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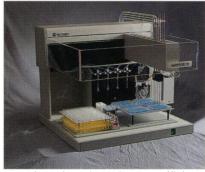
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tips when required, or use washable fixed tips whenever possible. Ultra-sensitive liquid level sensing tips further eliminate any risk for DNA cross-contamination.

#### **Clinical Testing**

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# Looking for the right angle on cell analysis?

The special twist of this puzzle is that each entry in the puzzle grid makes one 90-degree turn somewhere along its length. It's up to you to determine where each word or phrase makes this turn and in which direction. The starting direction of each answer (before it makes a turn) is indicated by a letter following the clue number – N for north, S for south, E for east and W for west.

1E	Cytokine
2E	Apoptosis
3W	Multiparamete
48	Stat
58	Receptor
GN	Biotin
7N	Avidin
88	Lyse
98	FITC
105	Specific
11E	Epitope
12N	Chain
138	Cell
14N	Viable
15N	Laser
16N	FACS
17W	Fluorochrome



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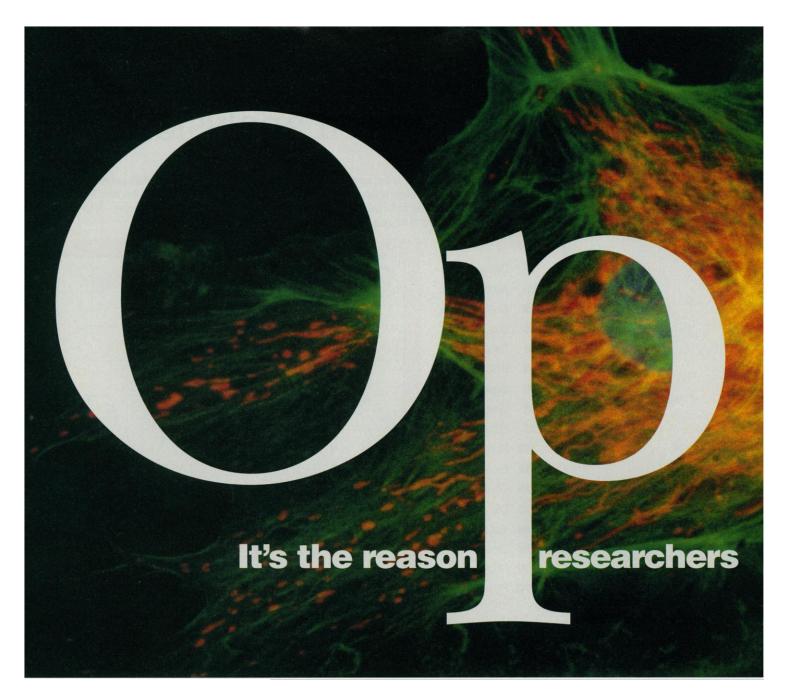
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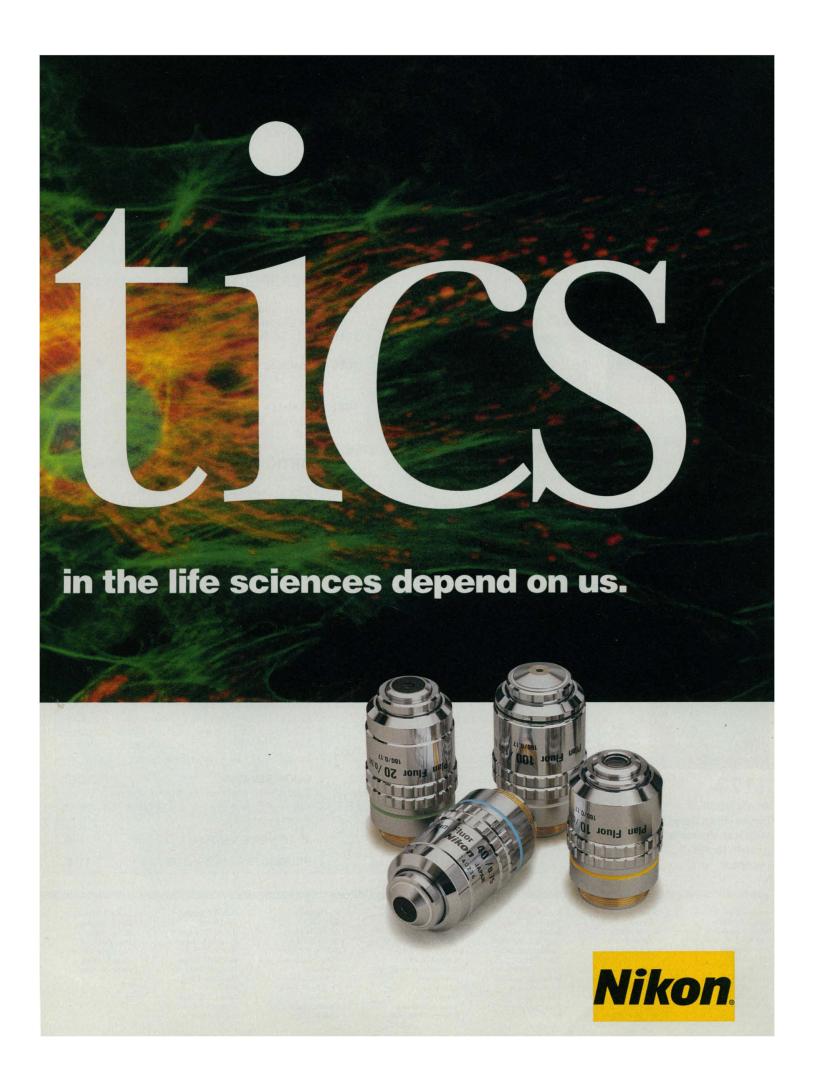
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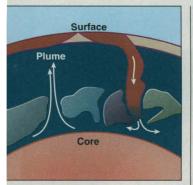


