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150 Years • 1848-1998

# SCIENCE

1 May 1998

Vol. 280 • Pages 641–788

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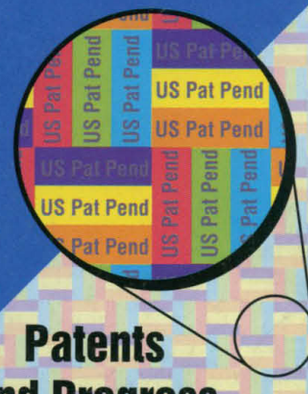


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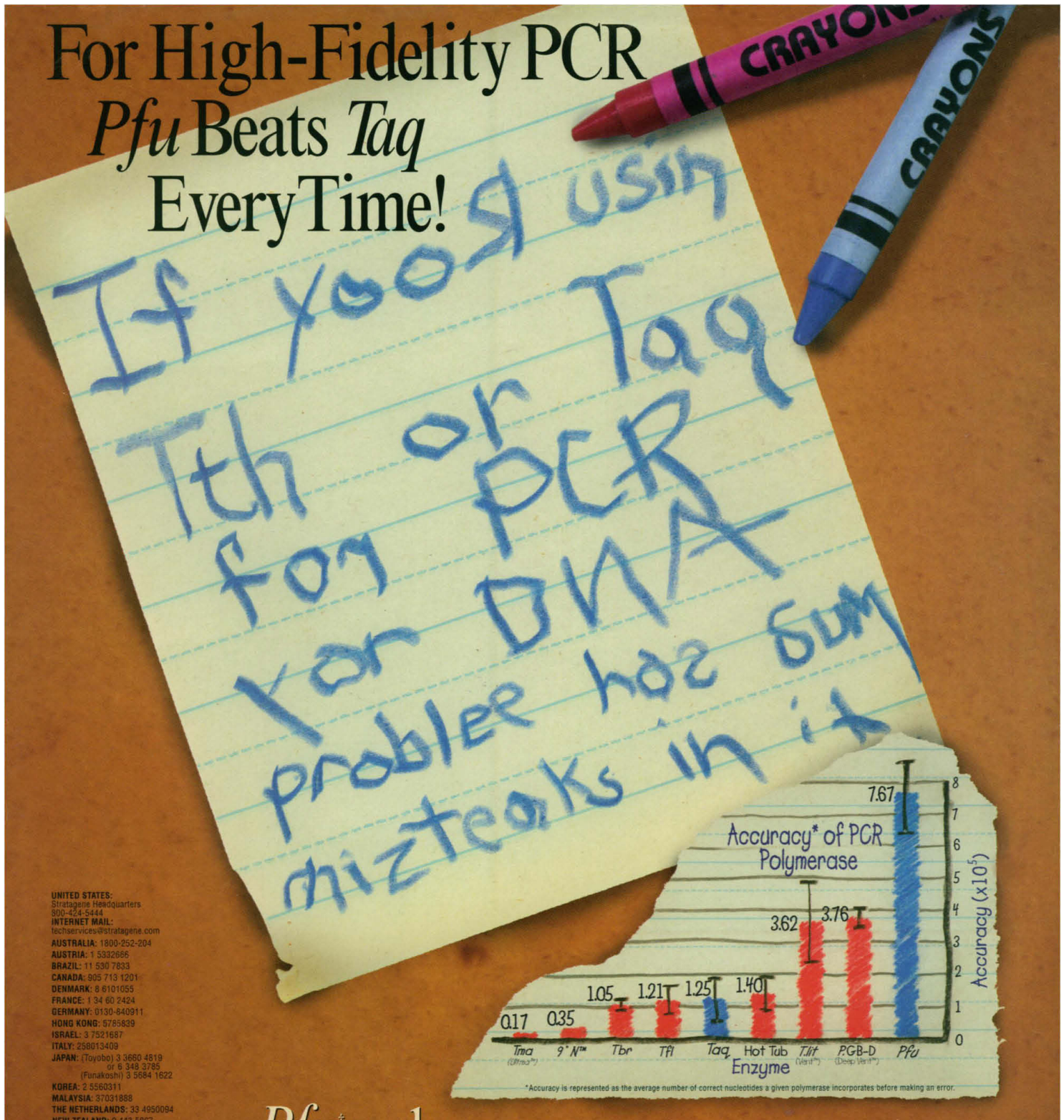


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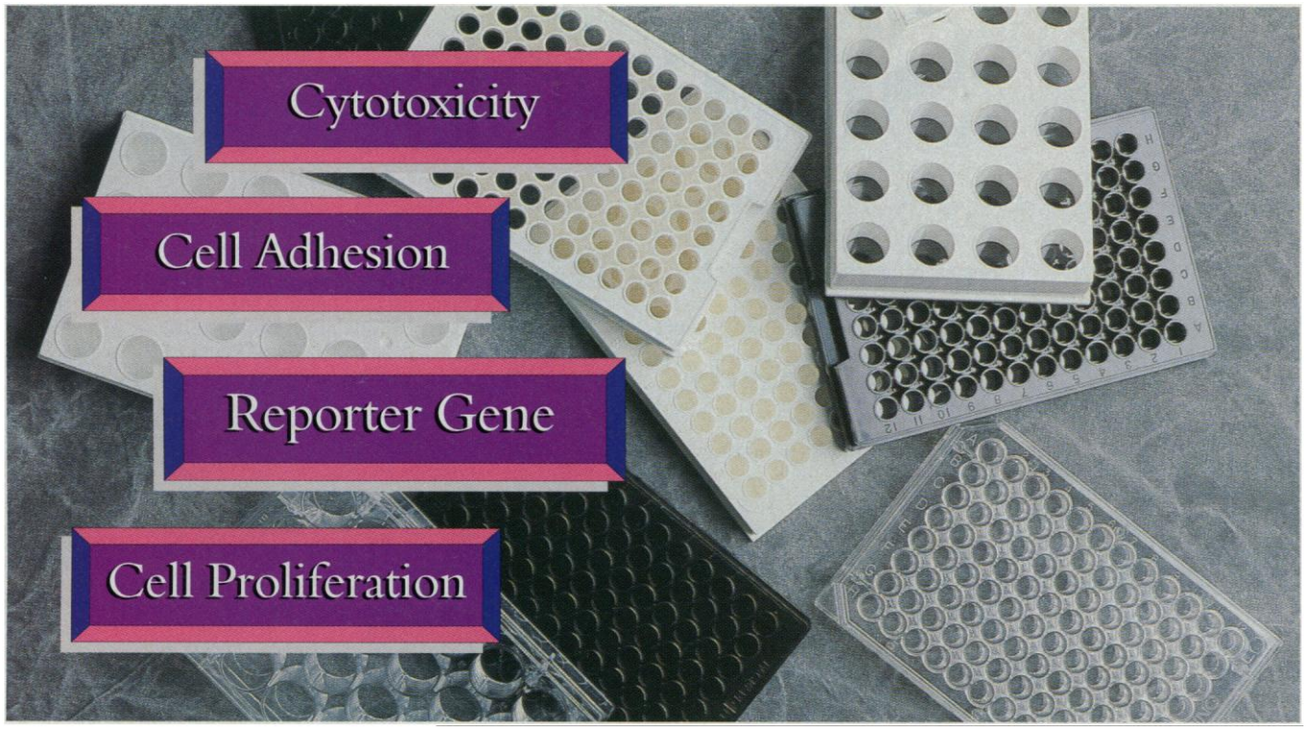


