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Science

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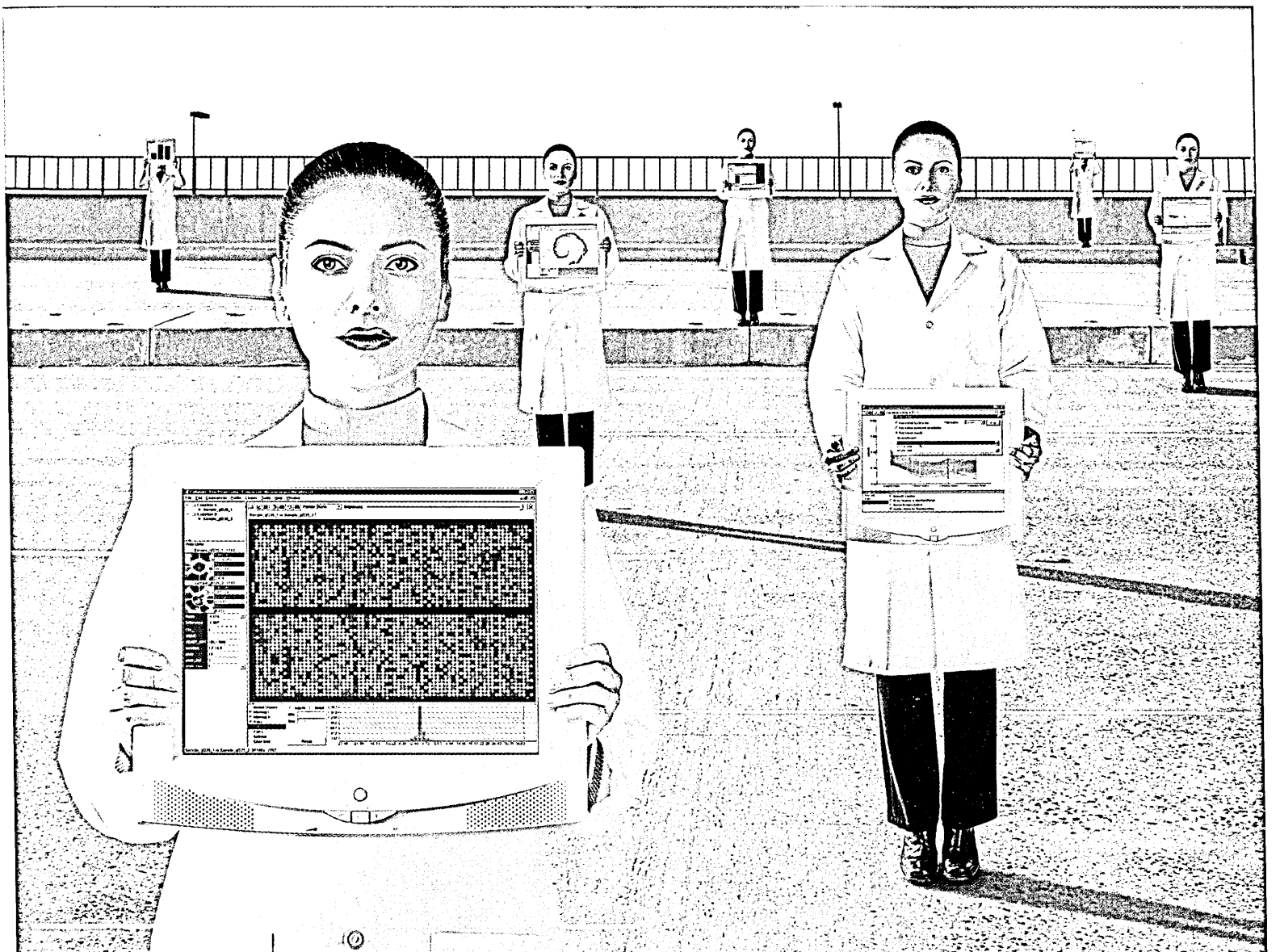
Lipid Biology

American Association for the Advancement of Science



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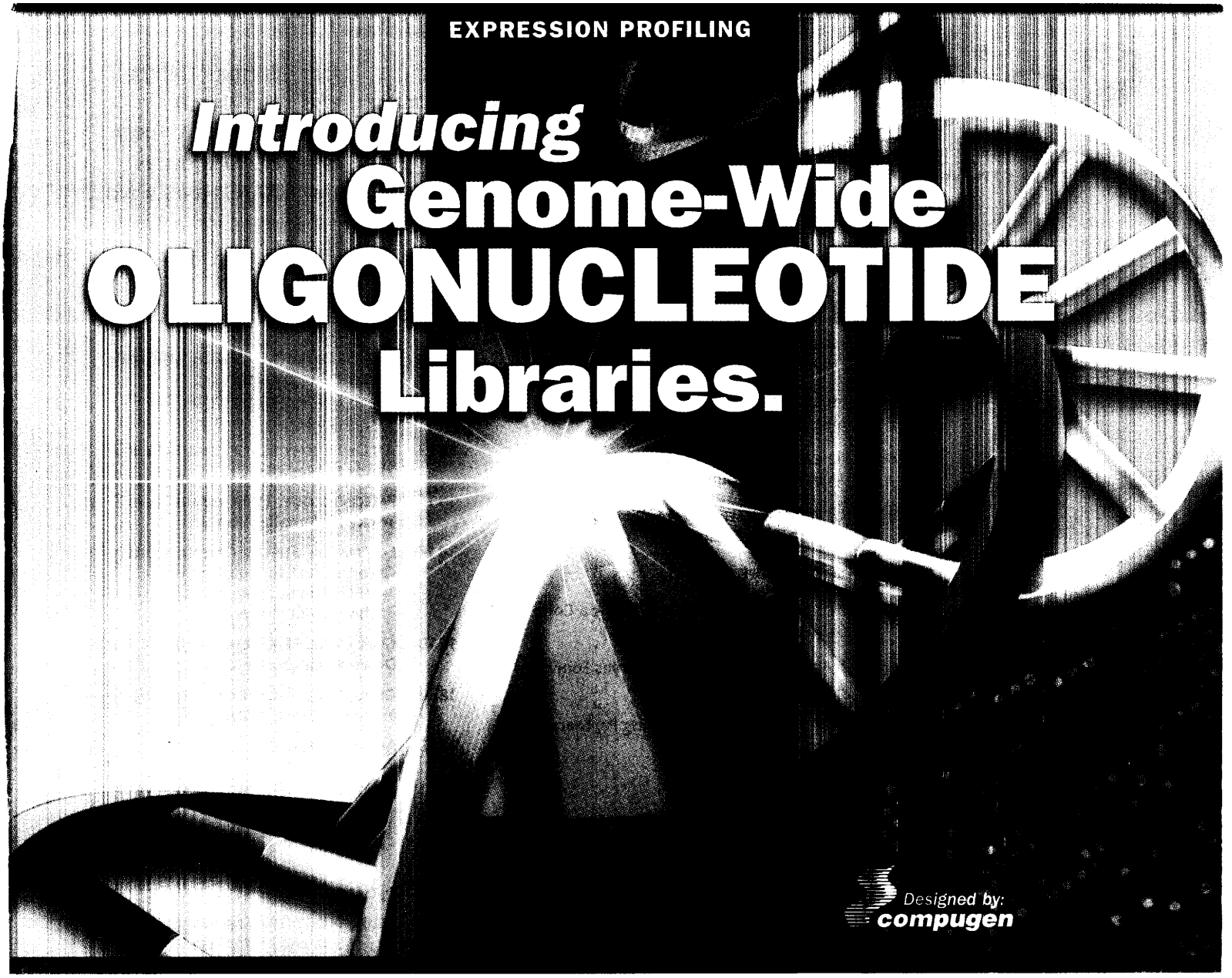

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Science

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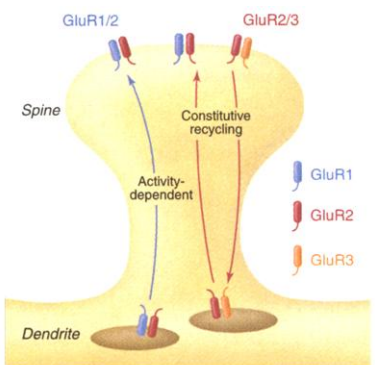

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1838 COMPUTING: ***The Unfinished Revolution*** *Human-Centered Computers and What They Can Do For Us* M. Dertouzos, reviewed by M. Greenberger

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▼1848 1936 IMMUNOLOGY: **A Molecular Gut Reaction** F. Lambolez and B. Rocha

1849 NETWORK ANALYSIS: **The Structure of the Web** J. Kleinberg and S. Lawrence

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LIPID BIOLOGY

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Caveolin-3 Helps Build Muscles

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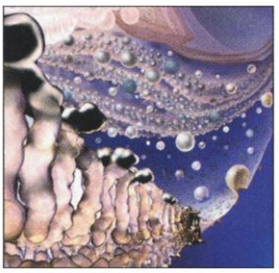
1871 **Prostaglandins and Leukotrienes: Advances in Eicosanoid Biology** C. D. Funk

1875 **Lysophospholipids—Receptor Revelations** T. Hla *et al.*

1879 **Hedgehog Signaling: A Tale of Two Lipids** P. W. Ingham

1881 **Location, Location, Location: Membrane Targeting Directed by PX Domains** T. K. Sato *et al.*

See also Perspective on p. 1845, Reports on pp. 1939 and 1942, and by Baron and Malhotra published online in Science this week (www.sciencexpress.org), and content in Science's STKE (stke.sciencemag.org; see p. 1783).



COVER 1861

Lipids are the fundamental structural components of cellular membranes, but they also have roles in signal transduction, intracellular transport, and gene transcription. The special section in this issue focuses on lipid biology, an area that has become a fertile meeting ground for diverse scientific fields. [Image: C. Slayden]

RESEARCH

NEW FEATURE

BREVIA

Science's newest section features short, peer-reviewed papers of particularly broad general interest.

1893 **Cloned Cattle Can Be Healthy and Normal** R. P. Lanza, J. B. Cibelli, D. Faber, R. W. Sweeney, B. Henderson, W. Nevala, M. D. West, P. J. Wettstein

1894 **Endangered Right Whales on the Southeastern Bering Sea Shelf** C. T. Tynan, D. P. DeMaster, W. T. Peterson

RESEARCH ARTICLE

▼1895 1841 **Delineation of mRNA Export Pathways by the Use of Cell-Permeable Peptides** I. E. Gallouzi and J. A. Steitz

REPORTS

1901 **Photoinduced Conversion of Silver Nanospheres to Nanoprisms** R. Jin, Y. W. Cao, C. A. Mirkin, K. L. Kelly, G. C. Schatz, J. G. Zheng

▼1904 1842 **Total Synthesis of Ciguatoxin CTX3C** M. Hirama, T. Oishi, H. Uehara, M. Inoue, M. Maruyama, H. Oguri, M. Satake

1907 **Engineering Crystal Symmetry and Polar Order in Molecular Host Frameworks** K. T. Holman, A. M. Pivovar, M. D. Ward

1911 **Seismic Detection of Rigid Zones at the Top of the Core** S. Rost and J. Revenaugh

▼1914 1843 **Detection of Molecular Hydrogen in the Atmosphere of Mars** V. A. Krasnopolsky and P. D. Feldman

▼1917 1844 **Mediterranean Sea Surface Radiocarbon Reservoir Age Changes Since the Last Glacial Maximum** G. Siani, M. Paterne, E. Michel, R. Sulpizio, A. Sbrana, M. Arnold, G. Haddad

▼1920 1807 **Effects of Marine Reserves on Adjacent Fisheries** C. M. Roberts, J. A. Bohnsack, F. Gell, J. P. Hawkins, R. Goodridge

▼1923 1847 **Ecological Meltdown in Predator-Free Forest Fragments** J. Terborgh *et al.*

1926 **Matching Spiracle Opening to Metabolic Need During Flight in *Drosophila*** F.-O. Lehmann

▼1929 1803 **Real-Time Single-Molecule Imaging of the Infection Pathway of an Adeno-Associated Virus** G. Seisenberger, M. U. Ried, T. Endreß, H. Büning, M. Hallek, C. Bräuchle

1933 **Physiological Migration of Hematopoietic Stem and Progenitor Cells** D. E. Wright, A. J. Wagers, A. P. Gulati, F. L. Johnson, I. L. Weissman

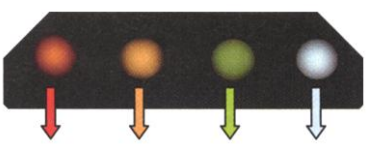
▼1936 1848 **T Cell Responses Modulated Through Interaction Between CD8αα and the Nonclassical MHC Class I Molecule, TL** A. J. Leishman *et al.*

