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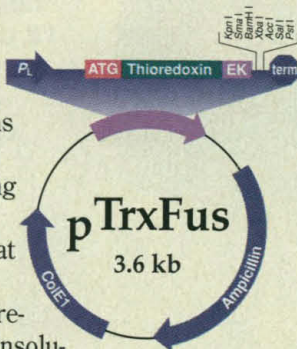
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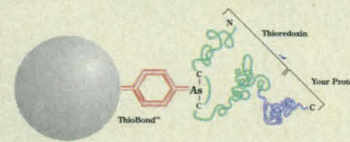


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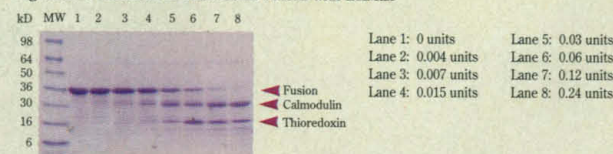
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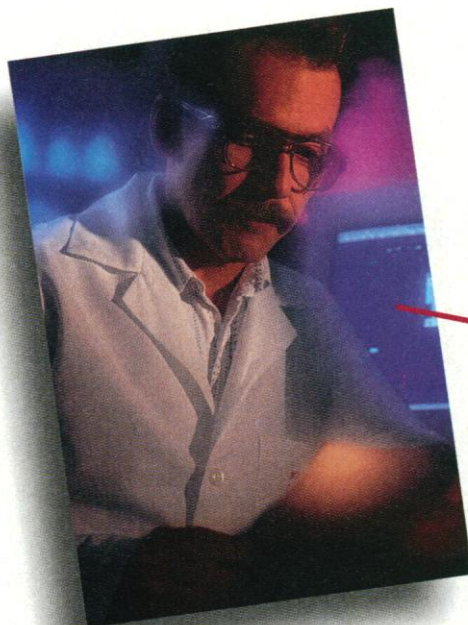
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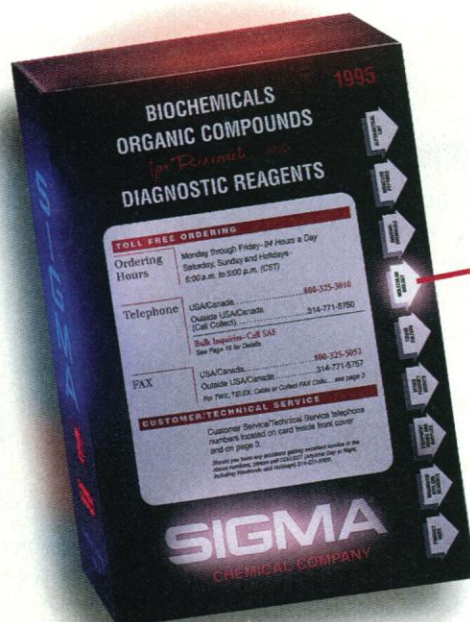
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Brian Ward, Ph.D.

- Presently working on DNA sequence recognition methods.
- Invented a novel method to qualitatively and quantitatively determine a DNA sequence recognition event.
- Solved dideoxy sequencing stalling by temperature ramping the termination reactions.
- Has worked in the Molecular Biology Department of Sigma for eight years.
- Received his Ph.D. from Michigan State University.



