



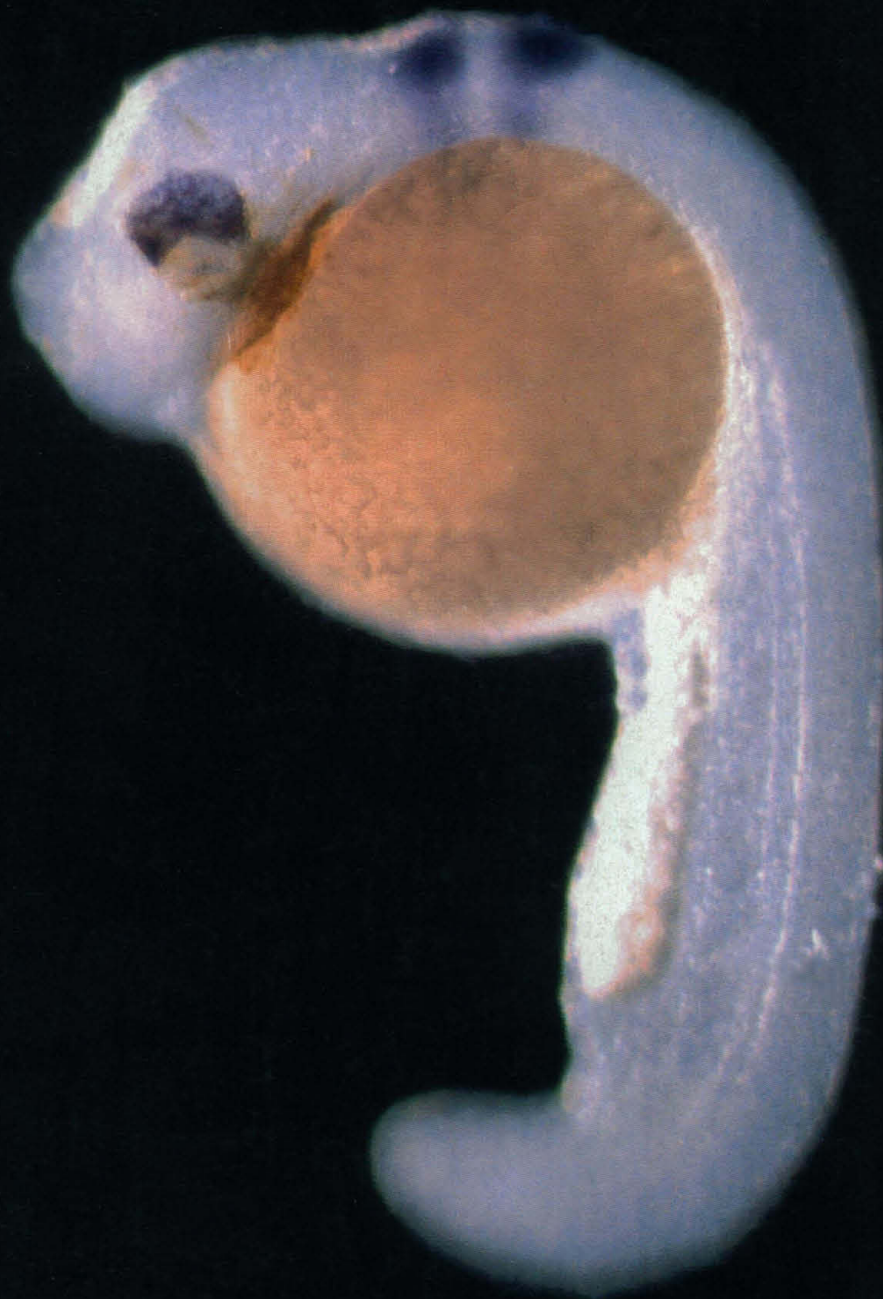
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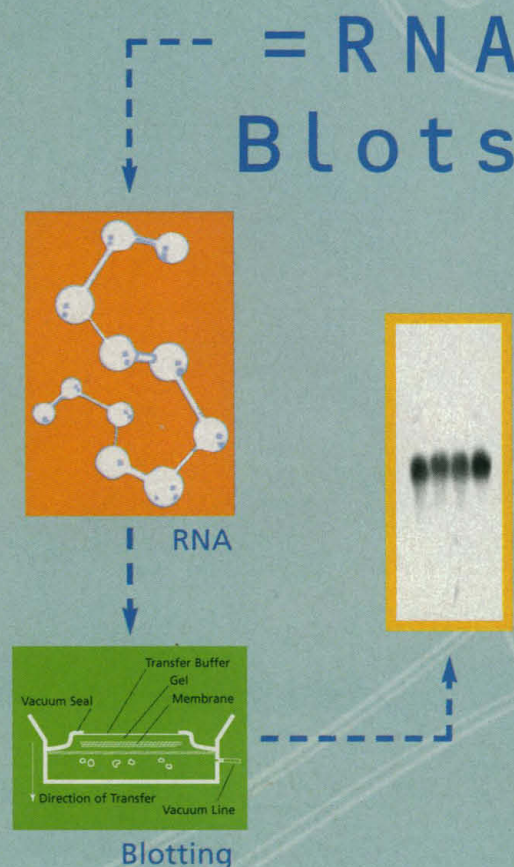
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Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University
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Fig. 1.