▼1939 1845 1861 **RGS-PX1, a GAP for $G\alpha_s$ and Sorting Nexin in Vesicular Trafficking** B. Zheng *et al.*

▼1942 1861 **Phosphatidic Acid–Mediated Mitogenic Activation of mTOR Signaling** Y. Fang, M. Vilella-Bach, R. Bachmann, A. Flanigan, J. Chen

1945 **Regulation of Cell Survival by Secreted Proneurotrophins** R. Lee, P. Kermani, K. K. Teng, B. L. Hempstead

1948 **Lobster Sniffing: Antennule Design and Hydrodynamic Filtering of Information in an Odor Plume** M. A. R. Koehl *et al.*



1901
Red scattering from triangular silver particles

1948
Lobster antenna smells odor plume

New on *Science* Express

Watery martian gullies: slippery when wet

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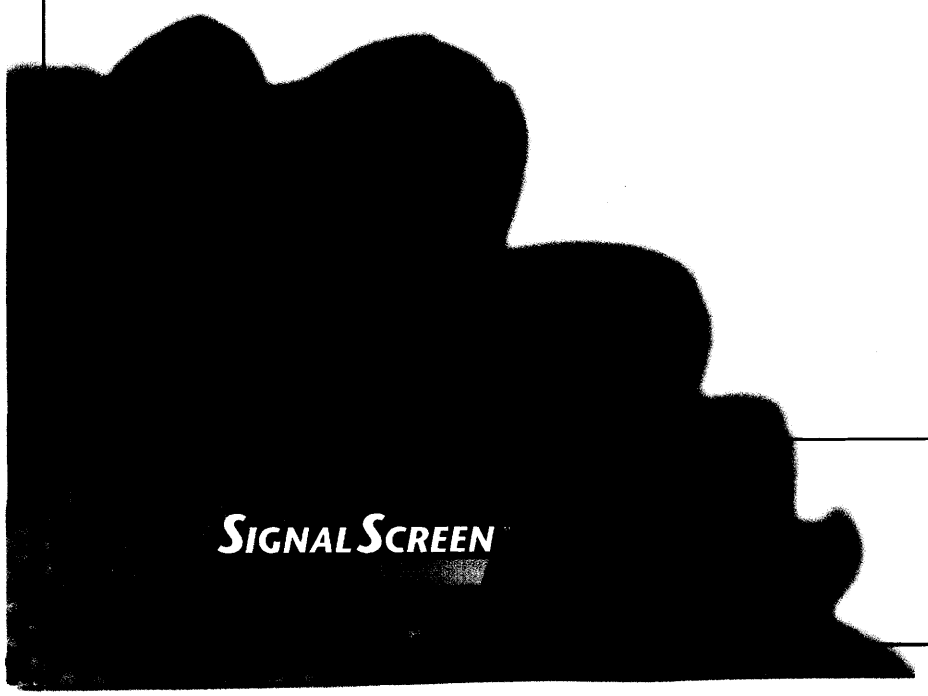

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CONTENT HIGHLIGHTS AS OF 30 NOVEMBER 2001

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SCIENCE EXPRESS

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Formation of Recent Martian Debris Flows by Melting of Near-Surface Ground Ice at High Obliquity F. Costard, F. Forget, N. Mangold, J. P. Peulvast

Terrestrial analogs and global climate models suggest that the gullies on Mars form by the melting of water ice.

Earthquake Recurrence and Rupture Dynamics of Himalayan Frontal Thrust, India S. Kumar *et al.*

Paleoseismic data show evidence for three large earthquakes along the Himalayan Frontal Thrust in India, reinforcing concerns regarding seismic hazard.

Role of Diacylglycerol in PKD Recruitment to the TGN and Protein Transport to the Plasma Membrane C. L. Baron and V. Malhotra

1861 It is demonstrated that the lipid diacylglycerol plays a key role in recruitment of protein kinase D to the trans-Golgi network, thereby allowing intracellular transport from the trans-Golgi network to the cell surface.

TECHNICAL COMMENTS

Role of Apoptosis in *Pseudomonas aeruginosa* Pneumonia

Grassmé *et al.* (Reports, 20 Oct. 2000, p. 527) found that *P. aeruginosa*, a bacterium responsible for pneumonia and sepsis in susceptible individuals, induces extensive apoptosis of lung epithelial cells through interaction with the CD95/CD95 ligand system—and that the epithelial cell death conferred a survival benefit on infected mice. Hotchkiss *et al.* comment that the TUNEL method used in the study to demonstrate epithelial cell apoptosis "may yield false positives," and that they were unable to confirm epithelial cell apoptosis in pneumonia using alternative methods. They also found that "extensive lymphocyte apoptosis ... occurred in lung, spleen, and thymus during pneumonia"—a pattern that suggests, according to Hotchkiss *et al.*, that "extensive lymphocyte apoptosis may ... contribute to the accompanying immune suppression and mortality" of bacterial sepsis, irrespective of infection site. Grassmé *et al.* respond with results of additional, non-TUNEL tests that "confirm induction of apoptosis in lung epithelial cells by *P. aeruginosa*." The difference between their results and those of Hotchkiss *et al.*, they suggest, may lie in the fact that the two groups used bacteria in different growth phases.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/294/5548/1783a

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career resources for scientists

Singapore: On Being a Responsible Scientist J. Wong

Some of the more common ethical issues encountered by young scientists—and suggestions on how to deal with them.

UK: Chemists Storm Parliament C. Sansom

A special event at the Palace of Westminster gave young scientists the opportunity to show MPs the relevance of their work.

Germany: German Ph.D. Students—Free But Lonely S. von Aichberger

Too much freedom can be a bad thing when it comes to preparing your Ph.D., as Germany's doctoral students attest.

Canada: Under One Roof, Part 4—Biotech in the Prairies L. McKarney

This week, we head west to look at the flourishing biotech industry in Saskatchewan and Alberta.

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Cortical Basal Ganglionic Degeneration: A Case Study N. Scarmeas, S. S. Chin, K. Marder

This rare neurodegenerative disease is categorized under both parkinsonian syndromes and frontal lobe dementias.

Best of Aging on the Web

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signal transduction knowledge environment

Perspective: Phospholipid Signaling in Plants—Holding on to Phospholipase D T. Munnik and A. Musgrave

Does phospholipase D link membranes and microtubules? Lessons from the plant.

Review: The Complex and Intriguing Lives of PIP_2 with Ion Channels and Transporters D. W. Hilgemann, S. Feng, C. Nasuhoglu

Highlighting the role of PIP_2 in regulating and organizing transmembrane proteins.

Forum: Lipid Rafts—Real or Artifact?

An open discussion about membrane microdomains with an Opening Statement by Michael Edidin.

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THIS WEEK IN Science

edited by Phil Szuromi

Rigidity in the Liquid Core

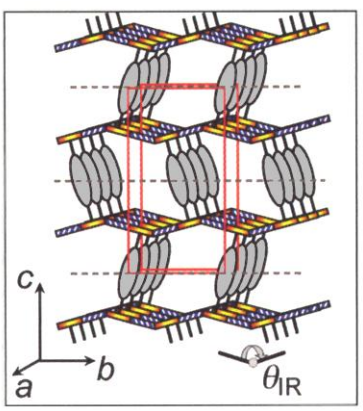
Earth's outer core is composed of an iron-rich liquid, but differences in its chemistry and structure could have effects on core convection and nutation (the slight nodding of Earth toward the Sun as the Earth precesses on its axis). Rost and Revenaugh (p. 1911) have detected thin (about 0.2 kilometer) rigid zones at the top of the outer core and infer that these zones are mixtures of liquid iron alloys and solid grains of iron alloys and iron oxides.

Tackling Ciguatoxin Synthesis

Many marine fish are vectors for ciguatera neurotoxins produced by the dinoflagellate *Gambierdiscus toxicus*, which produce more than 20,000 cases of seafood poisoning in subtropical and tropical regions. The development of antibodies to these toxins has been hampered by the extremely low content of these poisons in fish. Hirama *et al.* (p. 1904; see the Perspective by Markó) now report the total synthesis of one ciguatoxin, CTX3C, through the convergent assembly of two comparably complex fragments.

Polarizing Organic Frameworks

Polar crystals, in which molecular dipoles align in one direction, should exhibit useful properties such as ferroelectricity and frequency doubling of light. Organic crystals offer the opportunity for the more rational design of bonding in the solid, but the dipoles of organic molecules tend to cancel in crystals and create nonpolar structures. Holman *et al.* (p. 1907) show that an organic host structure for the inclusion of guest molecules can be modified by using achiral banana-shaped bridging molecules to create a structure with an overall polarity. By properly choosing guest molecules, they can create crystals that exhibit second-harmonic generation of light.



1901 Photogenerating Triangular Silver Nanoprisms

An important challenge in the solution-phase synthesis of nanoparticles is to control particle size and shape while maintaining a high overall yield of product. Jin *et al.* (p. 1901) show that spherical silver particles can be almost completely converted by visible light into thin triangular prisms with edge lengths of 100 ± 15 nanometers. The triangular shape of these nanoparticles leads to unusual optical properties, such as the presence of two distinct quadrupole plasmon resonances and Rayleigh scattering in the red, rather than in the blue as is typical for spherical particles.

And in Brevia ...

The highly endangered North Pacific right whale (*Eubalaena japonica*) has changed both its habitat and prey during the last 50 years, according to Tynan *et al.* (p. 1894), and remains posed on the brink of extinction.

Careful records kept on cloned cattle by Lanza *et al.* (p. 1893) reveal that the 24 adult cattle that survived from 110 pregnancies appear to be completely healthy, in spite of a higher-than-usual mortality rate during gestation and at birth.

Hydrogen on Mars

Molecular hydrogen on Mars, although a relatively minor species in the CO_2-dominated atmosphere, stabilizes the chemistry of the atmosphere and soil and provides estimates of past water abundance. Krasnopolsky and Feldman (p. 1914; see the Perspective by Hunten) measured the H_2 abundance of Mars' upper atmosphere using the Far Ultraviolet Spectroscopic Explorer (FUSE). They found that there is enough H_2 to prevent the buildup of CO and O_2 in the atmosphere, to explain the presence of hydrogen-based oxidants in the soil, and to suggest that Mars may have initially had more water (as a proportion of the planet's mass) than Earth.

Revising CD8 Function

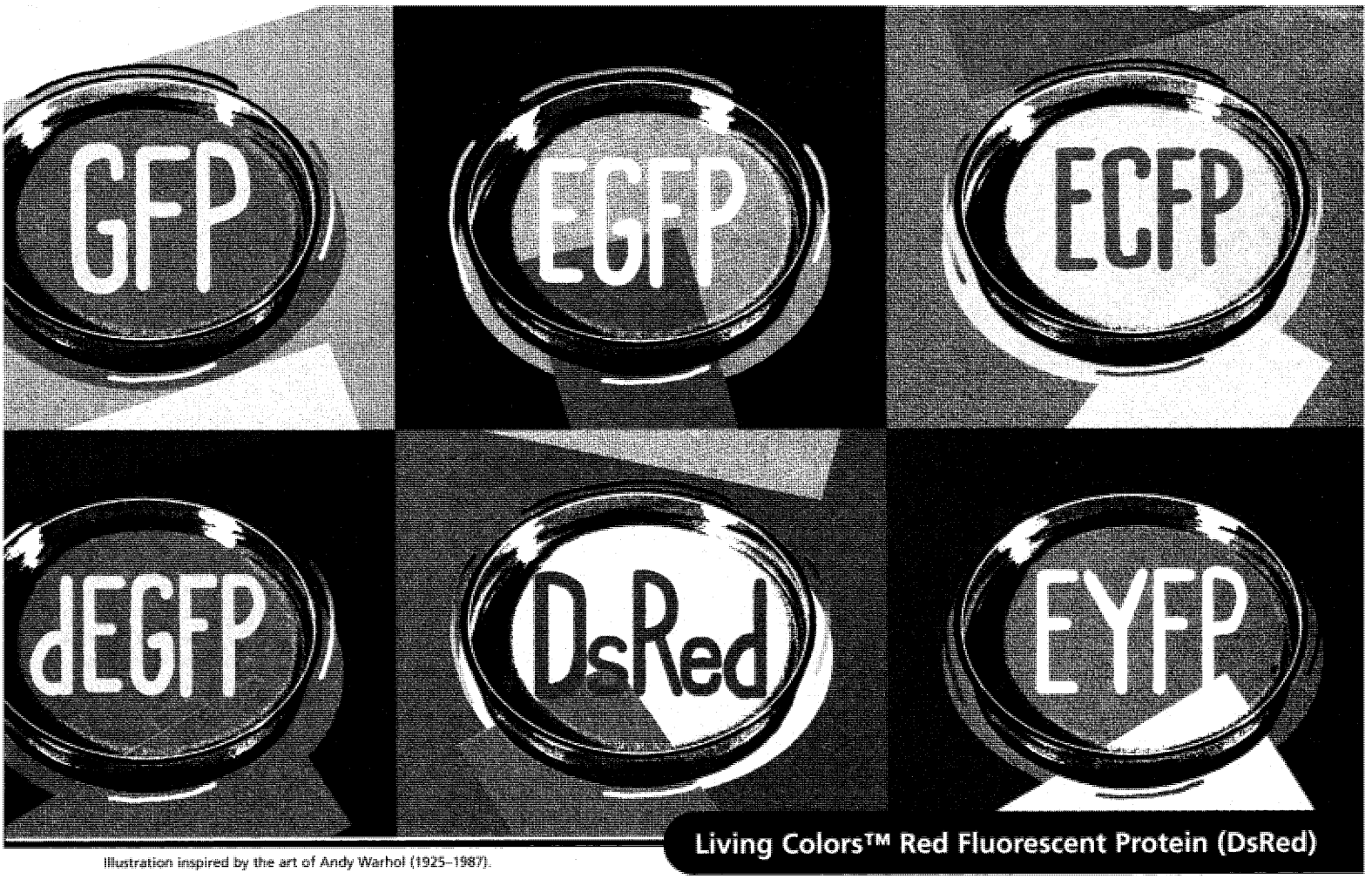
Intestinal intraepithelial lymphocytes (IELs) reside at epithelial surface along the gut, and many members of this class of T cells express a homotypic form of the CD8α molecule whose role had been unexplained in the context of IEL biology. Leishman *et al.* (p. 1936; see the Perspective by Lambolez and Rocha) show that CD8αα homodimers interact specifically with a major histocompatibility complex–like molecule, termed TL, expressed on intestinal epithelial cells. When CD8αα engaged TL, cell division and cytokine production of antigen-specific IEL were increased, and other effector functions, such as cytotoxic activity, were inhibited. Thus, CD8αα may not act as a typical coreceptor but rather as a regulatory molecule that modulates that activity of intestinal T cells

