24 July 1998

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COVER Real-space visualization of a molecular rotor (1.5 nanometers in diameter). The ringlike structure is a high-resolution scanning tunneling microscope image of a single molecule rotating at high speed. The two cone-like objects in the upper right corner are part of another group of molecules that acts as a bearing. The image is a pseudo-three-dimensional colored rendition. [Image: J. K. Gimzewski and V. Langlais]

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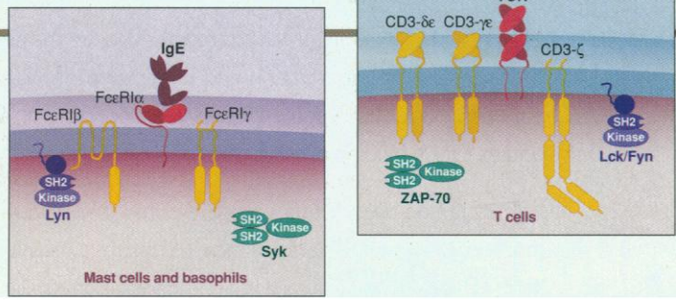
Change the affinity, change the immune response



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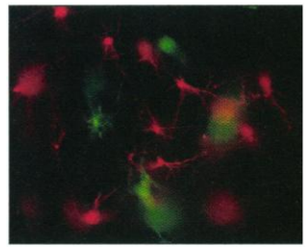

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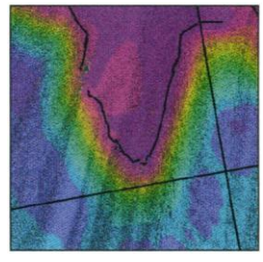
Transient connections in development



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Rapid glacial retreat in Antarctica

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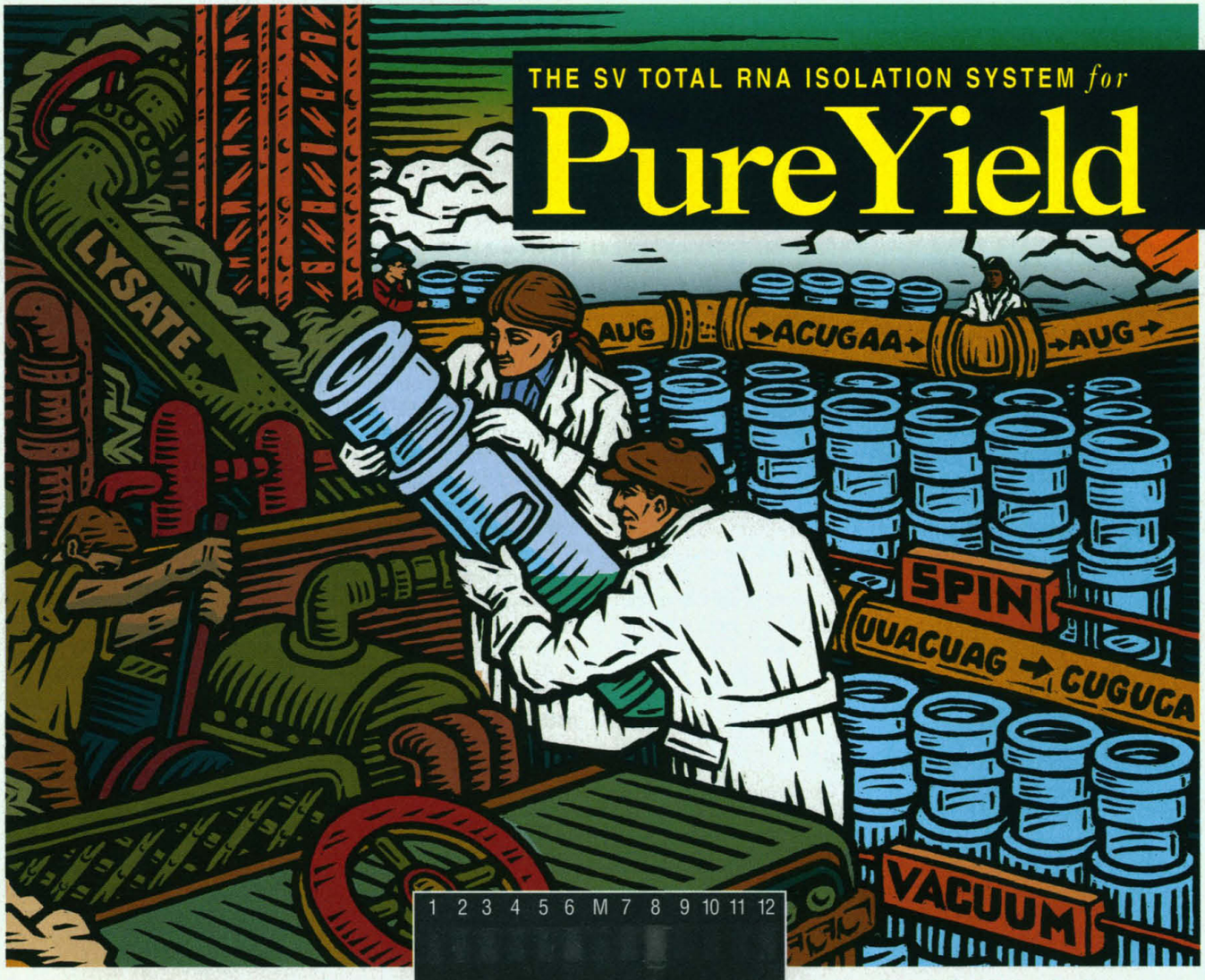

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MINUTE BEARING

One route to the miniaturization of mechanical devices is the use of single molecules for performing the various tasks required in the device, in a manner analogous to biological molecular motors. Gimzewski *et al.* (p. 531; see the cover) have designed propeller-shaped molecules 1.5 nanometers in diameter and show that a scanning tunneling microscope tip can be used to switch the molecules between two nearby but different sites within an incomplete monolayer on a surface. In one site, the molecule is immobilized, whereas in the other the molecule rotates too fast to be clocked experimentally. The surrounding molecules thus constitute a bearing for a single rotating molecule. The rotation appears to be wearless and can be stopped very quickly because of the small inertia of the rotor.