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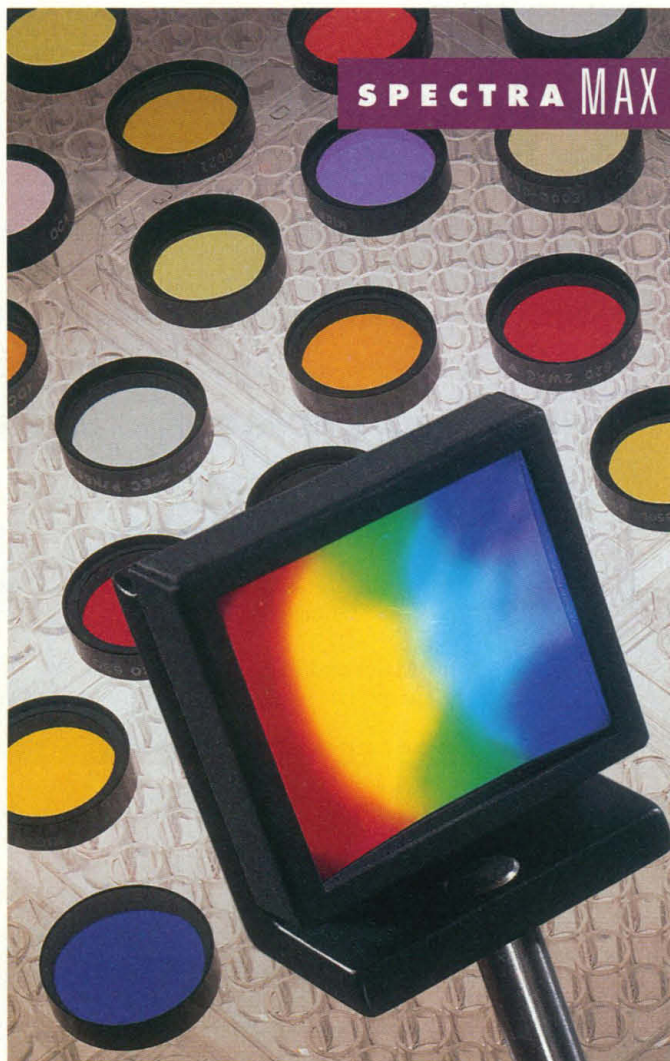


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Brian is presently concentrating his efforts on DNA sequence recognition methodologies. In addition, he is also an important part of a team working with nucleic acid isolation, recombinant protein expression, and transcription/translation technologies. You can find the products of Brian's work, as well as his co-workers', in the Molecular Biology section of the Sigma Catalog. And just like all the Sigma products you know and trust, your satisfaction is guaranteed.

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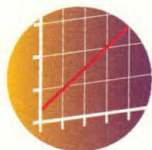
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1822

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NEWS

- Conflict Marks Crime Conference 1808
- French Budget: Research Given
an 'Apparent Increase' 1809
- Democrats Urge Clinton to Stand Up
for R&D Programs 1810
- Commission Proposes New Definition
of Misconduct 1811
- International Experts Help Probe
Haiti's Bloody Past 1812
- Tracing Croatia's 'Disappeared' 1812
- Mass Migration Plan for Neutrinos 1813
- Chambon Builds Institute With
U.S. Funds and Eye for Detail 1814
- Riding the Waves of Molecular Biology 1815
- Butterfly Biomechanics: Wing Scales
May Help Beat the Heat 1816
- Another Blow Weakens
EMF-Cancer Link 1816

Is the Most Distant Galaxy a Star Factory? 1817

Is Hale-Bopp the Next Great Comet? 1818

SPECIAL NEWS REPORT

SEX DETERMINATION

- Tracing How the Sexes Develop 1822
- Snaring the Genes That Divide the
Sexes for Mammals 1824
- How Males and Females Achieve
X Equality 1826

PERSPECTIVES

- Tuning into Better Catalysts 1833
J. A. Labinger
- Baculovirus Bounty 1834
L. E. Volkman

ARTICLE

- From Molecular Diversity to Catalysis:
Lessons from the Immune System 1835
P. G. Schultz and R. A. Lerner

DEPARTMENTS

- THIS WEEK IN SCIENCE** 1797
- EDITORIAL** 1799
Science in the Stationary Phase
A. Kornberg
- LETTERS** 1801
Multiple-Use Physics Facilities: J. C. Browne and
R. Pynn; J. M. Carpenter; L. Rosen • The Endan-
gered Species Act: P. F. Torrence • Garlic and
Mosquitoes: F. Crowe • "Not-Even-a-Draft?": R. L.
Park; Editors • Pioneering Work: W. Fiers; J. C.
Venter
- SCIENTESCOPE** 1807

- RANDOM SAMPLES** 1819
Jewish Breast Cancer Gene? • Lasker Honors T Cell
Pioneers • Lady in Amber • Potential Animal Model
for AIDS • Folding Proteins Fast • Materials Sci-
ence—Live on the Net • Shrinking National Labs

- BOOK REVIEWS** 1891
Crusading for Chemistry, reviewed by P. T. Carroll •
Factories of Death, A. D. Coox • *Corals in Space and
Time*, R. W. Grigg • Books Received • Publishers'
Addresses

- INSIDE AAAS** 1897

- PRODUCTS & MATERIALS** 1899

- QUARTERLY INDEX** 1901

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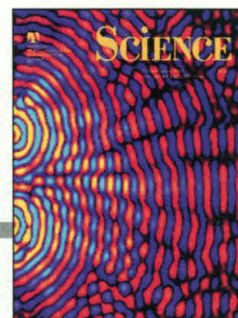
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COVER