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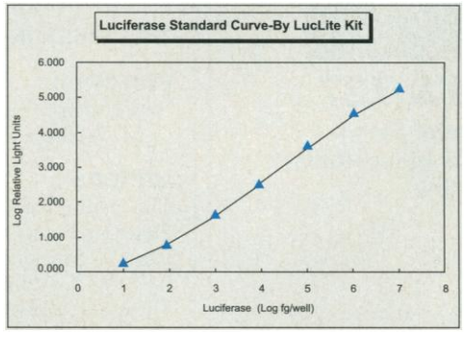


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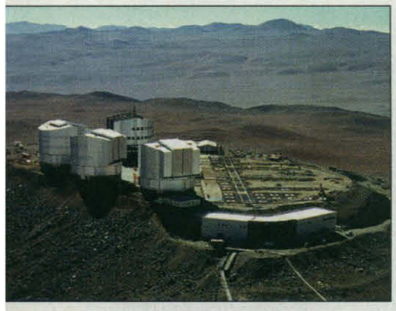
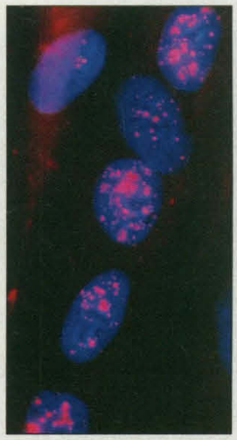


**670**
**Four eyes**



**696 & 737**
**Molecular pathogenesis of myotonic dystrophy**

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## RESEARCH NEWS



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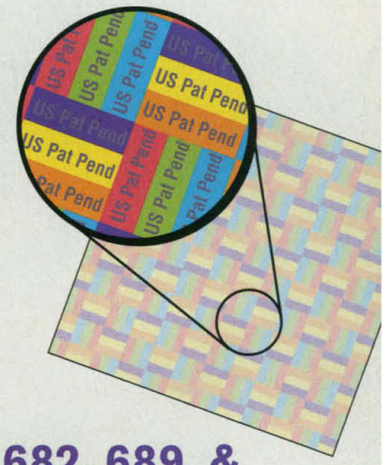
COVER

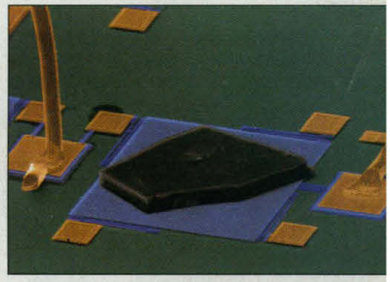
A specimen of the deep-sea coral *Desmophyllum cristagalli* Milne Edwards and Haime, 1848. This 6.7-centimeter-high individual is from the collections at the Smithsonian Institution and was recovered in 1964 by the *Eltanin* from a depth of 550 meters in the southern Pacific Ocean. Coupled uranium series and radiocarbon ages from deep-sea corals provide information about the rate of ocean circulation and the timing of rapid climate change. See page 725 and the News story on page 679. [Photo: Tom Kleindinst, Woods Hole Oceanographic Institution]





**682, 689, & 698**
**In the world of patents, does the "commons" model apply?**


**720**
**Getting a jump on large magnetic pulses**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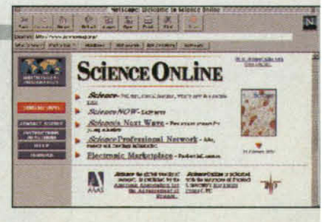

9-98 MMC

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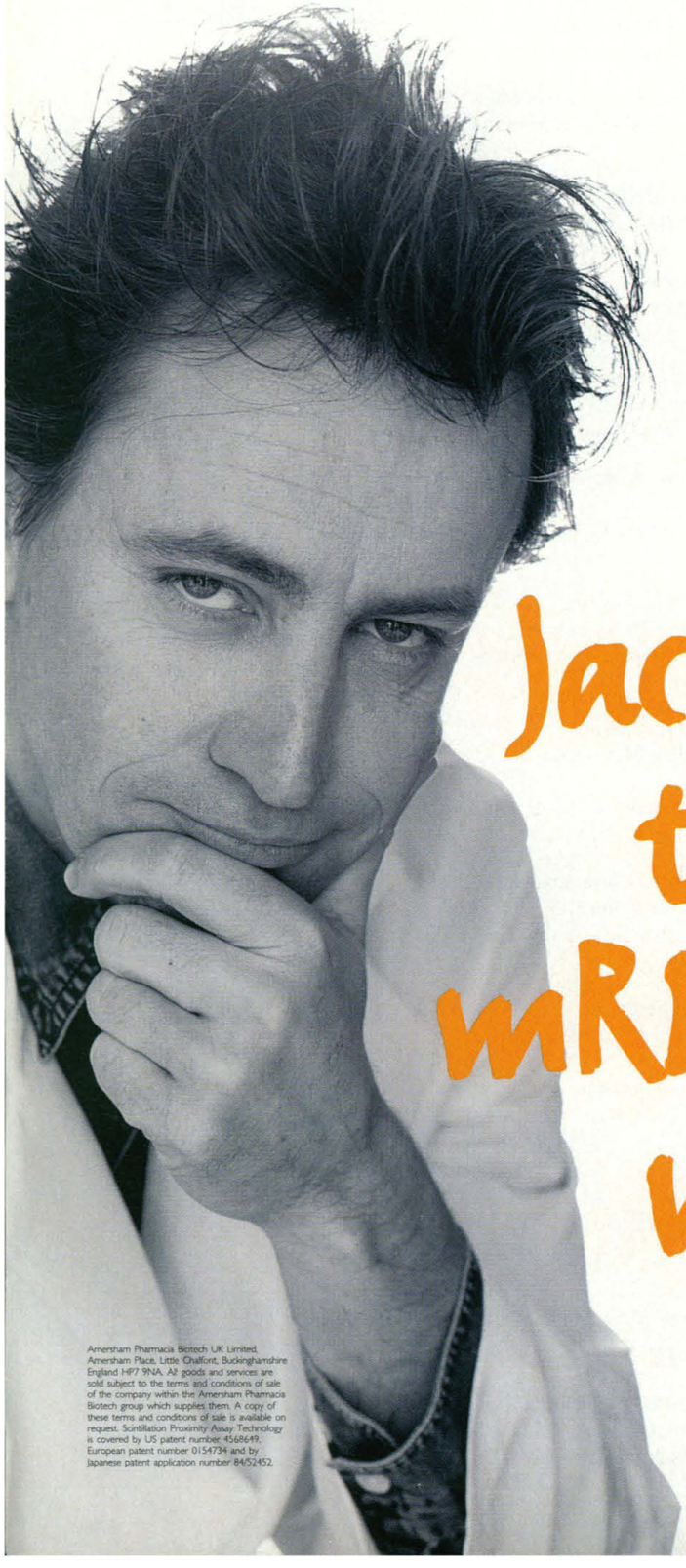

