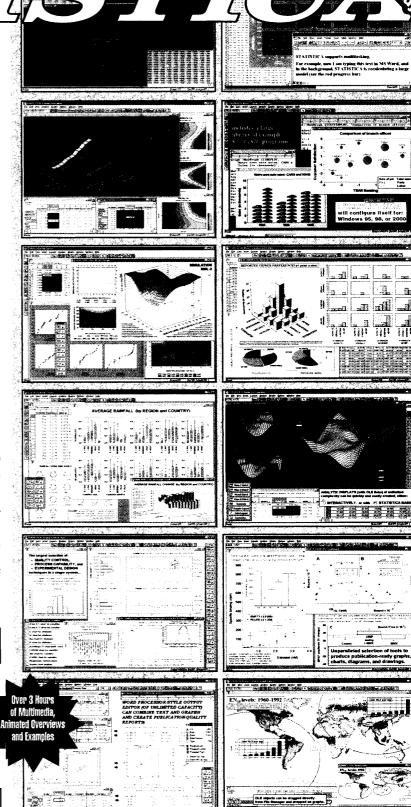
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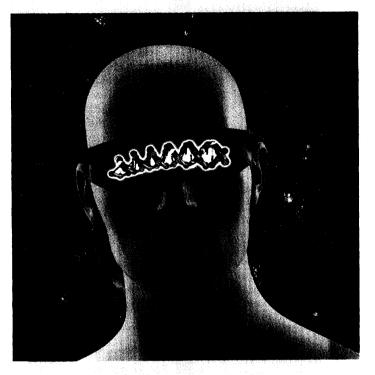
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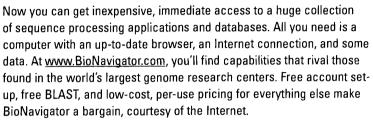
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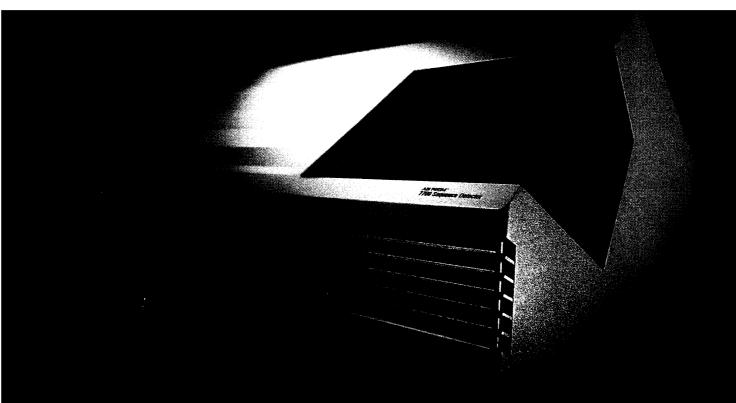
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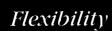
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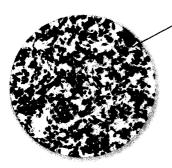
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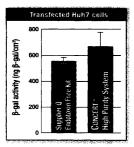
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Monday, August 14, 2000

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7:30	Pre-Conference Symposia Registration (Open All Day)
8:30 - 12:00	Symposium A: Managing Information in Drug Discovery for Better Decision Making Sponsored by: Contended BackAnd
	Symposium B: The Art and the Science of Pharmaceutical and Biotechnology Collaborative Ventures
1:15 - 4:45	Symposium C: Cutting-Edge Technologies
	Symposium D: The Impact of Gene and Technology Patents on Drug Discovery
4:45 - 7:30	Exhibit/Poster Opening Night and Reception Sponsored by: modemdrugdiscovery
	Exhibit Hall Hours: 4:45pm - 7:30pm

Tuesday, August 15, 2000

7:00	Main Conference Registration		
8:00 - 9:30	Keynote Presentations		
	J. Craig Venter, Ph.D., Celera Genomics Frank Douglas, Ph.D., Aventis Pharmaceuticals		
10:15 - 12:50	Parallel Sessions		
	Track 1: Genomics and Target Validation Sponsored by: GENE< 7 ⁴ / LOGIC		
	Track 2: Lead Generation and Optimization		
12:50 - 3:15	Poster/Exhibit Viewing and Lunch in the Exhibit Hall Sponsored by: modemdrugdiscovery		
3:15 - 5:30	Technology Workshops		
5:45 - 6:15	Mystery Keynote Speaker		
6:15 - 7:45	Exhibit/Poster Viewing and Networking Reception		
	Exhibit Hall Hours: 9:30am - 7:45pm		
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Wednesday, August 16, 2000