Propagating acoustic strain waves depicted by magnetic resonance imaging (MRI). The dual-source interference pattern arose from 500-hertz mechanical shear waves applied to a tissue-simulating gel at two points (54 millimeters apart, at left). The MRI technique used

can quantitatively depict mechanical waves with amplitudes on the order of hundreds of nanometers and could lead to the development of a medical imaging modality that emulates the clinical technique of palpation. See page 1854. [Image: Richard L. Ehman]



RESEARCH ARTICLE

Hemoglobin Allosteric: Resonance Raman Spectroscopy of Kinetic Intermediates

V. Jayaraman, K. R. Rodgers, I. Mukerji, T. G. Spiro

REPORTS

Understanding C-H Bond

Oxidations: H[•] and H⁻ Transfer in the Oxidation of Toluene by Permanganate

K. A. Gardner and J. M. Mayer

Global Distribution of Persistent Organochlorine Compounds

S. L. Simonich and R. A. Hites

Magnetic Resonance Elastography by Direct Visualization of Propagating Acoustic Strain Waves

R. Muthupillai, D. J. Lomas, P. J. Rossman, J. F. Greenleaf, A. Manduca, R. L. Ehman

Anisotropy and Spiral Organizing Centers in Patterned Excitable Media

O. Steinbock, P. Kettunen, K. Showalter

Replicator Neural Networks for Universal Optimal Source Coding

R. Hecht-Nielsen

Circadian Oscillations of Cytosolic and Chloroplastic Free Calcium in Plants

C. H. Johnson, M. R. Knight, T. Kondo, P. Masson, J. Sedbrook, A. Haley, A. Trewavas

Modulation of Transcription Factor Ets-1 DNA Binding: DNA-Induced Unfolding of an α Helix

J. M. Petersen, J. J. Skaliky, L. W. Donaldson, L. P. McIntosh, T. Alber, B. J. Graves

A Specialized Pathway Affecting Virulence Glycoconjugates of *Leishmania*

A. Descoteaux, Y. Luo, S. J. Turco, S. M. Beverley

Interaction of Tyrosine-Based Sorting Signals with Clathrin-Associated Proteins

H. Ohno, J. Stewart, M.-C. Fournier, H. Bosshart, I. Rhee, S. Miyatake, T. Saito, A. Gallusser, T. Kirchhausen, J. S. Bonifacino

Jak-STAT Signaling Induced by the *v-abl* Oncogene

N. N. Danial, A. Pernis, P. B. Rothman

Lateral Interactions in Primary Visual Cortex: A Model Bridging Physiology and Psychophysics

M. Stemmler, M. Usher, E. Niebur

An Internal Model for Sensorimotor Integration

D. M. Wolpert, Z. Ghahramani, M. I. Jordan

FFA-1, a Protein That Promotes the Formation of Replication Centers Within Nuclei

H. Yan and J. Newport

Inhibition of ICE Family Proteases by Baculovirus Antiapoptotic Protein p35

N. J. Bump, M. Hackett, M. Hugunin, S. Seshagiri, K. Brady, P. Chen, C. Ferenz, S. Franklin, T. Ghayur, P. Li, P. Licari, J. Mankovich, L. Shi, A. H. Greenberg, L. K. Miller, W. W. Wong

TECHNICAL COMMENTS

Honeybees and Magnetoreception

H. Nichol and M. Locke; J. L. Kirschvink and M. M. Walker; M. H. Nesson; C.-Y. Hsu and C.-W. Li

1883

Control of DNA replication center formation



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Cooperative Protein-DNA binding studies

van Dijk, M.A. and Murre, C. (1994) *Cell*, **78**, 1.

DNA-Protein complex formation, immunoprecipitation

Sif, S. and Gilmore, T.D. (1993) *J. Virol.* **67**, 7612.

Protein-RNA binding assays

Lutz, C.S. and Alwine, J.C. (1994) *Gen. Devel.* **8**, 576.

DNA binding

Loh, L.C. *et al.* (1994) *Virology* **200**, 413.

Protein-protein interaction, Mapping protein binding sites

Patrick, D.R. *et al.* (1994) *J. Biol. Chem.* **269**, 6842.

Fusion protein binding assays

Lukac, D.M. *et al.* (1994) *J. Virol.* **68**, 5184.

