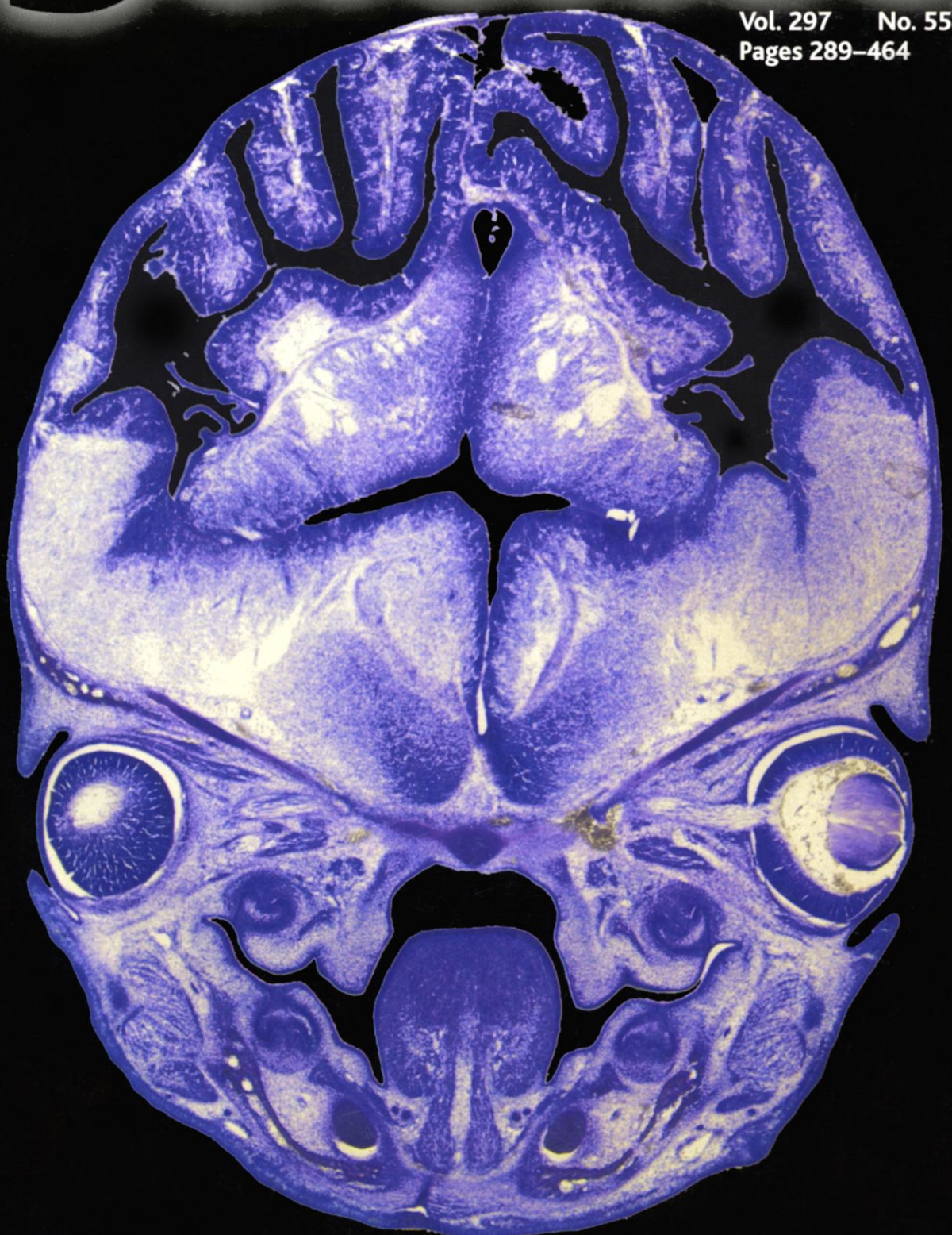
2003 KEYSTONE SYMPOSIA CALENDAR PAGE 419

19 July 2002

Science

Vol. 297 No. 5580
Pages 289–464 $9



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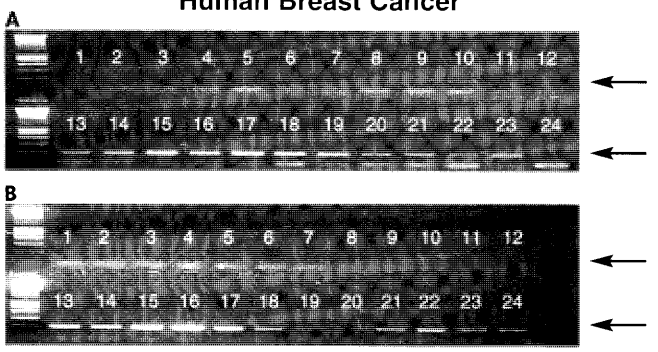

Lanes 1–12 represent normal breast epithelium samples from different individuals.
Lanes 13–24 represent breast cancer samples from different individuals.

A and B represent analyses of 2 individual genes whose expression is up regulated in breast cancer samples.

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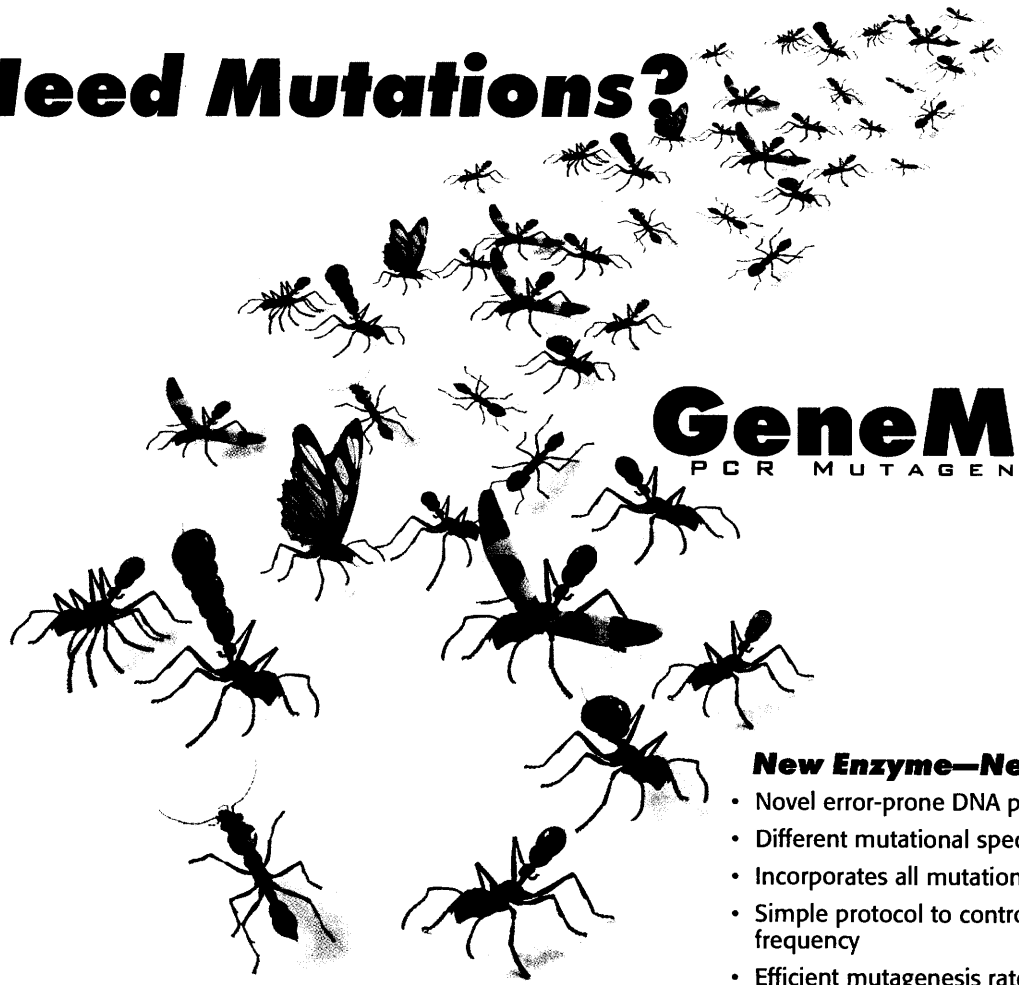

