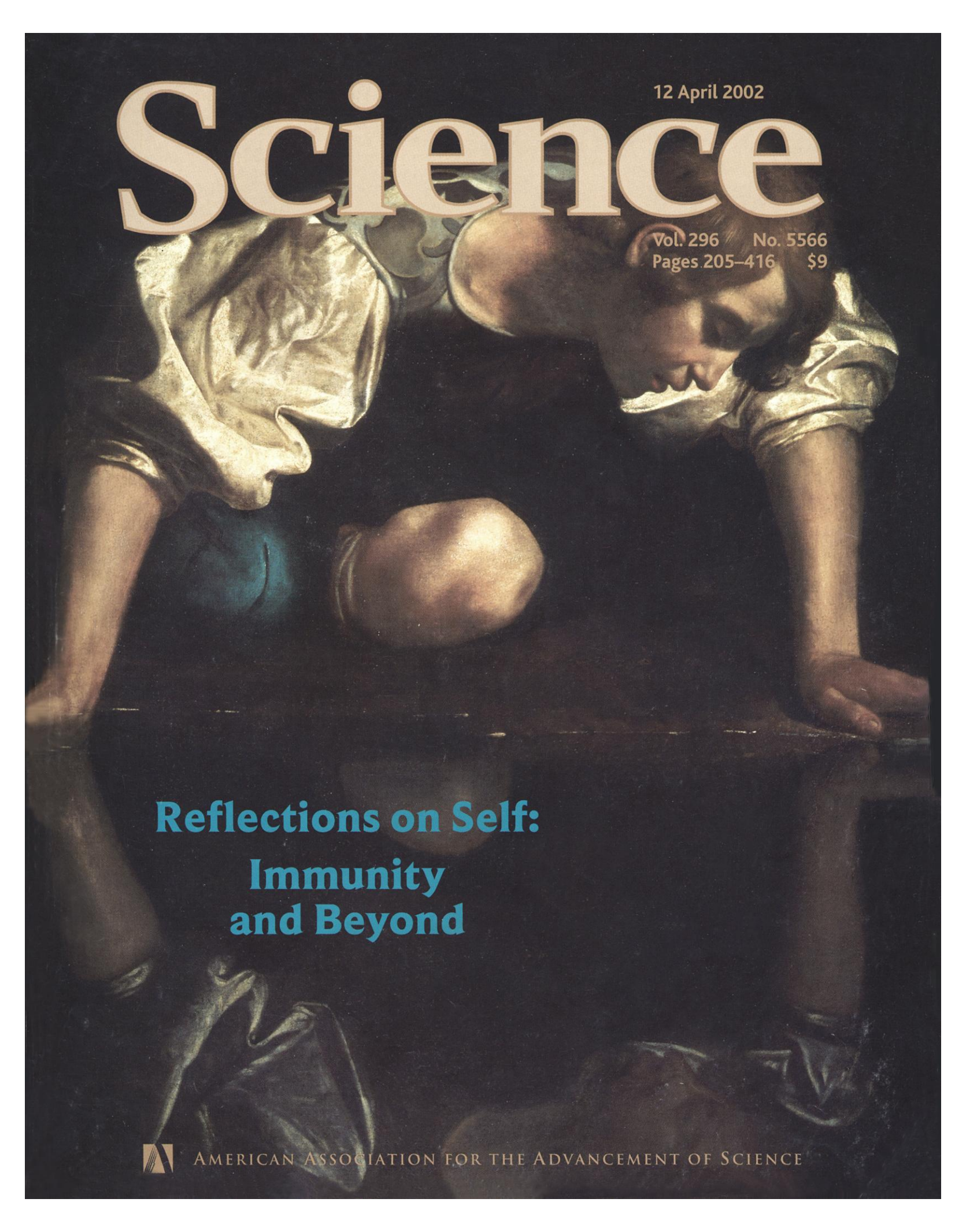




Science

12 April 2002

Vol. 296 / No. 5566
Pages 205-416 \$9

Reflections on Self: Immunity and Beyond



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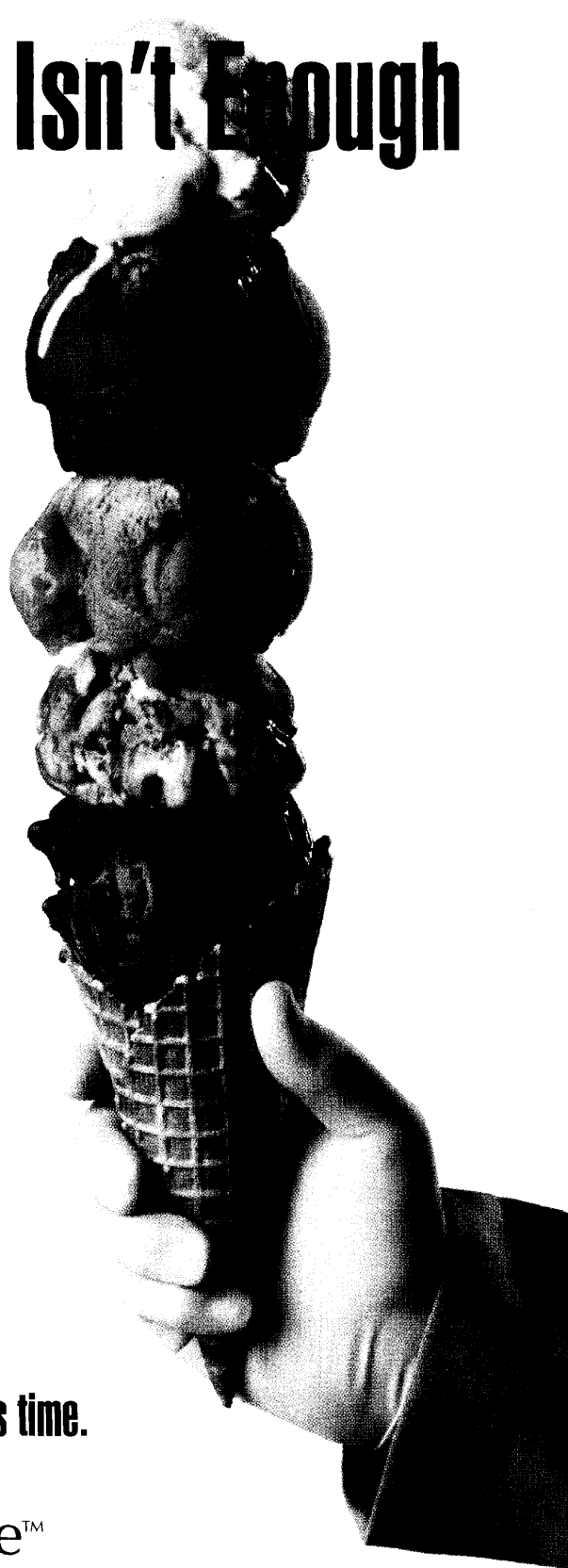
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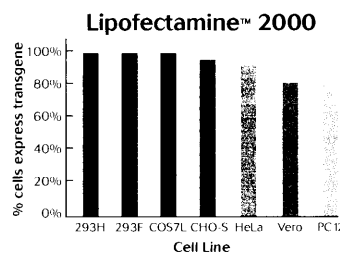




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NEWS

NEWS OF THE WEEK

- 232 **CLIMATE CHANGE: Battle Over IPCC Chair Renews Debate on U.S. Climate Policy**
White House Shakes Up U.S. Program
- ▼233 **PRIMATE EVOLUTION: Transgenes Clocks Brain's Fast Evolution**
340
- 235 **SCIENCESCOPE**
- ▼236 **ARCHAEOLOGY: Early Cowboys Herded Cattle in Africa**
336
- 236 **MEXICAN MAIZE: Transgene Data Deemed Unconvincing**
- 237 **U.S. EXPORT CONTROLS: Rules Eased on Satellite Projects**
- 238 **EMBRYONIC STEM CELLS: Australian Agreement Allows New Lines**
- 238 **ASTRONOMY: If It Quarks Like a Star, It Must Be...Strange?**
- 239 **GENOME CANADA: New Awards Bolster Canada's Global Role**

236

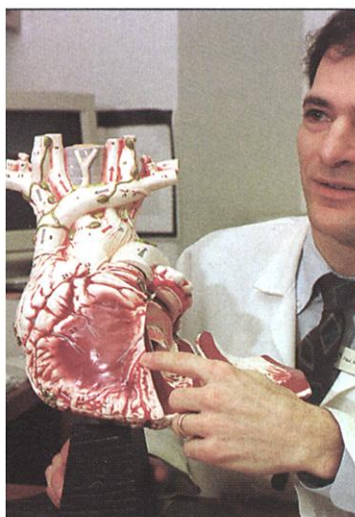
Roots of African cattle



- 241 **TOXICOLOGY: Fruit Bats Linked to Mystery Disease**
- NEWS FOCUS**
- 242 **CARDIOVASCULAR DISEASE: Does Inflammation Cut to the Heart of the Matter?**
- 245 **MARINE ECOLOGY: Picturing the Perfect Preserve**
- 246 **TECHNOLOGY: Microchips That Never Forget**
A Bit of This and That
- 250 **MATERIALS SCIENCE: Biology Reveals New Ways to Hold on Tight**
- 253 **RANDOM SAMPLES**

242

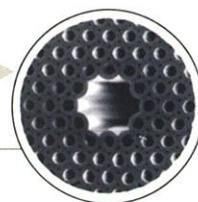
New marker for heart disease risk



SCIENCE'S COMPASS

276

Optical fibers go photonic



261 LETTERS

A Human Genome Diversity Cell Line Panel H. M. Cann, C. de Toma, L. Cazes, M.-F. Legrand, V. Morel, L. Piouffre, J. Bodmer, W. F. Bodmer, B. Bonne-Tamir, A. Cambon-Thomsen, Z. Chen, J. Chu, C. Carcassi, L. Contu, R. Du, L. Excoffier, G. B. Ferrara, J. S. Friedlaender, H. Groot, D. Gurwitz, T. Jenkins, R. J. Herrera, X. Huang, J. Kidd, K. K. Kidd, A. Langaney, A. A. Lin, S. Q. Mehdi, P. Parham, A. Piazza, M. P. Pistillo, Y. Qian, Q. Shu, J. Xu, S. Zhu, J. L. Weber, H. T. Greely, M. W. Feldman, G. Thomas, J. Dausset, L. L. Cavalli-Sforza. **Trees, Homologs, and Poisons** S. H. Strauss. **Stocking the Stacks** A. K. Bashirulla. **Italy's Annual AIDS Budget Appropriation** G. Sirchia. **A "Water" Model for Nuclei Still Holds Water** V. Viola and K. Kwiatkowski. **Biotech Poetry** M. Grayson. **Corrections and Clarifications**

POLICY FORUM

- 265 **EMBRYONIC STEM CELLS: The Debate in Germany** J. G. Reich

BOOKS ET AL.

