8 February 2002

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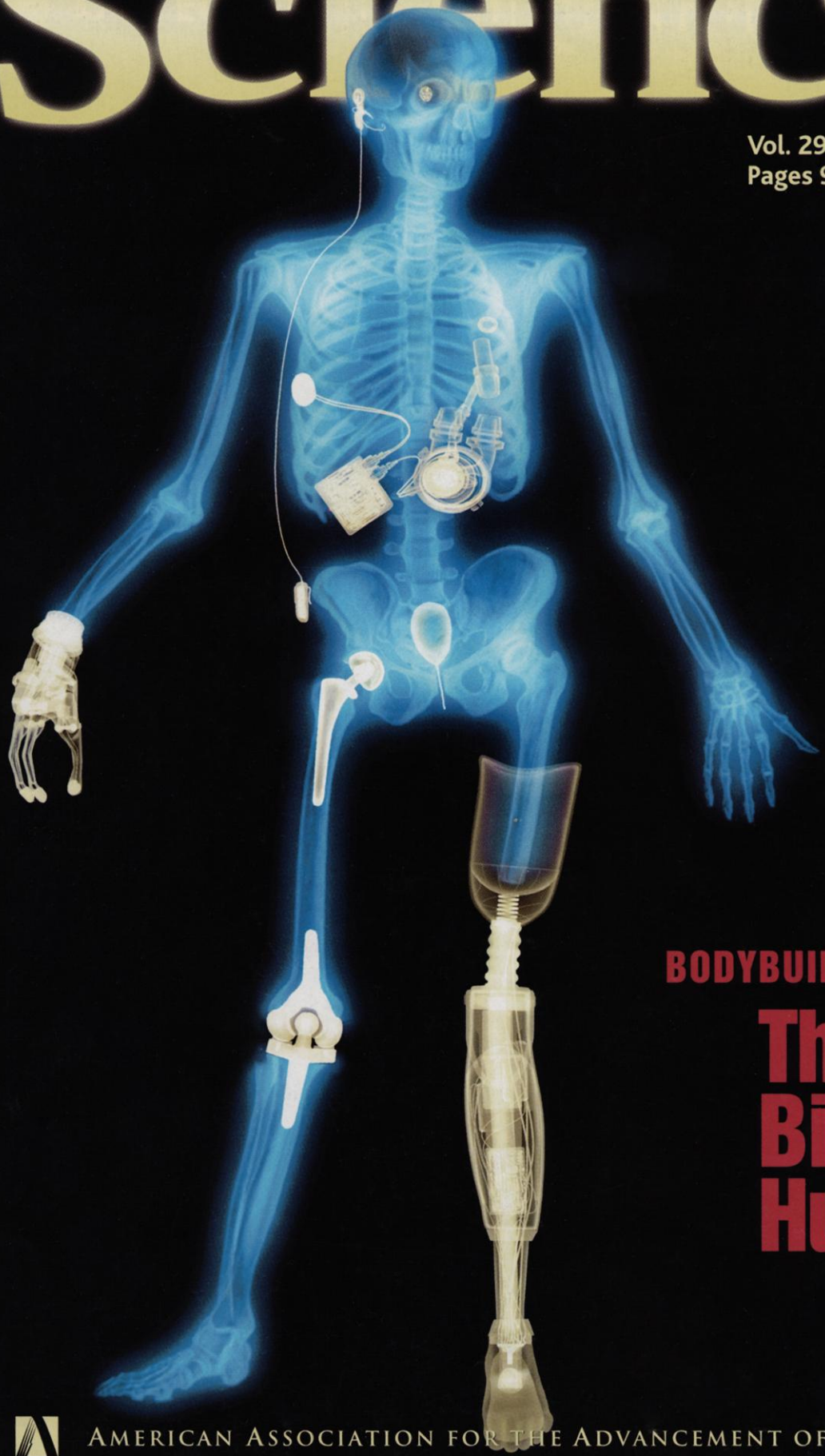

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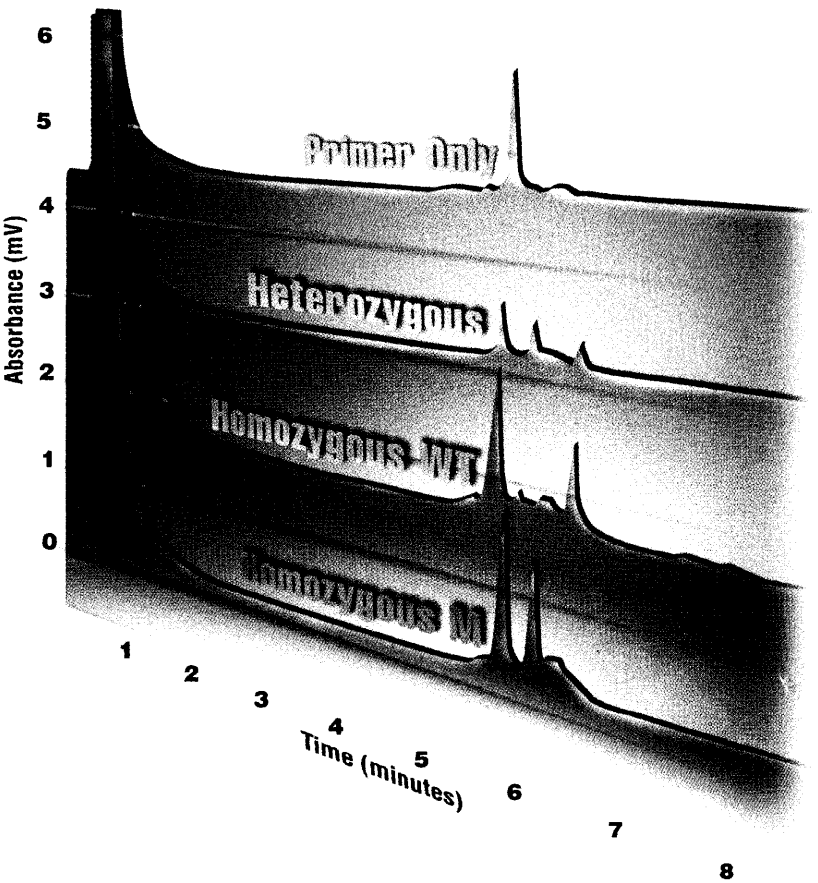

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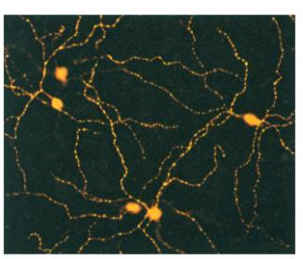

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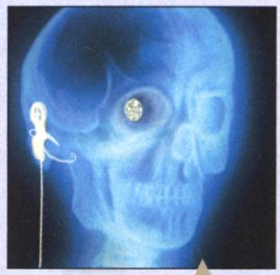
A glaucoma gene expands horizons

BODYBUILDING: THE BIONIC HUMAN

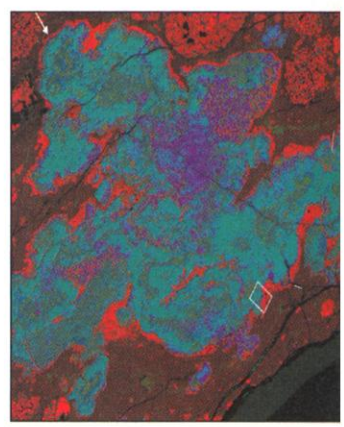
See also **Science's *STKE* on p. 923**



COVER 995

Will off-the-shelf body parts routinely replace injured or diseased tissue? This representational cover illustration and our special section highlight how far we have come and how far we have yet to go to accomplish this. [Illustration: Cameron Slayden; design: Nathalie Cary]

RESEARCH



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Exotic relics of the early solar system

New on *Science* Express A gene for systemic RNA interference

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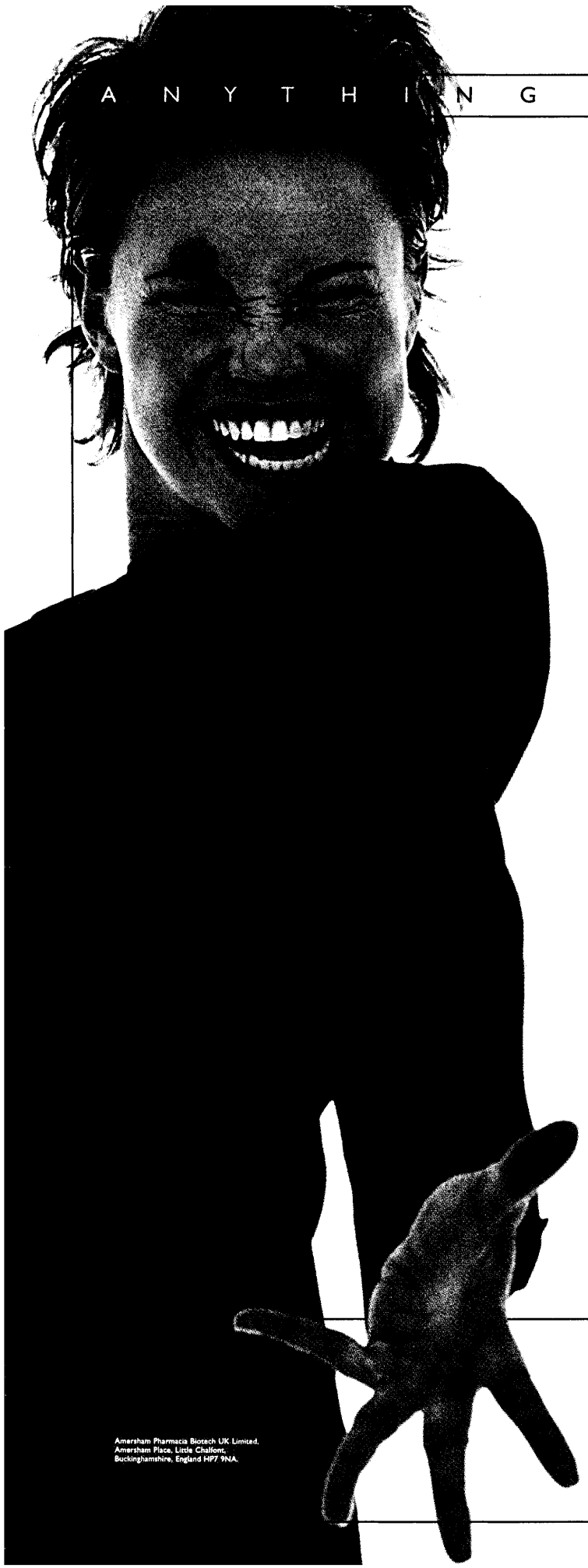

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Protein Nanoarrays Generated By Dip-Pen Nanolithography K.-B. Lee, S.-J. Park, C. A. Mirkin, J. C. Smith, M. Mrksich

The atomic force microscope has been used to spot and screen nanoscale arrays of proteins.

