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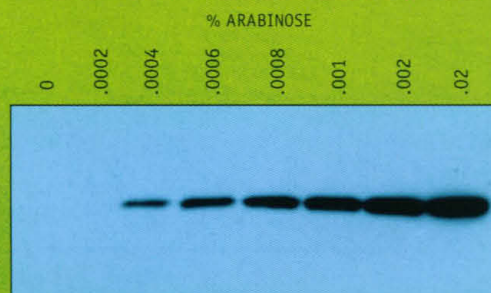
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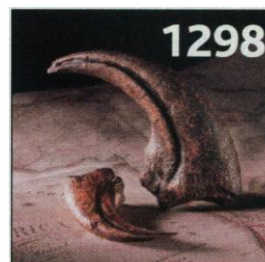


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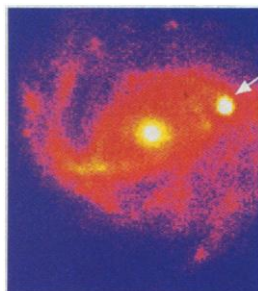
Science

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COVER Massive thumb (33 centimeters along outer arc) and smaller third claw from the hand of an ~11-meter-long dinosaur that was recently discovered in the remote Ténéré Desert of the Niger Republic. This sail-backed predator apparently used its long, narrow snout to capture fish along the banks of broad rivers around 100 million years ago. [Photo: Paul Sereno, Michael Roberts, Hans Larsson]



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Exploding stars' message undimmed

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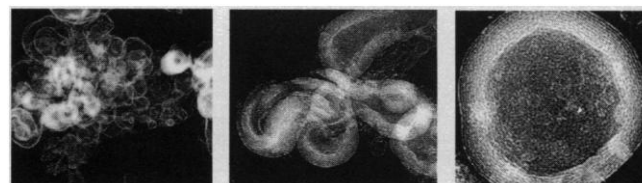
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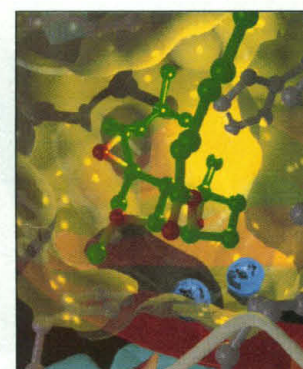
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Structural basis of fumagillin action

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STAR EJECTA IN METEORITES

Micrometer-sized refractory grains with anomalous isotopic ratios have been discovered in primitive meteorites and are associated with material ejected from stars. The measurement of multiple isotopic ratios in such grains can be used to constrain stellar nucleosynthesis models. Choi *et al.* (p. 1284) have developed a nondestructive technique based on scanning electron microscopy and energy-dispersive x-ray analysis to augment ion probe analysis, which can rapidly consume a micrograin. They determined isotopic abundances of oxygen, magnesium, aluminum, calcium, and titanium from 14 circumstellar grains in two ordinary chondrites. The isotopic composition of one corundum grain is consistent with mixing of the helium-carbon zone and the hydrogen envelope in a type II supernova, and other grains with anomalous titanium isotopic abundances may have been derived from asymptotic giant branch stars with high metallicity (abundance of elements heavier than hydrogen greater than that of our sun).

BROWN DWARF AROUND A RED STAR

A brown dwarf candidate has been identified orbiting around a young star by Rebolo *et al.* (p. 1309; see the news story by Helleman) through optical and infrared studies. Its distance (about 300 Earth-sun distances) and low mass (about 25 Jupiter masses) relative to the star suggest that the binary system formed by fragmentation of a collapsing molecular cloud. The lower limit on the estimated age of the star (about 100 million years) suggests that substellar mass companions can form on relatively short time scales.

LONG-SNOUT DINOSAURS

Spinosaurids are an enigmatic group of fish-eating dinosaurs, characterized in part by a long narrow snout. Early fossils first used to describe spinosaurids were lost in World War II; scattered remains have been found elsewhere since. Sereno *et al.* (p. 1298; see the cover, the Perspective by Holtz, and the related news story by Stokstad) describe new Lower Cretaceous fossils from the Ténéré Desert of Niger, including much of a snout and other parts of the skeleton, from a spinosaurid. The spinosaurid remains are closely related to fossils discovered previously in England, implying that there was dispersal across the Tethys Ocean separating Eurasia from Africa at this time.

LIBERATING SIGNALING PROTEINS

Some intercellular signaling molecules are synthesized in a form anchored to the cell membrane and to be released later by proteolysis. Tumor necrosis factor- α (TNF- α) converting enzyme (TACE) is a metallo-



proteinase that catalyzes such processing of TNF- α . Peschon *et al.* (p. 1281; see the Perspective by Werb and Yan) generated mice with mutated TACE that lacked protease activity. TACE was required for normal development, and analysis of immortalized fibroblasts from the mice showed that TACE processes other important regulatory molecules as well. The cells had defects in release of transforming growth factor- α , the adhesion molecule L-selectin, and a TNF receptor. Thus, TACE appears to function in shedding of a group of structurally and functionally diverse proteins.