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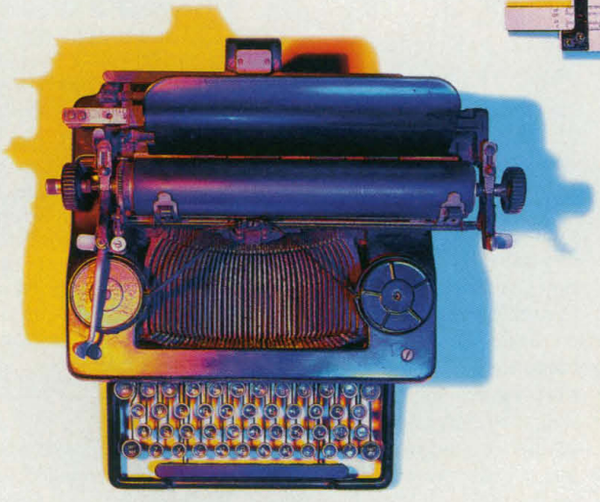

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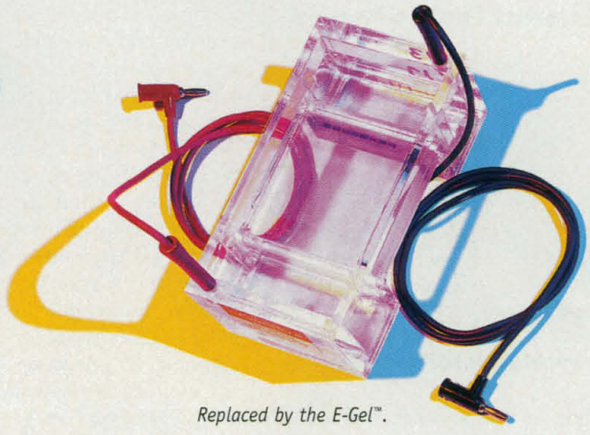

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# THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

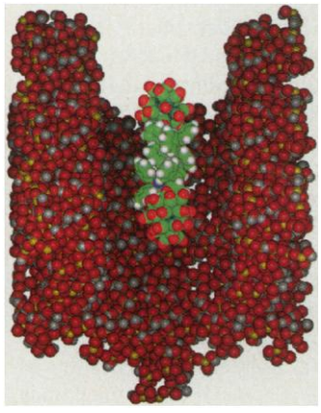
## Patent and perish?

Holding physical property in common, such as natural resources, can lead to destructive overuse, as pointed out by Hardin 30 years ago (see essay on p. 682). Heller and Eisenberg (p. 698), in a review, discuss a related effect in intellectual property—that the patenting process in biomedical research creates an "anticommons" in which scarce intellectual resources go unused because numerous patent owners can all block each others progress to market. Doll (p. 689), in a policy commentary, argues that similar issues did not deter innovation in polymer research 30 to 40 years ago and that patenting of DNA is needed for companies to raise capital and protect their investments and also helps disclose new information.

■

## Ordered in the pores

Zeolites, important industrial catalysts with angstrom-sized pores, have more recently been complemented by mesoporous



materials whose larger nanometer-sized pores may allow catalysis of reactions involving larger molecules. Zhou *et al.* (p. 705) show how ruthenium carbonyl cluster compounds can be introduced into mesoporous silica channels, to form chains of clusters that are highly ordered both along and perpendicular to the cylindrical pores. This ordering allows high loading of the mesoporous material with catalytically active species.

■

## Wreaking havoc at the RNA level

Myotonic dystrophy is a dominantly inherited neuromuscular disease caused by expansion of a CTG sequence in a noncoding region of the protein kinase gene, *DM*. Transcripts of the expanded *DM* allele accumulate in the nucleus of DM cells, but the mechanism by which these transcripts exert their trans-dominant pathogenetic effect has remained mysterious. Work by Philips *et al.* (p. 737; see the commentary by Singer, p. 696) indicates that an RNA binding protein, CUG-BP, may play a critical role by regulating the alternative splicing of the cardiac troponin T (*cTNT*) gene, which is disrupted in DM cells. The aberrant *DM* transcripts may interfere with the normal function of CUG-BP, and, in so doing, alter the expression of other genes regulated by this protein.

## Strength in numbers

Two reports focus on cooperativity effects in receptor-ligand binding, which may be of importance in issues ranging from signal transduction to drug design. Polyvalent ligand-receptor interactions may result in much tighter binding than the equivalent monovalent systems. Rao *et al.* (p. 708) have designed a trivalent ligand-receptor pair based on vancomycin and D-Ala-D-Ala and show that the binding is significantly tighter than not only the monovalent equivalent but also biotin-avidin, a benchmark for small molecule tight binding. Cooperative binding is often invoked in molecular recognition, such as when one molecule binds another more strongly as a dimer than as a monomer. Williams *et al.* (p. 711) use nuclear magnetic resonance data to analyze a series of glycopeptide antibiotic monomers and dimers and their interaction with suitable ligands. The free energy of ligand binding is closely related to the strength of the dimerization in the absence of the ligand. Loosely bound dimers gain free energy by tightening the dimer interface upon binding the ligand; strongly bound dimers gain free energy largely by tightening the ligand-antibiotic interface compared to the monomer.

■

## DDT degradation

The pesticide DDT is known to transform by dechlorination in the environment to form a by-product, DDE, but this species was thought to be stable and persist. Together DDT, DDE, and other related compounds pose environmental problems in several locations. Quensen *et al.* (p. 722) present laboratory studies showing that DDE in marine sediments can be dechlorinated further by bacteria under anaerobic conditions and thus is not environmentally stable.

■

## Strained surfaces

The atoms at a crystal surface can be strained relative to the position of atoms in the bulk, and even surfaces that rearrange the atoms can still be under stress. Such stress can affect adsorption of gas-phase species. Gsell *et al.* (p. 717) investigated the sensitivity of adsorption from the gas phase to surface strain by inserting subsurface argon bubbles in a ruthenium (0001) surface. The layers above the bubbles are strained relative to their normal surface termination positions. Oxygen preferentially adsorbs above the bubbles, whereas carbon monoxide preferentially adsorbs on the surrounding terraces, illustrating the change in the energy of adsorption as a result of the strain imposed on the surface.

■

## Coping with bigger beasts

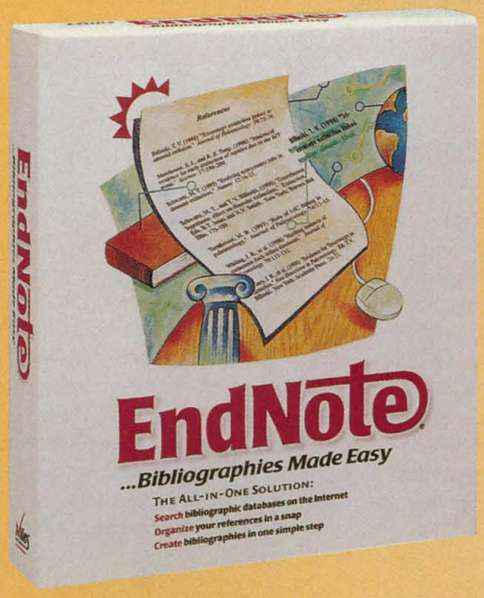
Cope's rule states that lineages of animals tend to increase in body size with evolution. However, most studies have tended to show little support for this rule. Alroy (p. 731) investigated body mass and thus Cope's rule for a large sample of Cenozoic North American mammals. The results imply that body mass of new species were about 9 percent greater than for older species within a genera. Large mammals show a dramatic size increase, a trend not evident in small mammals. Cenozoic evolution of mammals seems to have persistently favored larger species.