KONDO EFFECT TUNING IN QUANTUM DOTS

Recent studies have presented evidence for the Kondo effect, the coupling of magnetic impurities to conduction electrons observed in bulk semiconductors, in quantum dots. Cronenwett *et al.* (p. 540; see the Perspective by Inoshita) show that quantum dots can be converted from a Kondo to a non-Kondo state by changing the number of electrons on the dot from odd to even, that is, from a magnetic state with one unpaired spin to a nonmagnetic state with all paired spins. The Kondo temperature could also be tuned by means of a gate voltage, and the observed magnetic field and temperature dependence of the effect was in good agreement with theoretical predictions.

HOT SPOTS OVER SLOW WAVES

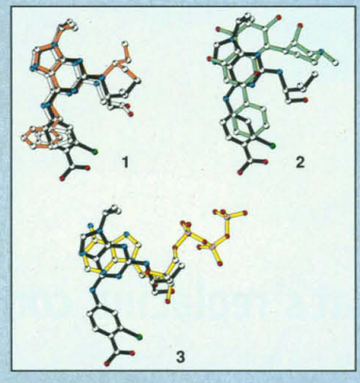
Convection in the mantle is a manifestation of the cooling of the Earth and drives plate tectonics, but even the basic geometry of the overall convection pattern is uncertain at depth. In one model, hot buoyant plumes are thought to rise from near the base of the mantle and produce volcanic hot spots on the surface, such as Hawaii. Williams *et al.* (p. 546) examined the spatial relation between surface hot spots and presumed hot or partially molten regions at the base of the mantle, as indicated by low seismic velocities (this region of the mantle is still not completely mapped by seismic waves). Most of the surface hot spots overlie regions of low seismic velocity near the mantle base, suggesting a plume connection.

FAST ROUTE TO MACROPOROUS MATERIALS

Macroporous materials (pore sizes greater than 25 nanometers) have been synthesized in a single fast step using polystyrene spheres as templates. Holland *et al.* (p. 538) formed millimeter-thick films of ~0.5-micrometer spheres by vacuum filtration and then covered them with solutions of metal alkoxides; heating to 575°C created microcrystalline networks of titania, zirconia, or alumina containing close-packed spherical voids approximately 320 to 360 nm in diameter.

CLOSING IN ON KINASE INHIBITORS

Selective kinase inhibitors are useful for analyzing signaling pathways and have potential therapeutic value. Gray *et al.* (p. 533) describe an approach for developing new inhibitors based on the purine olomoucine, which binds in an unusual fashion to the adenosine triphosphate site of cyclin-dependent kinases (CDKs). Screening of chemical libraries that modified the 2, 6, and 9 ring positions led to the identification of several strong CDK2 inhibitors, including purvalanol B, which is 30 times more potent than flavopiridol, an inhibitor in clinical trails. Structural studies suggest further synthetic targets, and cellular effects of these inhibitors were investigated by screening yeast genome messenger RNA expression well as in 60 human tumor cell lines.



A HASTY RETREAT

The Pine Island Glacier in West Antarctica has been thought to be particularly susceptible to retreat because its bed is below sea level and it is not constrained by a large ice shelf, as is much of the West Antarctic Ice Sheet. Rignot (p. 549; see the news story by Kerr) presents satellite radar measurements showing that the hinge-line position of the Pine Island Glacier (marking the limit of tidal flexing of the glacier) retreated rapidly, by more than 1 kilometer per year, between 1992 to 1996 (the period of data coverage). The retreat is likely caused by an influx of warm seawater that enhanced melting at the base of the glacier.

EARLY DISTANCE CUES

The early stages of cortical visual processing focus on features of visual stimuli, such as orientation and color, and the later stages begin to provide information about spatial relations of objects in the visual field and object identity. Dobbins *et al.* (p. 552; see the news story by Barinaga) uncover a surprising influence of viewing distance (that is, the spatial relation of objects to the observer's body) on the activity of neurons in V1, the earliest station in the visual cortex. Although it is known that the combination of input from the two eyes in the early stages allows for processing of binocular disparity, the effect of object distance remains even with monocular viewing, indicating that monocular depth or scene cues may be important. An additional possibility is that neurons may be tuned to respond preferentially to objects on the basis of their perceived distance within a scene.

UNRAVELING IMMUNE RECEPTOR RESPONSES

How cells of the immune system can respond to ligands with widely varying affinities is the subject of two reports (see the Perspective by Malissen). Multichain antigen receptors must recruit kinases to their complex so that they can initiate signals to the cell when they bind their ligands. Low-affinity ligands can disrupt the signaling of high-affinity ligands, but the mechanism is not clear. With the use of the Fc receptor system, Torigoe *et al.* (p. 568) determined that this inhibition need not be direct competition for the same receptor. An excess of a non-crossreacting low-affinity ligand clustered receptors together to the exclusion of the receptors clustered by high-affinity ligand. This process efficiently horded the associated kinases, such that the more distal signaling events normally initiated by high-affinity ligand failed to proceed. This "selfish" seizing of resources that it cannot utilize,

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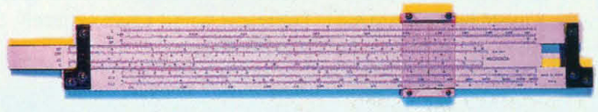