COPING WITH STRAIN

Many materials undergo a brittle-to-ductile transition below a specific temperature. It is unclear whether the propagation of a crack introduced into the material is controlled by the nucleation of dislocation sites around the crack front or by the mobility of these dislocations. Cleavage experiments on single crystal tungsten by Gumbsch *et al.* (p. 1293) show that, at low temperature, the nucleation density is the limiting factor—additional dislocation sites around the crack can arrest its propagation by giving some degree of plasticity to the material. Near the transition temperatures, however, sufficient dislocation sites exist and their mobility becomes the limiting factor in preventing further propagation.

HOT OUT OF THE PRESS

Composites of silicon carbide fibers in a ceramic matrix exhibit high strength, but the effects of heat and oxidation limit

their high-temperature use in air to below 1500°C, and fibers under load in the matrix are subject to creep failure. Ishikawa *et al.* (p. 1295; see the Perspective by Tredway) now show how to eliminate the matrix; amorphous silicon-aluminum-carbon-oxygen fibers, obtained through polymer synthesis, can be hot-pressed to form densely packed, hexagonal columnar fibers. The material shows high strength up to 1600°C in air and also exhibits high thermal conductivity.

MAKING MESOPOROUS MATERIALS STABLE

The high thermal stability of zeolites, which have angstrom-scale pores, allows their use in demanding industrial applications. Mesoporous materials, with larger nanometer-scale pores, have had much more limited stability, especially under hydrothermal conditions. Kim *et al.* (p. 1302) prepared mesoporous vesicles (pore sizes of 2.7 to 4 nanometers) that have very high cross-linking of the silicate tetrahedral network and that remain stable after 150 hours in boiling water.

