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Issues in
Public Health
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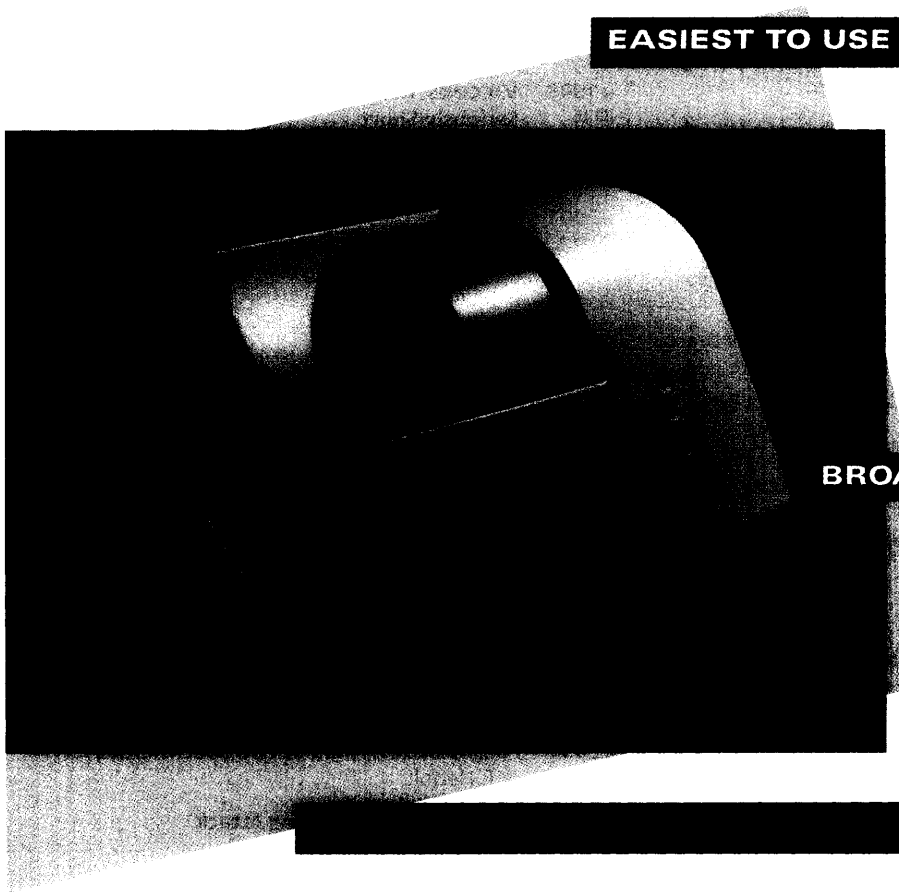

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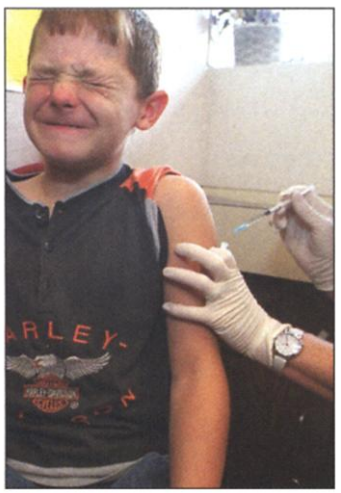
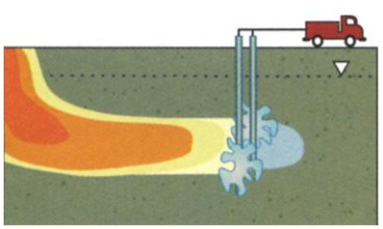
NEWS

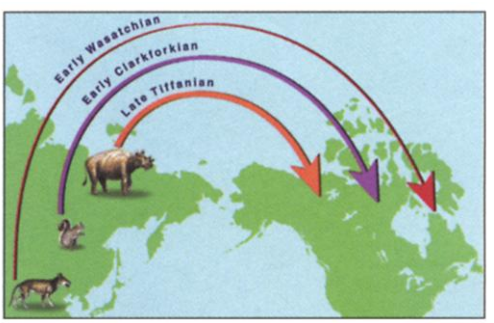


1998
Booster shot needed

SCIENCE'S COMPASS



2024
Tracking groundwater pollution

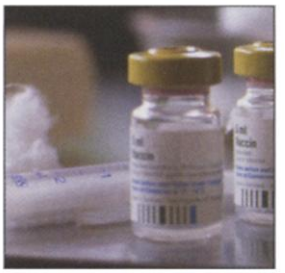


2028
On the dispersal of modern mammals

RESEARCH

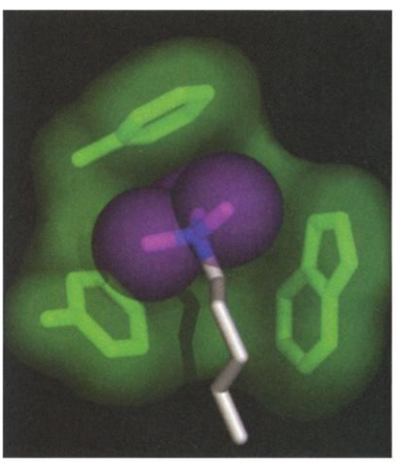
ISSUES IN PUBLIC HEALTH

See also News on pp. 1998, 2000, and 2001.



COVER 2035

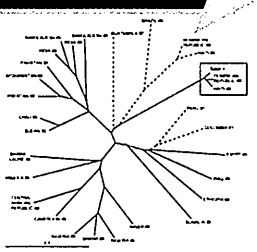
Vaccination drugs on a hospital tray, for use in a vaccination program run from Bujumbura Health Clinic, Burundi. The challenge of controlling the world's infectious diseases is as difficult today as it has ever been, as highlighted in the collection of articles on global public health in this issue. [Photo: Howard Davies/CORBIS]



2080

A chromodomain cage for a histone tail

New on *Science* Express Vaccine-derived paralytic poliomyelitis



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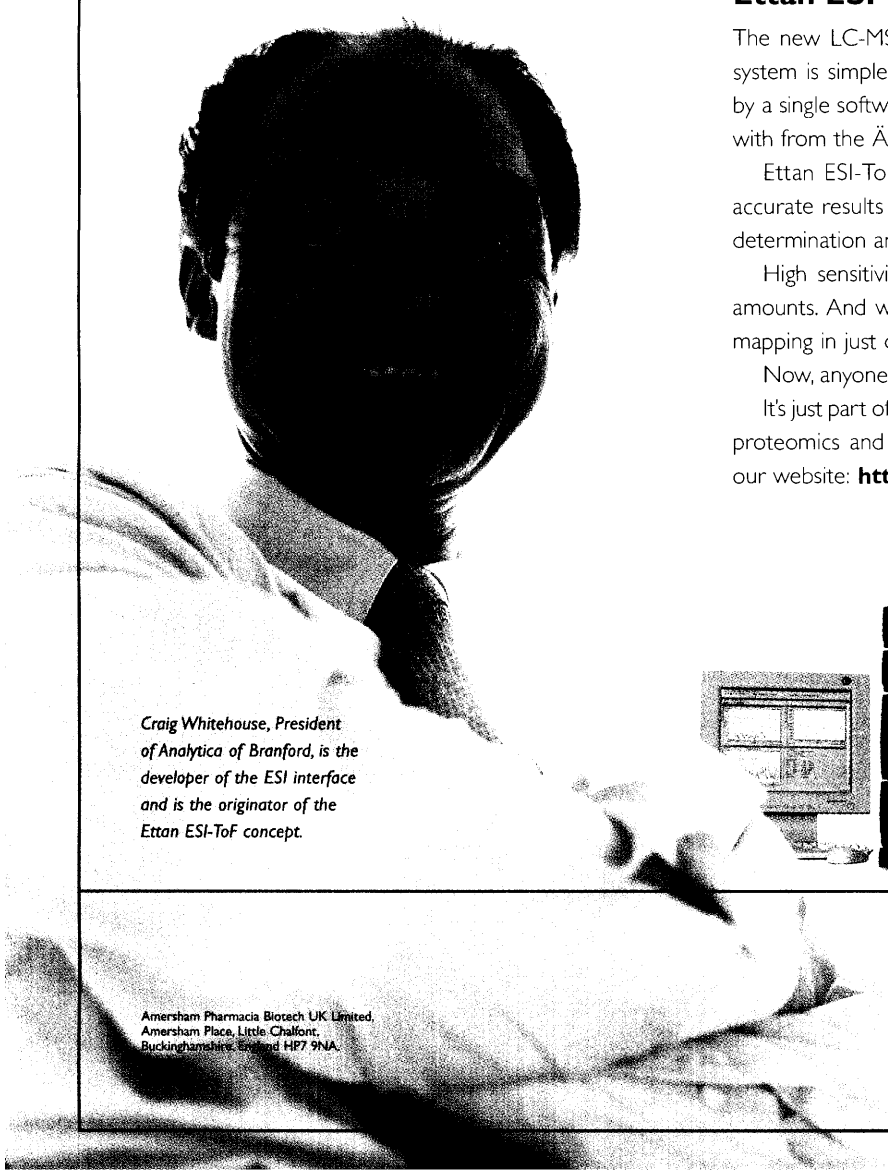
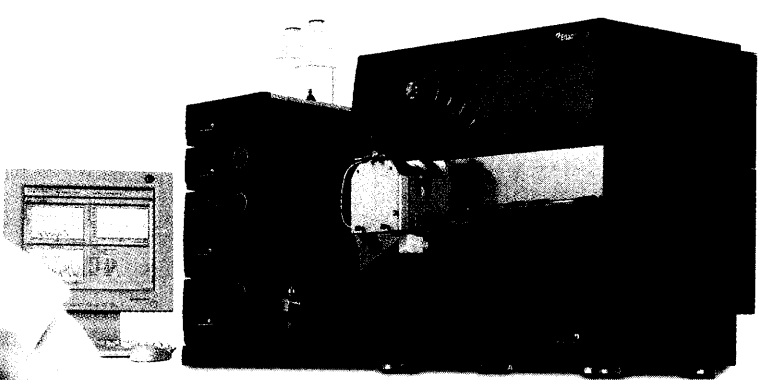