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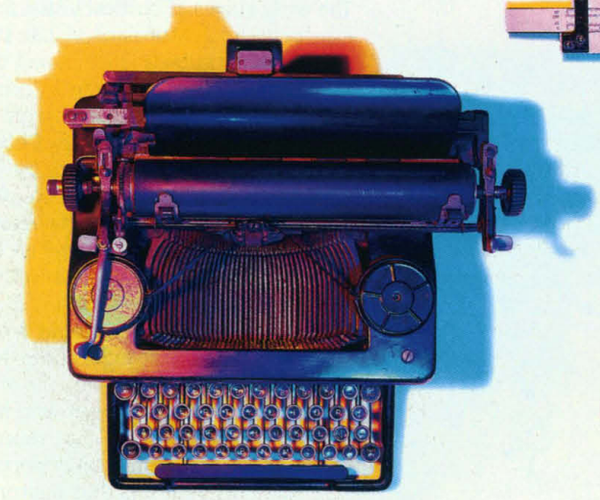

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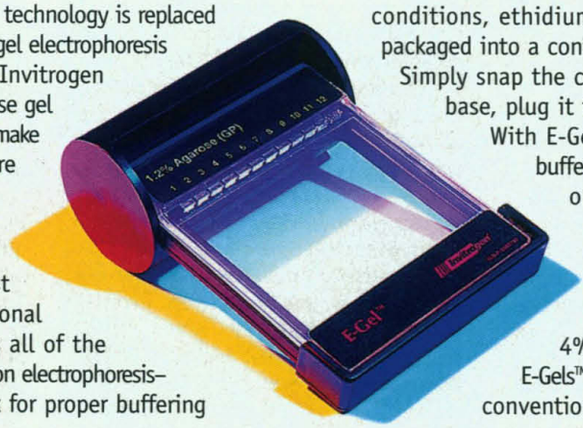

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THIS WEEK IN *SCIENCE*

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like Aesop's "Dog in the Manger," may also help to explain the response to T cell receptors to antigens of different affinities. The ab antigen receptor on T cells contains the two antigen-binding chains and additional γ, δ, ε, and ζ subunits. The ζ subunit has six tyrosine phosphorylation sites. Because multiple forms of phosphorylated ζ can be detected, but could not previously be examined individually, the connection between various phosphorylation and activation states has not been clear. Neumeister Kersh *et al.* (p. 572) have generated antisera to each phosphorylation site and found that the tyrosines are phosphorylated in a particular order, with the phosphorylation of some sites dependent on the previous phosphorylation of others. Peptide antigens that do not fully activate T cells are not able to complete the series of ordered phosphorylations. This process may be the root of the signaling differences that lead to functional differences in T cells presented with altered peptide ligands.

PUTTING *SALMONELLA* TO WORK

To facilitate the production of oral vaccines, attenuated versions of the intracellular bacteria *Salmonella typhimurium* have been developed as "carriers" of the genes or genomes from other pathogenic organisms. Rüssmann *et al.* (p. 565) use the bacterium's own specialized secretion system, the type III system, to generate cytotoxic T cells that protect against an otherwise lethal viral infection in mice. The type III secretion system ensures that the "hitchhiking" viral proteins get injected into the cytoplasm of the host cell. The proteins are then processed and transported to the cell surface as peptides bound to class I major histocompatibility molecules, where they stimulate a cellular immune response. *Salmonella* now has the potential to be an easy-to-administer vaccine for generating cytotoxic protection.

BEETLE-MANIA

Insects of the order Coleoptera, beetles, are the most diverse of all animal and plant groups. Seeking an explanation for this diversity, Farrell (p. 555; see the news story by Morell) constructed the diversification history of a large clade of plant-eating beetles, the Phytophaga, using a combination of DNA sequences and morphological characters. This procedure identified a series of origins for angiosperm feeding, each of which was associated with dramatically enhanced beetle diversity. Such radiations support a coevolutionary model in which a proliferation of beetle life-history traits accompanies the development of flowering plant diversity.

VIRAL INTERFERENCE WITH SIGNALING

Many genes in viruses are thought to have originated in their host's genomes, but viruses then turn their use around to further the propagation of the virus, often at the expense of the host. Miskin *et al.* (p. 562) have determined that a protein from African swine fever virus, A238L, can inhibit signaling pathways that are critical for the production of immunomodulatory cytokines by binding to the catalytic subunit of calcineurin. This finding implies that mammalian cells may contain homologous genes for proteins that would regulate cytokine production during immune responses.

TECHNICAL COMMENT SUMMARIES

β-Chemokine MDC and HIV-1 Infection

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/281/5376/487a

R. Pal *et al.* (Reports, 24 Oct., p. 695) found that macrophage-derived chemokine (MDC) "suppresses infection" of blood cells by some strains of the human immunodeficiency virus–type 1 (HIV-1). They suggested that β-chemokines could be "responsible for a major proportion of HIV-1–specific suppressor activity produced by primary T cells."

B. Lee *et al.* comment that, in their experiments, "even high concentrations of [recombinant] MDC did not inhibit productive infection of peripheral blood mononuclear cells, or macrophages by ... HIV-1 strains." F. Arenzana-Seisdedos *et al.* also found that MDC did not show "suppressive activity against [coreceptors] CCR5 or CXCR4–dependent HIV strains."

In response, A. L. DeVico *et al.* state that, in more recent experiments, their "findings are in agreement with those of the other groups." But they ask "which molecule in the native MDC preparations is responsible for the antiviral effect" observed? They discuss several possibilities—including a contaminant, "a cryptic factor," or "other isoforms" of MDC—that could be explored.