Managing Messenger RNA Traffic

Two classes of proteins, receptors and adapters, recognize properly processed messenger RNAs (mRNAs), and facilitate their export through pores in the nuclear membrane in the cytoplasm. The adapters bind directly to the mRNAs, and the receptors interact with the nuclear pore complex (NPC) and the adapters. The multiplicity of potential protein-protein interactions has hindered efforts at assigning pairwise combinations of adapters and receptors, both of which must also be recycled through the NPC for repeated use (see the Perspective by Moore and Rosbash). Gallouzi and Steitz (p. 1895) have now developed cell-permeable peptides that inhibit pair-wise interactions between receptors and adapters selectively without perturbing the overall movement of mRNAs into the cell.

CONTINUED ON PAGE 1787

CREDITS: (TOP TO BOTTOM) LANZA *ET AL.*; HOLMAN *ET AL.*



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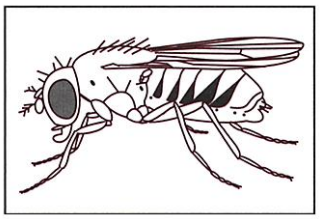
Losses Coming from the Top Down

Fragmentation of a natural habitat has been shown to create a community-level trophic cascade caused by the absence of predators. Terborgh *et al.* (p. 1923; see the Perspective by Diamond) show that for fragments of tropical forest created by the Guri dam project in central Venezuela, predator populations become unsustainable. Herbivores then become hyperabundant and severely suppress the recruitment of canopy trees, presaging wholesale degradation of the vegetation and loss of species diversity.

Controlling Air Intake During Flight



The tiny fruit fly, which has a diffusion-based respiratory system, must avoid excessive water loss during flight while maintaining sufficient gas exchange to fuel intense respiration. Is the opening of spiracles, which mediate gas exchange, tuned to match the intensity of force generation? To find out, Lehmann (p. 1926) glued individual female *Drosophila* to a support in a gas-tight chamber and indirectly measured spiracle opening by monitoring the release of water and CO_2. The author interprets the results to indicate that the flies do not hold their spiracles open during flight as previously suggested, but somehow adjust the size of the spiracle opening to correspond to the fly's metabolic requirements.

Watch a Virus Make Its Moves

For many of us, early instruction in microbiology included watching a movie of *Paramecia* engulfing their prey. Seisenberger *et al.* (p. 1929; see the news story by Beckman) now provide us with a real-time fluorescence video recording of a single virus particle adhering to a cell, being taken inward via endocytosis, breaking through into the cytoplasm, and reaching the nucleus where the wholesale takeover of host functions begins. The unexpectedly rapid transit time is of special interest because this invader, adeno-associated virus, is a prime candidate for virus-based gene therapy approaches.

G Proteins and Vesicle Trafficking

Attenuating a cellular signal is just as critical as inducing it. For example, regulator of G protein signaling (RGS) proteins modulate the signaling output from receptor-coupled heterotrimeric G proteins. Zheng *et al.* (p. 1939; see the Perspective by von Zastrow and Mostov) have identified what has been an elusive RGS for the $G\alpha_s$ class of G proteins. Named RGS-PX1, it also contains a membrane-interacting PhoX domain whose presence suggests a link between G protein signaling and vesicle trafficking in cells.

Lipids and Immunosuppression

Mitogens and other stimuli to cells cause generation of the lipid phosphatidic acid (PA), which acts as a second messenger to promote various cellular responses. Fang *et al.* (p. 1942) identify a new target regulated by PA binding that appears to account for the mitogenic effects of the lipid. In cells treated with PA, the mTOR protein (so named because it is mammalian target of the immunosuppressant rapimycin), which is a phosphatidylinositol kinase–like enzyme, becomes activated. Stimulation of human cells with mitogens increased accumulation of PA and inhibitors of PA production inhibited signaling through mTOR. The results indicate that PA mediates the effects of mitogens to activate mTOR and that rapimycin may interfere with mTOR function by blocking binding of PA.

How to Catch a Smell

Lobsters capture odors with small hairy arrays in their antennules. Does the movement of these antennules disrupt the spatial pattern of odors? Koehl *et al.* (p. 1948) used laser light and high-speed video imaging to visualize fluorescent dye flow through these antennules and found that small spatial patterns of dye enter the receptor area with little initial disturbance during the fast downstroke of the antennule. The spatial patterns only get blurred during the return stroke and the subsequent pause.

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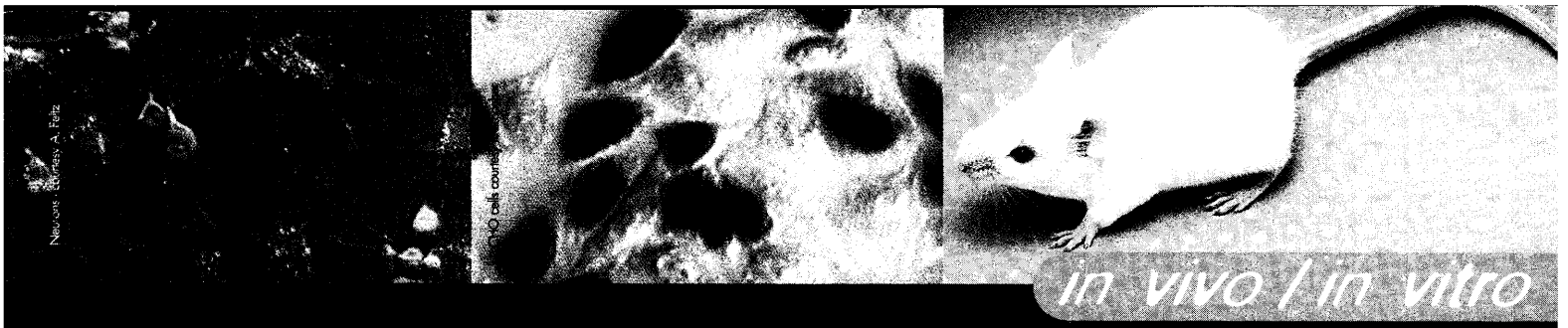

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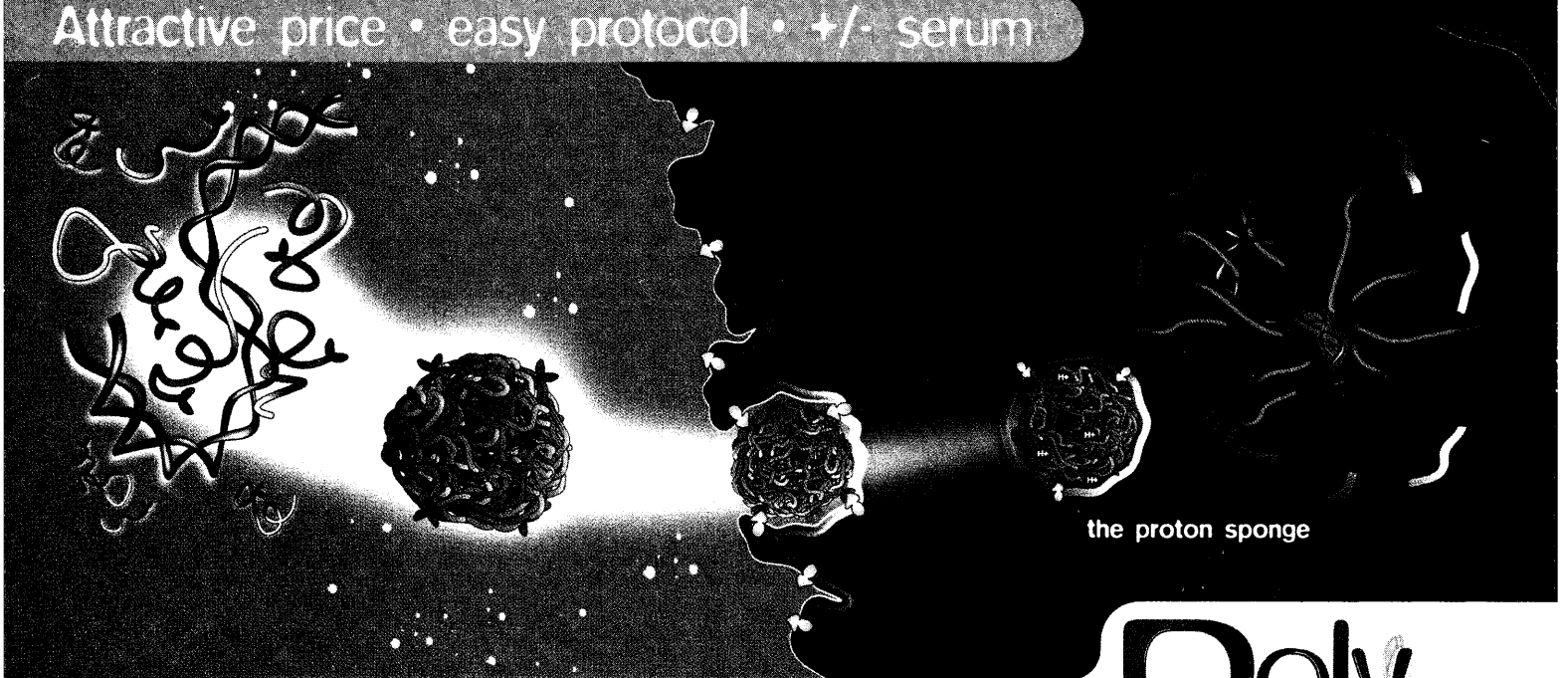

