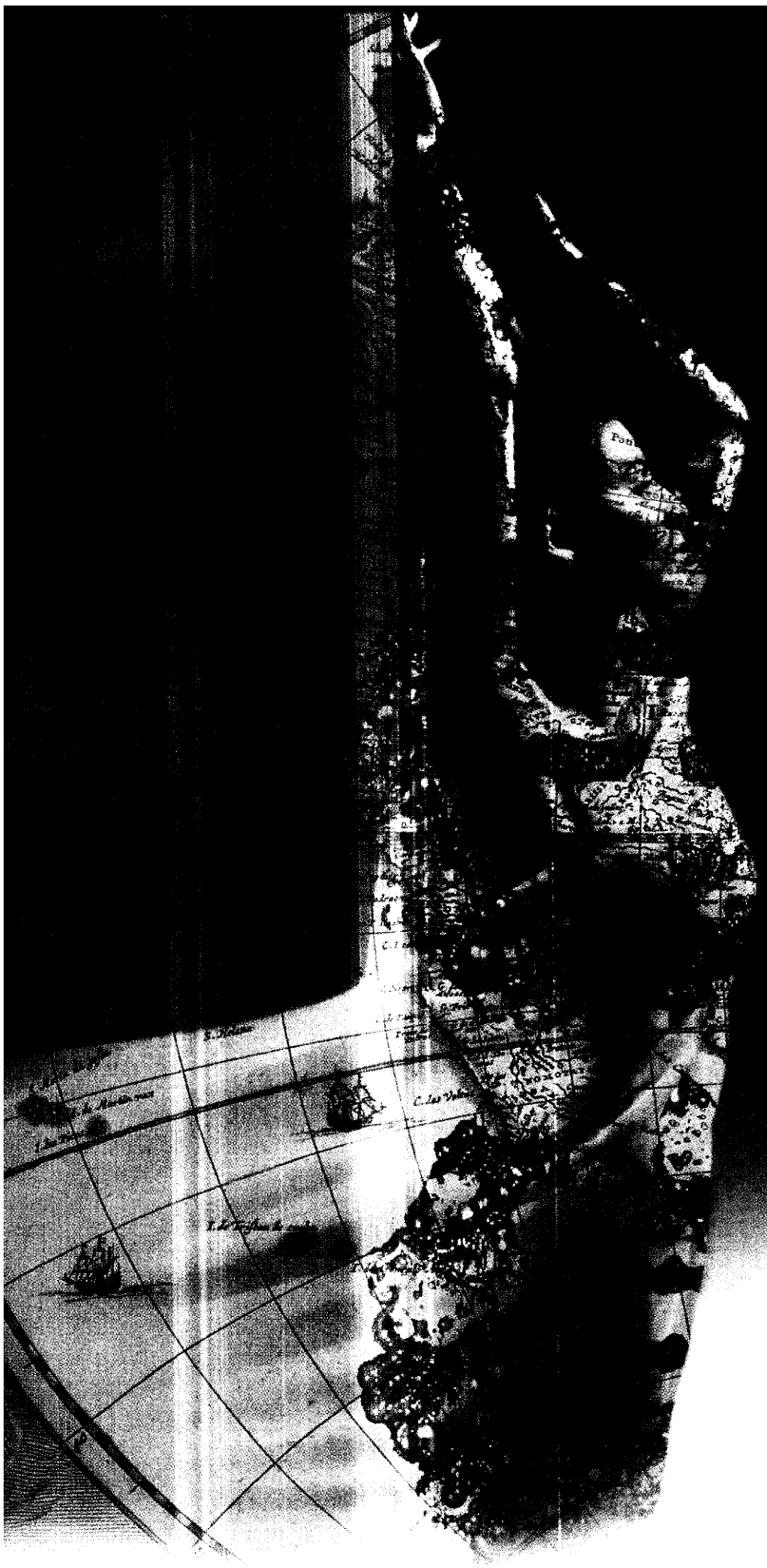
23 March 2001

Science

Vol. 291 No. 5512
Pages 2263–2502 $9

Carbohydrates and Glycobiology

American Association for the Advancement of Science



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Science

Volume 291 23 March 2001 Number 5512

2298
Containing foot-and-mouth disease

NEWS

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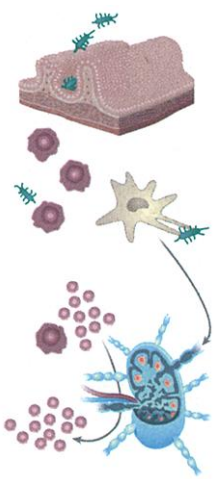

2323
Immune memories of pathogen invaders

2321
Parasite tales

RESEARCH

RESEARCH ARTICLE

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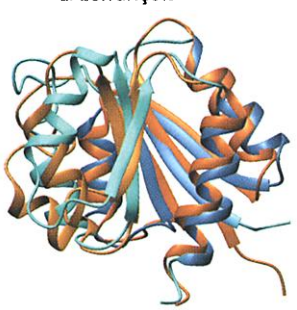


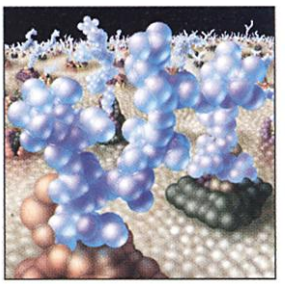
2429
Dynamics and activation

CARBOHYDRATES AND GLYCOBIOLOGY

NEWS

REVIEWS

VIEWPOINT



COVER 2357

The cell surface landscape is richly decorated with oligosaccharides anchored to proteins or lipids within the plasma membrane. Cell surface oligosaccharides mediate the interactions of cells with each other and with extracellular matrix components. The important roles that carbohydrates play in biology and medicine have stimulated a rapid expansion of the field of glycobiology, the focus of the special section in this issue. [Illustration: Cameron Slayden]

2381
Still on the rebound

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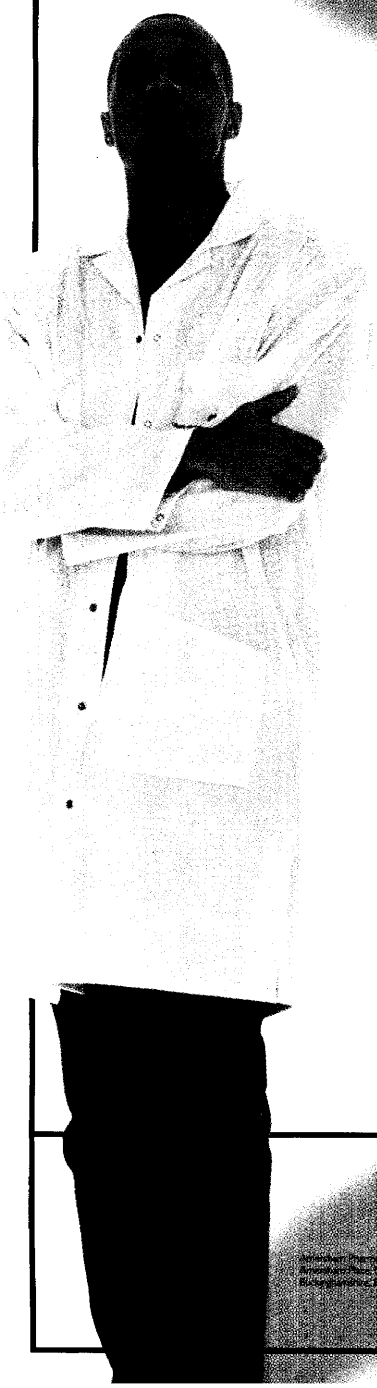

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Direct Detection of Galactic Halo Dark Matter B. R. Oppenheimer, N. C. Hambly, A. P. Digby, S. T. Hodgkin, D. Saumon
2293 Subluminous stars, or old, cool white dwarfs, have been detected in our galaxy and likely represent some of its missing dark matter.

Observation of Vortex Lattices in Bose-Einstein Condensates J. R. Abo-Shaeer, C. Raman, J. M. Vogels, W. Ketterle
2301 Large and ordered vortex lattices are obtained in a rotating Bose-Einstein condensate.

A Bose-Einstein Condensate of Metastable Atoms A. Robert, O. Sirjean, A. Browaeys, J. Poupard, S. Nowak, D. Boiron, C. I. Westbrook, A. Aspect
2301 Spin polarization is used to suppress inelastic collisions in an ultracold cloud of metastable helium, forming a Bose-Einstein condensate.