■

## Rapid changes below

The surface-ocean circulation and atmospheric circulation changed greatly and rapidly—within a few years to a decade—at the beginning of the large change in climate that marked the most recent deglaciation. Although a change in thermohaline circulation has been implicated in this climate change, evidence of a change in deep-ocean circulation of such rapidity has been lacking.

*(Continued on page 651)*

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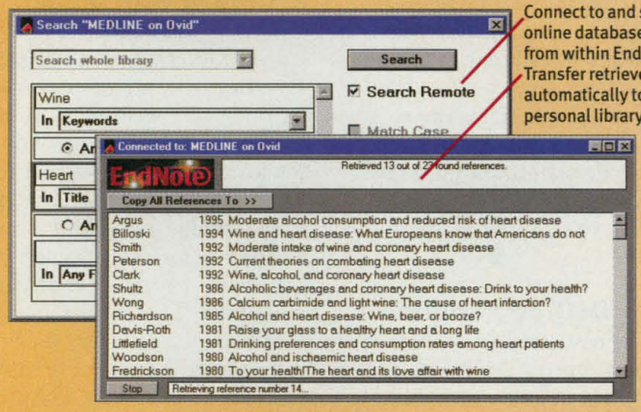


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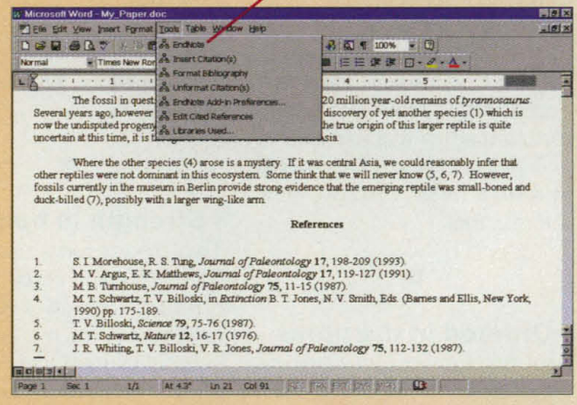


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(Continued from page 649)

Adkins *et al.* (p. 725; see the cover and the news story by Kerr, p. 679) studied deep-ocean corals that grew at depths of about 1800 meters in the North Atlantic during this time. Thorium-230 dates on the corals provide independent age control. Carbon-14 dates on different parts of the coral, along with cadmium-calcium ratios, provide a record of changes in the ventilation rate of deep water during deglaciation. During the lifetime of some corals of 30 to 160 years, abrupt and large changes in carbon-14 ages occurred. These data imply that the deep-ocean circulation is changing over annual time scales, along with changes in the surface ocean and atmosphere.

■

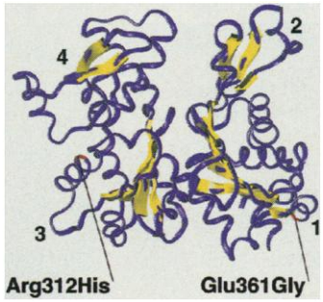
## Southern start

Climate records seem to consistently show that the Southern Hemisphere (and particularly the Antarctic) warms slightly before the Northern Hemisphere during deglaciations and cools first during glaciations. This problem is perplexing because the most extreme cooling seems to be associated with reduced summer solar forcing in the Northern Hemisphere associated with precession—at these times, summer solar forcing is at a maximum in the Southern Hemisphere. Kim *et al.* (p. 728), using a coupled atmosphere-ocean climate model, demonstrate that the initial sensitivity of the Southern Hemisphere can be explained by the interaction of precessional solar forcing with the seasonal cycle of sea ice around the Antarctic. During summer, the sea ice around the Antarctic is near its melting temperature, and thus slight changes in forcing are amplified.

■

## Cardiomyopathy gene

Heart failure affects 700,000 individuals per year in the United States and accounts for $10 to $40 billion in medical




costs. Olson *et al.* (p. 750) have found that an inherited form of heart failure, idiopathic dilated cardiomyopathy, is associated with missense mutations in the gene encoding cardiac actin. This result raises the possibility that defective transmission of force may lead to myocyte dysfunction and heart failure.

■

## Anthrax toxin target

Anthrax is a potentially fatal disease caused by a toxin secreted by the bacterium *Bacillus anthracis*. Anthrax primarily affects herbivorous animals such as sheep and cattle, but in certain settings can also affect people. The anthrax toxin consists of three protein components. Duesbery *et al.* (p. 734; see the news story by Strauss, p. 676) show that one of these components, lethal factor, is a protease that cleaves and inactivates mitogen-activated protein kinase kinase (MAPKK), a key player in cellular signal transduction.

## Surprise ending

The Ku protein is the regulatory component of the DNA-dependent protein kinase (DNA-PK). Ku binds to double-stranded (ds) DNA ends and participates in ds break repair and nonhomologous DNA end-joining. Through genetic and biochemical analyses, Gravel *et al.* (p. 741) show that yeast Ku binds directly to telomeric DNA and is required for the formation of G tails, a key telomerase-independent event at chromosome ends. End-joining reactions at telomeres would be deleterious to genome stability, so the precise role of telomeric Ku remains to be determined.

■

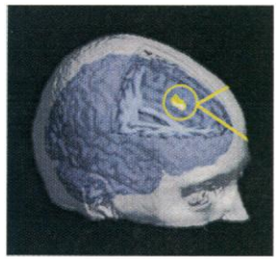
## Shedding light on diversity

Many ecosystems are under stress from anthropogenic threats such as habitat fragmentation and eutrophication, so there is a need to identify ecological mechanisms that bolster species diversity within such ecosystems. Collins *et al.* (p. 745; see the news story by Kaiser, p. 677) demonstrate the positive influence that grazing bison can have on the diversity of grasslands. They experimentally isolated the effects of different factors and showed that grazing or its surrogate, mowing, is required in addition to fire (the major current restoration tool) to maintain diversity. Grazing and mowing reduce the canopy of dominant $C_4$ grasses, allowing more light to reach the soil surface. This effect, the authors suggest, explains how species diversity is maintained.

■

## Managing complexity

The anterior cingulate cortex, part of the frontal lobe of the brain, is thought on the one hand



to participate in tasks in which a subset of stimuli must be attended to and on the other hand to serve as an error-detection comparator of correct and incorrect responses. Carter *et al.* (p. 747) reconcile these two views by proposing, on the basis of functional imaging experiments, that this region monitors the complexity of performance and not errors per se. In particular, they find that activity in the anterior cingulate is associated with increased competition among available responses even when performance remains relatively error free.