Craig Whitehouse, President of Analytica of Branford, is the developer of the ESI interface and is the originator of the Ettan ESI-ToF concept.



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CONTENT HIGHLIGHTS AS OF 15 MARCH 2002

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SCIENCE EXPRESS www.sciencexpress.org

Solution of a 20-Variable 3-SAT Problem on a DNA Computer R. S. Braich, N. Chelyapov, C. Johnson, P. W. K. Rothemund, L. Adleman

An electrophoretic DNA computer has been used to solve a 20-variable, 24-clause logic problem.

A Thymic Precursor to the NKT Cell Lineage K. Benlagha, T. Kyin, A. Beavis, L. Teyton, A. Bendelac

Natural killer T cells migrating from the thymus undergo major expansion and display unusual profiles of cytokine expression.

Outbreak of Poliomyelitis in Hispaniola Associated with Circulating Type 1 Vaccine-Derived Poliovirus O. Kew *et al.*

Vaccine-derived polio virus used in Hispaniola has recombined with wild enterovirus to restore virulence, resulting in disease and fatalities in children.

TECHNICAL COMMENTS

Superconductivity in a Spin-Ladder Cuprate

Schön *et al.* (Reports, 28 Sep. 2001, p. 2430) reported that, through field-effect doping of molecular beam epitaxy (MBE)–grown thin films, they had induced superconductivity in the nominally insulating spin-ladder compound $[CaCu_2O_3]_4$. In a comment, Ingle *et al.* argue that the work referenced by Schön *et al.* provides "no unequivocal evidence of a spin-ladder arrangement of the Cu and O atoms in the film studied," and conclude that "without such evidence, any claim for superconductivity due to doping of a spin ladder is premature." Schön *et al.* respond that additional work has confirmed a very close fit between the ladder-plane unit cell parameters in their thin films and those in a variety of two-leg ladder cuprates reported elsewhere in the literature. They also review other lines of evidence that lead them to conclude that they "have observed clear evidence of a spin-ladder arrangement."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/295/5562/1967a

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career resources for scientists

US: Science Bytes—The Latest Bits of U.S. Job Market News R. Weibl

Featuring a report from the latest Survey of Earned Doctorates, a Job Market Outlook, and notes on a field in which 49% of tenure-track positions went unfilled in 2000–2001.

US: Take Your Worst Estimate and Double It—Project Management for Postdocs R. Price

Sketching plans on the back of a towel while holding a pipettor is a recipe for experimental disaster.

SINGAPORE: Undergraduate Scholarships Special J. Wong

A compilation of undergrad scholarships for Singapore's 2002–2003 academic year.

UK: Your First "First-Author" Paper, Part Two—Submission and Peer Review P. H. Dee

Writing your paper is only the start of getting it published. Our columnist shares his experience of dealing with editors and referees.

CANADA: Science Bytes—The Latest Bits of Canadian Job Market News L. McKarney

A bundle of Innovation Strategy announcements; human genetics research collaborations; PromoScience awards; postdoc fellowship competitions; and more.

KNOWLEDGE ENVIRONMENTS

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More Than a Hot Flash R. J. Davenport

Sex hormones control a wide range of physiological processes, and replacement therapy might exert similarly broad benefits.

Bulletin Board

View one researcher's list of studies on potential interventions to combat the effects of aging—and register your opinion.

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signal transduction knowledge environment

Perspective: Dancing with Multiple Partners D. G. Woodside

GPCRs and integrins signal through noncompeting partners.

Perspective: Argosomes—Intracellular Transport Vehicles for Intercellular Signals? J. L. Christian

Cells use more than just simple diffusion to create gradients.

Connections Map: Differentiation Pathway in PC12 Cells Pathway Authorities: D. Vaudry, P. J. S. Stork, P. Lazarovici, L. E. Eiden

A specific pathway describing how nerve growth factor and PACAP stimulate differentiation in PC12 cells.

Connections Map: B Cell Antigen Receptor Signaling Pathway Pathway Authorities: S. B. Gauld, J. M. Dal Porto, J. C. Cambier

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THIS WEEK IN Science

edited by Phil Szuromi

High-Pressure Photopolymerization

1,3-Butadiene is highly unsaturated and very reactive. It readily dimerizes at ambient conditions, and polymerization produces a mix of cis and trans isomers. Citroni *et al.* (p. 2058) show that in a diamond-anvil cell under high-pressure conditions (above 0.7 gigapascals), the constrained molecular environment limits the reaction outcomes of *trans*-butadiene. Under dark conditions, only the cycloaddition product, vinylcyclohexene forms, and when irradiated with 488-nanometer light, pure *trans*-polybutadiene forms. The authors interpret the polymerization results in terms of an extended lifetime of the S_1 excited state.

2062 Radiation from Asia

The diversity and range of mammals increased greatly after the Paleocene/Eocene boundary (about 55 million years ago), and new groups appeared on continents throughout the Northern Hemisphere. On the basis of primarily phylogenetic analyses, Asia has been suggested as a likely center of origin. Bowen *et al.* (p. 2062; see the Perspective by Beard) now provide paleontologic evidence pointing to an Asian origin for a major mammal family, the Hyaenodontidae, which includes a number of large extinct carnivores, and implying an Asian origin for other major mammal groups, including the primates.

And in Brevia ...

Analysis of the fungi that inhabit the roots of a grass by Vandenkoornhuyse *et al.* (p. 2051) reveal an extraordinary diversity of species, from every major fungal group, as well as yet unidentified species.

Rates for Attaining Fit States

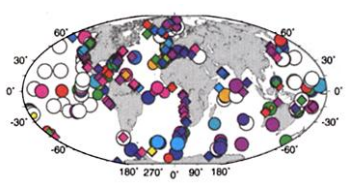
Hexavalent chromium, such as the chromate anion, can be toxic in high doses and resides in many contaminated groundwater systems (as made famous by the movie *Erin Brockovich*). One source has been leakage or waste from large baths or ponds of chromium used to electroplate metals. Reduction to Cr^{3+} reduces its mobility and hazard. Ellis *et al.* (p. 2060; see the Perspective by Blowes) survey the distribution of stable isotopes of chromium in groundwater and the Earth and show that the isotopic ratio in ground water can be used to assess rapidly the rate of ongoing reduction.

Catalytic Metals and Their Supporting Casts

Recently, a transmission electron microscope has been developed that allows high-resolution analysis of catalytic metal nanoparticles dispersed on oxide supports in the presence of reactive gases and at high temperatures. After some further modification, Hansen *et al.* (p. 2053) now achieve 0.14-nanometer resolution, which allows them to study nanoparticles of metals with lower atomic numbers, such as iron, nickel, and copper, with atomic resolution. The authors show that nanoparticle dynamics and their interactions with the supporting material influence the performance of catalytic systems such as the industrial methanol synthesis catalyst.

