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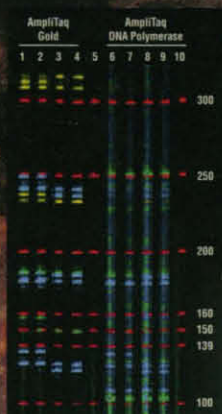
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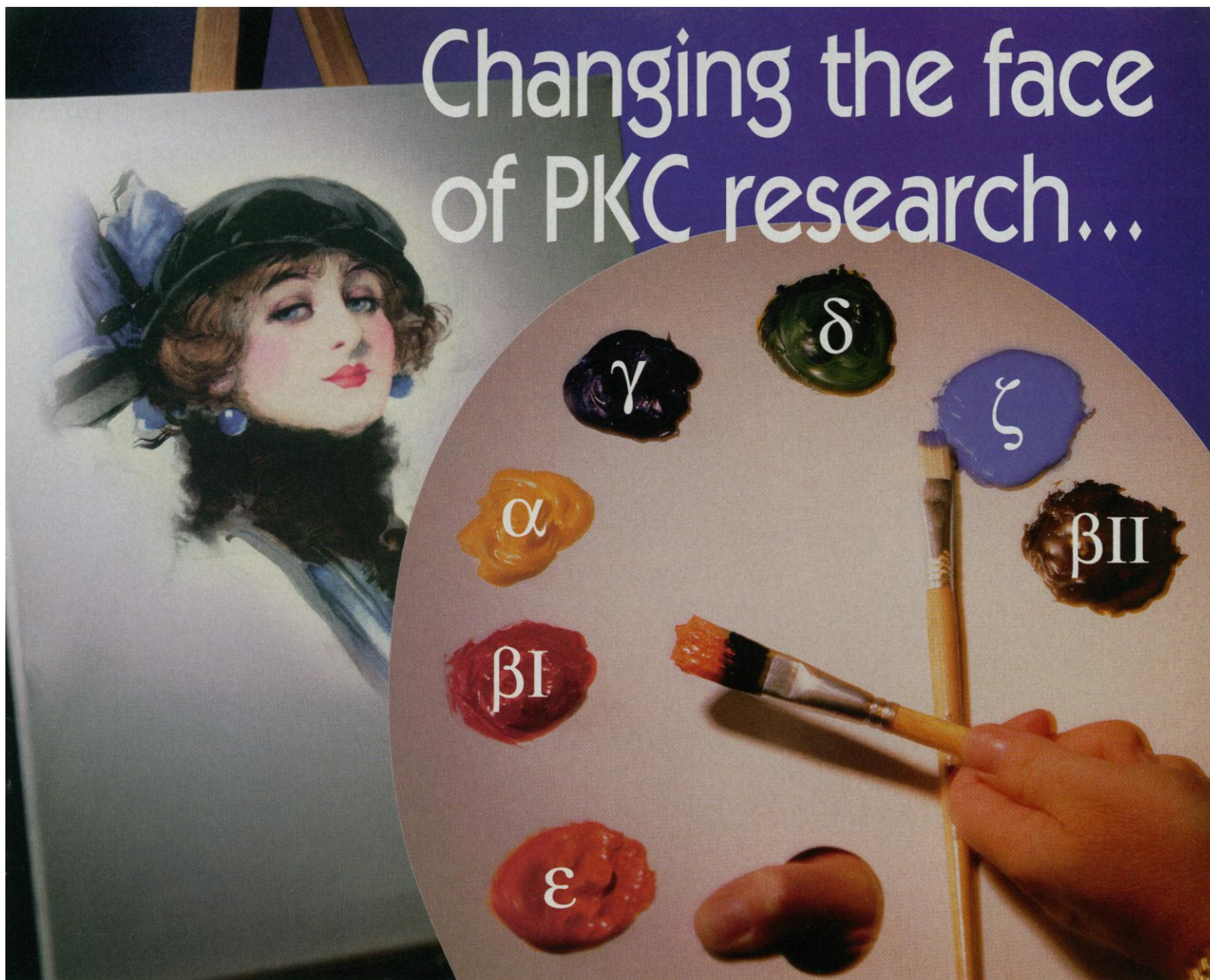
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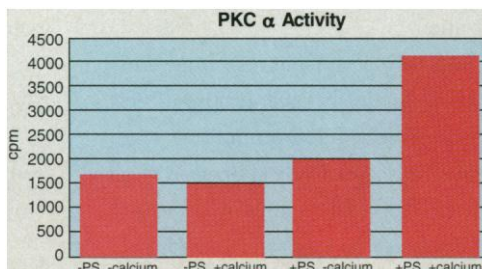
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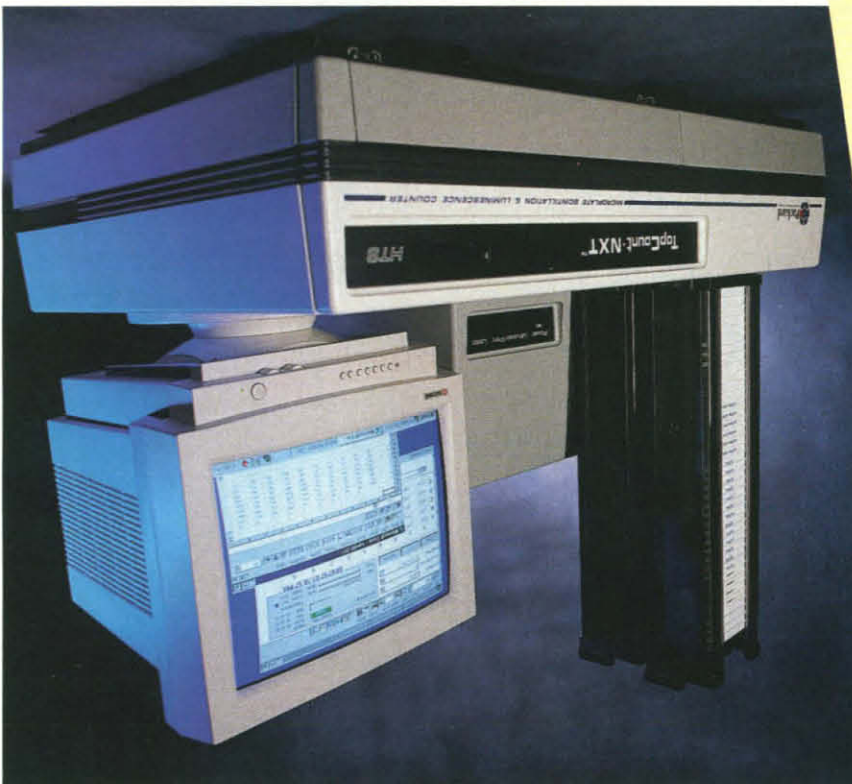


