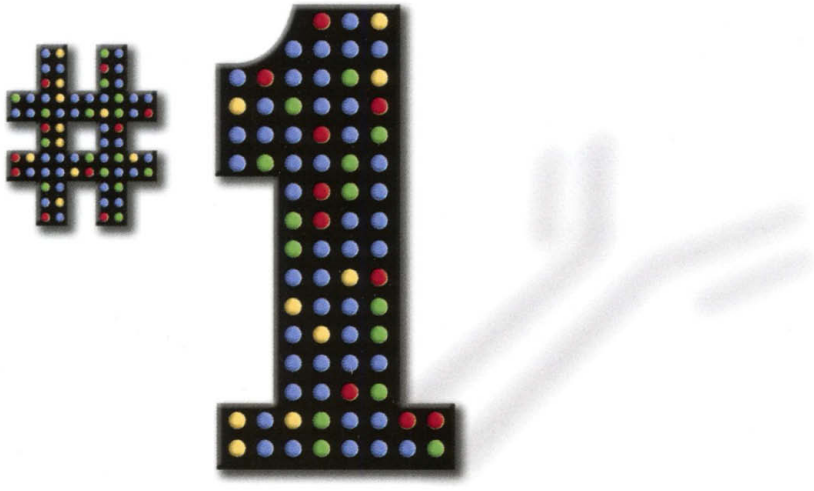
Drug Discovery | Research | Clinical Screening

Protein Microarrays



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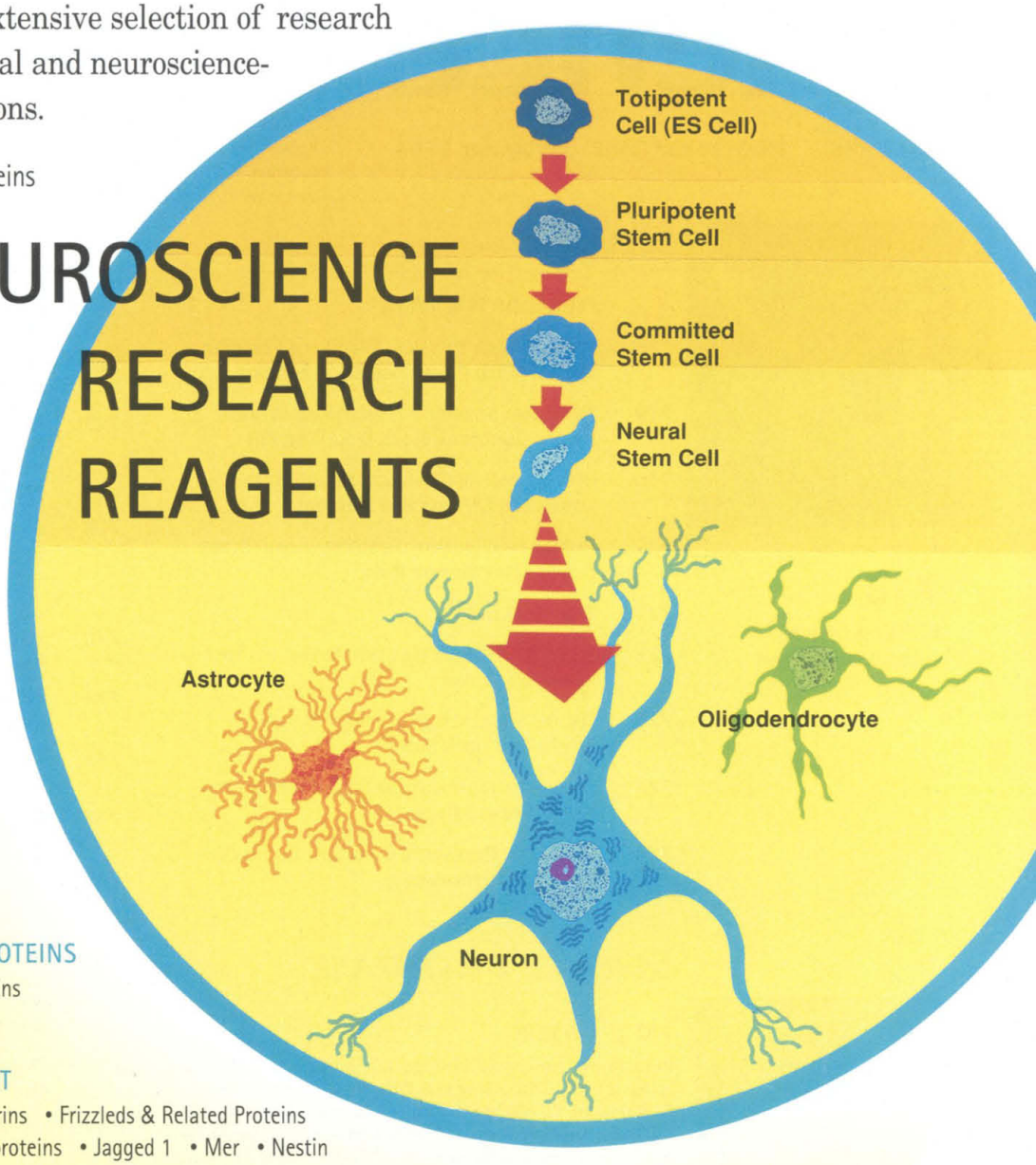

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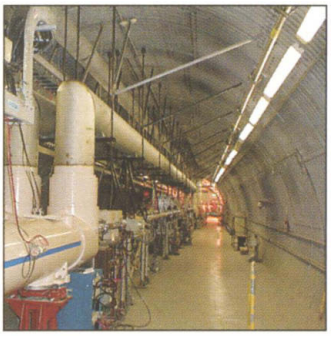
Science

Volume 298 25 October 2002 Number 5594



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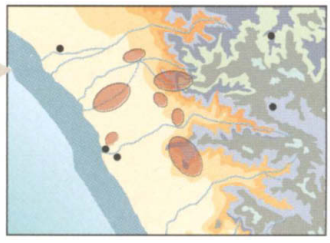


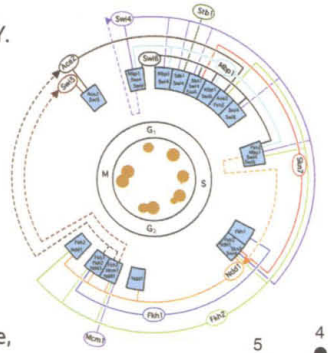
RESEARCH

THE DYNAMIC SYNAPSE

See also Science's *STKE* on p. 697.

COVER 769

The synapses that connect neurons in the nervous system are dynamic entities. The special section in this issue focuses on aspects of synapse formation and development and the dynamic processes that occur at synaptic connections throughout the lifetime of an individual. [Image: Kosi Gramatikoff]



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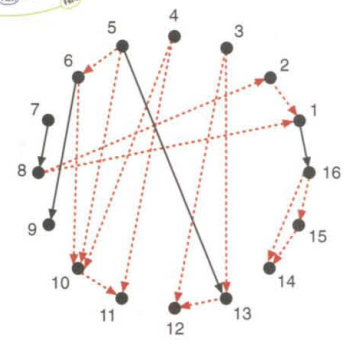
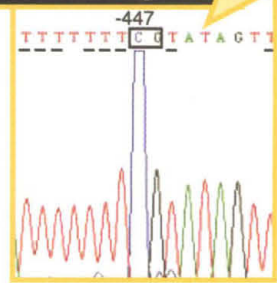
Finding structure in networks



New on *Science* Express Methylation-dependent silencing of neuronal genes



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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices.