TECHNICAL COMMENTS

Noble Gases in Mantle Plumes

Drawing on experiments that showed, in mantle and plume-derived rocks, neon isotope ratios indistinguishable from those of meteorites, Trieloff *et al.* (Reports, 12 May 2000, p. 1036) argued that Earth's solar-type rare gas inventory likely was acquired "during accretion from small planetesimals previously irradiated by solar wind" rather than directly from the solar nebula. Ballentine *et al.* suggest that the signal found by Trieloff *et al.* may reflect limitations of the ball mill crushing technique they employed, as other release techniques have revealed higher neon isotope ratios, and that the data reported by Trieloff *et al.* do not show an expected correlation with argon isotope data. Trieloff *et al.* respond that the high neon isotope ratios cited by Ballentine *et al.* represent "the high-value tail of a statistical distribution," the Gaussian center of which agrees well with their reported value, and that the argon isotope data can be reconciled with their neon data when all available popping rock data are considered.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/291/5512/2269a

SPECIAL FEATURES www.sciencemag.org/feature/data/carbohydrates.shl

Carbohydrate Chemistry and Glycobiology: A Web Tour

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Review: Intracellular Signaling by the Killer Immunoglobulin-Like Receptors (KIR) and Ly49 D. W. McVicar and D. N. Burshtyn

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Canada: Picking Stocks C. Boulakia

In our "Financial Planning for Scientists" column, we explore some common methods for evaluating and picking stocks that should work no matter what the markets are doing.

US: A Match Made in Heaven M. Sincell

In this month's "Survive and Thrive," find out how to identify the perfect Ph.D. advisor—do your research and trust your instincts.

UK: Kingdom Come K. Urquhart

An interview with the U.K.'s new Chief Scientific Adviser, Professor David King, who talks salaries and offers advice for early caree · scientists.

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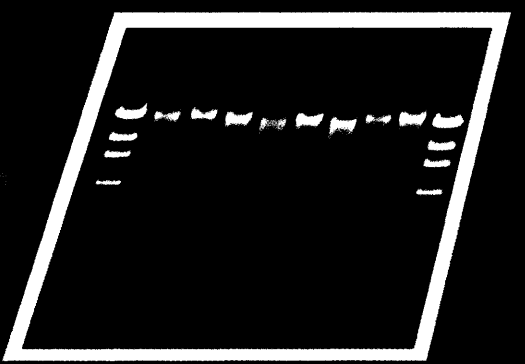

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THIS WEEK IN Science

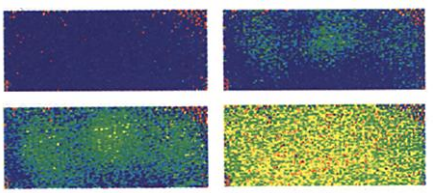
edited by Phil Szuromi

Squeezing Condensates

Measurements in quantum mechanics are limited by the Heisenberg uncertainty relations, but these limits hold as a time average. It is possible to "squeeze" quantum-mechanical states so that the uncertainty limit for an observable, such as position, is beaten periodically. Quantum optics has created squeezed states for photons, and because the de Broglie wavelengths associated with atoms are much shorter than those of photons, the creation of squeezed atomic states should have an impact on areas such as high-resolution interferometry. Orzel *et al.* (p. 2386; see the news story by Voss and the related *Science* Express reports by Abo-Shaeer *et al.* and Robert *et al.*) show that the number states of atoms in a Bose-Einstein condensate can be squeezed, thus greatly reducing the variance in the number of atoms trapped in a particular well.

2395 Potential for Turing Patterns

Chemical waves and patterns observed in solution for certain reactions can be explained by a mechanism proposed in the early 1950s by Turing. A critical ingredient for pattern formation in solution is that one species must diffuse much more rapidly than the others—a somewhat difficult requirement for small molecules. Recent theoretical work has suggested that reactions at electrodes could also exhibit Turing-type patterns if the electrode potential took the place of the rapidly diffusing species and if field-induced migration replaced diffusion. Li *et al.* (p. 2395) now experimentally verify this theory for the reduction of periodate on gold electrodes in the presence of camphor, an organic molecule that can condense on the electrode at certain potentials and inhibit reduction. Such pattern formation should be observable in many electrochemical systems and could operate at biological membranes that exhibit potential gradients. ℰ



SOURCE: Y.-J. LI *ET AL.*

Catching Fennoscandia on the Rebound

Fennoscandia has been rising since the retreat of a massive glacier at the end of the Pleistocene. Although there are decades' worth of tide gauge records for the coast of Sweden and Finland, it has been difficult to extract an estimate of sea level rise by subtracting the ground surface uplift. Milne *et al.* (p. 2381) completed a 7-year global positioning system (GPS) campaign and combined these land-surface deformation measurements with the tide gauge records to derive a more accurate regional sea level rise of 2.1 ± 0.3 millimeters per year. This value is consistent with the global average and relevant to models of global warming. They also derived a refined viscosity for the mantle and an elastic thickness of the lithosphere, which are fundamental inputs for mantle convection and crustal flexure models.

Tiny Breaths

Marine biological control of the flux of CO_2 between the atmosphere and upper ocean is mediated by a combination of carbon uptake by phytoplankton photosynthesis, remineralization of organic carbon back to CO_2 (community respiration), and export of biogenic carbon to deeper waters. These processes also help control the distribution of biogenic carbon in the ocean. Rivkin and Legendre (p. 2398) show that there is an inverse relation between temperature and bacterial growth efficiency and that bacterial respiration accounts for nearly all of the community respiration. Besides their ecological implications, these results suggest that increases in sea surface temperatures will increase the proportion of the assimilated carbon that is remineralized and thus decrease the solubility of CO_2. These effects would then create a positive feedback between atmospheric CO_2 and temperature.

The Details of Taking a Hit

When a polycrystalline material is deformed, the individual grains change shape through the movement of dislocations and through grain rotation. Although many theories have been developed to model this process, experimental data for the actual grain evolution have been harder to obtain. Margulies *et al.* (p. 2392; see the Perspective by Heidelbach) used focused hard x-rays to map out the evolution of several grains in an aluminum sample undergoing tensile deformation. The results are inconsistent with the two classical models, those of Taylor and of Sachs, but provide needed inputs for more detailed numerical models.

Turning On (and Off) a Nanocrystal

Quantum-confinement effects in semiconductor nanocrystals should make the electronic and optical properties of these materials more sensitive to the injection of extra charge carriers compared to the corresponding bulk materials. Wang *et al.* (p. 2390) demonstrate how electrochemical injection of extra carriers in CdSe nanocrystals quenched their photoluminescence. The photoluminescence could be recovered by reversing the bias, thus illustrating the potential of such an effect for optoelectronic applications.

Turning Over a New Leaf

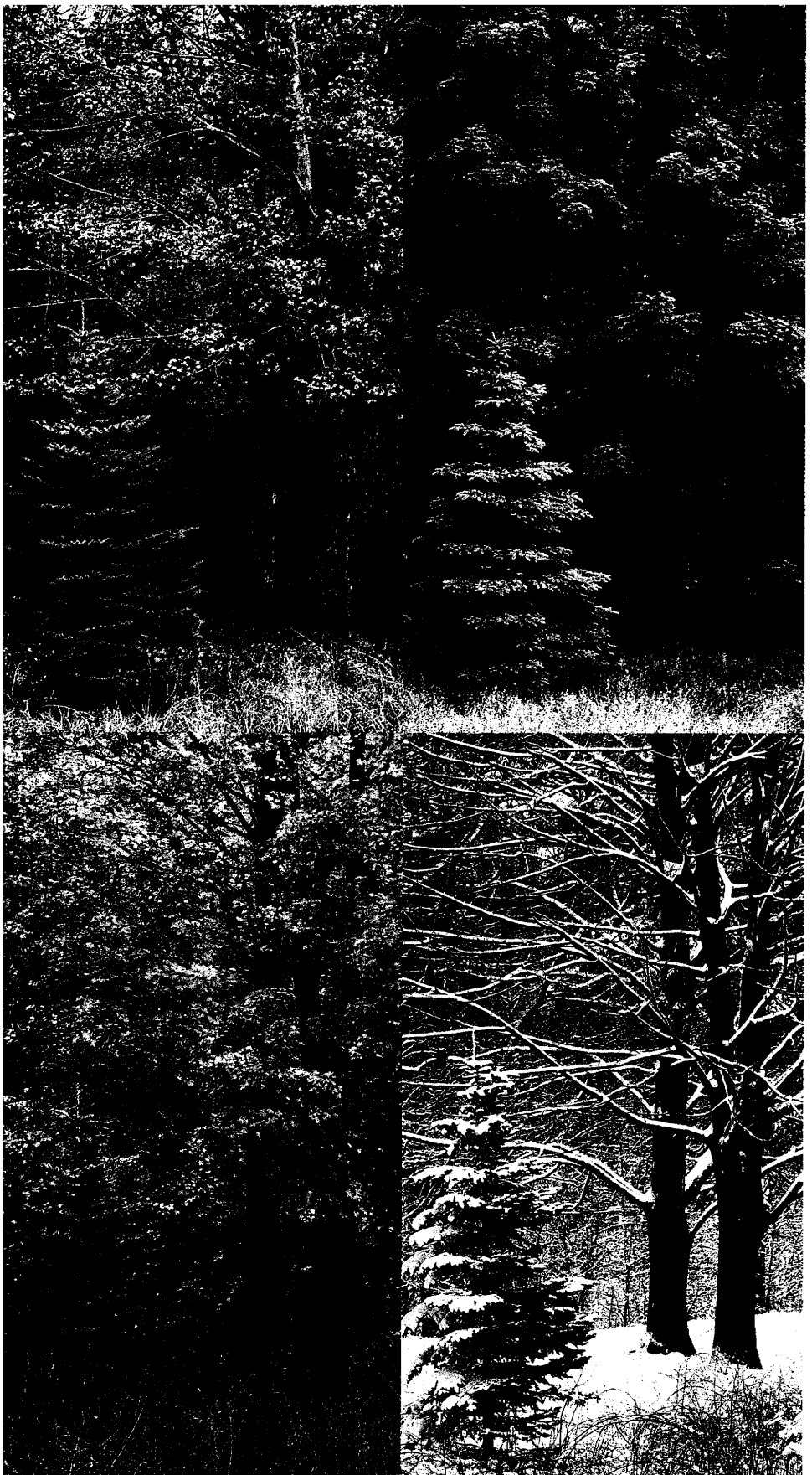
In plant development, the growing shoot changes from a juvenile, or reproductively incompetent state, to an adult state. Mechanisms governing this change were examined by Berardini *et al.* (p. 2405), who found that a protein termed squint, a chaperone-like protein, was involved. In mutants lacking squint protein, leaves exhibited adult properties early, but flowering time was unaffected. Surprisingly, the mutant plants expressed elevated levels of another heat shock chaperone protein, Hsp90, but the response of seedlings to heat shock was not affected