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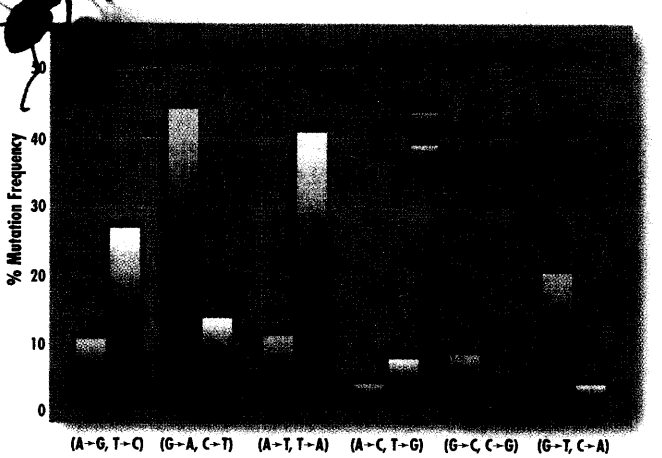

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* Shafikhani, S., et al. (1997) BioTechniques 23: 304-310
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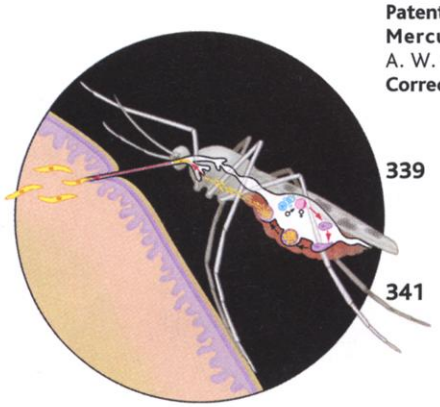

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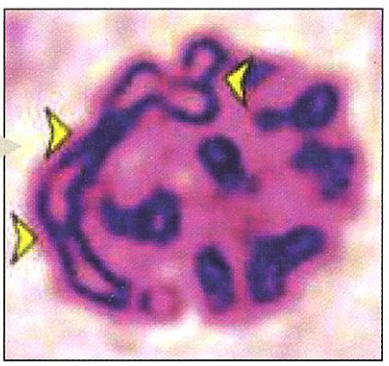

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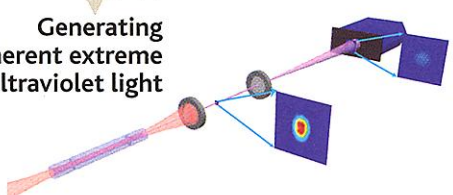

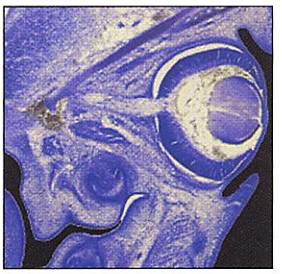

COVER 365

The head of an embryonic transgenic mouse expressing a stabilized β-catenin protein in neural precursor cells (coronal section, stained with cresyl violet). The cortical surface of the brain is enlarged, with increased surface area and folding of the cortex, indicating that β-catenin can regulate whether neural precursor cells proliferate or differentiate. [Image: A. Chenn]

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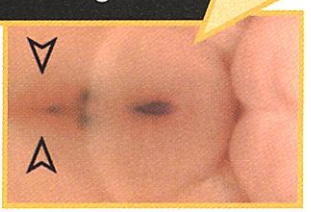
New on *Science* Express Control of organ size



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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $120 ($66 allocated to subscription). Domestic institutional subscription (51 issues): $390; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $85. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

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CONTENT HIGHLIGHTS AS OF 19 JULY 2002

science magazine www.sciencemag.org

SCIENCE EXPRESS www.sciencexpress.org

Probing Oxygen Motion in Disordered Anionic Conductors with ^{17}O and ^{51}V MAS NMR Spectroscopy N. Kim and C. P. Grey

The movement of oxide ions in ceramic oxygen-separation membranes has been followed using solid-state nuclear magnetic resonance methods.

Tissue-Specific Regulation of Retinal and Pituitary Precursor Cell Proliferation X. Li, V. Perissi, F. Liu, D. W. Rose, M. G. Rosenfeld

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365 A tissue-specific transcriptional repressor/corepressor complex provides an organ-specific strategy for the expansion of precursor cells.

Impaired B and T Cell Antigen Receptor Signaling in p110δ PI 3-Kinase Mutant Mice K. Okkenhaug *et al.*

The p110δ subunit of PI3K is critical for B and T cell receptor signaling.

TECHNICAL COMMENTS

Are Cells Viable at Gigapascal Pressures?

Using microbial formate oxidation "as a probe of metabolic viability," Sharma *et al.* (Reports, 22 Feb. 2002, p. 1514) presented evidence that strains of the bacteria *Shewanella oneidensis* and *Escherichia coli* can survive at pressures above 1 gigapascal, well beyond the currently known conditions for life on Earth. In a comment, Yayanos argues that formate oxidation is insufficient as a proxy for cell viability and that "although Sharma *et al.* referred to the cells as being viable and living, not a single observation they made supports that contention." Sharma *et al.* respond that the concerns expressed by Yayanos "appear in most instances to reflect differences in semantics" and that the controls used in the study verified "that the observed formate oxidation was primarily due to biological activity."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/297/5580/295a

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career resources for scientists

CANADA: Postdocs Gain Status, Benefits at University of Toronto L. McKarney

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GERMANY: Research on Agriculture and Society E. von Ruschkowski

An interdisciplinary group explores the implications of BSE and hormone scandals for German agriculture, ecology, and society.