ISSN 0036-8075 **23 FEBRUARY 1996** VOLUME 271 NUMBER 5252





ASSOCIATION FOR THE **ADVANCEMENT OF** SCIENCE



1053 New picture of the mantle





1120 Association of farnesyltransferase with transforming growth factor-β receptor

NEWS & COMMENT	Analyzing With Astro	
Big Science Is Booming in Japan Researchers, Book Your Flights	1046 1047	PERSPE
Clinton's R&D Achievements Tilt Toward Technology Science and the Balanced Budget	1049 1049	Molecular of Chemist T. W. Bel
MIT Torn by Bitter Dispute Over Missile	1050	Evolving C M. M. Da
Russia: Funding Crisis Provokes Street Protests	1052	Delivery of to Solid Tu R. K. Jain
RESEARCH NEWS	Margaretter	rt. rt. juiii
Putting Stiffness in Earth's Mantle	1053	ARTICLE
AAAS Gathering Explores Animals, Aliens, and Atoms	1055	The Galvan Growing A J. M. Berg
Regulating G Protein Signaling	1056	RESEAR
Infrared Astronomy: New Images Wet Researchers' Appetites	1058	The Immu Catalysis
A Split-Personality X-ray Beacon Tantalizes Theorists	1059	P. A. Pat Marks, G Stevens, I
	DEPART	MENTS
THIS WEEK IN SCIENCE	1033	SCIENCES
<b>EDITORIAL</b> Science and the American Dream Neal F. Lane	1037	RANDOM S Genes Conf Dictionary Trail • PN
LETTERS Superconductivity Researchers: R. L. Gr	1039	Journal of P
LETTERS Superconductivity Researchers: R. L. Gro Prediction of the Bose-Einstein Condens Donnelly • Air Quality in Mexico Guzmán, M. E. Ruíz, E. Vega; D. R. Blake Rowland • Climate Change and Consen tinued: M. J. Prather • HIV Viral Load As Fox; B. F. Haynes	eene • A sate: R. J. City: F. and F. S. sus: Con-	
Superconductivity Researchers: R. L. Gra Prediction of the Bose-Einstein Condens Donnelly • Air Quality in Mexico Guzmán, M. E. Ruíz, E. Vega; D. R. Blake Rowland • Climate Change and Consen tinued: M. J. Prather • HIV Viral Load As	eene • A sate: R. J. City: F. and F. S. sus: Con-	Journal of P BOOK REV Tempo and Larson • Pr Books Recei

Molecular Structure 1060 onomical Speed ECTIVES **Trees: A New Branch** 1077 try 11 Catalysts in Real Time 1078 ivis f Molecular Medicine 1079 umors EI inization of Biology: A 1081 Appreciation for the Roles of Zinc g and Y. Shi RCH ARTICLE inological Evolution of 1086 tten, N. S. Gray, P. L. Yang, C. B. J. J. Wedemayer, J. J. Boniface, R. C. P. G. Schultz SCOPE 1045 SAMPLES 1061 firm Archaea's Uniqueness • Antarctic • Piping in the Sun • On the Dinosaur JAS Opens Up Submission Process • lague Years • Bear Facts VIEWS 1075 Mode in Evolution, reviewed by A. rotein Kinases, J. T. Stull • Vignettes • ived