Molecular Ruler or Measuring Cup?

At the base of the bacterial flagellum, there is a hook structure onto which the flagellin subunits are assembled. The total length of the flagellum itself is highly variable, but the hook structure is

ℰ Published online in *Science* Express

CONTINUED ON PAGE 2273



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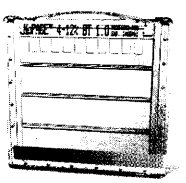

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remarkably homogenous in its size. In examining the mechanism for this relative constancy, Makishima *et al.* (p. 2411) found that rather than using a molecular ruler to determine hook length, *Salmonella* appears to regulate the amount of subunits secreted for hook assembly.

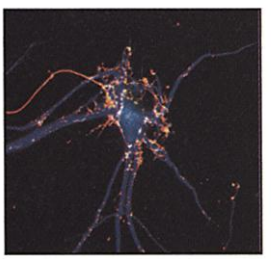
Having Trained Reserves in Place

Long after T cells first deal with a pathogen, small numbers persist so that immunological memory is not lost in the event of reinfection. Using fluorescently tagged antigenic tetramers, Masopust *et al.* (p. 2413; see the Perspective by MacKay and Andrian) tracked memory $CD8^+$ T cells and observed a marked preference of these cells for a range of nonlymphoid tissues, including the lung, liver, kidney, and gut. T cells from each site could respond immediately to antigen by producing interferon-γ and by killing target cells. Because most infections occur at such peripheral sites, these results emphasize the importance of having a ready supply of memory T cells that can be delivered to wherever the immunological action might be.

Learning and Relearning

Experimental extinction, the disappearance of a conditioned behavior after repetitive trials in the absence of the unconditioned stimulus, is not simply a kind of forgetting but rather a new learning phenomenon. To address the cellular mechanisms underlying this phenomenon, Berman *et al.* (p. 2417) studied conditioned taste aversion in the rat insular cortex. Both acquisition and extinction of conditioned taste aversion were impaired by inhibition of protein synthesis and involved β-adrenergic receptor activation. Acquisition, but not extinction, was decreased by antagonists of muscarinic receptors and *N*-methyl-D-aspartate receptors and also by mitogen-activated protein kinase inhibitors. There are thus clear differences between memory encoding and consolidation during retrieval.

Making the Transfer



The origin and movement of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) between nerve cells has been controversial. Kohara *et al.* (p. 2419) used BDNF tagged with green fluorescent protein to follow anterograde synaptic transport from axons of neurons to postsynaptic cells. This synaptic transport of the growth factor is absent when neuronal activity was blocked by tetrodotoxin and was enhanced after reduction of inhibition. These results constitute direct evidence for an anterograde, trans-synaptic transport of BDNF.

SOURCE: K. KOHARA *ET AL.*

Blocking a Survival Pathway

In several neurodegenerative diseases, proteins that bear expanded polyglutamine repeats aggregate, a process that somehow leads to the demise of neurons. Nucifora *et al.* (p. 2423) studied the interaction of aberrant versions of huntingtin (which is affected in Huntington's disease) and atrophin (which is affected in dentatorubral and pallidoluysian atrophy) containing expanded polyglutamine repeats. These aberrant proteins avidly bound to the transcriptional coactivator CREB-binding protein (CBP) and prevented the transcription of target genes known to be crucial for neuronal survival.

Exploiting a Preexisting Condition

Phosphorylation is usually assumed to regulate signal transduction by triggering a conformational switch. Volkman *et al.* (p. 2429; see the Perspective by Buck and Rosen) show that in the signaling protein NtrC, activation by phosphorylation involves stabilization of a preexisting conformation. Nuclear magnetic resonance measurements of backbone dynamics show that both active and inactive conformations are populated in unphosphorylated NtrC, with the inactive form favored. Phosphorylation shifts the equilibrium far toward the active conformation so that conformational exchange virtually disappears. Thus, allosteric regulation of single domains may be important in signal transduction.

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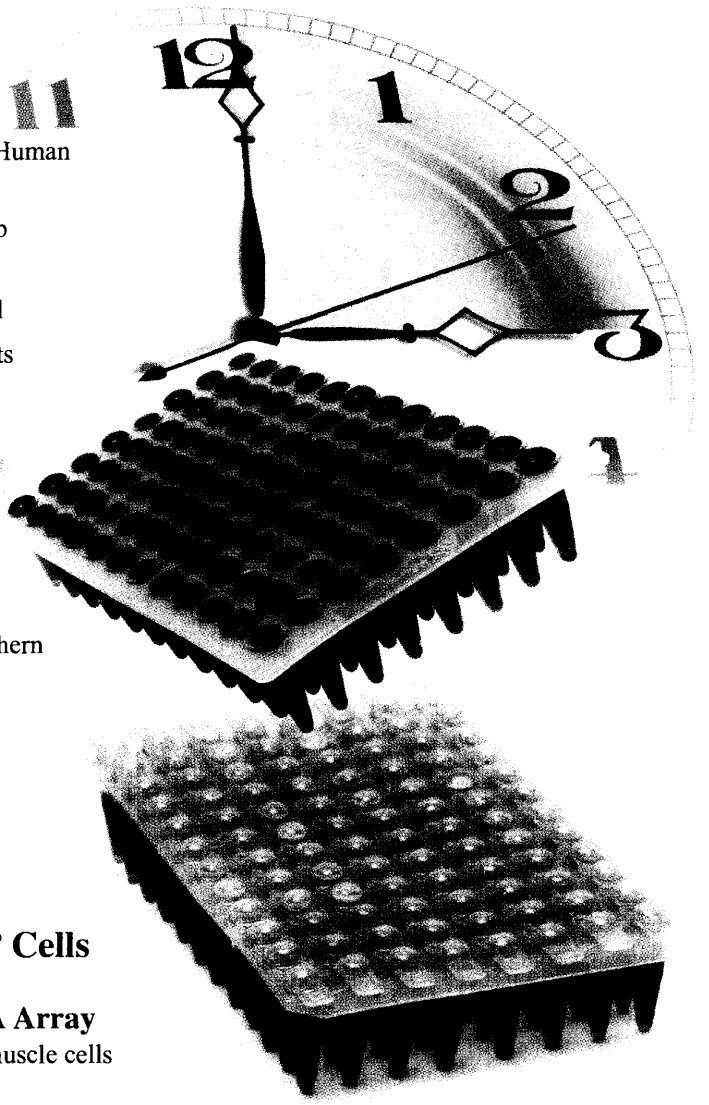