■

## Primitive protein in ribonuclease P

Ribonuclease P consists of a 400-nucleotide ribozyme and a 120-residue protein subunit. This enzyme processes the precursors of transfer RNAs and the 4.5S ribosomal RNA. Stams *et al.* (p. 752) have determined the high-resolution structure of the protein subunit which, together with cross-linking results, serves to characterize the three RNA binding motifs. One of the motifs, an unusual left-handed βαβ crossover, bears an intriguing resemblance to a portion of the ribosomal elongation factor G (EF-G). Because the 4.5S rRNA binds to the ribosome and displaces EF-G (which itself mediates translocation of the ribosome along the messenger RNA during protein synthesis), this motif may have arisen early in the evolution of translation.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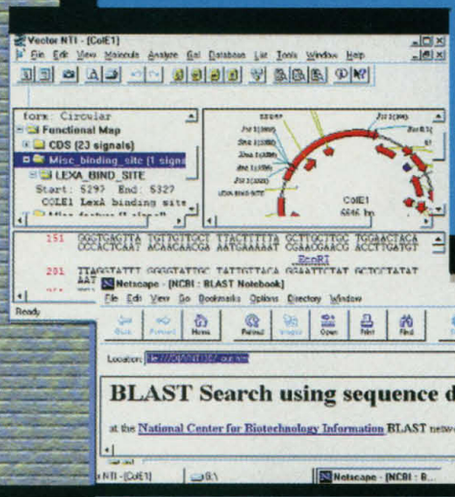


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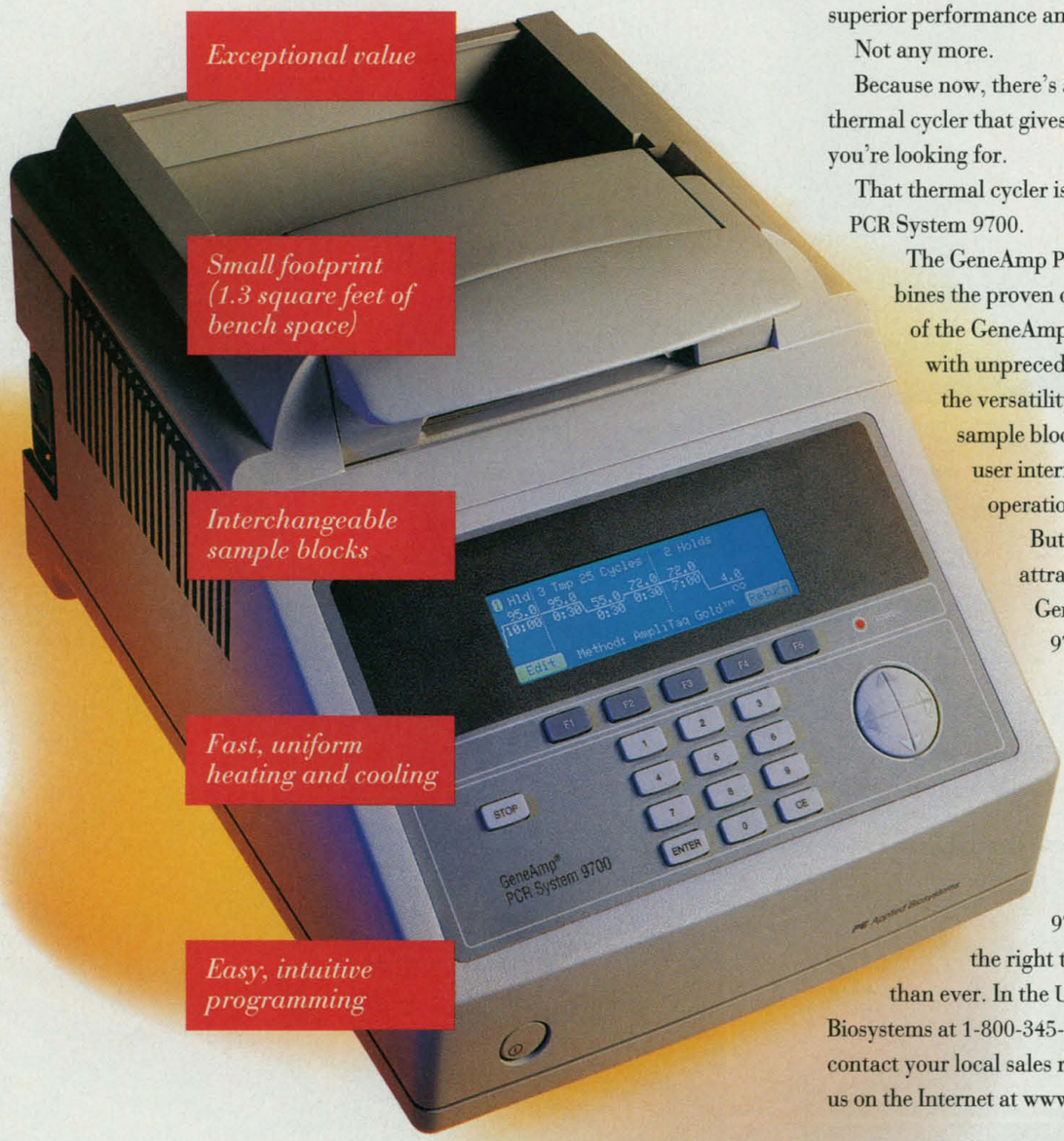


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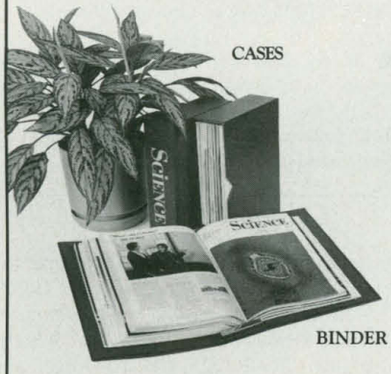


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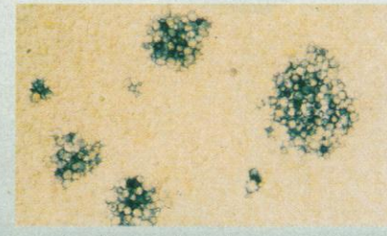

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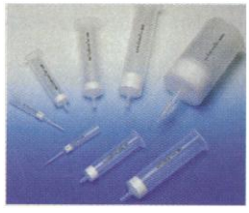

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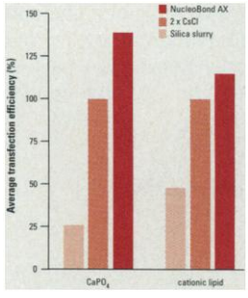