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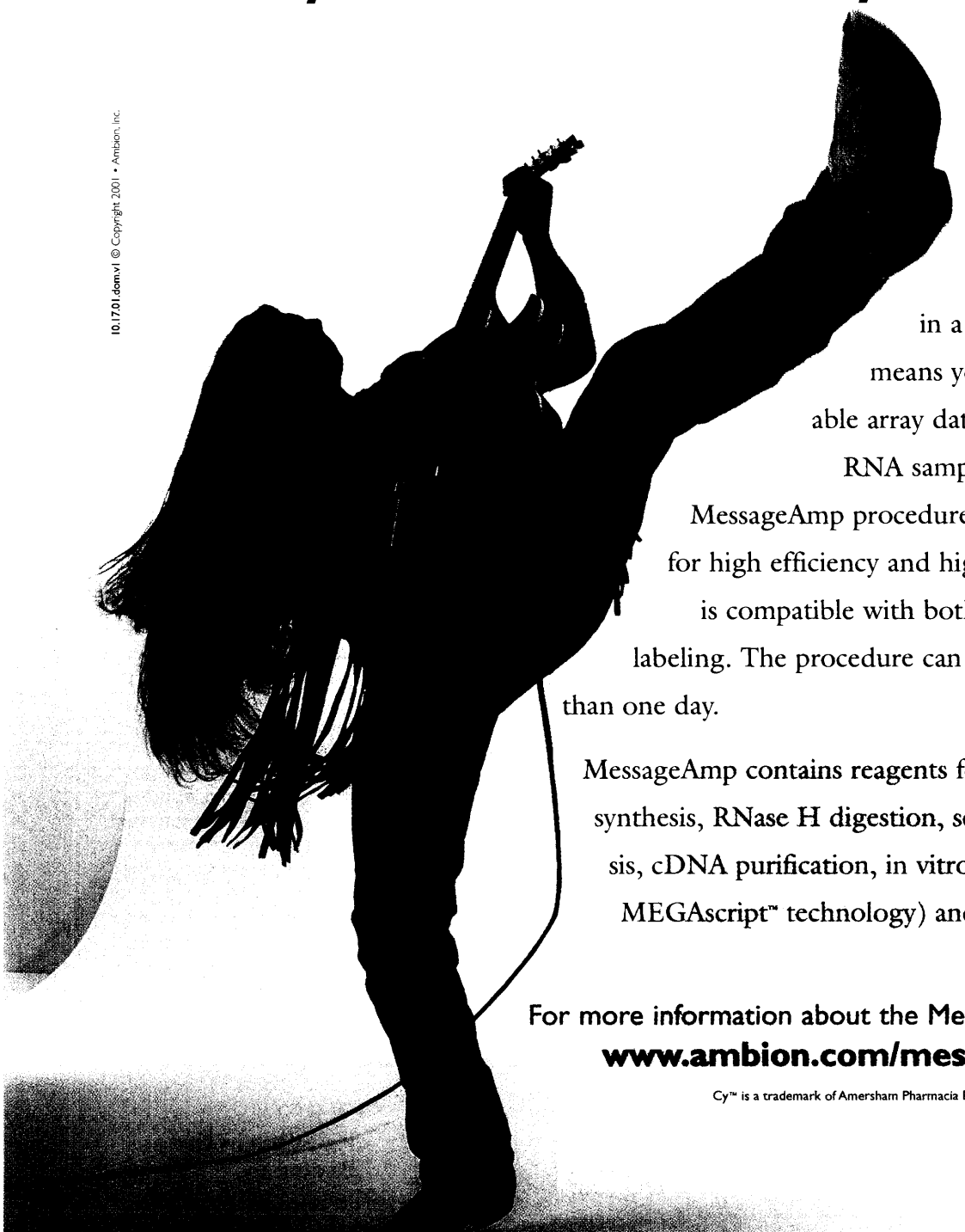

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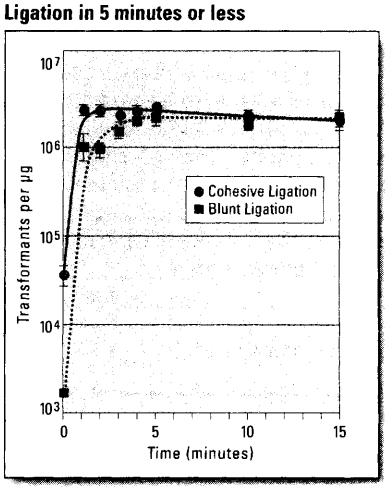

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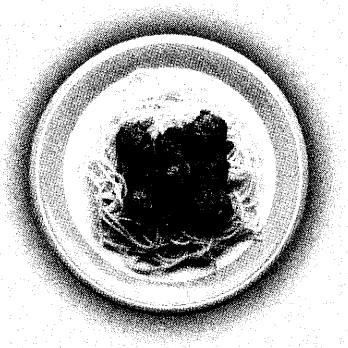

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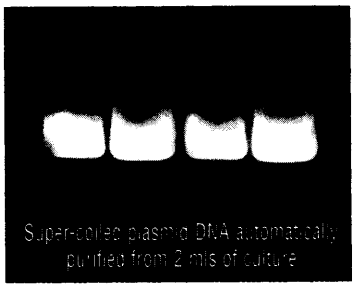

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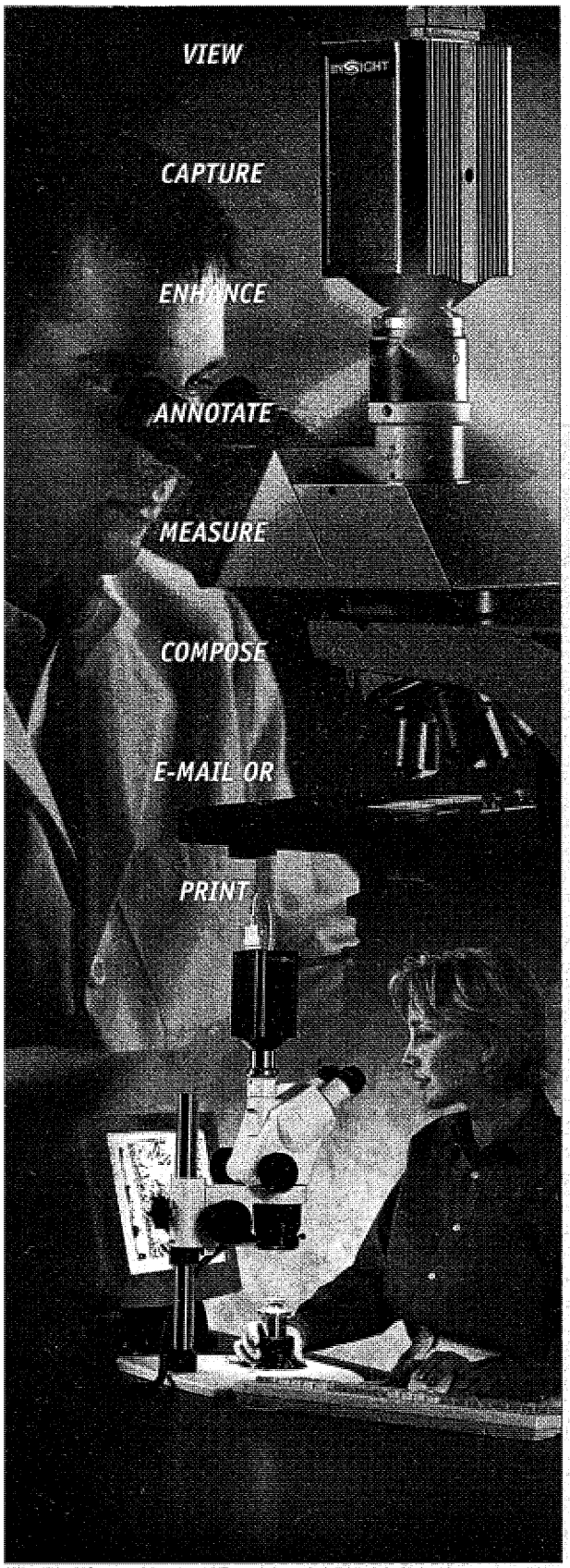

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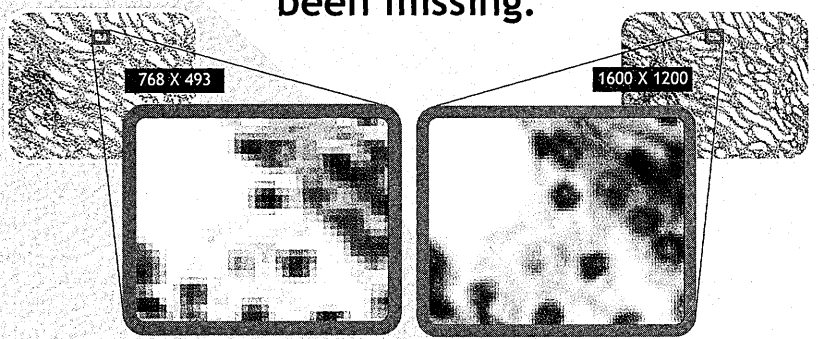

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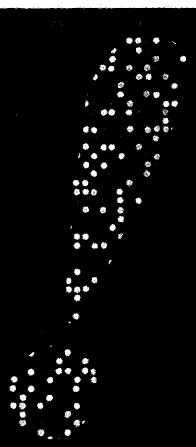

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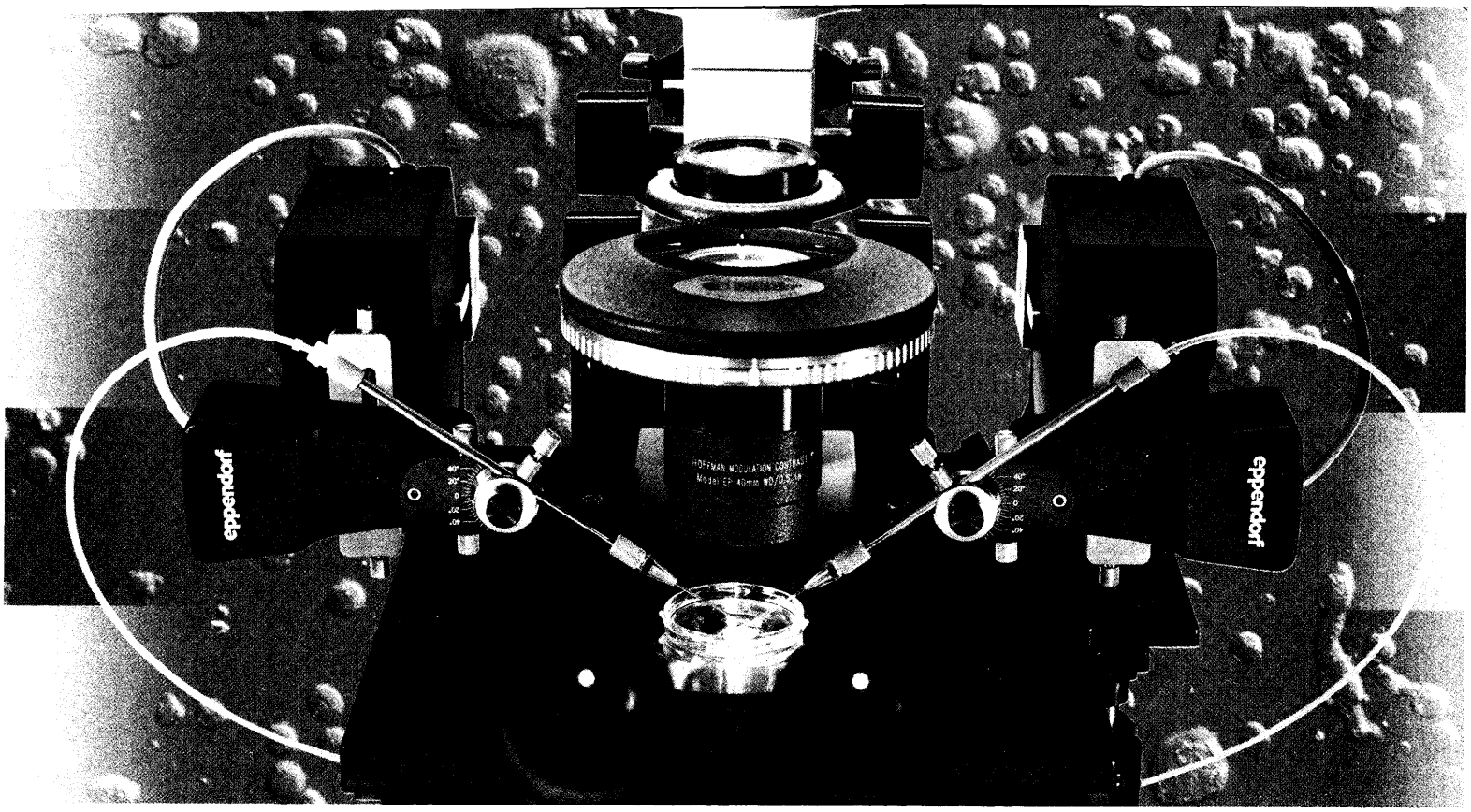

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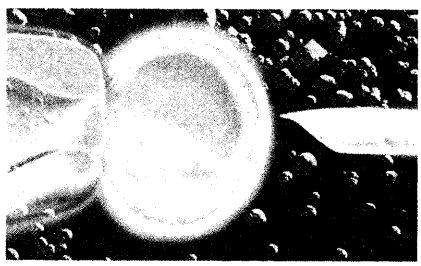

● ES cell transfer to blastocyst with the workstation above, using Eppendorf manipulators, Vacu Tip and Transfer Tip ES

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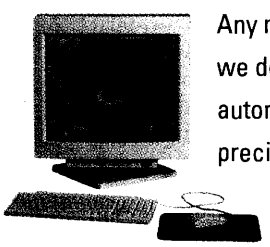

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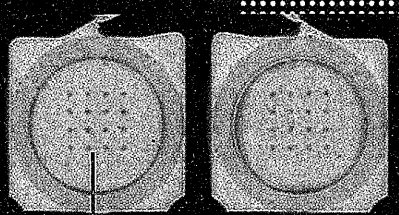
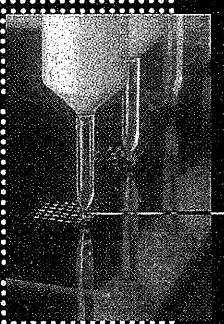


Flexibility of the BioChip Arrayer allows the researcher to develop unique applications, such as this microarray printed in the bottom of a 96 well microplate.



