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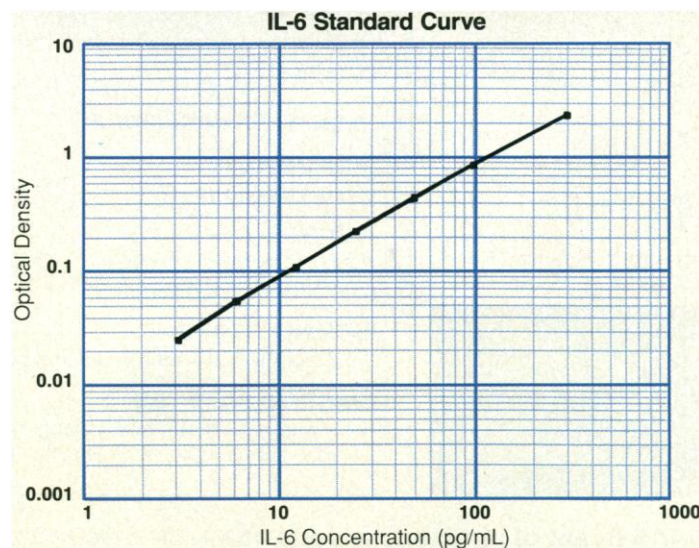
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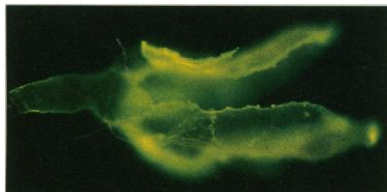
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1812

Leishmania adhesion
in the sandfly gut



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COVER

Agrobacterium tumefaciens VirE2 protein (fused to the β -glucuronidase reporter protein, which generates the blue stain) accumulates in the nucleus of a tobacco cell. VirE2, a single-stranded DNA binding protein that associates with *Agrobacterium* T-strand DNA, is pro-

posed to target this DNA directly into the plant nucleus during infection. See page 1802. Insight into how *Agrobacterium* infects plants may lead to better control over transformation and bioengineering of plants. [Photomicrograph: J. Zupan]



RESEARCH ARTICLE

Crystal Structure at 3.5 Å Resolution of HIV-1 Reverse Transcriptase Complexed with an Inhibitor

L. A. Kohlstaedt, J. Wang, J. M. Friedman, P. A. Rice, T. A. Steitz

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Reversal of the Orientation of an Integral Protein of the Mitochondrial Outer Membrane

J.-M. Li and G. C. Shore

Peptides Presented to the Immune System by the Murine Class II Major Histocompatibility Complex Molecule I-A^d

D. F. Hunt, H. Michel, T. A. Dickinson, J. Shabanowitz, A. L. Cox, K. Sakaguchi, E. Appella, H. M. Grey, A. Sette

Neurotransmitter Release from Synaptotagmin-Deficient Clonal Variants of PC12 Cells

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Involvement of the N-methyl D-aspartate (NMDA) Receptor in the Synapse Elimination During Cerebellar Development

S. Rabacchi, Y. Bailly, N. Delhay-Bouchaud, J. Mariani

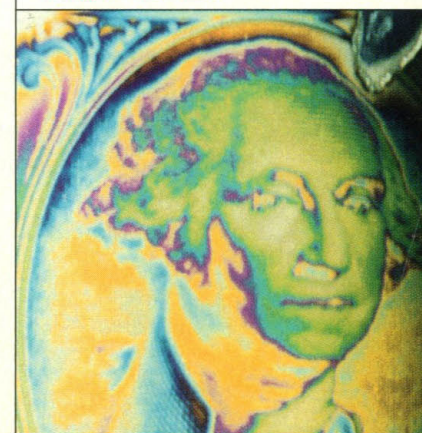
TECHNICAL COMMENTS

Expression of Intra-MHC Transporter (HAM) Genes and Class I Antigens in Diabetes-Susceptible NOD Mice

H. R. Gaskins, J. J. Monaco, E. H. Leiter, L. S. Wicker, P. L. Podolin, P. Fischer, A. Sirotina, R. C. Boltz, Jr., L. B. Peterson, D. Faustman, X. Li, H. Y. Lin, R. Huang, J. Guo