Life Below the Sea Floor

Live bacterial cells appear to inhabit sediments as far as 1 kilometer beneath the sea surface. These communities may account for as much as one-third of Earth's total biomass, but the biological activity of these cells is extremely low, and the bulk of any metabolic activity always takes place within the uppermost centimeters of the sediment. D'Hondt *et al.* (p. 2067) review the data on these sediments gathered from around the world during the past 15 years of the Ocean Drilling Program and found striking differences between two distinct realms of sediments. Although methanogenesis occurs in both, the methane is destroyed oxidatively when coupled to sulfate reduction. Hence, the open-ocean sediments are rich in sulfate and relatively methane-depleted, whereas the more strongly methanogenic, ocean-margin sediments are relatively sulfate-depleted.



CREDIT: D'HONDT *ET AL.*

Life-Styles and Variability

Why do different animal species vary so greatly in population variability? Sæther *et al.* (p. 1507; see the Perspective by Coulson *et al.*) identify two distinct demographic processes operating in bird populations and report a strong covariation between demographic processes and population variability. Recruitment-driven populations (in which there is a high reproductive rate) were characterized by weak density regulation and a large environmental stochasticity that resulted in high population variability. In survival-restricted populations (in which the reproductive rate is typically low and survival long), strong density regulation at high densities, and small estimates of the environmental variance were found, leading to small fluctuations in population size.

Caging the Histone Code

Chromatin plays an important role in the regulation of gene expression. Covalent modification of the tails of the histone proteins, which make up the nucleosome around which DNA is wrapped, can alter the response of a gene to the transcription machinery. For example, methylation of Lys^9 in the tail of histone H3 results in epigenetic repression of gene expression. The chromodomain-containing protein HP1 binds to methylated Lys^9, but it has not been clear why only a subset of chromodomain-containing proteins interact with chromatin. Jacobs and Khorasanizadeh (p. 2080; see the cover) have determined the structure of the HP1 chromodomain bound to a methylated H3 tail. The methylammonium group is recognized by a hydrophobic cage in HP1, and the H3 tail completes the β-sandwich architecture of the chromodomain.

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CONTINUED ON PAGE 1971

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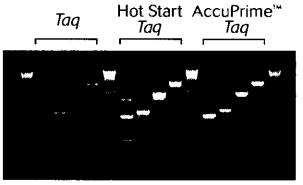

Comparison of PCR specificity with various *Taq* Polymerases.

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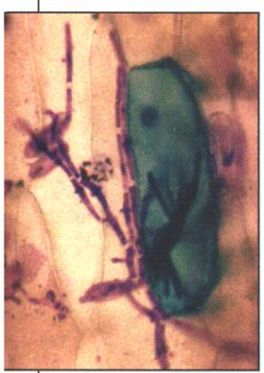
Protein Degradation Maintains Plant Defenses



The innate immune response by which plants defend against certain pathogens includes interactions between a signal from the pathogen and a specific resistance (*R*) gene in the plant. Although there are a variety of *R* genes, and a veritable multitude of pathogens, the plant tends to respond with a limited repertoire of physiological responses. Azevedo *et al.* (p. 2073) and Austin *et al.* (p. 2077) analyze the signaling cascade initiated by activation of disease resistance (see the Perspective by Nishimura and Somerville). Several R proteins trigger responses through the RAR1 protein, which in turn interacts with the SGT1 proteins. These results implicate SGT1 in ubiquitin-targeted protein degradation. The two SGT1 variants in *Arabidopsis* seem to have divergent functions. Thus, at least part of the signaling cascade triggered by response to a pathogen may involve protein degradation.

CREDIT: AZEVEDO *ET AL.*

Cutting and Pasting RNA

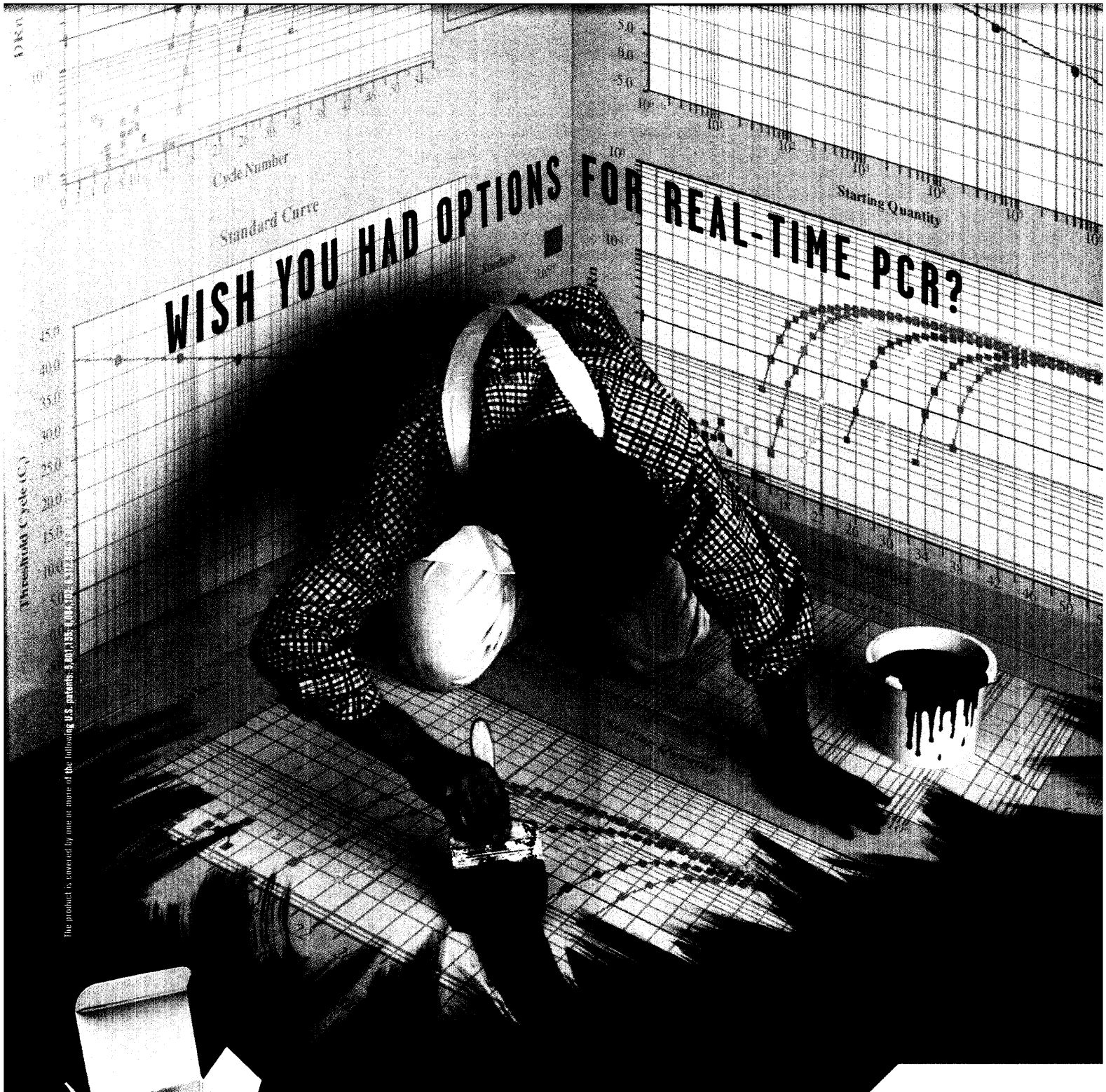
Although macromolecular complexes that decode messenger RNA (mRNA) and synthesize pre-mRNA have been resolved, one of the most enzymatically challenging reactions, the splicing of pre-mRNAs, has been difficult to assess structurally. Fortunately, the group II self-splicing introns follow a catalytic pathway similar to that of pre-mRNA splicing, and these introns display sequence similarities to the RNA components of the macromolecular spliceosome complex. Zhang and Doudna (p. 2084) describe the crystal structure of the catalytic core of the group II intron and find that the critical nucleophilic adenosine is part of an unpaired, two-nucleotide bulge, extruded from the RNA double-helical scaffold.