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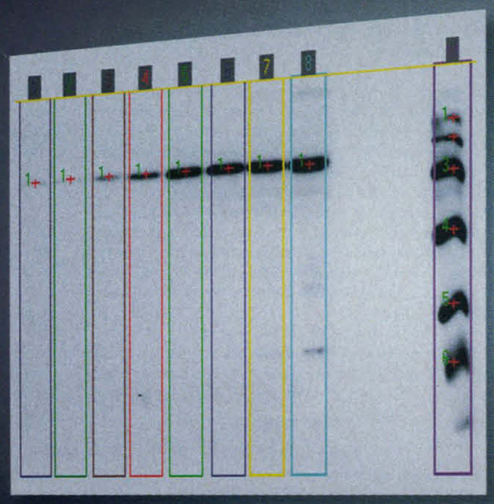
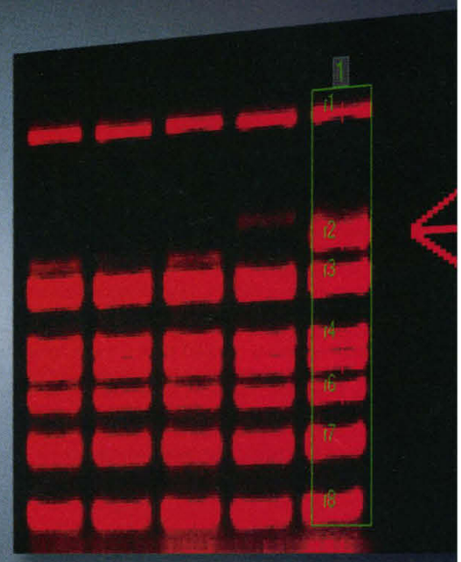


Chemiluminism 1998



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Bad (pS136)
Bad (pS112)

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STAT3 (pY704)
STAT3 (pS727)
STAT5 (pY694)
CREB (pS133)
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c-Jun (pS63)

Neurobiology

NR1 (pS896)
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Specific Immunocytochemical Labeling of Mitotic Cells. Exponentially-growing kangaroo rat Ptk1 cells were fixed with methanol and stained with Upstate Biotechnology polyclonal anti-phospho-Histone H3 (Mitosis Marker) and visualized with a rhodamine-conjugated secondary antibody. An anaphase nucleus is shown at high magnification.

Western Blot Analysis. Lysates of unstimulated cells (Lane A) and stimulated cells (Lane B) were resolved by electrophoresis, transferred to nitrocellulose and probed with phosphorylation state-specific antibodies.

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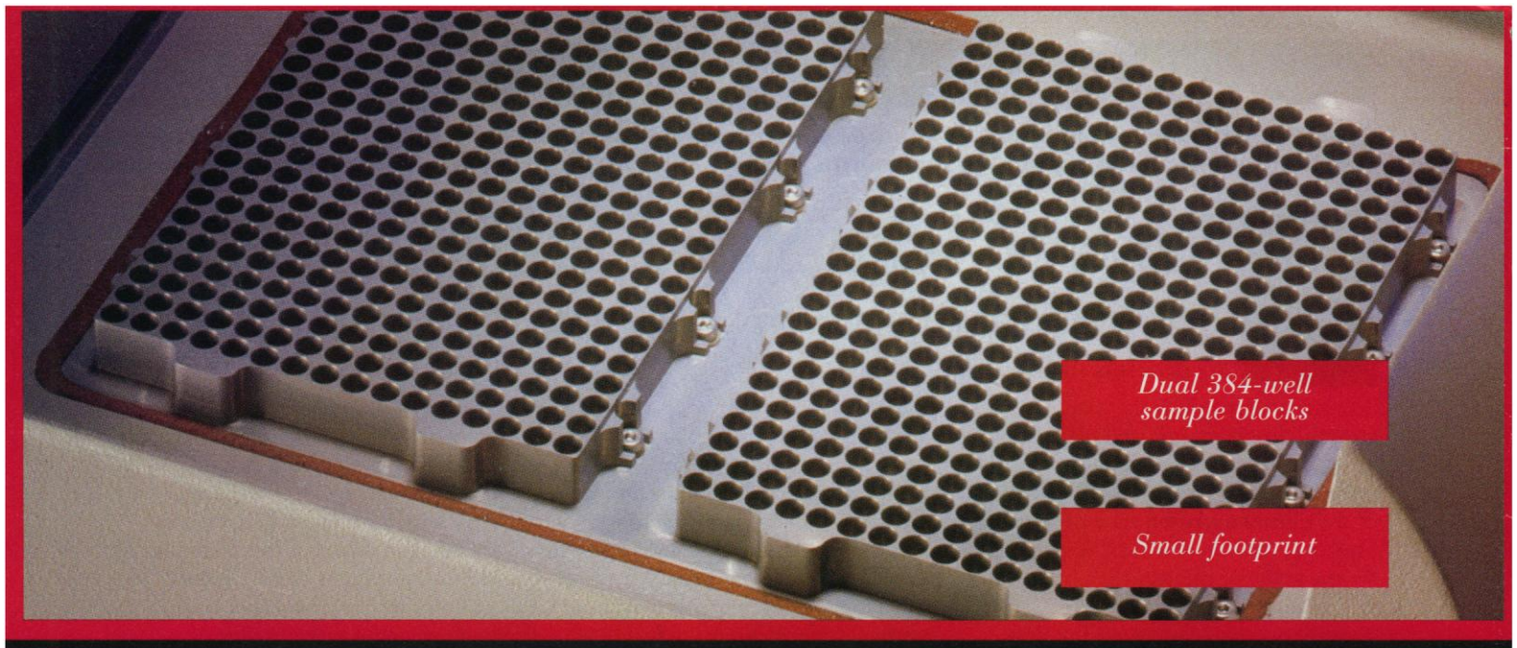