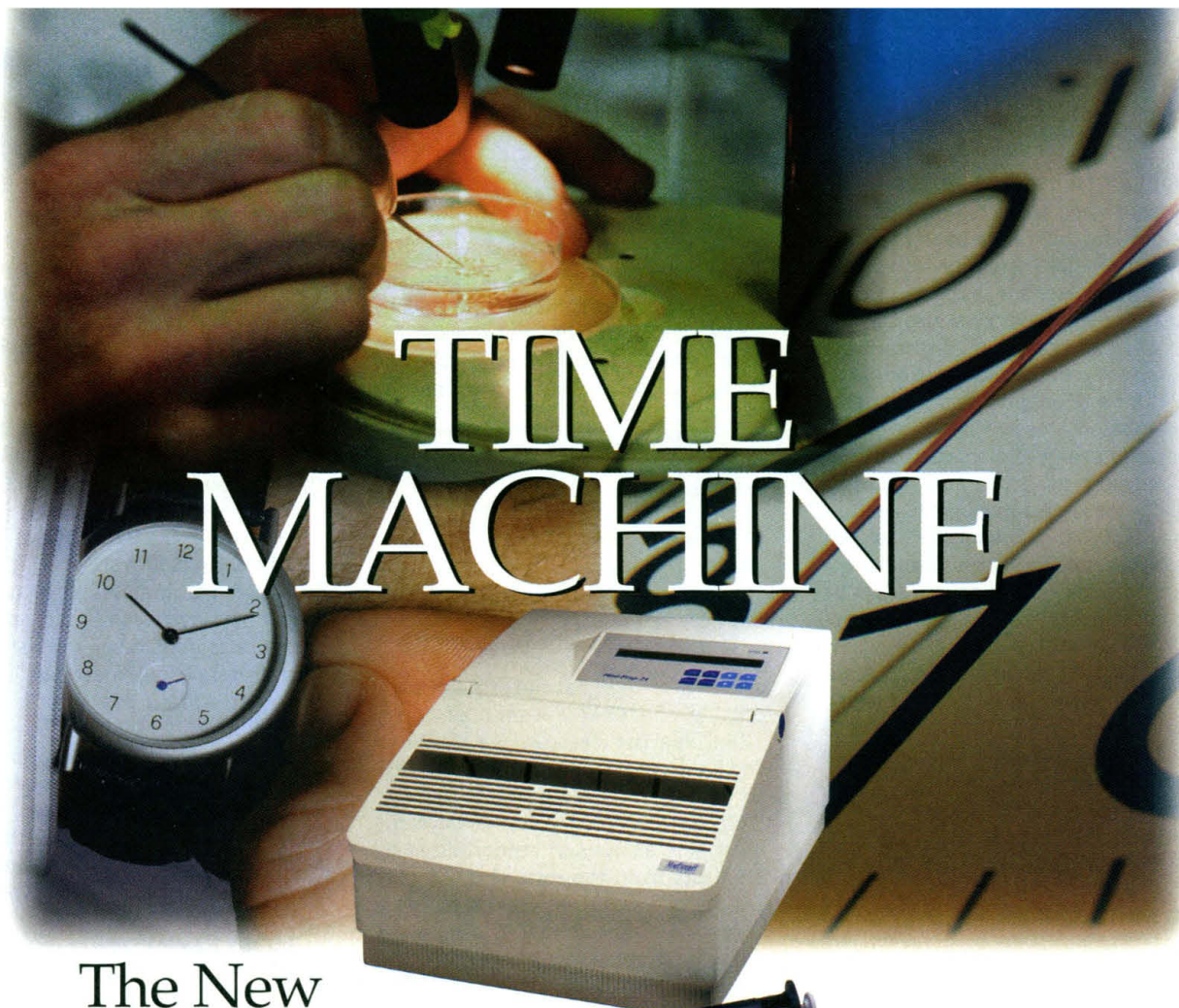
MOST REWARDING

The presentation of visual stimuli, with rewards linked to only one of several possible eye or hand movements, has made possible the identification and analysis of brain areas and cell subserving visual attention and directional motor output. Shima and Tanji (p. 1335) modified this approach to identify cells in the rostral cingulate motor area that are used when making a decision to switch to a more promising stream of rewards. The cingulate motor area receives input from the limbic system and prefrontal cortex, which contain information about motivation and internal state, and sends output to motor systems, and thus appears to be ideally positioned as an arbiter of reward evaluation.

CLOSE-UP OF A CANCER DRUG

Fumagillin is a fungal metabolite that was serendipitously discovered to inhibit angiogenesis, the formation of new blood vessels. Angiogenesis is required for the growth of solid tumors, and a derivative of fumagillin is now in clinical trial as an anti-cancer agent. Fumagillin specifically binds and inhibits methionine aminopeptidase-2 (MetAP-2), a metalloenzyme that cleaves methionine from the amino terminus of proteins. Liu *et al.* (p. 1324) determined the crystal structure of human MetAP-2 with and without bound fumagillin. The struc-

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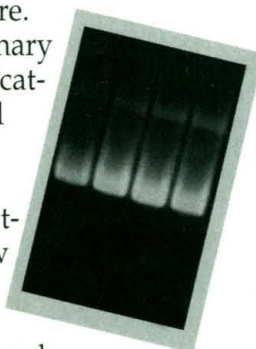
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tures provide insight into the drug's specificity and mechanism of action, information that may facilitate the design of more effective anticancer therapies.

EVADING APOPTOSIS

The caspase cascade, which plays a leading role in programmed cell death, is initiated through the cleavage of procaspase molecules. Cardone *et al.* (p. 1318) show that phosphorylation can regulate caspase activation and may contribute to the survival of some cancer cells. Both an activated form of the oncogene Ras and a kinase that it activates, Akt, can phosphorylate and thereby prevent the activation of pro-caspase-9.

VIRAL ATTACK ON CANCER

Reovirus is an RNA virus that infects and kills cells with an activated Ras pathway. Reasoning that this pathway is activated in most tumor cells, Coffey *et al.* (p. 1332; see the news story by Pennisi) investigated whether the virus could be used as a cancer therapy. Direct injection of reovirus into tumors growing in immune-deficient or immune-competent mice resulted in significant shrinkage of the tumors, although larger doses of virus were required in the latter case. Because reovirus is relatively nonpathogenic in humans, its anticancer activity may have clinical applications.

RECEPTOR CLUSTERING AND MOLYBDOENZYMES

Gephyrin, a neuronal protein, has been thought to be important in clustering neuronal glycine receptors. The gene for gephyrin also has homology to proteins involved in the generation of molybdenum cofactors required for activity of a variety of enzymes, including xanthine de-

hydrogenase and sulfite oxidase. Feng *et al.* (p. 1321; see the Perspective by Froehner) describe mice that totally lack gephyrin. The mice die within 1 day of birth and exhibit symptoms similar to those seen in human babies with stiff baby syndrome (they assume a rigid hyperextended posture in response to touch). In addition to the motor problems, the mice also lack functional molybdoenzymes.

ENZYMES THAT SWITCH

Various fatty acids differ by hydroxylation state and location of double bonds. Broun *et al.* (p. 1315), in analyzing some of the enzymes that synthesize fatty acids, identified six specific amino acids that determine which sort of chemical reaction an enzyme will catalyze. Changes in no single amino acid determine specificity, but combined changes in these various amino acids can switch the function of the enzyme from hydroxylase to desaturase. The identity of these critical amino acids suggests that the enzyme's specificity is determined by the geometry of its active site.