Analysis of truncation mutations in MDS

Screening for translation-terminating mutations in MDS
Roest, P.A. *et al.* (1993) *Human Mol. Gen.* **2**, 1719.

Mutational analysis

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Johnson, V.G. and Nicholls, P.J. (1994) *J Biol Chem.* **269**, 4349.

Confirmation of ligand-binding region, analysis of mutants

Kallio, P.K. *et al.* (1994) *Endocrinology* **134**, 998.

Gel shift analysis of deletion mutants

Palvimo, J.J. *et al.* (1993) *Mol. Endo.* **7**, 1399.

Verification of cloned genes

Verification that clone expressed a protein of the predicted size

Daigle, I. and Li, C. (1993) *Proc. Natl. Acad. Sci. USA*, **90**, 12045.

Verification of clone and immunoprecipitation

Greig, A. *et al.* (1994) *Circulation Research*, **74**, 41.

In vitro evolution studies

Joyce, G.F. (1993) *Pure & Appl. Chem.* **65**, 1205.

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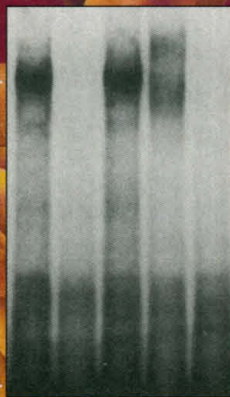
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Oxidizing C-H bonds

Oxidation is one way of activating normally unreactive carbon-hydrogen single bonds. Gardner and Mayer (p. 1849; see the Perspective by Labinger, p. 1833) have studied the mechanism of toluene oxidation by permanganate ion in water and inorganic solvent. In water, toluene transfers an H^\cdot species, but in neat toluene an H^\cdot atom is transferred. The energetics of O-H bond formation can be used to predict oxidation rates and may lead to understanding C-H bond oxidation by metalloenzymes and metal oxide surfaces.

Unwanted travelers

Organochlorine compounds, such as lindane and DDT, are widely used as pesticides. Some of these compounds are carcinogens or estrogen mimics, and their use may be restricted or even banned in many countries. However, the global distribution of the compounds through atmospheric transport leads to contamination even of remote regions such as the Arctic. Simonich and Hites (p. 1851) have analyzed tree bark samples from worldwide sites for 22 organochlorine compounds; their results relate the volatility of the compounds to their global distribution. Such data is vital for future restrictions on the use of these hazardous compounds.

Elastic images

Patterns of local mechanical response in a material are important for understanding wave propagation, but few methods exist for mapping this response. Muthupillai *et al.* (p. 1854) have used magnetic resonance imaging to quantitatively image the spatial distribution of displace-

Programming of chemical oscillations

Complex chemical systems often show oscillating behavior; the propagation of the resulting chemical waves is affected by inhomogeneities in the reaction system. This is of particular importance for biological systems because of their cellular nature. Steinbock *et al.* (p. 1857) have adapted an ink jet printer to study the effect of regular and irregular inhomogeneities on oscillating reactions. The methodology should be easily applicable to a variety of systems, giving important insight into the effects of local features on global behavior for wave propagation.

ment of a gel in response to mechanical excitation. The method was also used to map the mechanical properties of a tissue specimen. The technique offers a resolution of less than 200 nanometers and may find application in ultrasonics and medical imaging.

Sorted out

Integral membrane proteins are targeted to their final destination by sorting signals in their cytoplasmic domains (sequences of four to six residues that include a critical tyrosine residue). Ohno *et al.* (p. 1872) used a yeast two-hybrid approach to screen more than 2 million clones for proteins that interact with the tyrosine-based signal. The medium chains of the clathrin-associated protein complexes (μ_1 of AP-1 and μ_2 of AP-2) were found to specifically interact with the tyrosine signals of several integral membrane proteins and with isolated hexapeptide signals. The medium chains apparently serve as the signal-binding components in the clathrin-dependent sorting apparatus.