7:30	Breakfast Seminar Sponsor	red by: 🕂 Cy E	Bio
8:15 - 9:05	Keynote Presentation		
9:05 - 9:45	Steven V. Ley, FRS, Univer Innovative Investigator	•	
2.00 2.10	Award Presentation	Sponsored by:	Aventis

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10:30 - 12:45 Parallel Sessions

	Track 1: Target and Compound Prioritization and Early ADME and Toxicology Sponsored by:
	Track 2: Combinatorial/Medicinal Chemistry and Miniaturization and Chip-Based Technologies
12:45 - 3:00	Poster/Exhibit Viewing and Lunch in the Exhibit Hall
3:00 - 5:35	Parallel Sessions
	Track 1: ADME and Toxicology continued and Predictive and Simulation Tools Sponsored by: Instancatica
	Track 2: Miniaturization and Chip-Based Technologies continued and Screening/Assay Development
6:00	Drug Discovery Technology 2000 Dinner "A Taste of Boston"

Exhibit Hall Hours: 9:45am - 3:00pm

Thursday, August 17, 2000

7:15	Breakfast Seminar
8:15 - 12:00	Drug Discovery Case Histories
12:00	Close of Drug Discovery Technology 2000
12:00 - 6:00	American Chemical Society Short Courses
	ACS 1: Organic Chemistry of Drug Design and Drug Action
	ACS 2: Practical LC/MS and CE/MS
	ACS 3: Combinatorial Chemistry: Solid and Solution Phase Synthesis
	ACS 4: Drug Discovery Using Molecular Biology Techniques to Find Drug Targets
	ACS 5: The Role of Toxicology in Drug Discovery