Systemic RNAi in *C. elegans* Requires the Putative Transmembrane Protein SID-1 W. M. Winston, C. Molodowitch, C. P. Hunter

An extensive screen in *C. elegans* has revealed three genes specifically involved in the systemic RNA interference effect, and characterization of SID-1 reveals that it is a membrane protein conserved in mouse and man.

Placebo and Opioid Analgesia—Imaging a Shared Neuronal Network P. Petrovic, E. Kalso, K. M. Petersson, M. Ingvar

947 Neuronal mechanisms underlying the placebo response to pain.

TECHNICAL COMMENTS

Is the Dongwanzi Complex an Archean Ophiolite?

Kusky *et al.* (Reports, 11 May 2001, p. 1142) interpreted an extensive complex of rocks in China of Archean age, dating from ~2.5 billion years ago, as a complete ophiolite (a characteristic suite of rocks that form in extensional plate tectonic settings such as oceanic spreading centers). The find, the study argued, suggests that plate tectonic processes "similar to those of today" were operating in the Archean. Zhai *et al.* comment that much of the supposedly Archean complex is actually of younger age, take issue with a number of field and petrographic observations of Kusky *et al.*, and conclude that interpretation of the complex as an ophiolite "needs to be further examined before it can be used as a hallmark of Archean plate tectonics." Kusky and Li, in their response, acknowledge that subsequent mapping has revealed that the complex does indeed include Mesozoic intrusives, but hold that the overall interpretation of the complex as an Archean ophiolite remains sound. They suggest that some of the discrepancies between their observations and those of Zhai *et al.* may stem from insufficiently detailed sampling by the latter group.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/295/5557/923a

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career resources for scientists

US: Flag Waivers J. Gallini and J. Goldman

In the second article of a series on immigration law for scientists, our experts explain how to get a green card without employee sponsorship by winning a "National Interest Waiver."

Singapore: Confessions of a Writer M. Rajen

A pharmacist writes about his moonlighting experiences as a newspaper columnist and journal editor.

UK: Mind the Gap K. Urquhart

The Art of Crazy Paving explains how to fill skills gaps in your CV through volunteering.

Germany: Good Fortune for Young Scientists E. von Ruschkowski

The Alexander von Humboldt Foundation has recently awarded 29 young scientists with 3-year grants of up to € 1.2 million each so that they may establish their own research groups in Germany.

Canada: Science, Technology, and the Arts—A Well-Rounded Career M. Lee

As managing editor with an online, peer-reviewed scientific journal, the author discovered that the endless possibilities of online publication quenched her thirst for creativity.

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Review: Knowing How to Navigate—Mechanisms of Semaphorin Signaling in the Nervous System Z. He, K. C. Wang, V. Koprivica, G. Ming, H.-J. Song

995 Axons utilize semaphorins to get from here to there.

Perspective: Mechanotransduction—All Signals Point to Cytoskeleton, Matrix, and Integrins F. J. Alenghat and D. E. Ingber

995 How structural connections between a cell's internal architecture and extracellular environment allow perception and transduction of mechanical force.

Perspective: ECM Remodeling Regulates Angiogenesis—Endothelial Integrins Look for New Ligands D. G. Stupack and D. A. Cheresh

995 Integrins for adhesion, migration, and survival of endothelial cells.

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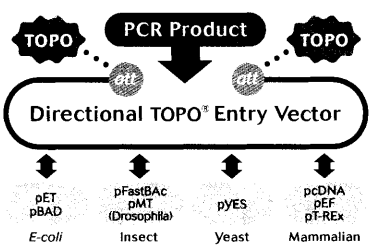

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THIS WEEK IN Science

edited by Phil Szuromi

Mantle Flow, To and Fro

The relative motions of tectonic plates are well established, but the motion of the underlying mantle is poorly known. Silver and Holt (p. 1054) determined the motion of the mantle beneath western North America by combining observations of surface deformation with upper-mantle seismic-velocity anisotropy. The upper mantle is flowing to the east, opposite the westward motion of the North American plate. Thus, the upper mantle is decoupled from the plate and its flow is primarily related to the subduction of the Farallon plate.

1039 Incorporating Chlorine Naturally

Organic chlorine compounds found in the environment have been thought to derive primarily from industry and agriculture. Furthermore, identifying nonvolatile chlorinated organic species that are produced in soils in situ has been problematic, and most naturally occurring chlorine compounds were thought to be inorganic. Myneni (p. 1039; see the Perspective by Casey) has used near-edge x-ray absorption fine-structure spectroscopy to identify and characterize chlorine-containing compounds in a variety of forest soils and other natural samples. Chlorine-bearing organic compounds are produced rapidly in leaf litter and are more abundant than inorganic chlorine compounds.

And in Brevia ...

A comparison by Dubrova *et al.* (p. 1037; see the news story by Stone) of families exposed to nuclear fallout in Kazakhstan to control groups in similar but uncontaminated areas of the country revealed a roughly doubled germline mutation rate.

Back at You

Many characteristics of volatile atmospheric aerosols, which have various impacts on climate and air quality, depend on aspects of their physical chemistry, such as the partitioning of elements between the surface and the interior of the particle. Krieger *et al.* (p. 1048) demonstrate that these profiles can be made nondestructively and in situ using Rutherford backscattering spectrometry for liquids and solids under conditions similar to those found in Earth's atmosphere.

Spin Resonance in Single-Layer Cuprate

One way to explore the underlying nature of the pairing mechanism in high-temperature superconducting cuprates is to identify common features of the various compounds that would place restrictions on other theories that predict specific behavior only in specific compounds. One such feature is a spin resonance seen in neutron scattering that has so far been seen only in bilayer and trilayer compounds. The absence of this feature in the single-layer cuprates, particularly the highly studied $La_{1-x}Sr_xCuO_2$, has provided formidable arguments against theories that postulate the necessity of the resonance. Preparing a mosaic of high-quality crystals of $Tl_2Ba_2CuO_{6+\delta}$, a single-layer cuprate, He *et al.* (p. 1045; see the 25 January news story by Voss) provide unambiguous evidence that the spin resonance is present, thus indicating that any proposed theory must consider the spin resonance as an essential ingredient.

Magnetic X-ray Microprobe

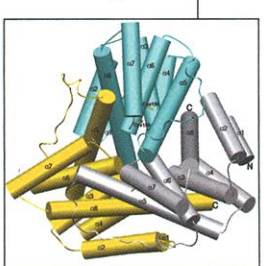
Understanding antiferromagnetic behavior on the microscopic scale is becoming increasingly important because of applications in magnetic memory devices. Evans *et al.* (p. 1042) present a new technique based on microfocused x-ray beams that can be used to image the structure and evolution of individual domains. They studied the intriguing but little understood spin-flip transition in chromium in which the spins are rotated 90° from their original orientation. The transition takes place near the domain wall and then works its way into the bulk of the domain.

Birds of Feather, Flocking Together

Tropical deforestation may be harming migratory bird species that breed in temperate latitudes and overwinter in the tropics. However, for most such species, it has proved difficult to differentiate among and track populations using different parts of the wintering range, and hence to pinpoint how these effects operate. Rubenstein *et al.* (p. 1062; see the Perspective by Hobson) use stable isotope signatures in the feathers of an American migrant songbird, the black-throated blue warbler, to show that birds from different parts of the breeding range have distinct migratory patterns. For example, birds from the northern part of the breeding range in North America wintered in Cuba and Jamaica, while those from the southern parts of the breeding range wintered in Hispaniola and Puerto Rico.

A Bucket-Brigade Defense

Mycobacterium tuberculosis defends itself against oxidative attack (primarily peroxides and peroxynitrite) by sacrificing reducing equivalents in the form of the cysteine residues of alkyl hydroperoxide reductase (AhpC). Bryk *et al.* (p. 1073) show that these cysteines are regenerated with the aid of three other essential components drafted from basic intermediary metabolism. Analysis of the crystal structure of the protein AhpD, which is encoded by the open reading frame downstream of *AhpC*, suggested a similarity to thioredoxin. This insight led to the identification of dihydrolipoamide dehydrogenase (Lpd) and dihydrolipoamide succinyltransferase (SucB) as go-betweens in conveying reducing equivalents derived from the oxidation of α-keto carboxylic acids, such as pyruvate, to the adapter AhpD, and finally to the antioxidant defender AhpC.



CREDIT: BRYK *ET AL.*

Shedding Light on Clocks

Rods and cones are not the only photoreceptor cells in the mammalian retina (see the news story by Barinaga). Berson *et al.* (p. 1070) have identified a subset of retinal ganglion cells that are

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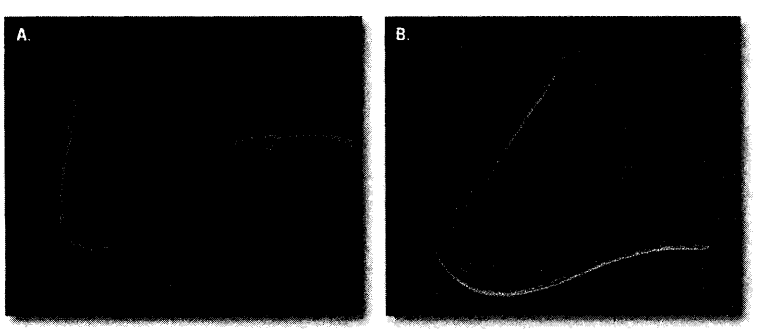
CONTINUED ON PAGE 927

NEW ENGLAND BIOLABS

Sense and Antisensibility.



RNAi in *C. elegans*
Fluorescence microscopy of a *C. elegans* adult female with a transgenic GFP reporter gene (green) highly expressed in the pharynx (A). Double-stranded RNA corresponding to the GFP coding region was produced using the HiScribe RNAi Transcription Kit and injected into the syncytial gonad of transgenic adult worms. RNAi is demonstrated by the reduction of GFP expression in the progeny (B).