**VS & NOTES** S & MATERIALS Kim Nasmyth Gottfried Schatz Roger A. Nicoll Staffan Normark Stuart L. Pimm

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Yoshinori Tokura Emil R. Unanue

Terrence J. Sejnowski

Geerat J. Vermeij Bert Vogelstein Arthur Weiss Zena Werb George M. Whitesides Owen N. Witte William A. Wulf

1149

1150

Frederick W. Alt Don L. Anderson Michael Ashburner Stephen J. Benkovic Alan Bernstein David E. Bloom Piet Borst Henry R. Bourne Michael S. Brown James J. Bull Kathryn Calame Dennis W. Choi

David Clapham Adrienne E. Clarke Adrienne E. Clarke John M. Coffin F. Fleming Crim Paul J. Crutzen James E. Dahlberg Robert Desimone Paul T. Englund G. Ertl Richard G. Fairbanks Douglas T. Fearon Harry A. Fozzard

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SCIENCE • VOL. 271 • 23 FEBRUARY 1996

1030

#### COVER

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Representation of a hexameric assembly of dendrimers (hyperbranched polymers, shown with four layers or generations). Hydrogen-bonding contacts at the core of each dendrimer and peripheral van der Waals interactions stabilize the assembly, whose size rivals

#### that of a small protein. White, hydrogen; black, carbon; red, oxygen; and blue, nitrogen. See page 1095 and the Perspective on page 1077. [Image created by Paul A. Thiessen with PovChem (see http:// ludwig.scs.uiuc.edu) on a Silicon Graphics Indigo]

#### REPORTS

Olig	ling and Dating New Jersey gocene-Miocene Sequences: Ice Volu bal Sea Level, and Exxon Records	1092 1me,	S. Faha Linhard
Sh	G. Miller, G. S. Mountain, the I hipboard Party, and Members of the rsey Coastal Plain Drilling Project		The p21 <sup>®</sup> in TGF-f T. Wan S. D. Ki
S.	-Assembling Dendrimers Z C. Zimmerman, F. Zeng, D. E. C. R V. Kolotuchin	<b>1095</b> eichert,	Locus Co Heteroch Effect Va
and	<b>Os Ages of Group IIA, IIIA, IVA,</b> <b>IVB Iron Meteorites</b> . I. Smoliar, R. J. Walker, J. W. Morga	<b>1099</b>	R. Fest Mamala Jones, I
Sim Mor S.	Swelling of Clays: Molecular ulations of the Hydration of ntmorillonite Karaborni, B. Smit, W. Heidug, J. n Oort	<b>1102</b> Urai, E.	Congenit with a M Resistand C. C. F C. T. M
CO Mat	dle to Late Paleozoic Atmospheric 2 Levels from Soil Carbonate and Or ter I. Mora, S. G. Driese, L. A. Colarusso		Scheper IRAK: A Interleuk Z. Cao,
Obs Usin E. Le Sc C.	ial Results of Radio Occultation ervations of Earth's Atmosphere ng the Global Positioning System R. Kursinski, G. A. Hajj, W. I. Bertig roy, T. K. Meehan, L. J. Romans hofield, D. J. McCleese, W. G. Me L. Thornton, T. P. Yunck, J. R. Eyr agatani	s, J. T. lbourne,	TECHN How Mu Clouds A G. L. St Pilewsk Interheli
	ervations of Carbon Monoxide	1110	Stability, P. Lavig
	Comet Hale-Bopp Jewitt, M. Senay, H. Matthews	7	Hodges
D. Imit Rec of the	Comet Hale-Bopp	1113 rs	Hodges

#### AAAS Board of Directors

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leparin Structure and Interactions	1116
with Basic Fibroblast Growth Factor	1110
S. Faham, R. E. Hileman, J. R. Fromm, Linhardt, D. C. Rees	R. J.
The p21 <sup>RAS</sup> Farnesyltransferase $\alpha$ Subunit TGF- $\beta$ and Activin Signaling	1120
T. Wang, P. D. Danielson, Bv. Li, P. C.	Shah.