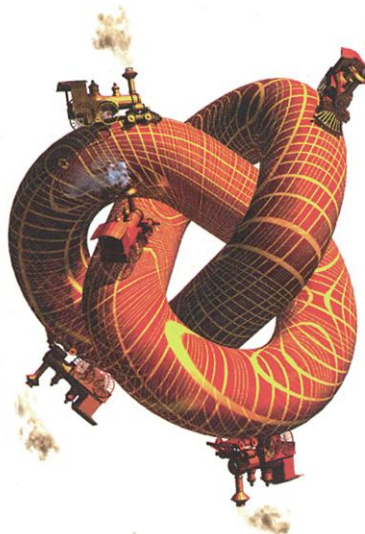
- 267 **COSMOLOGY: The Universe in a Nutshell**
Stephen Hawking, reviewed by
M. Kamionkowski
- 268 **NEUROSCIENCE: Synaptic Self How Our Brains Become Who We Are** J. LeDoux, reviewed by
R. J. Davidson

PERSPECTIVES

- ▼269 **VIROLOGY: Poliomyelitis Eradication—a Dangerous Endgame** N. Nathanson and P. Fine
356
- ▼270 **CHEMISTRY: Catalytic Degradation of Chlorinated Phenols** B. Meunier
326
- ▼271 **PLANETARY SCIENCE: A New Solar System Basalt** H. Palme
334
- ▼273 **IMMUNOLOGY: Pathogen Surveillance—the Flies Have It** R. S. Khush, F. Leulier, B. Lemaître
297
359
- ▼275 **PLANT BIOLOGY: MADS-Box Genes Reach Maturity** B. Causier, M. Kieffer, B. Davies
343
- 276 **APPLIED OPTICS: New Ways to Guide Light**
J. C. Knight and P. St. J. Russell
- ▼277 **PALEOCLIMATE: Corals, Chemistry, and Climate**
331
D. P. Schrag and B. K. Linsley
- 279 **VIROLOGY: Rafting with Ebola** E. O. Freed

REVIEW

- 280 **MATERIALS SCIENCE: Thermal Barrier Coatings for Gas-Turbine Engine Applications**
N. P. Padture, M. Gell, E. H. Jordan
- 285 **FLOWERING: Arabidopsis, the Rosetta Stone of Flowering Time?** G. G. Simpson and
C. Dean



267

Time in Hawking's curvy Universe

RESEARCH

BREVIA

- 319 **Dietary Restriction in Long-Lived Dwarf Flies** D. J. Clancy, D. Gems, E. Hafen, S. J. Leivers, L. Partridge

REPORTS

- 321 **Formation of the Three-Ring Structure Around Supernova 1987A** T. Tanaka and H. Washimi
- 323 **Fabrication of a Cylindrical Display by Patterned Assembly** H. O. Jacobs, A. R. Tao, A. Schwartz, D. H. Gracias, G. M. Whitesides
- ▼326 **Rapid Total Destruction of Chlorophenols by Activated Hydrogen Peroxide** S. Sen Gupta, M. Stadler, C. A. Noser, A. Ghosh, B. Steinhoff, D. Lenoir, C. P. Horwitz, K.-W. Schramm, T. J. Collins
- 328 **Organic Molecules Acting as Templates on Metal Surfaces** F. Rosei, M. Schunack, P. Jiang, A. Gourdon, E. Lægsgaard, I. Stensgaard, C. Joachim, F. Besenbacher
- ▼331 **The Effect of Algal Symbionts on the Accuracy of Sr/Ca Paleotemperatures from Coral** A. L. Cohen, K. E. Owens, G. D. Layne, N. Shimizu
- ▼334 **A New Source of Balsatic Meteorites Inferred from Northwest Africa 011 A** Yamaguchi, R. N. Clayton, T. K. Mayeda, M. Ebihara, Y. Oura, Y. N. Miura, H. Haramura, K. Misawa, H. Kojima, K. Nagao
- ▼336 **African Pastoralism: Genetic Imprints of Origins and Migrations** O. Hanotte, D. G. Bradley, J. W. Ochieng, Y. Verjee, E. W. Hill, J. E. O. Rege
- ▼340 **Intra- and Interspecific Variation in Primate Gene Expression Patterns** W. Enard, P. Khaitovich, J. Klose, S. Zöllner, F. Heissig, P. Giavalisco, K. Nieselt-Struwe, E. Muchmore, A. Varki, R. Ravid, G. M. Doxiadis, R. E. Bontrop, S. Pääbo
- ▼343 **A MADS-Box Gene Necessary for Fruit Ripening at the Tomato Ripening-Inhibitor (*Rin*) Locus** J. Vrebalov, D. Ruzinsky, V. Padmanabhan, R. White, D. Medrano, R. Drake, W. Schuch, J. Giovannoni
- 346 **Alteration of Lymphocyte Trafficking by Sphingosine-1-Phosphate Receptor Agonists** S. Mandala, R. Hajdu, J. Bergstrom, E. Quackenbush, J. Xie, J. Milligan, R. Thornton, G.-J. Shei, D. Card, C. Keohane, M. Rosenbach, J. Hale, C. L. Lynch, K. Rupprecht, W. Parsons, H. Rosen



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REFLECTIONS ON SELF: IMMUNITY AND BEYOND

- 297 **Self-Discrimination, a Life and Death Issue**

VIEWPOINTS

- 298 **Decoding the Patterns of Self and Nonself by the Innate Immune System** R. Medzhitov and C. A. Janeway Jr.
- 301 **The Danger Model: A Renewed Sense of Self** P. Matzinger
- 305 **Recognition and Rejection of Self in Plant Reproduction** J. B. Nasrallah
- 308 **Self-Representation in Nervous Systems** P. S. Churchland
- 311 **The Many Selves of Social Insects** D. C. Queller and J. E. Strassmann
- 314 **Human Cloning and Our Sense of Self** D. W. Brock

See also Science's STKE on p. 211, Perspective on p. 273, and Report on p. 359.

- 349 **Regulation of Mitochondrial Biogenesis in Skeletal Muscle by CaMK** H. Wu, S. B. Kanatous, F. A. Thurmond, T. Gallardo, E. Isotani, R. Bassel-Duby, R. Sanders Williams

- 352 **Structure of a Cofactor-Deficient Nitrogenase MoFe Protein** B. Schmid, M. W. Ribbe, O. Einsle, M. Yoshida, L. M. Thomas, D. R. Dean, D. C. Rees, B. K. Burgess

- ▼356 **Outbreak of Poliomyelitis in Hispaniola Associated with Circulating Type 1 Vaccine-Derived Poliovirus** O. Kew, V. Morris-Glasgow, M. Landaverde, C. Burns, J. Shaw, Z. Garib, J. Andre, E. Blackman, C. J. Freeman, J. Jorba, R. Sutter, G. Tambini, L. Venczel, C. Pedreira, F. Laender, H. Shimizu, T. Yoneyama, T. Miyamura, H. van der Avoort, M. S. Oberste, D. Kilpatrick, S. Cochi, M. Pallansch, C. de Quadros

- ▼359 **Requirement for a Peptidoglycan Recognition Protein (PGRP) in Relish Activation and Antibacterial Immune Responses in *Drosophila*** K.-M. Choe, T. Werner, S. Stöven, D. Hultmark, K. V. Anderson



COVER 297

Narcissus gazes at his reflection, as depicted by Michelangelo Merisi da Caravaggio (1573–1610). As the story from Greek mythology reminds us, and as discussed in the special section in this issue, effective recognition of self is important to general survival and to successful immune surveillance, reproduction, community structure, and philosophical integration of the individual. [Image: Scala/Art Resource]

343

Fruit and floral development in tomato



New on Science Express

Mouse model of premature aging



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Binary Asteroids in the Near-Earth Object Population

J. L. Margot *et al.*

Radar images reveal several binary asteroids near Earth that may have formed by tidal disruption and that make up about 16% of the near-Earth population.

Direct Recognition of Cytomegalovirus by Activating and Inhibitory NK Cell Receptors

H. Arase, E. S. Mocarski, A. E. Campbell, A. B. Hill, L. L. Lanier

Viral resistance in mice is conferred directly through the interaction of a virus protein with a natural killer cell receptor.

Premature Aging in Mice Deficient in DNA Repair and Transcription

J. de Boer *et al.*

PERSPECTIVE: Genomic Priorities in Aging P. Hasty and J. Vijg

A mouse model provides strong support for the hypothesis that aging is caused by wear and tear on DNA.

TECHNICAL COMMENTS

Questioning the Evidence for Genetic Recombination in the 1918 "Spanish Flu" Virus

In a molecular and phylogenetic analysis of the virus that caused the 1918 influenza pandemic, Gibbs *et al.* (Reports, 7 Sep. 2001, p. 1842) found evidence for a recombinant origin for the virus's hemagglutinin (HA) gene, and suggested that the recombination event, "which probably changed the virulence of the virus," may have triggered the pandemic. Worobey *et al.*, in a comment, conclude from an alternative phylogenetic analysis that "there is no evidence that the HA gene . . . had a recombinant origin" in this virus, and argue that the "apparent recombination" observed by Gibbs *et al.* actually stemmed from "a difference in the rate of evolution" between the globular domain and the stalk region of the HA gene. Gibbs *et al.* respond that the alternative proposal of Worobey *et al.*, although interesting, is "not yet proven," and offer several arguments in defense of the techniques and conclusions of the original study.

The full text of these comments can be seen at
www.sciencemag.org/cgi/content/full/296/5566/211a

SPECIAL FEATURE

Quarterly Author Index

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GERMANY: Take Your Mind Off Your Ph.D.—Organize a Conference!

A. Shaw and S. Curado

Two coordinators of the European Molecular Biology Organisation's Ph.D. student symposium share the pros and cons of the experience.

CANADA: Canadian Science Bytes

L. McCarney

Carleton's cheating scandal; Genome Canada funding announcements; campus news; scholarships; and more research chair announcements.

US: The Insider's Edge—Are Job Fairs Fair?

D. Bomzer

Next Wave's Tooling Up columnist offers tips designed to help you stand out in the crowd.

US: From HBCU to Majority Institution—A Journey

K. Hamilton

An individual perspective on doing science in minority-deficient and minority-rich environments.

SINGAPORE: Better Business with a PhD?

L. Lim

Two of Singapore's Science Park technopreneurs insist that their scientific backgrounds helped pave their business success.

UK: Physiology—Back in Fashion

E. Pain

A recent conference in London examined the renewed interest in integrative physiology in the postgenomic era.

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An Untwister's New Twist

R. J. Davenport

Disease-causing helicase displays unanticipated talents.

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M. Leslie

Compound might shield neurons during stroke.

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Perspective: CTLA-4 Negative Signaling via Lipid Rafts—A

New Perspective C. E. Rudd, M. Martín, H. Schneider

CTLA-4 regulates how strongly T cells can signal by regulating the access of lipid rafts to immune synapses.

Review: Controlling the Immune System Through

Semaphorins G. Bismuth and L. Boumsell

The immune system and the nervous system share a guidance network.

Protocol: Flow Cytometric Analysis of T Cell Receptor Signal Transduction

T. Zell and M. K. Jenkins

A method of detecting physiologically relevant TCR signaling *ex vivo*.

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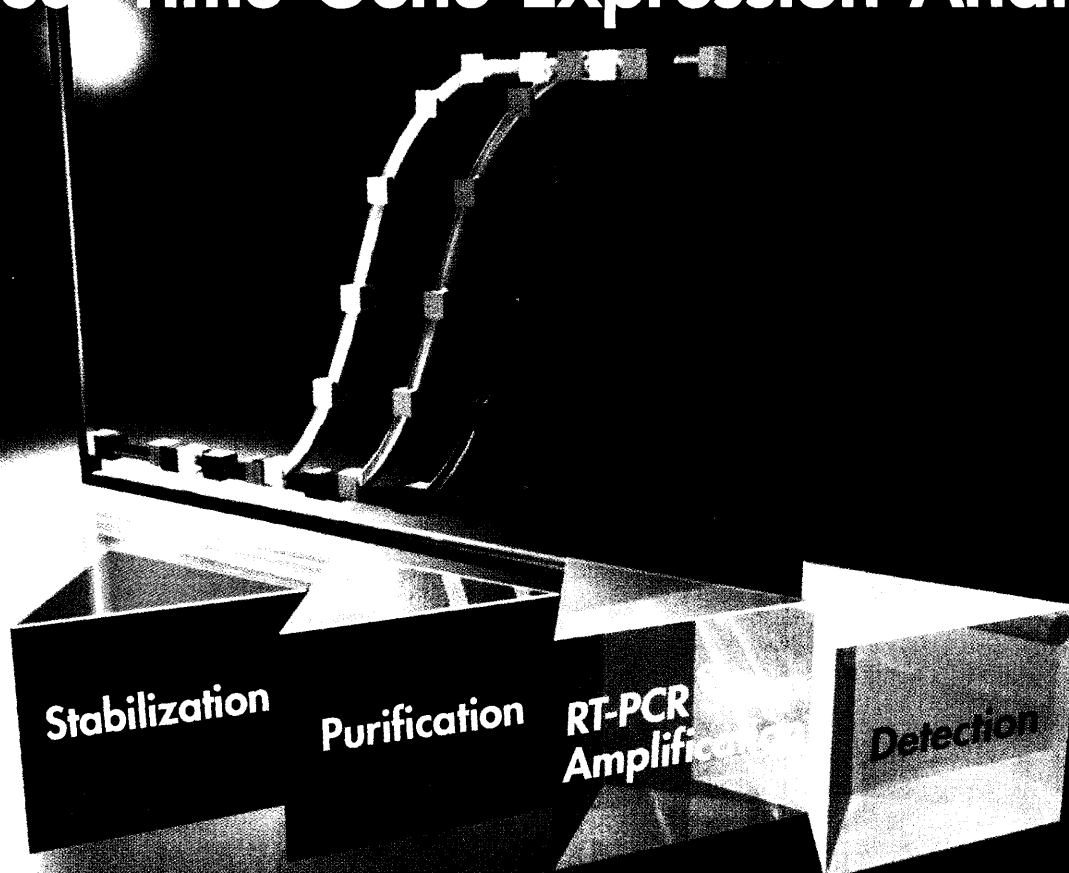
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THIS WEEK IN Science