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# COVER

Aided by sophisticated molecular genetic techniques, researchers are assembling an increasingly detailed profile of the molecular changes that characterize human cancer cells. The cover illustration portrays our struggle to understand and apply this informa-

tion to defeat the disease. The Editorial (page 995), News stories, and Articles (see the special section beginning on page 1035) review current efforts in prevention, diagnosis, and treatment of cancer. [Illustration: Celia Johnson]



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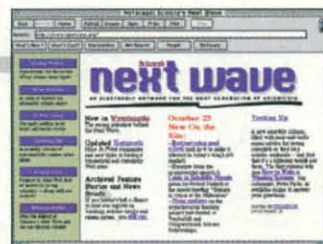
**1093**  
A cutaway view of the ribosome

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# THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

## Lunar time

The moon has generally been thought to have formed following the impact of a Mars-sized planetesimal into the early Earth. Lee *et al.* (p. 1098) investigate this early planetary history by measuring tungsten-hafnium isotopes in many lunar samples. This isotope system is useful for assessing early planetary evolution because tungsten-182 has a short half-life (about 9 million years) and tungsten tends to fractionate into a metal core if it forms. The data imply that the moon formed about 4.5 billion years ago.

## Good alignment

The direct measurement of bond distances and angles in macromolecules by nuclear magnetic resonance (NMR) is reported by Tjandra and Bax (p. 1111; see the news story by Service, p. 1014). They dissolved macromolecules in dilute aqueous solutions containing discotic nematic liquid crystals and magnetic particles. When the magnetic field was applied, the liquid crystalline media tended to align the macromolecule (in this case, the protein ubiquitin) so that dipolar couplings between nuclei, instead of canceling to zero, could be measured. The structure obtained is in excellent agreement with the known x-ray structure of ubiquitin, and the method should extend the size range of molecules that can be studied by solution NMR.

## Eurasian climate record

Long-term records of continental climate stretching back beyond even about 1 million years ago have been obtained from Antarctica and the Chinese loess sequences. Williams *et al.* (p. 1114) now describe a record for Lake Baikal in central Eurasia that extends back about 5 mil-

## Taking the measure of the ribosome

During translation, transfer RNAs (tRNAs) bind through their anticodon stem-loops to the codons of messenger RNA, but ribosomal RNA (rRNA) itself also plays a role in tRNA binding. Joseph *et al.* (p. 1093) have used a cleavage method to map out regions of rRNA near the tRNA binding sites. RNA probes were constructed that consisted of stem-loops and 4 to 33 base pairs of RNA; Fe(II) ions attached to the end of RNA helix were used to generate hydroxyl radicals that cleaved nearby rRNA. The cleavage patterns were then used to model the three-dimensional structure of rRNA near the A and P sites.

lion years. Analysis of the records, primarily of biogenic silica accumulation, implies that the climate response to orbital variations in the interior of the Eurasian continent was similar to that in the oceans throughout the long record.

## Selenium in soil

Selenium is a major contaminant in many watersheds and soils, and its mobility depends on its oxidation state. Many soils and sediments also contain an iron oxide called green rust. Myneni *et al.* (p. 1106) show that a series of abiotic reactions involving green rust reduce selenium in sediments and thus affect selenium cycling and perhaps the cycling of other trace elements in soil.

## Follows convention

Low-barrier hydrogen bonds (LBHBs) consist of a proton that is shared equally between two atoms. Although LBHBs are known to exist in the gas phase, they also have been proposed to exist within the active sites of enzymes and help stabilize the transition state, thus accelerating the reaction. Ash *et al.* (p. 1128), using nuclear magnetic resonance spectroscopy, reexamine this issue as it applies to the catalytic triad of a serine protease as well as a small molecule model of the catalytic amino acids. The hydrogen bond formed

by the aspartate-histidine dyad appears to be of the conventional kind and not LBHB-like.

## Cold tongue

For endotherms such as whales to flourish in richly productive high-latitude waters, they must have overcome a considerable potential constraint—loss of heat through the tongue. The tongues of baleen whales can be particularly large and, unlike the skin, cannot be insulated by a thick blubber layer. Heyning and Mead (p. 1138) show that the tongues of gray whales contain a large countercurrent heat exchanger. Temperature measurements at the oral cavity of a live gray whale suggest that this heat exchanger can considerably reduce such heat loss when the whale feeds in cold polar and subpolar waters.