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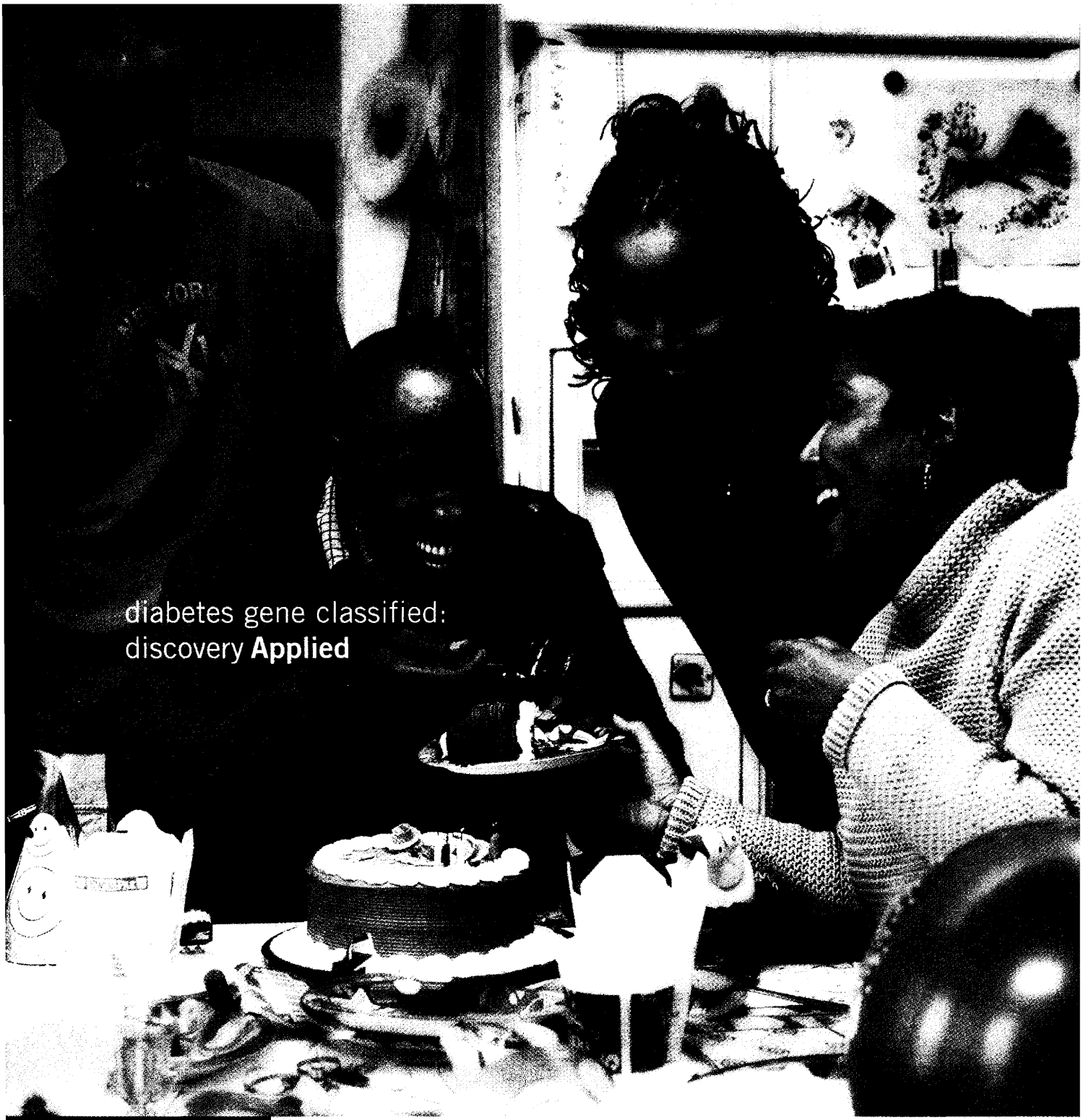

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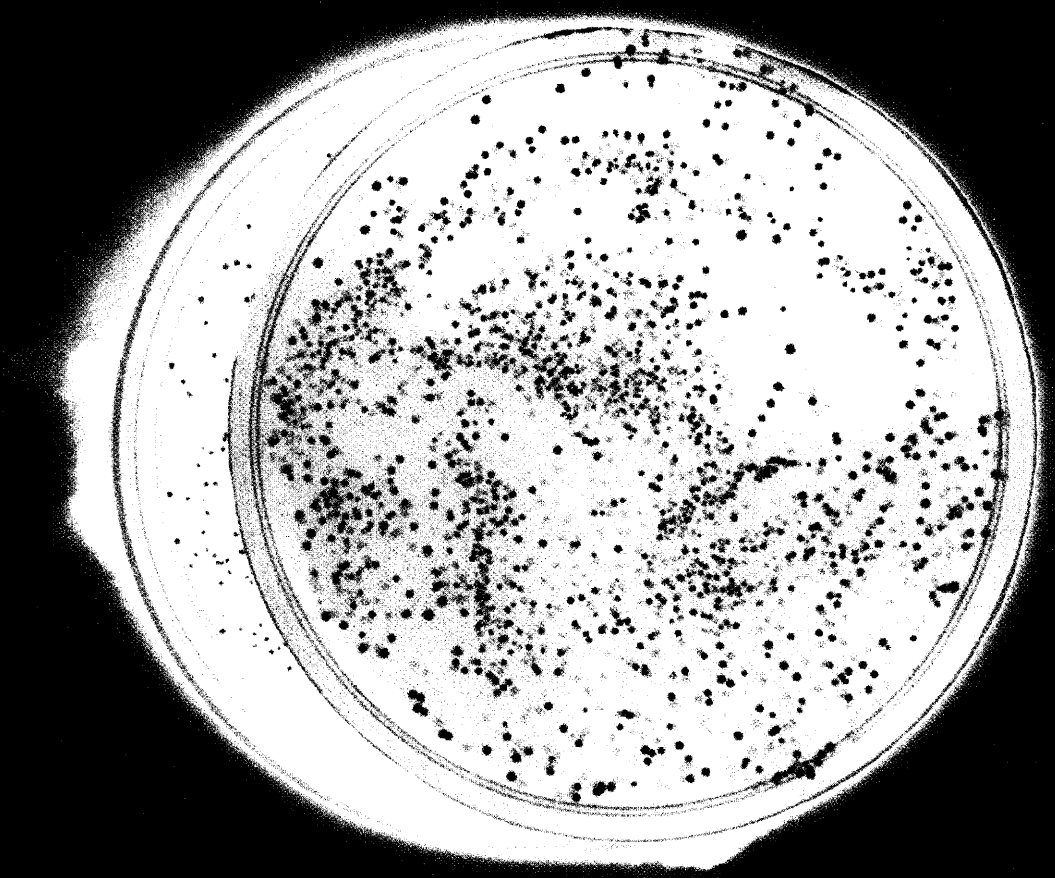

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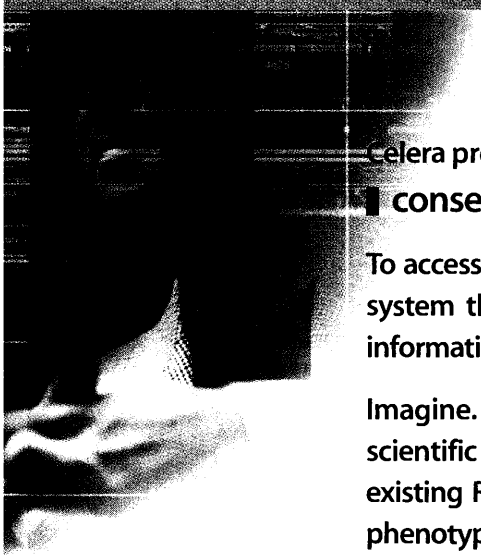

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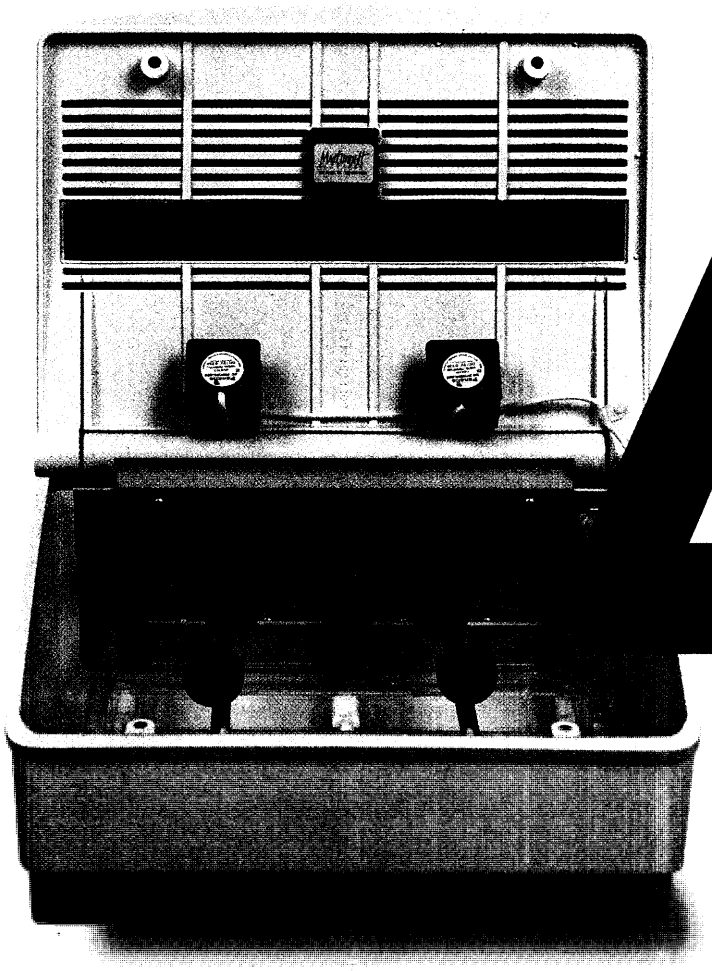