SINGAPORE: Ethical Issues in Research, Part I—Research by Stealth D. Evans

A research ethics specialist shares his views on ethical reviews of innovative treatment.

US: Teaching Doctoral Students About Industrial Careers J. Shulman

A new course provides an overview of career opportunities in industry and lessons on the job search.

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News Synthesis: "Gero-Tech" Sprouts, But Will It Bloom? R. J. Davenport and J. Toy

Researchers plant seeds, hoping to bring their academic work to market.

News Focus: High-Octane Endurance—Yeast in the Metabolic Fast Lane Live Longer E. Strauss

Unorthodox finding prods researchers to rethink old ideas about metabolism and longevity.

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Protocol: Analysis of Phosphorylation-Dependent Protein-Protein Interactions Using a Bacterial Two-Hybrid System A. J. Shaywitz, S. L. Dove, M. E. Greenberg, A. Hochschild

Quantifying protein interactions and screening libraries for binding influenced by kinases.

Events

Online submission form for meetings and conferences is now available.

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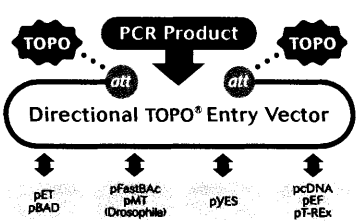

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THIS WEEK IN Science

edited by Phil Szuromi

A Switch in Time Saves Lines

In most nuclear magnetic resonance (NMR) experiments, a uniform magnetic field is applied to the sample, and radio frequency pulses are used to manipulate particular nuclear spins. Under ex situ conditions, such as deep in a bore hole, it is difficult to apply high magnetic fields or to do so uniformly, and, thus, approaches in which signals are generated by suddenly reversing the applied magnetic field prove useful. Unfortunately, background fields (such as Earth's field) are difficult to shield, and the resulting signals last only a few milliseconds. Brill *et al.* (p. 369) show that when two nearly orthogonal fields are reversed in such a way so as to compensate for the background field, spin echoes form that persist for more than 600 milliseconds, which allows accurate measurement of spin-relaxation times.

Taking Coherence to Extremes

High-harmonic generation is a promising approach for generating coherent light in the extreme ultraviolet, a region of interest in spectroscopy and lithography, but the highly ionized medium used to create the light produces a changing refractive index that degrades coherence. Bartels *et al.* (p. 376) now show that the high-harmonic generation of extreme ultraviolet emitted by ionized argon atoms, when contained in a hollow fiber and phase-matched, maintains temporal and spatial coherence sufficient for the formation of holographic images.

There's the Rub

How much does adhesion or friction between two polymer surfaces depend upon the geometry of the polymer chains? Maeda *et al.* (p. 379) studied both nonpolar and polar materials using a surface force apparatus to determine how the friction changes when the polymers are cross-linked and when the surface loops were subsequently cut. Both adhesion and friction were dominated by free surface ends, which rearranged and tangled as the two surfaces were brought into contact.

Measuring Melting

The meltwater input from the glaciers of coastal Alaska is a major contributor to global sea-level rise, but also one that is difficult to quantitate directly. Arendt *et al.* (p. 382; see the Perspective by Meier and Dyurgerov) now present laser-altimetry data on 67 Alaskan mountain glaciers (covering about 20% of the glaciated area there) and show that their contribution to rising sea level is much greatly than previously realized. The estimated amount is ~78% more than that from the entire Greenland Ice Sheet from the mid-1950s to the mid-1990s. Moreover, the rate of melting appears to have increased considerably during the past decade.

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The Front Lines

In the push for increased device density on chips, the features written in lithographic resists are approaching the scale of individual polymer chains. Lin *et al.* (p. 372; see the Perspective by Reichmanis and Nalamasu) have developed a combined x-ray and neutron reflectometry technique to examine the reaction front in a deuterated chemically amplified photoresist. They obtained both compositional and density profiles for the resists on the nanometer scale, information that should aid the design of improved materials.

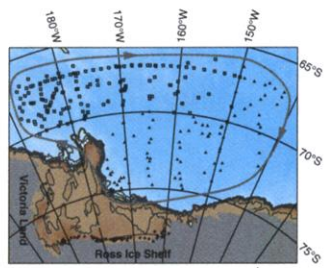
And in Brevia ...

Lichen assemblages have been grouped by Rikkinen *et al.* (p. 357) into guilds in which different fungal species share a common cyanobacterial partner.

Skimming for Fish?

Pterosaurs, an extinct group of flying lizards, lived during the reign of the dinosaurs, but a poor fossil record has limited our understanding of their behavior. Kellner and Campos (p. 389) have discovered a new taxon of pterosaur, *Thalassadromeus sethi*, which had an unusually large crest and a distinctive, streamlined skull and jaw. The crest, which is decorated with grooves that suggest an extensive blood vessel system, may have functioned to regulate body temperature. The streamlined skull and jaw are similar to that of the extant bird *Rynchops*. Like the bird, *Thalassadromeus* may have skimmed the surface of lakes and seas, dipping its head into the water to catch fish and crustaceans.

Getting Fresher



Measurements made in the Pacific Ocean have shown that Antarctic Intermediate Water has become less salty during recent decades. Jacobs *et al.* (p. 386) document decreases in the salinities of shelf water in the Ross Sea and surface water in the Ross Gyre during the past 40 years. They suggest that a combination of increased precipitation, reduced sea ice production in response to increasing air temperature, and increased melting of the West Antarctic Ice Sheet could explain this freshening.

Coding of Smell in the Insect World

The mushroom bodies in the insect brain function in olfactory learning and in other types of memory formation, but the cellular mechanisms underlying information processing in this structure are still poorly understood. Perez-Orive *et al.* (p. 359) analyzed the computational functions of the antennal lobe–mushroom body system in locusts. A combination of excitatory inputs from antennal lobe projection neurons and feed-forward inhibition from lateral horn interneurons sculpts the functional properties of Kenyon cells in the mushroom bodies.