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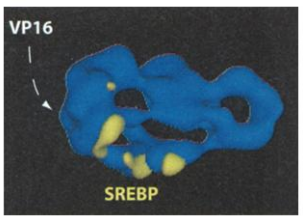
also sensitive to light and directly innervate the central circadian pacemaker in the brain. Hattar *et al.* (p. 1065) further show that the intrinsic photosensitivity of these cells depends on their expression of the photopigment melanopsin. The findings solve the long-standing puzzle of whether circadian photoreceptors underlie the light-dark cycle entrainment mechanism of mammals.

Glaucoma Gene in Sight

Glaucoma affects nearly 70 million people worldwide and is the second leading cause of blindness. One of the major subtypes of this disorder, primary open-angle glaucoma (POAG), is manifested clinically as a gradual loss of peripheral vision and at the cellular level by the death of retinal ganglion cells. Rezaie *et al.* (p. 1078; see the Perspective by Friedman and Walter) identified the gene responsible for a hereditary form of adult-onset POAG. The culprit gene, located at chromosome 10p14, codes for optineurin, a 66-kilodalton protein of unknown function that has previously been implicated in the tumor necrosis factor–α signaling pathway and may be playing a neuroprotective role.

Lifting the Veil

Veil-like projections at the leading edge of moving cells, the lamellipodia, are propelled by the dynamics of actin filaments. Watanabe *et al.* (p. 1083) used sophisticated fluorescent microscopy techniques to analyze the precise details of actin polymerization and breakdown. Contrary to previous expectations, the majority of actin filaments within the lamellipodia are generated away from the very tip, which raises questions about how the leading edge is actually pushed forward.



CREDIT: TAATJES *ET AL.*

Getting into Shape

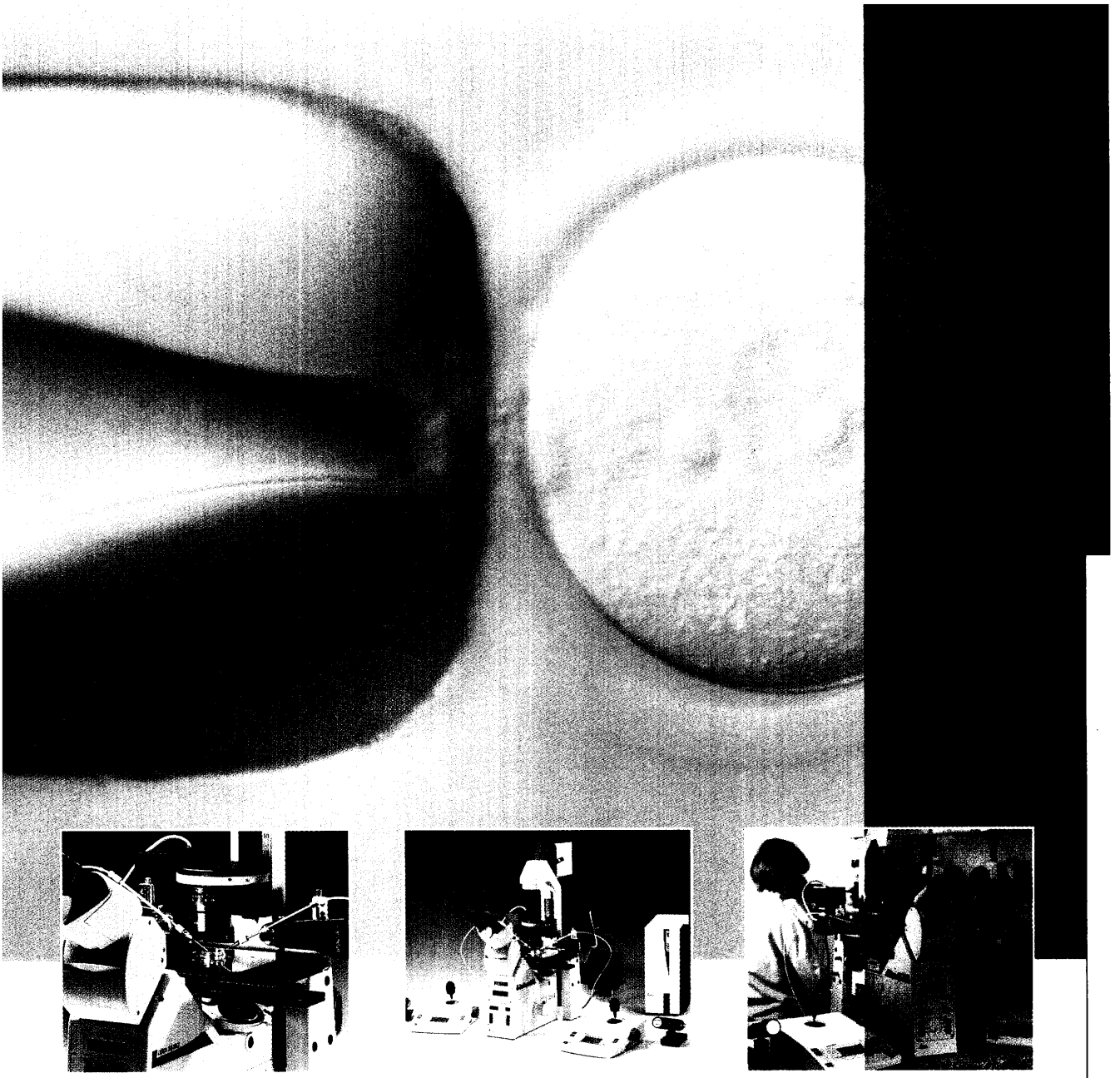
The cofactor complexes such as ARC (activator-recruited cofactor) and CRSP (cofactor required for Sp1) share several common subunits and mediate interactions between activators and the basal transcription apparatus. Taatjes *et al.* (p. 1058; see the Perspective by Meisterernst), using biochemical assays and electron microscopy, found that the larger complex ARC is composed of two multisubunit complexes, ARC-L and CRSP, and that transcriptional activity is only observed with CRSP. Structural determinations indicate that distinct conformations are induced in the CRSP complex by various activators. Therefore, different activators may allow for different transcriptional readouts based on the specific conformations that form.

Small by Design

The search for effective small molecule inhibitors of protein-protein interactions is a major goal in pharmaceutical research. Gadek *et al.* (p. 1086) describe the design of a small molecule that mimics an epitope of the ligand of the integrin LFA-1. The lead compound (*ortho*-bromobenzoyl tryptophan), originally identified as inhibiting LFA-1, was optimized using information gained from the separate evolution of a noncontinuous peptide epitope of ICAM-1. The final result of the modifications led to a compound that retained characteristics of the small molecule and bound LFA with high affinity. The compound also effectively blocked lymphocyte proliferation and contact hypersensitivity in mice.

Overcoming Rejection

Shortages in human organs for transplantation has led to consideration of other species as possible donors. The ability to use pig organs has been hampered by the presence of galactose α(1,3) galactose residues on the surface of pig cells, which result in their rejection by primate recipients, who lack the enzyme that creates this linkage. Lai *et al.* (p. 1089) knocked out one allele of the α(1,3) galactosyltransferase in fetal fibroblasts in vitro and then used these cells to clone transgenic pigs by nuclear transfer. The next step will be the creation of a homozygous pig that completely lacks these residues. In addition to their eventual impact in the field of xenotransplantation, these pigs serve as models for genetic modifications of the porcine genome for other medical and agricultural purposes.



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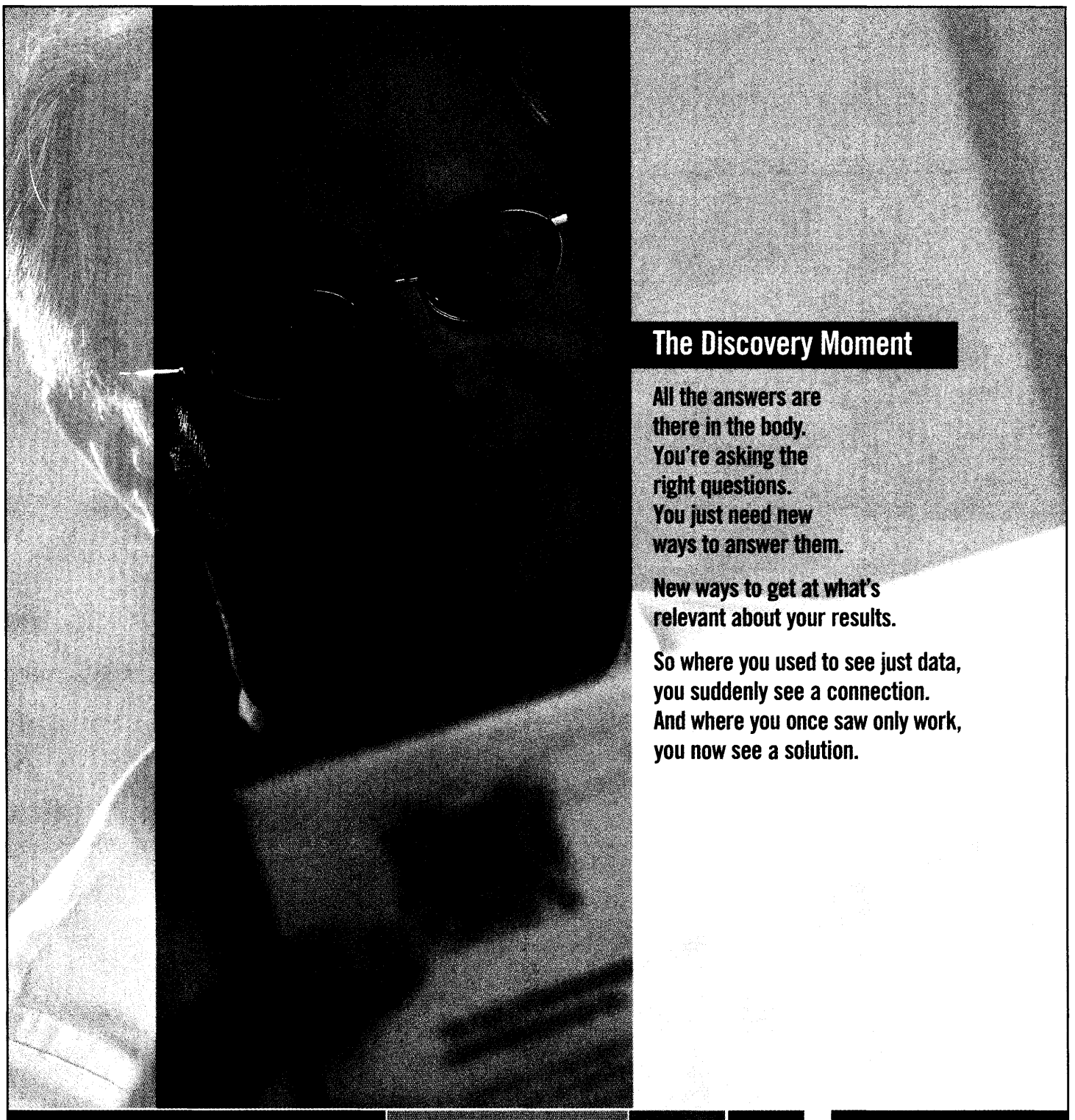