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Pradeep P. A. Mammen, MD
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Helen C. Kales, MD
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Christine E. Koval, MD
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School of Medicine and Dentistry

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Julia S. Seng, PhD
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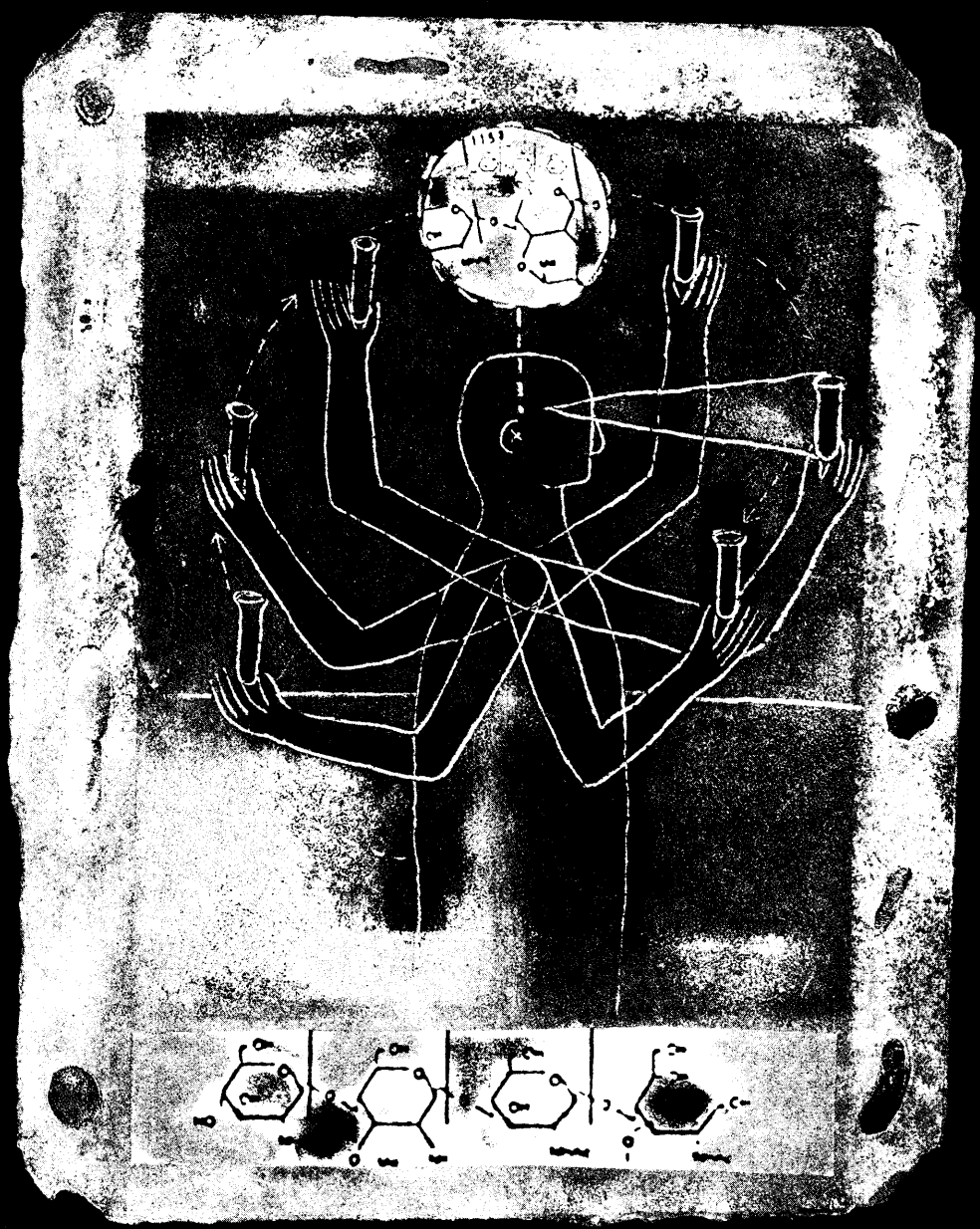

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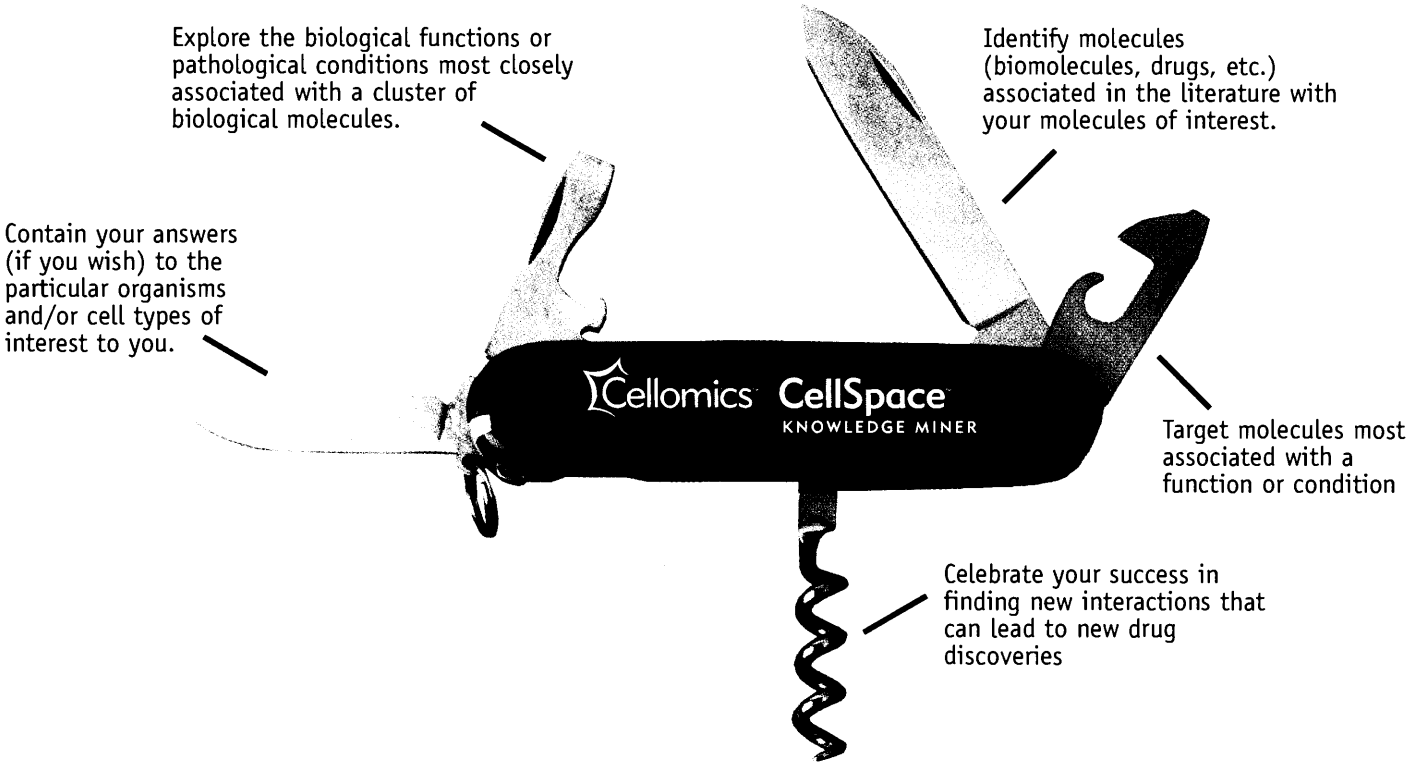

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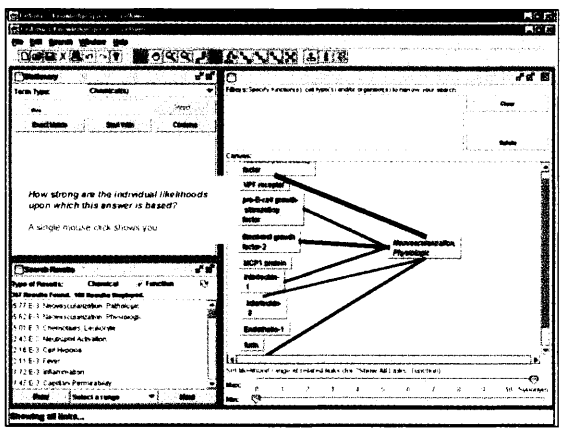

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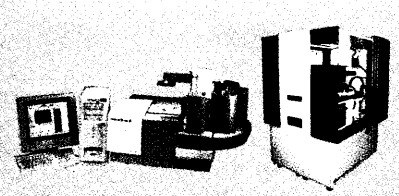

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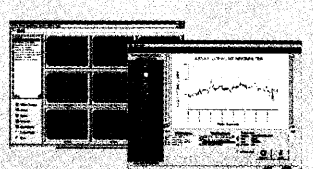
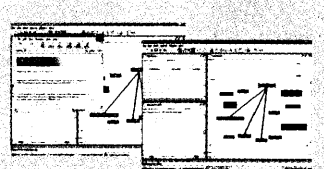
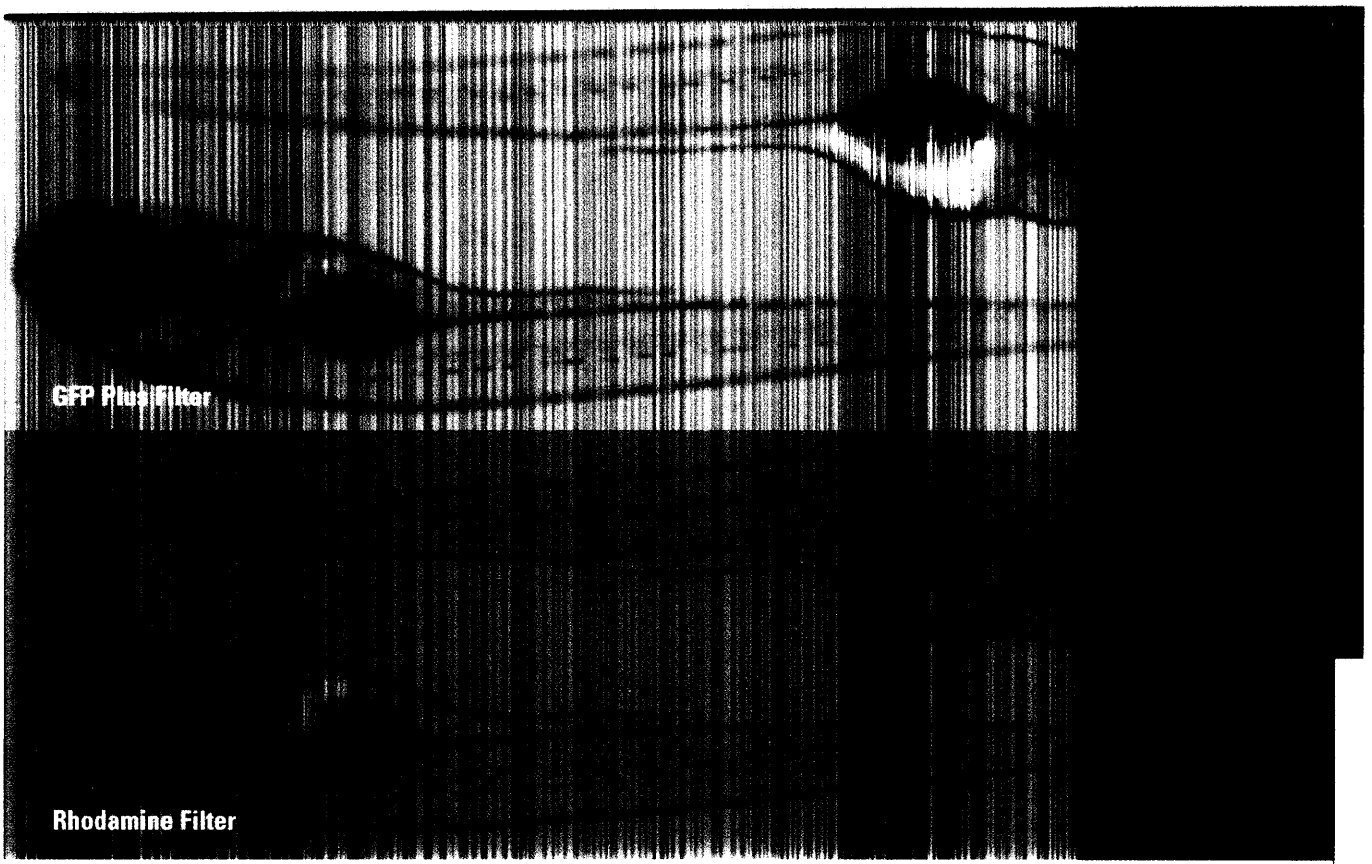
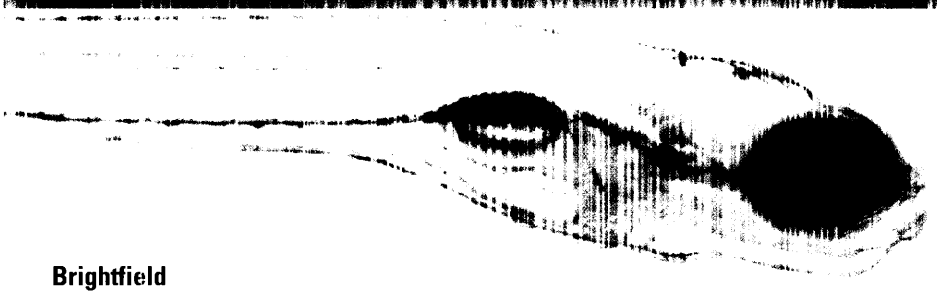