I. Wang, P. D. Danielson, B.-y. Li, P. C. Shah, S. D. Kim, P. K. Donahoe

#### Locus Control Region Function and 1123 Heterochromatin-Induced Position Effect Variegation

R. Festenstein, M. Tolaini, P. Corbella, C. Mamalaki, J. Parrington, M. Fox, A. Miliou, M. Jones, D. Kioussis

#### Congenital Jaundice in Rats 1126 with a Mutation in a Multidrug Resistance–Associated Protein Gene

C. C. Paulusma, P. J. Bosma, G. J. R. Zaman, C. T. M. Bakker, M. Otter, G. L. Scheffer, R. J. Scheper, P. Borst, R. P. J. Oude Elferink

#### IRAK: A Kinase Associated with the 1128 Interleukin-1 Receptor Z. Cao, W. J. Henzel, X. Gao

#### **TECHNICAL COMMENTS**

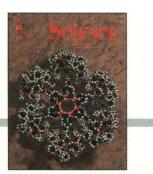
How Much Solar Radiation Do Clouds Absorb?	1131
G. L. Stephens; R. D. Cess and M. H. Zha Pilewskie and F. P. J. Valero	ang; P.
Interhelical Salt Bridges, Coiled-Coil Stability, and Specificity of Dimerization	1136
P. Lavigne, F. D. Sönnichsen, C. M. Kay Hodges; K. J. Lumb and P. S. Kim	, R. S.

**1110** Hale-Bopp in a CO coma

#### Indicates accompanying feature

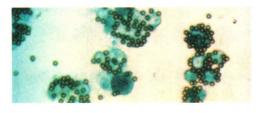
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### This Week in Science

edited by PHIL SZUROMI

#### **Clay swelling**

Some clays can swell to several times their original thickness in the presence of water, but the details of water adsorption between the layers within the clay are poorly understood. Kara-



borni *et al.* (p. 1102) present simulations of sodium-montmorillonite, an abundant clay that affects the stability of oil wells during drilling. Particularly strong swelling of this clay may result from the occurrence of two different types of stable structures, depending on the number of water layers between the clay layers. Switching between these two different stable states may facilitate the swelling of the clay.

#### On the level

Reconstructing past changes in sea level has proven difficult, yet it is critical for evaluating causes of sea-level changes (for example, tectonic versus climatic) and controls on deposition. Two controversial studies by Vail and Haq and their coworkers had correlated sequence boundaries and other features in marine stratigraphic records distributed globally to try to delineate past changes in sea level. Miller *et al.* (p. 1092) now test

#### Steps toward catalytic antibodies

Highly specific recognition of antigens by antibodies results during affinity maturation, in which an expanding population of different B cell clones compete for the same antigen. Patten *et al.* (p. 1086; see the Perspective by Davis, p. 1078) cloned and expressed nine affinity mutations from germline cells that occurred during the generation of an antibody that catalyzes ester hydrolysis. A kinetic analysis revealed that as the antibody evolved, its affinity for the transition-state analog increased by a factor of  $10^4$ , and the reaction rate for the ester substrate increased by about a factor of  $10^2$ . A crystal structure of the antibody revealed that these mutations were not in direct contact with the hapten and thus likely played a conformational role.

this interpretation by comparing the oxygen isotope curve, an indicator of sea-level changes due to glaciation, with ages of sequence boundaries in Oligocene-Miocene sediments along the New Jersey coast. The ages of unconformities are correlated with indications of a lowering of sea level inferred from oxygen isotope values.

#### Listening to the air

A recently completed network of 24 Global Positioning System satellites has been used to listen to the structure of the Earth's atmosphere using radio occultation. Kursinski et al. (p. 1107) determined preliminary vertical temperature and water vapor profiles that illustrate the enhanced resolution of this technique over limited groundbased balloon radiosonde and model data. Additional measurements should contribute to our understanding of the structure of the stratosphere and enhance weather forecasting.

#### CO in a comet coma

The development of sensitive millimeter-wave telescopes has allowed astronomers to observe distant comets to understand what produces their gaseous comas when they are too cold to sublimate water-ice. Jewitt *et al.* (p. 1110) have determined that the bright coma of comet Hale-Bopp is due to the outgassing of CO. This rare observation of CO outgassing may be a transient brightening that will evolve into an even brighter water outgassing, visible with the naked eye, as Hale-Bopp makes its closest approach to the sun in April 1997.