Brainier Mice

The normal mouse brain lacks the folds and gyrations that characterize the surface of the human brain. Chenn and Walsh (p. 365; see the cover and the news story by Vogel) now show that expression of

CREDIT: JACOBS *ET AL.*

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CONTINUED ON PAGE 299

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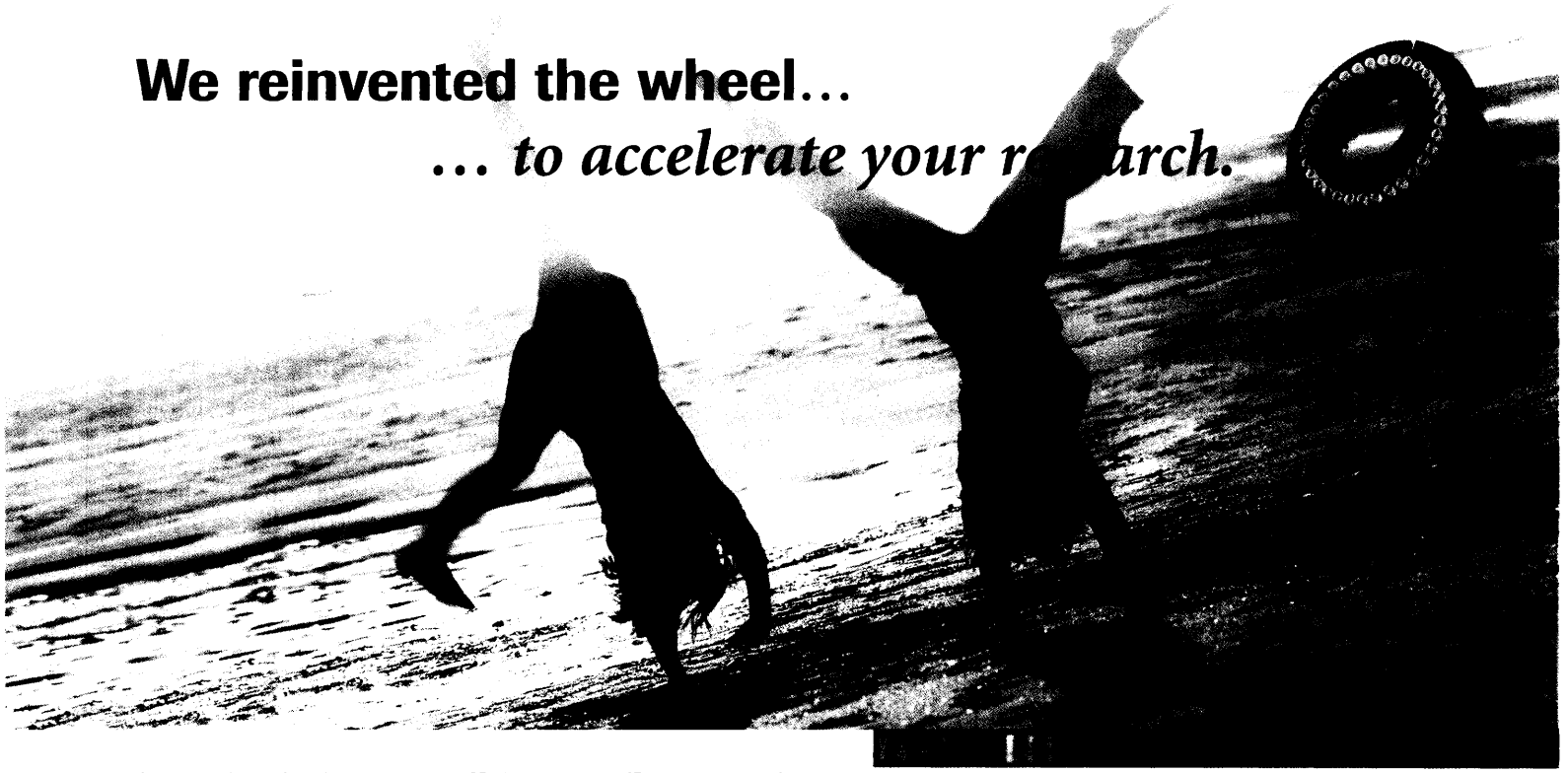

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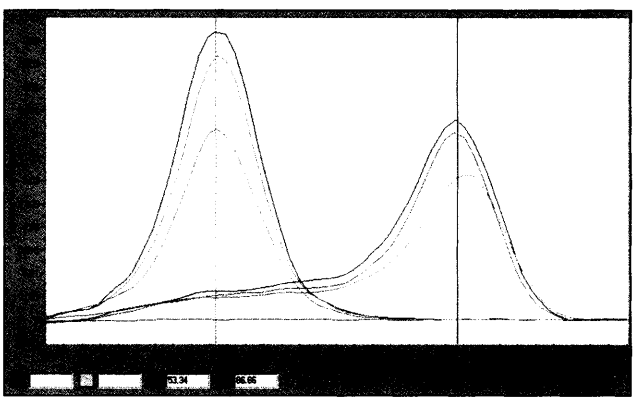

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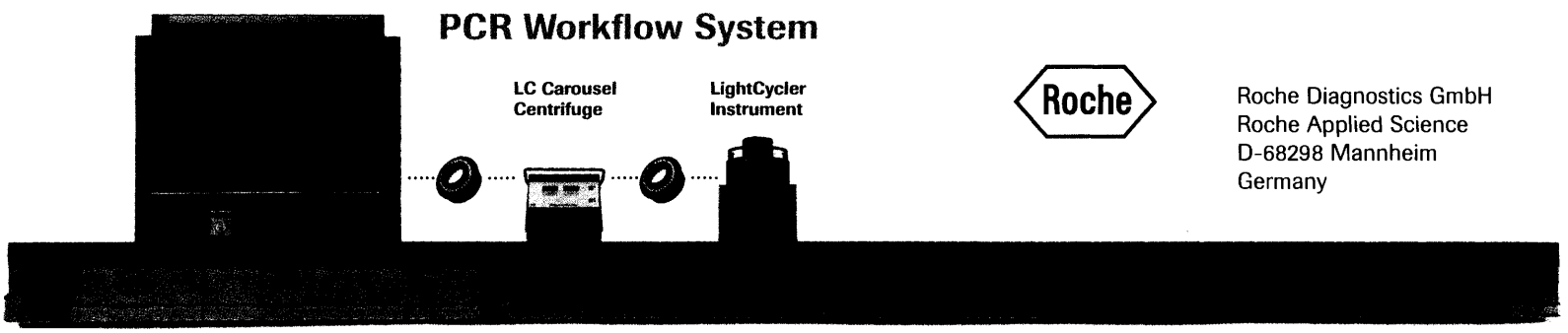

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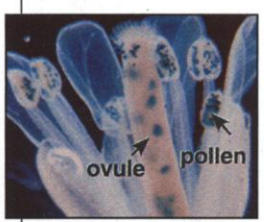
a constitutively active variant of β-catenin, a component of cellular adherens junctions, in transgenic mice resulted in lateral expansion of the mouse cerebral cortex. The brain surface buckled and folded to fit into the cranial cavity. Although the sequence of neuronal differentiation appears to be approximately normal, the numbers of cells are much greater and reflect an expanded pool of neural progenitor cells. The extra β-catenin signaling appears to encourage neural precursors to proliferate rather than differentiate.