edited by Phil Szuromi

More Differentiated Bodies

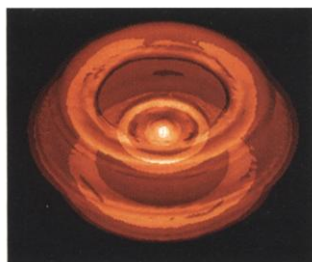
Basaltic meteorites are thought to be derived from a parent body that differentiated early in the solar system to form a dense core, a silicate mantle, and a basaltic crust. Most of these parent bodies are planets or our own Moon, but one group, the eucrites, derives from the only known differentiated asteroid, Vesta. Yamaguchi *et al.* (p. 334; see the Perspective by Palme) measured an anomalous oxygen isotopic concentration in the recently recovered basaltic meteorite, Northwest Africa 011 (NWA011), which shows that it arose in a different region of the early solar system than did the eucrites. Thus, there may be other differentiated bodies (Vesta-like asteroids) orbiting in our solar system.

Algae Fouls a Thermometer

The uptake of strontium (Sr) during the crystallization of coral skeleton aragonite (calcium carbonate) is controlled thermodynamically, and thus Sr/Ca ratios should provide a reliable measure of estimating past sea surface temperatures (SSTs). However, calibrations derived from different studies can give temperatures that can disagree by as much as 5°C or more. Cohen *et al.* (p. 331; see the Perspective by Schrag and Linsley), in an attempt to identify possible sources of error in these types of measurements, report that algal symbionts are responsible for as much as 65% of the variation of the Sr/Ca of *Astrangia poculata* coral growing in coastal waters of New England. This finding suggests that a reexamination of this method will require additional care in sampling. 

From Winds to Rings

A supernova, the final uncontrolled explosion and death of a star, leaves behind a highly luminous remnant of gas and ejecta that traces the stellar dynamics. Tanaka and Washimi (p. 321) performed a magnetohydrodynamic simulation of the 1987A explosion and reproduced the distinctive three-ring structure of SN 1987A. A wind-wind interaction occurred between the slowly expanding red supergiant and the rapidly expanding blue supergiant phases that preceded the explosion. A magnetic pinch,



326 Cleaning Up Chlorophenols

Chlorophenols have been used in many product formulations and are by-products of wood-pulp bleaching. Although a number of biological and chemical approaches have been developed to clean up these toxic compounds from the environment, most are either slow, ineffective at high pollutant concentrations, or can, in some cases, create other more toxic products. Sen Gupta *et al.* (p. 326; see the Perspective by Meunier) show that activation of hydrogen peroxide by iron catalysts that bear a tetraamidomacrocyclic ligand (TAML) can completely convert two of the most common of these pollutants, trichlorophenol and pentachlorophenol, to inorganic species (CO, CO₂, and Cl⁻) or to less harmful organic species on time scales of minutes under ambient conditions.

And in Brevia ...

Using the fruit fly *Drosophila*, Clancy *et al.* (p. 319) show that slowing of aging by a mutation in an insulin/insulin growth factor-like signaling pathway and by dietary restriction occurs through overlapping but distinct mechanisms of life-span extension.

the twisting of the magnetic field lines caused by the winds and stellar rotation, enhances the wind-wind interaction.

Shake and Make

Construction of an integrated semiconductor device, such as a display, requires the assembly and interconnection of a large number of components. Jacobs *et al.* (p. 323) show that assembly processes used to combine centimeter-scale objects can also be applied to much smaller objects (~300 micrometers). Light-emitting diodes (LEDs), which were formed on a single gold-coated surface, were immersed in solution with a flexible substrate that was patterned with a solder array. Under gentle agitation, the LEDs attached to the solder. The few defects that formed during the initial assembly could be readily

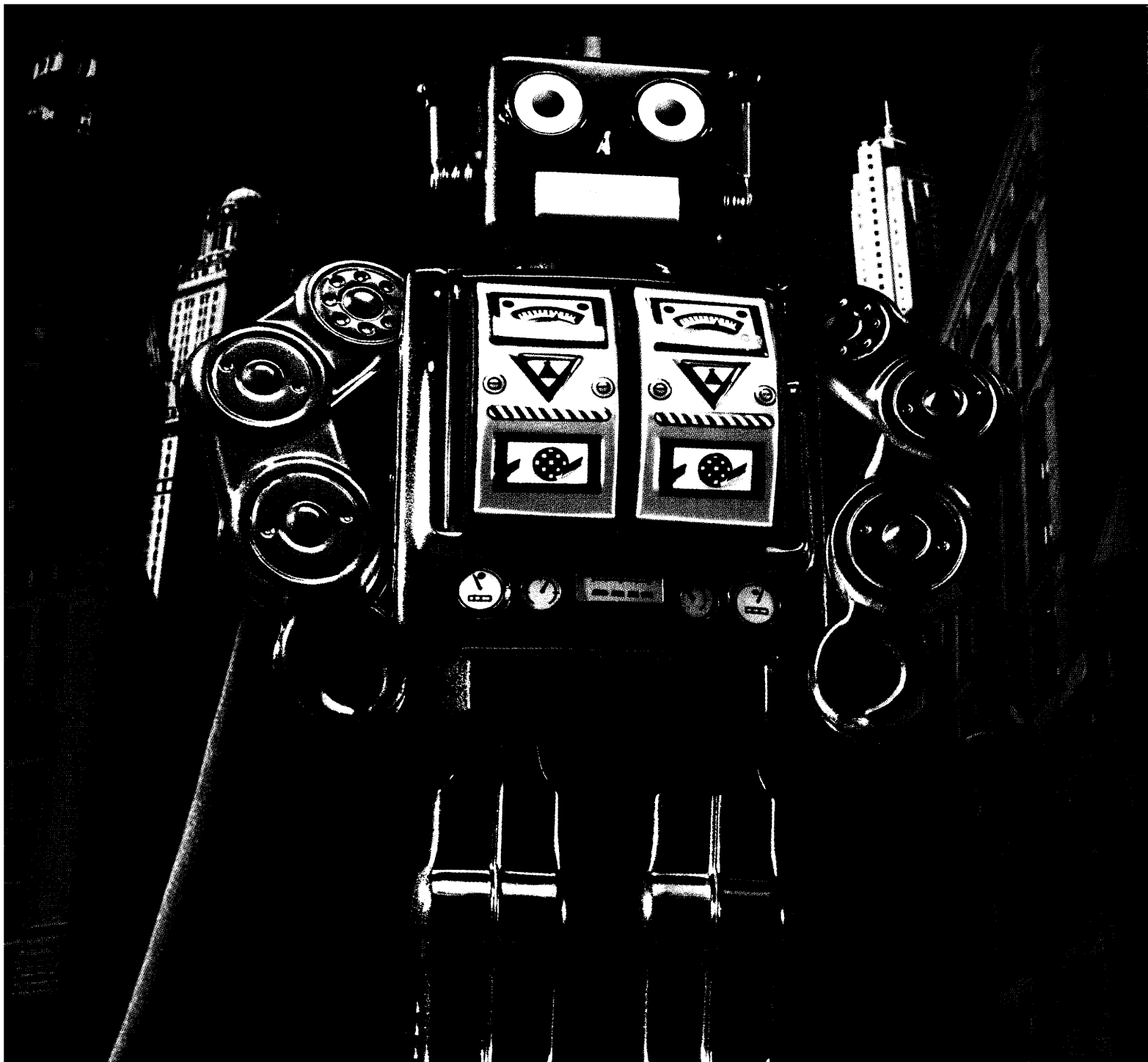
corrected through a more vigorous agitation and a repeat of the initial deposition cycle. The process was demonstrated for both a 113-element and a 1600-element substrate. Although for the latter case the assembly was not perfect, in both cases the entire process was complete within a few minutes, which suggests that with optimization this process can be scaled up to form large devices.

Cattle Called

Despite the central role of cattle pastoralism in many African cultures, its origins have remained largely unknown. Hanotte *et al.* (p. 336; see the news story by Stokstad) used molecular data from a comprehensive sampling of the African continent's cattle populations to unravel different strands of genetic variation. The initial dispersal of the earliest cattle from an indigenous domestication center was followed by a secondary influx from the Near East and Europe. Two phases of Asian zebu introgression into African cattle populations also occurred, and the recent introduction of pastoralism to southern Africa proceeded via an eastern rather than western migration corridor.

Expression Making the Difference

Chimpanzees and humans share more than 98% of their genetic material, yet differ strikingly in morphology and cognitive ability. Enard *et al.* (p. 340; see the news story by Pennisi) explore how differences in the expression patterns of shared genes might account for such differences between the species. Using microarrays carrying 18,000 human complementary DNAs, they compare gene expression patterns in the brains, liver, and blood of humans, chim-



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panzees, and macaques. The differences in the expression patterns in liver and blood corresponded to the evolutionary distance between the species. However, in the brain there was a much greater difference in expression patterns between chimp and human than between macaque and chimp. The divergence between the chimps and humans was accompanied by an accelerated evolution of expression patterns in human brain.

Going Against the Flow

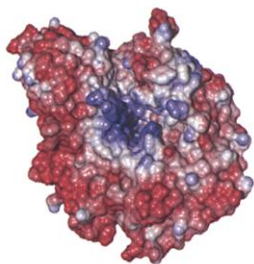
The mechanism of action of a drug already used for immunosuppression reveals a new level of regulation of lymphocyte migration. Mandala *et al.* (p. 346) show that the active form of the drug FTY720 becomes phosphorylated once administered and resembles sphingosine 1-phosphate, a lipid whose activation of cognate receptors has been implicated in modulating the immune response. The drug and lipid achieve immunosuppressive effects by inhibiting the circulation of lymphocytes in the body. **X**

Powering Up Muscle

Endurance training enhances the oxidative capacity of skeletal muscle by stimulating the production of mitochondria, the organelles that supply fuel to cells. The molecular signals that mediate this adaptive process are not well understood. Through a study of transgenic mice that express a hyperactive form of calcium, calmodulin-dependent protein kinase IV (CaMKIV*) in their skeletal muscle, Wu *et al.* (p. 349) establish that calcium-regulated signaling pathways play a key in controlling mitochondrial biogenesis in muscle.

Making Way for a Cluster

The metalloenzyme nitrogenase catalyzes the reduction of unreactive atmospheric nitrogen into bioavailable ammonia. Nitrogen binds to the FeMo cofactor (FeMoco) cluster, which contains one Mo atom, seven Fe atoms, and nine S atoms. This cluster is synthesized in vivo and incorporated into the tetrameric MoFe protein. Schmid *et al.* (p. 352) describe the crystal structure of the MoFe protein isolated from an *Azotobacter* strain deficient in producing FeMoco. They observe a positively charged funnel of a size that would allow insertion of the negatively charged FeMoco, the last step in assembling a catalytically competent nitrogenase.