Informatics Solutions



Cellular Bioinformatics





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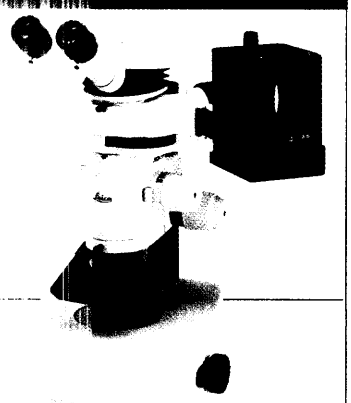

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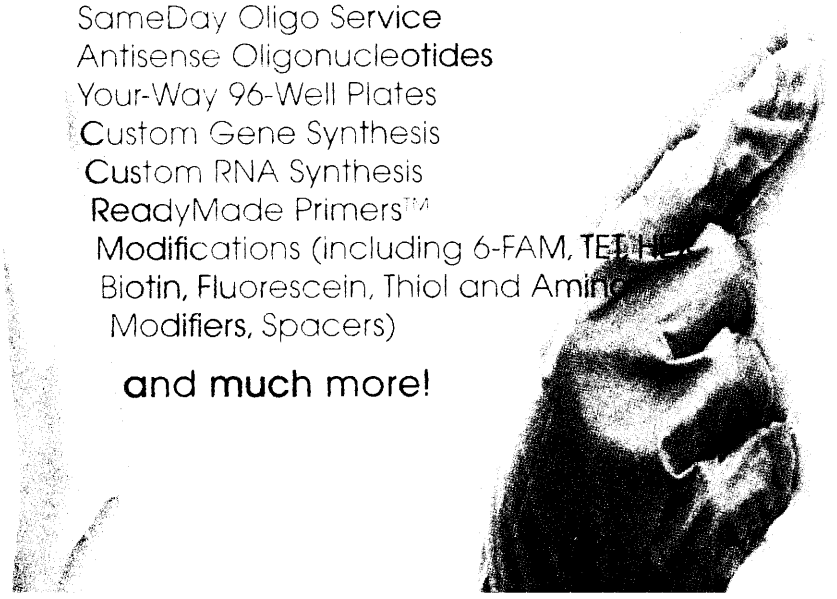

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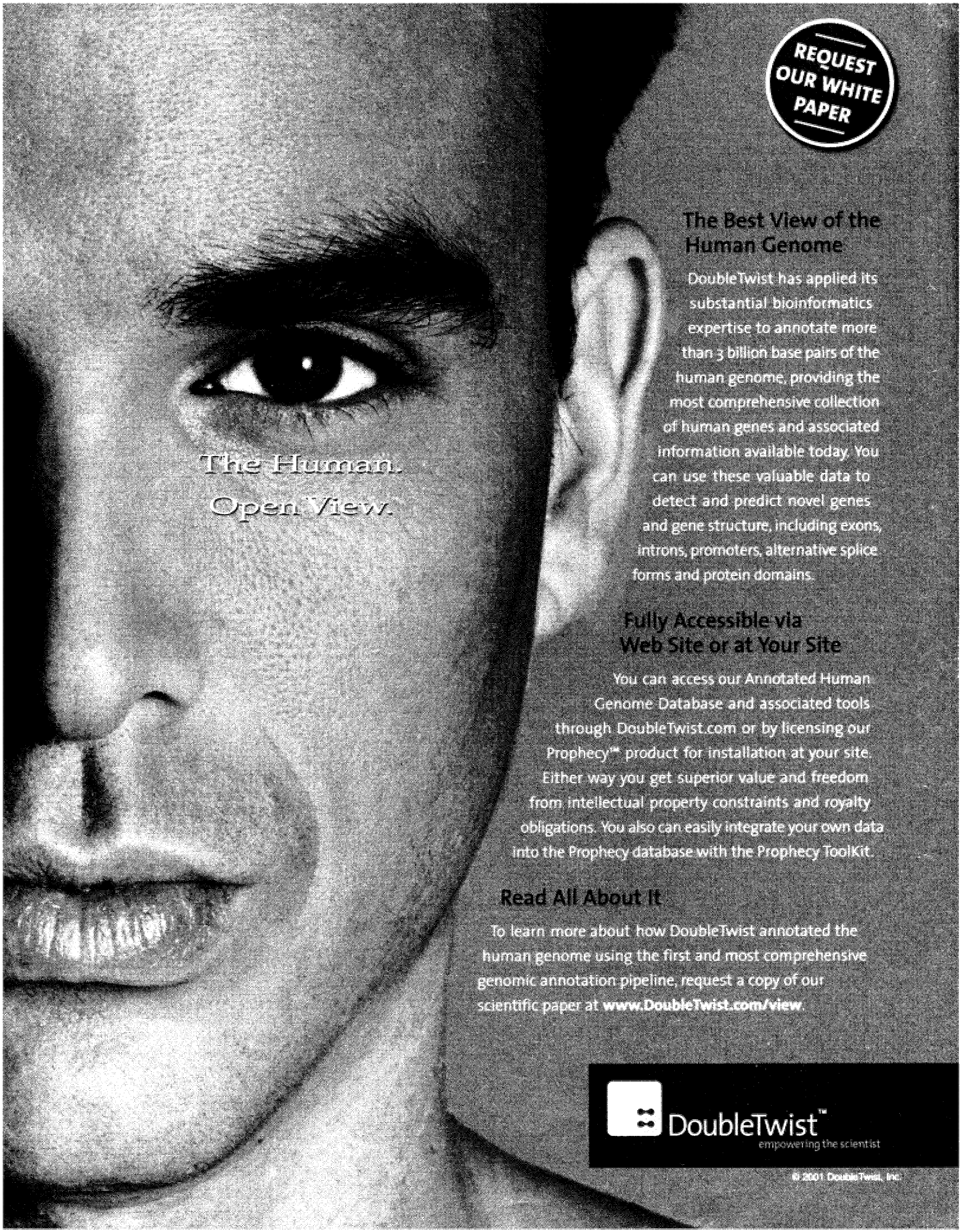
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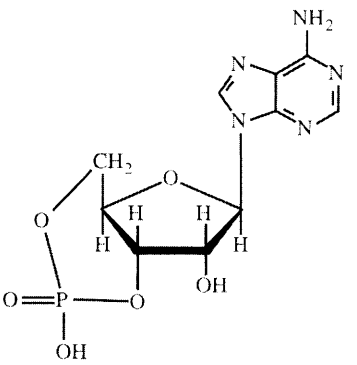

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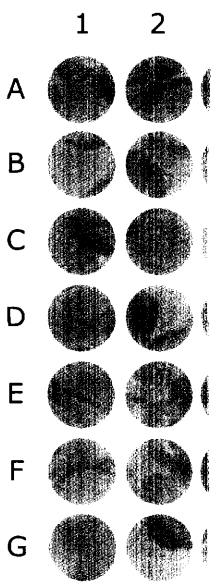

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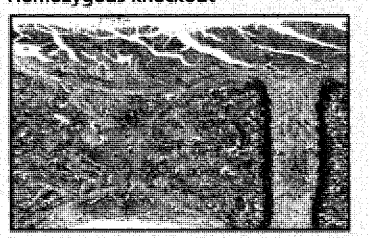
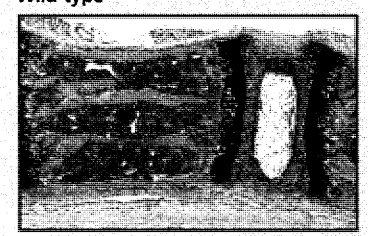
Target: Bone

Phenotypic analysis
Gene: Ion channel

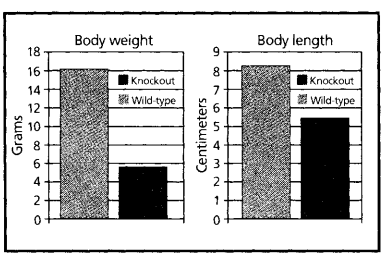
Homozygous knockout



Wild-type



All homozygous knockout mice are runted and exhibit osteopetrosis. Severe fibro-osseus proliferation is present in the cranial bones, femur, tibia, vertebrae and/or sternum. Homozygous knockout mice also show diminished bone marrow hematopoietic cells within the marrow spaces (myelophthisis). An example from the sternum is shown here. A wild-type sternum is presented for comparison.



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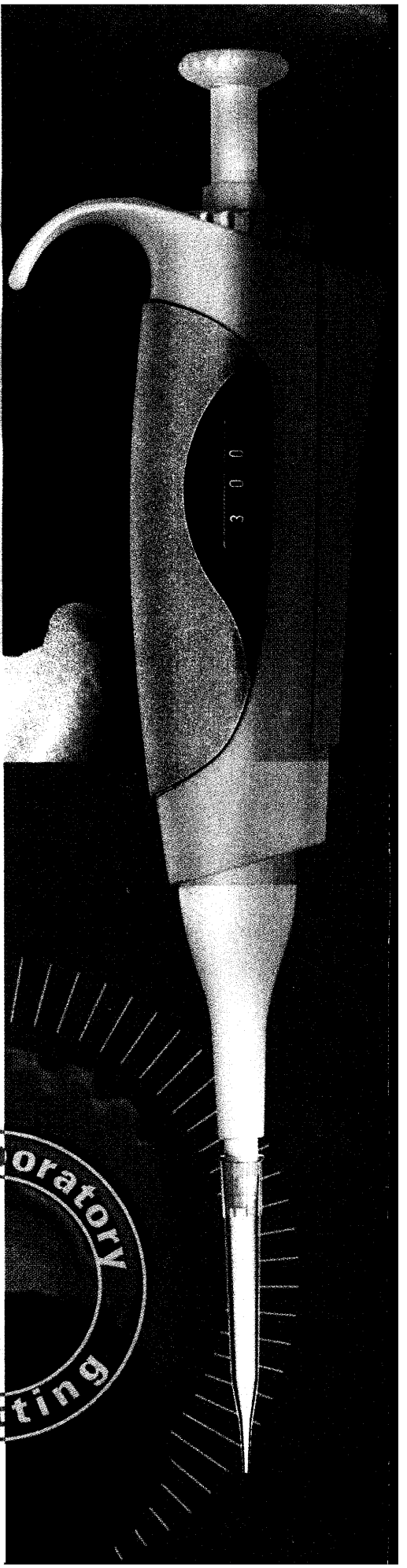

