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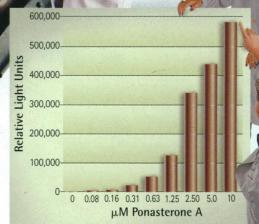
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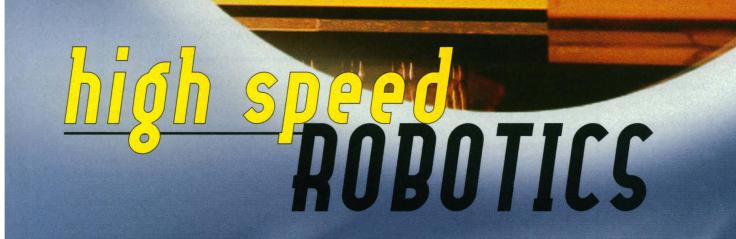
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Set for Radiation Victim

Inflammatory Agent

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Sciences Take a Hit

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**EPIDEMIOLOGY: Groups Race to Sequence** 

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### COVER Oblique aerial view of raised beaches along the Scott Coast, Antarctica. Ages and elevations of these beaches suggest that the final unloading of ice occurred about 7600 years ago. These data, coupled with other evidence from the southern Ross Sea Embayment, indicate Holocene (and perhaps ongoing) recession of the West Antarctic Ice Sheet. [Photo: G. Denton]

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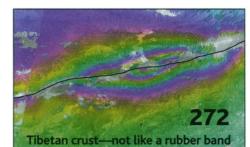
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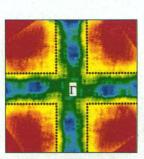
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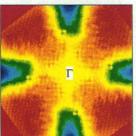
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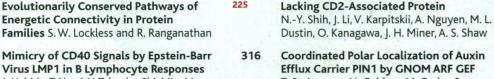




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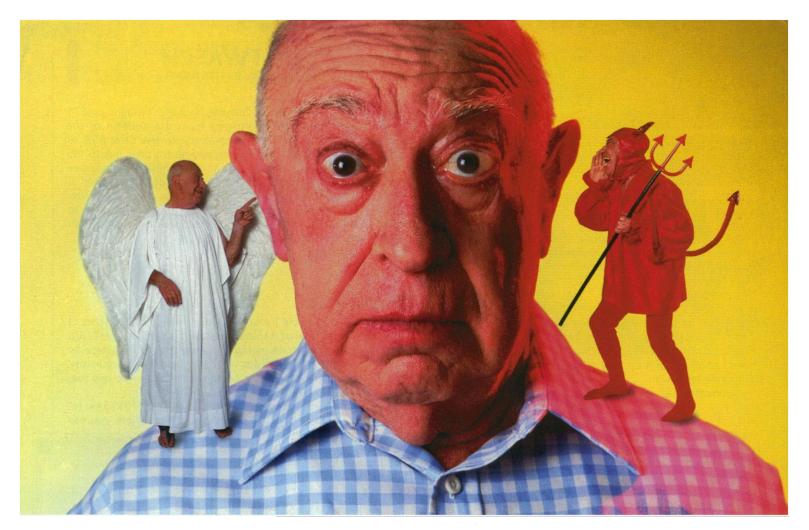
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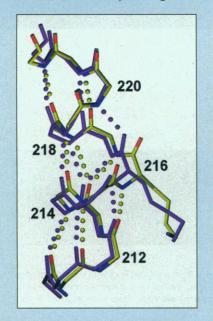
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### SHIFTING PROTONS UPHILL

Bacteriorhodopsin, a bacterial membrane protein, catalyzes the conversion of the energy of a single photon into electrochemical potential energy by transporting a single proton across the membrane. This proton gradient



can then be used via other transport proteins to accumulate nutrients or to synthesize adenosine triphosphate directly. Leucke et al. (p. 255; see the Perspective by Gennis and Ebrey) describe the atomic-resolution structure of this protein in two statesprior to absorbance of the photon and midway through the catalytic cycle. What they observe is that the isomerization of a single chemical bond produces conformational changes that result in sequential shifting of a pattern of hydrogen bonds between portions of the protein and specific water molecules. These shifts alter the acidity constants of several carboxylic acids so that a proton is released on the extracellular side of the membrane while another is absorbed on the cytoplasmic surface.