Vaccine-Derived Polio in Hispaniola

From July 2000 to July 2001, there were 21 cases of paralytic poliomyelitis, with two fatalities, in Haiti and the Dominican Republic. Kew *et al.* (p. 356; see the Perspective by Nathanson and Fine) show that these cases appear to have arisen from a type 1 virus shed by a vaccine about 3 years ago in Haiti, which then recombined with wild enteroviruses to regain virulence. Poor maintenance of vaccine coverage in these countries over the past several years (there were cases among teenagers) led to the epidemiological circumstances that allowed the recombinant virus to circulate among poorly immunized children. This outbreak sounds a warning for the careful development of immunization strategies and comprehensive monitoring of paralysis cases in the last stages of the global polio eradication scheme. **X**

Microbial Defense in Flies

Two branches of innate immune response have evolved in *Drosophila* to recognize molecular patterns encoded either in fungi or in the cell walls of bacteria. Each activates distinct sets of genes encoding peptides with specific antimicrobial activity. Choe *et al.* (p. 359; see the Perspective by Khush *et al.*) investigated two mutant alleles (*ird7¹* and *ird7²*) that inhibited genes normally activated by the *imd* pathway by preventing the cleavage and nuclear translocation of the transcription factor Relish. The *ird7* alleles mapped to a region of chromosome 3 containing peptidoglycan recognition protein (PGRP) genes and encoded truncations in PGRP-LC that could account for disruption of its function in each of the mutants. Phenotype rescue by transgenic overexpression of wild-type PGRP-LC in *ird7* mutant flies and RNA interference analyses in cell lines confirmed that PGRP-LC is a critical component of the antimicrobial response of *Drosophila*. **X**

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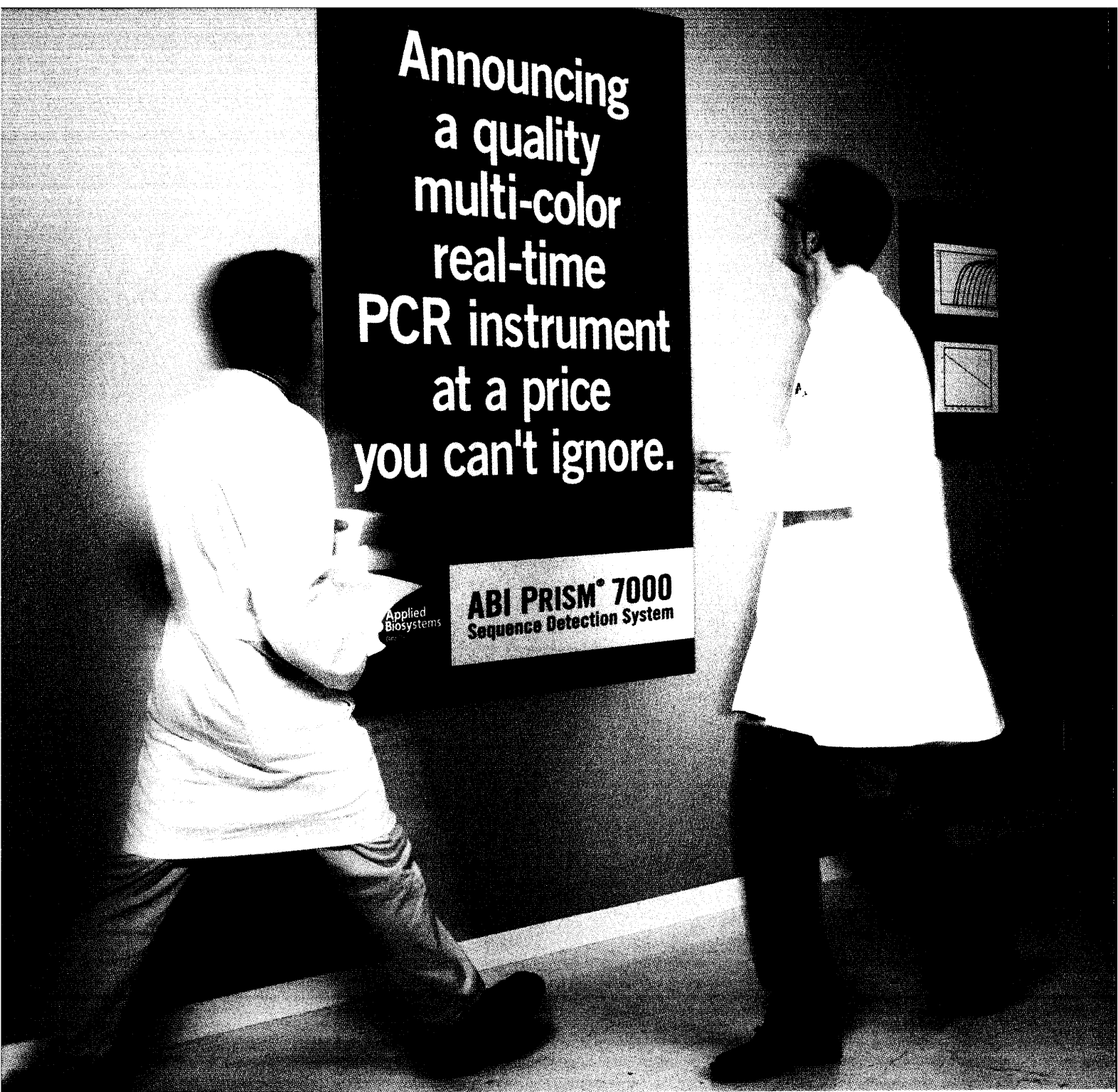
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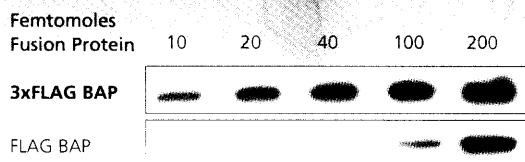
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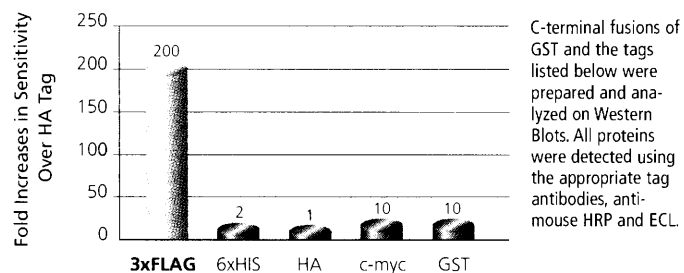
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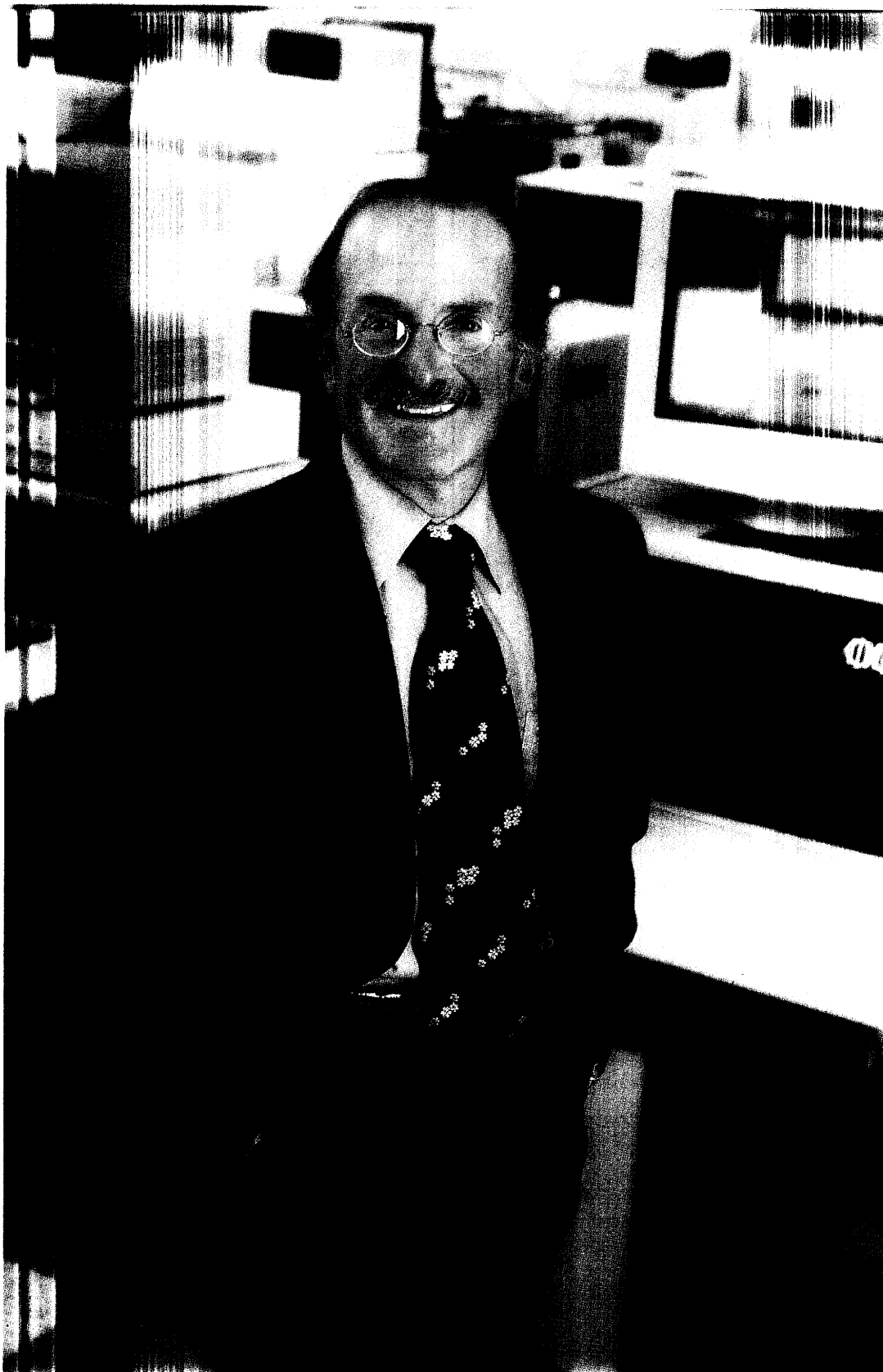


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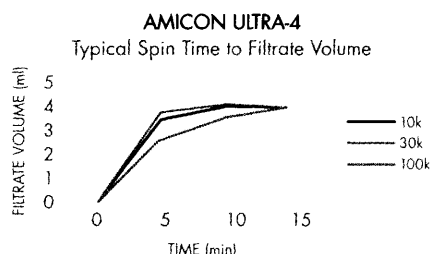


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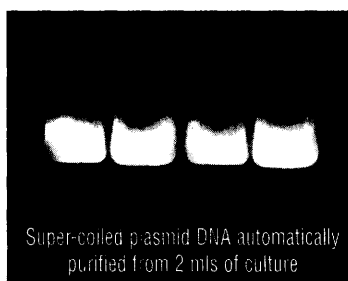
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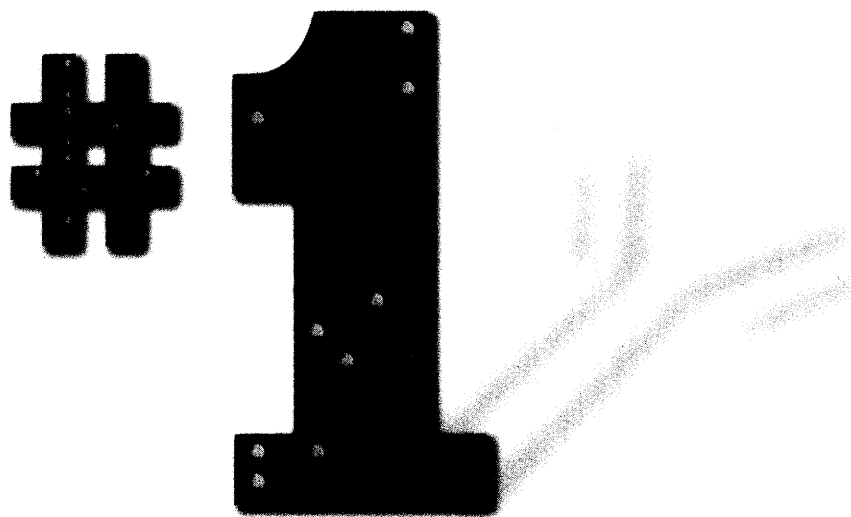
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1. Morris, M. et al. (2001) *Nature Biotech.* 19: 1173-1176.
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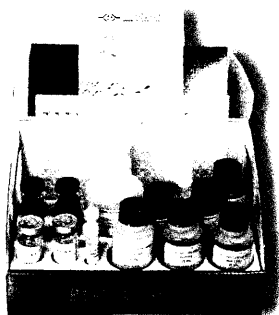
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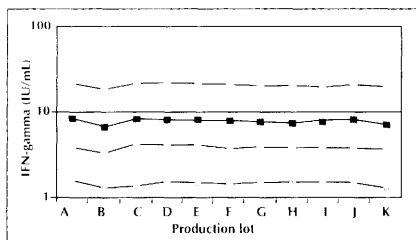
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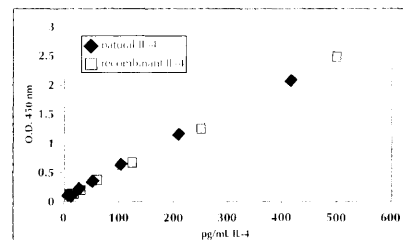