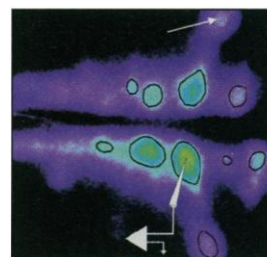
## Class distinctions

The enzymes that charge transfer RNAs (tRNAs) with their amino acids (tRNA synthetases, or RSs) have appeared to distribute into two classes in the same way in all organisms. In certain Archaea species (methanogens), however, no lysyl RSs, a class II RS, could be identified. Ibba *et al.* (p. 1119) have purified this enzyme from one organism and cloned the corresponding gene, which was found to correspond to unassigned open-reading frames in two other methanogens. The se-

quence suggests that this lysyl RS actually belongs to class I, which also raises questions concerning RS evolution.

## Skin-deep response

Control of limb movement involves a complicated interchange between sensory and motor neurons and muscles. Viana Di Prisco *et al.* (p. 1122; see the Perspective by Grillner and van der



Plicht, p. 1087) examined how sensory inputs from the skin translated into tail movements in lamprey. At a certain threshold of stimulation, inputs into reticulospinal neurons are transformed into motor commands.

## Evading attack

Pathogenic bacteria secrete virulence proteins that help them escape killing by the defenses of the host. Attempts to identify an amino acid sequence or other physical properties of such proteins that might target them to the appropriate secretion system have been unsuccessful. Anderson and Schneewind (p. 1140; see the Perspective by Silhavy, p. 1085) report that in *Yersinia enterocolitica*, a bacterium that infects animals and humans, translation and secretion of virulence factors appear to be closely coupled. Furthermore, frameshift mutations that completely alter the amino acid sequence in the critical region still allowed appropriate secretion. Thus, an intrinsic property of the messenger RNA during translation appears to provide the signal for secretion.



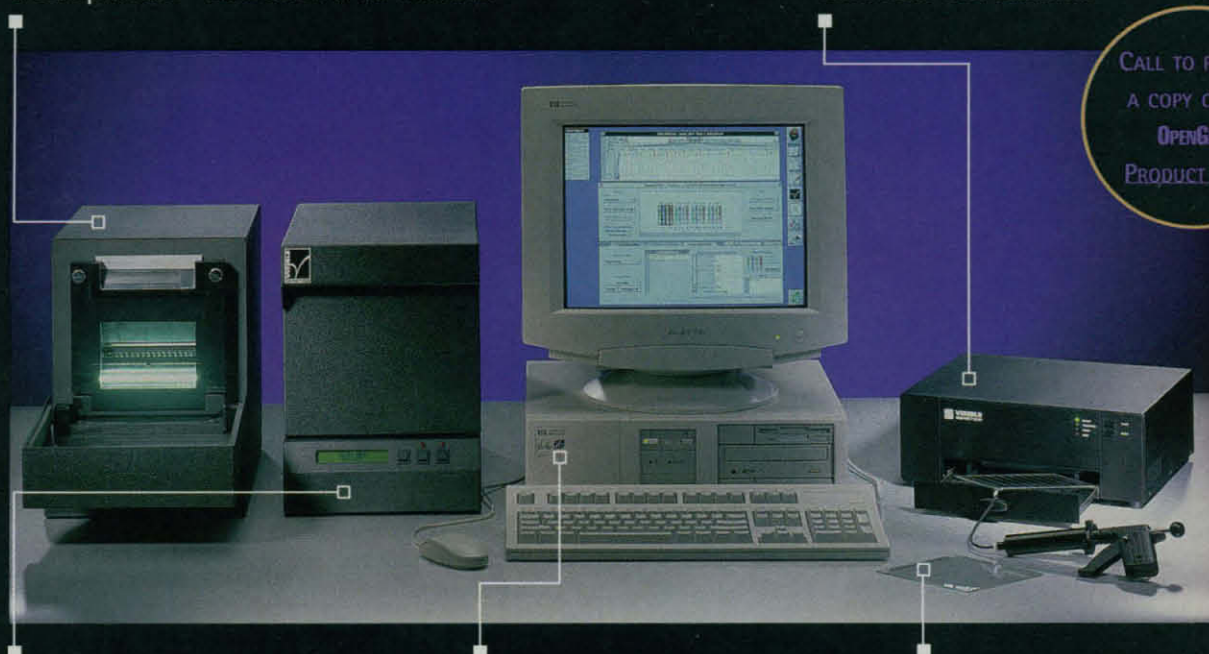
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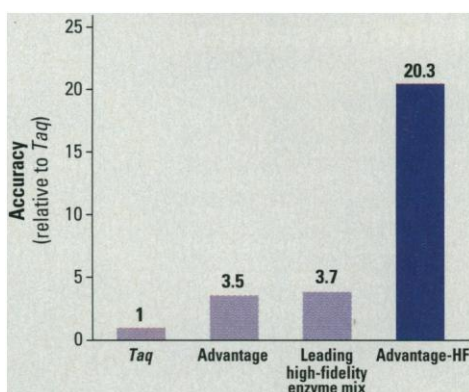
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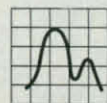
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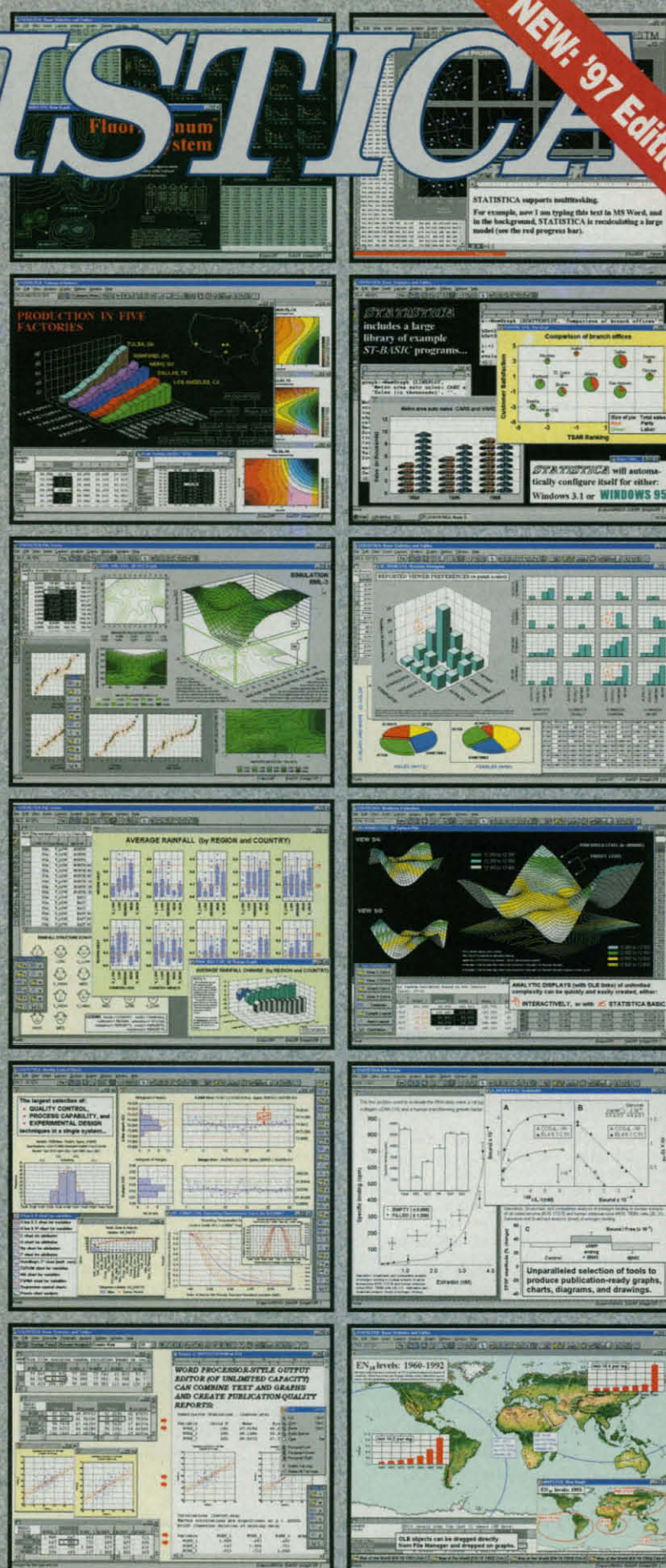
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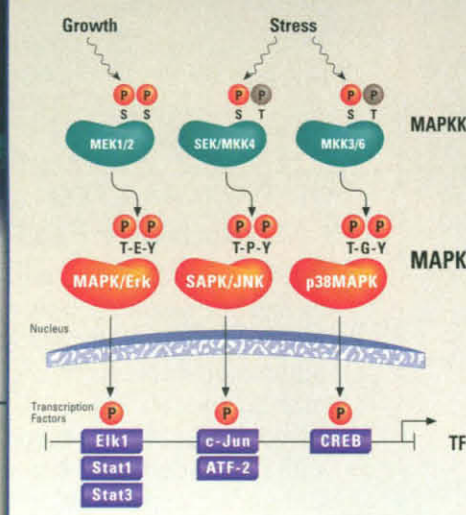