### NONLINEAR ELASTICITY AND EARTHQUAKES

Rocks such as sandstone and granite are structurally nonuniform and exhibit nonlinear elastic behavior—their Young's moduli under tension is about half of the value measured when the samples are

under compression (that is, they are stronger when compressed than when stretched). Peltzer et al. (p. 272) used satellite synthetic aperture radar interferometry to measure surface displacement after the magnitude 7.6 earthquake in Tibet in 1997. They found asymmetries in the amount of displacement on either side of the fault and could model this displacement successfully only by including nonlinear elastic responses. The authors attribute the nonlinear behavior in this case to the presence of heterogeneously distributed shallow cracks on either side of the fault. This rare example of nonlinear behavior on a scale of hundreds of kilometers suggests that earthquake modeling may normally need to take such effects into account.

### TREADING ON THICK ICE

The West Antarctic Ice Sheet has been retreating, but how rapidly and for how long? Its complete collapse could raise sea level by several meters. Three reports address the past retreat and current movement of this important ice sheet. Ackert et al. (p. 276) examined the early deglacial history of the Ice Sheet and determined its past elevation by dating the deposition of a lateral moraine on Mount Waesche. The age of 10,000 years for the high stand there, in conjuction with an ice sheet model, imply that melting of the West Antarctic Ice Sheet may not have contributed to a prominent sea-level rise in the Holocene. Conway et al. (p. 280; see the cover) examined the retreat of the grounding line of the Ice Sheet (where it contacts the floor of the Ross Sea Embayment) during the past several thousand years by dating exposed raised beaches and deltas. Most of the retreat began about 7500 years ago, and the grounding line passed Roosevelt Island about 3200 years ago. The rate of retreat seems to reflect long-term controls rather than any recent acceleration by climate warming. Thus, retreat may likely continue even in the absence of warming. Finally, Joughin et al. (p. 283) used radar interferometry to get a broad view of the inland ice flow that now feeds four Antarctic ice streams and related these results to the topography beneath the ice sheet. Their results show that streaming flow is fed by a network of smaller tributaries, which coincide with valleys in the subglacial floor where sediments and water are expected to occur, and originate from common source areas. Thus, mass balance calculations of ice flow that have assigned distinct catchment basins to individual ice streams must be revised.

### BISTABLE RADICAL MAGNETS

THIS WEEK IN SCIENCE edited by PHIL SZUROMI

> Although most organic molecules have their electron spins paired, some species contain an unpaired spin. Magnetic properties that may arise through the unpaired spins are usually hard to exploit near ambient conditions, but Fujita and Awaga (p. 261) show that the organic radical 1,3,5-trithia-2,4,6-triazapentalenyl (TTTA) exhibits a low-temperature diamagnetic phase that switches abruptly to a paramagnetic phase just above room temperature. Upon cooling, the material stays paramagnetic down to 230 kelvin, thus creating a wide hysteresis loop. This first-order magnetic phase transition is related to a structural transition that involves a change in the stacking of the molecules that also changes its color.

### CONTROL OF NANOTUBE

Recent experiments on single-walled carbon nanotubes connected across two superconducting contacts revealed that, at sufficiently low temperatures, a supercurrent could flow through the nanotube from one superconducting electrode to the other via the proximity effect. Morpurgo *et al.* (p. 263) now demonstrate that a bias voltage, supplied by a gate electrode located directly below the nanotube, can be used to switch the nanotube between high- and low-conductivity states.