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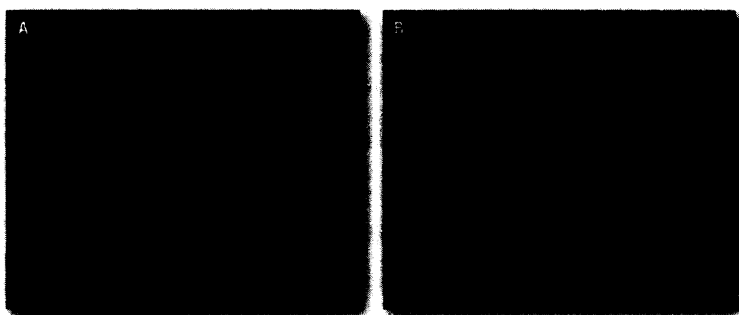
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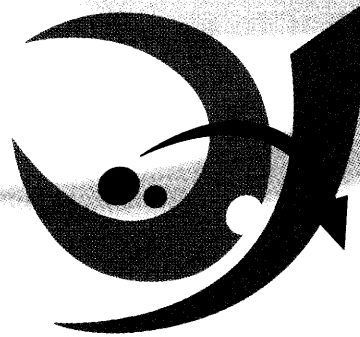
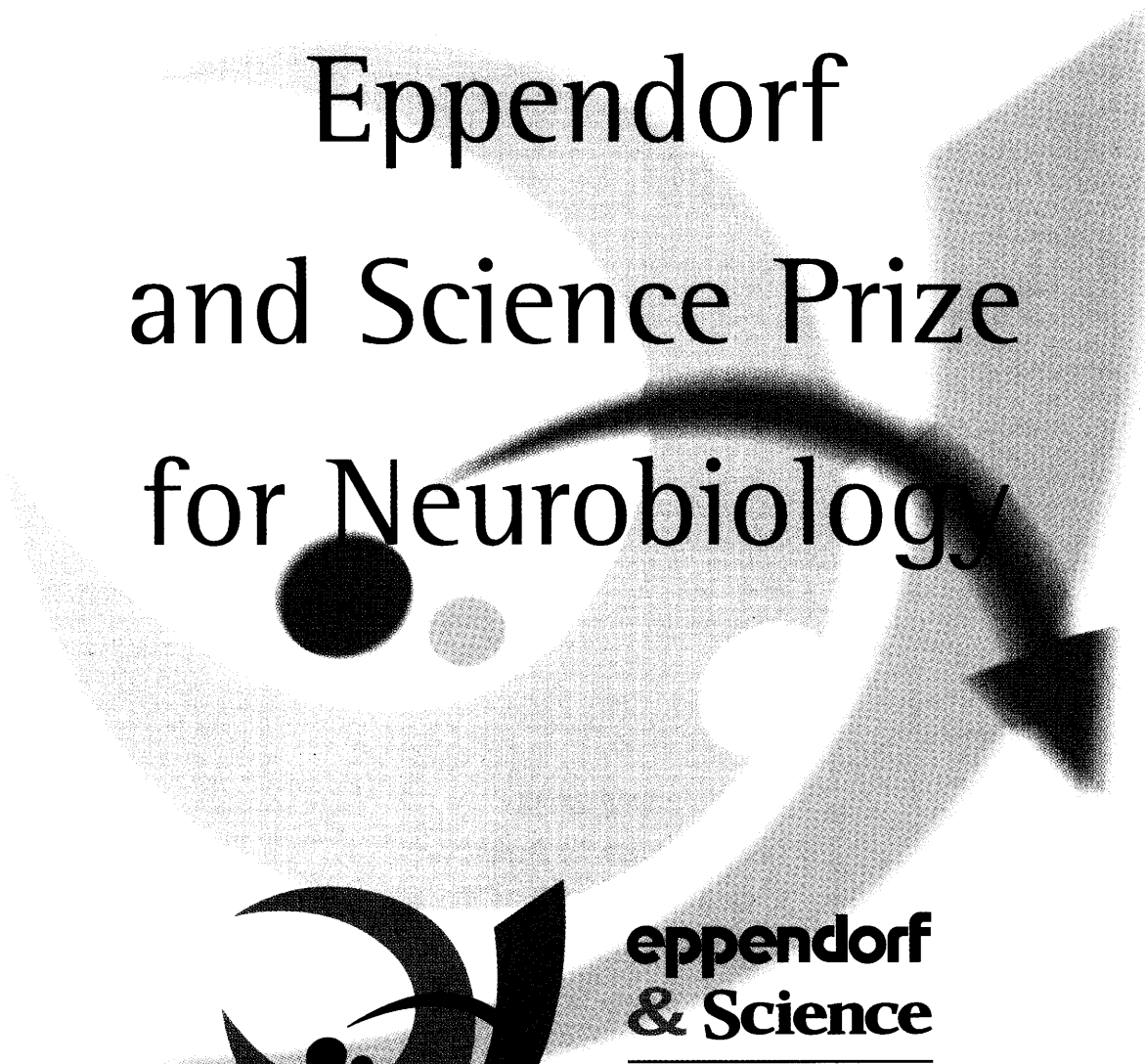
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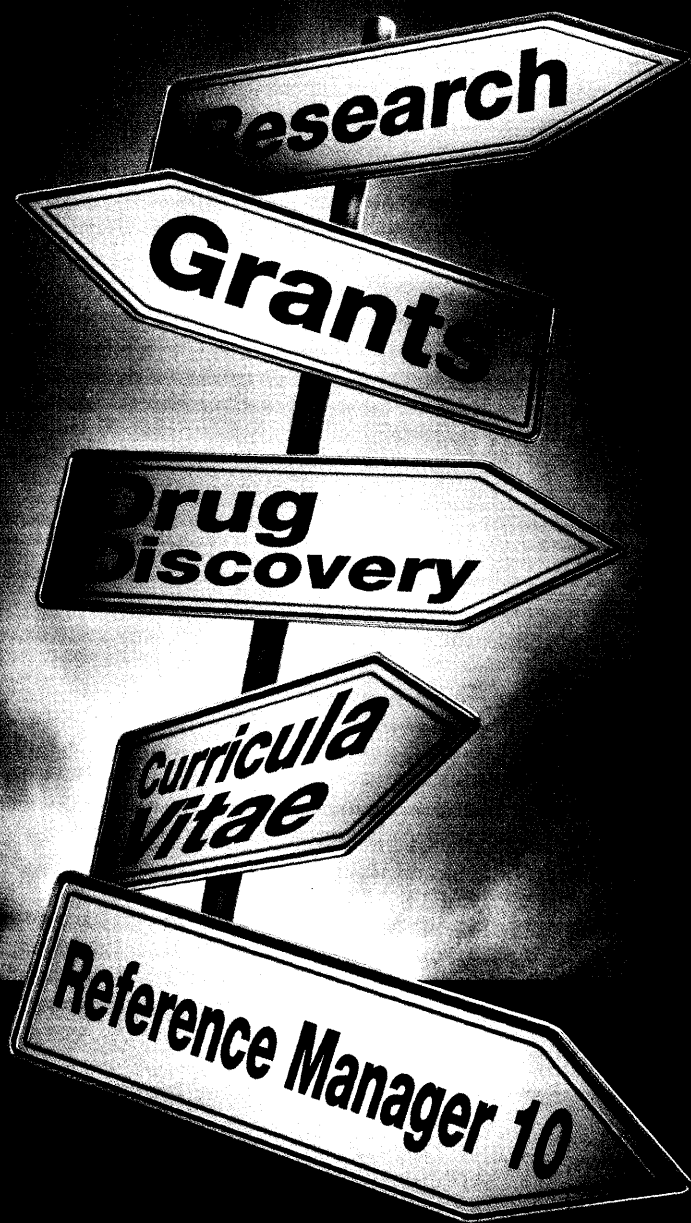
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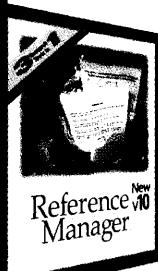
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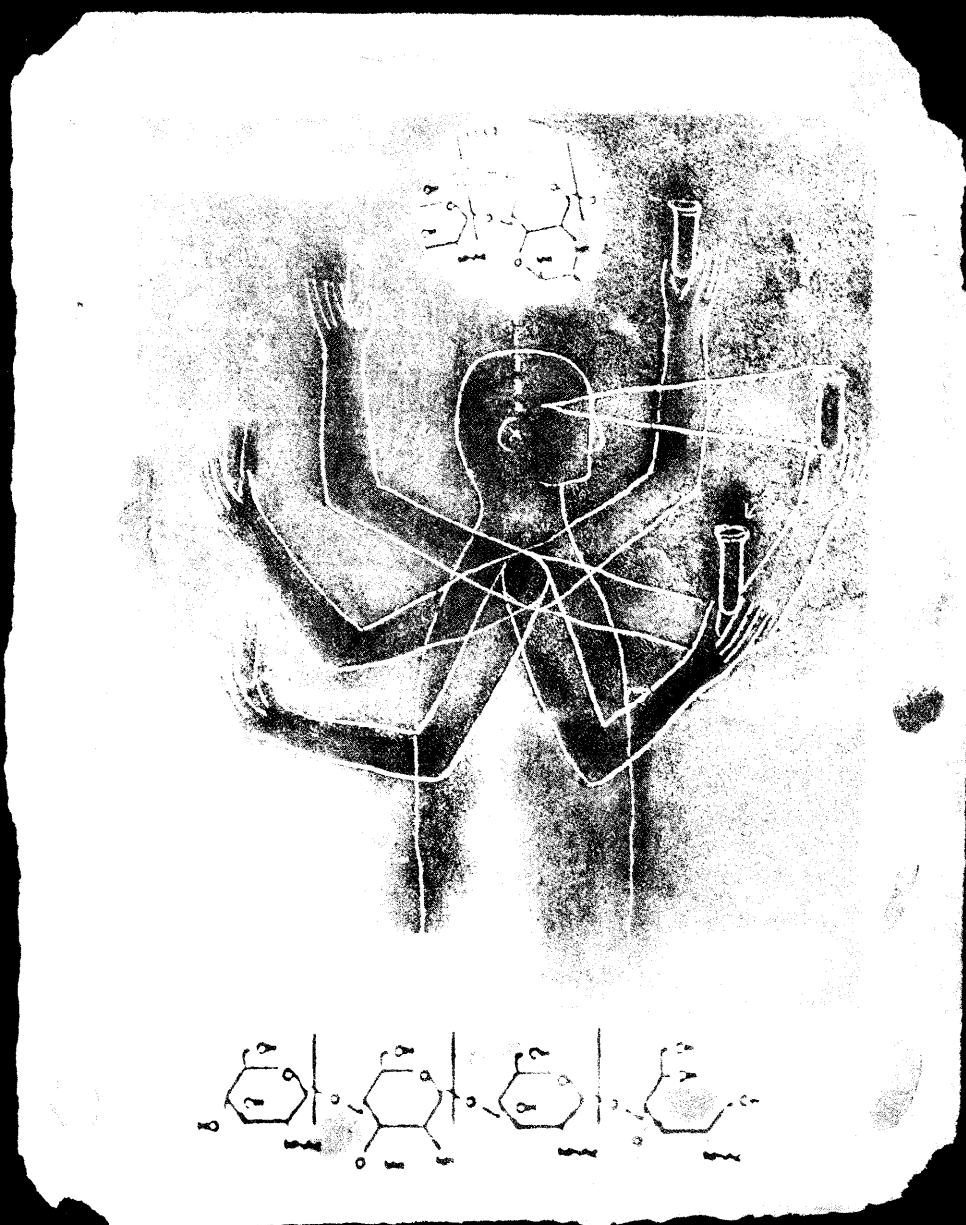
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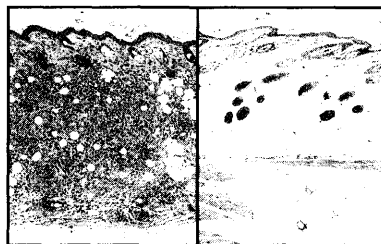
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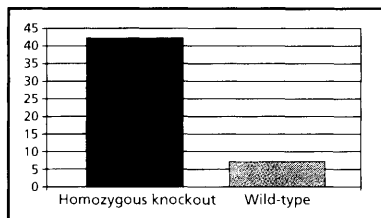
Phenotypic analysis Gene: Phosphatase