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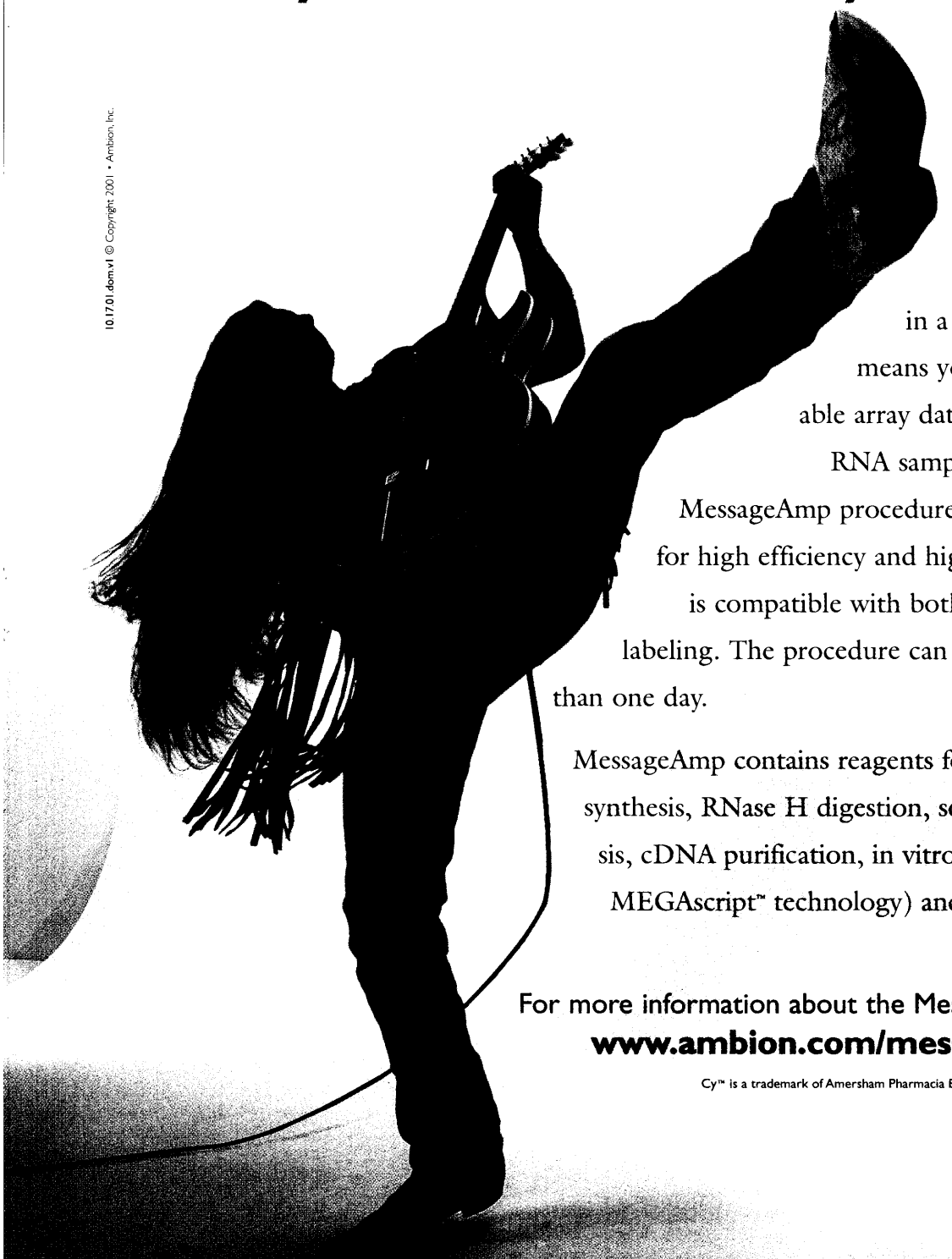

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USA-CyP in the splicing of pre–messenger RNA (pre-mRNA). USA-CyP binds to the human splicing factors hPrp4 and hPrp18. hPrP4 is required for assembly of the spliceosome complex that mediates the first half-reaction (separating the 5′ end of the intron from the pre-mRNA), and hPrP18 is required during the second half-reaction (removing the intron and joining exons). These structural interactions differ from those of cyclophilins and HIV capsid proteins, in that binding occurs at a site distinct from the catalytic center. Thus cyclophilin can be added to the list of choreographers who direct the sequential rearrangements of RNA and protein that occur during pre-mRNA splicing. — GJC

EMBO J. **21**, 470 (2002).

Imprints of ancient jellyfish in sandstone beds.

PALEONTOLOGY

Beached Jelly Bellies

Scyphozoan medusae or jellyfish are pelagic organisms that tend to congregate in near-shore, shallow water environments for reproduction, hunting, or during stormy weather. During the ebb of tides, large groups can be stranded. When a medusa realizes it is stuck in the sand, it turns belly-up and pumps its bell to try to escape, but this response only aggravates the sticky situation by filling the medusa with sand. The deceased medusa leaves a mound of sand and decomposing internal organs surrounded by concentric concave rings where it tried to repeatedly pump to flee.

Now, Hagadorn *et al.* have found rare and unusual traces of several strandings of large medusae from the late Cambrian, exquisitely preserved in coarse-grained sandstone beds in Wisconsin. The concentric concave rings surrounding sandy mounds, which in some cases show possible traces of internal organs, are commonly preserved on rippled bedding planes. Together, these features suggest a shallow lagoon environment, possibly a sandy barrier island, where frequent tropical storms may have caused the multiple strandings. Thus, these ancient sands provide a rare glimpse of rarely preserved soft-bodied life in Cambrian seas. — LR

Geology **30**, 147 (2002).

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Immunity **16**, 23 (2002).

CREDITS: HAGADORN *ET AL.*, *GEOLOGY* 30, 147 (2002)

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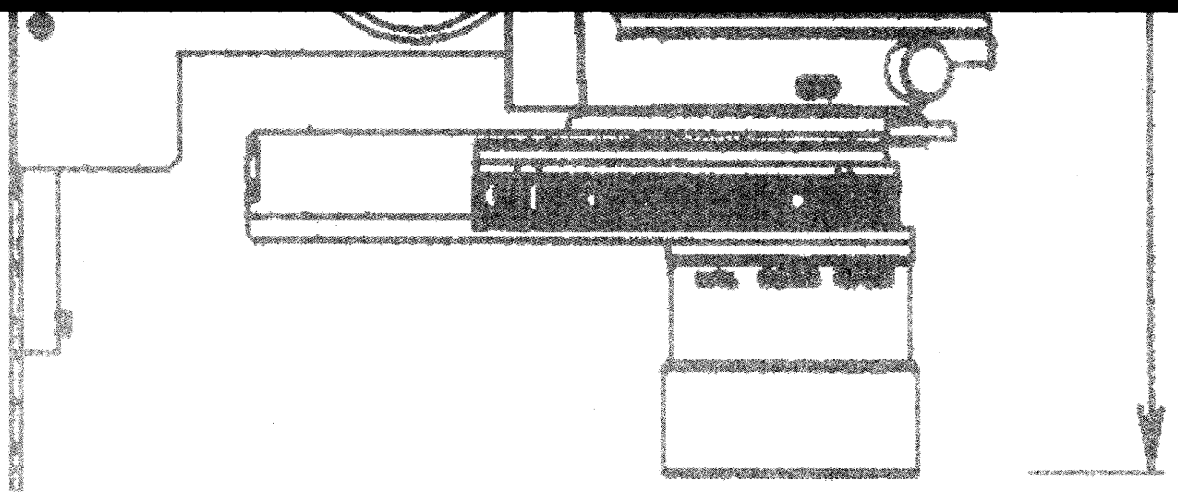