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Fig. 2

a. Standard fluorescent detection.

b. TSA-Enhanced fluorescent detection.

c. Standard chromogenic ISH.

d. TSA-Enhanced chromogenic ISH.

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Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads.
Figs. 2 c-d. *In situ* chromogenic detection of oxytocin in rat brain tissue sections.

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Fig. 3

a. Anti-EBA dilution is 1:25.

b. Anti-EBV dilution is 1:25,000. Enhanced by TSA.

Figs. 3 a-b. IHC of EBV antigen in Hodgkin's Lymphoma of mixed cellularity.
Courtesy of R. Von Wasielewski and S. Gignac, Pathologisches Institut der
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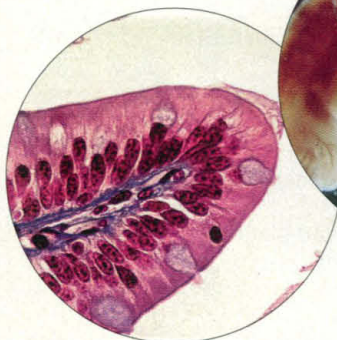
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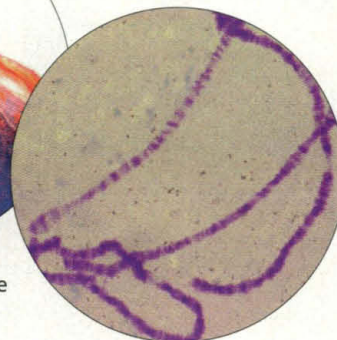
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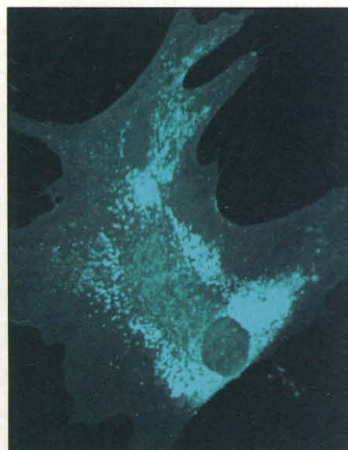
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COVER

A 24- to 26-hour zebrafish embryo (~2 millimeters long) whose left forebrain has been transformed into a section of the hindbrain, as indicated by the ectopic expression of a hindbrain-specific RNA marker (blue), in place of the eye. This posterior transformation of the

cells is caused by a patterning signal from nonaxial mesendodermal precursor cells transplanted to the presumptive forebrain region at the shield stage. See page 254. [Image: K. Woo and S. E. Fraser]