1791

Images in silicon



■ Indicates accompanying feature

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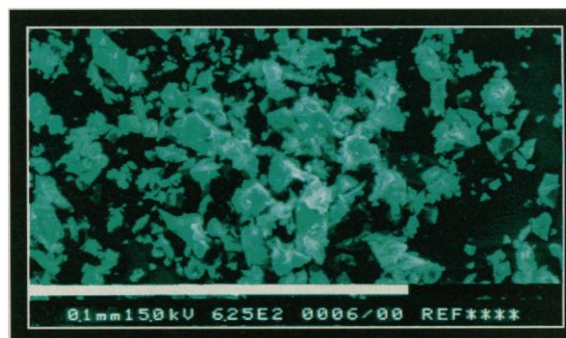
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After the flood

How do climate changes, streams, and tectonic processes such as uplifting and faulting interact to yield a sedimentary deposit? Koltermann and Gorelick (p. 1775) address the question by performing large-scale computer simulation of an alluvial fan in northern California. They examined a range of hydrologic systems throughout the state to infer likely climate changes. Paleoclimate fluctuations dominated the large-scale changes that occurred in the deposit.

HIV reverse transcriptase

A 3.5 angstrom resolution crystal structure of HIV reverse transcriptase, a target for many AIDS drugs, in a complex with an inhibitor has been reported by Kohlstaedt *et al.* (p. 1783). In a Perspective, Wlodawer (p. 1766) discusses some of the difficulties involved in obtaining this structure and as well as some of the insights gained from it, especially in the area of rational drug design.

Silicon images

When electrochemically etched, silicon can be made to emit visible photoluminescence. Doan *et al.* (p. 1791) find that black and white images can be transferred to a silicon surface by means of photoetching. Viewed in visible light the etched image exhibits false colors owing to thin film interference. Under blue light, the image photoluminesces with intensities corresponding to the light and dark regions of the original pattern. The authors were also able to photoetch a diffraction grating, a procedure that may find

application in holographic displays, waveguides, and data storage technology.

Bigger fullerenes

Theoretical calculations for larger fullerenes (from 60 to 240 carbon atoms) reveal that ball-shaped molecules are lower in energy than tubular structures. Adams *et al.* (p. 1792) performed first-principles calculations for spherical arrangements of atoms and for capsule structures (cylinders with hemispherical end caps) with different numbers of carbon atoms. These energies could be related by a single parameter that they call the planarity, which relates how well the p orbitals of the carbon atoms align and thus measures how complete the π -bond network is in the molecule.

Stuck in the solvent

Solvent viscosity can play a major role in the dynamics of protein conformational changes. Spectroscopic studies by Ansari *et al.* (p. 1796) of the dissociation of carbon monoxide (CO) from myoglobin at ambient temperatures and high viscosities showed that the rate of dissociation was approximately inversely proportional to the viscosity. Conformational changes in myoglobin that accompany CO dissociation may be slowed down in a viscous solvent, so much so that the conformations become "stuck" and that motion of the protein

through the solvent becomes the major barrier to release of the CO molecule. Both unimolecular rate theory and experimental data suggest that these results may explain in part the dissociation kinetics at low temperatures (below 200 K).

More complexes

Recognition of peptides by T cells requires presentation of the peptides to the immune system by association with the class I or class II molecules of the major histocompatibility complex (MHC). Hunt *et al.* (p. 1817), using microcapillary high-performance liquid chromatography coupled with electrospray tandem mass spectrometry, showed that a large number

of different peptides (between 650 and 2000) are presented to the immune system by the class II MHC molecule I-A^d, thus forming a much more complex system than was previously reported for the class II MHC molecule I-A^b. These peptides are 16 to 18 residues long, and sequencing revealed a six-residue binding motif that occurred at various positions within these peptides. The groove for peptide binding on I-A^d is probably open at both ends, based on binding data for truncated peptides.