Friday, August 18, 2000

8:00 - 5:00 American Chemical Society Short Courses

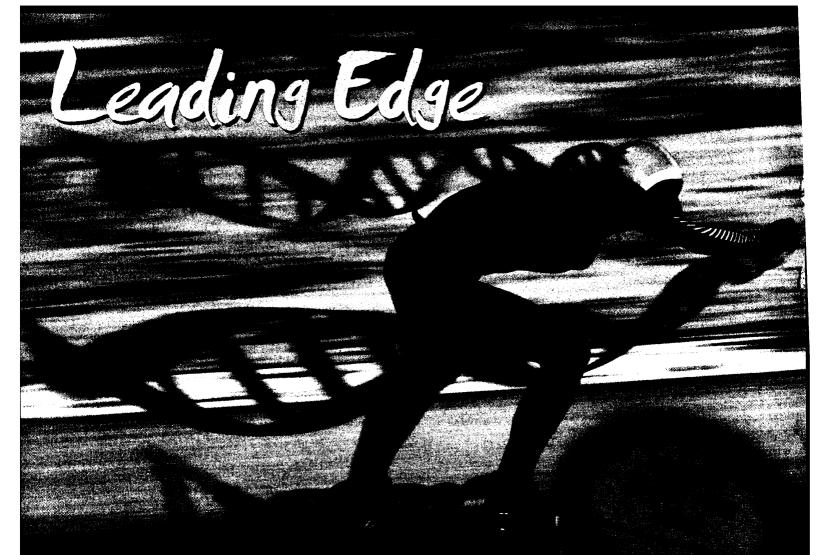
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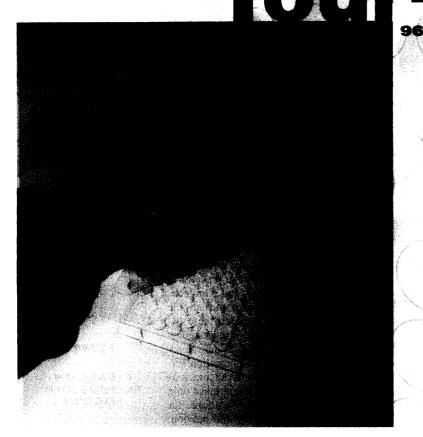
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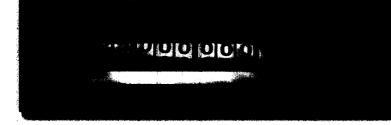
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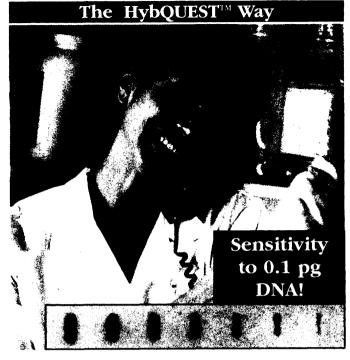
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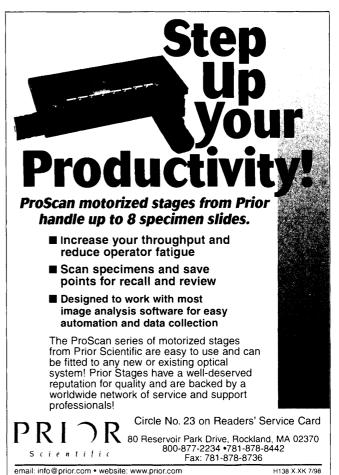
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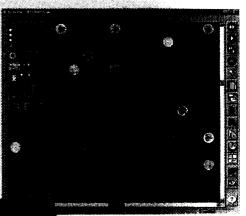
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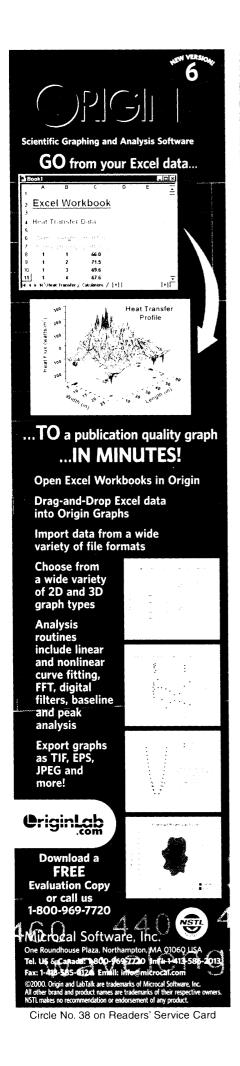
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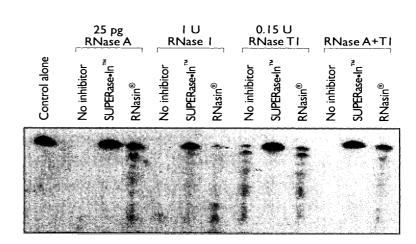
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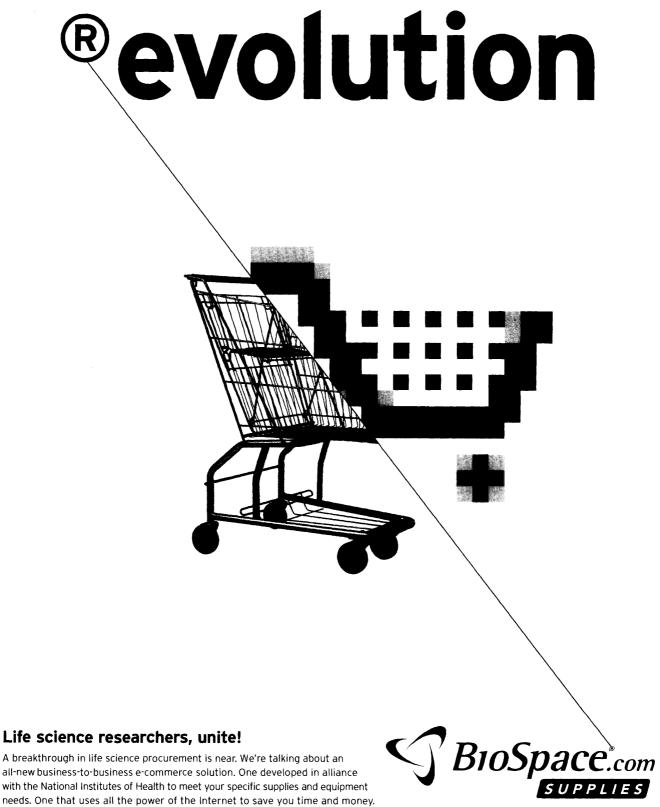
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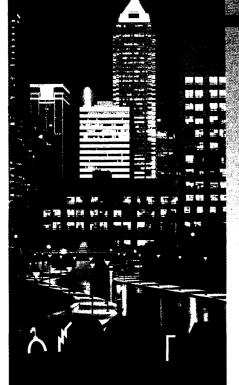


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