### SUPERCONDUCTING CUPRATES GET INTO LINE

Strong but indirect experimental and theoretical evidence has indicated that the charge carriers in the underdoped layered cuprate superconductors form ordered, conducting, one-dimensional stripes separated by antiferromagnetic insulating regions as the temperature is decreased below the transition temperature. Two reports present direct evidence for one-dimensional ordering in these materials (see the Perspective by Zaanen). Noda et al. (p. 265) present data from directional electrical measurements (resistivity and Hall measurements), and Zhou et al. (p. 268) probed the electronic structure by angle-resolved photoemission spectroscopy

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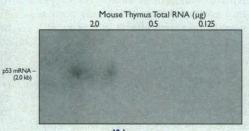
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1. Molecular Cloning: A Laboratory Manual, 1989. Sambrook, J. Fritsch, E.F., Maniatis, T. Cold Spring Harbor Laboratory Press.

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### THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 197

### **PROTEIN MIMICS**

Pathogenic bacteria and viruses must evade host defenses to survive; two reports show how mimicry of host protein function can aid in cell entry and interrupt immune system responses. Entry of the bacterial pathogen Yersinia pseudotuberculosis into eukaryotic cells is mediated by the bacterial outer-membrane protein invasin, which binds to host cell integrins with a higher affinity than natural substrates such as fibronectin. Hamburger et al. (p. 291) present the atomic-resolution structure of the invasin extracellular region. Comparison of this structure to fibronectin provides an example of convergent evolution. Although the proteins have different folding topologies, both form elongated structures comprised of tandem domains and have residues critical for integrin binding at similar locations. The structural comparison also reveals differences between invasin and fibronectin that might explain how the bacterial pathogen can compete with host proteins to exploit host cell receptors. Epstein-Barr virus infects epithelial and B cells and is associated with various cancers and B lymphomas. This DNA virus has a latent phase and expresses latent membrane proteins, such as LMP1, that are essential for transformation. LMP1 can interact with many of the signaling molecules that normally bind to CD40, a crucial activation signal for B cells. Uchida et al. (p. 300) report that LMP1 can mimic a constitutively active CD40 molecule and thus needs no ligation to aid in proliferation and antibody secretion of B cells. However, LMP1 blocks B cells from forming the germinal center, the site for affinity maturation and generation of memory B cells, and may increase the likelihood of viral survival.

### **RADICAL STEPS**

The overproduction of oxygen free radicals can damage cells and is associated with many diseases. These free radicals are normally removed in our bodies by the superoxide dismutase (SOD) enzymes. Salvemini et al. (p. 304; see the news story by Strauss) have synthesized a nonpeptidic manganese-based complex that is a functional mimetic of SODs and is stable in vivo. Injection of this compound into rodents in model studies of inflammation and ischemic injury protected the animals against tissue damage. This class of compounds may have therapeutic potential in diseases ranging from inflammation to cancer. The protection that SODs offer aerobic organisms is not appropriate for anaerobes because molecular oxygen is a product. Jenney *et al.* (p. 306; see the Perspective by Lloyd) purified a novel enzyme, superoxide reductase (SOR), from the hyperthermophilic anaerobe *Pyrococcus furiosus.* SOR reduces superoxide to hydrogen peroxide, which is then reduced to water by peroxidases. Genes encoding SOR homologs are found in most of the available anaerobic genome sequences but not in the genome sequences from aerobes.

### **MAKING THE TAG**

Receptor protein-tyrosine kinases are activated in response to binding of extracellular ligands and control many biological processes. Just as proper cellular regulation requires finely controlled activation of such receptors, the termination of such signals must be tightly controlled. The degradation of many key signaling proteins is controlled by covalent attachment of the small protein ubiquitin, which targets the protein for degradation. The protein c-Cbl associates with activated receptors such as the platelet-derived growth factor receptor or epidermal growth factor receptor and leads to ubiquitination and degradation of the receptor. Joazeiro et al. (p. 309; see the news story by Barinaga) report that c-Cbl is itself a ubiquitin-protein ligase or E3 enzyme. The c-Cbl protein was shown to promote transfer of ubiquitin from an E2 ubiquitin-conjugating enzyme to substrate proteins.