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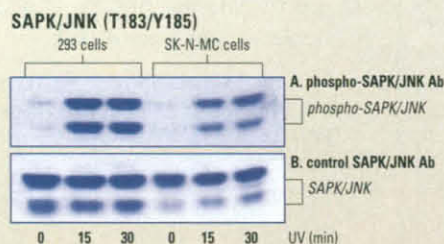
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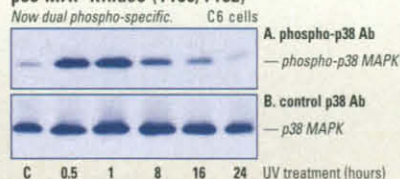


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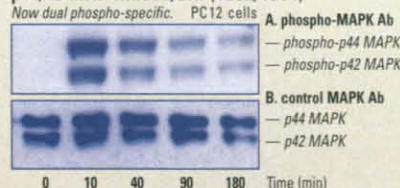


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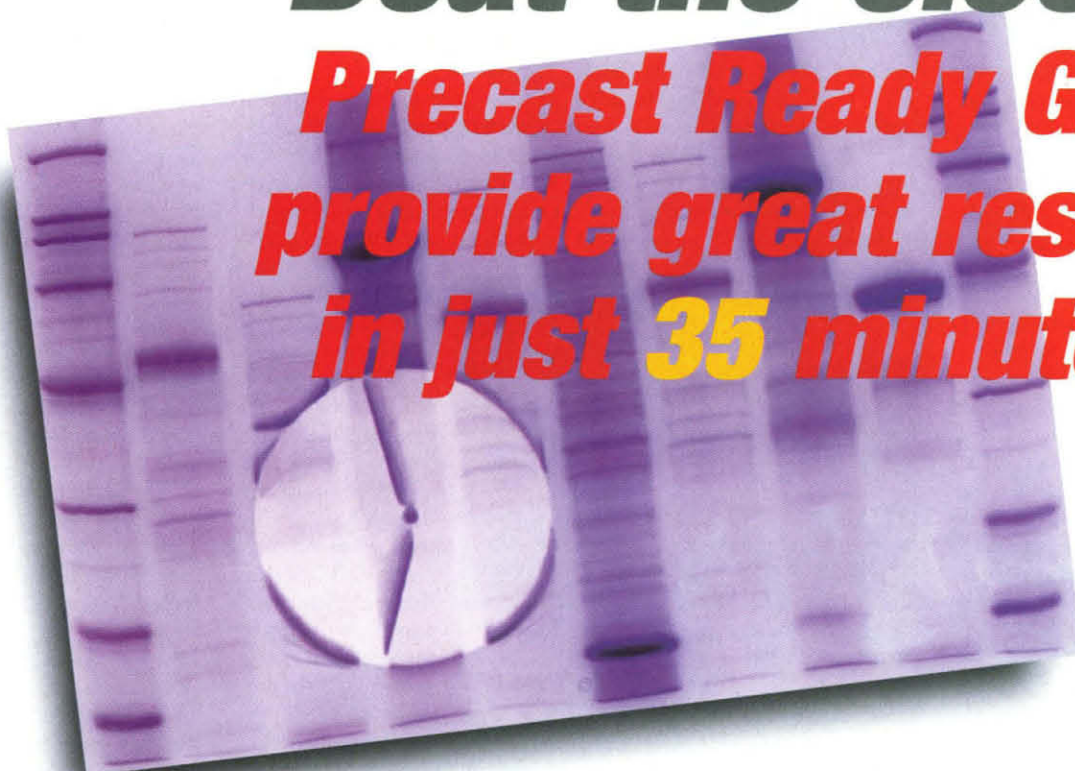