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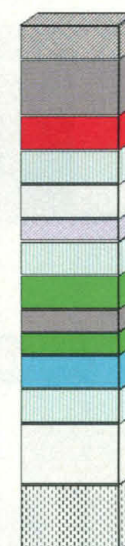
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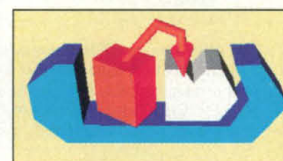
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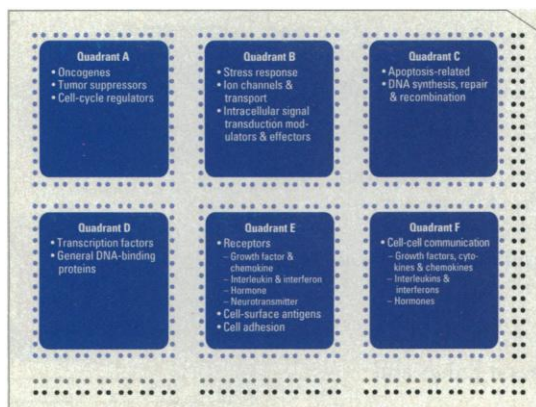
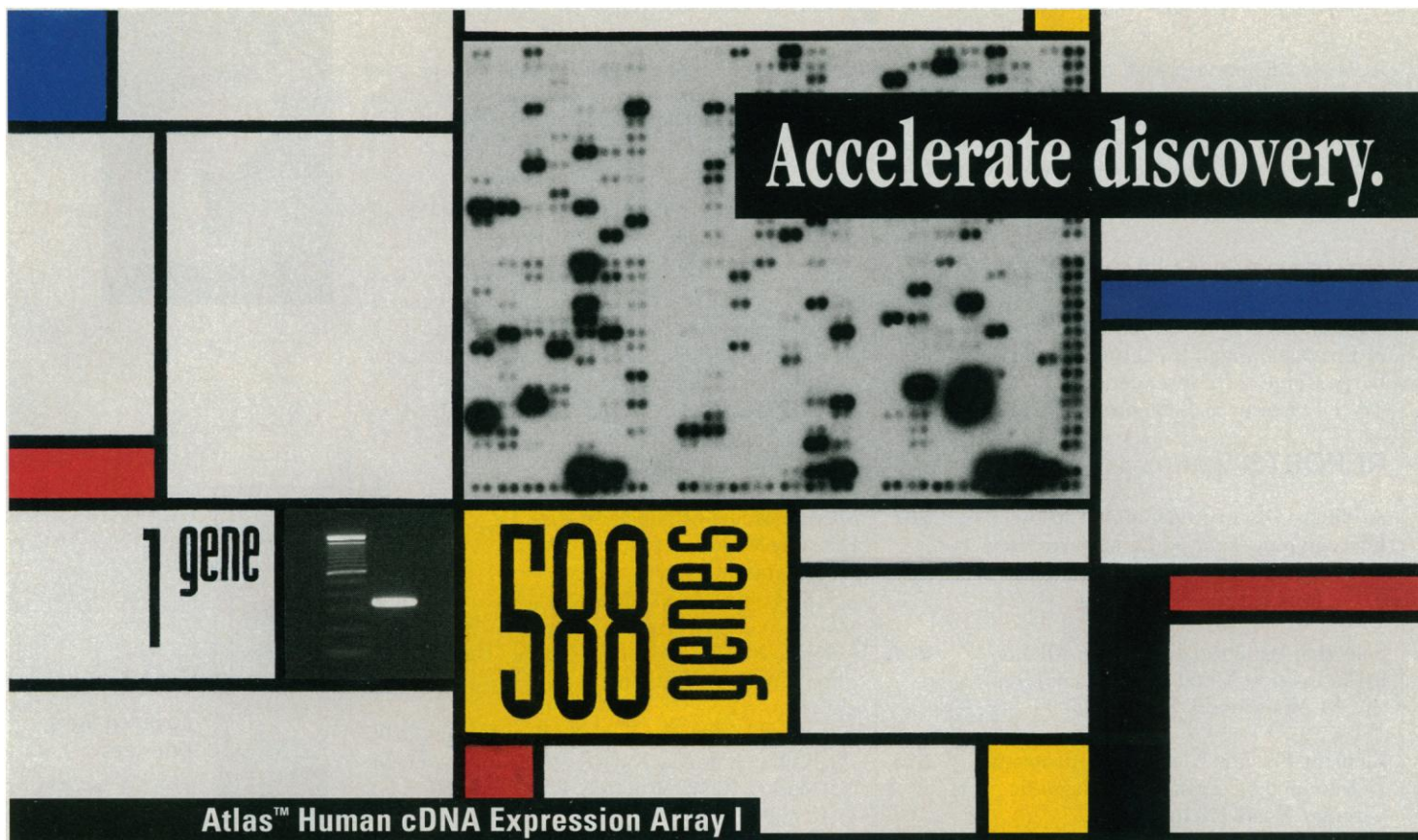
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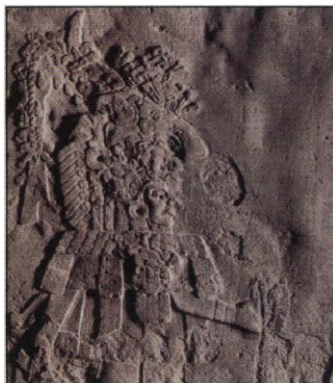
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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Deciphering additional clues