Not Too Big, Not Too Small

A brute-force approach has been used to address a classic problem in cell biology—how cell growth and the cell division cycle are coordinated so that cells maintain a certain size. Jorgensen *et al.* (p. 395; see the Perspective by Sudbery) performed a systematic analysis of the complete set of yeast haploid deletion strains that yielded strains (several thousand) that were either larger or smaller than their normal counterparts. Further genetic analysis revealed a dozen new regulators of Start, the point in the yeast cell cycle at which the cell commits to a new round of cell division. The groups of genes identified point to a key role of nucleolar genes and genes affecting ribosome biogenesis in control of cell size as well as cell growth.

Profiles in Fear

Linking genotype to phenotype has been particularly challenging in the realm of neurotransmitter metabolism and subjective assessments of human behavior and personality. Anxiety-related traits have been associated with the biogenic amine serotonin, an important mediator and modulator of emotion and mood, and a polymorphism in the serotonin transporter, which sequesters synaptic serotonin. Hariri *et al.* (p. 400; see the news story by Miller) present the results of a functional brain imaging of normal individuals. An increased responsiveness of the amygdala (a brain structure intimately involved in emotional processing) to fearful stimuli was seen in subjects carrying one or two copies of the "s" allele of the transporter, in contrast to those with two copies of the "l" allele.



CREDIT: HU *ET AL.*

Making the Most of the Light

Peroxisomes are small intracellular organelles involved in metabolism. In mammals, abnormal peroxisomes can cause effects ranging from skin disorders to neuropathologies. Studies in the plant *Arabidopsis* by Hu *et al.* (p. 405) now show that peroxisomes are critical for normal photomorphogenesis. The plant peroxisomal protein AtPex2p is required for normal growth. Mutations in its gene suppress growth defects caused by mutations in Det, which encodes a nuclear protein that regulates expression of photomorphogenesis genes.

Guarding Against Mutation

Deamination of 5-methylcytosine to thymine (T) at CpG sites is the most frequent cause of the point mutations in humans that lead to genetic disease and cancer. Millar *et al.* (p. 403) generated mice deficient in MBD4, a methyl-CpG binding protein that specifically removes T from G:T mismatches at CpG sites. C → T mutations within CpG sites occurred three times more frequently in mice lacking MBD4. When the mutant mice were crossed into a genetic background that increases cancer susceptibility, the progeny showed accelerated tumor formation. These results indicate that MBD4 is a major factor in helping cells cope with the mutability of 5-methylcytosine.

Staying Put

A large number of B cells inhabit the marginal zones (MZ) of the spleen, where they maintain steady contact with recirculating antigens in the blood. These lymphocytes respond rapidly to bacteria by mobilizing and differentiating into extensive clusters of antibody-producing plasma cells. Lu and Cyster (p. 409) show that two integrins involved in lymphocyte trafficking across endothelium, LFA-1 and $\alpha_4\beta_1$, appear to be responsible for the migration and localization of MZ B cells. Large-scale egress of B cells from the MZ occurred when interactions of these integrins with their respective ligands were blocked. The retention of lymphocytes within lymphoid niches suggests a wider role for some integrins associated with lymphocyte trafficking.

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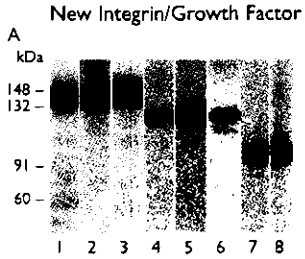

Lane:
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2: c-Met [pYpYpY1230/34/35]
3: c-Met [pY1365]
4: Integrin β_1 [pTpT788/789]
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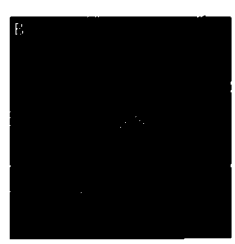

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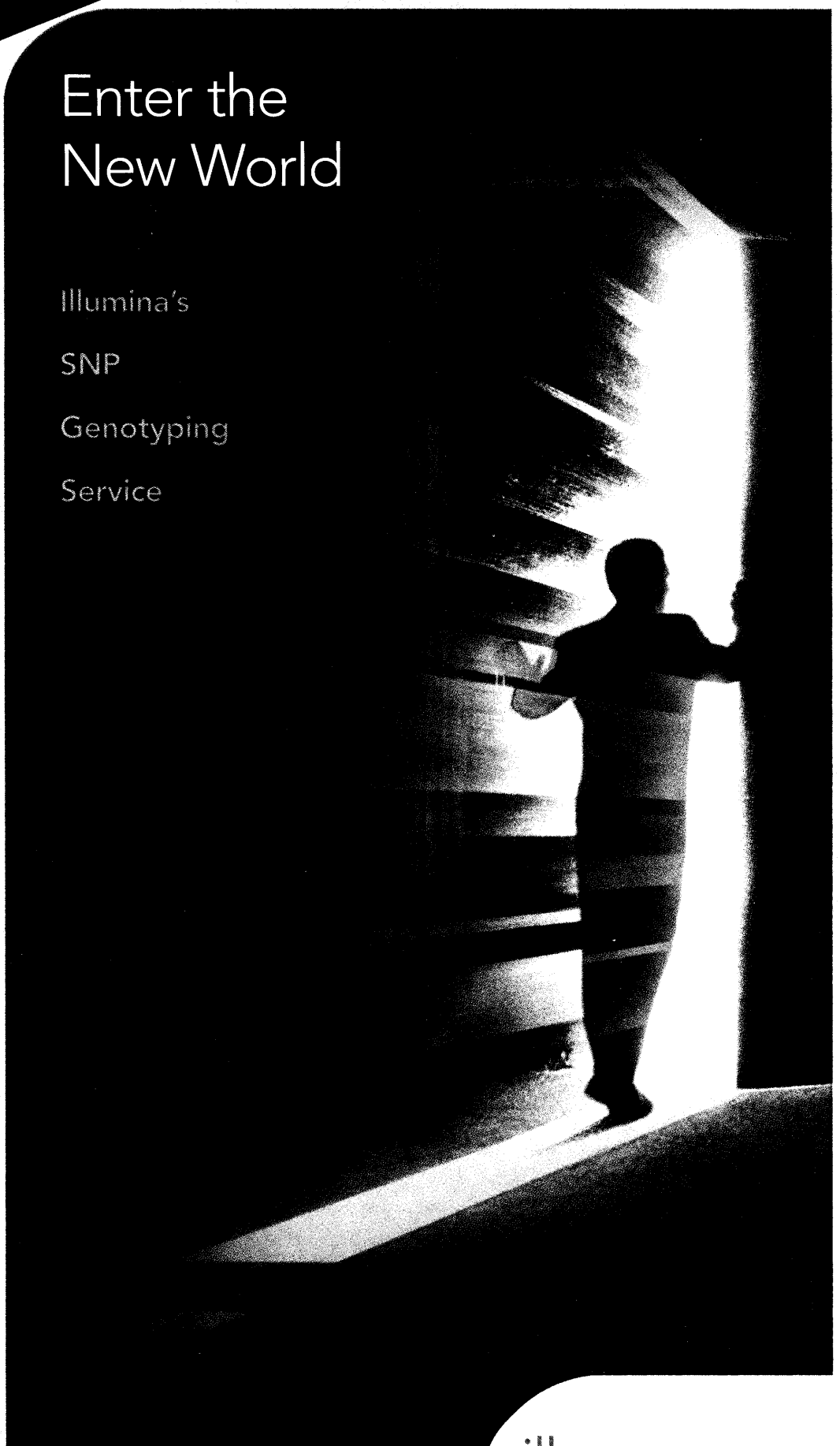