NMDA and synaptic elimination

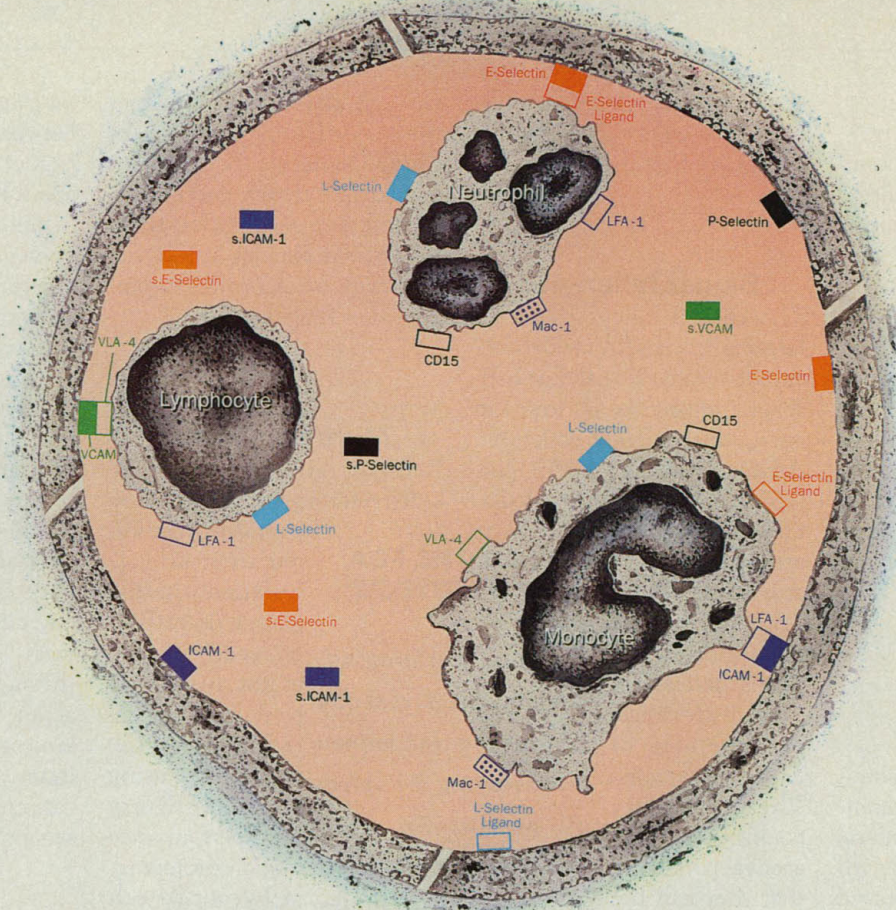
Highly specific connections between neurons form shortly after birth, either through rear-

angement of the connections between axons or by elimination of existing functional synapses. Rabacchi *et al.* (p. 1823) demonstrated the critical involvement of the *N*-methyl-D-aspartate (NMDA) receptor in synaptic elimination by using a selective antagonist of this receptor, D,L-2-amino-5-phosphonovaleric acid (D,L-APV). In the rat cerebellum, Purkinje cells are innervated by several olivary climbing fibers during the first week after birth, but after about 2 weeks each Purkinje cell is innervated by only one climbing fiber. Treatment with D,L-APV administered through an implant allowed about 50 percent of the Purkinje cells to remain multiply innervated by the fibers, implicating the NMDA receptor in synaptic elimination.

Diabetes: class I or class II?

Type I diabetes, an autoimmune disease in which the immune system destroys the pancreatic islet cells that produce insulin, has been genetically linked to the class II major histocompatibility complex (MHC) molecules. A recent article by Faustman *et al.* suggested that decreased expression of class I molecules may contribute to the disease process. In Technical Comments, Gaskins *et al.* (p. 1826) present new data from multiple mouse strains on the expression of the transporter genes that are located in the class II region of the MHC and that are thought to affect class I expression, and Wicker *et al.* (p. 1828) reexamine class I expression in diabetic mice. Faustman *et al.* (p. 1830) describe new data supporting their interpretation of the involvement of class I molecules.

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Gearing, A.J.H. et al, *In Press, Annals N. Y. Acad. Sci.*

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Cancer researchers report a growing interest in endothelial adhesins....