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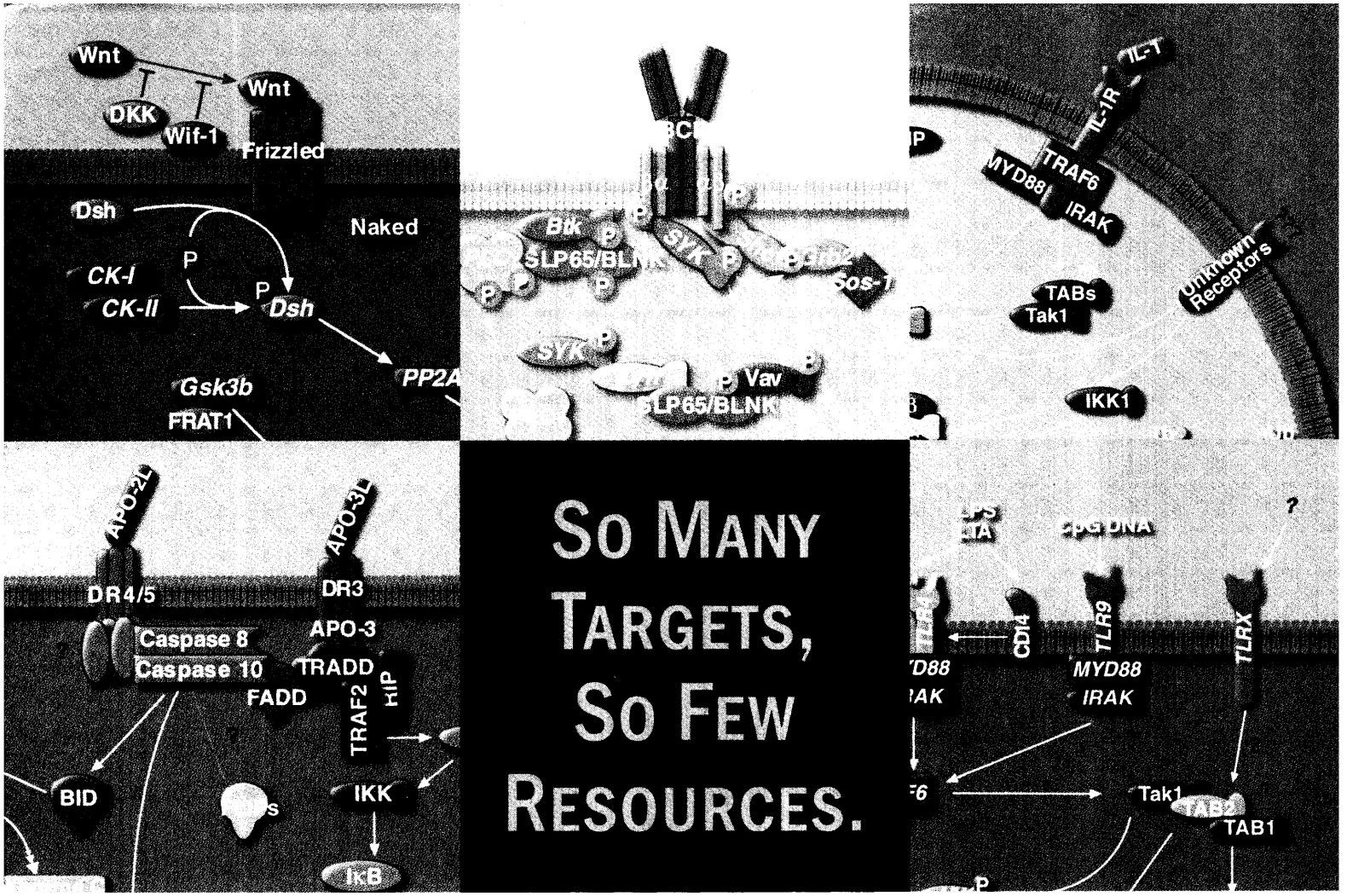

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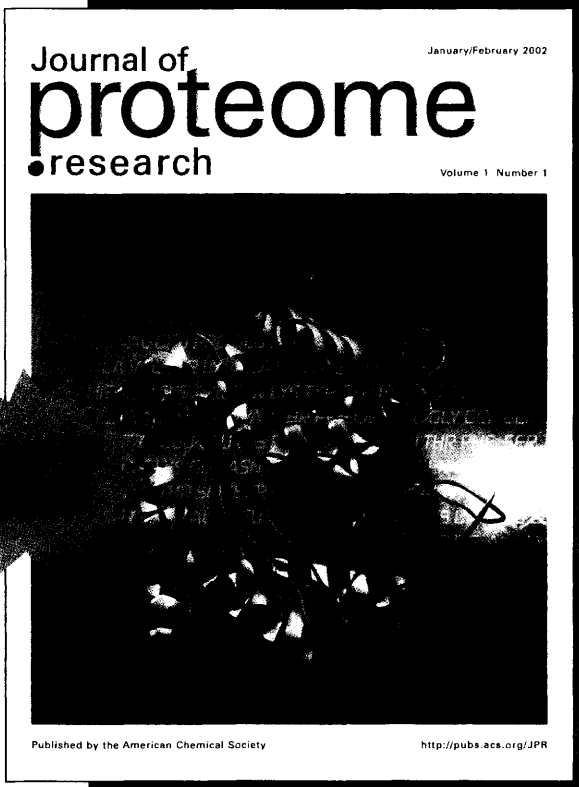

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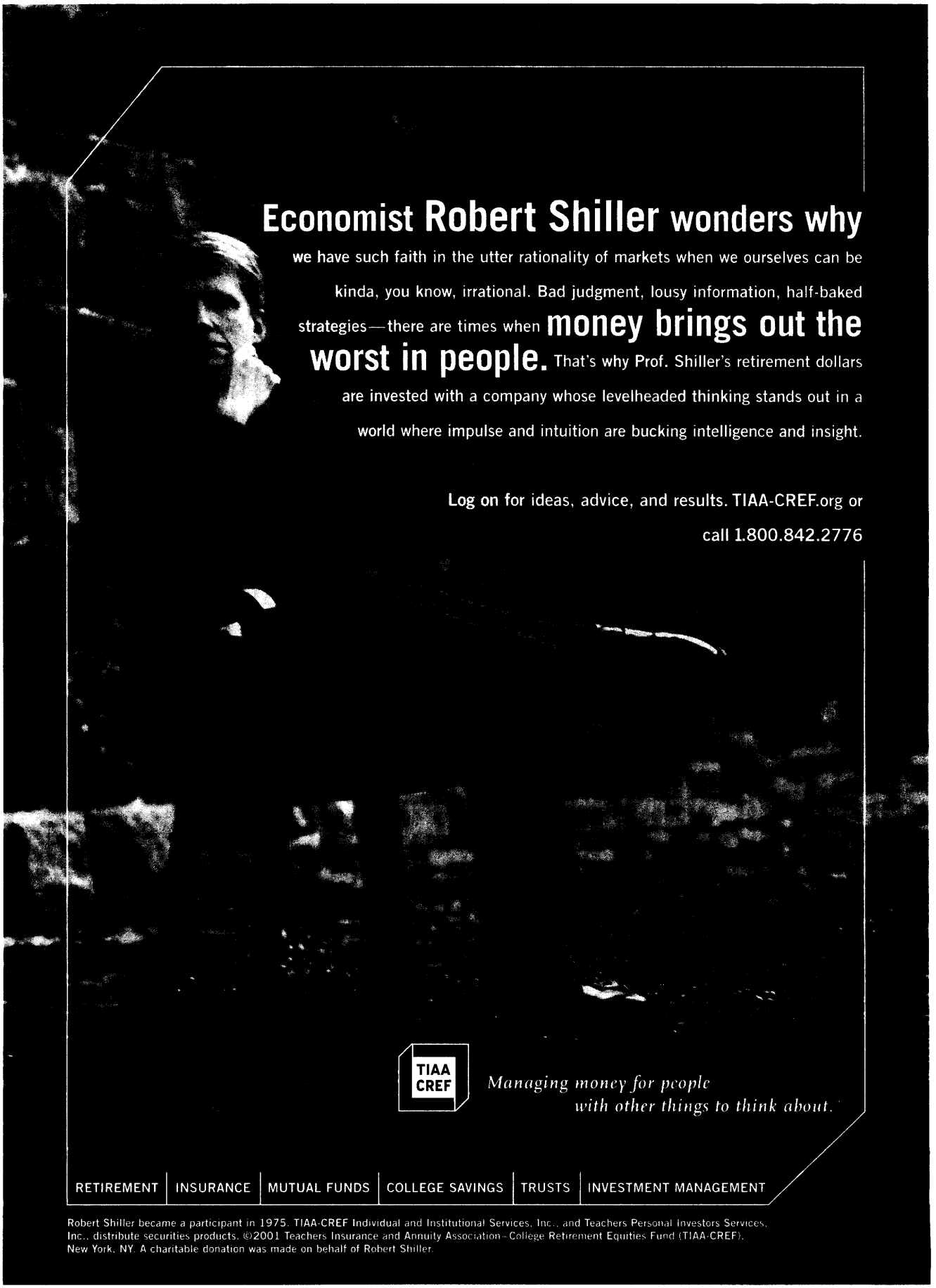

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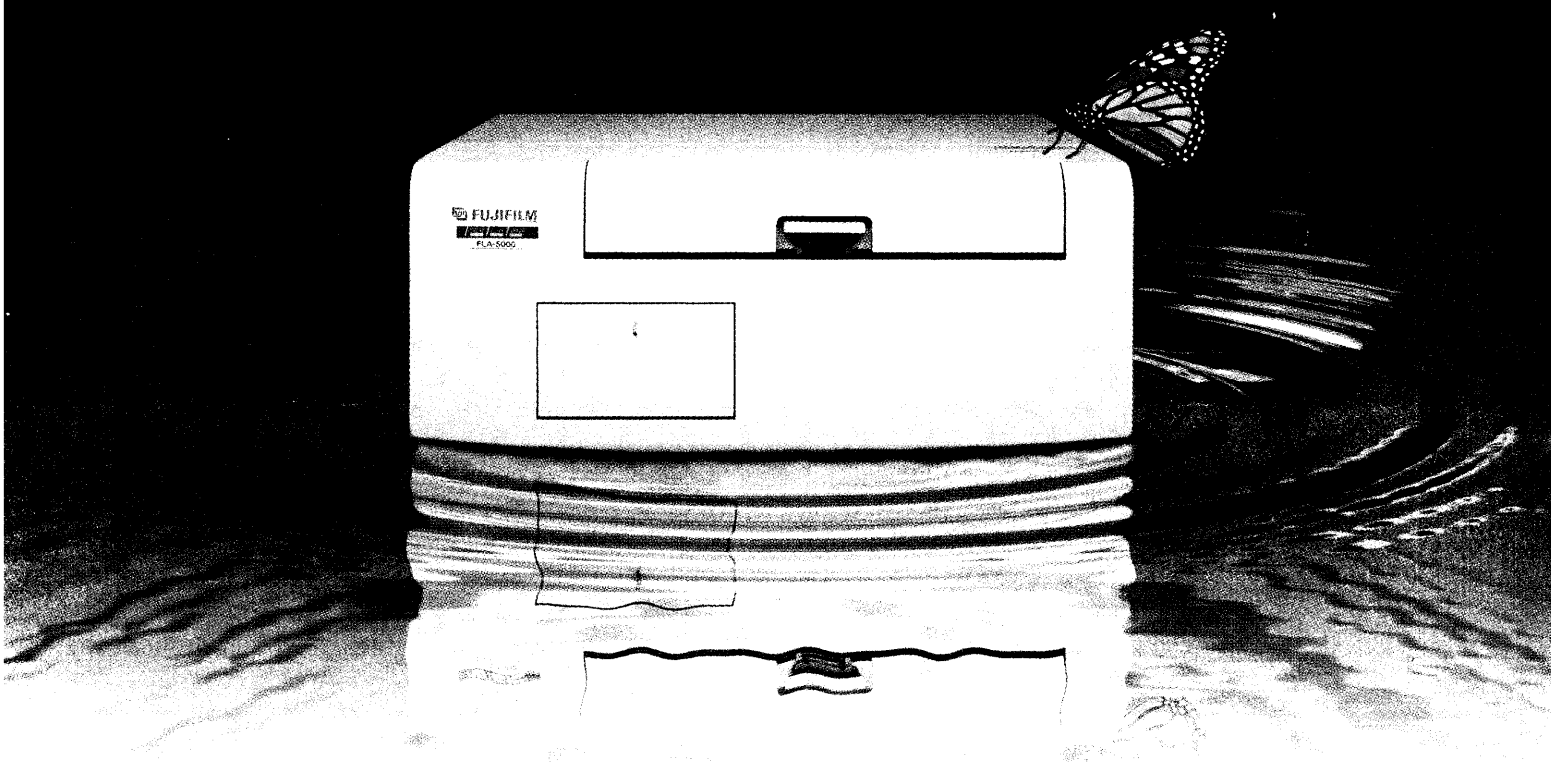