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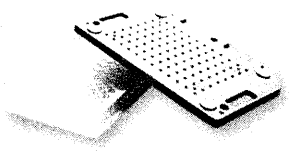

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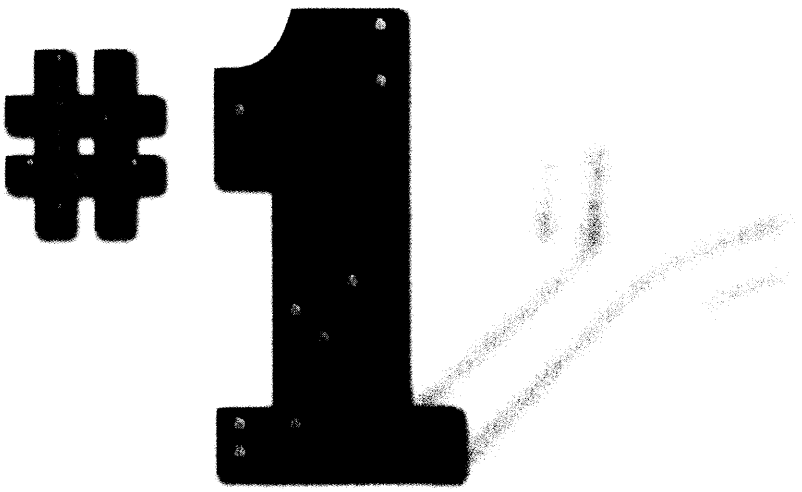

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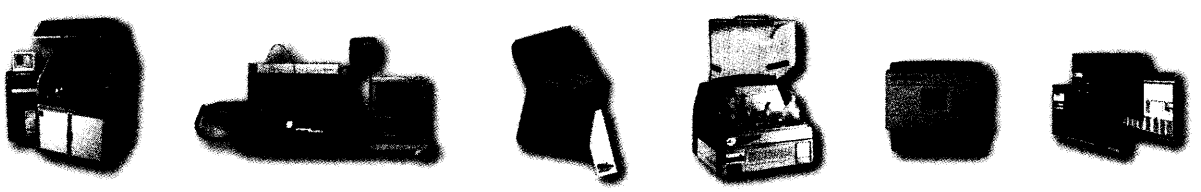

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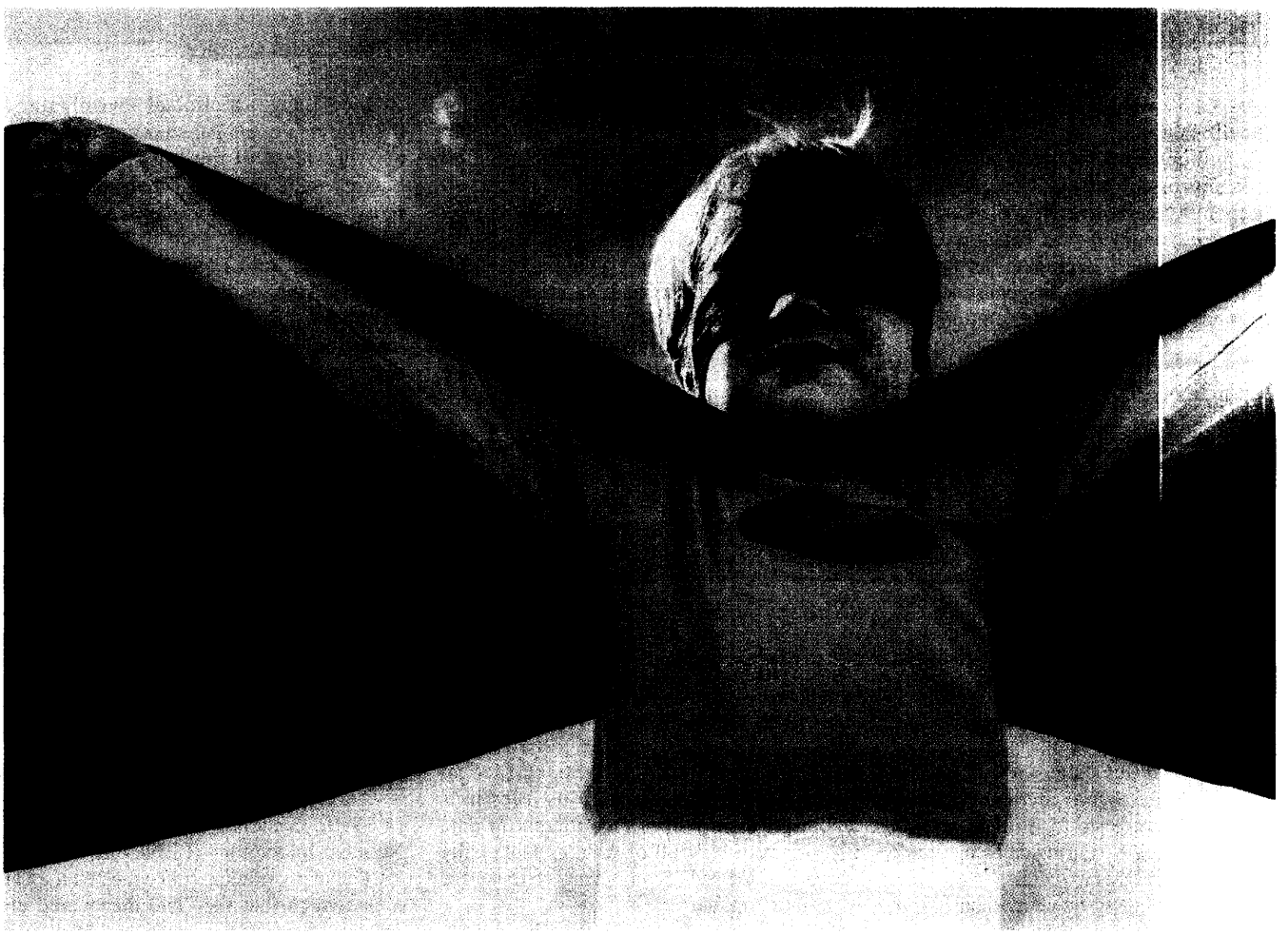