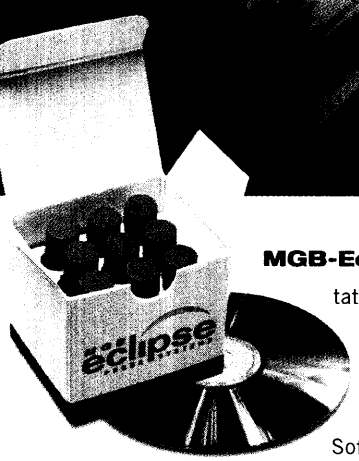
Little Fleas Have Lesser Fleas

Bordetella spp. cause significant human respiratory disease, and to accommodate the changing environments they encounter, they cycle through a series of phenotypic changes, including changing the nature of the surface molecules that also act as receptors for the tails of bacteriophages that prey on these bacteria. Liu *et al.* (p. 2091; see the Perspective by Hatfull) have discovered a family of phage that have a marked tropism for a phase in the *Bordetella* life cycle when several virulence and colonization factors are produced; here, pertactin is the primary virus receptor. However, they also found phage that have tropism for a motile phase of the bacterium's life cycle, as well as various intermediate forms. Thus, the phage can generate variants that can infect the bacterium at different stages in its life cycle by means of a reverse transcriptase–driven mechanism that causes mutations in a tail assembly protein.

Natural Killer Cells Overcome Rejection

Reconstitution of the hematopoietic system by bone marrow (BM) transplantation operates on a knife edge. Engraftment can be improved by allowing some degree of mismatch between the tissue antigens of the donor and recipient. In diseases such as leukemia, engraftment can also provide a powerful means for helping to destroy host-derived cells. However, the greater the mismatch, the more vigorously residual T cells in the donor BM will react against the recipient tissues, leading to graft-versus-host disease (GVHD). Two reports address how natural killer (NK) cells help prevent rejection (see the Perspective by Kärre). Ruggeri *et al.* (p. 2097) observed that for NK cells, a greater level of NK cell reactivity against host antigens correlated with a higher incidence of successful transplantation. In mice, preconditioning with purified host-reactive NK cells removed the need for usual preablation of recipient bone marrow by irradiation, and these animals did not develop T cell–mediated GVHD seen in control mice. Host-reactive NK cells may ablate antigen-presenting cells in the host and, in so doing, prevent them from inducing antihost T cells. Activation of NK cells can also be prevented by ligands that bind inhibitory receptors on the NK cell surface. Wang *et al.* (p. 2094) observed that in mice lacking the phosphatase SH2-containing inositol phosphatase (SHIP), the repertoire of inhibitory NK receptors was skewed in favor of select receptors that could recognize foreign as well as self ligands. When transplanted with bone marrow, these mice failed to reject bone marrow from a mismatched donor. Incidence of GVHD was also absent in these mice, suggesting a possible role for host-derived NK cells in GVHD.





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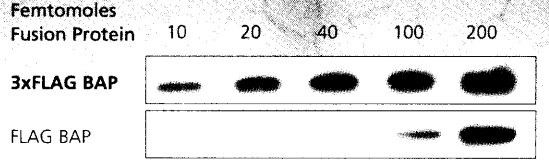

Western blot of purified 3xFLAG bacterial alkaline phosphatase and FLAG bacterial alkaline phosphatase transferred on to nitrocellulose membrane. Detection was performed with ANTI-FLAG M2 monoclonal antibody as primary, anti-mouse-HRP secondary antibody, and ECL™ chemiluminescent substrate.

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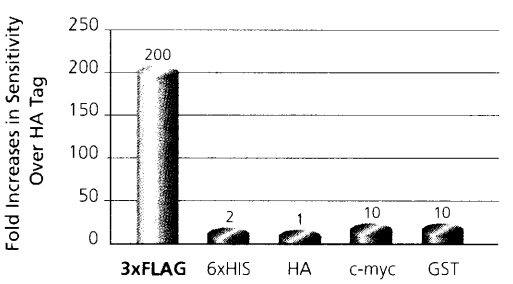

C-terminal fusions of GST and the tags listed below were prepared and analyzed on Western Blots. All proteins were detected using the appropriate tag antibodies, anti-mouse HRP and ECL.

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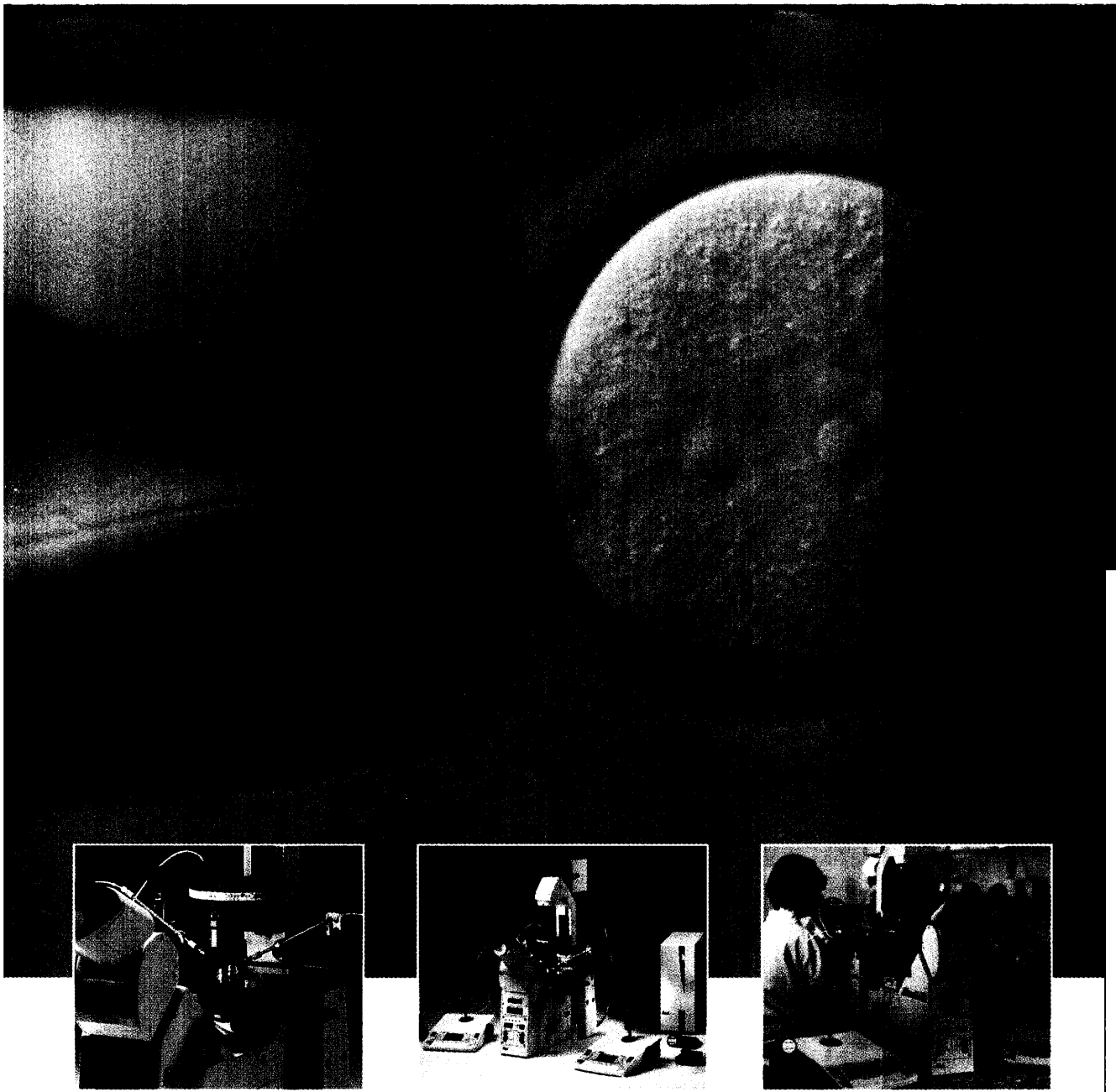