The writing system known as epi-Olmec has provided researchers in Mesoamerican studies a number of important and controversial puzzles. In 1993, Justeson and Kaufman published their decipherment of epi-Olmec texts on a stone monument



from La Mojarra, Mexico. Now these authors (p. 207) have uncovered an additional text on the same monument that expands the available corpus of epi-Olmec writing and confirms various aspects of the original decipherment.

Orbit and climate

Variations in the amount and distribution of solar energy arising from cyclic changes in the precession, obliquity, and eccentricity of Earth's orbit are thought to drive glacial climate cycles. One open question has been the origin of the major 100,000-year glacial cycles that developed about 1 million years ago—the forcing by variations in Earth's eccentricity is weak. Muller and MacDonald (p. 215; see the news story by Kerr, p. 183), in an analysis of several ocean climate records, show that before about 1 million years ago, the spectrum of the obliquity cycles closely matched those of the major climate cycles. However, variations in the inclination of Earth's orbital plane can better account for the spectral shape of the 100,000-year cycle.

Cholesterol traffic tie-up

Niemann-Pick C disease (NP-C) is a rare inherited disorder that, at the cellular level, is characterized by an inability to mobilize cholesterol. Patients with NP-C develop neurologic abnormalities including ataxia, seizures, and loss of speech, and typically die as children. Carstea *et al.* (p. 228) (see the news story by Pennisi, p. 180) have identified the human gene responsible for NP-C, and, in parallel work, Loftus *et al.* (p. 232) show that the same gene is defective in two independent mouse models of the disease. The predicted NPC1 protein has more than 10 putative transmembrane domains and has sequences in common with other proteins involved in cholesterol metabolism. The NPC1 sequence suggests that it participates in cholesterol trafficking from lysosomes to other cellular membranes.

Magnetic origins

The magnetic properties of alloys and thin layered materials, such as direction of easy magnetization, can result from complex interactions between components, and the individual contributions can be difficult to resolve. Dürr *et al.* (p. 213) have used transverse magnetic circular x-ray dichroism to resolve the magnetic contributions of cobalt and nickel layers in a thin film structure by using the different x-ray absorption edges for each element. The much thinner cobalt overlayer changed the easy magnetization direction of the entire film.

Out of sight but not out of mind

How do we know where things are when we are not looking at them, as when the lights go out in a room? Graziano *et al.* (p. 239; see the Perspective by Rizzolatti *et al.*, p. 190) have located neurons in the monkey premotor cortex—an area known to be involved in integration of sensory and motor function—that register the presence of an object seen when the lights are on and that continue to maintain their activity after the lights have been turned off. Only after the lights are turned on again and the monkey sees that the object actually had been removed silently under the cover of darkness do the neurons cease

responding. Thus, these neurons can code for “object permanence,” an aspect of spatial perception developed by Piaget.