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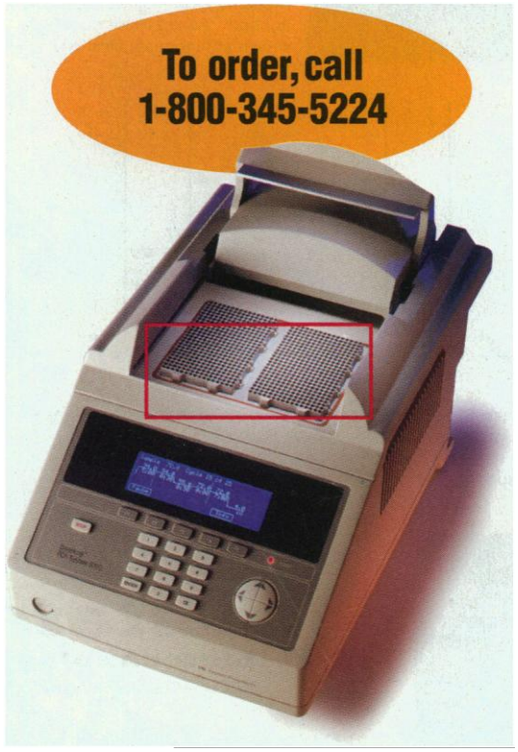

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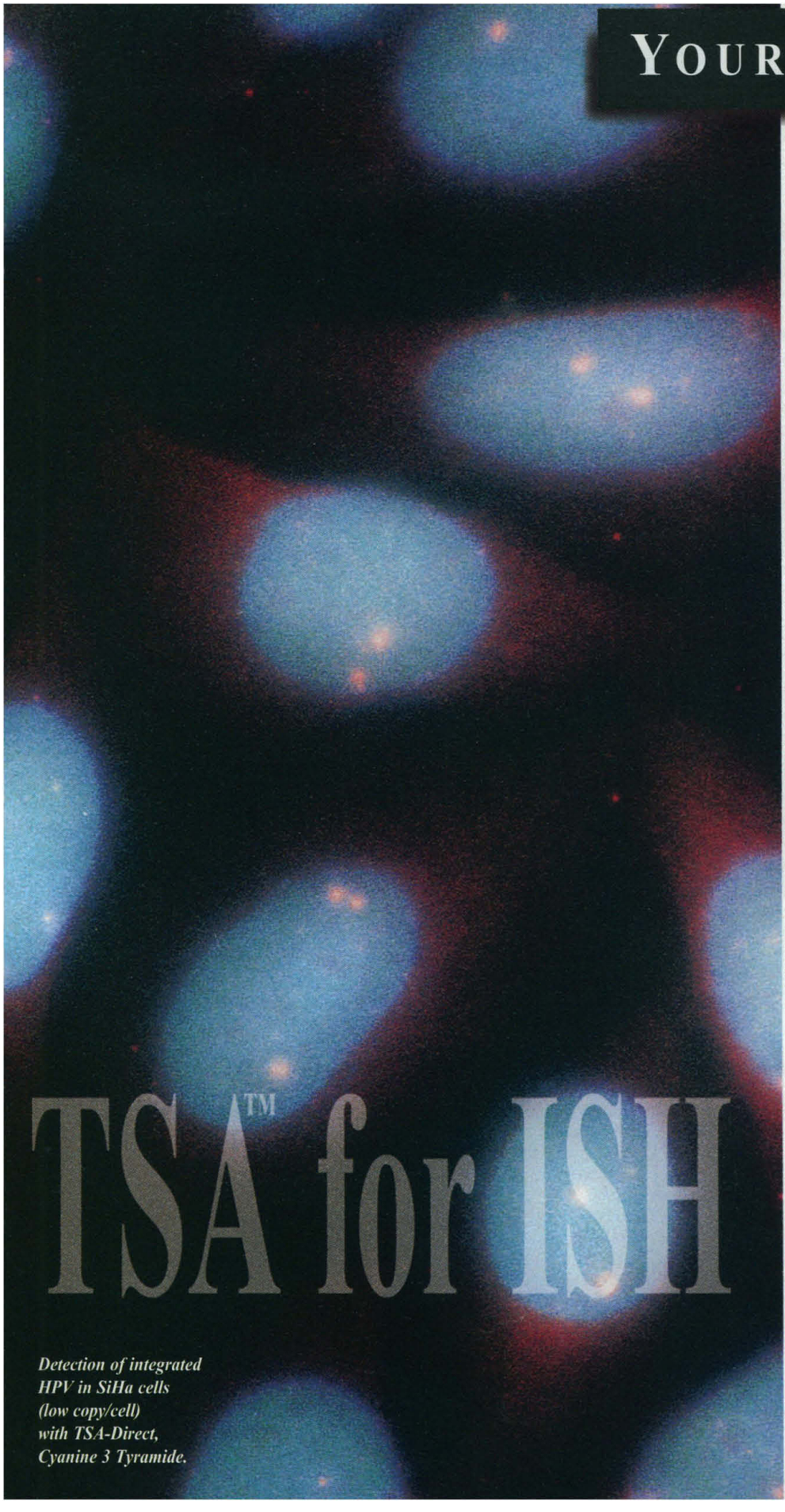