- Current reports have suggested a role for intracellular adhesion molecule 1 (ICAM-1) in the progression of human malignant melanoma and other cancers. Stage I, II and III patients with histologically diagnosed malignant melanoma had significantly increased serum levels of circulating ICAM-1, (cICAM-1). We suggest that elevated levels of serum cICAM-1 may be of diagnostic and prognostic importance in patients with malignant cutaneous melanoma.◀◀

Harning, R. et al, *Cancer Research* (1991) 51, 5003-5005.

On-going studies into inflammatory diseases cite soluble adhesins as an area of potential importance....

- Studies have shown differences in intensity related to age and to particular inflammatory conditions (Such as rheumatoid arthritis, systemic lupus erythematosus, metastatic cancer, and acute urolithiasis) of both ICAM-1 and VLA (unpublished).◀◀

Seth, R. et al, *The Lancet* (1991) 338, 83-84.

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Diseases where Cytokines are important may also have a role for adhesins....

- Tumour necrosis factor, interleukin-1 and γ -interferon cause the release of soluble ICAM-1.◀◀

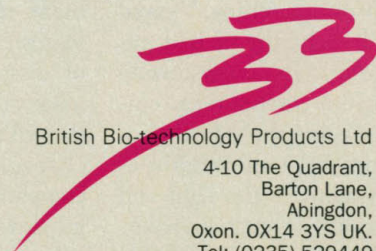
Giavazzi, R. et al, *Cancer Research* (1992)

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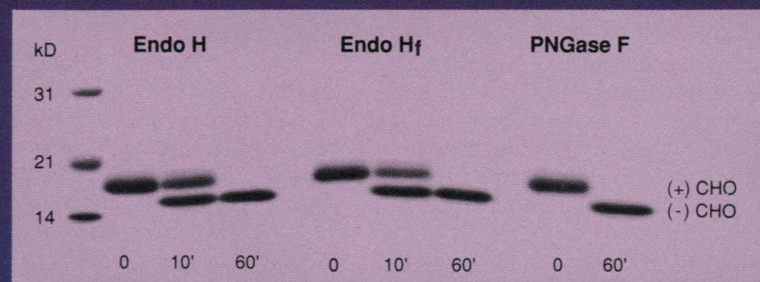
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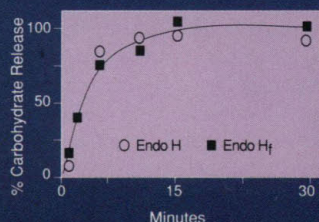
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60 mg of RNase B was incubated with 3,000 units of Endo H or Endo H_f under standard assay conditions. Aliquots were removed at various time points and measured for released carbohydrate. (Dubois et. al [1956] Anal. Chem. 28, 350-356).