#### Varying variegation

Locus control regions (LCRs) permit the tissue-specific expression of linked genes at high levels. Festenstein *et al.* (p. 1123) have studied the LCR



from the human CD2 gene in transgenic mice. They find that the CD2 LCR was necessary to prevent variegated expression (expression in some cells of a tissue but not others) when the gene was inserted into centromeric heterochromatin. Such variegated expression was associated with a closed chromatin configuration. They conclude that the LCR functions by establishing or maintaining an open chromatin domain.

#### **Regulation by release**

Like other receptors, the transforming growth factor (TGF)- $\beta$  receptor is expected to transmit signals to the interior of the cell through its interaction with associated proteins. Wang et al. (p. 1120) searched for proteins that interacted with the TGF- $\beta$  receptor and found the  $\alpha$  subunit of farnesyltransferase (FNTA). FNTA regulates the activity of small guanine nucleotide-binding proteins like Ras that participate in many signaling pathways. When TGF- $\beta$ bound to its receptor, FNTA was released. Thus, signaling by the TGF- $\beta$  receptor may be mediated, at least in part, by ligand-induced release of FNTA and consequent regulation of small guanine nucleotide-binding proteins.

#### Liver-specific multidrug transporter

Formation of bile requires the secretion of bile acids from the liver through a canalicular multiorganic anion transporter (cMOAT) that has been defined physiologically but whose molecular definition has remained elusive. Deficiencies in bile acid secretion leads to disease. Paulusma et al. (p. 1126) have described the isolation of the sequence that encodes cMOAT. The protein is related to known multidrug transporters and is specifically expressed in the canalicular membrane of liver cells.

#### Research Notes from

# Nikon

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Like all Nikon optics, the new CF PLAN FLUOR Objectives correct all the various chromatic aberrations from the center to the edges of the image, providing extreme sharpness over the entire field of view. Nikon is the only microscope

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The new CF PLAN FLUOR Objectives also offer higher numerical apertures to capture more of the available light emitted by the specimen. The N.A. of the 40X PLAN FLUOR, for for the 40X Plan Achromat. The N.A. of the 100X oil PLAN FLUOR is 1.3 of the 100X oil PLAN FLUOR is 1.3 compared with 1.25 for the 100X Plan compared with 1.25 for the 100X Plan Achromat oil.

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#### Smaller objects, finer details

Using fluorescence, scientists can resolve images that cannot be observed with ordinary light. The diameter of a single DNA molecule, for example, is about 2nm, while the optical lenses is about 200nm. However, if a fluorescent dye is conjugated with the DNA molecule and the specimen is viewed with a fluorescence microscope, the molecule can be easily detected and measured.

Although it is a very powerful and relatively easy to use tool, fluorescence places extreme demands on the microscope's optics. The nearultraviolet wavelengths that are used in energy. At the same time, the light emitted from the specimen is of much lower intensity than the light used to be designed to transmit as much light as possible. Care must also be taken to prevent autofluorescence taken to prevent autofluorescence emissions, which can mask and rob emissions, which can mask and rob

#### Special objectives required

Because today's ultrasensitive techniques place extreme demanda on optics, the emitted fluorescence requires specially designed objecenhanced brightness and higher UV light transmission than those used with other techniques. The new Wikon CF<sup>®</sup> PLAN FLUOR Universal Objectives have these characteristics.

> more powerful technique. promise to make it an even advances in optics design increasingly popular. Recent nanometers, it is becoming with resolution down to several and analysis of these substances cence permits selective imaging and DNA. Because fluoresantibodies, microtubules, RNA cellular organelles, proteins, smaller entities such as some are not adequate for imaging of individual cells, but they techniques work well for studies for microscopic studies. These most popular techniques used and phase contrast were the Until fairly recently, brightfield

DNA sequences in mammalian cells. number, size and location of specific chromosomes and determining the played a key role in identifying (FISH), for example, which has as Fluorescence in situ Hybridization has made possible techniques such ed and observed separately. This men, each substance can be targetdifferent substances within a specichromes, are absorbed selectively by Because fluorescent dyes, or fluoroto be an exceptionally powerful tool. fluorescence microscopy is proving to explore smaller and smaller entities, As biomedical researchers continue