Domestic individual membership and subscription (51 issues): $120 ($66 allocated to subscription). Domestic institutional subscription (51 issues): $390; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $85. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

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CONTENT HIGHLIGHTS AS OF 25 OCTOBER 2002

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SCIENCE EXPRESS

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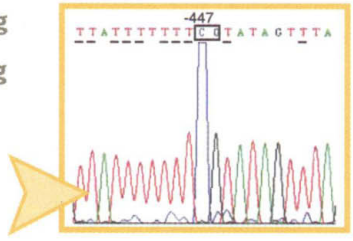
Corepressor-Dependent Silencing of Chromosomal Regions Encoding Neuronal Genes V. V. Lunyak *et al.*

The transcription factor REST/NRSF uses two different mechanisms to repress neuron-specific genes.



Molecule Cascades A. J. Heinrich, C. P. Lutz, J. A. Gupta, D. M. Eigler

An STM tip can nudge patterns of CO molecules on a copper surface into "hopping," a movement that can be engineered to perform one-time computational logic functions.

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career resources for scientists

UK: Leaving the Lab The CareerDoctor

Exploring the options for postdocs looking to leave bench science.

GERMANY: Private Universities—Better than the Rest? S. Steghaus-Kovac

How different are the facilities for researchers at Germany's private institutions?

CANADA: The Academic Consultant S. Cheung

Tools and tips for academics wishing to develop a complementary consulting business.

US: Coming Out in the Sciences—A Graduate Student's Perspective M. Hughes

For a gay student, the decision to come out to colleagues cannot be taken lightly.

SINGAPORE: BioMed-Singapore—A One-Stop Shop J. Wong

Singapore's national Web portal for the biomedical sciences is a great resource for students, scientists, and investors.

EUROPE: Serial Postdoc Killer? K. Urquhart

Does an EC directive mean the end of successive short-term contracts and the beginning of greater job security for academic researchers?

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NOTEWORTHY THIS WEEK: Deadly Giveaway R. J. Davenport

Protein linked to Parkinson's disease squanders clearance molecules.

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signal transduction knowledge environment

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769 Changing the glutamate receptor complement at the synapse contributes to long-term potentiation and long-term depression.

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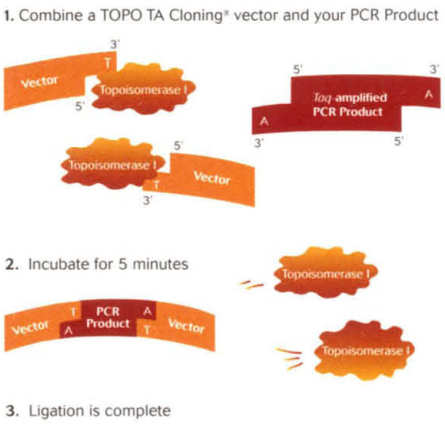

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THIS WEEK IN Science

edited by Phil Szuromi

Mediterranean Air Pollution

A large, international field measurement campaign—MINOS, the Mediterranean Intensive Oxidant Study—was conducted in 2001 to investigate anthropogenic contributions to environmental stresses affecting rainfall, ecosystems, agriculture, and drinking water supplies. Atmospheric chemistry–transport model simulations suggest that summertime tropospheric ozone is enhanced across the entire Mediterranean basin and contribute substantially to the radiative forcing of climate. Lelieveld *et al.* (p. 794) used a coastal station in north Crete and two aircraft to measure a wide range of gases, aerosols, radiation, and meteorological parameters. They conclude that European pollution of the Mediterranean lower troposphere has a strong impact on air quality and climate, particularly during summer, and that pollution in the free troposphere is largely determined by intercontinental transport, with upper tropospheric pollution from Asia by monsoons sometimes reaching into the stratosphere.

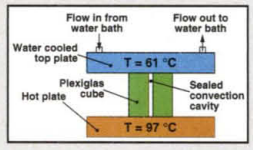
807

Shear Surprise

The elastic modulus of a material is a measure of how much tensile force is required to deform a sample and should generally be a good predictor of shear strength. However, first-principles calculations by Ogata *et al.* (p. 807) show that because of differences in atomic bonding, aluminum, which has a lower modulus than copper, can undergo larger strains before yielding and thus has the greater shear strength. External pressure is also shown to harden or soften the metals, depending on the crystal direction of the applied force, contrary to the common wisdom that such effects should be negligible.

And in Brevia ...

Continuous cycling in the polymerase chain reaction (PCR) amplification of DNA has been achieved by Krishnan *et al.* (p. 793) by using convection to shuttle the reaction volume through temperature zones associated with denaturation and annealing.



Magnetic Evolution in Manganites

The colossal magnetoresistance effect, in which the material's resistance drops rapidly in response to an applied magnetic field, is currently being developed for the applications in memory elements. Despite the complex phase diagram of such materials, a picture is developing based on the seeding, growth, and percolation of magnetic domains to explain the results. However, such an interpretation has so far relied on indirect experiments. Using magnetic force microscopy, Zhang *et al.* (p. 805) present direct evidence supporting the above scenario, but surprisingly find that the domains evolve at temperatures far away from the transition region.

CREDIT: ZHANG *ET AL.*

Second Time Around

Secondary organic aerosols particles form in the atmosphere through gas-phase reactions of volatile organic compounds associated with photochemical oxidant cycles. These aerosols have potentially negative health effects, contribute to the formation of visibility-reducing haze, and affect Earth's radiative balance. Jang *et al.* (p. 814) report that the formation of acidic surfaces on atmospheric organic aerosols can lead to large increases in secondary organic aerosol mass. Their experimental observations confirm that inorganic acids, such as sulfuric acid, catalyze particle-phase heterogeneous reactions of atmospheric organic carbonyl species. These reactions lead to a large increase in secondary organic aerosol mass and help stabilize the organic layers as the particles age. Climate models that do not take these reactions into account will likely underpredict radiative forcing caused by aerosols.

Robotic Eyes

Windblown dust may carry minerals such as iron that are often the limiting nutrient of productivity in many areas of the world ocean. Bishop *et al.* (p. 817 describe results obtained with a new generation of robotic ocean sensors. They deployed 3000 autonomous profiling floats, which can function for years at a time, in the North Pacific just prior to the storms that swept dust from the Gobi desert across the Pacific Ocean in April and May 2001. They present observations of biomass variability between the surface and 1000 meters depth that show a likely biotic response to fertilization of high nutrient–low chlorophyll waters by iron and other micronutrients in the Asian dust.

High But Not Dry

The peopling of the New World after deglaciation appears to have followed patterns that reflect the response of early settlers to environmental conditions. Nuñez *et al.* (p. 821; see the Perspective by Dillehay) describe the discovery and survey of many new early sites in the Atacama Desert region of northern Chile at elevations exceeding 4000 meters. Most of the sites are concentrated in caves or around paleolakes. Settlement of the region about 13,000 years ago apparently coincided with a change from arid to humid conditions, and sites were abandoned starting about 9500 years ago when aridity returned.