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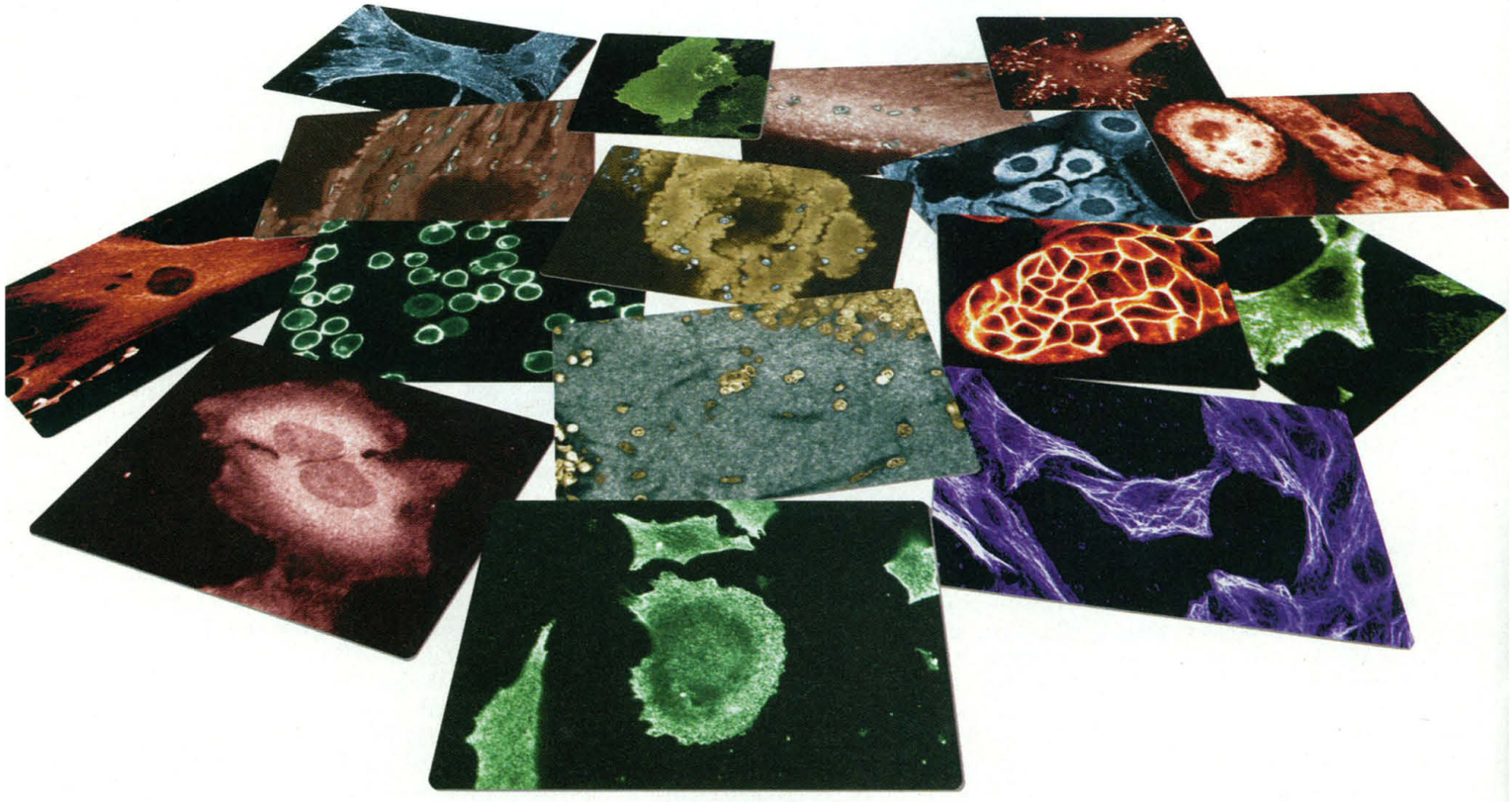