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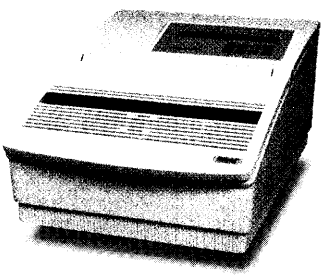

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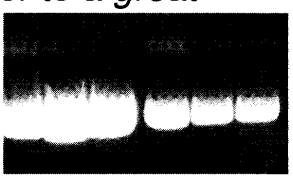

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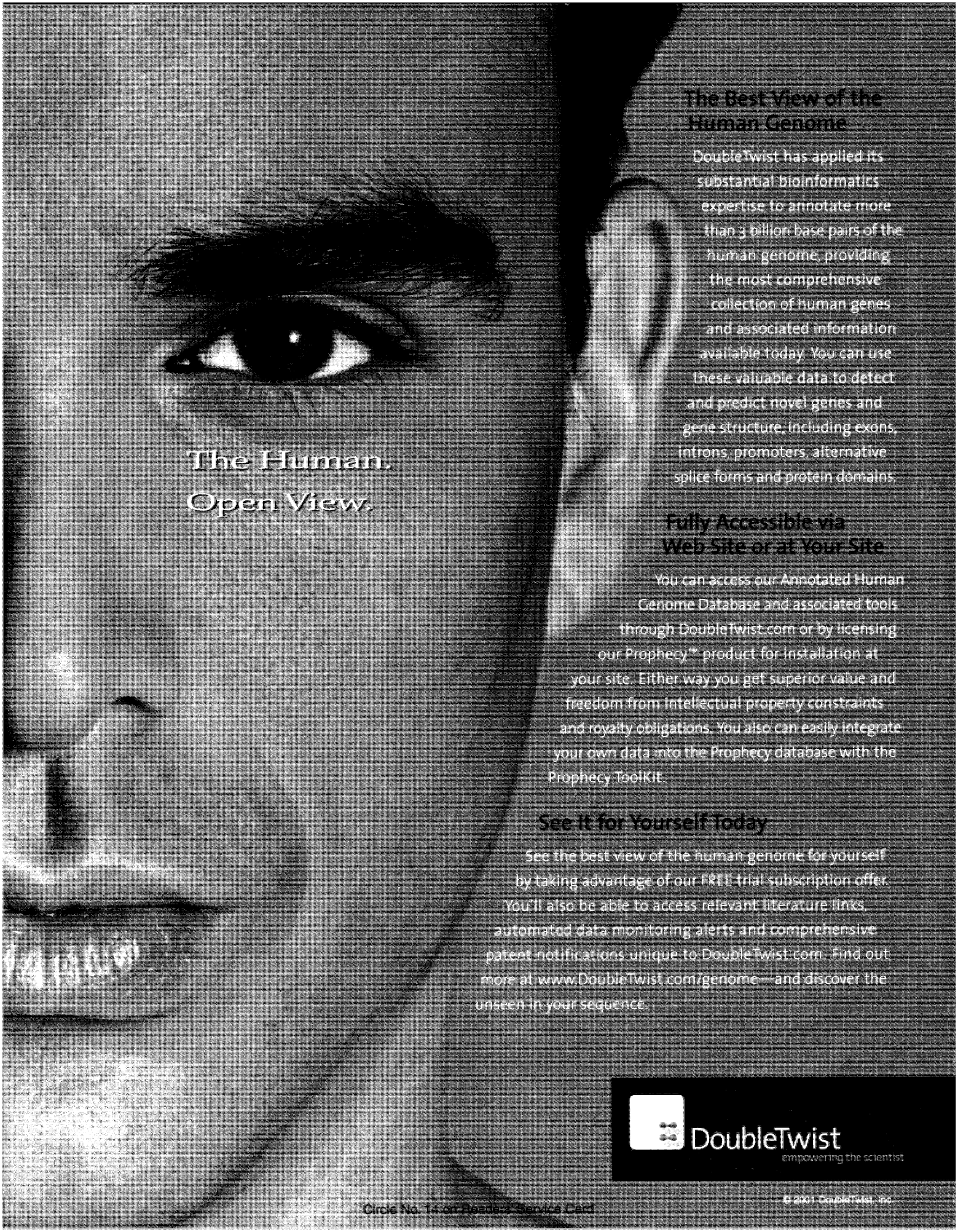

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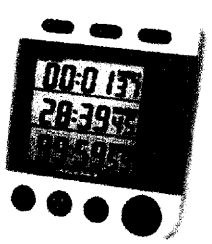

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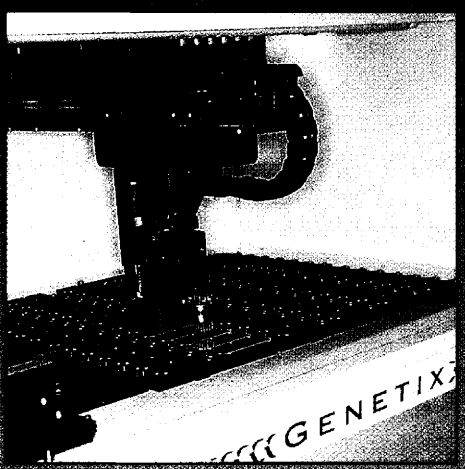

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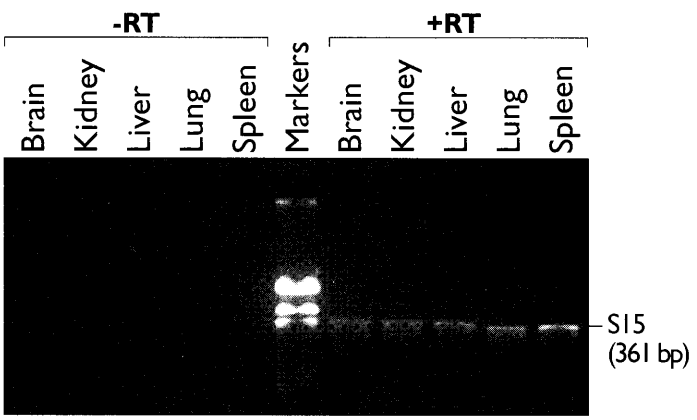

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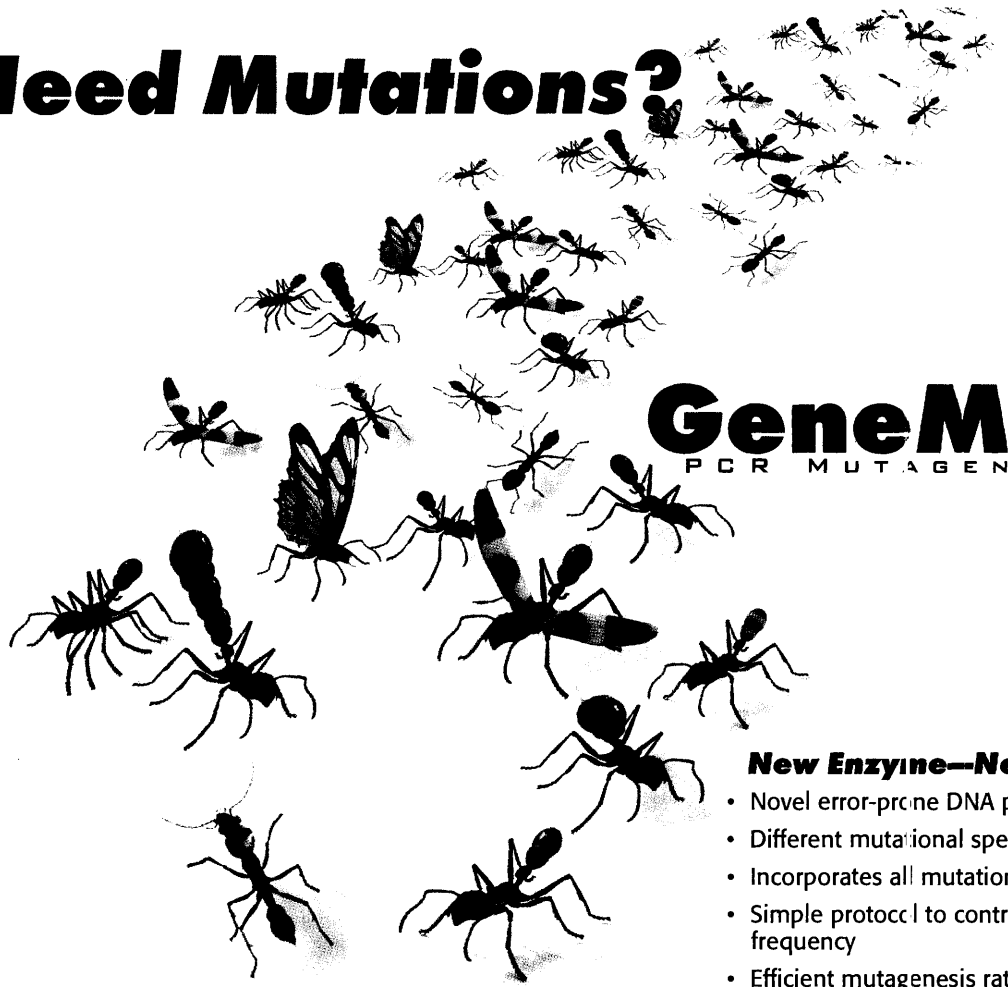