Transcriptional Networks and Their Relatives

Living cells are the product of gene expression programs involving regulated transcription of thousands of genes. Lee *et al.* (p. 799) used immunoprecipitation and microarray studies to build a global analysis of transcriptional regulatory networks in *Saccharomyces cerevisiae*. Patterns observed were characterized as motifs that were then combined by an automatic process into a net-

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CONTINUED ON PAGE 701

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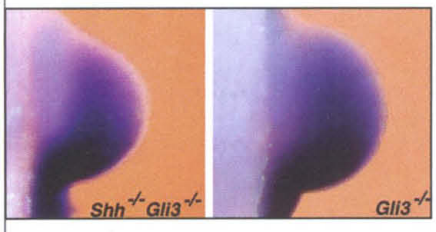
work structure. Such transcriptional regulation represents a network of interactions, and similar networks underlie apparently unrelated systems such as food webs and electronic circuits. To examine their fundamental design features, Milo *et al.* (p. 824; see the Perspective by Oltvai and Barabási) looked at local organizing principles of networks, expressed as motifs of how different interactors are joined, that occurred at more than random frequencies. Motifs shared by food webs had features that were not shared by transcription networks from yeast and from *Escherichia coli* or by electronic circuits, although similarities were seen in information-processing circuits.



CREDIT: TE WELSCHER *ET AL.*

Digital Programming

Digit duplications (polydactyly) are seen in mice with defects in the transcription factor *Gli3*, and excess digits can be induced by ectopic expression of *Sonic Hedgehog* (*Shh*) in mouse limb buds. It was previously thought that the *Gli3* mutant phenotype was caused by ectopic *Shh* expression. Using mouse genetics and molecular analyses, te Welscher *et al.* (p. 827) examine the relative mechanisms for *Shh* and *Gli3* in limb patterning. When Shh function was eliminated, the digits were severely truncated, whereas loss of *Gli3* function caused polydactyly. Mouse embryos lacking both *Shh* and *Gli3* were polydactylous. Digits can form by two completely different mechanisms, one of which is SHH dependent and another that is SHH independent (represented by the GLI3 mutation). Thus, a major function of SHH is to counteract the repressive action of GLI3.

Live Long and Reproduce

Insulin and other insulin-like growth factors signal through a pathway that involved phosphatidynlinositol 3-kinase and the forkhead transcription factors. This pathway is a critical regulator of life-span and reproduction in many organisms. Dillin *et al.* (p. 830) have now determined that in the nematode *Caenorhabditis elegans*, life-span can be regulated through this pathway only in the adult and reproduction only in the developmental phases. Thus, the long-standing notion that life-span can be lengthened only at the expense of reproductive fitness is almost certainly false.

Power Gliding

The role of the motor protein myosin A in the pathogenesis of *Toxoplasma gondii* has been examined by Meissner *et al.* (p. 837), who regulated the expression of a target protein to maintain the possibility of parasite propagation in the presence of a mutation of a gene required for invasion and parasite growth. They confirmed that myosin A is required to power the invasion of host cells and is a virulence factor in a mouse model system.

Strong Bones via Tailored Hormones

Interest in alternative preventive strategies against bone loss has intensified in light of the recent announcement of risks associated with hormone replacement therapy. Previous cell culture studies showed that estrogen and androgen protect bone through a mechanism distinct from the DNA-mediated mechanism underlying their effects on reproductive organs. Kousteni *et al.* (p. 843; see the news story by Miller) now show that a synthetic compound (estren) that mimics these "nongenotropic" effects can increase bone mass in estrogen- or androgen-deficient mice without adverse effects on reproductive organs.

A Gentler Treatment for Stroke

Although *N*-methyl-D-aspartate (NMDA) receptors play an important role in stroke, simply blocking them would lead to many unwanted side effects. Aarts *et al.* (p. 846) suggest a novel approach to treat ischemic brain injury without blocking NMDA receptors. They constructed peptides that bind to molecular domains governing the interaction of NMDA receptors with the postsynaptic density protein PSD-95. Normal synaptic activity and the subsequent postsynaptic calcium influx remain intact but deleterious downstream neurotoxic signaling events are inhibited.

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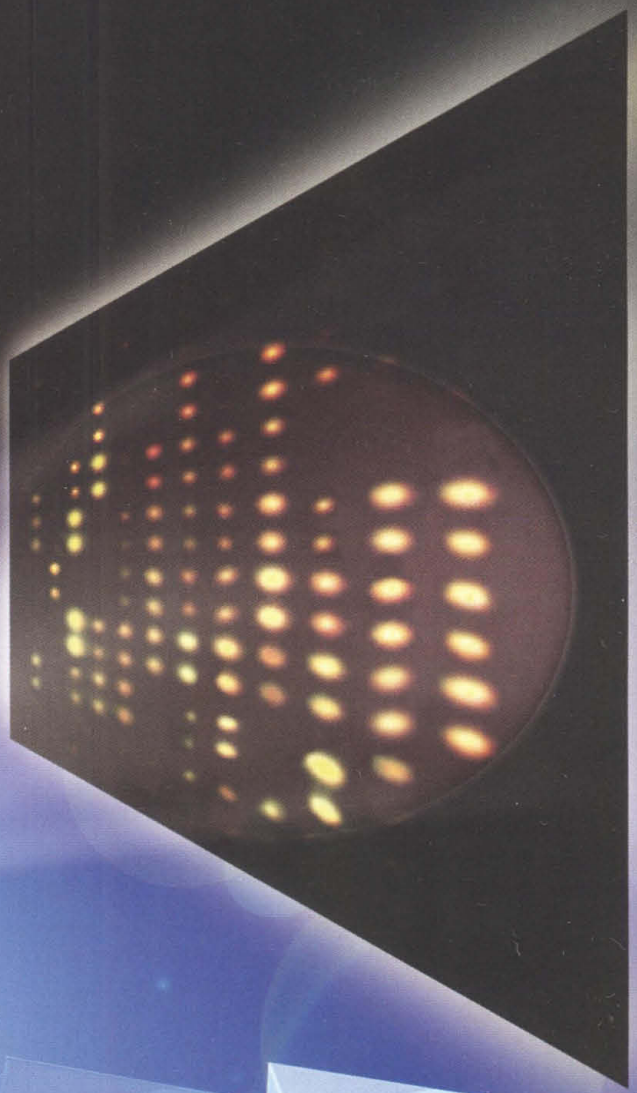

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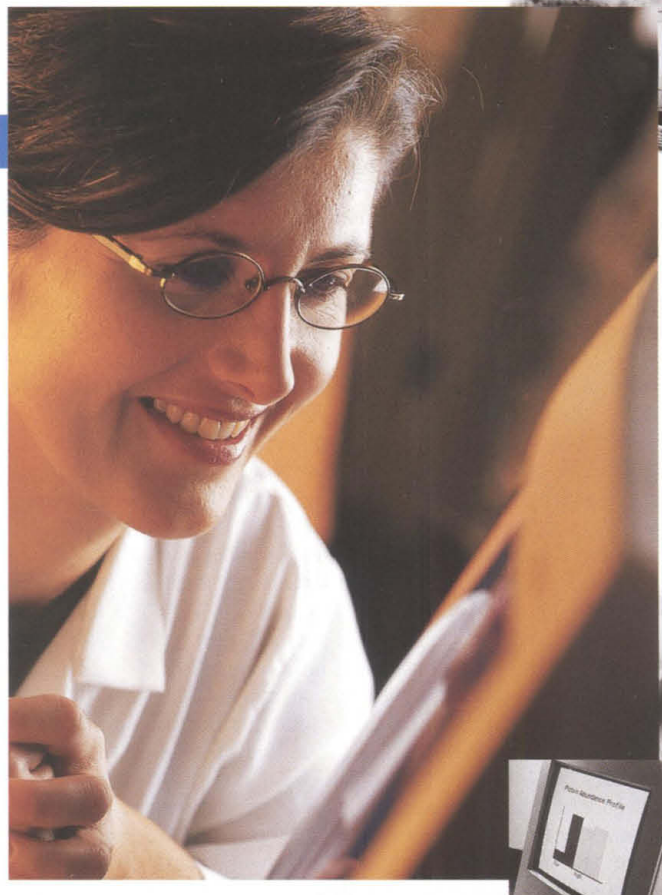