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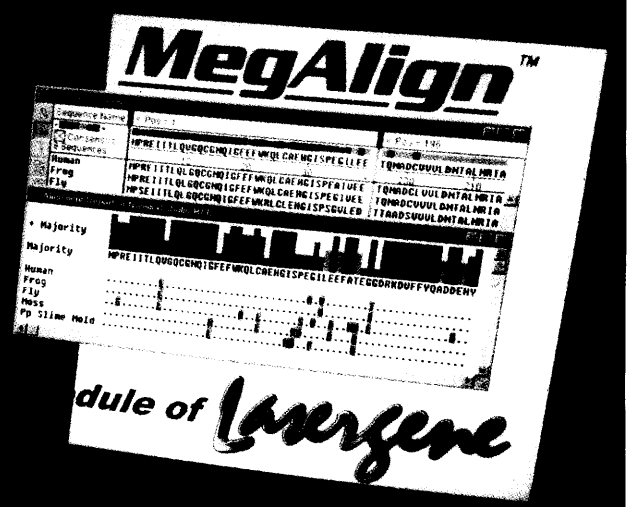

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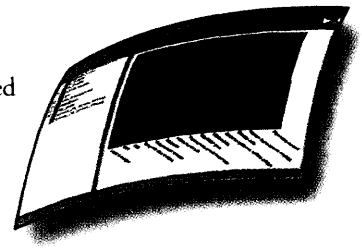

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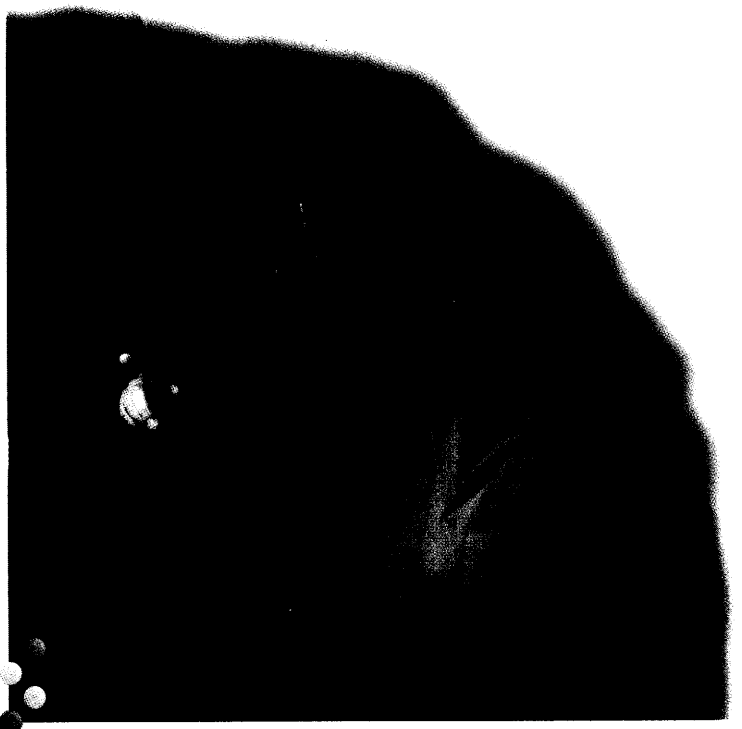

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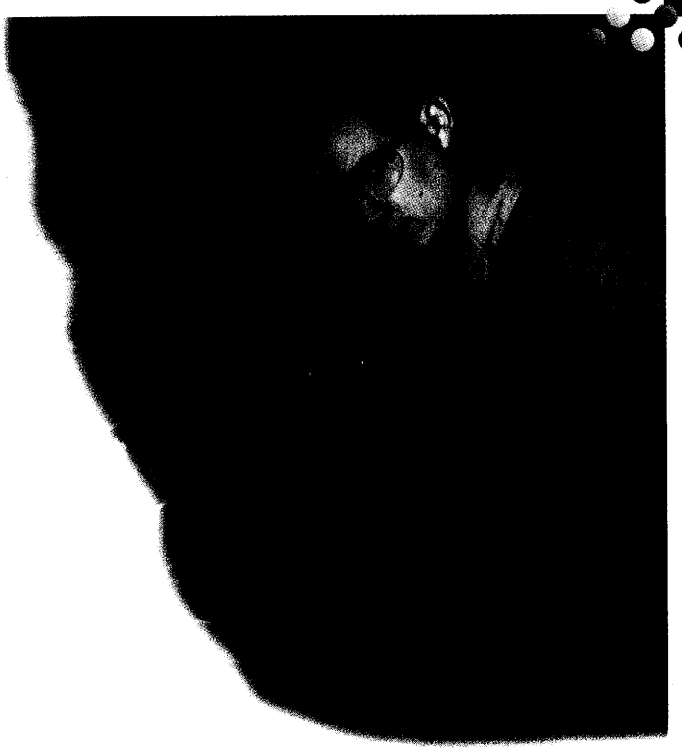

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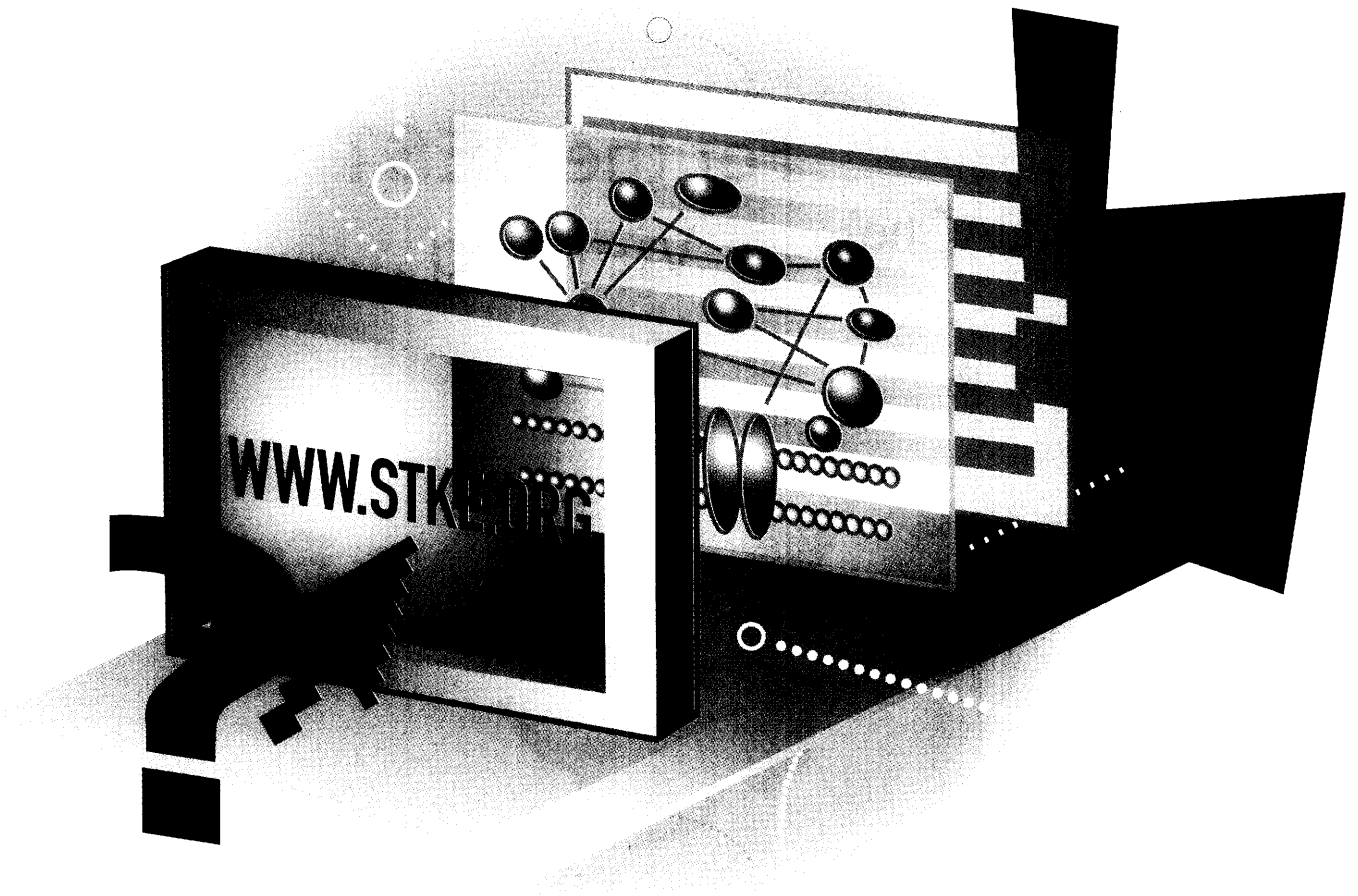

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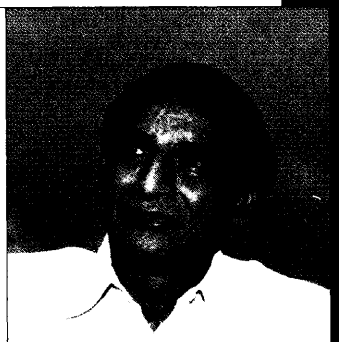

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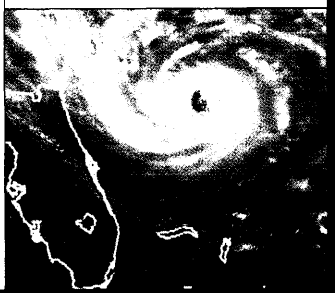

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Hyperefficient researchers institute and enforce strict organizational protocols and tracking procedures. The less organized may find their labs slipping into borderline chaos. BOXIT, a database created in FileMaker Pro, is a program designed for the latter group. It allows a lab to track their items conveniently. Designed to work on Macintosh or Windows computers, the database is available in versions that either work with FileMaker Pro or work independent of it.

BOXIT contains eight categories of items: antibodies, cells, strains, oligonucleotides, plasmids and hosts, stuff, protocols, and orders. Within each of these subsections are records with fields that are common to each category. For example, records in "Oligonucleotides" contain fields identifying to whom the item belongs, the gene locus on which it is used, for what techniques it is designed, the name of its primer partner (for PCR uses), the sequence, the melting temperature (T_m), and so forth. The program allows one to track oligos within boxes, towers, drawers, or even different refrigerators. In many place, BOXIT has been streamlined to provide pop-up menus, making entry of common values easy. Clicking in a field of a record can bring up more information—a property of the program that is its only drawback. There are so many options that one can sometimes get lost by following all the links.

Output options permit users to print lists of the contents of entire freezers, or just the individual records, as desired. Information can be imported from tab-separated databases, such as Excel. Export options include tab- or comma-delimited, DIF, SYLK, and even HTML tables. Through the program, users can print out order forms but BOXIT will not remind a user to order items as they are running out. Perhaps this will be an option in future versions of the program.

The best solution to lab disorder is a good system of tracking. BOXIT is a step in the right direction. **—Kevin Ahern**

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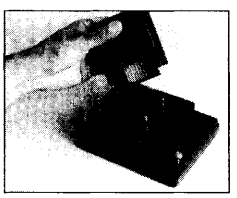

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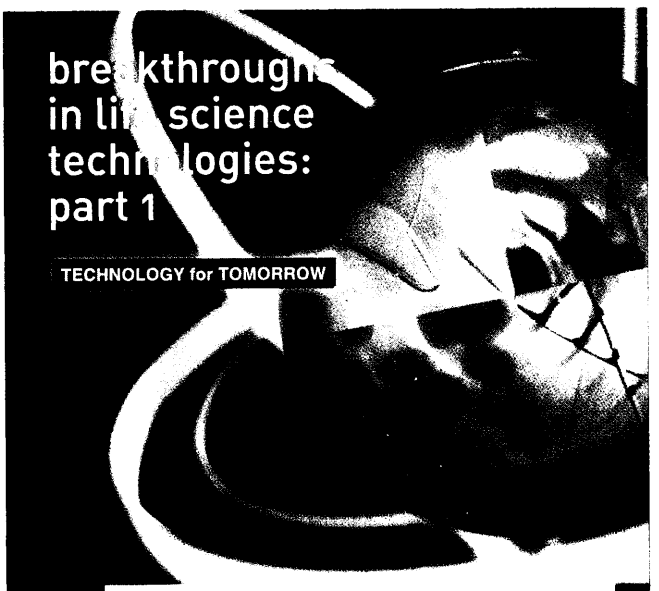

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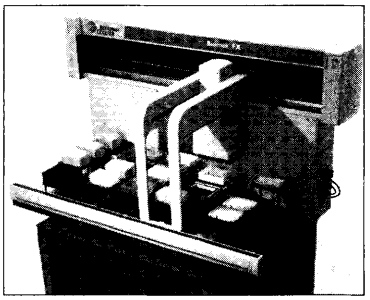

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