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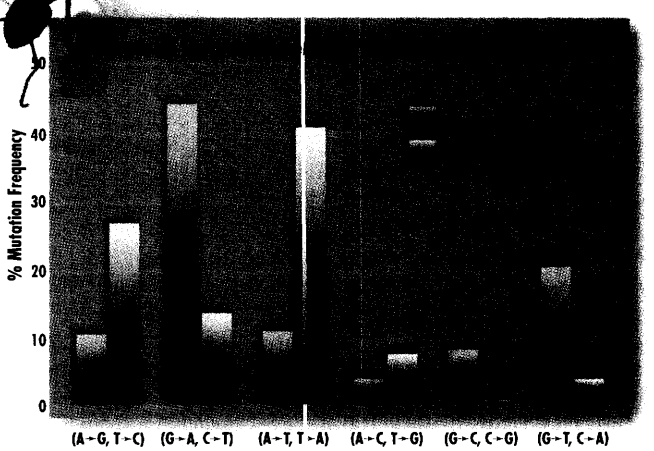

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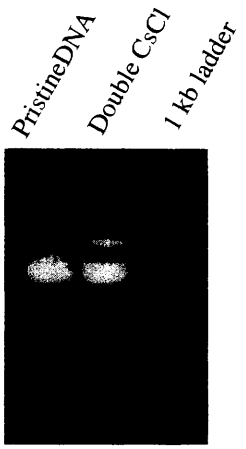

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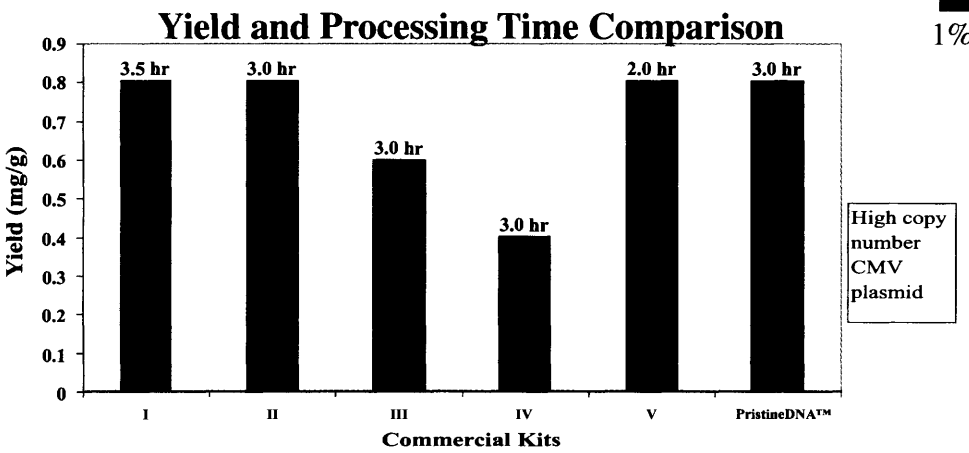

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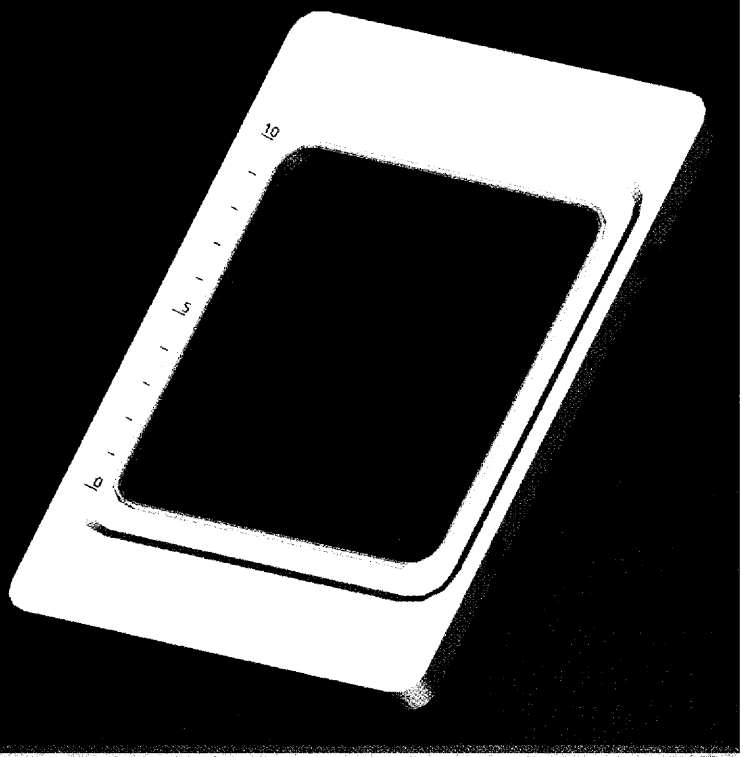

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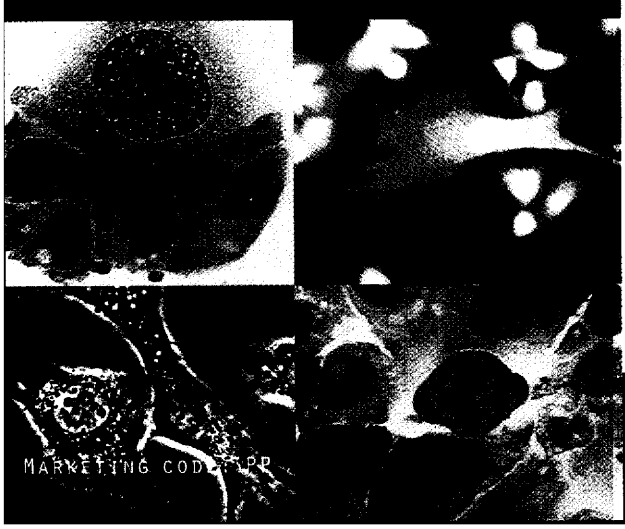

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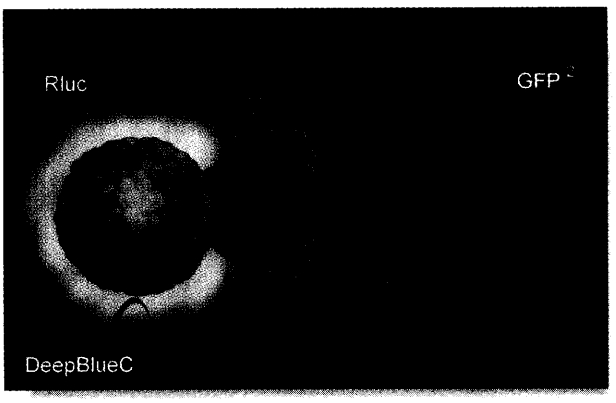

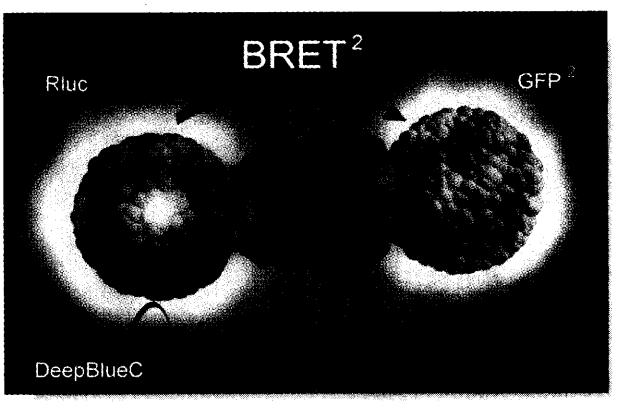

Interaction between two proteins respectively fused to Rluc and GFP² brings them into close proximity, allowing energy transfer and GFP² light emission.

Advanced BRET² technology

- Whole cell functional assays
- Proximity interaction based on fully licensed *Renilla* luciferase† and GFP²*
- Bioluminescence, no excitation required
- Ratiometric measurement
- Large selection of vectors for easy assay assembly
- DeepBlueC™, new coelenterazine for a large Stokes shift

...for Proteomics applications

- Developed for mammalian cells
- Monitor protein-protein interactions (activation or inhibition)
- Measure interactions in all cell compartments
- Validate yeast 2-hybrid results
- Screening (HTS)
- Use our Gene2Screen™ contract services for your cell line development

The new Multimode Fusion Microplate Analyzer from Packard BioScience is optimized to detect all BRET² chemistries.