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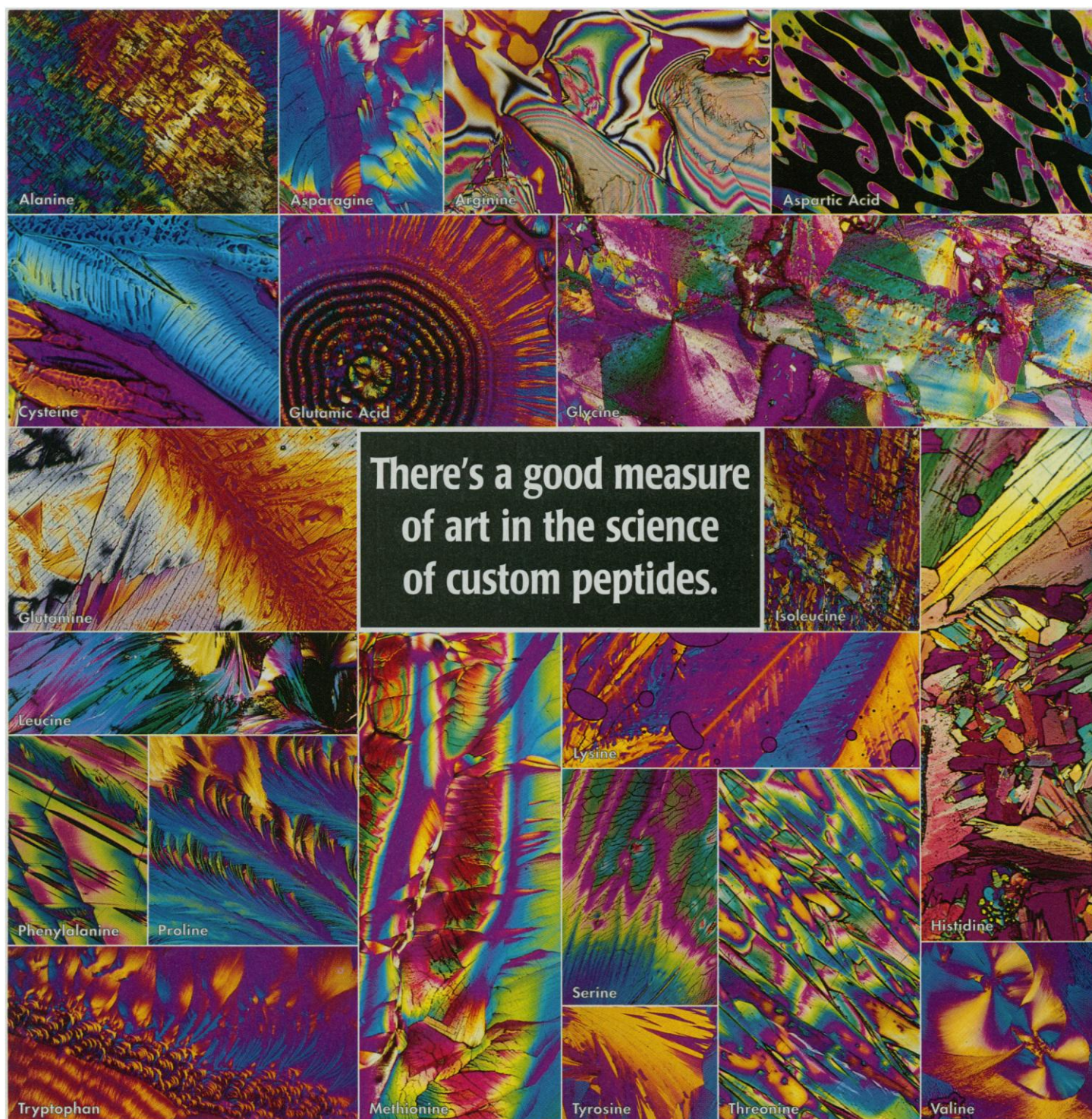
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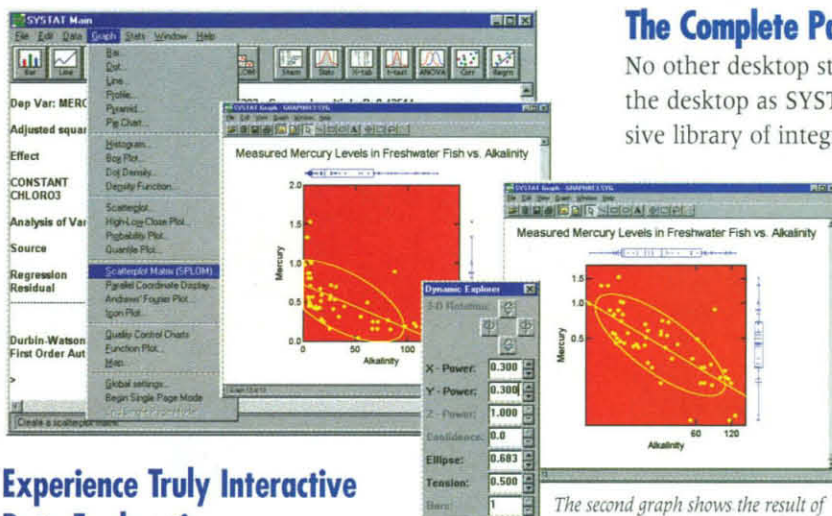
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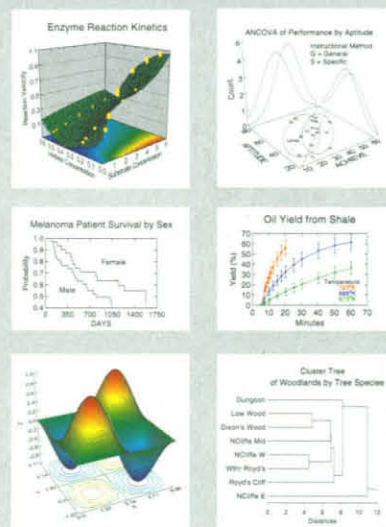
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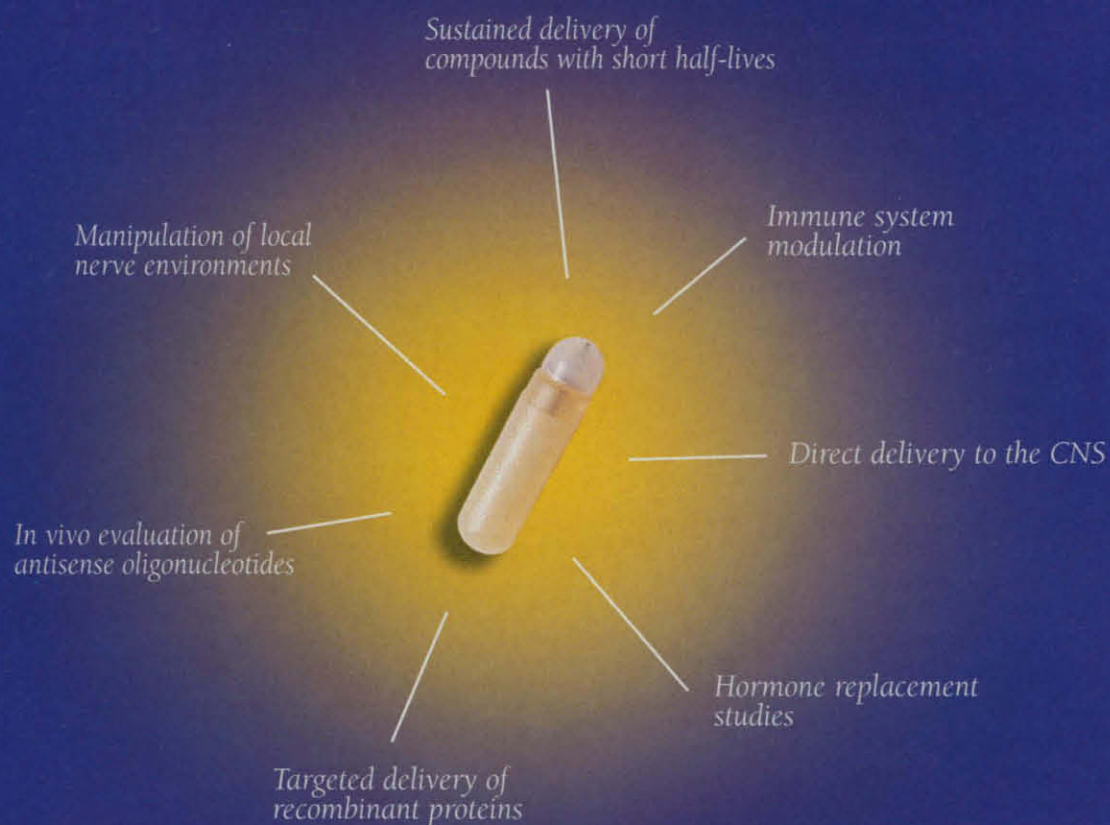
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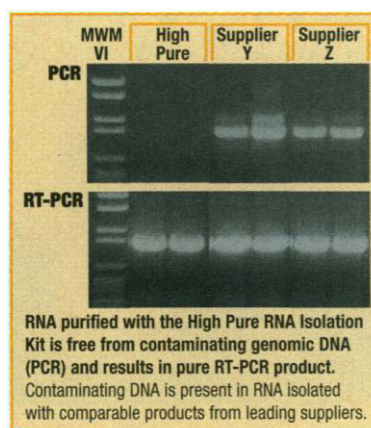




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<sup>1</sup> Noppen, C. et al. (1997) *Biochemica* **1997**(4):11-13.

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\* Lennon, G., Aufray, C., Polymeropoulos, M., Soares, M.B. 1996. The I.M.A.G.E. Consortium: An Integrated Molecular Analysis of Genomes and their Expression. *Genomics* 33, 151-152.