EXPLORATORY IMMUNITY

How does the immune system learn to ignore its own antigens while responding quickly to antigens expressed by microbes or on grafts from nonidentical donors? Alferink *et al.* (p. 1338) show that the neonatal immune system has different trafficking patterns for lymphocytes than does the adult system. For a short period of time after birth, T cells have much greater access to the skin, for example. This trafficking depends on the selectin adhesion molecules that are expressed on the endothelium and allows the immune system to become tolerant to antigens found only in that location.

TECHNICAL COMMENT SUMMARIES

Detecting Possible Rotation of Earth's Inner Core

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5392/1227a

A. Souriau (*Science's* Compass, Perspectives, 3 July, p. 55) discussed evidence, from several recent studies, purporting to show that the solid inner core of the Earth might rotate faster than the mantle. She noted that "the problem is far from simple" and concluded "the differential rotation of the inner core is not yet firmly established."

P. G. Richards *et al.* describe new data in support of the hypothesis of a rotating inner core, noting that "for three seismic paths through the inner core ... the estimated rate of change is consistently negative." Richards *et al.* "agree in general" with Souriau "that anisotropy variation within the inner core must be better understood before significant improvement can be made in estimates of the rotation rate."

In response, Souriau describes, point by point, why the results of various studies to date should be considered ambiguous (because of methodological and statistical problems). She concludes that "there is no undeniable demonstration of the existence of inner core rotation. But there is also no undeniable demonstration of the absence of rotation."