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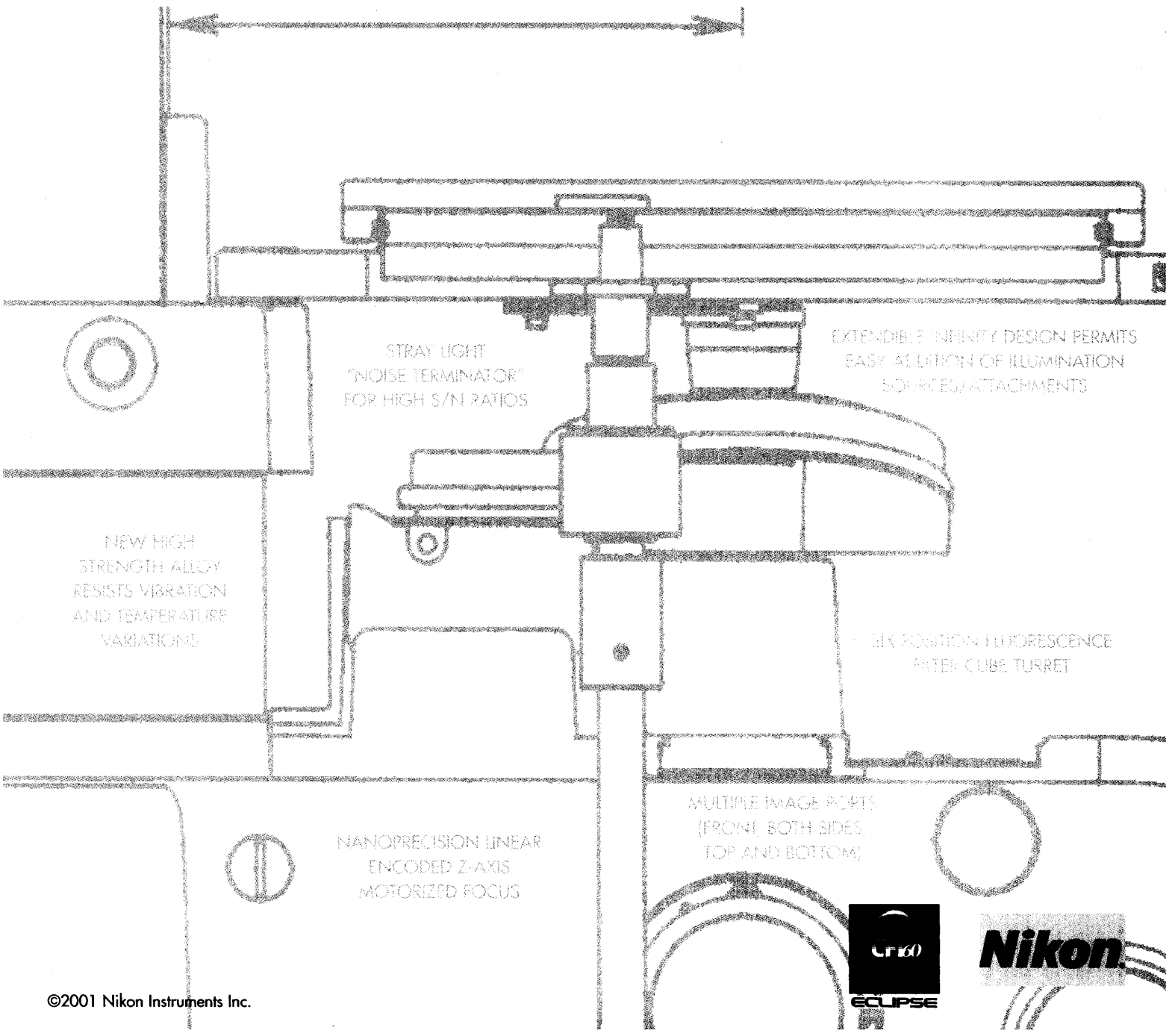

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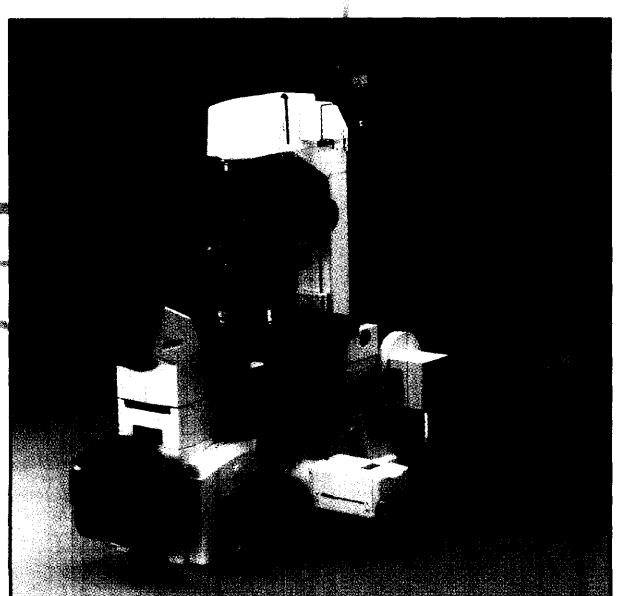

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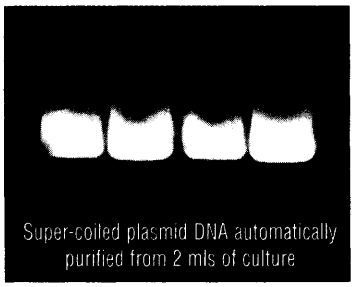

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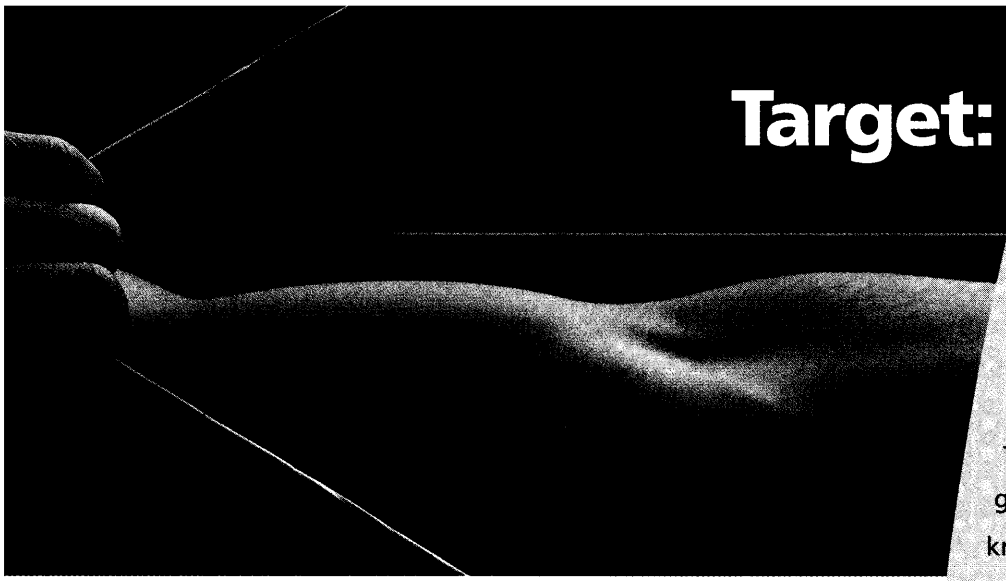

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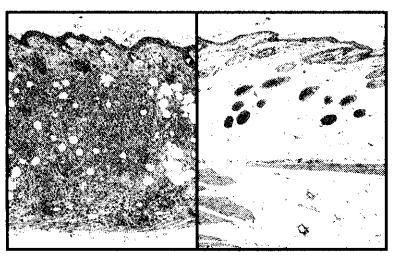
Phenotypic analysis

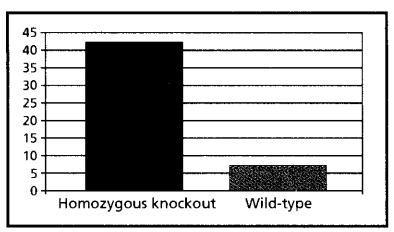
Gene: Phosphatase

Homozygous knockout **Wild-type**



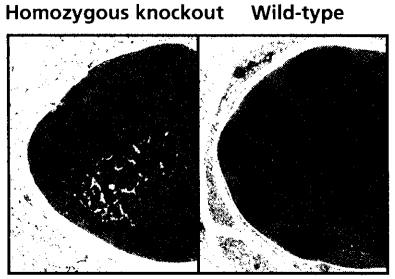
At 11-14 days of age homozygous mice develop flaky skin lesions. This pattern of inflammation is often associated with immune diseases. Examination reveals panniculitis with neutrophilic infiltrates and areas of overlying ulceration.

Differential cell count — % neutrophils



The differential cell count reveals an increased percentage of neutrophils among homozygous mice.

Homozygous knockout **Wild-type**



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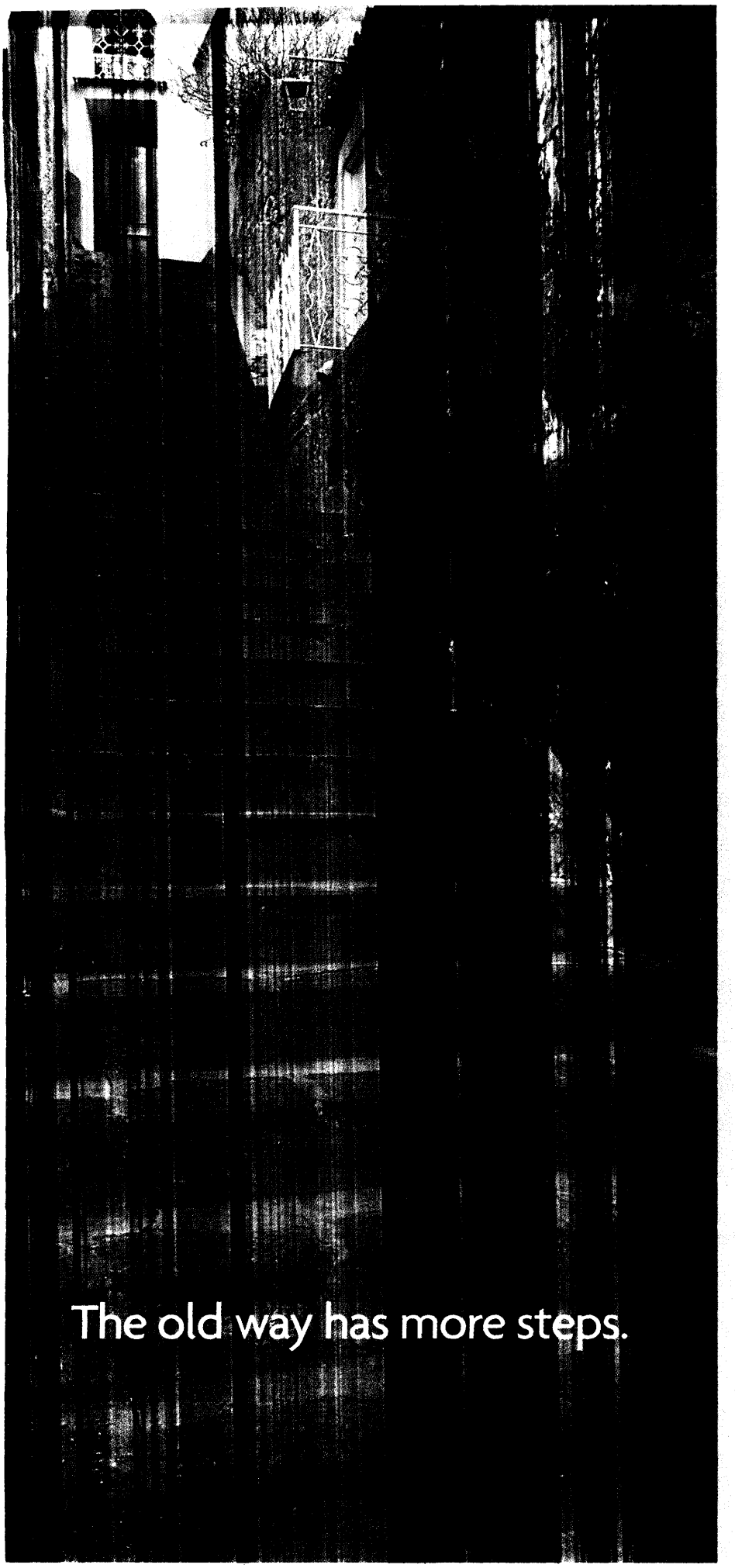