Making lignin the hard way

The production of paper and pulp from trees requires the removal of lignin, which stabilizes the cell walls of woody plants. Ralph *et al.* (p. 235) show that although loblolly pine trees carrying a naturally occurring mutation are deficient in an enzyme thought to be critical for lignin biosynthesis, the mutant trees get around the problem by co-opting an unusual subunit to synthesize lignin. Efforts to genetically engineer plants with lower amounts of lignin may be complicated by the apparent flexibility of these metabolic pathways.

Capillary creation

The tiny capillaries that carry blood throughout our tissues develop first as outgrowths of endothelial cells from larger vessels. Lindahl *et al.* (p. 242) found that the next step, recruitment of pericyte cells to the capillaries, is dependent on platelet-derived growth factor (PDGF) signaling and is ultimately critical to the structural stability of the capillaries. In mice lacking PDGF-B, the capillaries

lack pericytes, and innumerable microaneurysms form when the fetal blood pressure rises near the time of birth.

Simulates stress

In unstressed cells, heat shock factors (HSFs) are present as inactive monomers in the cytoplasm. Upon heat shock treatment, the factors multimerize, translocate to the nucleus, and activate gene transcription. Kanei-Ishii *et al.* (p. 246) show that, in the absence of cellular stress, an HSF can be converted to an active form. HSF3 can associate directly with the proto-oncogene product c-Myb in unstressed cells. This complex stimulates translocation of HSF3 to the nucleus for subsequent gene activation. The association of HSF3 and c-Myb may provide a link between the stress response and proliferation control.

Manages without cAMP

During *Dictyostelium* development, cyclic adenosine monophosphate (cAMP) is used as a signal both outside and inside the cell. Extracellular cAMP triggers a signaling pathway that activates adenyl cyclase, an enzyme involved in the production of cAMP. Previous work suggested that extracellular cAMP is crucial for *Dictyostelium* tissue formation, morphogenesis, and terminal differentiation. Wang and Kuspa (p. 251; see the news story by Gura, p. 181) have demonstrated that when protein kinase A is expressed in cells in which all extracellular and intracellular cAMP were absent, normal *Dictyostelium* development was observed. Extracellular cAMP was not found to be essential for *Dictyostelium* development, and all intracellular cAMP signaling was mediated through protein kinase A.

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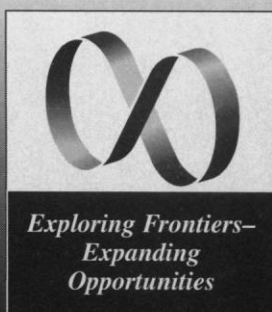