Vital for virulence

Leishmania are heteroxenous parasites: One stage of their lives is spent in the blood or tissues of

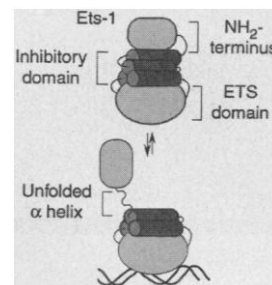
a vertebrate host, while other stages live in the intestines of bloodsucking invertebrates. The infectious cycle is controlled in part by surface glycoconjugates, such as lipophosphoglycan (LPG), and regulation of expression of these molecules is a topic of keen interest. Descoteaux *et al.* (p. 1869) report a novel gene, *LPG2*, which encodes a Golgi membrane protein. *LPG2* is specifically involved in the intracellular compartmentalization and assembly of LPG and other virulence-associated glycoconjugates. This may represent an evolutionarily specialized activity, as the yeast homologs of *LPG2* are required for general Golgi function.

Foci on replication

In eukaryotic cells, DNA replication is initiated at many discrete subnuclear locations called foci. These foci contain an aggregation of 300 to 1000 DNA loops. The single-stranded DNA binding protein RP-A that is required for the initiation of DNA replication is associated with foci before replication initiation. Yan and Newport (p. 1883) have isolated a protein, focus-forming activity 1 (FFA-1), that is required for the association of RP-A with foci. In association with other components of the foci, FFA-1 may generate binding sites for RP-A.

Molecular foldout

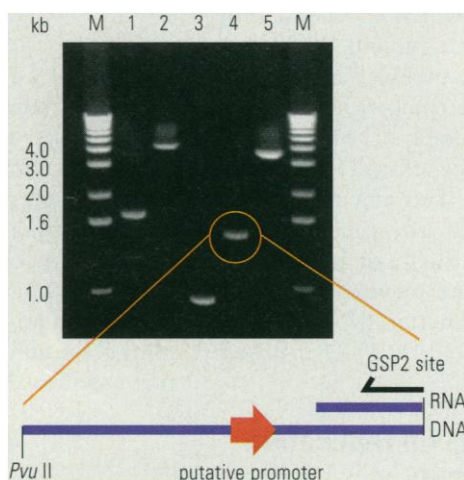
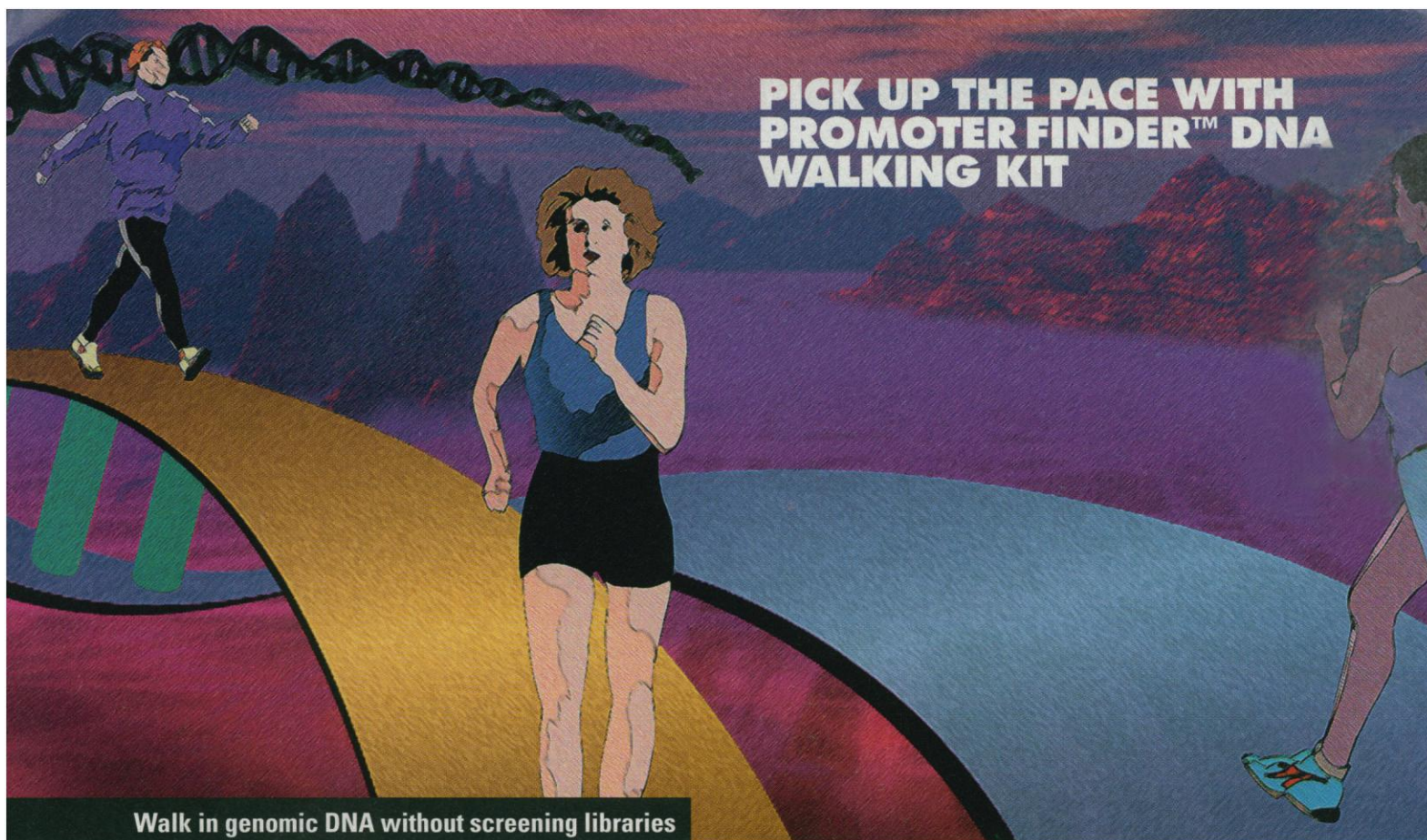
Members of the *ets* family of transcription factors contain a winged helix-turn-helix DNA-binding domain. Many members are negatively regulated by inhibitory sequences that affect the DNA-binding domain. Petersen *et al.* (p. 1866) have examined the conformational changes that occur during the DNA binding of Ets-1. Although the secondary structure