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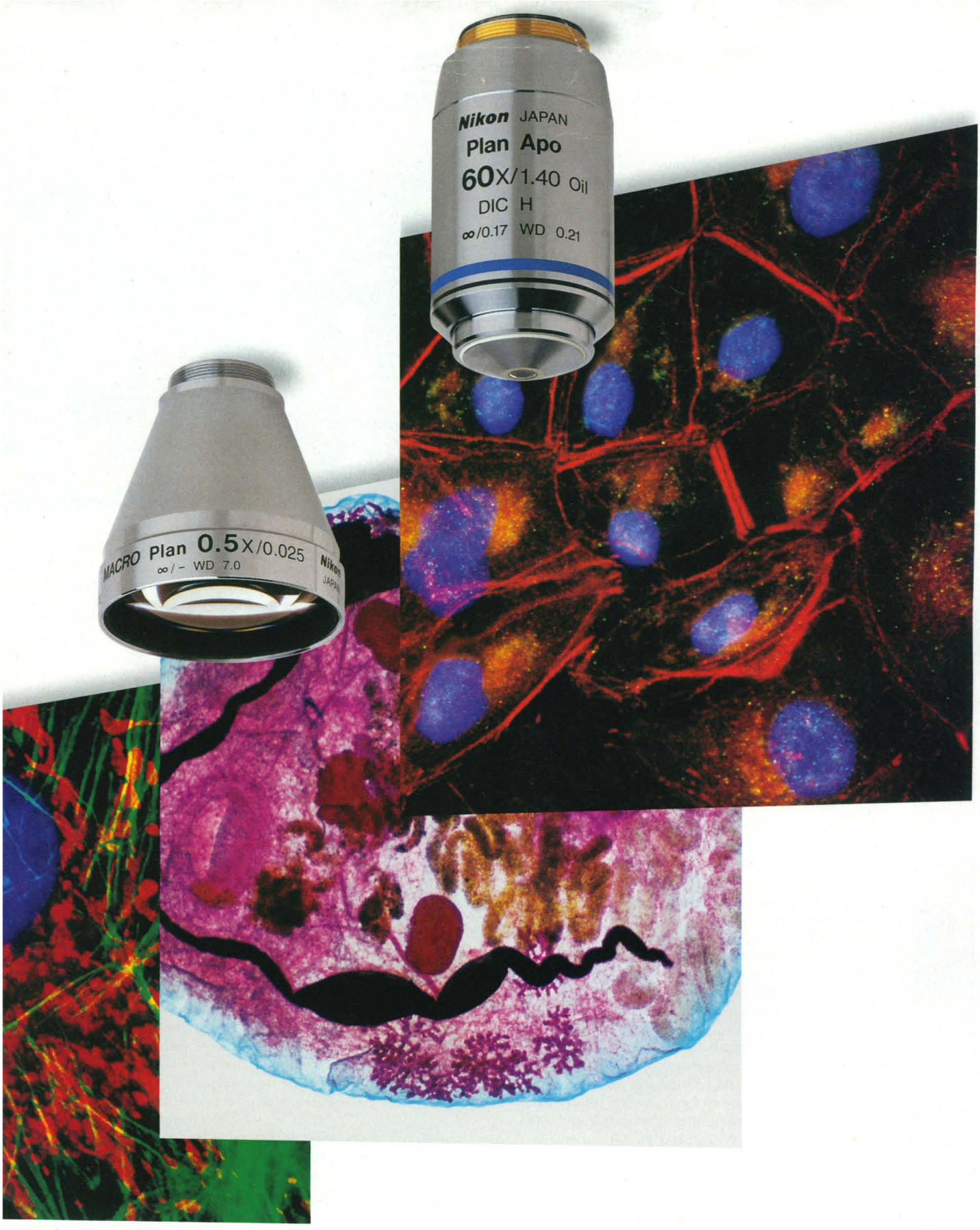
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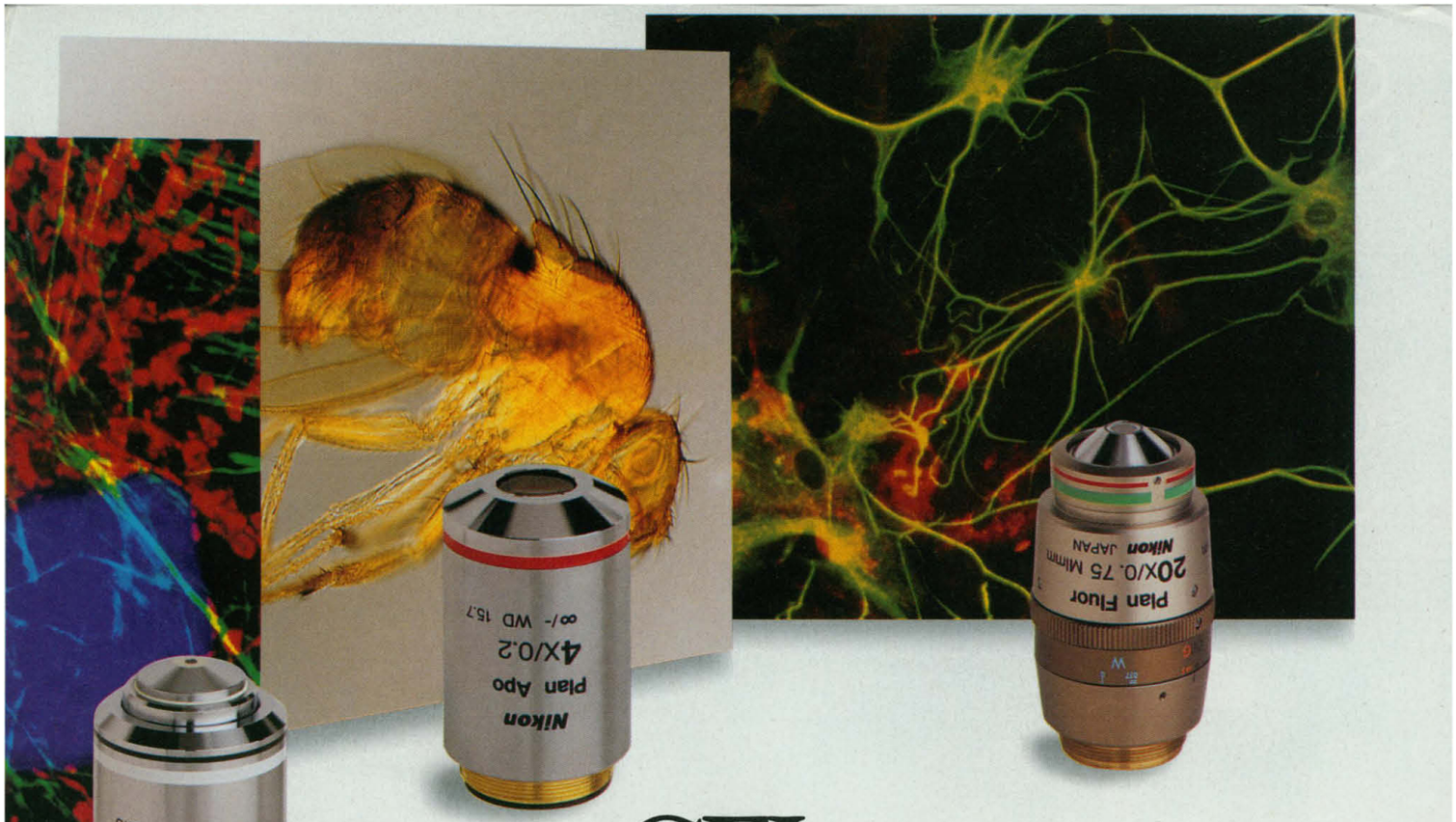


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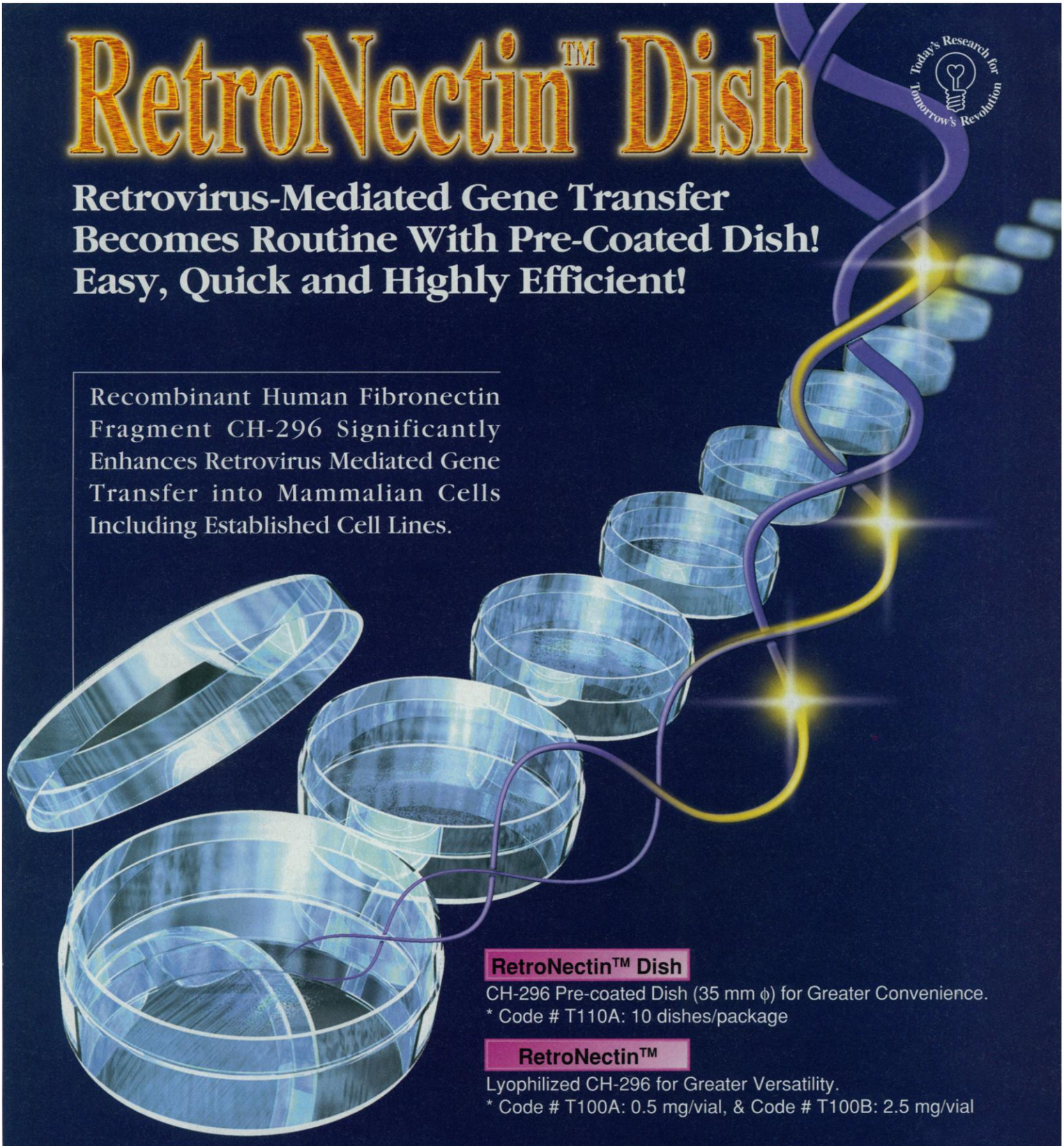