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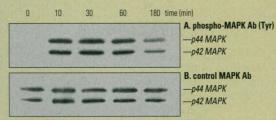
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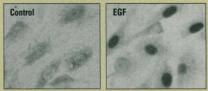
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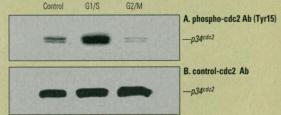
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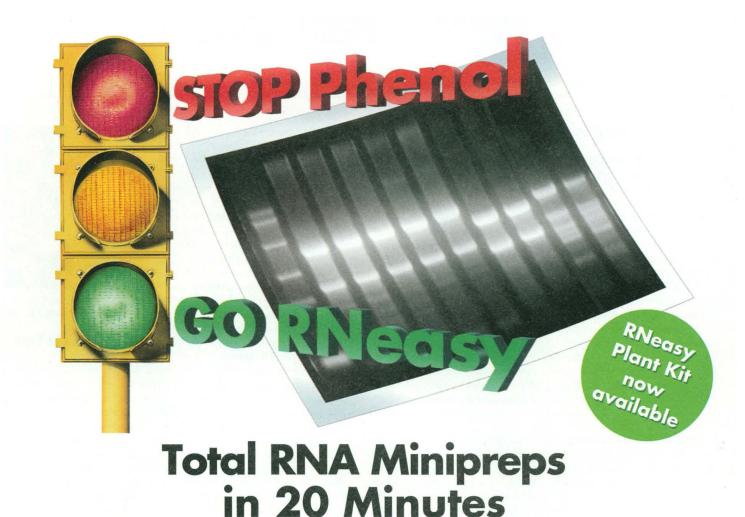
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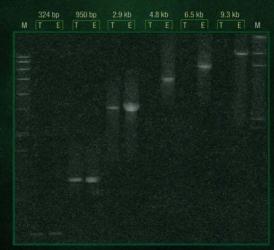
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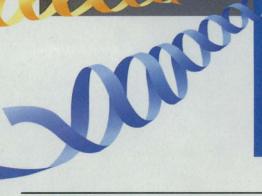
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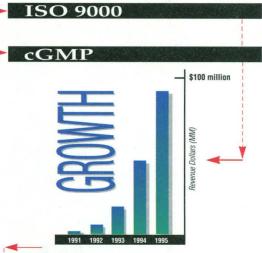
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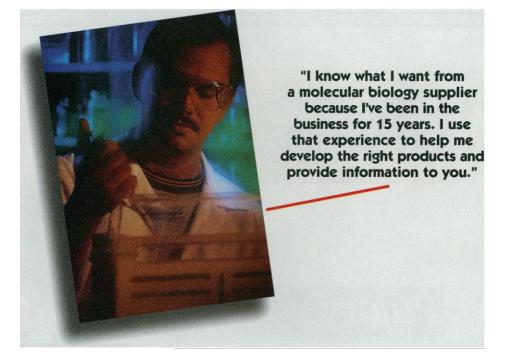


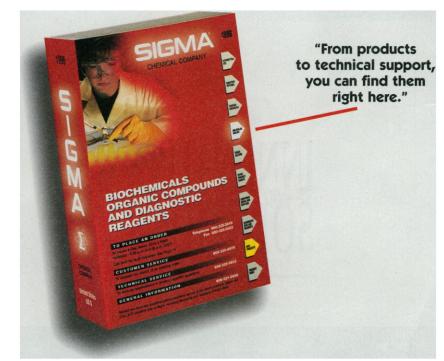
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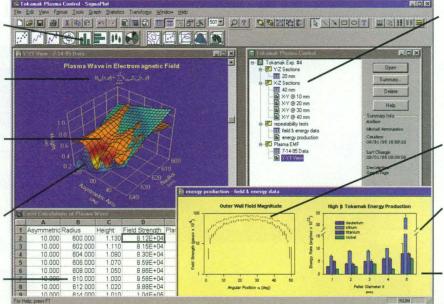
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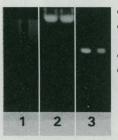
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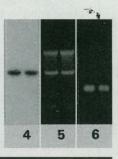


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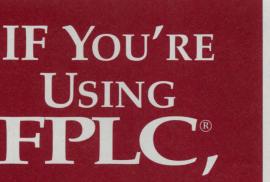


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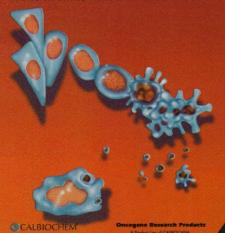


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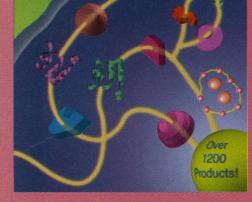
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