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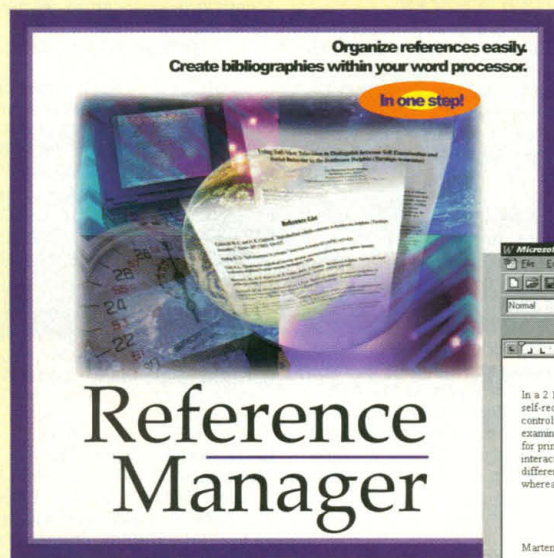
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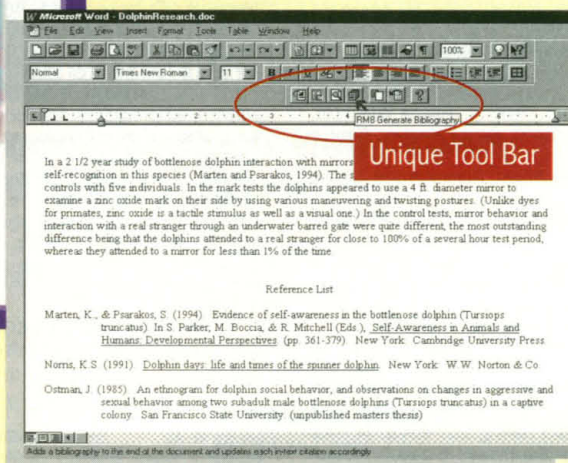