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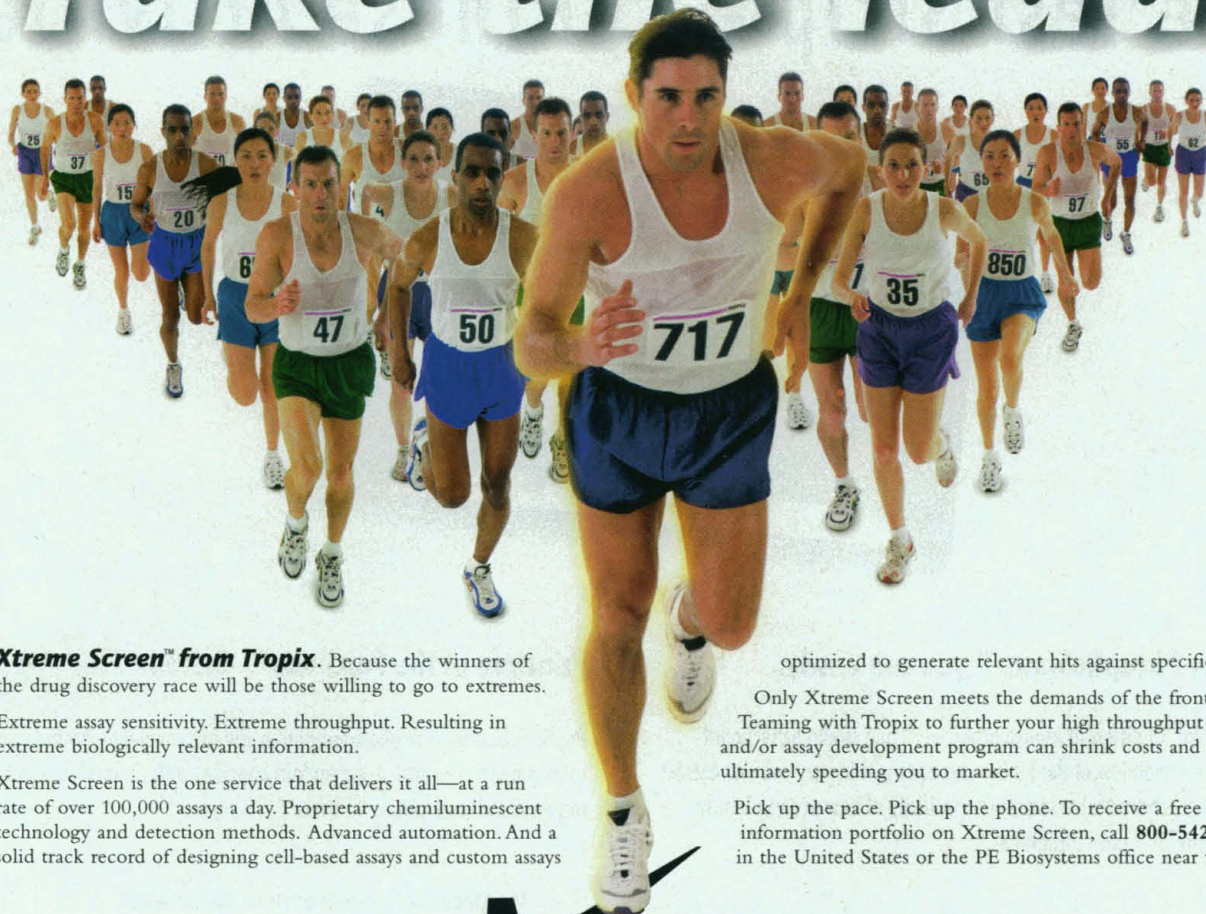
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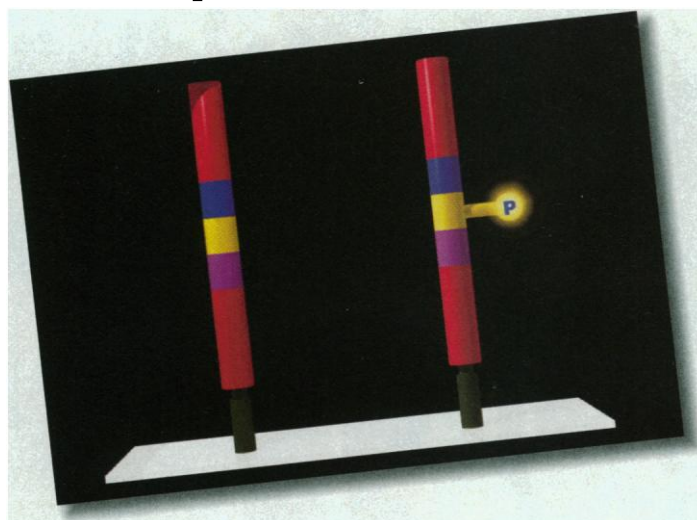
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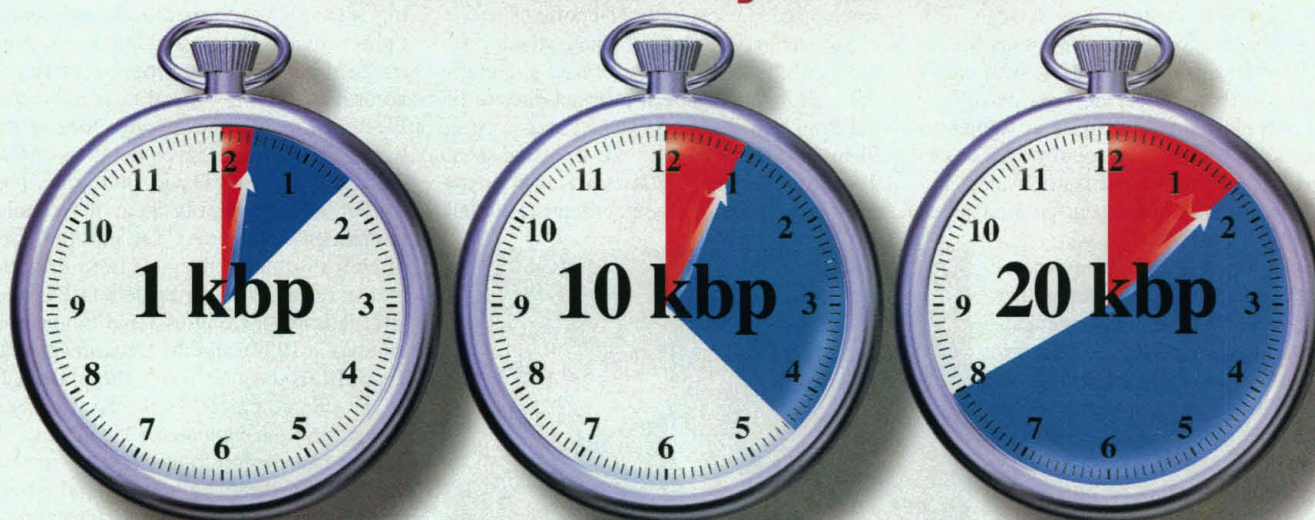
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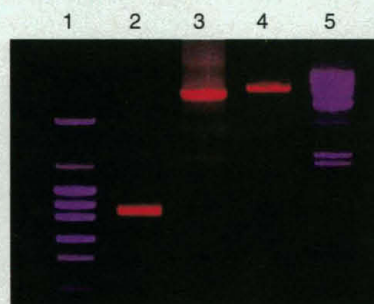
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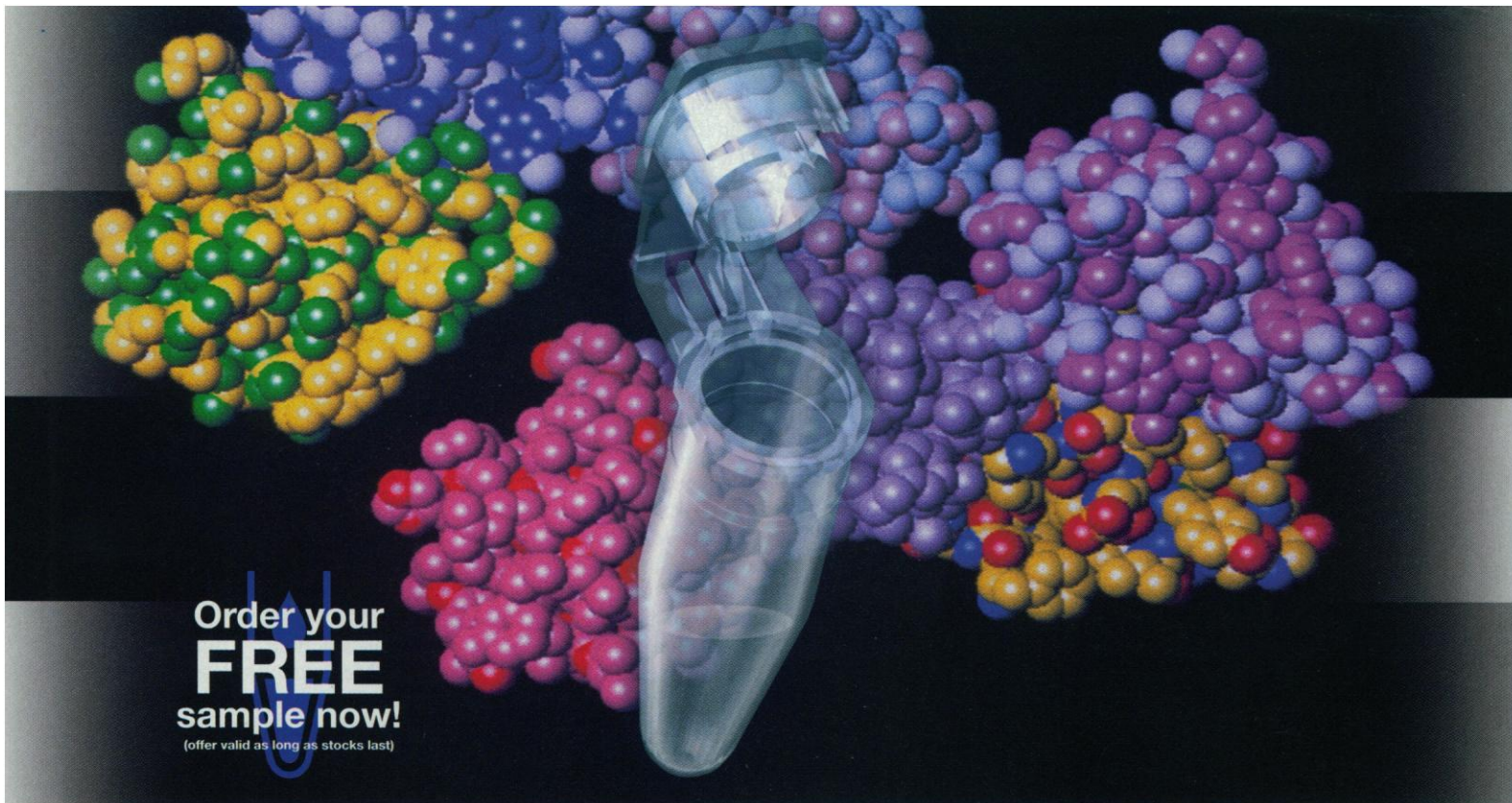
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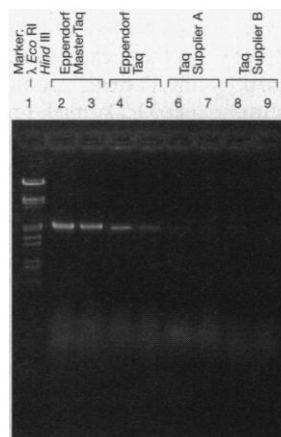
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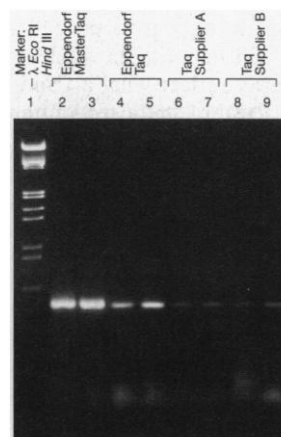
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● Fig. 1: Amplification of a SSU rRNA gene from total genomic algae DNA. PCR was performed from genomic algae using different Taq DNA Polymerases. Equal volumes of the PCR reactions were analyzed by gel electrophoresis.