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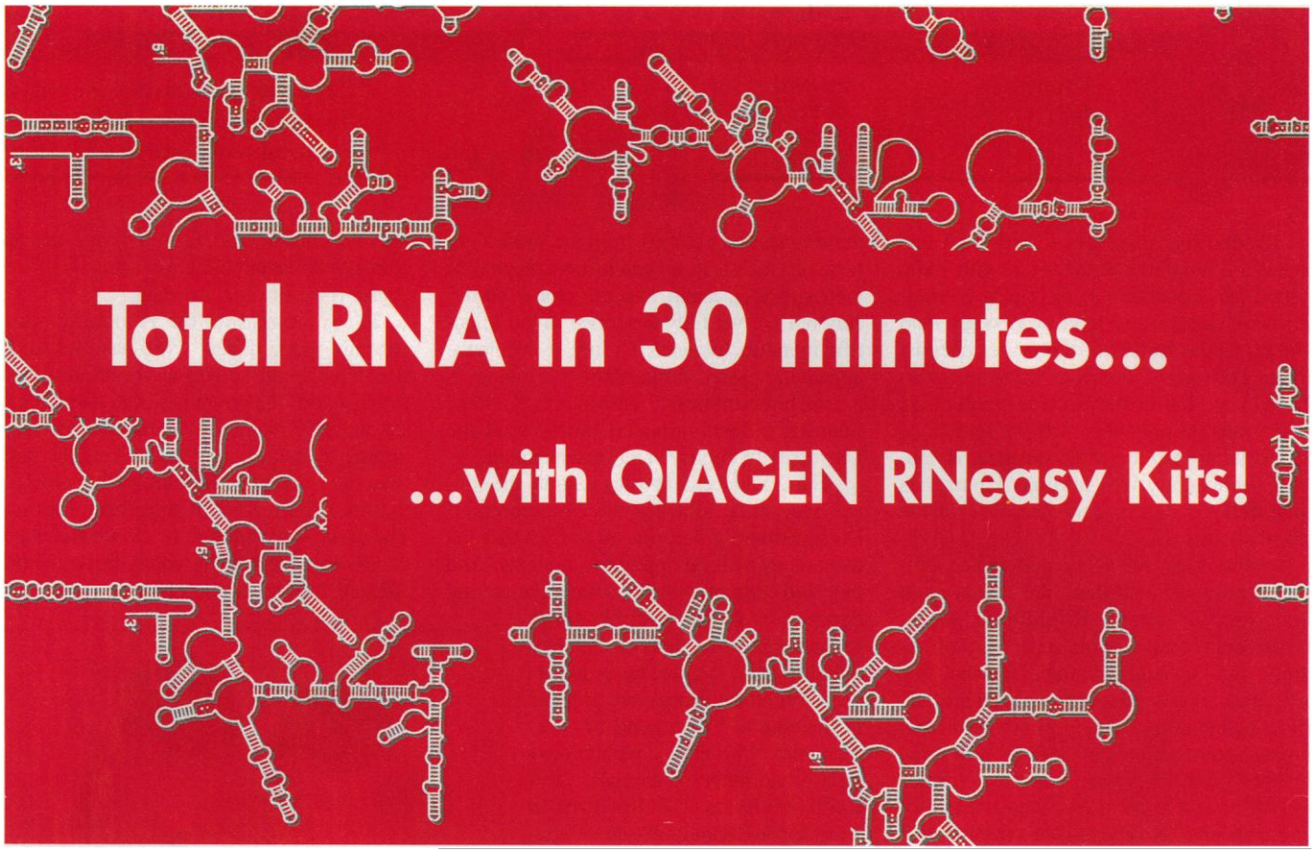

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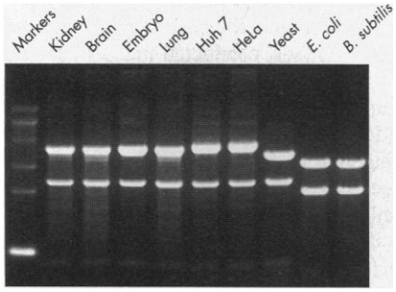

Formaldehyde agarose gel of total RNA isolated with the RNeasy Maxi Kit from the indicated sources. All tissues were from mouse.

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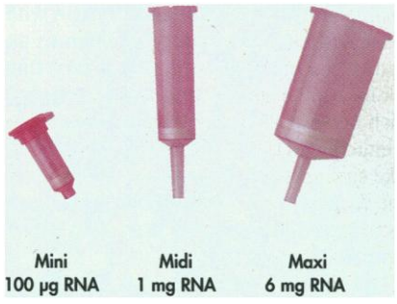
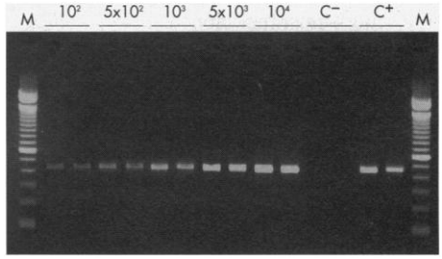