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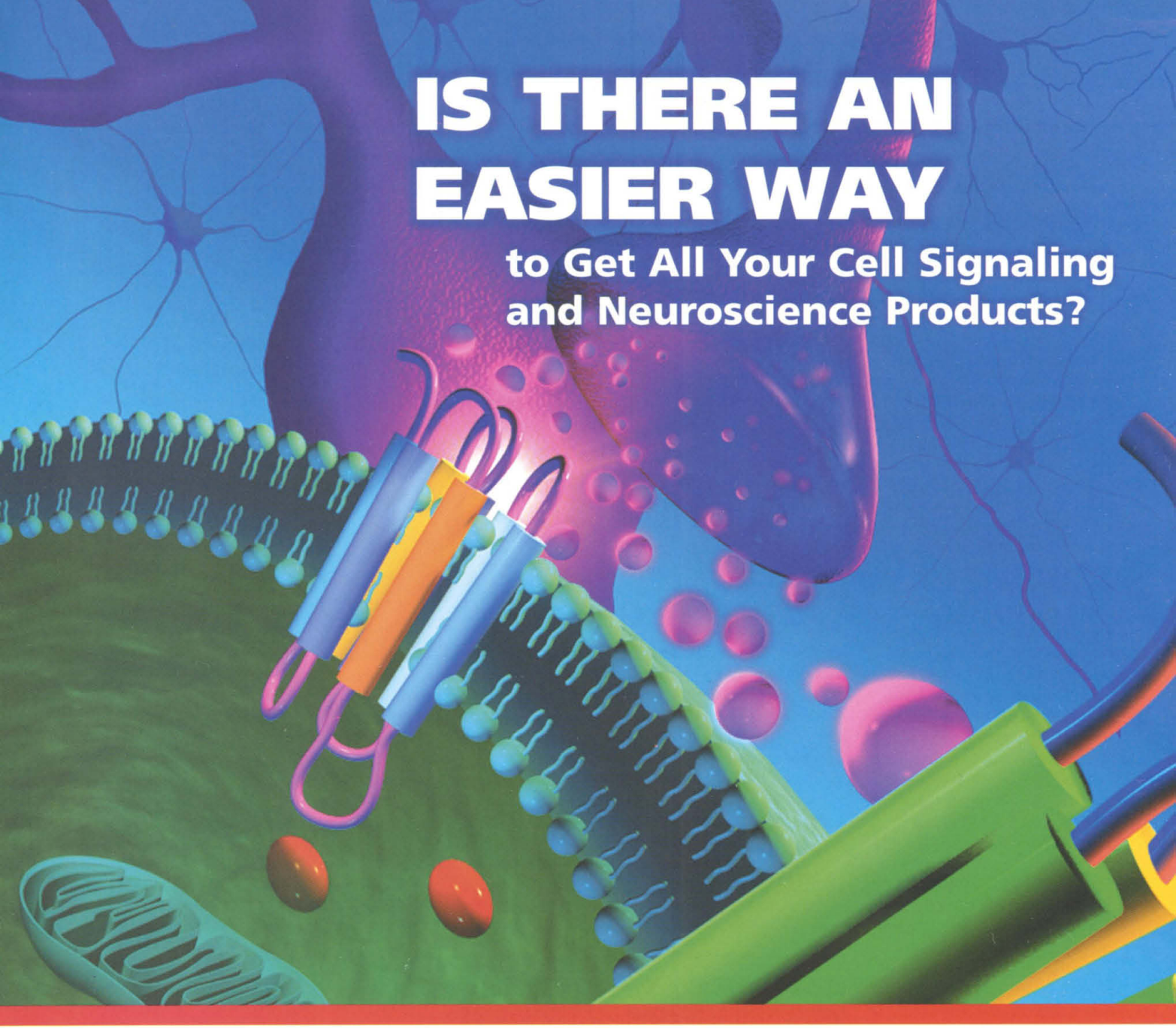

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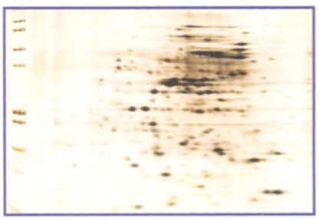

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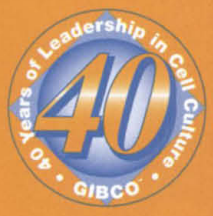

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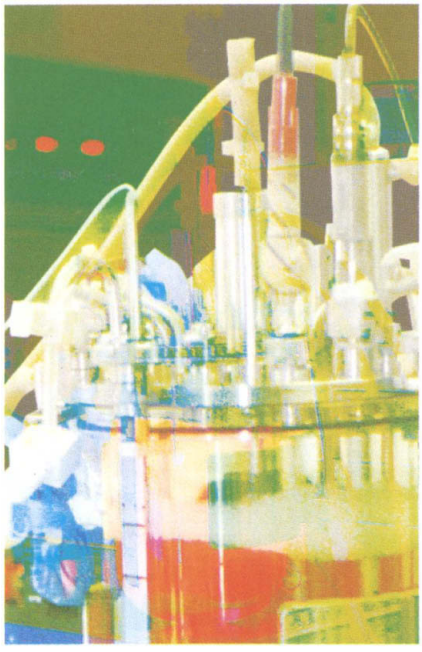

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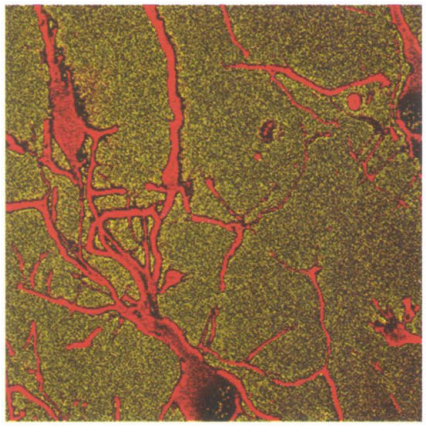

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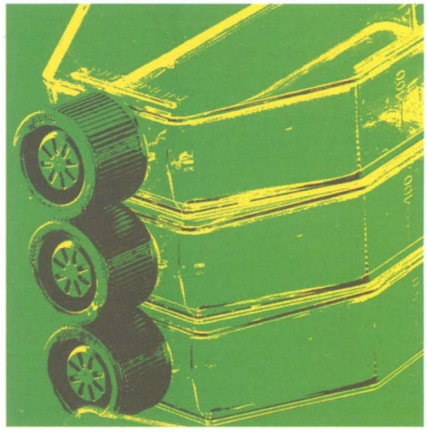