● Fig. 2: Amplification of a GAPDH specific DNA fragment from genomic blood DNA. PCR was performed from human genomic blood with different Taq DNA Polymerases. Equal volumes of the PCR reactions were analyzed by gel electrophoresis.

The Polymerase Chain Reaction (PCR) is protected by patent. The patent is held by Hoffmann-La Roche. Products marked "licensed for PCR" are sold under licensing arrangements with F. Hoffmann-La Roche Ltd., Roche Molecular Systems, Inc. and The Perkin-Elmer Corporation.

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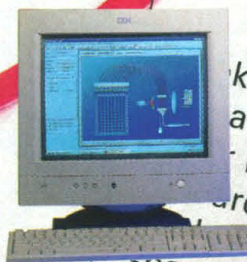
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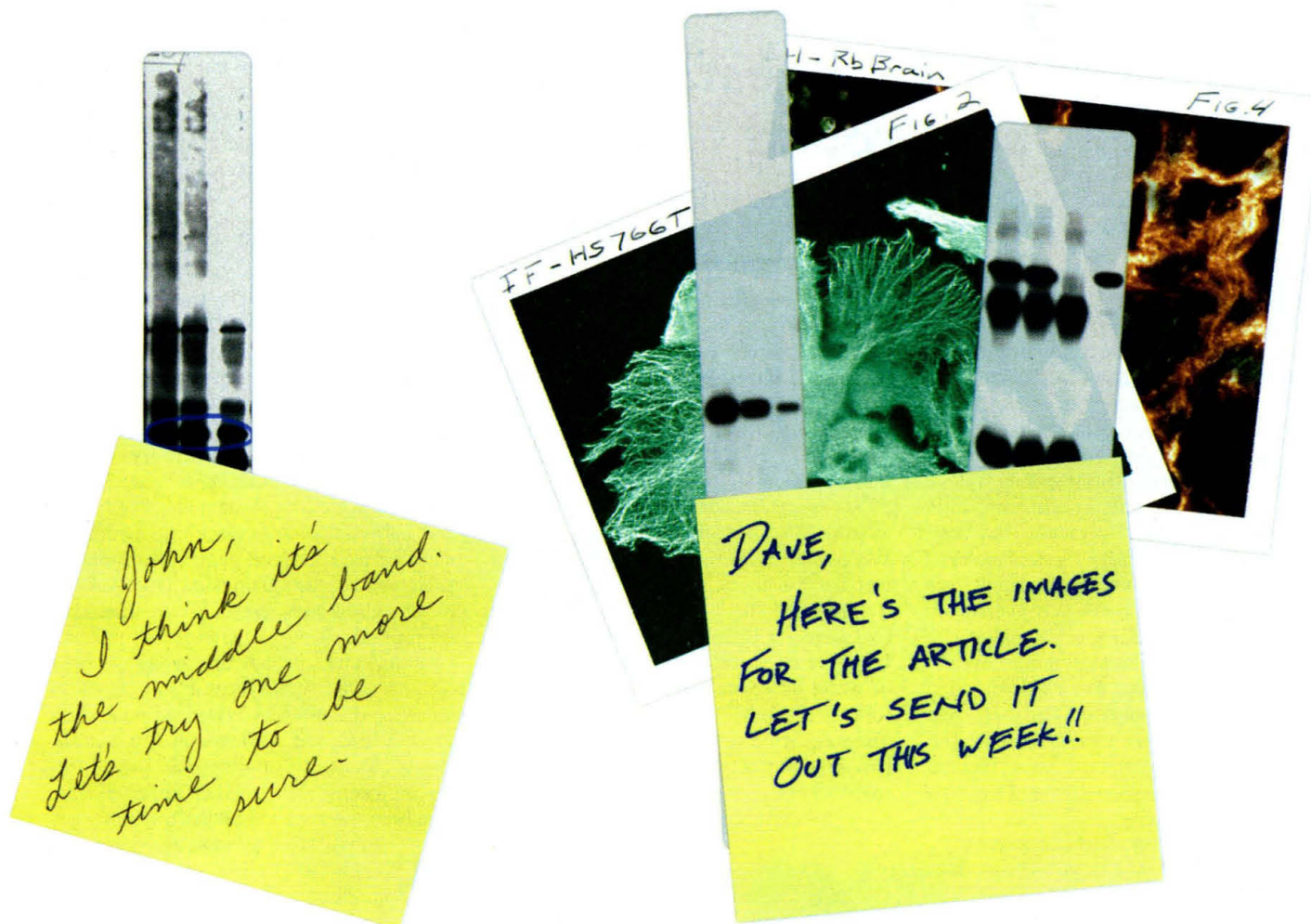
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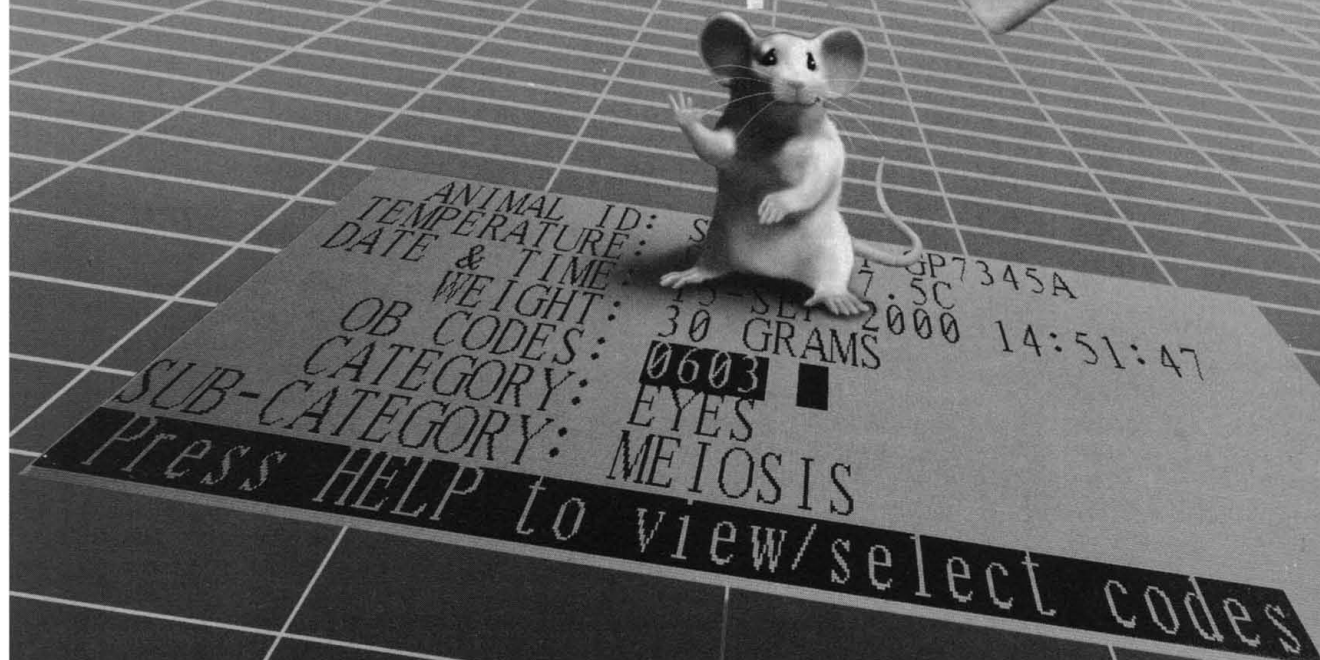
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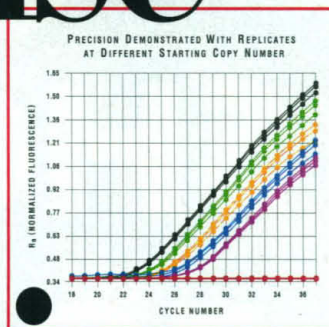
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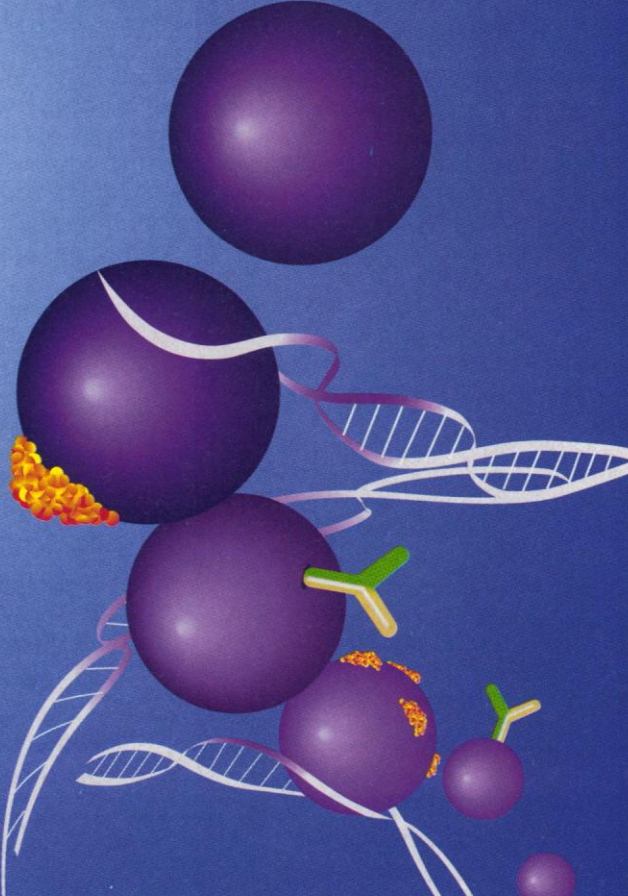
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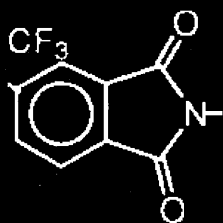
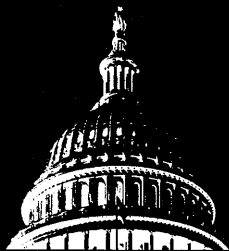
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