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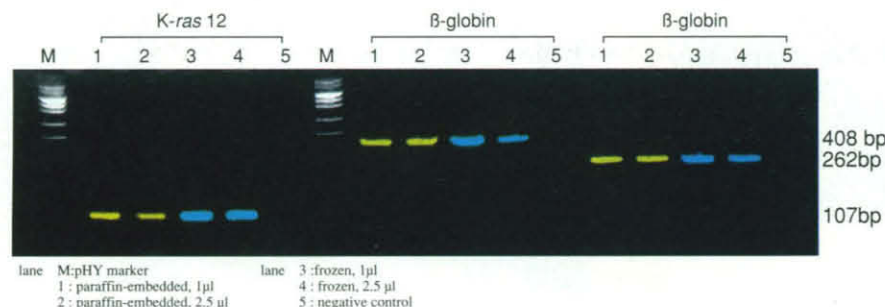
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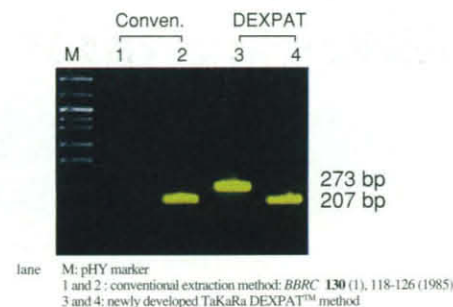
#### Comparison of Section Preparations

for K-ras 12 (107 bp) and β-globin (408 bp and 262 bp) Amplification from Human Tonsil: 1 μl or 2.5 μl extracts used for 25 μl PCR



#### Comparison of Extraction Methods

for p53 exon 5 (273 bp) and exon 6 (207 bp) Amplification from Paraffin-embedded Tissues of Colon Cancer After a 10-year Preservation



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Fig. 1. Sensitive detection of integrated HPV in SiHa cells using TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe (1000 bp) hybridized to cultured SiHa cells. TSA fluorescence detection used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slide counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using separate tetramethylrhodamine and DAPI filters. Photo taken on KODAK 1000 speed film with 5 second (Cyanine 3 Tyramide) and 0.5 second (Hoechst 33342) double exposure using a 100X objective.

Fig. 1

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Figs. 2a-d. Comparison of HPV fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe hybridized to cultured CaSki cells.

2a-b. Standard fluorescence detection carried out with Cy™3-conjugated Streptavidin (Jackson ImmunoResearch Laboratories, Inc.). TSA-enhanced fluorescence used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slides counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using a tetramethylrhodamine filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

2c-d. Protocol same as above but counterstained slides evaluated using a multiband pass filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

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Fig. 3a-b. Comparison of standard fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3). Courtesy of Kevin Roth, M.D., Ph.D., Washington University School of Medicine, St. Louis, MO. Bouin's fixed, paraffin embedded mouse intestinal tissue, deparaffinized and incubated with biotinylated wheat germ agglutinin. Sections incubated with Cy3-conjugated Streptavidin (3a) or with Streptavidin-HRP followed by Cyanine 3 Tyramide (3b). Wheat Germ Agglutinin labels intestinal epithelial cells at the base of the crypts.