of the Ets-1 DNA-binding domain is unchanged in the presence of DNA, an α helix in the inhibitory domain is unfolded. Unfolding represents a means of transcription factor regulation. Both specific and nonspecific DNA sequences can change the conformation, so Ets-1 sampling of the unfolded conformation can precede recognition.

Freezing out ICE

The p35 protein encoded by baculovirus can block apoptosis, a defense mechanism against infection in multicellular organisms. Bump *et al.* (p. 1885) used a recombinant form of p35 to show that this protein blocks the proteolytic activity of interleukin-1 β converting enzyme (ICE) and three of its homologs. This enzyme acts autocatalytically by cleaving its proform. Because p35 blocks several apoptotic pathways, ICE and related proteins may play a central role in apoptosis.



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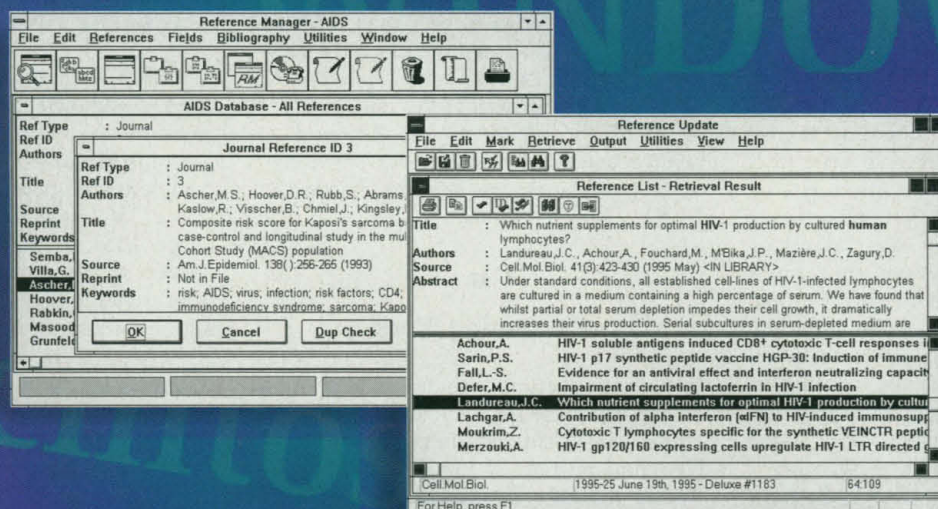
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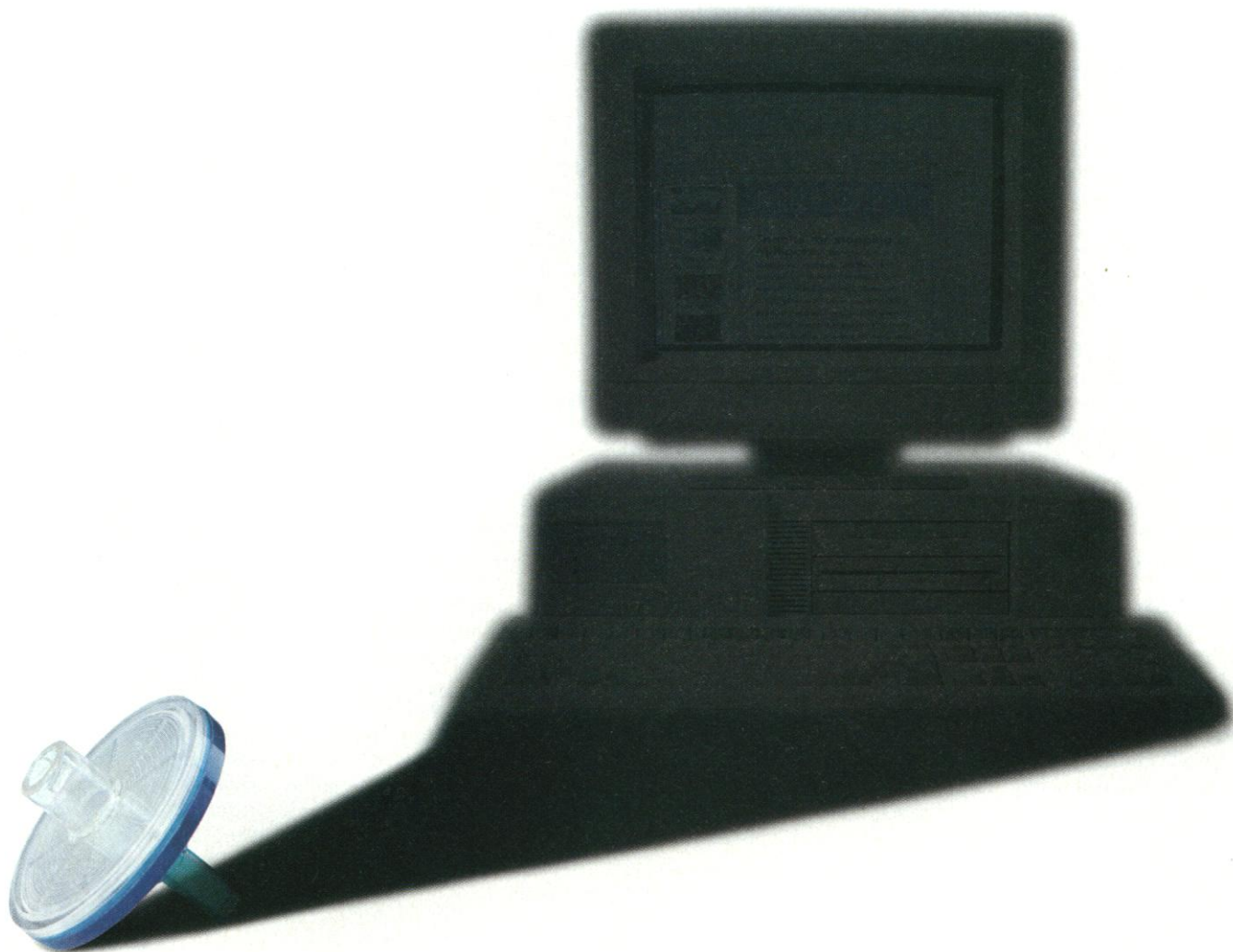