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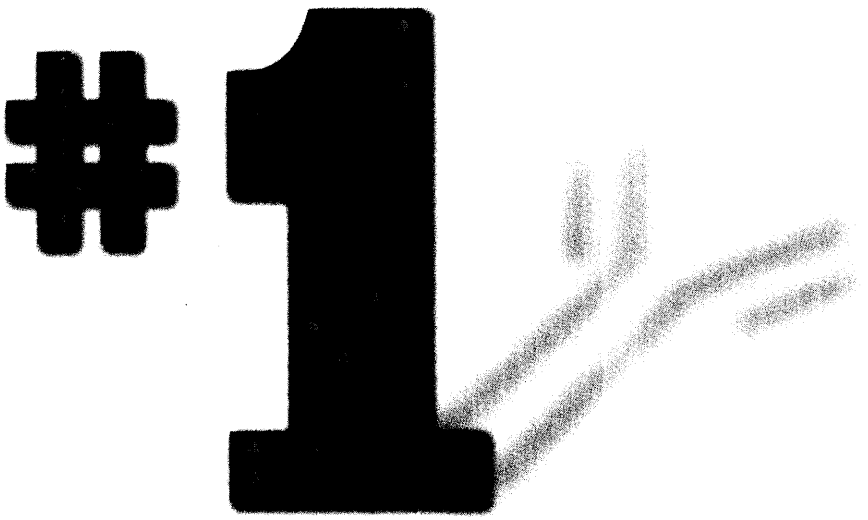

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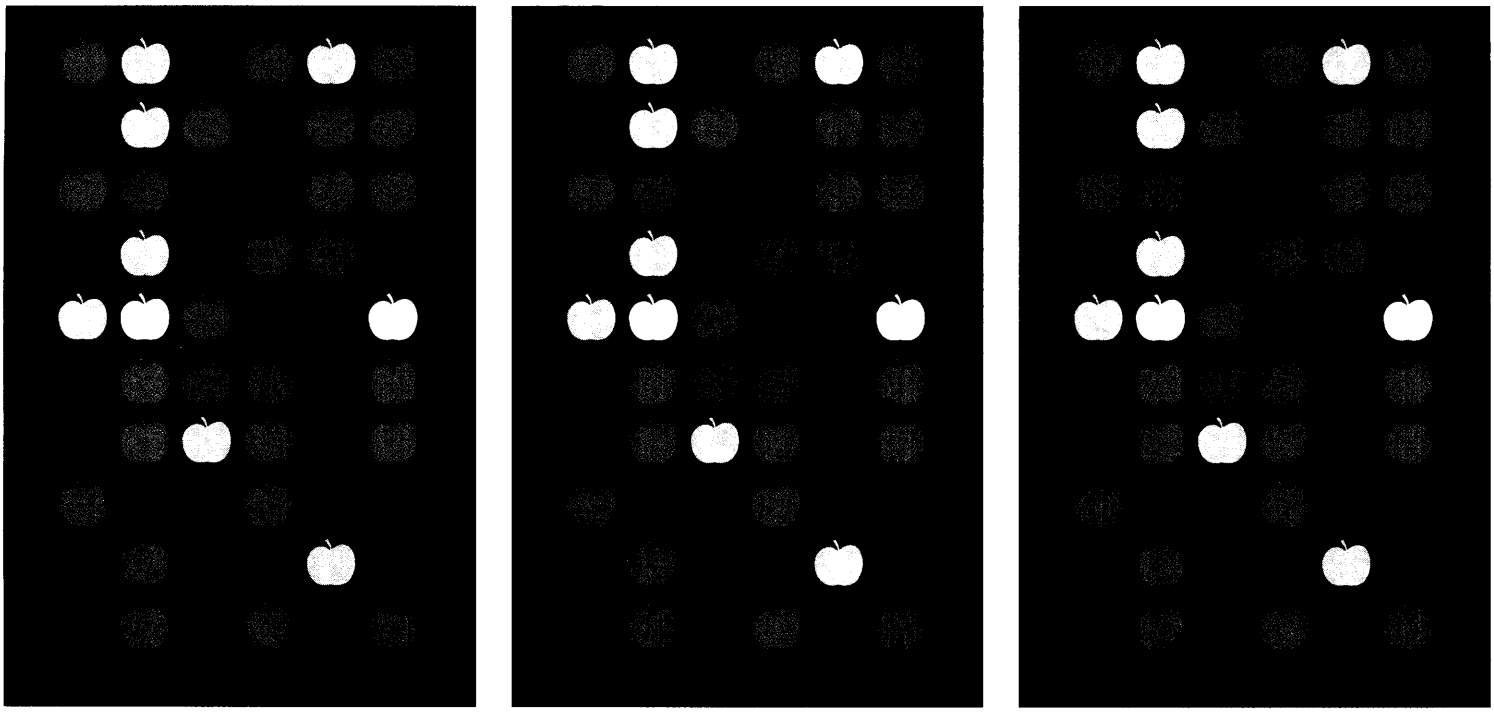

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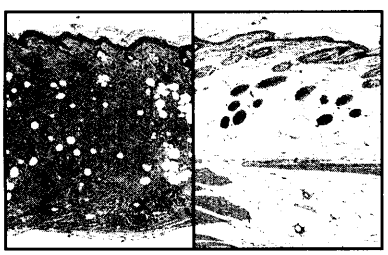
Phenotypic analysis

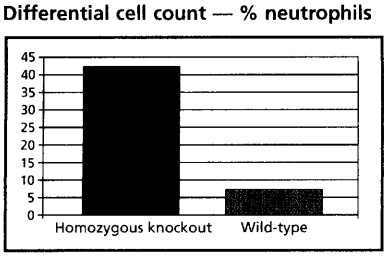
Gene: Phosphatase

Homozygous knockout **Wild-type**



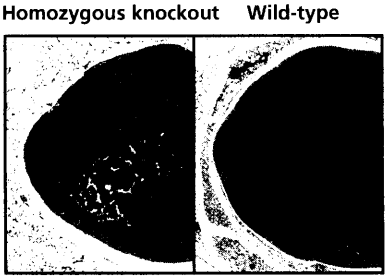
At 11-14 days of age homozygous mice develop flaky skin lesions. This pattern of inflammation is often associated with immune diseases. Examination reveals panniculitis with neutrophilic infiltrates and areas of overlying ulceration.

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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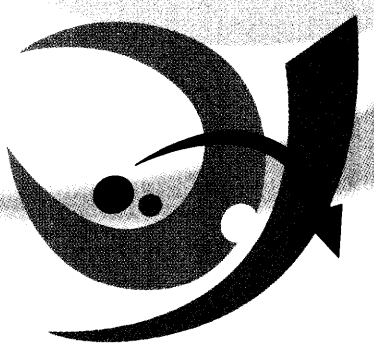

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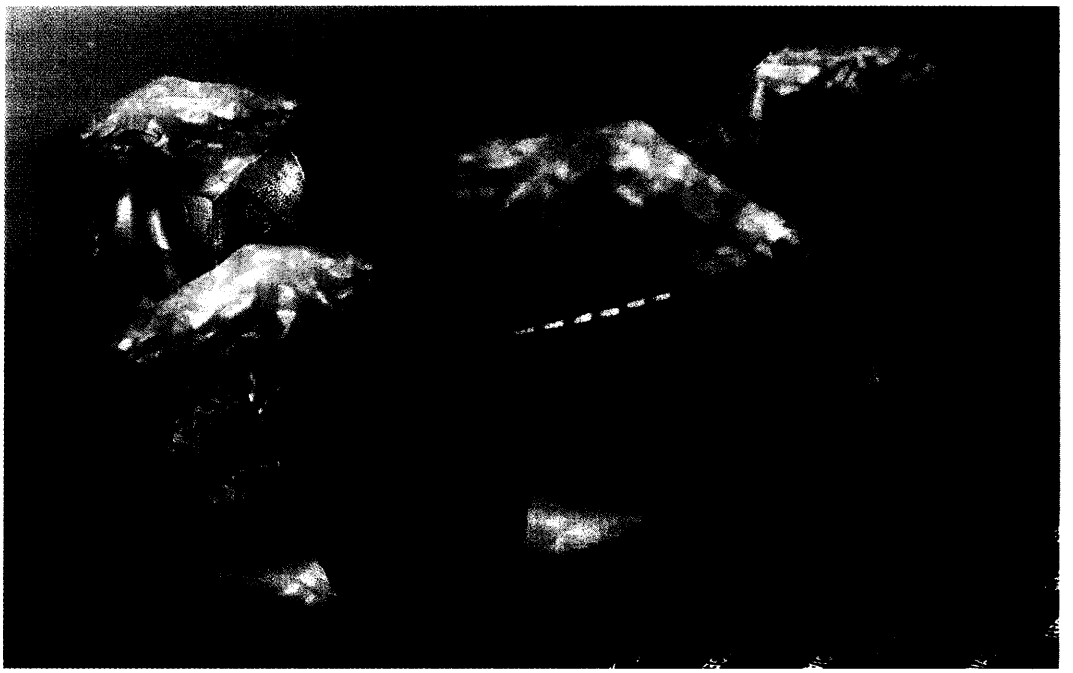