### FILTER FAILURE

Regions in the kidney called the glomeruli filter blood during urine formation. Glomerular epithelial cells called podocytes establish a filtration barrier by extending protrusions that interact to form a tight web called the slit diaphragm. Shih et al. (p. 312; see the news story by Wickelgren) report that mice that do not express a cytoplasmic protein called CD2AP die of renal failure due to defects in these podocyte contacts. CD2AP was first characterized as a protein that assists in T cell adhesion to antigen-presenting cells in the immune system. The authors report that CD2AP localized to podocyte processes in the kidney as well. CD2AP also interacted with nephrin, a membrane protein thought to maintain the integrity of the slit diaphragm. Hence, CD2AP may have a general role in facilitating specialized cell-cell adhesion complexes and may be implicated in certain nephrotic syndromes.



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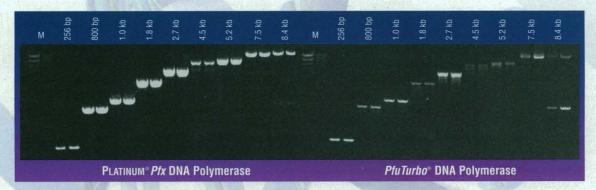
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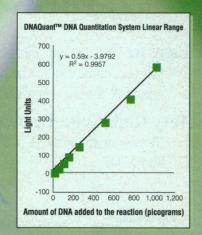
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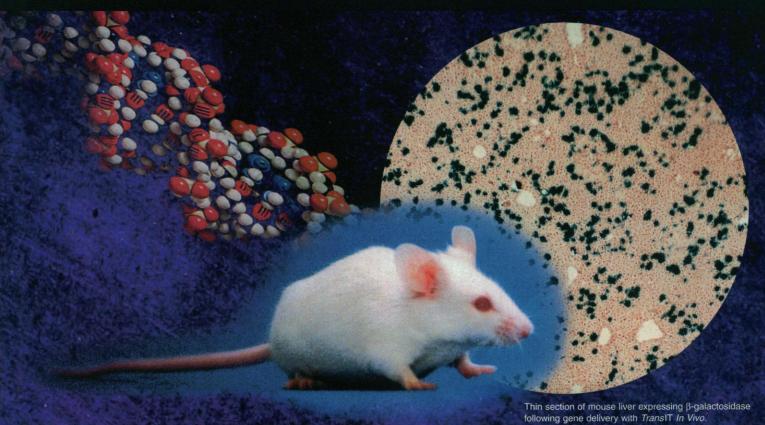
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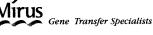
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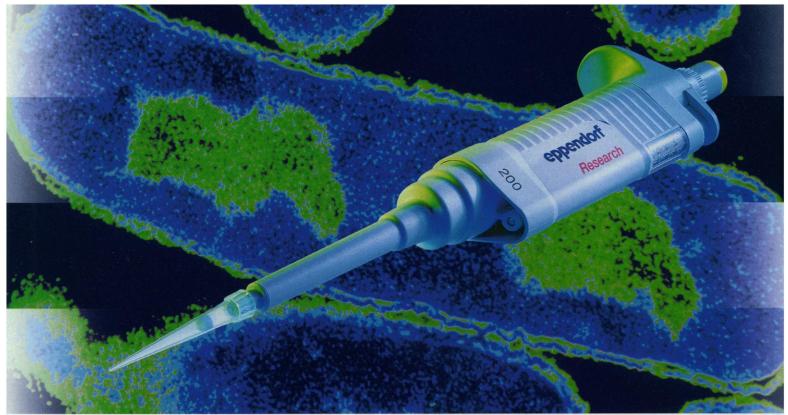
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Background picture: Color-adapted, electron-microscopic image of E.coli bacteria

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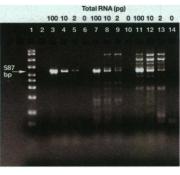
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Lanes 7, 8, 9, 10: RNA PCR; with MuLV and Taq DNA Polymerase, no Hot Start