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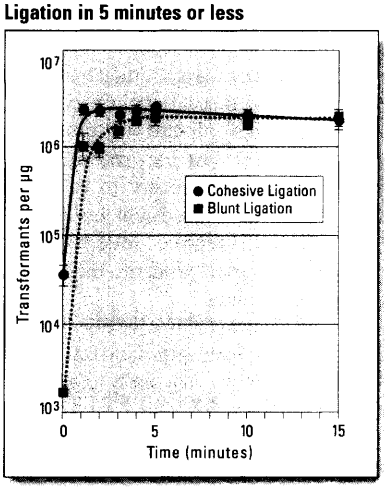

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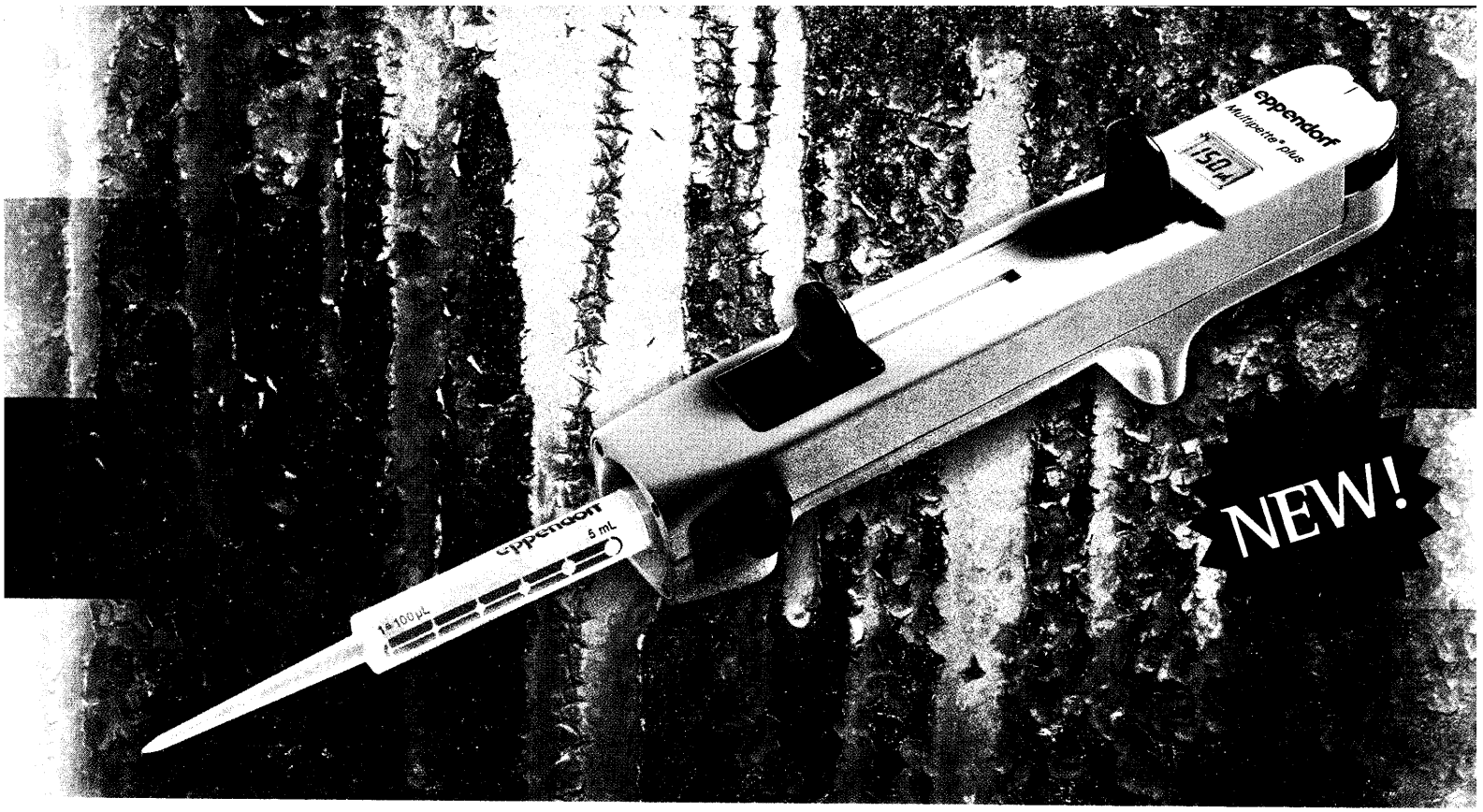

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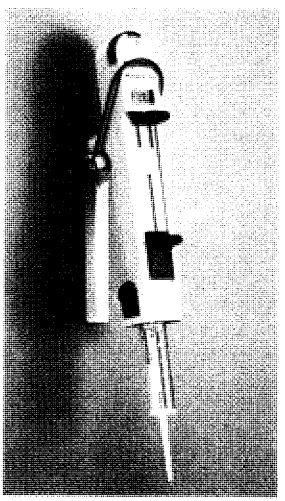