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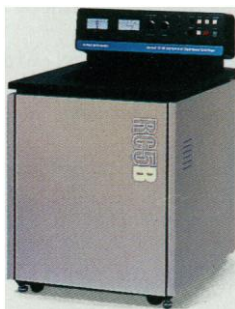
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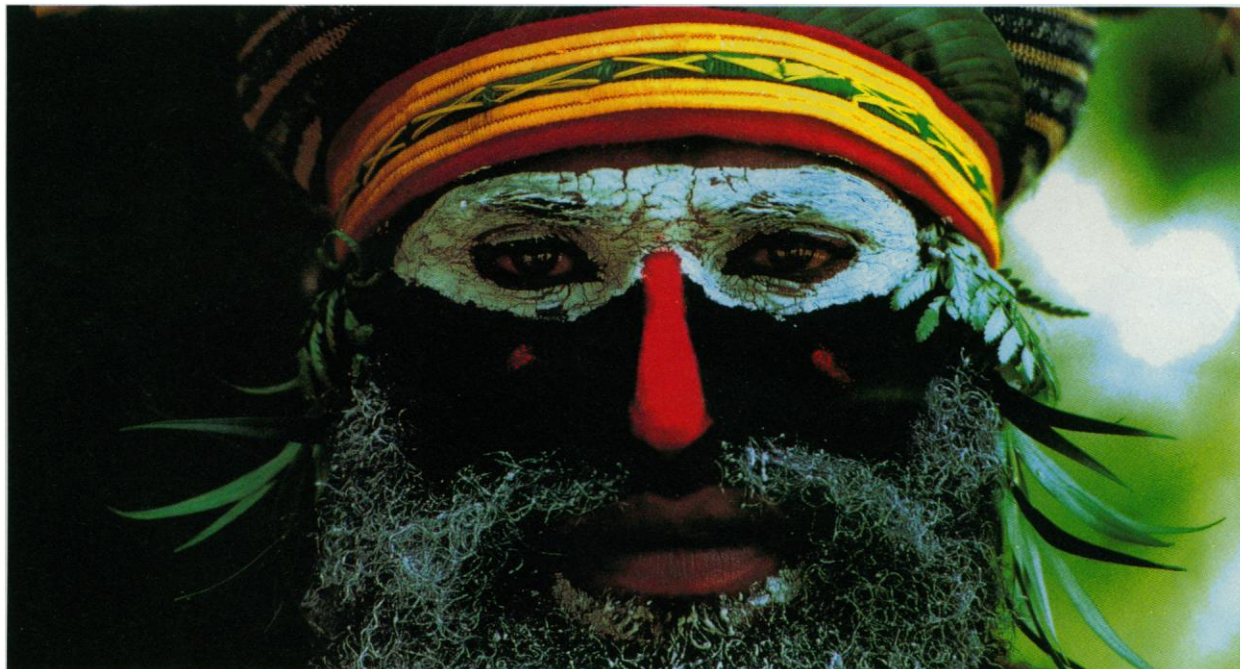
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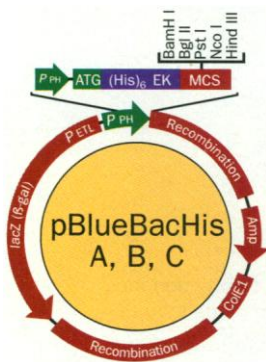