Lanes 11, 12, 13, 14: RNA PCR; AMV and enzyme blend, no Hot Start

Lane 1: Size Standard







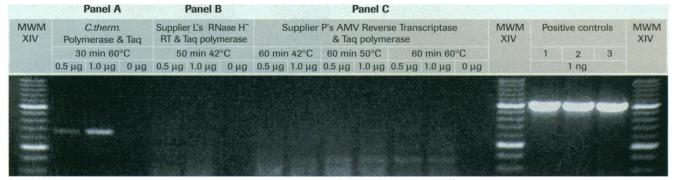
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Comparison of C.therm. Polymerase, Supplier L's RNase H<sup>-</sup> Reverse Transcriptase, and Supplier P's AMV Reverse Transcriptase for RT-PCR. (Template: Total RNA isolated from K562 cell line; Primer: TGFß; Target: 650 bp product; 1.5 M betaine to dissolve secondary structure; Positive Controls: 1 ng of a 997 bp ß-actin fragment from mouse).

Panel A: C.therm. Polymerase & Tag polymerase for 30 min at 60°C **Panel B:** Supplier L's RNase H<sup>-</sup> Reverse Transcriptase & Tag polymerase for 50 min at 42°C Panel C: Supplier P's AMV Reverse Transcriptase & Tag polymerase for 60 min at 42°C