Homozygous knockout Wild-type



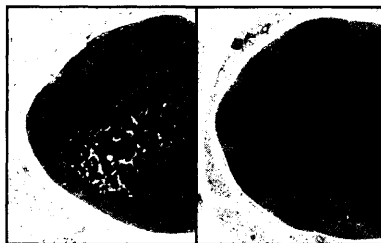
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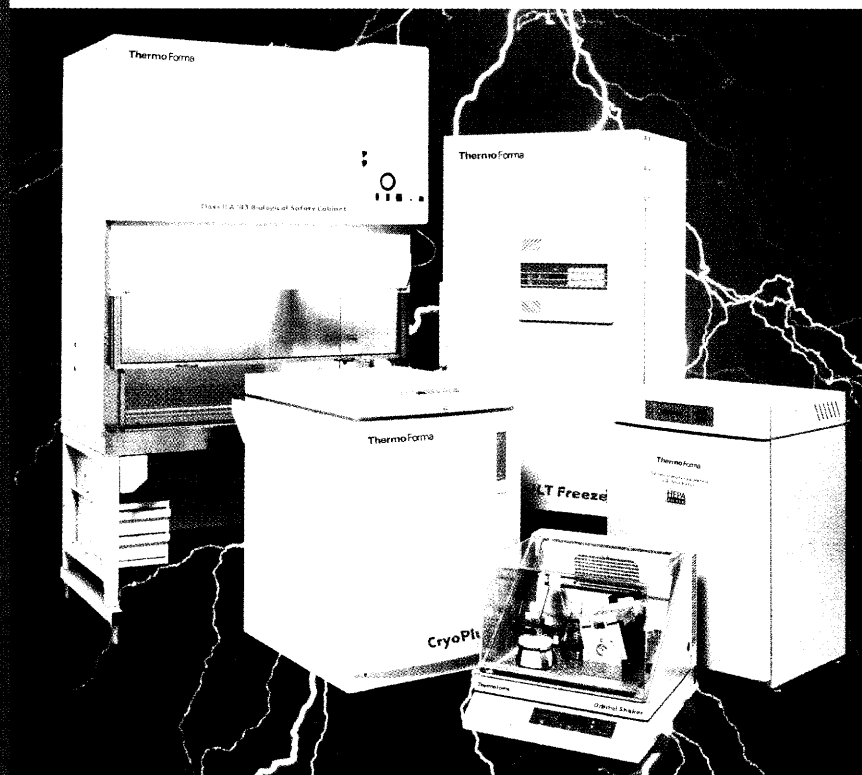
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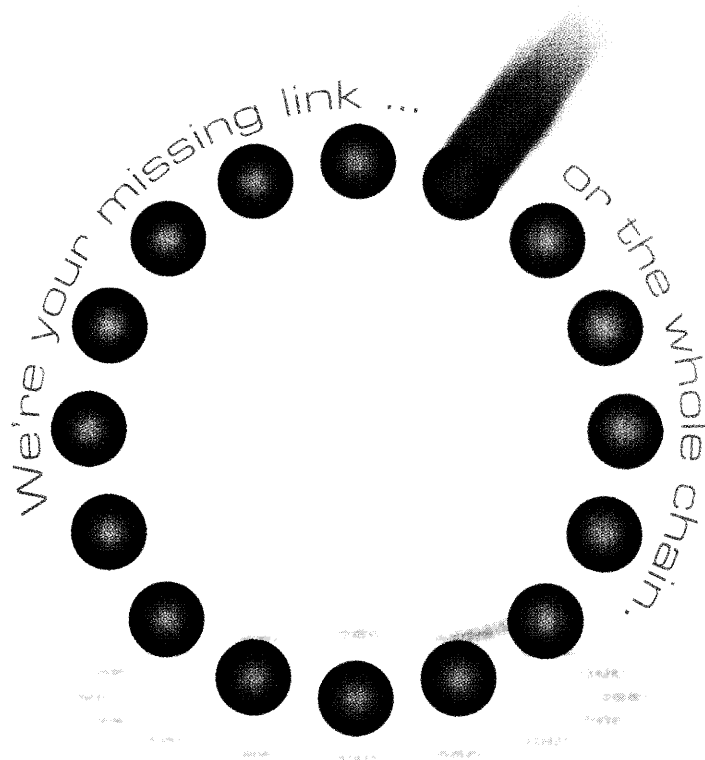
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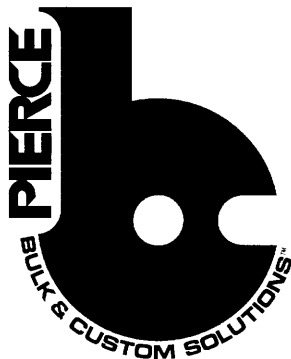
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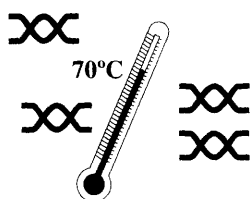
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Fig. 1

Pfu fails to amplify a GC-rich template. (far right)

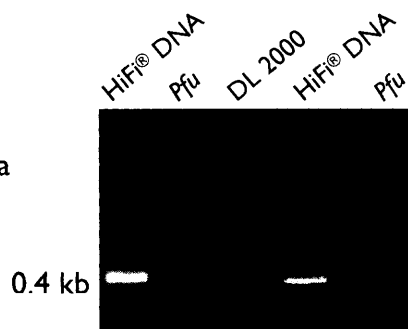


Fig. 2

Taq fails to amplify a 2.3 kb GC-rich template. (far right)

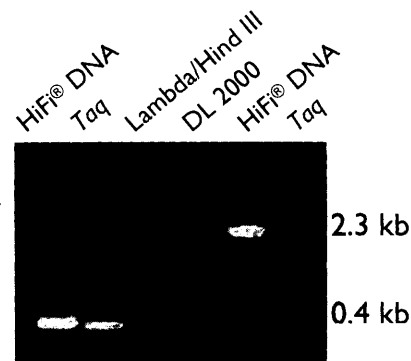


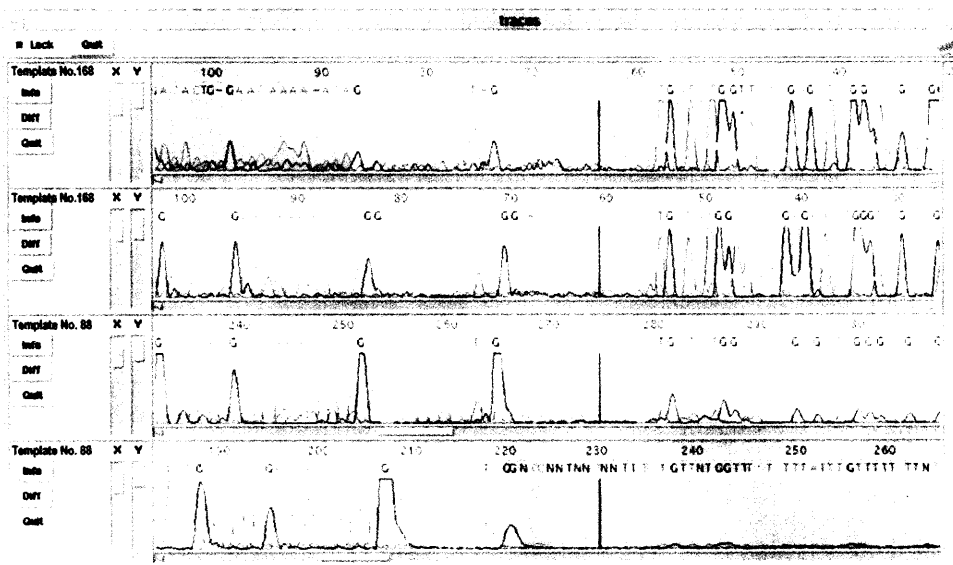
Fig. 3

ThermoSequenase II fails in the extension/termination after the GC-rich segment. (on the left)

HiFi® DNA polymerase in LoTemp™ cycle sequencing continues extension/termination. (on the left)

HiFi® DNA polymerase in LoTemp™ cycle sequencing overcomes this GC-rich segment. (on the right)

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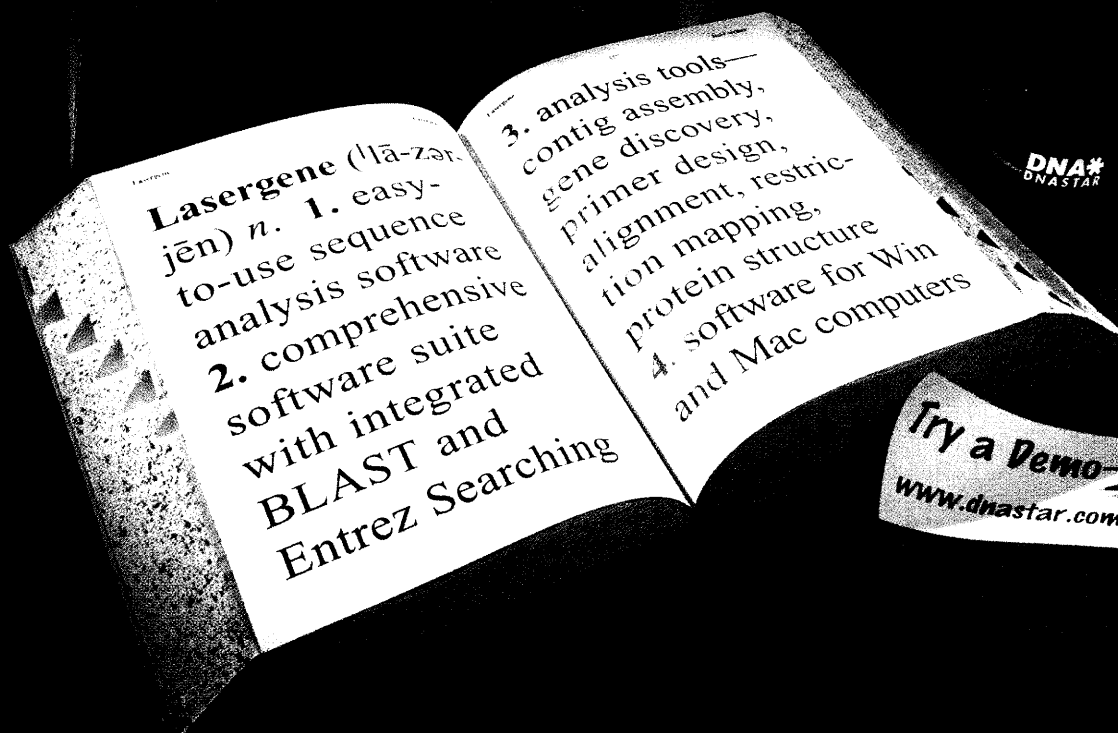
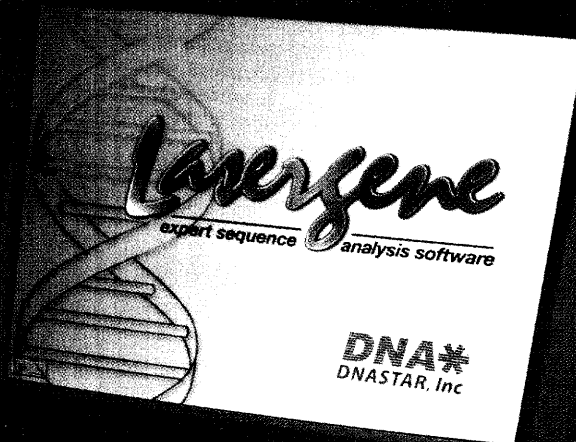