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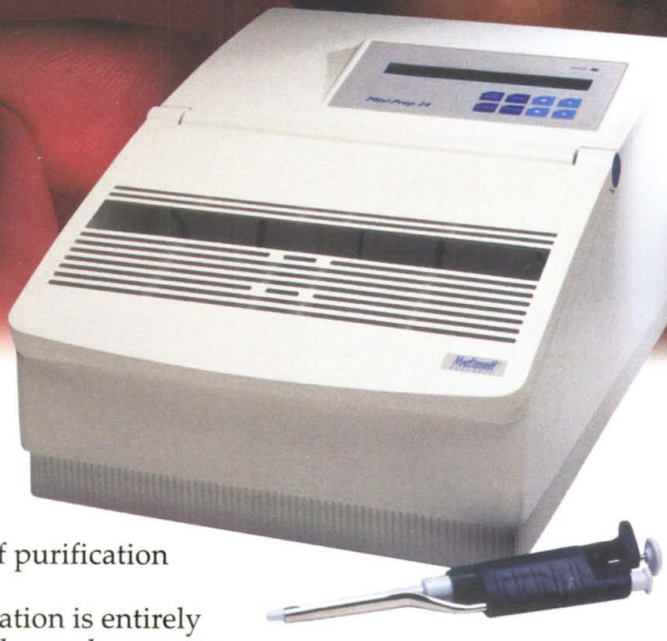

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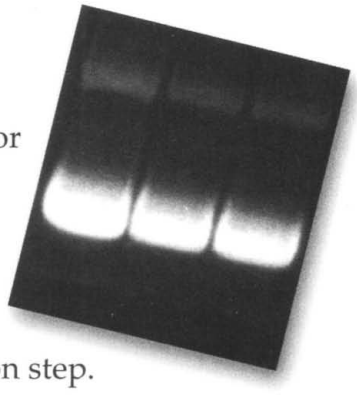

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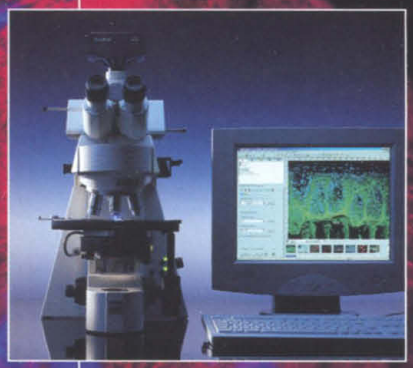

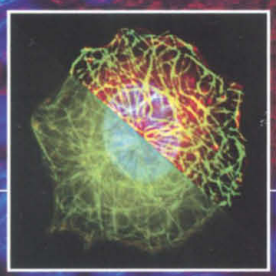

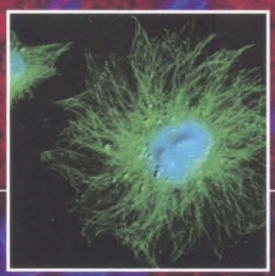

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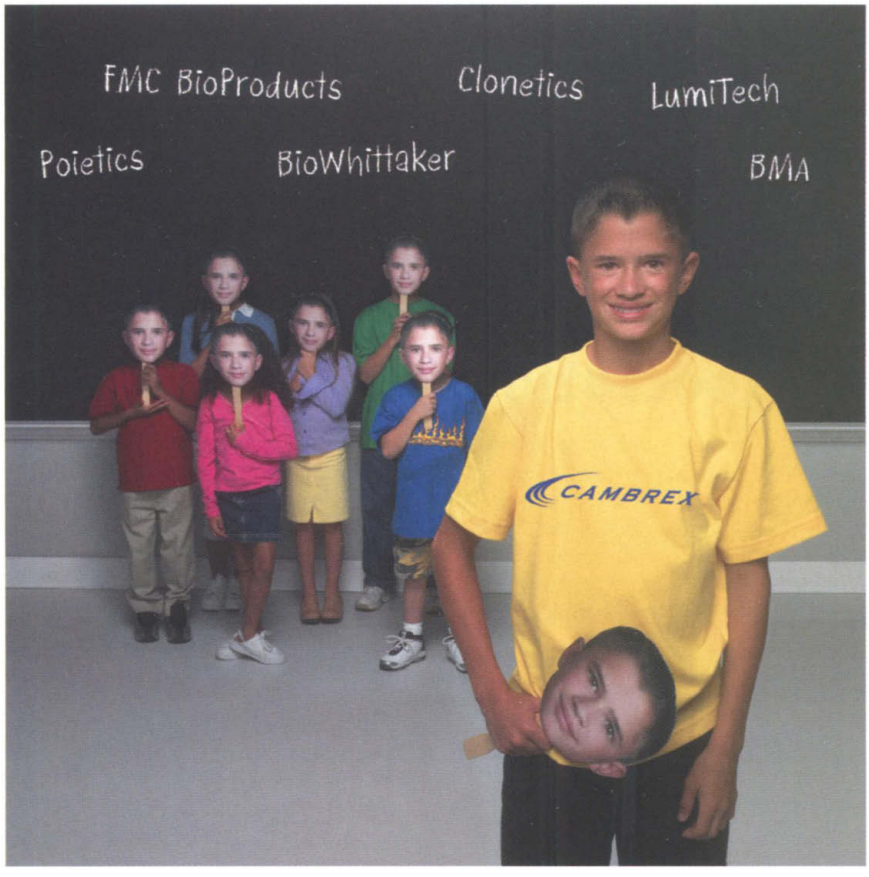

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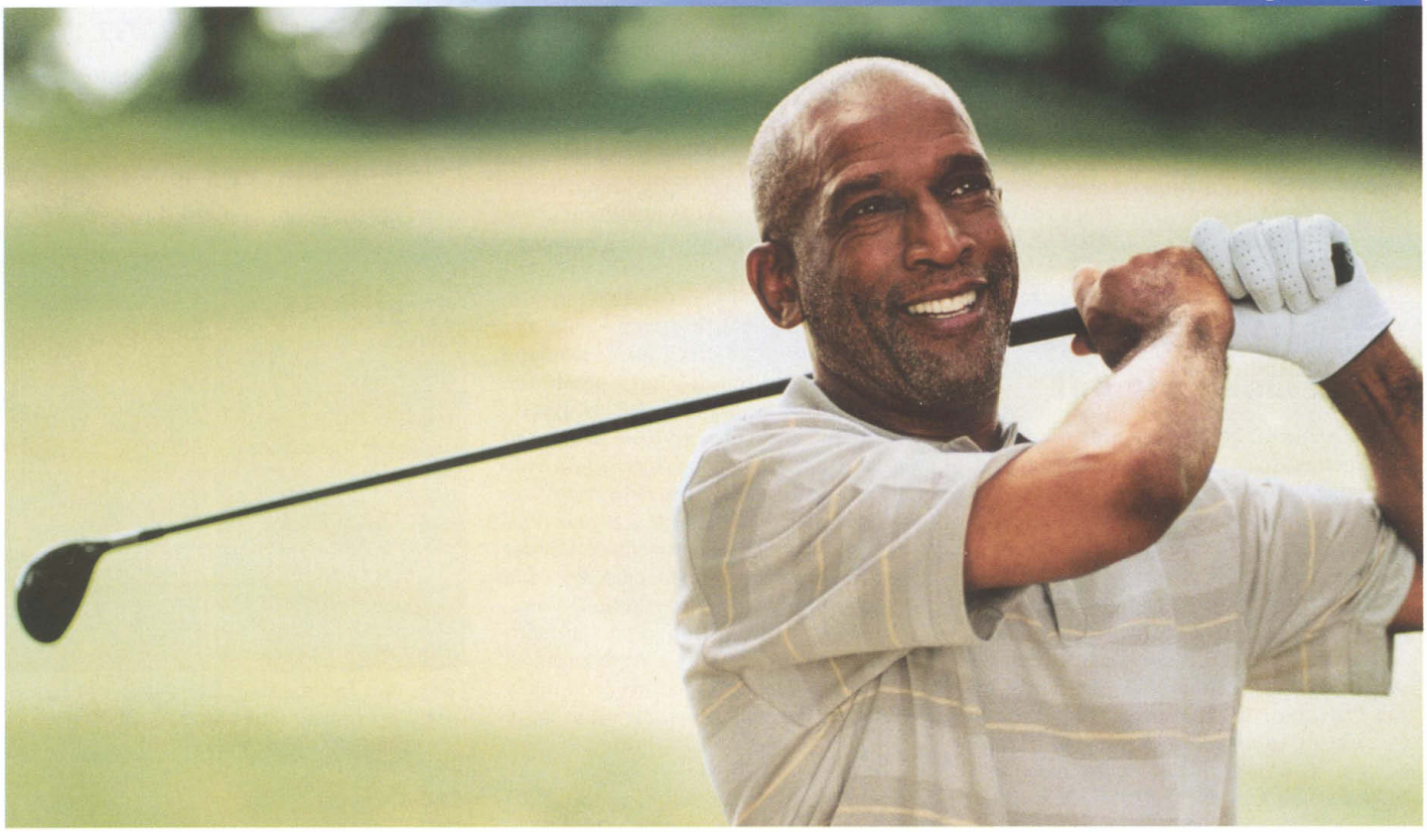