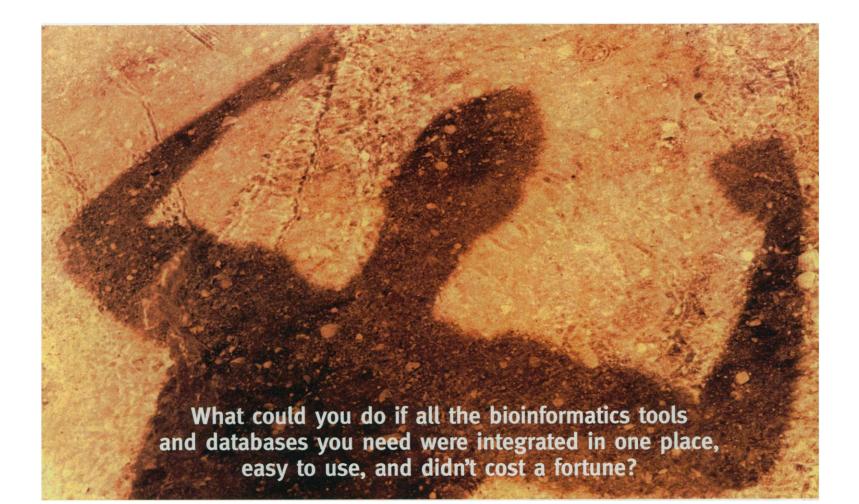


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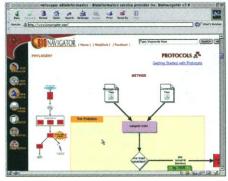
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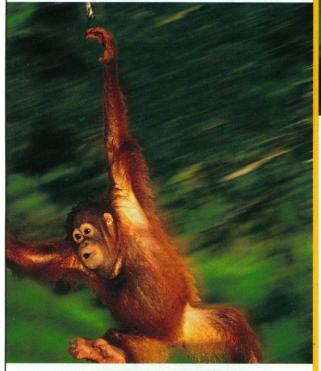
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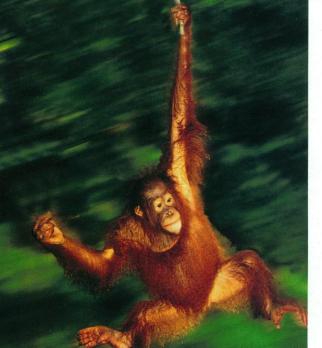
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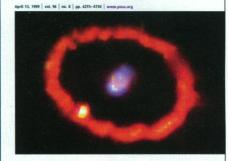
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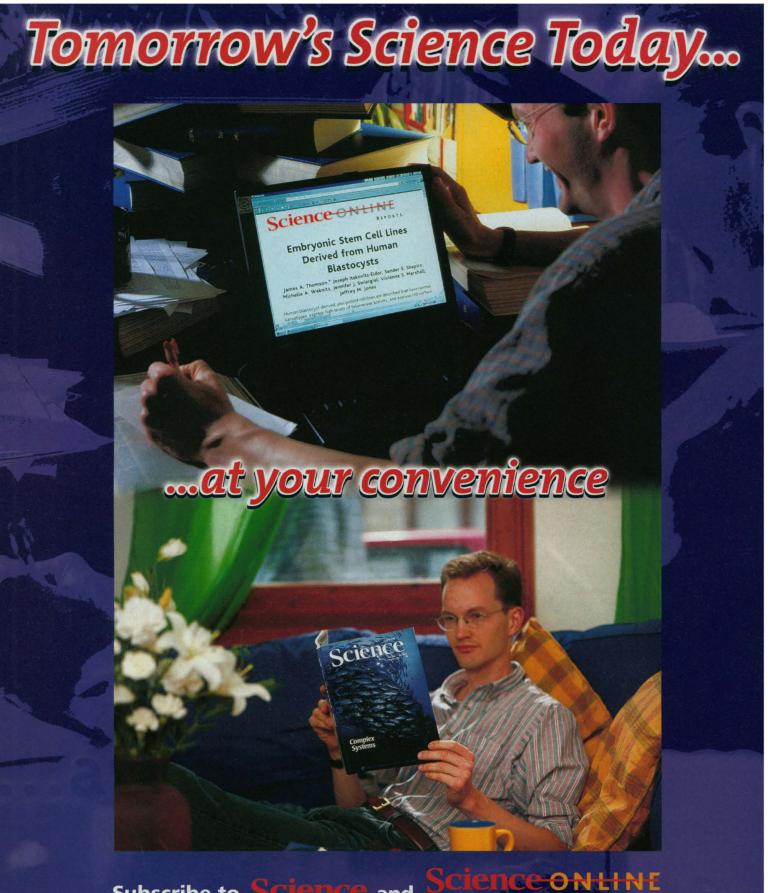
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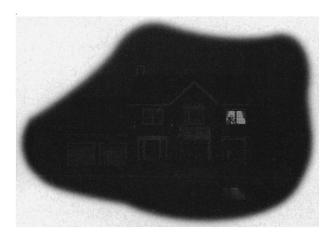
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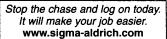
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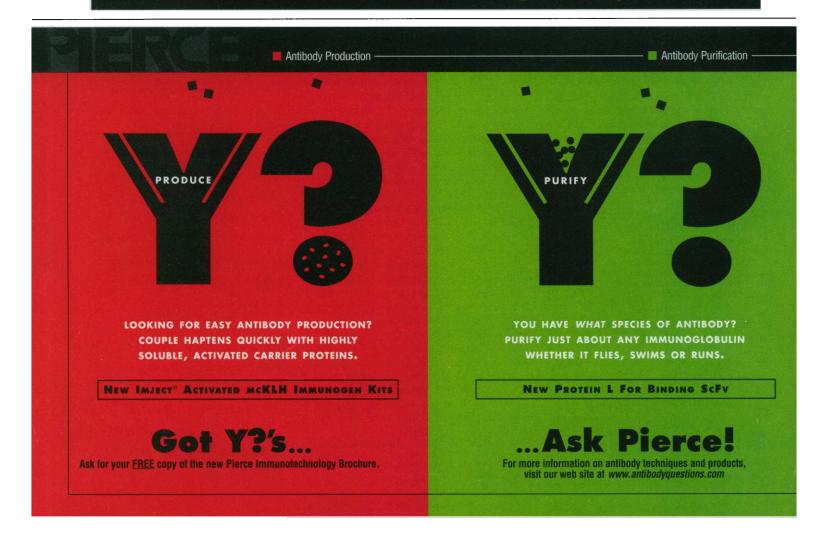
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