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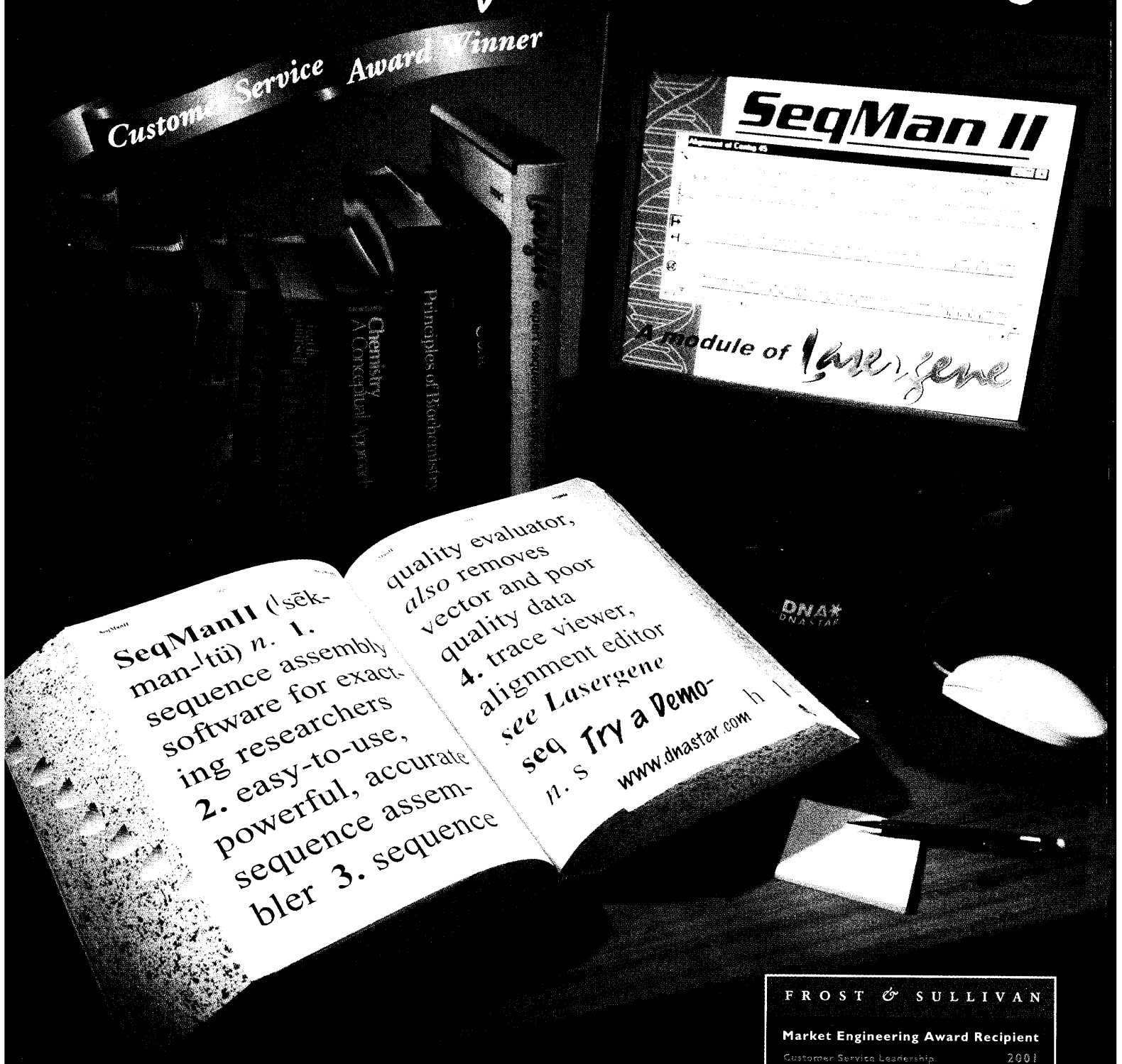

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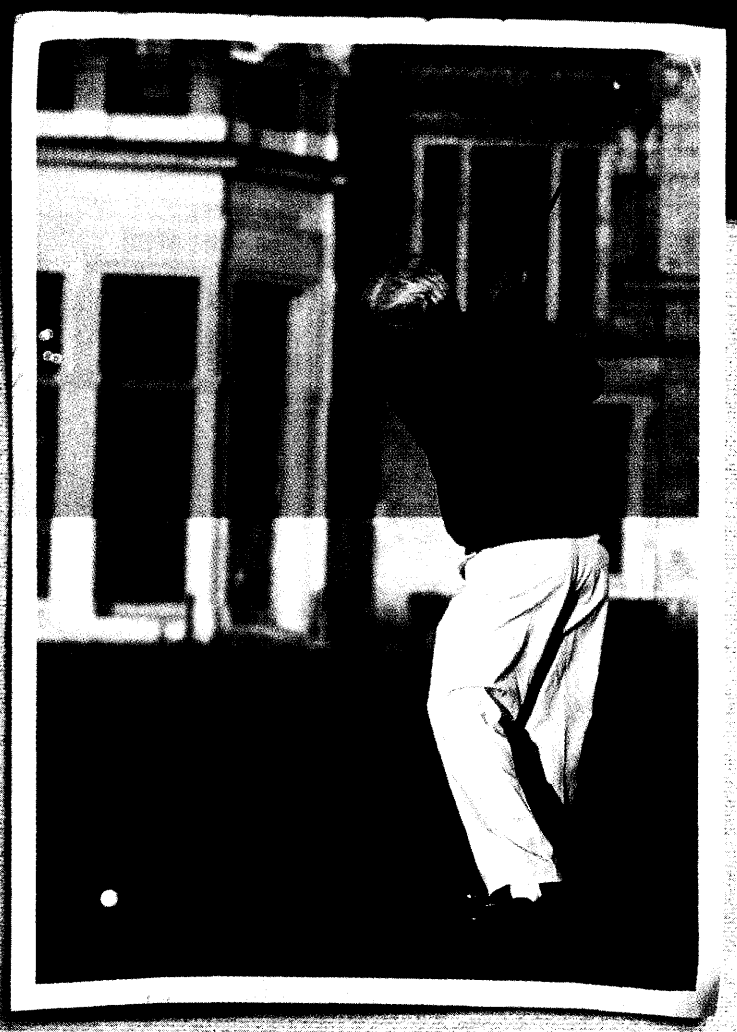

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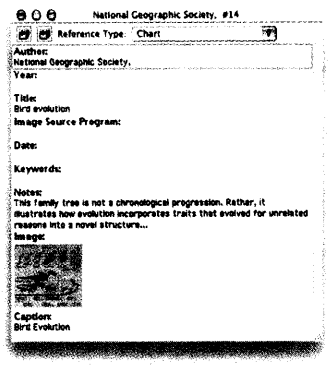

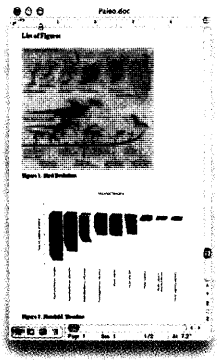

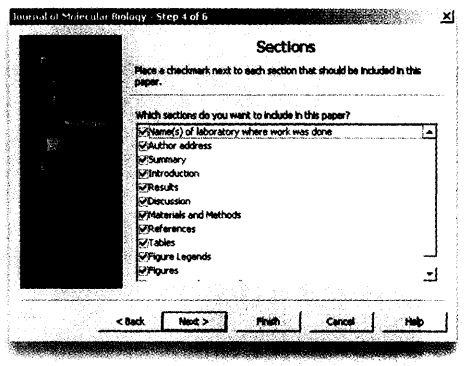

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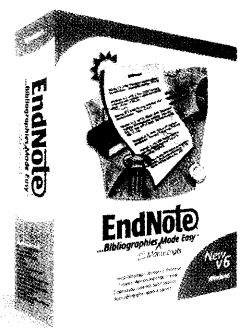

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