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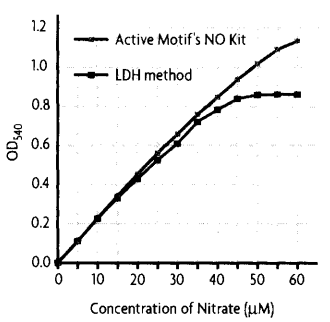

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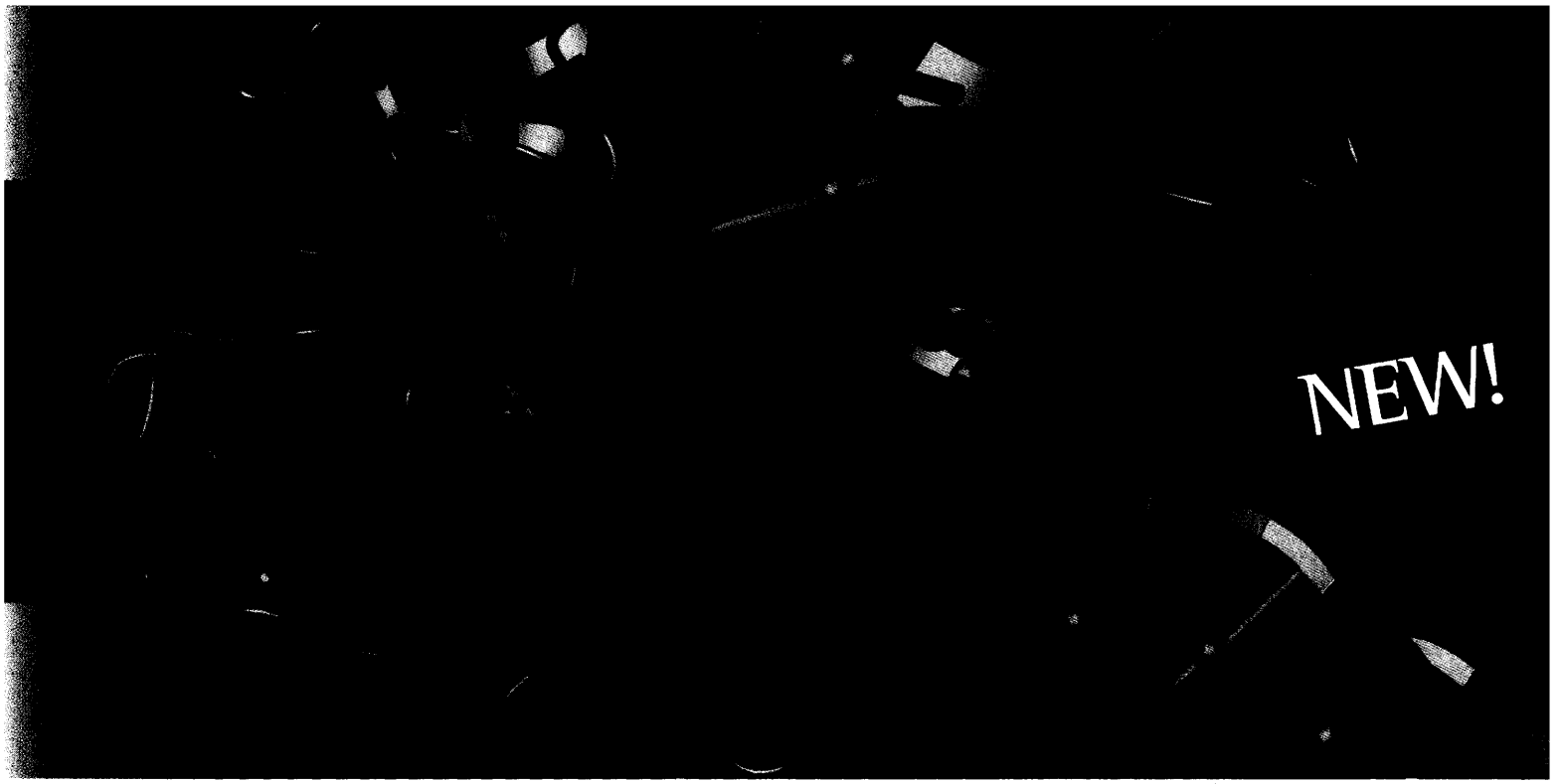

Picture: Model of a Taq DNA Polymerase with a DNA strand.
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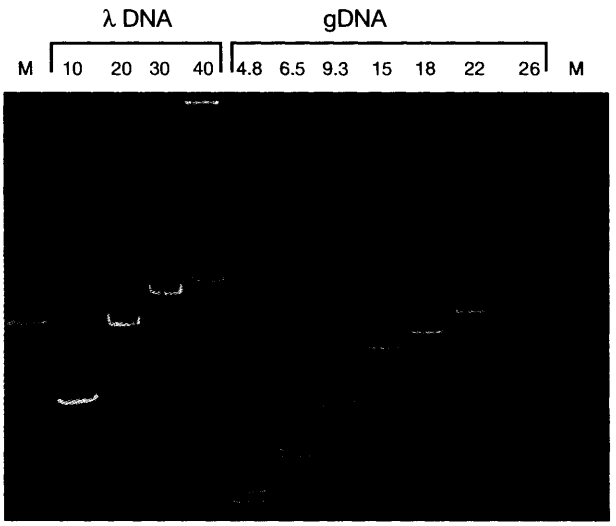

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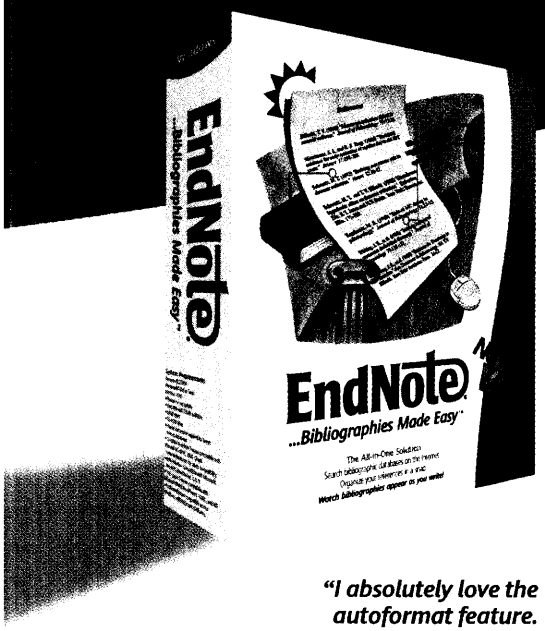

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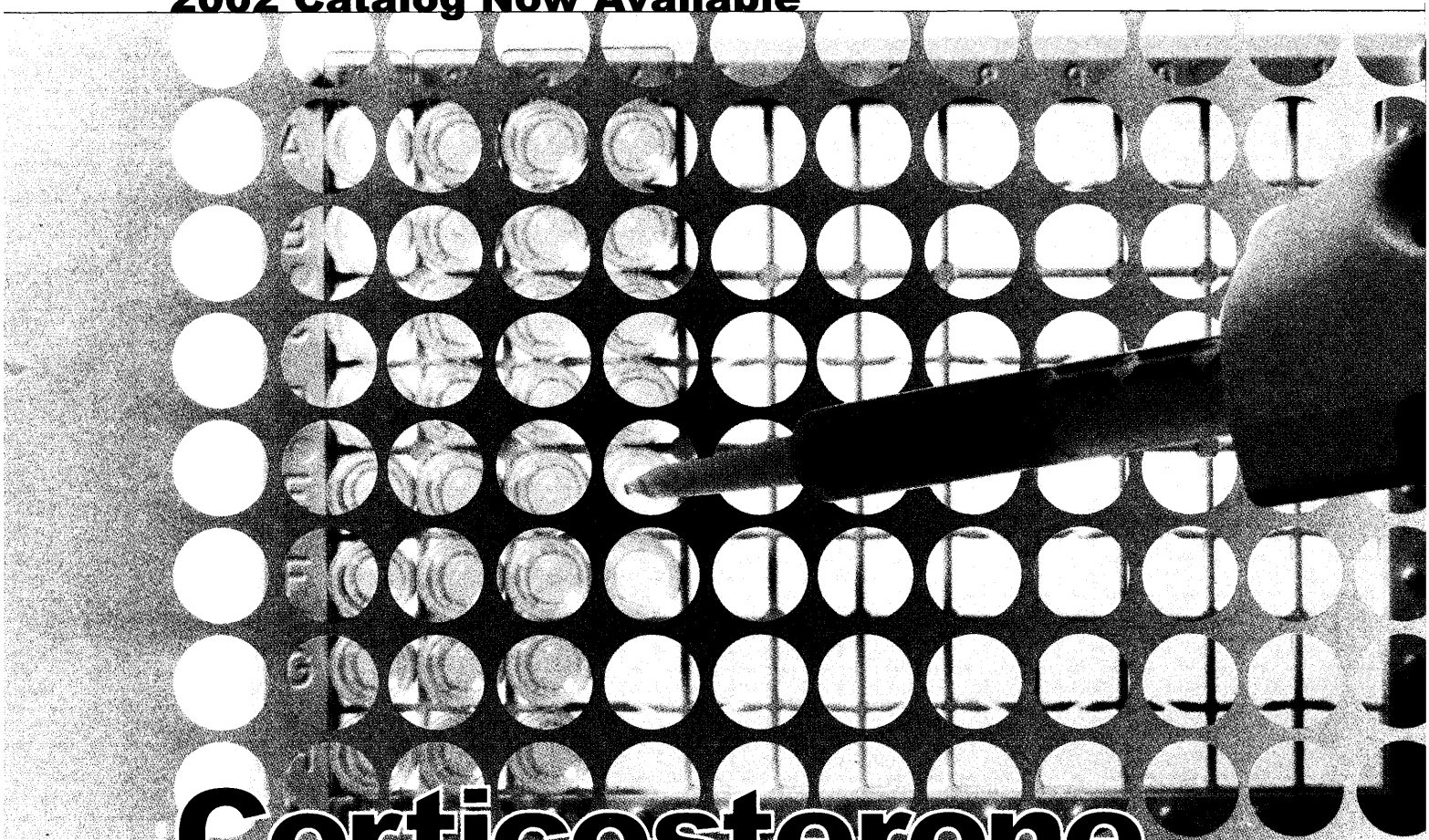