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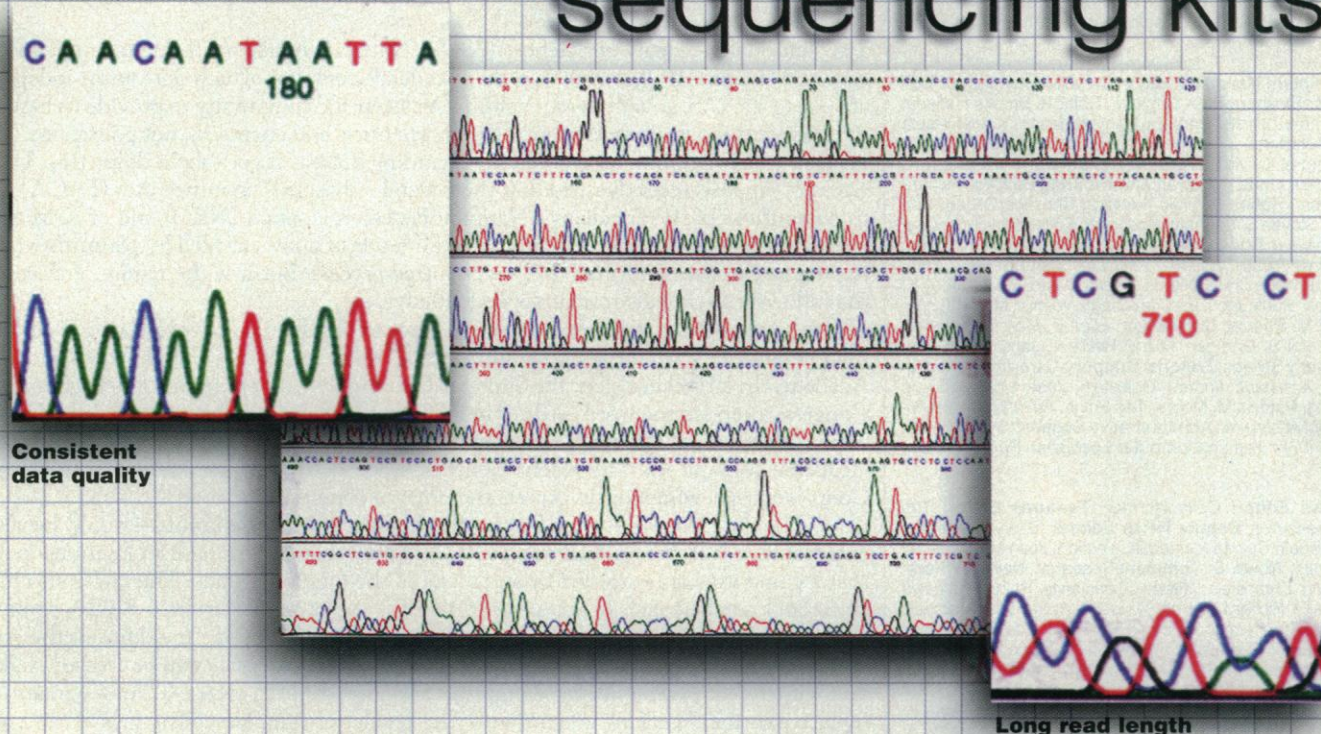
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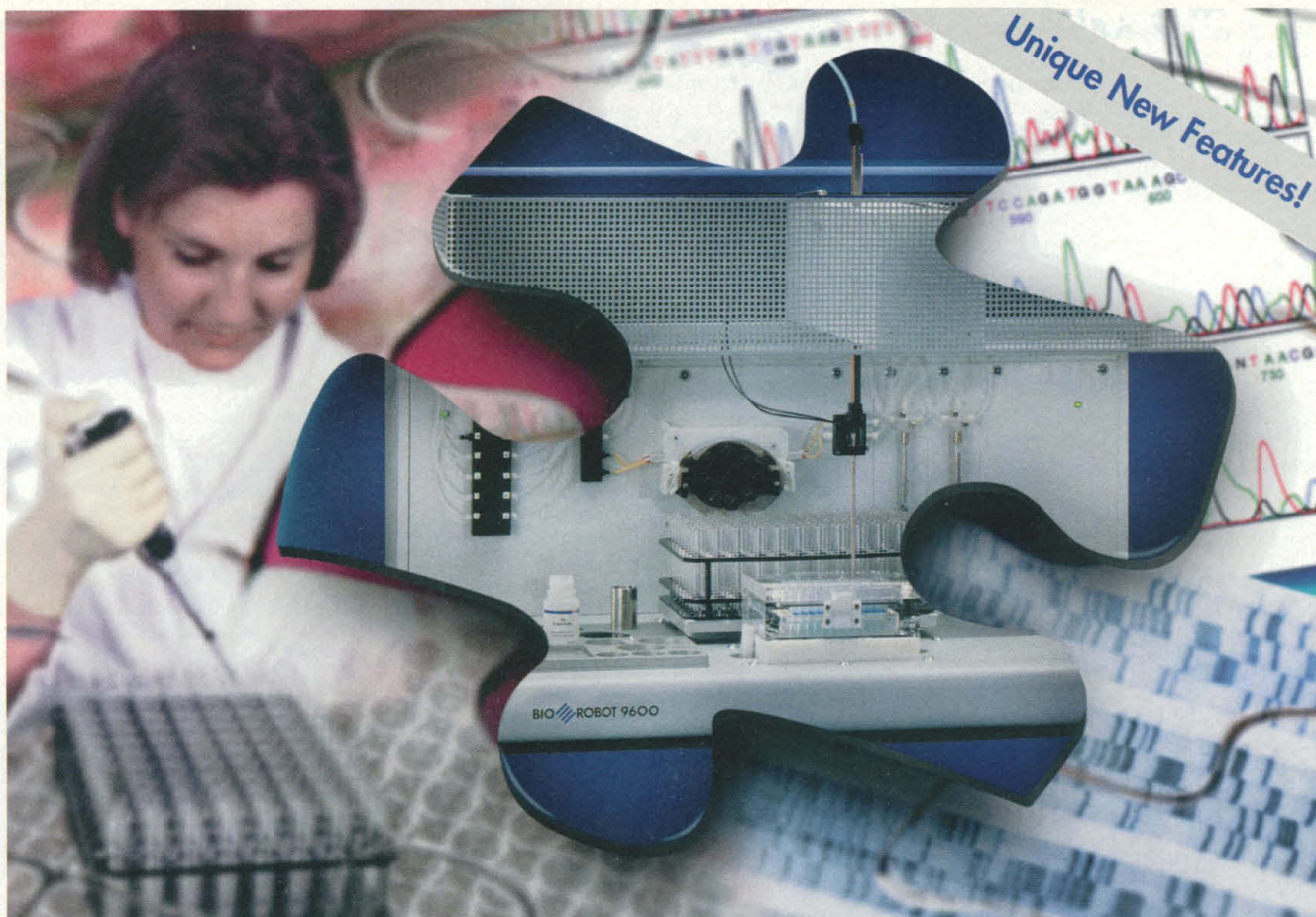
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