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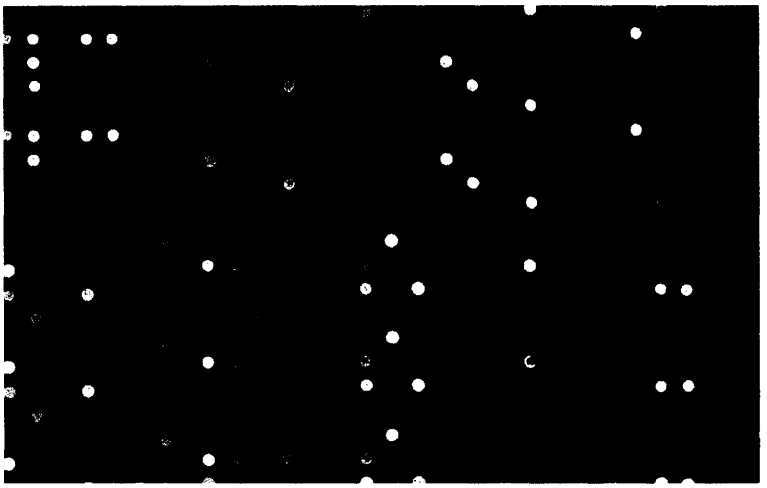

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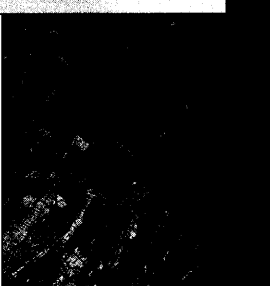

Professor Robert A. Holton, organic chemist.

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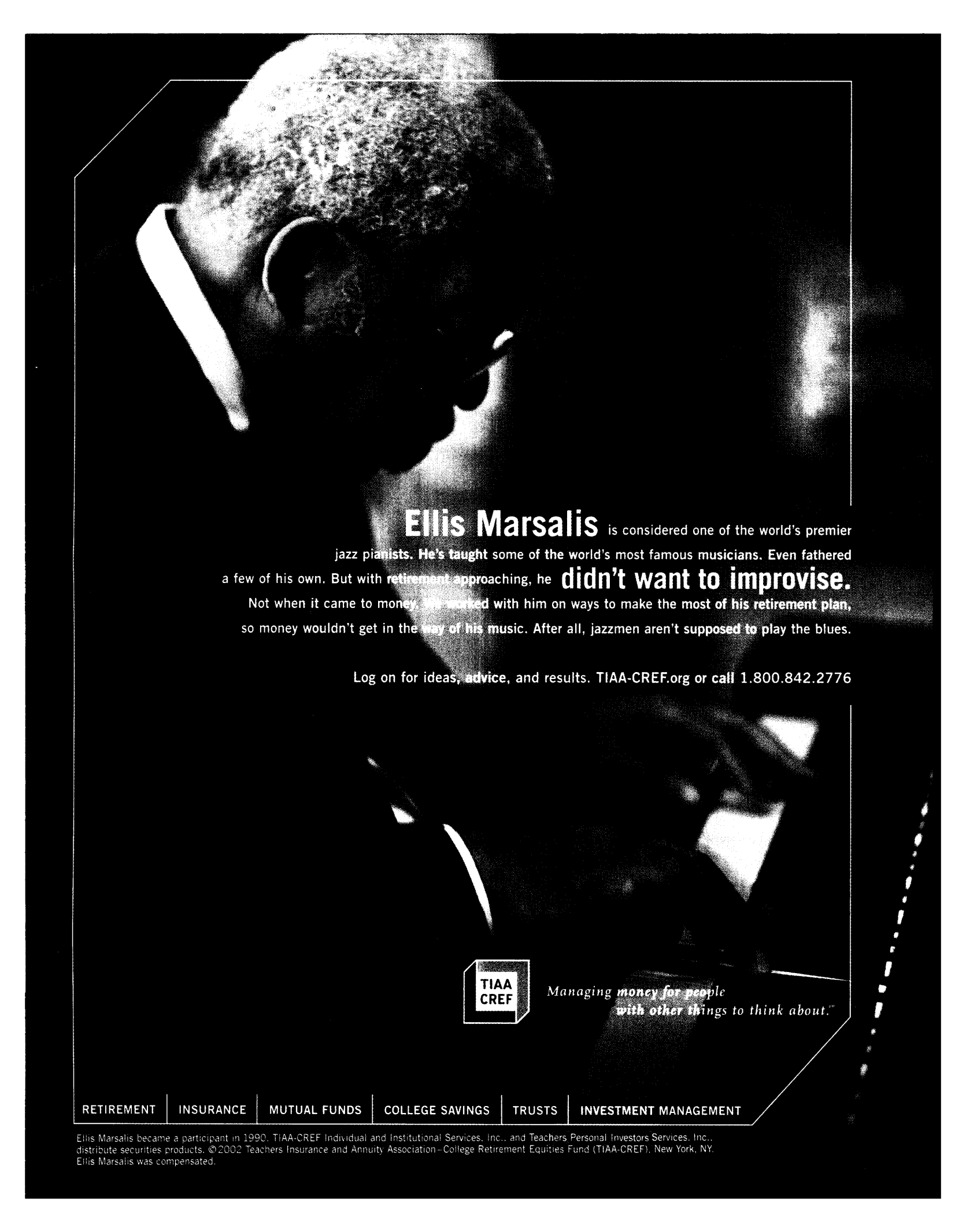
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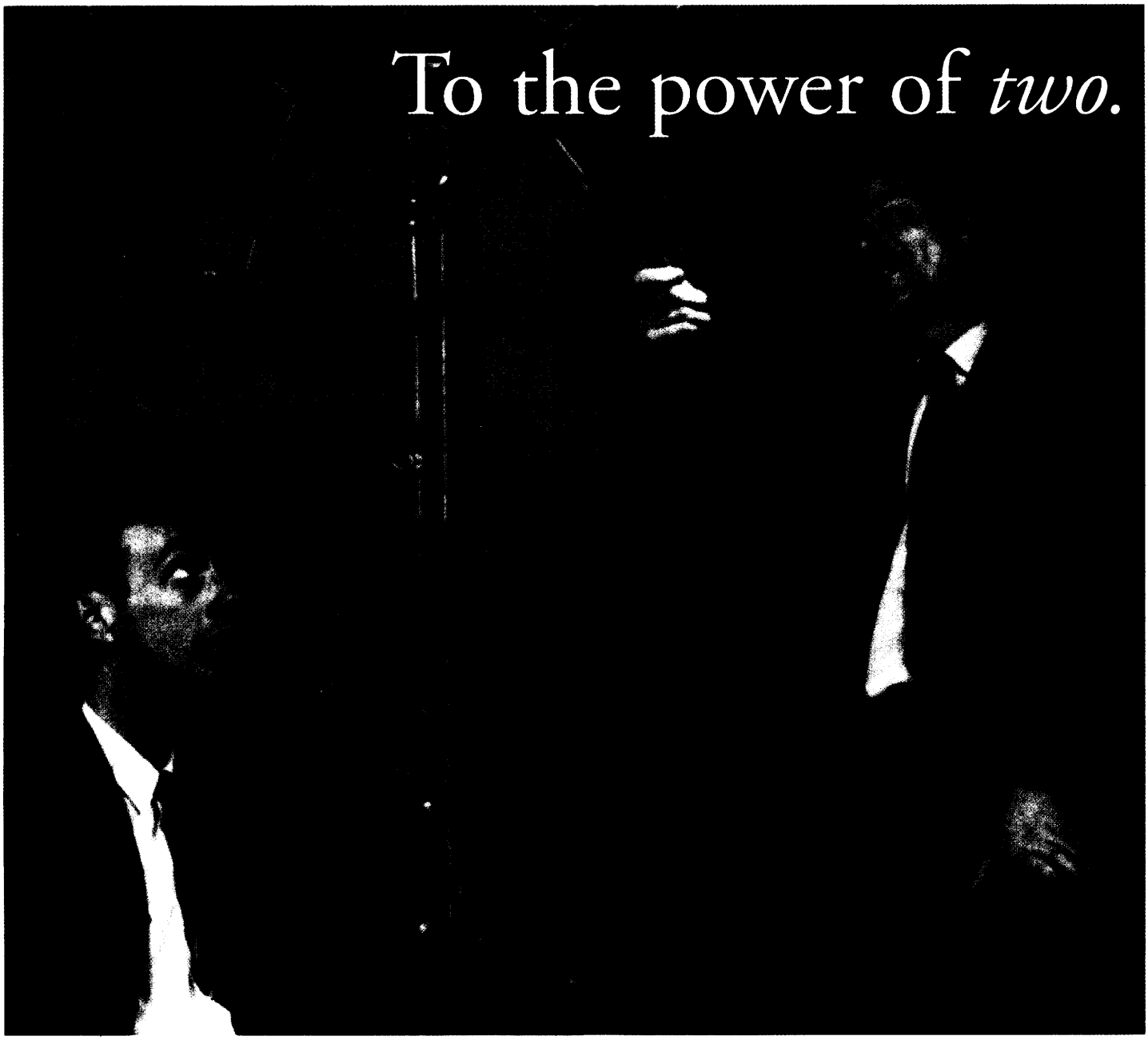