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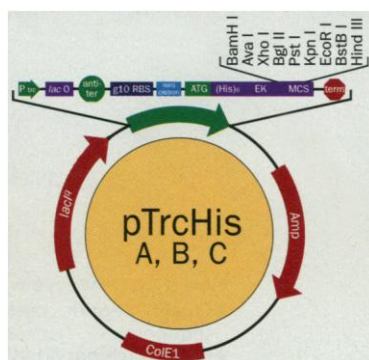
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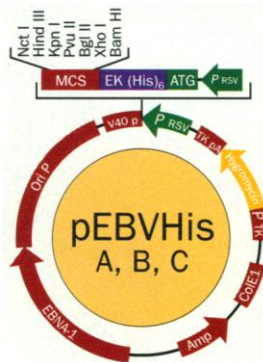
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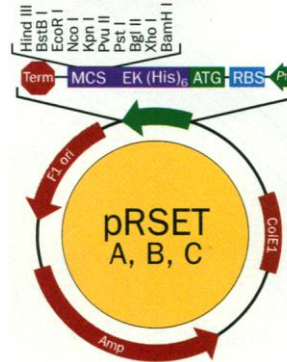
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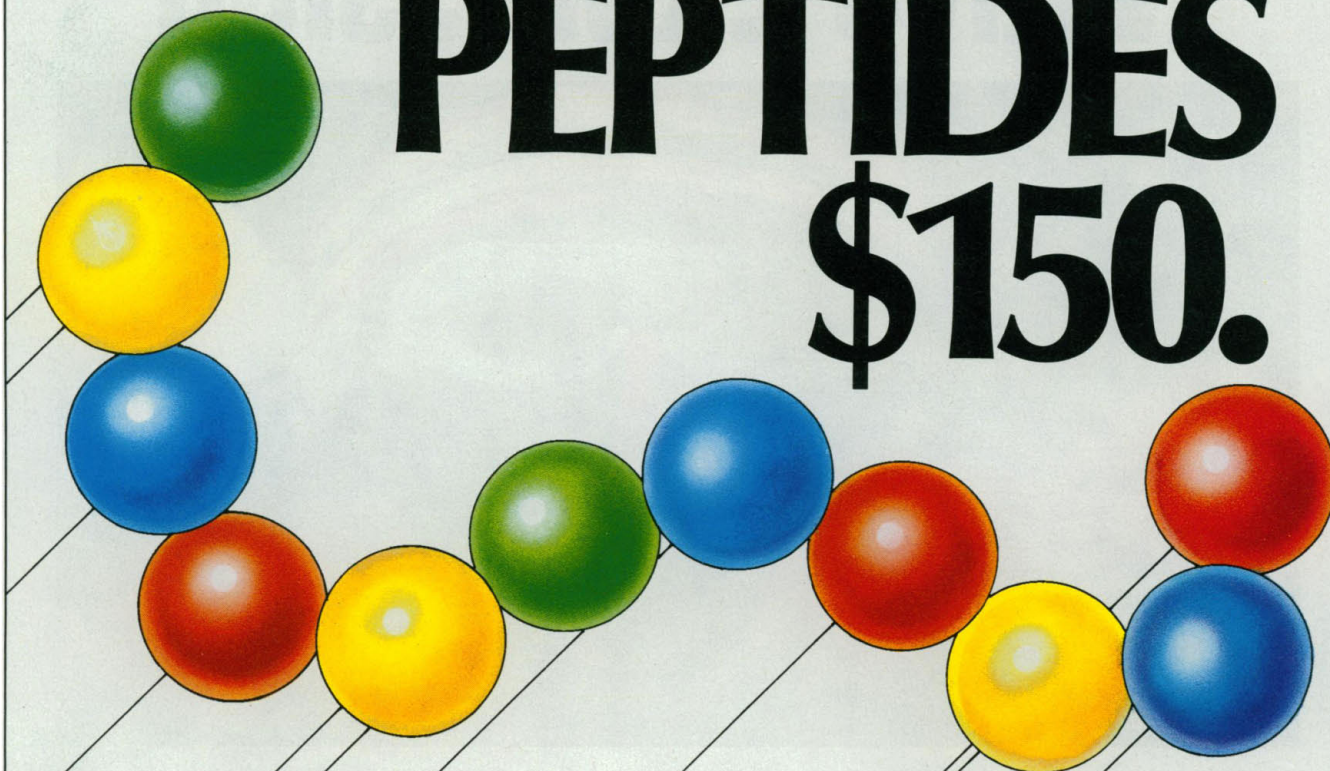
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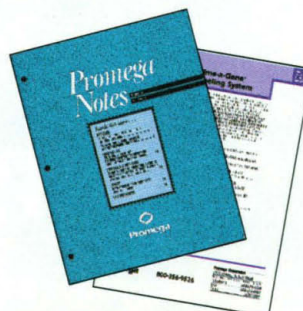
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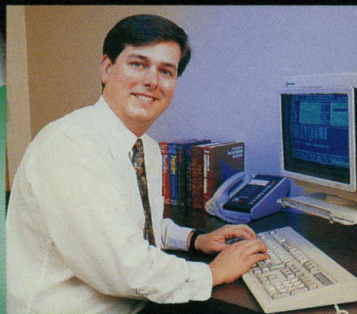
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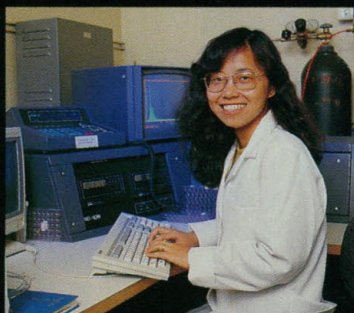
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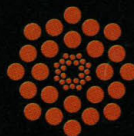


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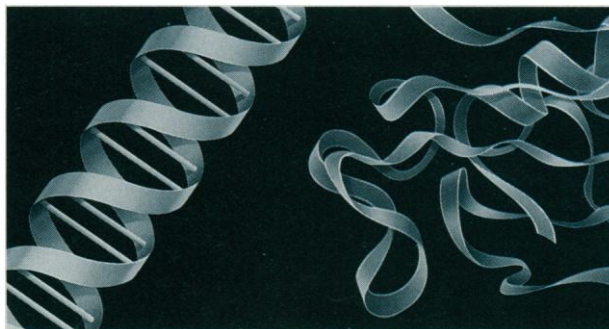
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