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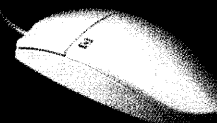
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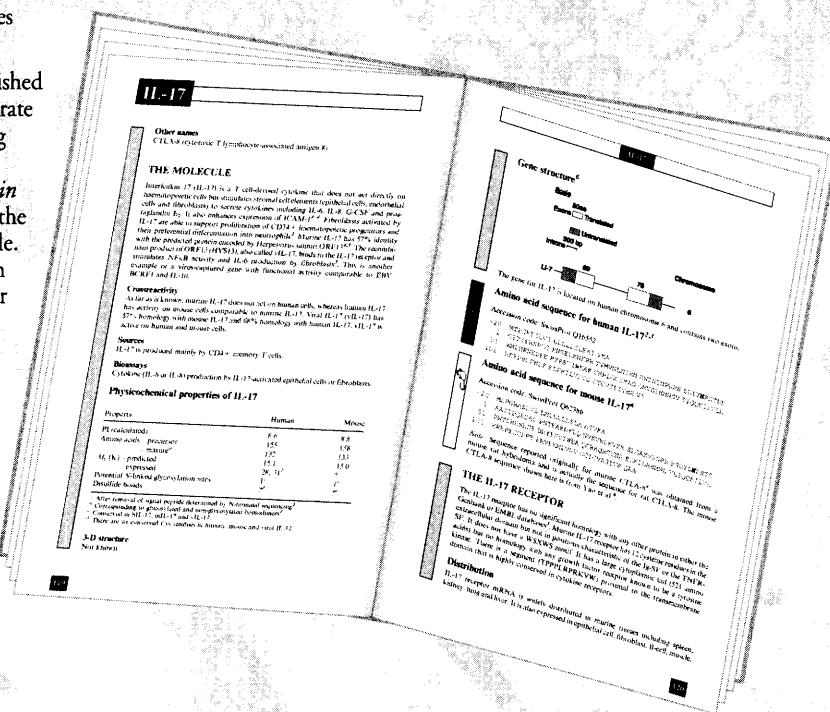
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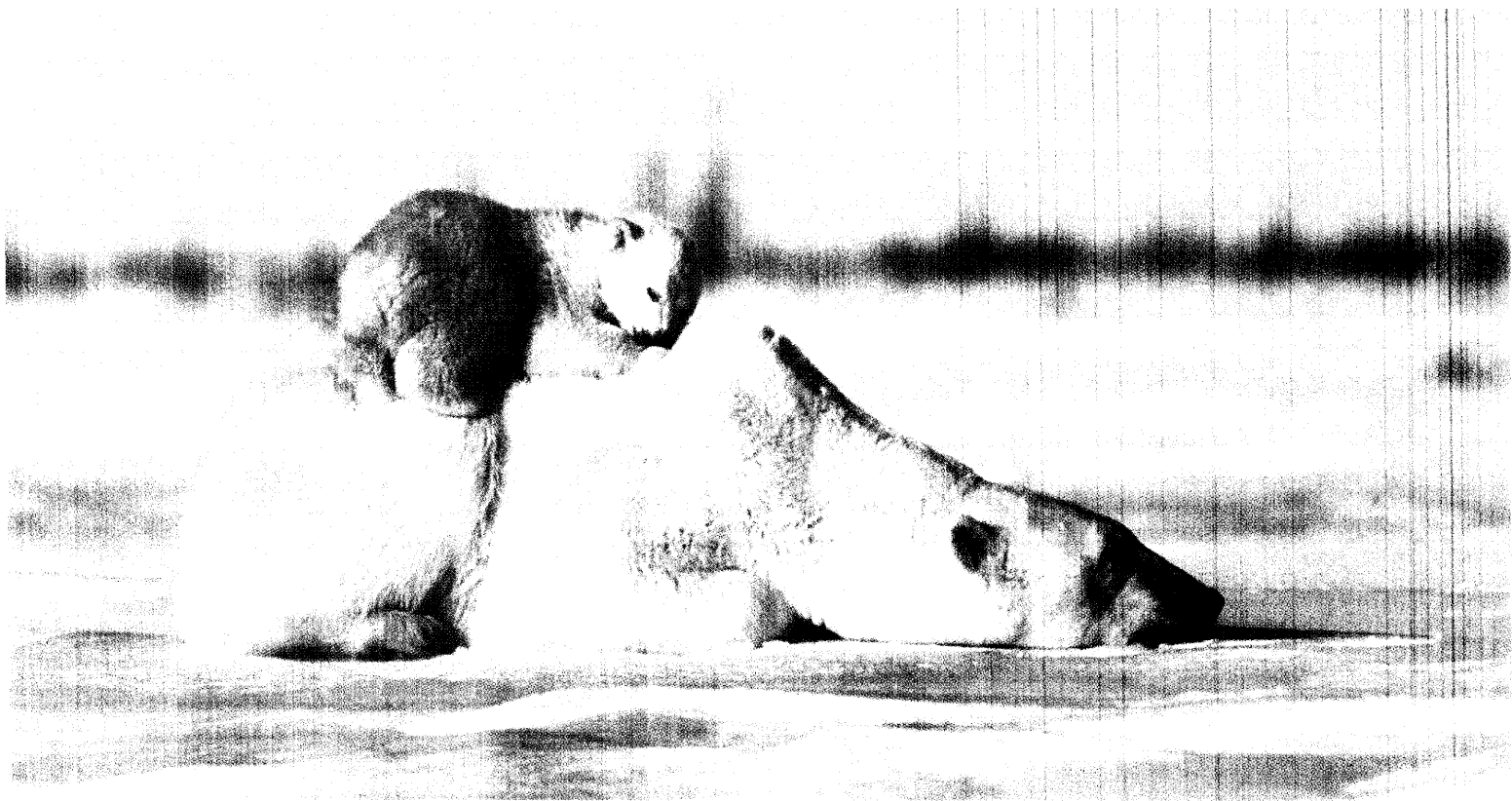
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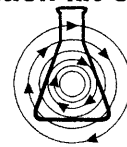
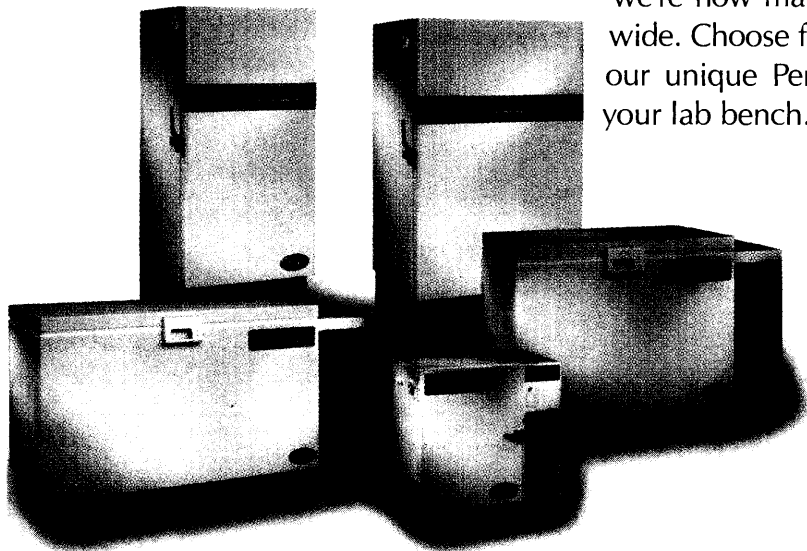
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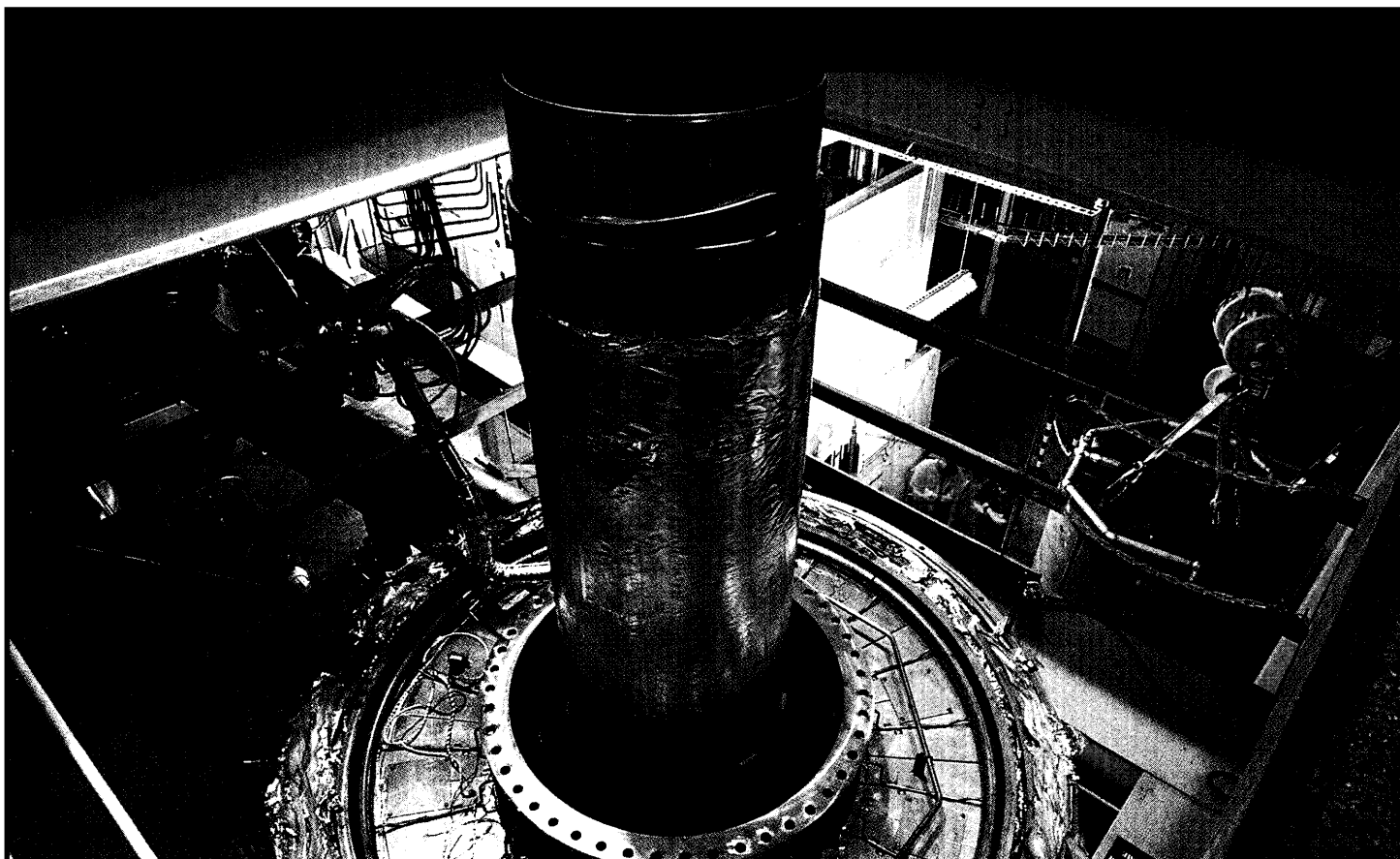
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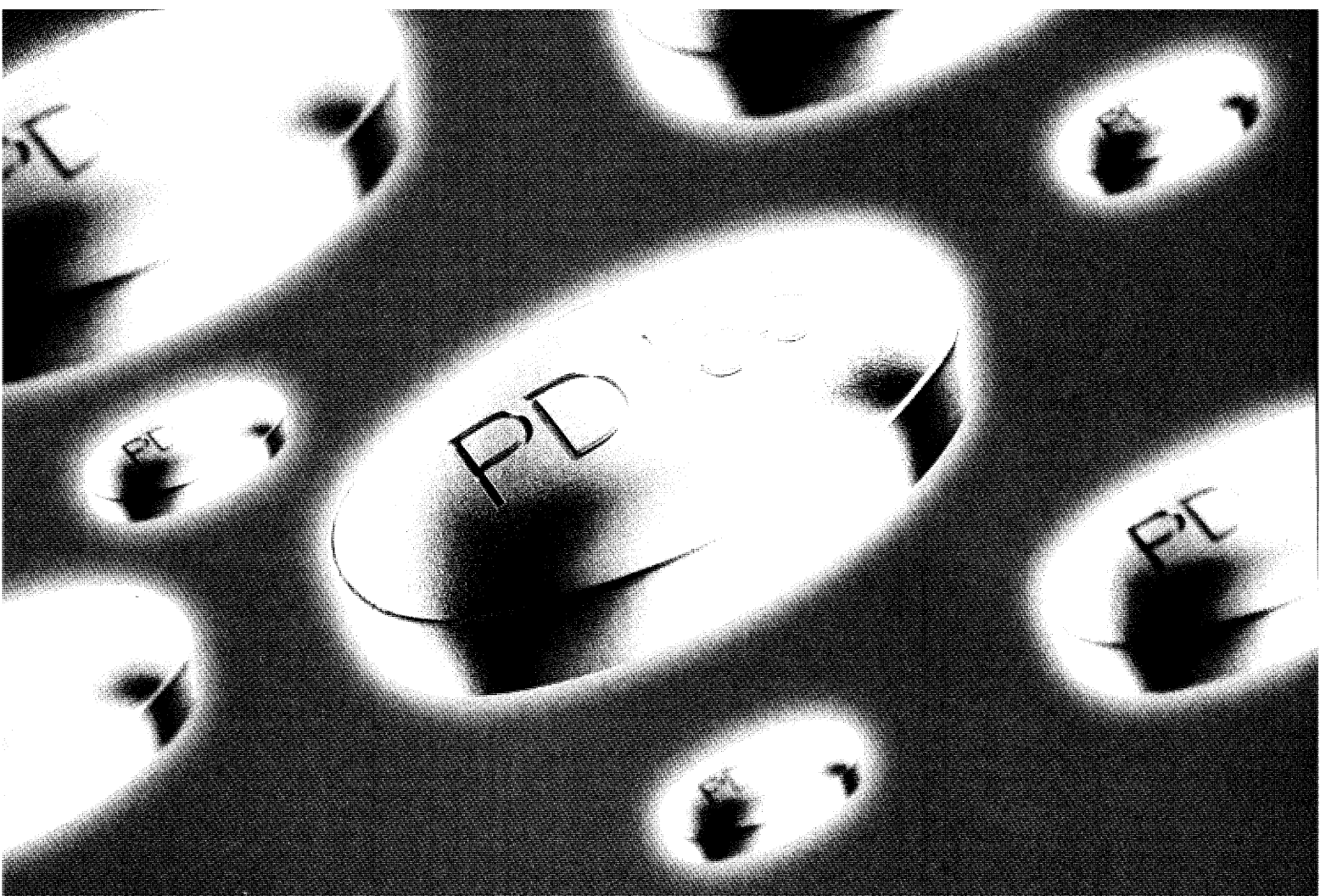
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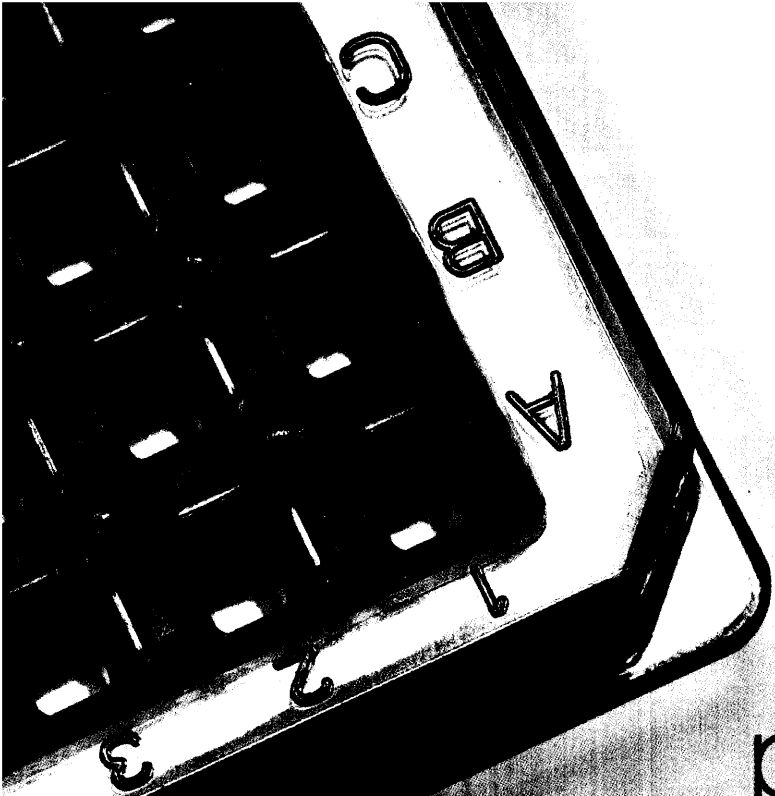
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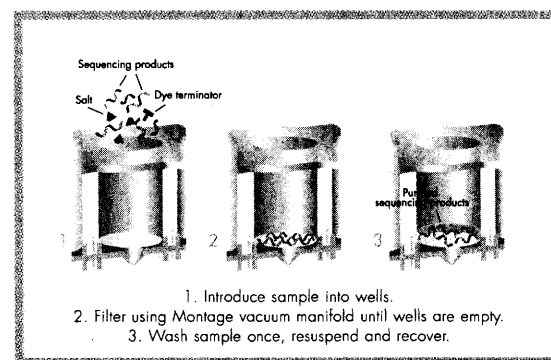
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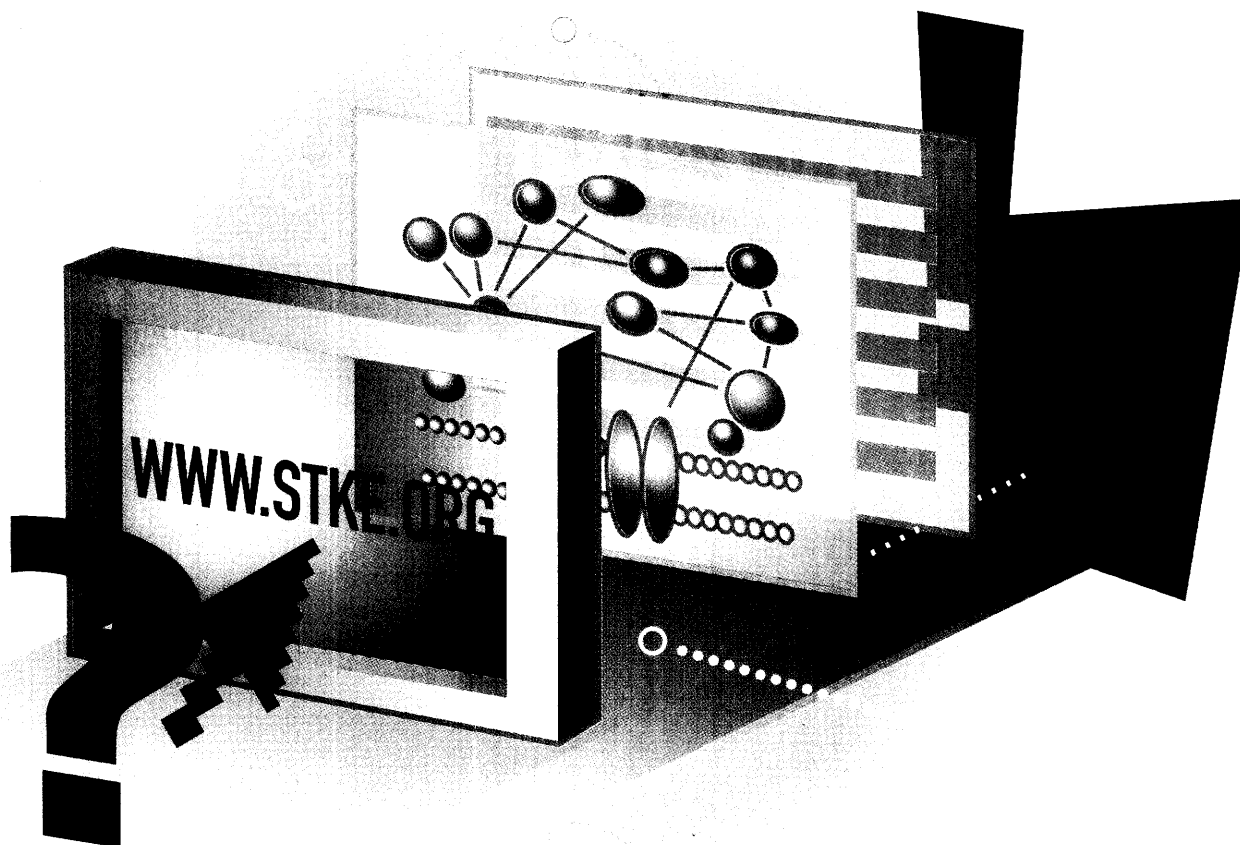
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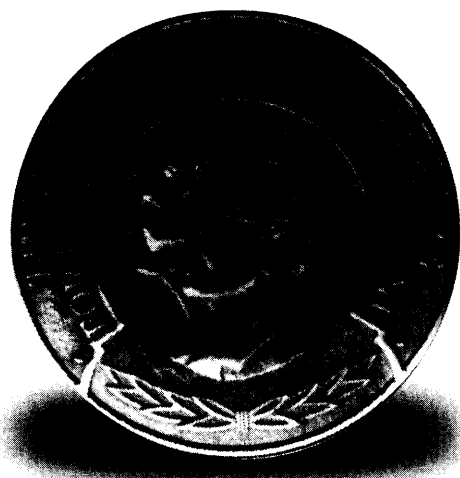
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Dr. Broecker, Newberry Professor of Earth and Environmental Sciences at Lamont-Doherty Earth Observatory, of Columbia University, has pioneered the use of a wide range of geochemical tracers to describe basic biological, chemical and physical processes that govern the behavior of carbon dioxide in the oceans and the interactions of oceanic carbon dioxide with the atmosphere. His studies on glacial/interglacial climate change provided the first definitive evidence that variations in earth's orbit around the sun and the resulting changes in insolation induce the glacial/interglacial climate cycle. Broecker proposed the concept of a global oceanic "conveyor belt" and identified the importance of changes in North Atlantic deep water formation as a leading candidate for the trigger of abrupt climate changes over the last few million years. Dr. Broecker was awarded the National Medal of Science in 1996.

Dr. Liu, Professor in the Institute of Geology and Geophysics at the Chinese Academy of Sciences has been a trailblazer in developing ways to measure paleoclimatic change over the last 2.5 million years through studies of loess, a windblown dust, that forms thick deposits over much of central China. The Chinese loess record contains an unparalleled terrestrial record of global environmental change. Liu's accumulated work on the loess/paleosol sequences has led to a deeper knowledge of the Southeast Asia monsoon system. Liu has also been recognized for his group's innovative discovery of the cause of Keshan's disease, which affected thousands of people and vexed the medical community for decades. Liu's research linked this disease to deficiencies in trace elements and nutrients in local soils and water, particularly selenium. Dr. Liu is a past President of the International Union for Quaternary Research (INQUA) and a founding member of the International Geosphere-Biosphere Programme on Past Global Changes (PAGES).

For additional information contact Dr. Linda E. Duguay, Executive Director, The Tyler Prize
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