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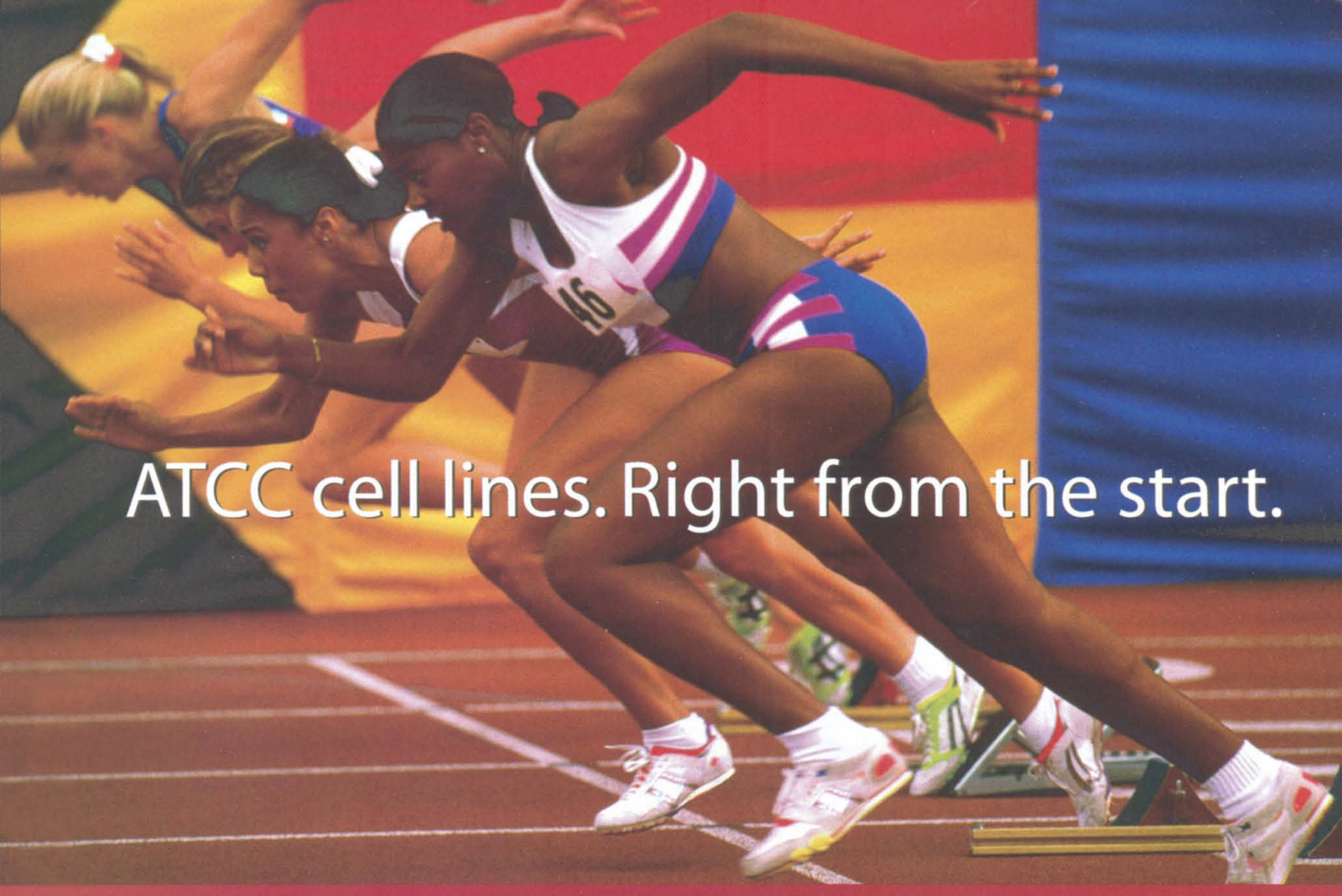

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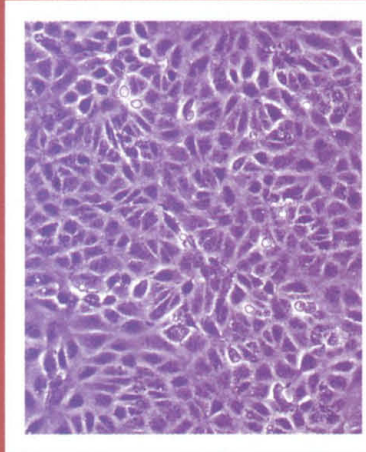

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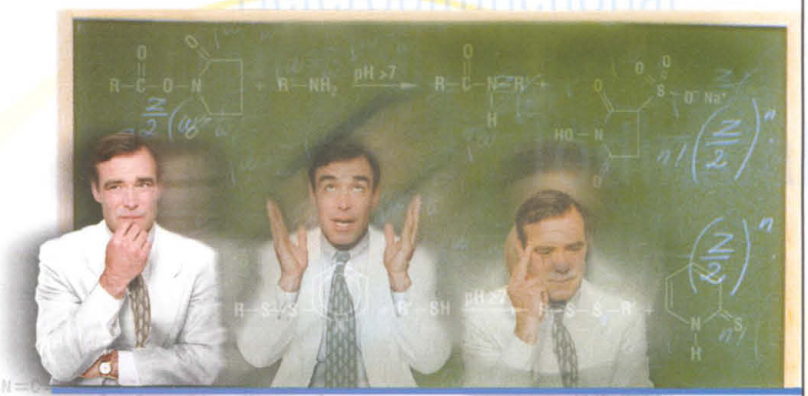

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Hermanson, G.T. (1995). *Bioconjugate Techniques.* Academic Press: New York. (Product # 20002)

Hermanson, G.T., *et al.* (1992). *Immobilized Affinity Ligand Techniques.* Academic Press: New York. (Product # 22230)