† *Renilla* Luciferase is produced and sold under license, U.S. Patent Nos. 5,292,658 & 5,418,155; CA Patent No. 2,105,984; EPO Patent No. 91 908378.2; JP Patent No. 506544/91 exclusively licensed from Chemicon International, Inc.

* GFP² is produced and sold under license, U.S. Patent Nos. 6,020,192; 5,968,750 & 5,874,304.

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For more information on BRET² contact your local Packard BioScience office or visit our Web site at

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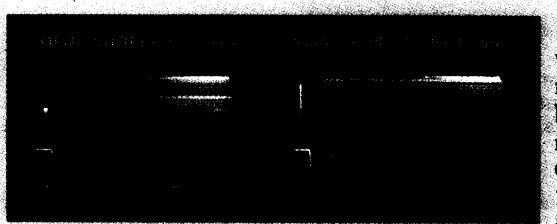

You asked for it and like our One Cage™ System, Super Mouse 750™ was designed to incorporate the same modular features into a cage exclusively for mice.

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*Guide for the Care and Use of Laboratory Animals. Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, 1996.

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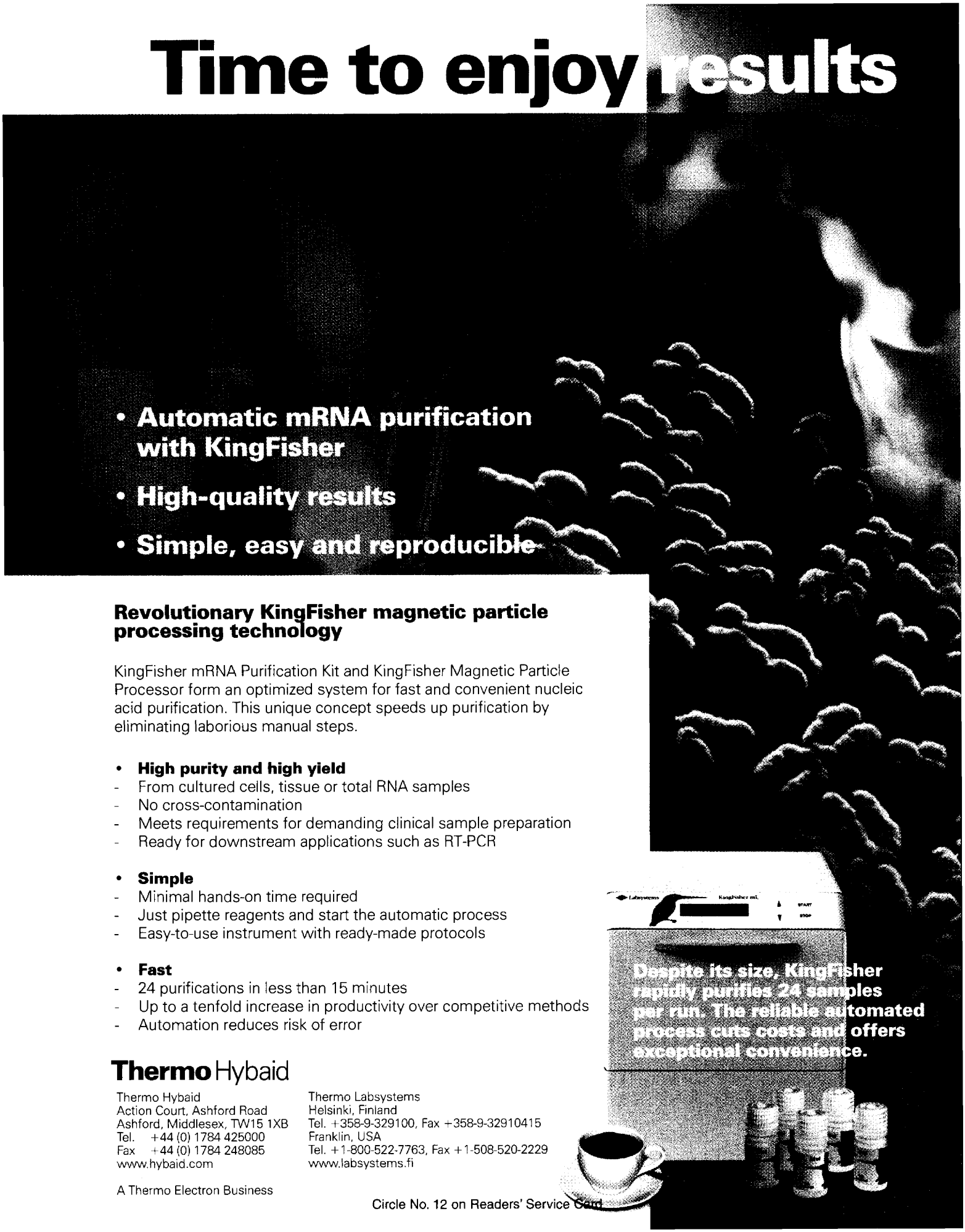

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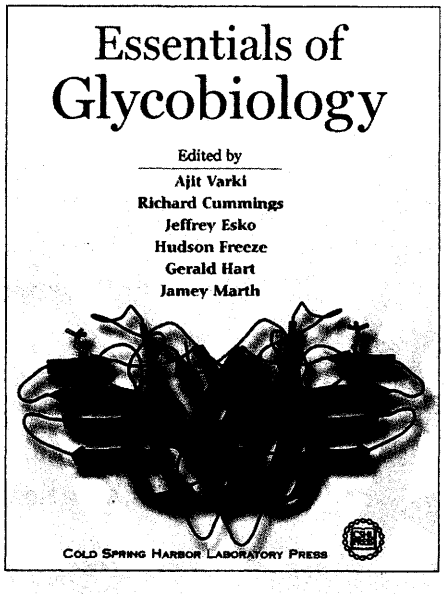
Essentials of Glycobiology



Edited by Ajit Varki, *University of California, San Diego;* Richard Cummings, *The University of Oklahoma, Oklahoma City;* Jeffrey Esko, *University of California, San Diego;* Hudson Freeze, *The Burnham Institute;* Gerald Hart, *Johns Hopkins University School of Medicine;* Jamey Marth, *University of California, San Diego*

Foreword by Stuart Kornfeld, *Washington University School of Medicine, St. Louis*

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Sugar chains (glycans) are often attached to proteins and lipids and have multiple roles in the organization and function of all organisms. They participate in activities as diverse as protein folding, leukocyte physiology, and microbial pathogenesis. Genetic defects in their assembly are at the root of a growing list of human diseases. *Essentials of Glycobiology* is an ideal gateway to the understanding of glycans, and is the first textbook approach to describing their biogenesis and function. Written and edited by glycobiologists with experience in both teaching and research, this volume will be invaluable for students and established investigators in developmental biology, cell biology, neuroscience, immunology, and biochemistry, who need a complete yet concise introduction to this burgeoning field.

— Here's what the reviewers have to say:

"*Essentials of Glycobiology* fills a longstanding need for a basic textbook in glycobiology and will be most welcome to many scientists who give courses in glycobiology to undergraduate and graduate students. The book is aimed primarily at the relative novice who wishes to obtain a solid introduction to this very complicated and rapidly growing field. In this respect the book is unique and differs from the many advanced reviews, monographs and books that have preceded it. However, the book summarizes much of the current state of the art in glycobiology, although often in a rather abbreviated format, and will therefore also be of value to the expert."

—*Carbohydrates in Europe*

"*Essentials of Glycobiology* should be required reading for any biologist aspiring to understand the molecular basis of cell and tissue function. It provides an excellent introduction into carbohydrate biology for a novice, and it will be useful for university level teachers seeking additional breadth to their courses in biochemistry or cell biology.... *Essentials of Glycobiology* is one of the first books to have the newly coined term 'glycobiology' in its title. The authors succeed in giving the word a specific context without being too limiting. They also make clear that through new model systems and recent methodological and conceptual advances, the field is gaining momentum and recognition. New investigators are entering with novel questions and insights. At a deeper level, this book may also help newcomers and other interested readers to appreciate the mind-set needed for thinking constructively about glycans, and for approaching this 'last frontier' of biochemistry and cellular biology."

—*Cell*

1999, 668 pp., illus., glossary, index
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Printed hardcover $99

ISBN 0-87969-559-5
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PCR clean-up

PCR clean-up.