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| 48231-3 | Hardback | $125.00 |
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## Molecular Aspects of Host-Pathogen Interactions
***Malcolm A. McCrae, J. R. Saunders, C. J. Smyth,*** *and*
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| CG | 1 | | | | | | | |
| CGα | 1 | | | | | | | |
| CGβ | 1 | | | | | | | |
| FSH | 1 | 1 | 1 | 1 | 1 | | 1 | 1 |
| FSHα | 1 | 1 | | 1 | 1 | 1 | 1 | 1 |
| FSHβ | 1 | 1 | | 1 | 1 | 1 | 1 | 1 |
| GH | 1 | 1 | 1 | 1 | | 1 | 1 | |
| GH, 20K | 1 | | | | | | | |
| LH | 1 | 1 | 1 | 1 | | 1 | 1 | 1 |
| LHα | 1 | 1 | | 1 | 1 | 1 | 1 | 1 |
| LHβ | 1 | 1 | | 1 | 1 | 1 | 1 | 1 |
| LPHβ | 1 | | | | | | | |
| NEUROPHYSINS | 1 | | | | | | | |
| PL | 1 | | | | | | | |
| PRL | 1 | 1 | 1 | 1 | | 1 | | |
| TSH | 1 | 1 | 1 | 1 | 1 | 1 | | |
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| CG, recomb (Serono) | 0.5 mg | | | | | | |
| CGα & CGβ, recomb | 0.1 mg | | | | | | |
| FSH, pituitary | 0.1mg, 0.25mg[1] | | | 0.3 mg/0.25 mg[1] | 0.1 mg | 0.1 mg | |
| FSH, recomb (Serono) | 0.1 mg | | | | | | |
| GH | 10 mg | 5 mg/1 mg[1] | 0.5 mg | 50 mg | 2 mg, 10 mg | 2 mg, 10 mg | 1 mg |
| GH, 20K Variant | 1 mg | | | | | | |
| LEPTIN | | | 0.5 mg | | | | |
| LH | 0.5 mg[1] | | | 10 mg | 1 mg, 5 mg | 1mg, 5 mg | |
| PL | 5 mg, 2 mg | | | | | | |
| PMS Gonadotropin | | | | | | | 2000 IU<br>10000 IU |
| PRL | 0.1 mg, 0.5 mg[1] | 1 mg/1 mg[1] | 0.5 mg | 50 mg, 10 mg | 2 mg, 10 mg | 2mg, 10 mg | |
| PRL, Glycosylated | 0.1 mg | | | 1 mg | | | |
| TSH | 0.5 mg[1] | | | 1 mg | 1 mg | 1 mg | |

[1] SIAFP quality, (Selective Immuno Affinity Purified); i.e. devoid of hormonal contaminants.

## MISCELLANEOUS PEPTIDES

| | | | |
|---|---|---|---|
| **Human Activin A (recombinant)** | 50 µg | **Porcine Folliculostatin** | 0.2 U |
| **Human Follistatin (recombinant)** | 0.1 mg | **Bovine PTH** | 1 mg |
| **Human Inhibin A (recombinant)** | 10 µg, 25 µg | **Porcine Relaxin** | 1.0 mg |

## ANTIBODIES for IMMUNOCYTOCHEMISTRY, WESTERN BLOT, etc.

| IMMUNOCYTOCHEMISTRY & WESTERN BLOT | | | | MISCELLANEOUS |
|---|---|---|---|---|
| Peptide Antiserum | Human | Rat | Ovine | anti-Aldosterone[3] |
| ACTH | 1 | 1 | | anti-Somatomedin-C (polyclonal) |
| β Endorphin | 1 | | | anti-cAMP |
| Estrogen & Androgen Receptor[4] | | 1 | | **ImmunoAffinity-Purified Ig (Rabbit) to Rat PRL, Rat TSHβ, Rat LHβ, Rat LHα, Human PRL, Human TSHβ, Human LHβ.** |
| Follistatin | 1 | | | |
| FSHβ | 1 | 1 | 1 | **Guinea Pig antisera to all Rat & Human pituitary peptides.** |
| GH (natural) | 1 | 1[1,2] | 1 | |
| GH (synthetic) | 1 | | | |
| LHβ | 1 | 1[1,2] | 1 | |
| Oxytocin | 1 | 1 | 1 | |
| PRL | 1 | 1 | 1 | |
| α Subunit | 1 | 1 | 1 | |
| TSHβ | 1 | 1 | 1 | |
| FSH, LH[2], TSH[2] | | 1 | | |
| Vasopressin | 1 | 1 | 1 | |

All the above antisera were raised in rabbits, except for [1] monkey, [2] guinea pig, [3] sheep.
[4] A vial of rat Estrogen receptor peptide (amino acid residues 270-284) is included with this reagent.

**Submit requests for reagents on an NHPP Application Form by FAX to (310) 222-3432**
**or by mail to Dr. A. F. Parlow, Scientific Director, National Hormone & Pituitary Program.**
**APPLICATION FORMS are OBTAINABLE at WEB ADDRESS http://www.humc.edu/hormones**
**or by EMAIL or FAX or PHONE request to Dr. Parlow.**
**Direct all inquiries to Dr. Parlow at**
**PHONE (310) 222-3537 FAX (310) 222-3432 E-MAIL "PARLOW@HUMC.EDU"**
**All reagents from NHPP are supplied free of charge. The reagents are sent free via U.S. Mails (unless otherwise specified & paid for by the requesting researcher). Exceptions: - Activin A & Inhibin A are sent refrigerated, via FEDEX, at requester's expense.**

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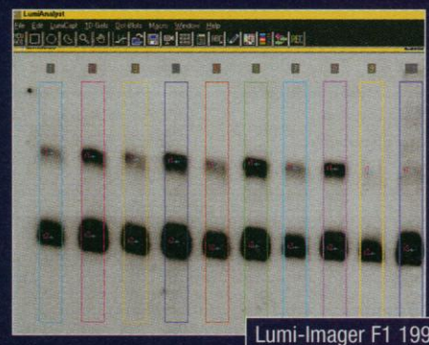
Botticelli 1482

Da Vinci 1503

Miro 1949



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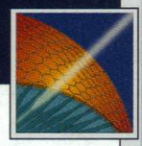

*Image data Northern blot by courtesy J. Bergemann, Beiersdorf AG, Germany

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