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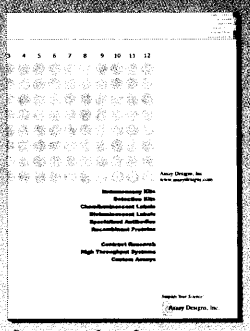

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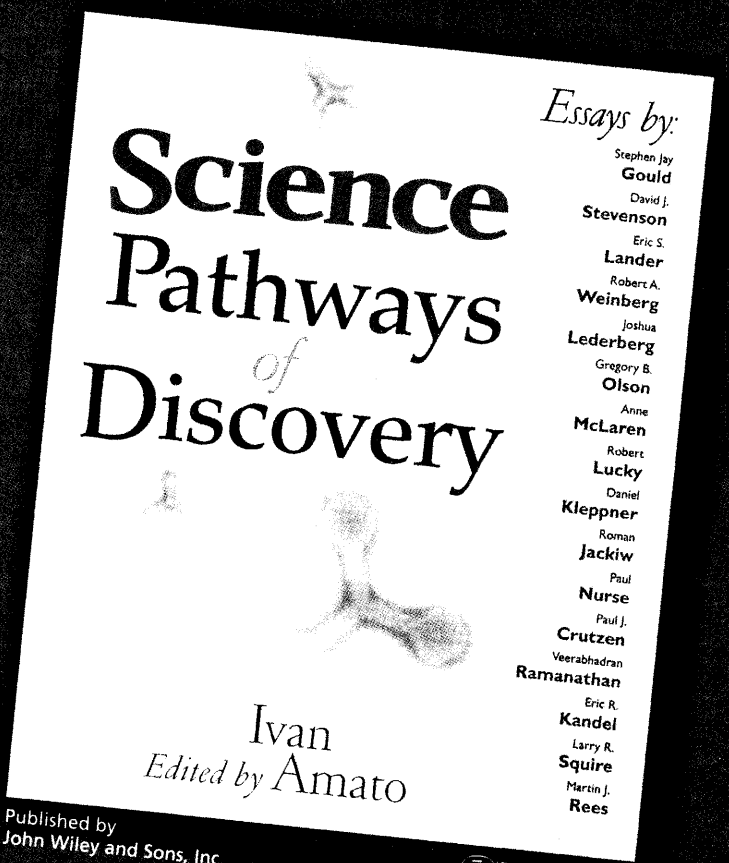

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REGISTER NOW by completing and returning the enclosed form. For further information, contact: Directorate for Science and Policy Programs, AAAS, 1200 New York Ave, NW, Washington, DC 20005 ▪ *Fax:* 202-289-4950 ▪ *E-mail:* slita@aaas.org ▪ *Phone:* 202-326-6600 (for information). A more detailed version of the Colloquium program can be found on the AAAS homepage on the World Wide Web: **www.aaas.org/spp/colloquium**. Online registration is also available at that site.

PROGRAM OVERVIEW

THURSDAY, APRIL 11

(Registration opens 8:00am; program starts at 9:00am.)

KEYNOTE

John H. Marburger, III, Director, White House Office of Science and Technology Policy (confirmed)

BUDGETARY AND POLICY CONTEXT FOR R&D IN FY 2002 (Plenary Symposium)

- The 107th Congress and Implications for S&T Issues
- AAAS Overview of Federal Budget Proposals for R&D in FY 2003
- Where Science and Technology Fit in the National Agenda: Past, Present, Future
- National Priorities for S&T: A View from the Industrial R&D Community

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Gary Hart, co-chair, U.S. Commission on National Security/21st Century (invited)

CONCURRENT SYMPOSIA

- **Technological Challenges to Governance**
  Proliferation of technological innovations • Impacts on society, the economy, and governance • How can governance systems cope? • Making governance functions more responsive and flexible
- **The Regulatory Environment for Science: Conflict-of-Interest Issues**
  What's driving the push for conflict-of-interest regulations in science? • Who should be covered? • Under what circumstances? • Balancing public responsibility with scientific/technological freedom
- **Rethinking the U.S. S&T Policy System: Can It Be More Responsive While Maintaining Excellence?**
  Strengths and weaknesses of the U.S. system for S&T policy • Post-9/11 reassessments • Proposals for "reform" • Is the U.S. system, despite its weaknesses, better than the alternatives?

POLICY ROUNDTABLES WITH AGENCY OFFICIALS (Concurrent small group sessions)

DOD • NIH • NSF • DOE

THE WILLIAM D. CAREY LECTURE (public invited)

(Speaker to be announced)

RECEPTION

FRIDAY, APRIL 12

BREAKFAST AND ADDRESS

Senator Pat Roberts (KS) (invited)

SCIENCE AND TECHNOLOGY'S ROLES IN THE WAR ON TERRORISM AND HOMELAND DEFENSE (Plenary Session)

Bioterrorism and the adequacy of public health systems • Cyberterrorism and how to deal with it • Technologies for surveillance and identification • S&T needs of the intelligence community • Assistance to developing nations • Social-behavioral science contributions

LUNCHEON AND ADDRESS

Sean O'Keefe, Administrator-Designate, NASA (confirmed)

FORBIDDEN SCIENCE: SHOULD SOME RESEARCH BE OUTLAWED? (Plenary Session)

Human reproductive cloning • Race and IQ • Genetically engineered bio-weapons • What have we learned from the past?

(Adjournment at 3:30 p.m.)

Details and updated program information may be obtained by visiting the Colloquium Website, www.aaas.org/spp/colloquium

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Cancellations must be made by March 21, 2002.

Please Note

- Refund requests for registration fees and meal tickets must be submitted in writing (to the address or fax number above) by March 21, 2002, and will be processed after the Colloquium. **No refunds will be made for cancellations received after March 21, 2002.**
- After March 21, register in person at the Omni Shoreham Hotel (Connecticut Ave. and Calvert St., NW) beginning at 8:00AM, April 11. On-site registration fees are $15 higher than advance registration fees.
- Publications: All registrants receive *AAAS Report XXVII: Research and Development, FY 2003*; the *2003 AAAS Science and Technology Policy Yearbook*, and *Congressional Action on R&D in the FY 2003 Budget* in the fall. Please fill in your full mailing address above to ensure delivery of these publications to you.

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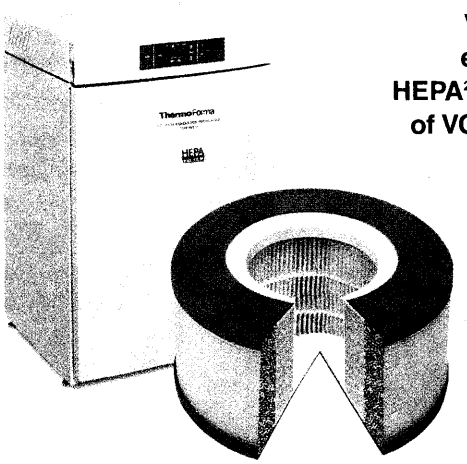

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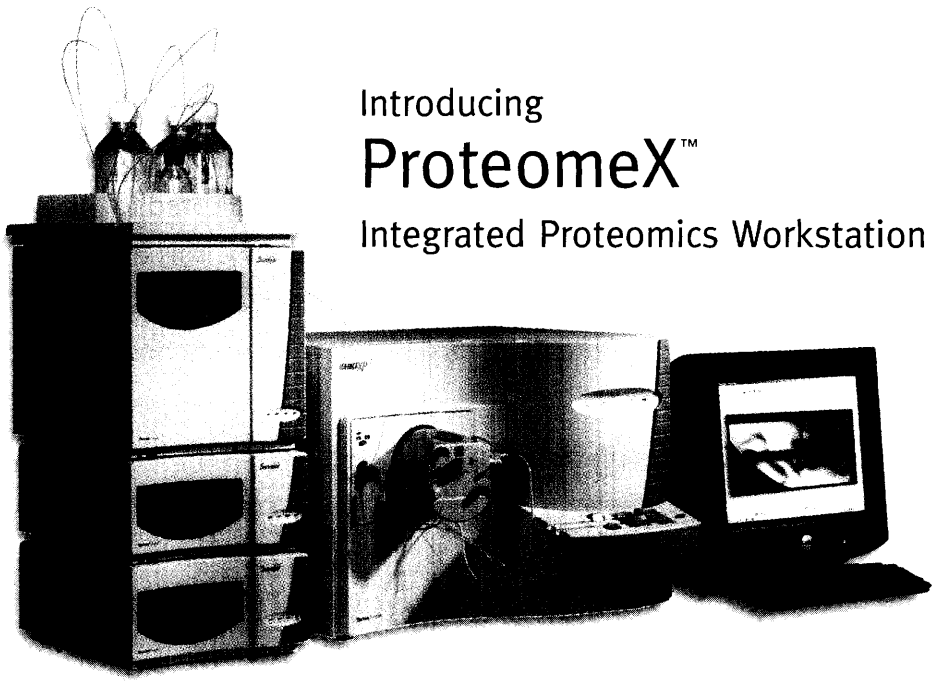

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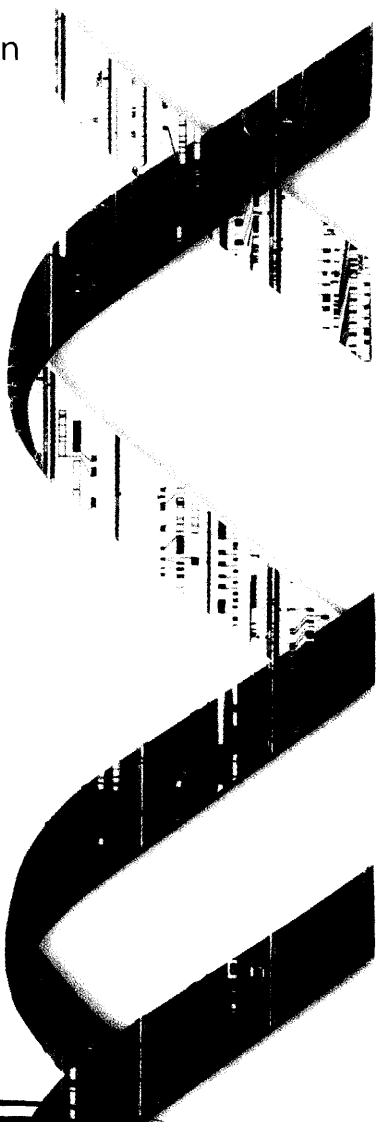