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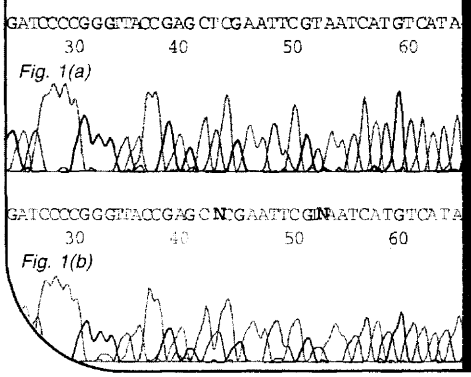
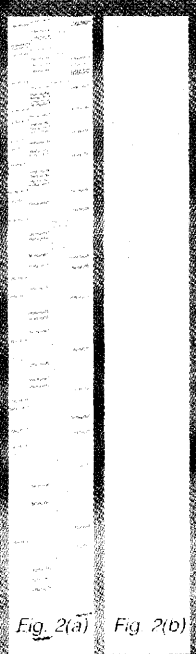
Fig.1. Fluorescent sequencing results of a 100 bp pUC18 PCR fragment sequenced with a -20 Fwd primer using the DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech). Data generated for USB by Cleveland Genomics (clevelandgenomics.com), a research service company. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up. Base miscalls in (b) are due to inherently low yields of short PCR products when using columns.

Fig. 2. Autoradiograms of a 20.7 kb Lambda PCR fragment sequenced with MBL202 Fwd primer using USB's Thermo Sequenase Radiolabeled Terminator Cycle Sequencing Kit. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up.





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† The Polymerase Chain Reaction (PCR) is covered by patents owned by Roche Molecular Systems and F. Hoffmann-La Roche Ltd. ‡Patent pending on product. The method of use is covered by the following patents: 5,756,285 and 5,741,676.

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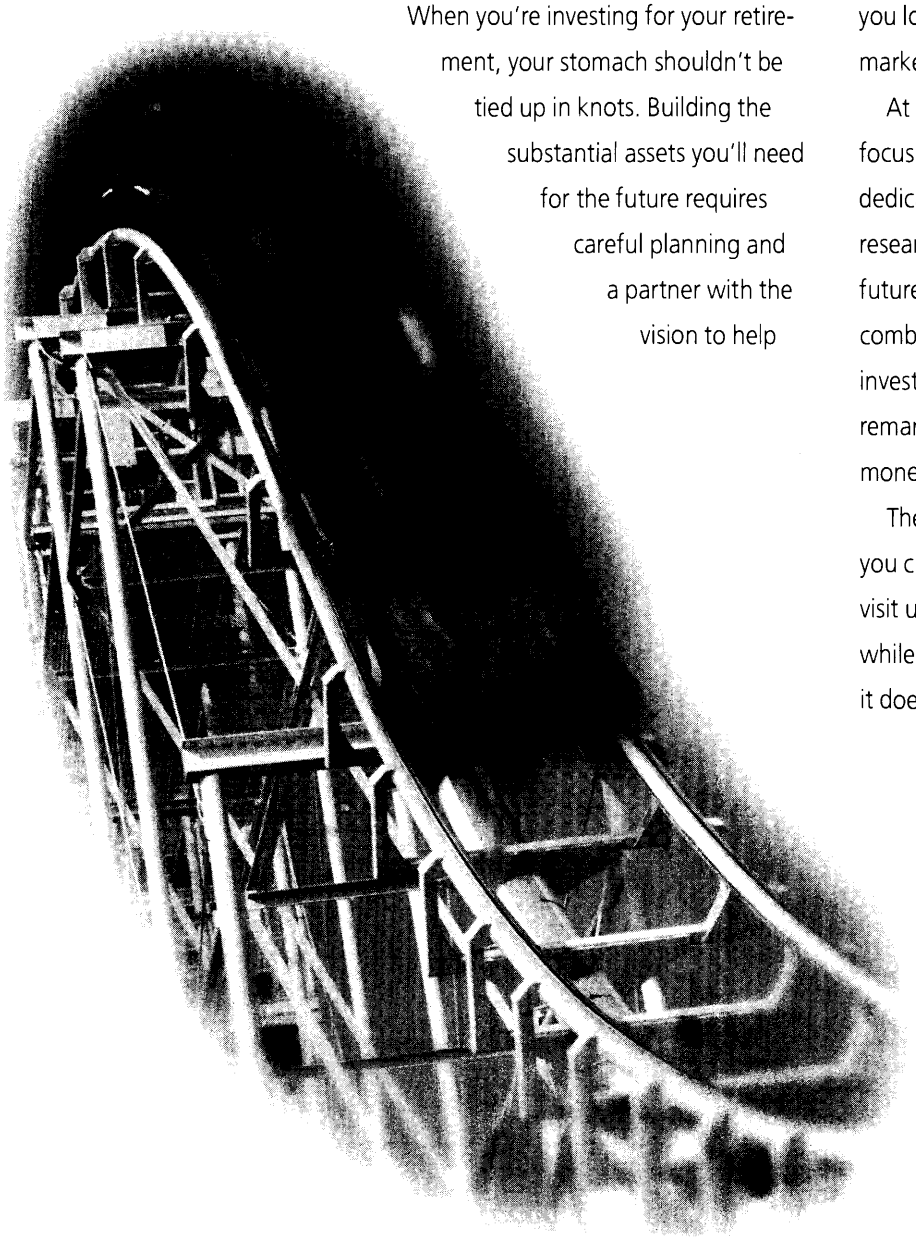

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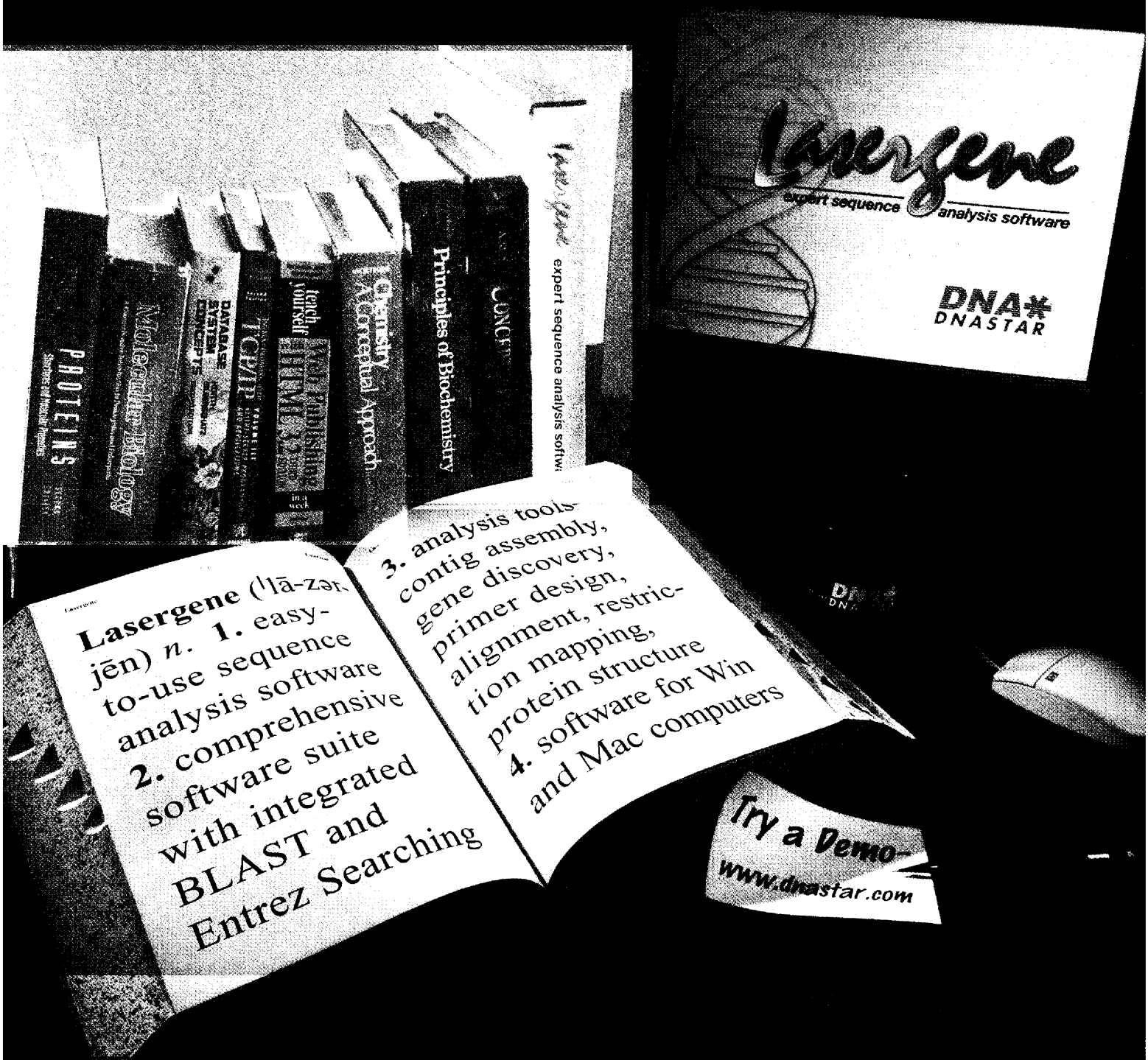

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