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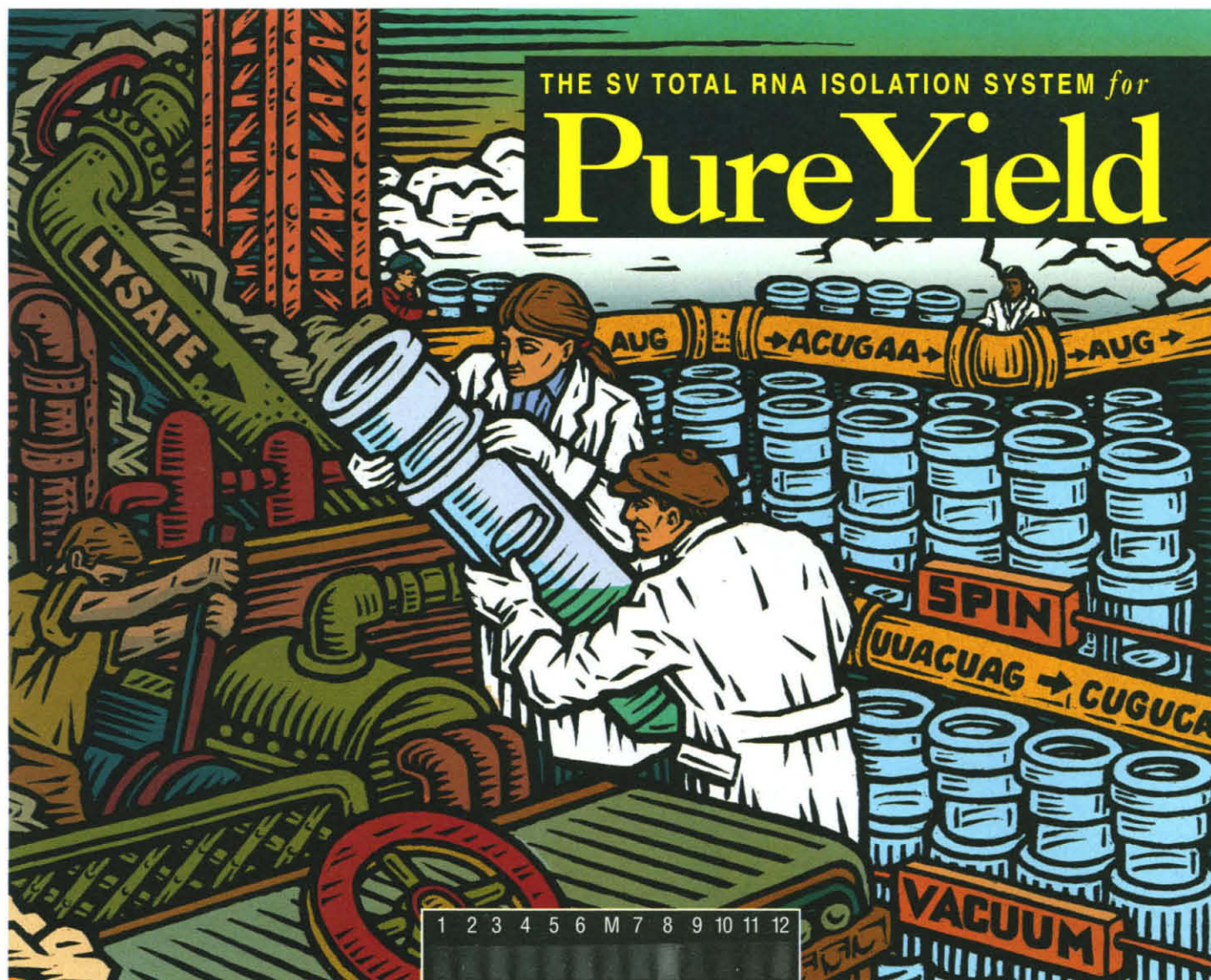
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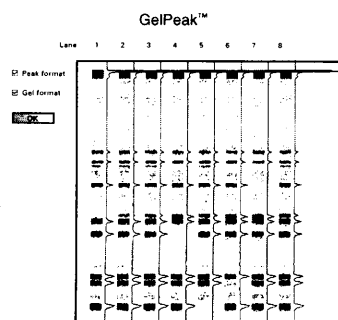
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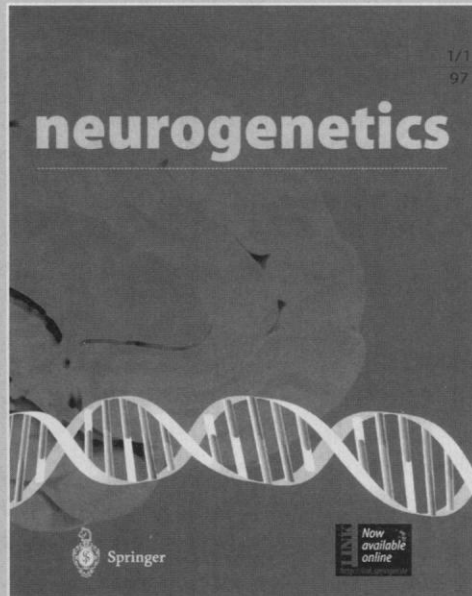
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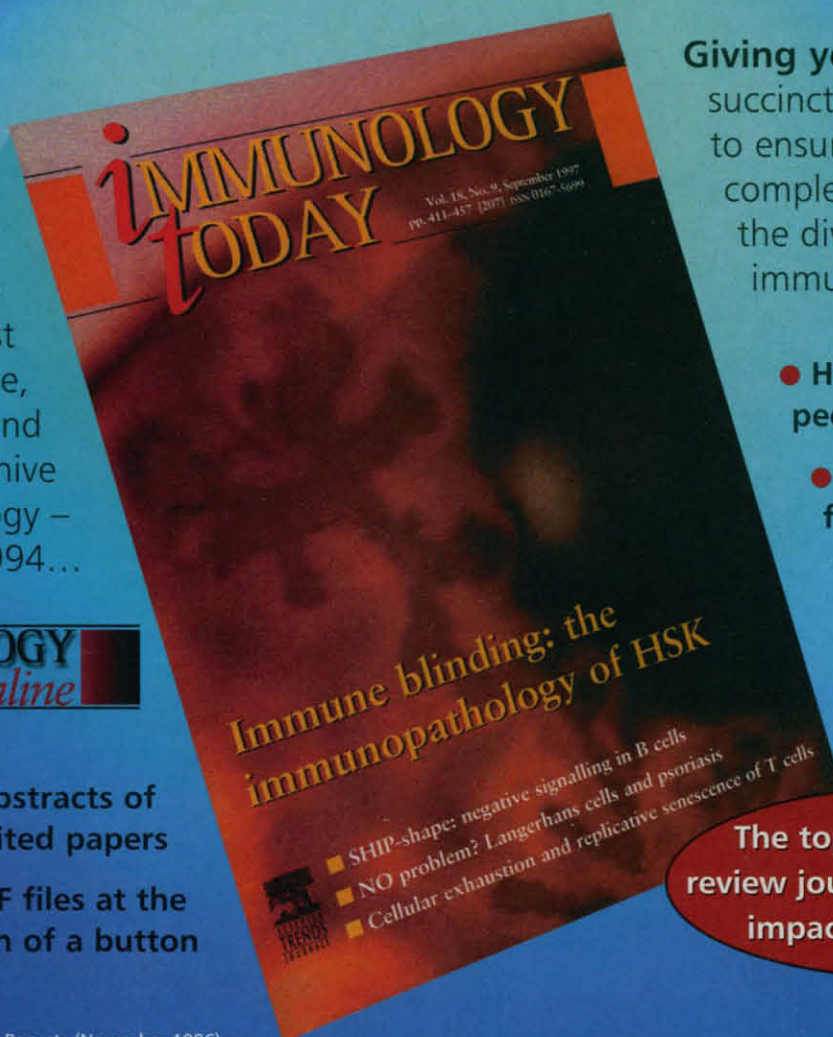


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