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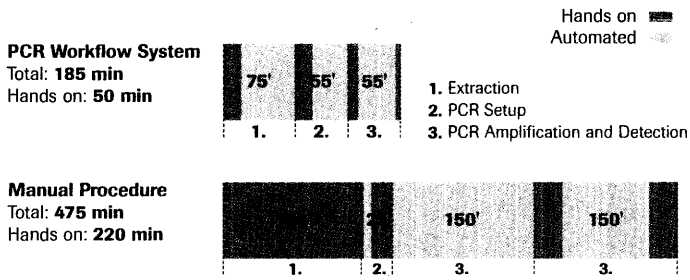

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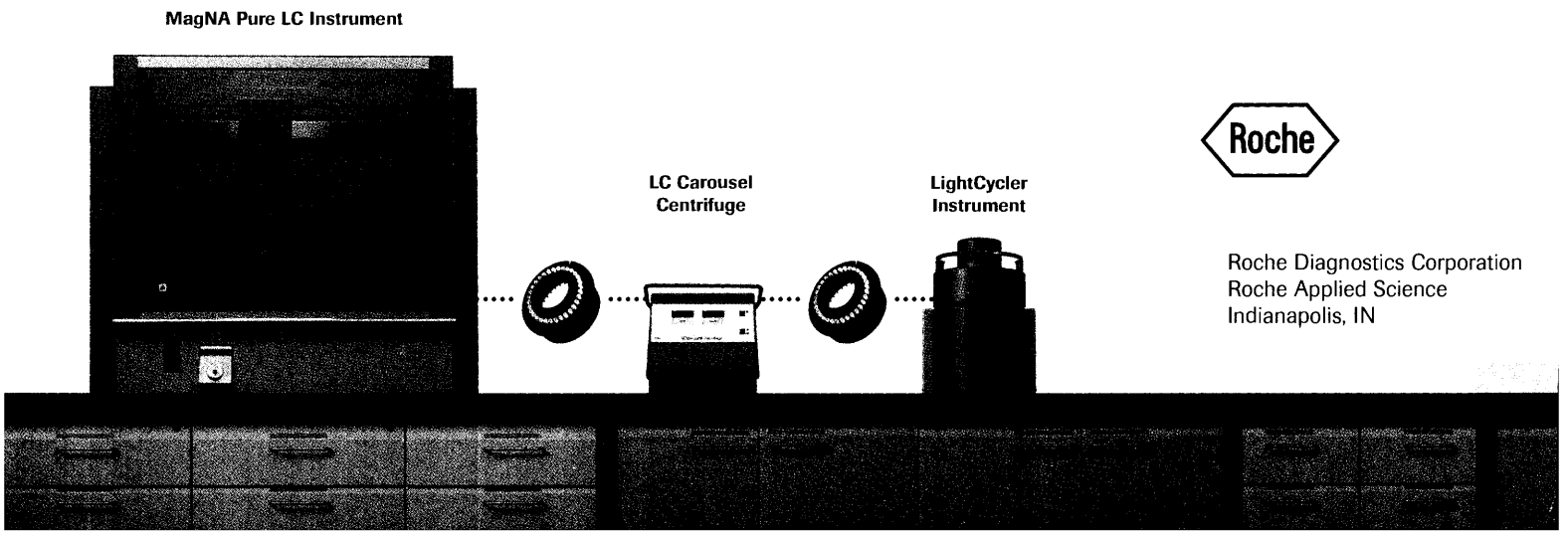

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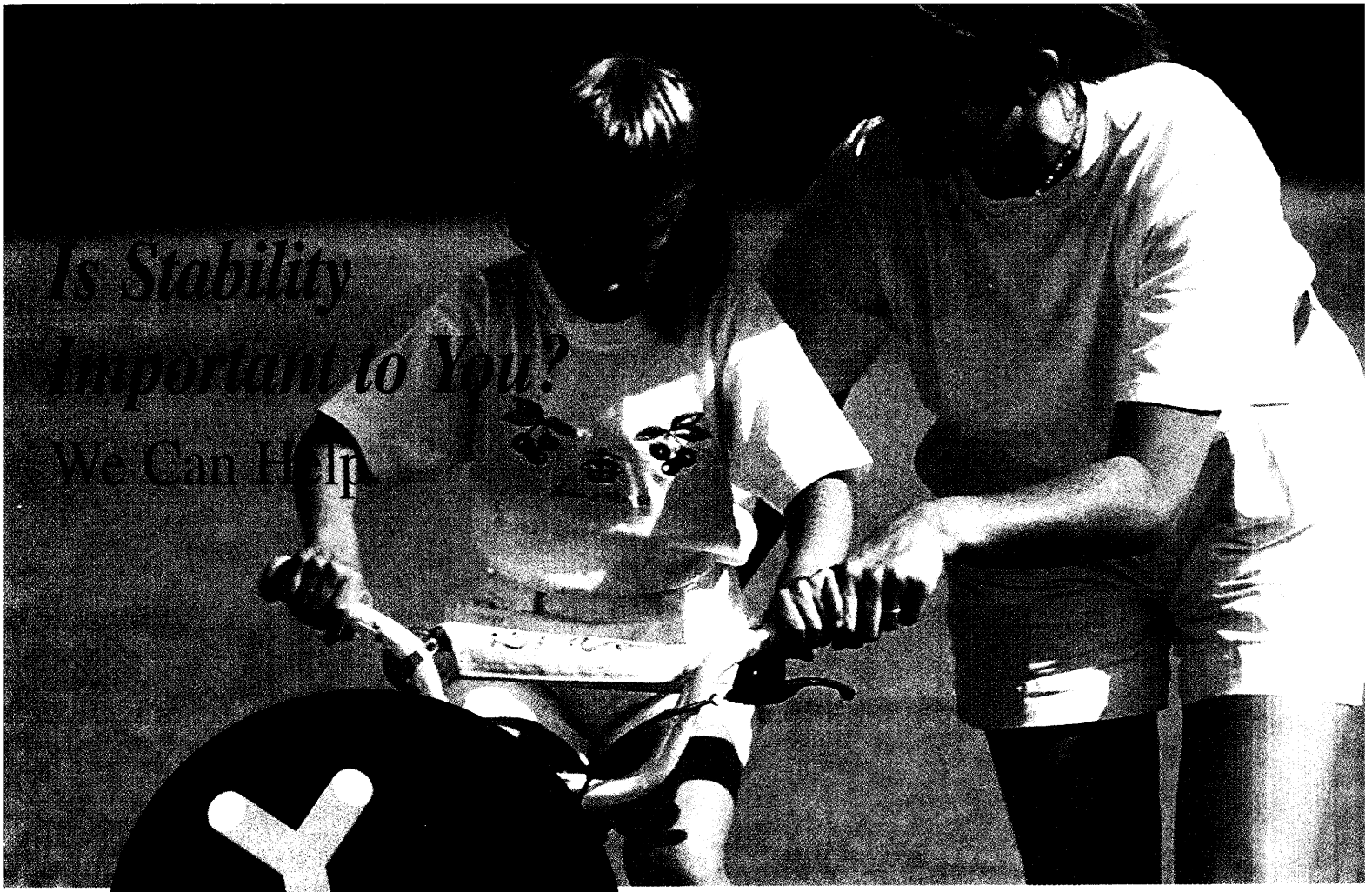