RT-PCR of RNA from ≥100 cells



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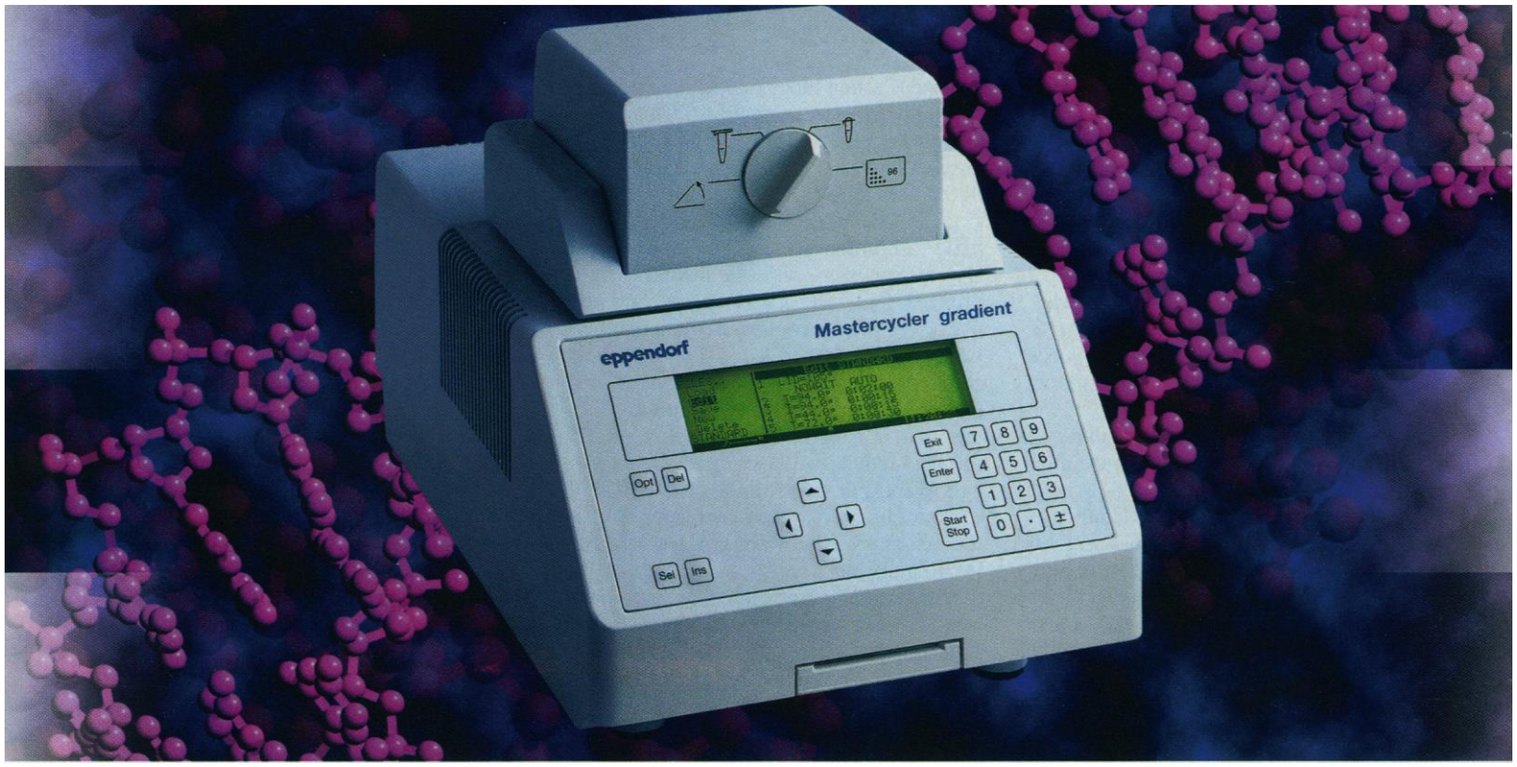

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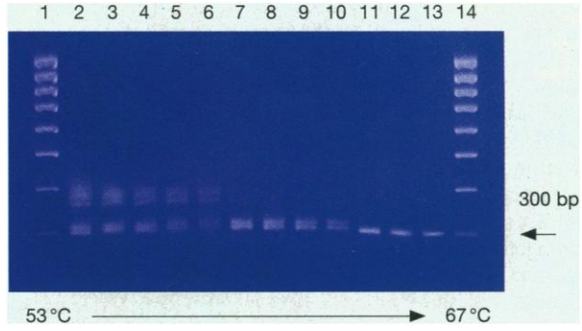

● Experimental determination of optimal annealing temperature. The calculated primer annealing temperature was 56.5 °C, the actual annealing temperature is 63.5 °C. The ribosomal spacer region of mycoplasms from H9 cell cultures was amplified.

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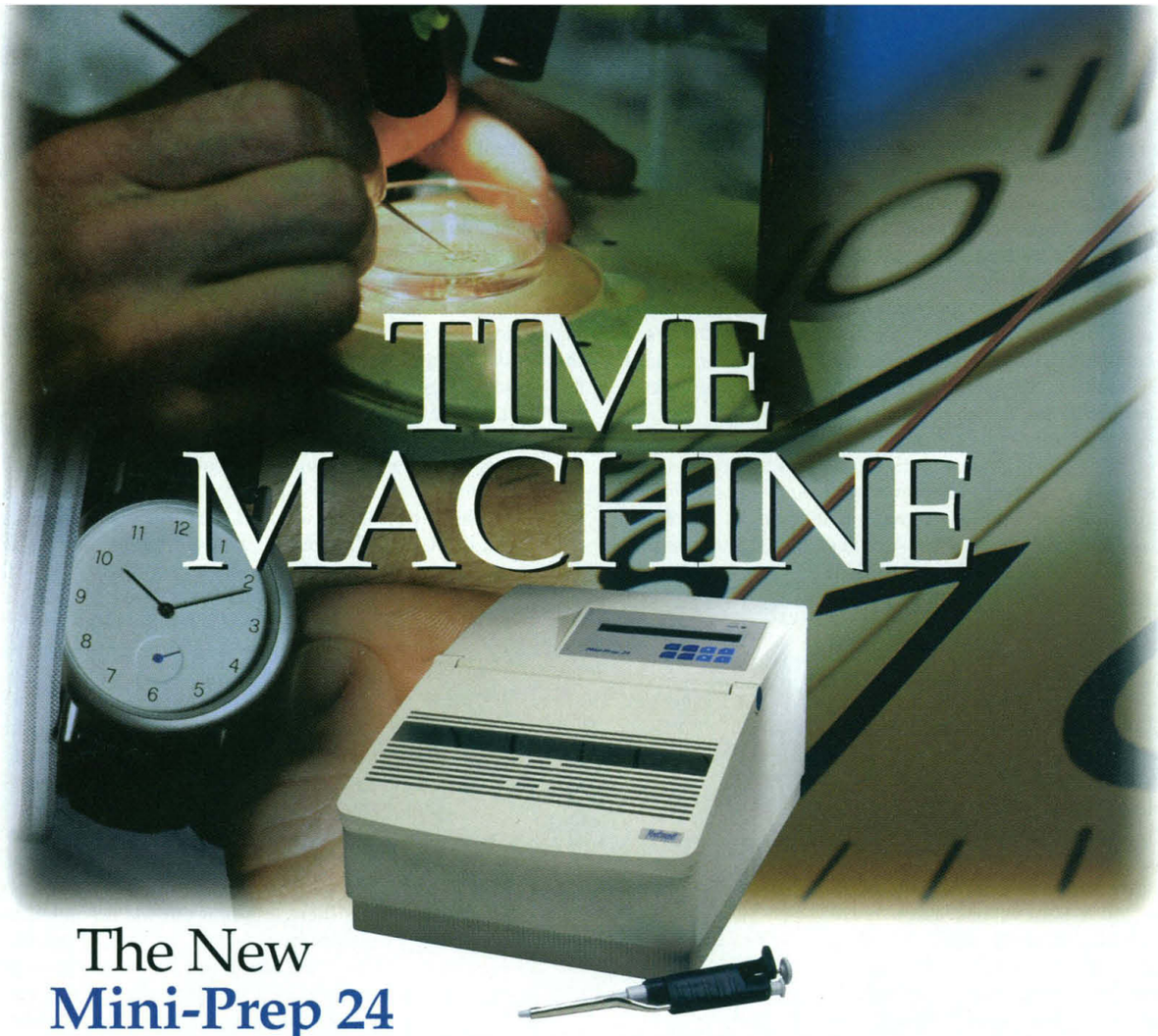