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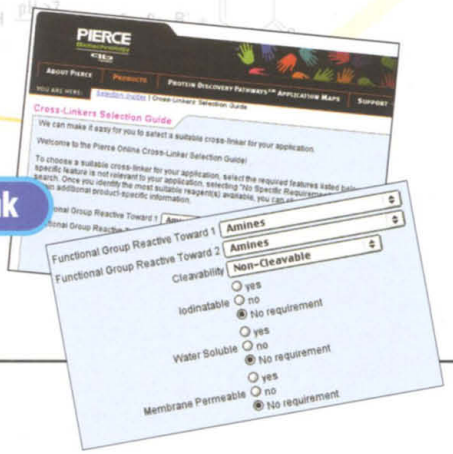

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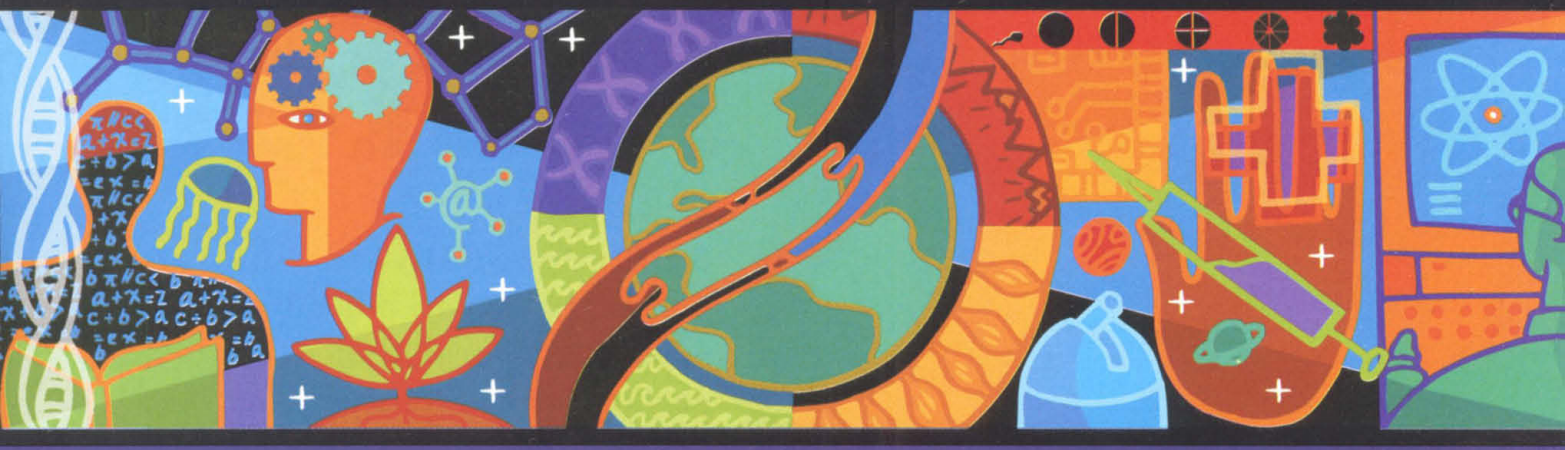

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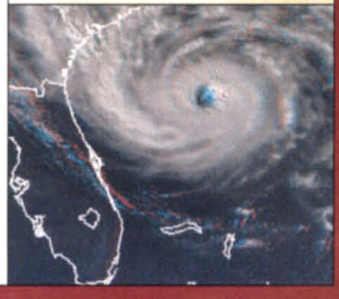

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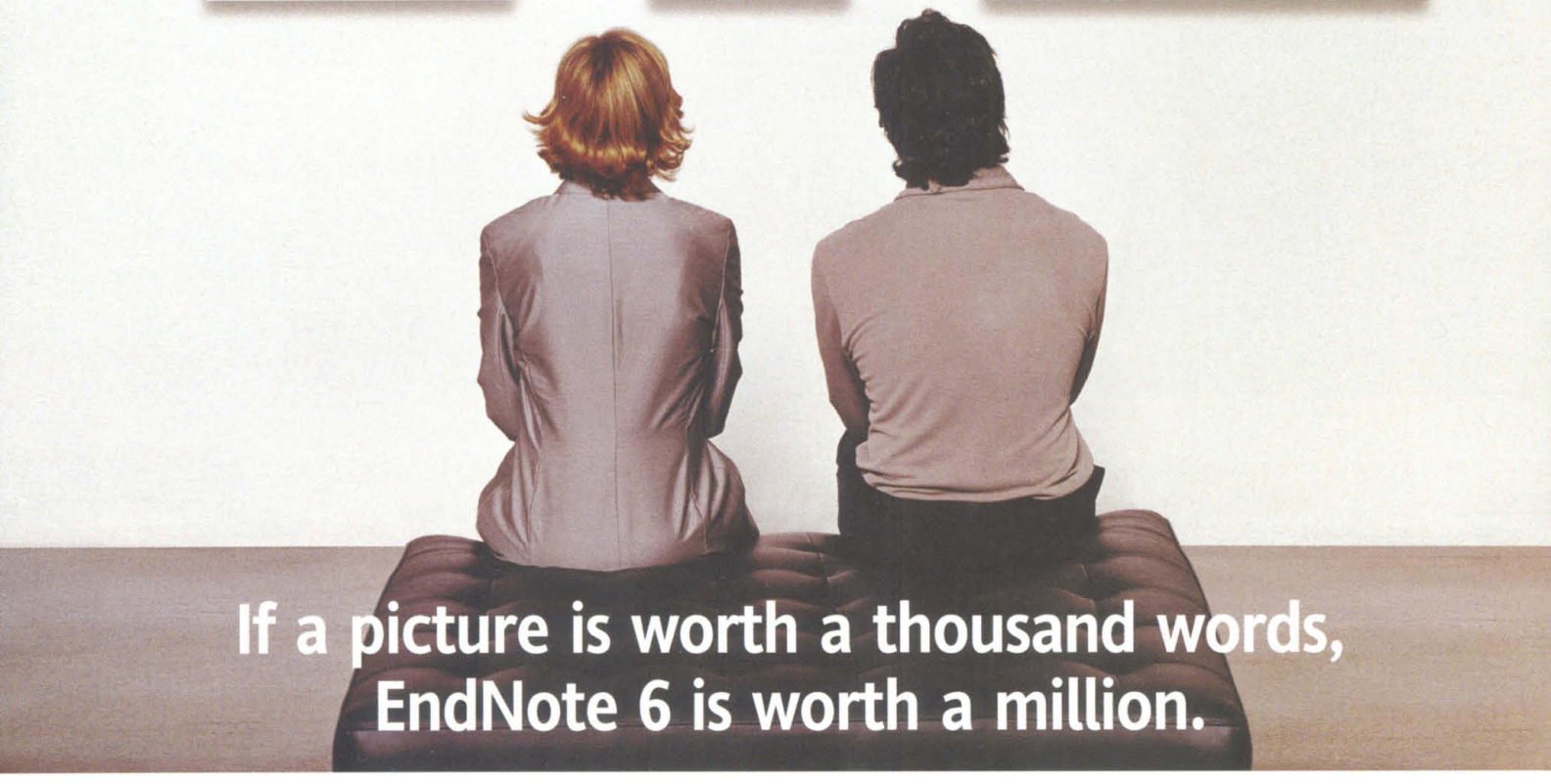