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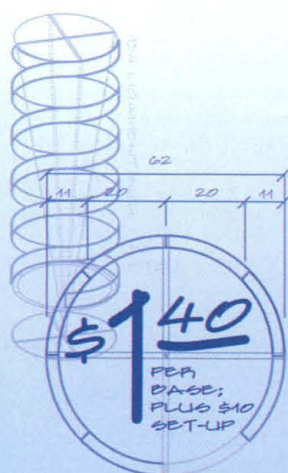
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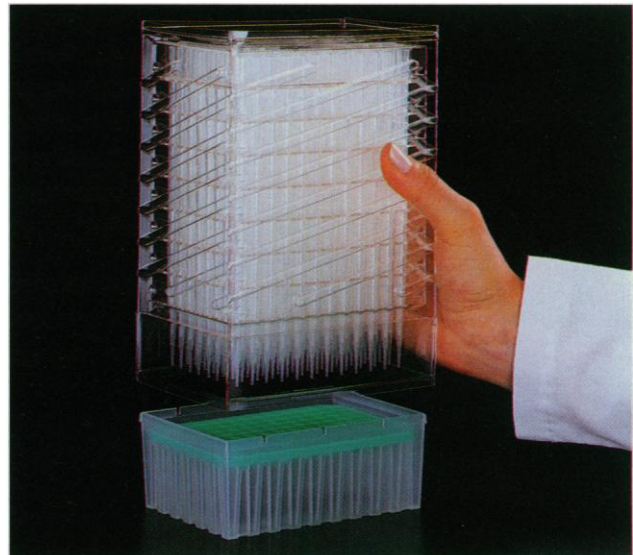
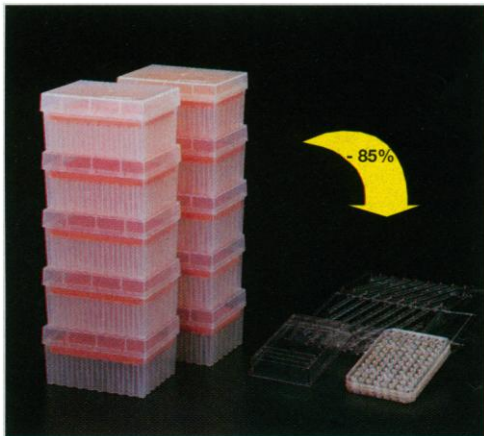
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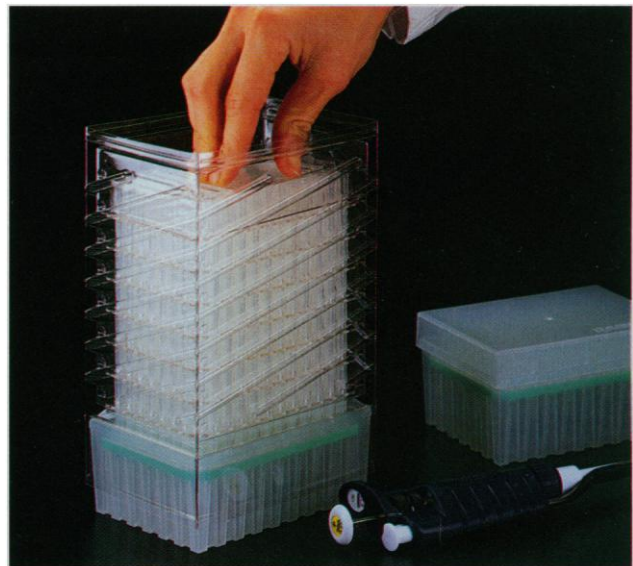
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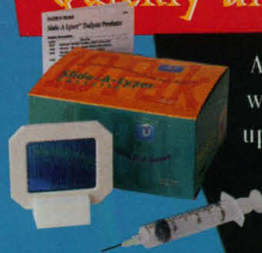
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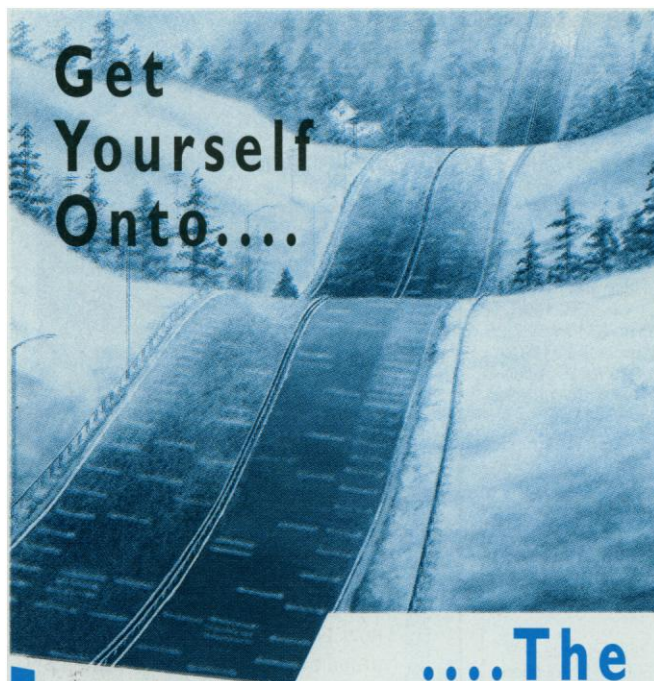
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