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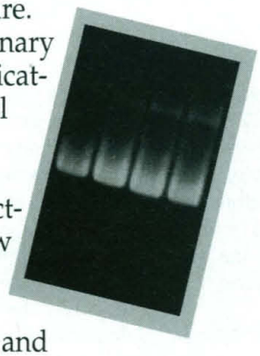

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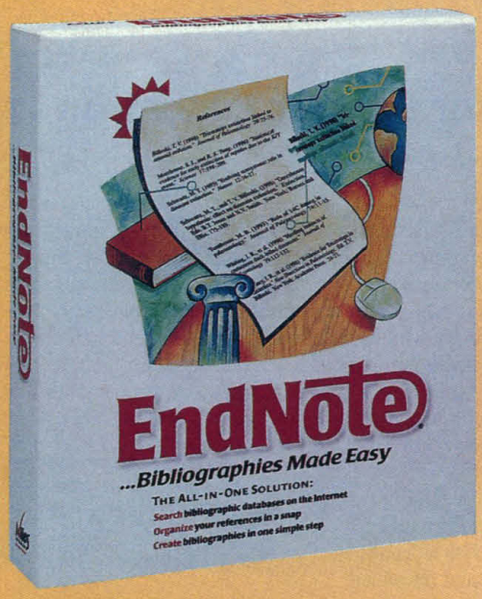

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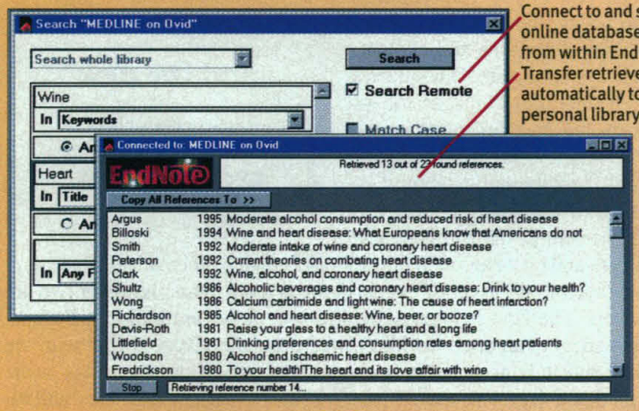
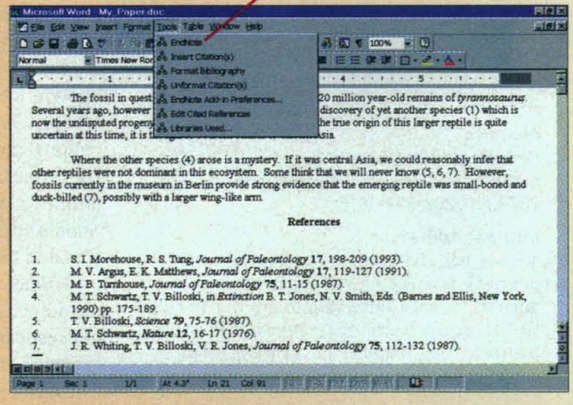
✓**1-Step Reference Organization**

✓**1-Step Bibliographies**



Connect to and search online databases from within EndNote. Transfer retrieved references automatically to your personal library.

Access EndNote commands and create **ONE-STEP BIBLIOGRAPHIES™** from within Microsoft Word & WordPerfect.



Online Search Tool *New!*

EndNote includes more than 100 connection files, enabling you to seamlessly access remote bibliographic databases such as MEDLINE, PsycINFO, and many university library catalogs from within EndNote. Search these and other databases using EndNote's simple search window-then transfer your results directly into your EndNote database. No additional importing steps!

Reference Database

EndNote makes organizing references easy. Create your own EndNote databases (as many as you wish) and store up to 32,000 records in each. Store abstracts, keywords, and notes, and link records to full-text articles or other material on the World Wide Web. At the click of a button, EndNote launches your web browser (e.g. Netscape, Microsoft Internet Explorer) directly from EndNote records.

1-Step Bibliography Maker

EndNote creates 1-Step Bibliographies™ from within Microsoft Word (Macintosh and Windows) and WordPerfect (Windows), allowing you to insert citations and format bibliographies without leaving your word processing documents. For journal article submissions, grant proposals, thesis preparation and a wide variety of academic writing projects, EndNote is an invaluable time-saving tool. You can choose from over 300 pre-defined bibliographic styles (e.g., APA, Science, Nature), or create a style to suit your needs. You can revise your document as many times as needed—EndNote will update the in-text citations and bibliography quickly and easily. And EndNote will also generate bibliographies in HTML for publication on the Internet!

More than 150,000 users prefer EndNote.

Compatible with Windows 95, Windows NT, Windows 3.1 and Mac OS. To use EndNote as an online search tool: Remote databases must be z39.50 compliant; System must have Internet access and ability to run standard Internet applications.

Visit our website at www.niles.com to download a free 30-day trial version of EndNote.

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