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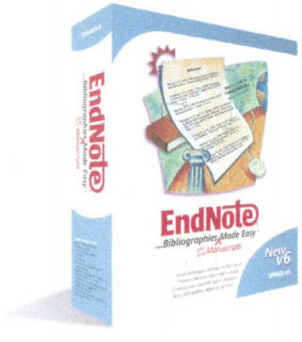

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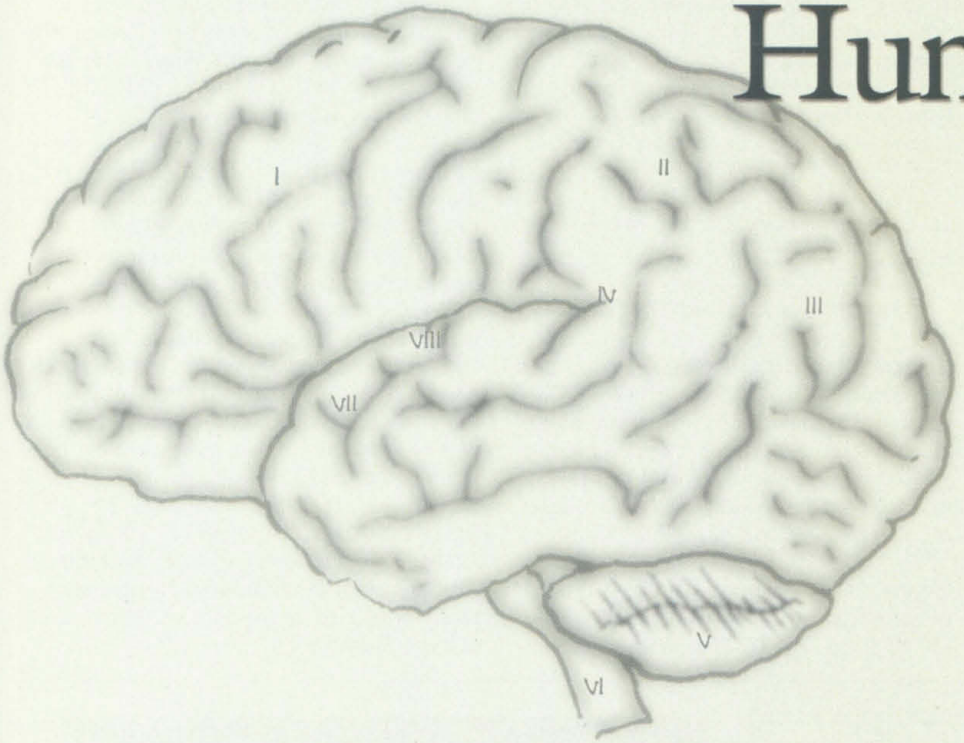

- Frontal Cortex(I)
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- Basal Ganglia(IV)
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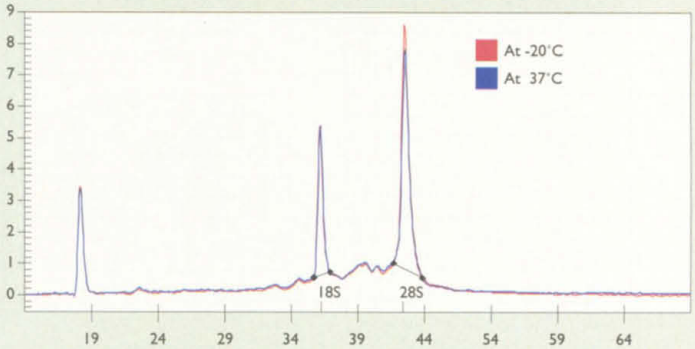

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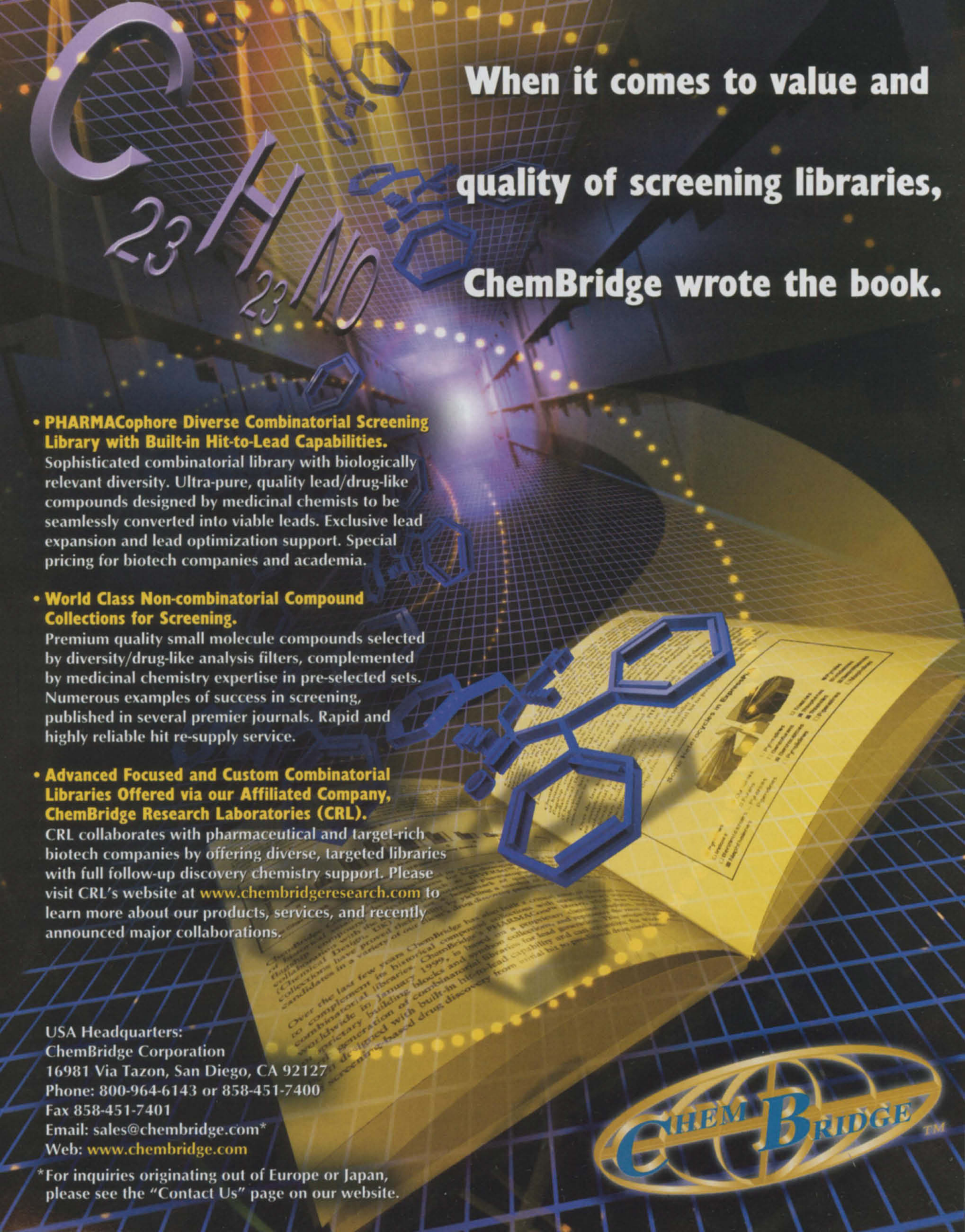
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