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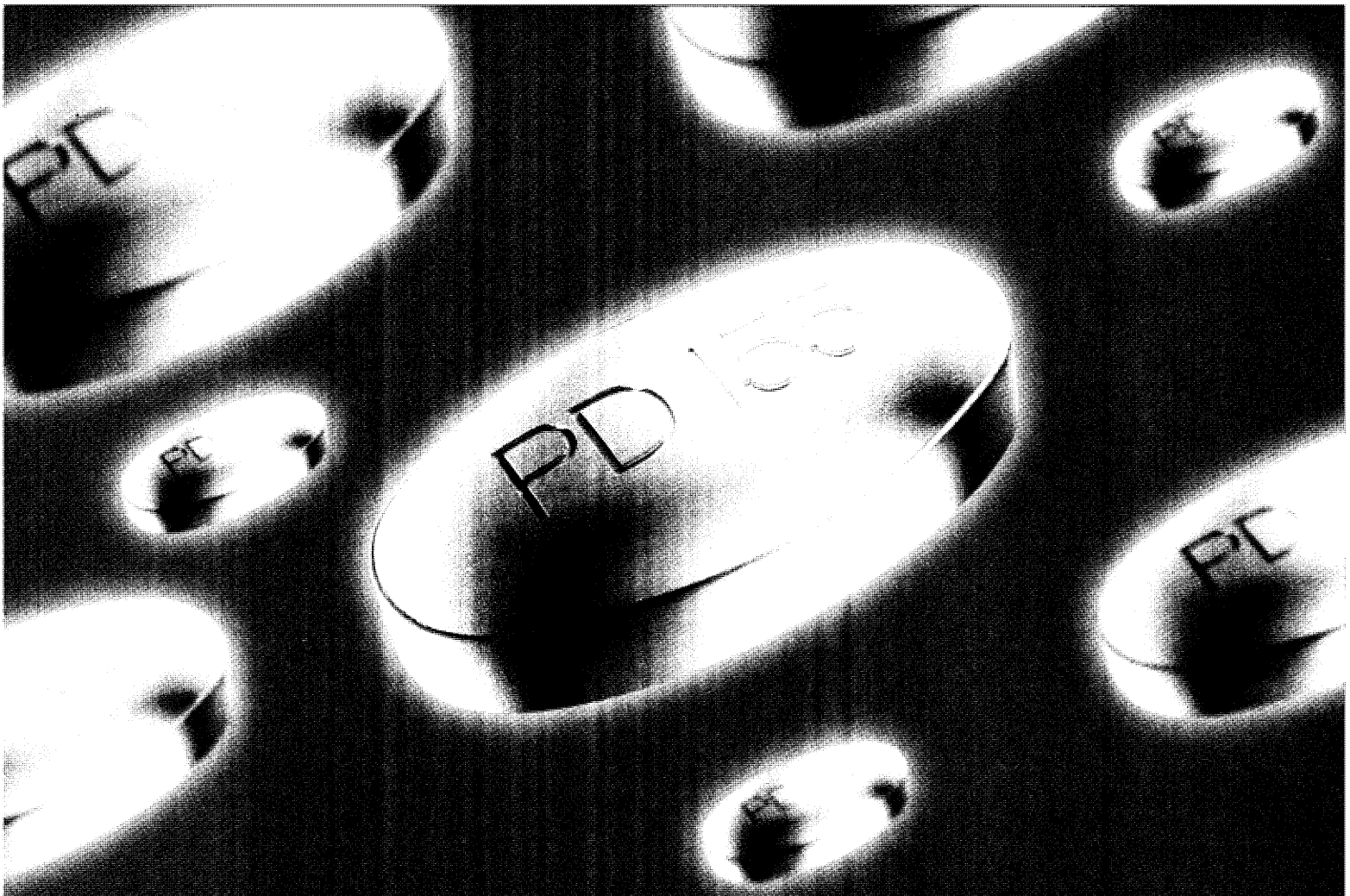

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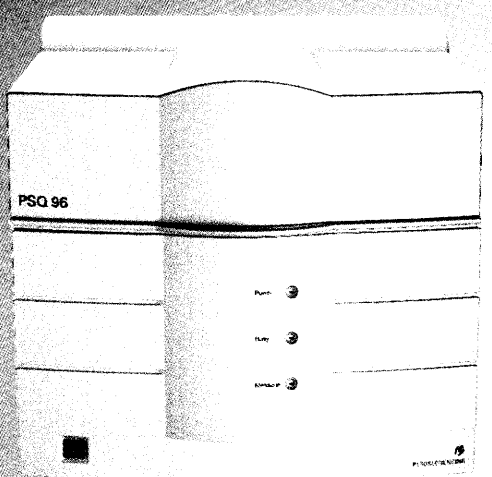

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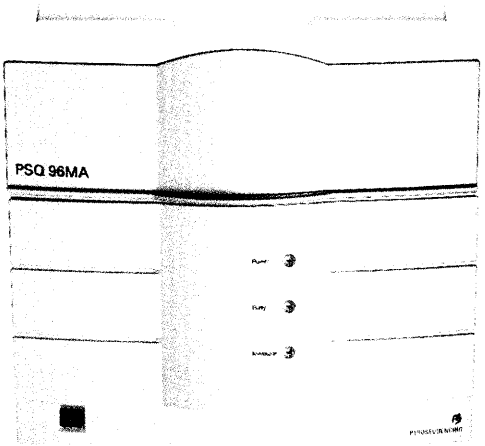

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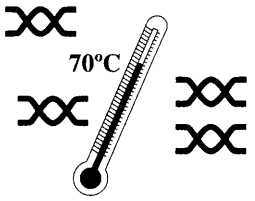

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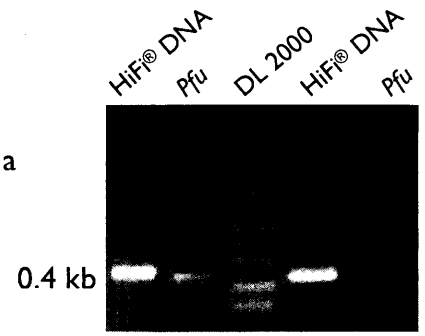


Fig. 1
Pfu fails to amplify a GC-rich template. (far right)

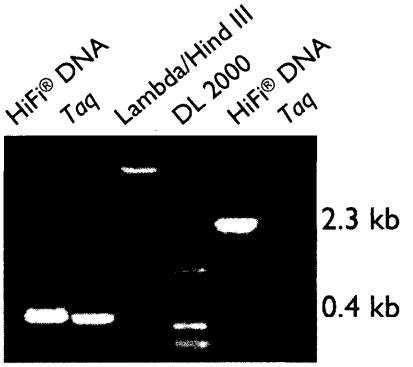


Fig. 2
Taq fails to amplify a 2.3 kb GC-rich template. (far right)

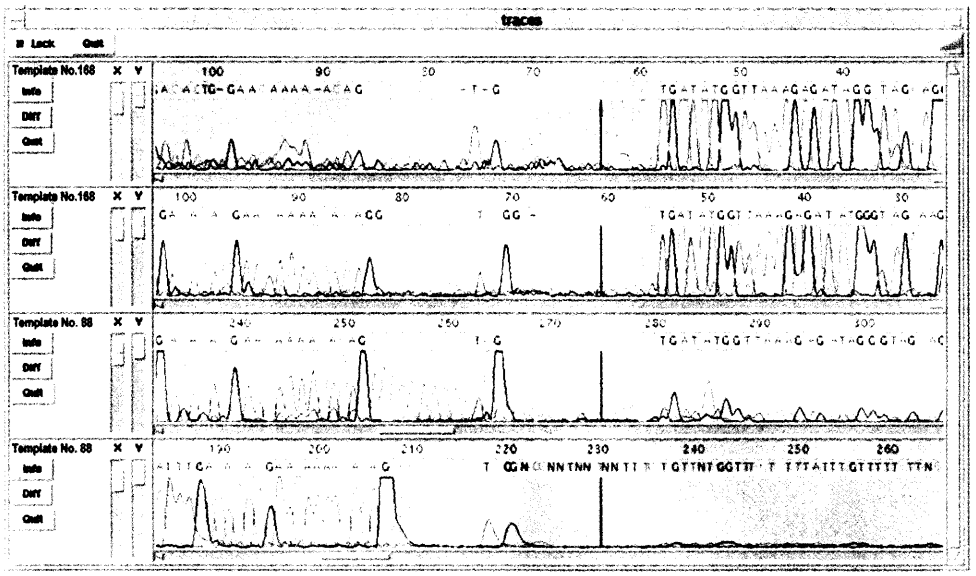
Fig. 3

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)

AmpliTaq, FS fails to overcome this GC-rich segment in cycle sequencing. (on the right)



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