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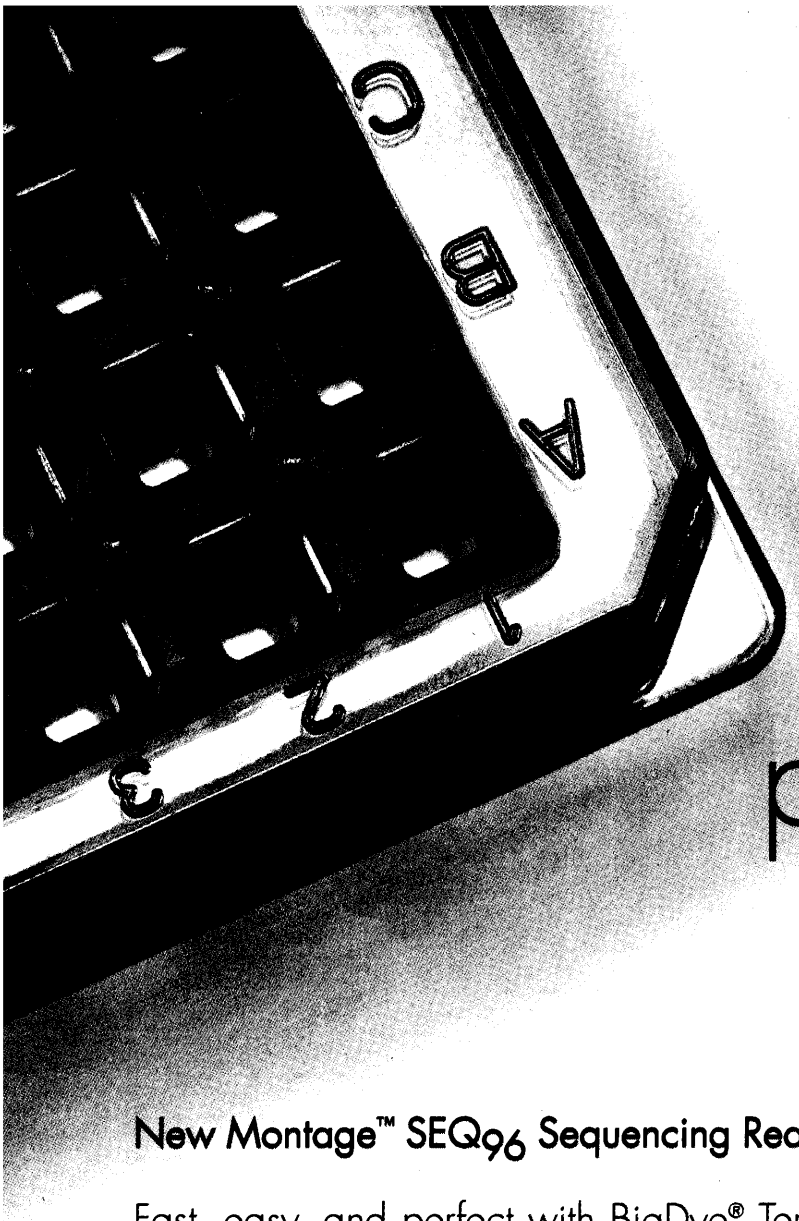

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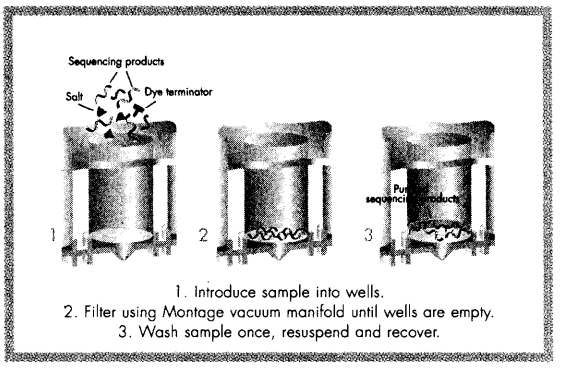

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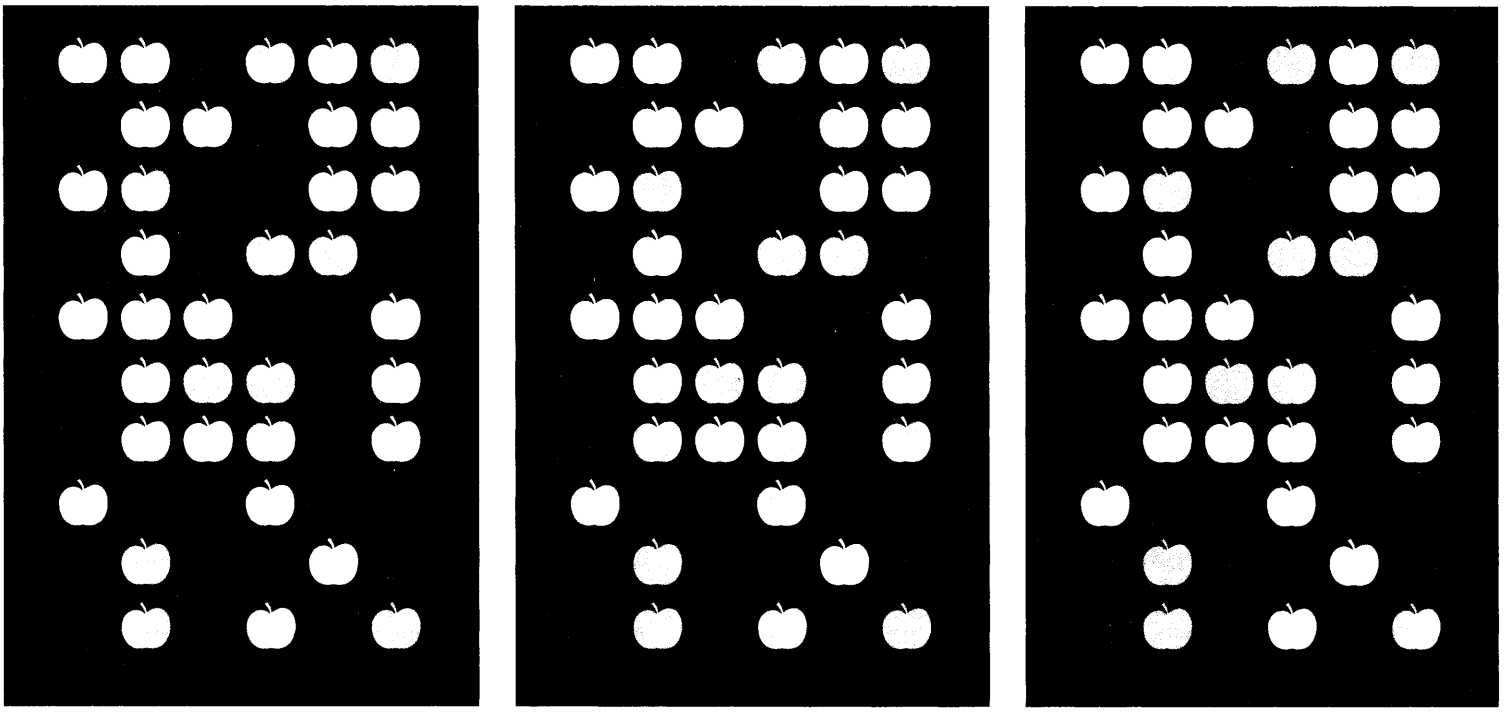

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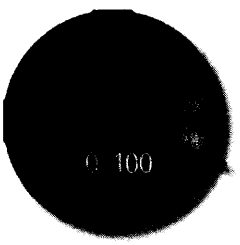

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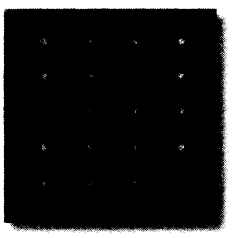

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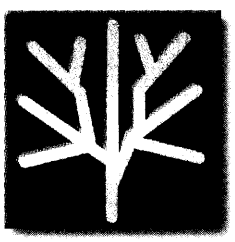

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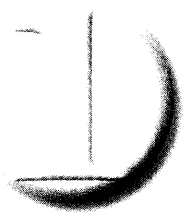

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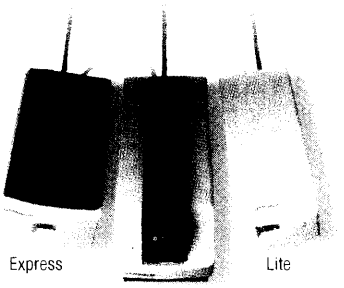

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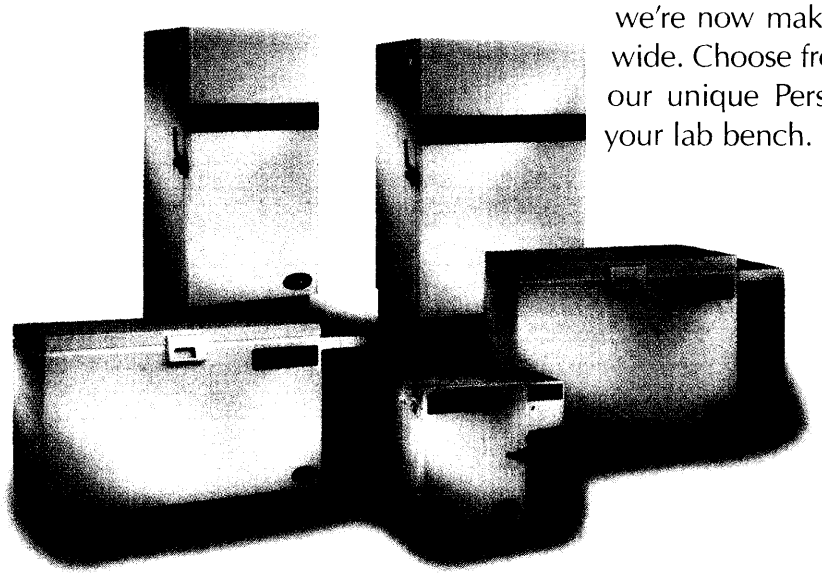

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