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SCIENCE

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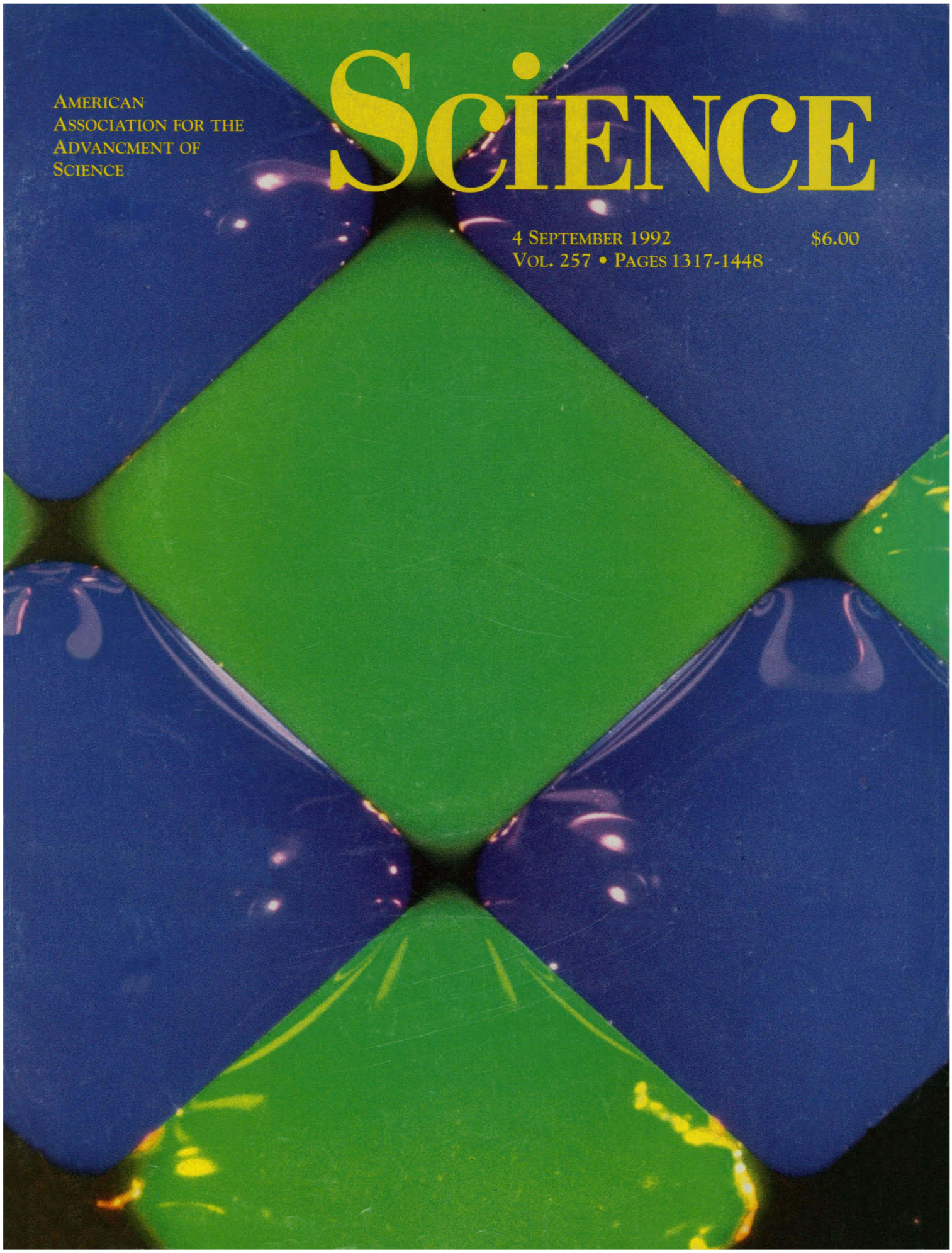

Double-Stranded Mutagenesis

Feel Stranded with M13?

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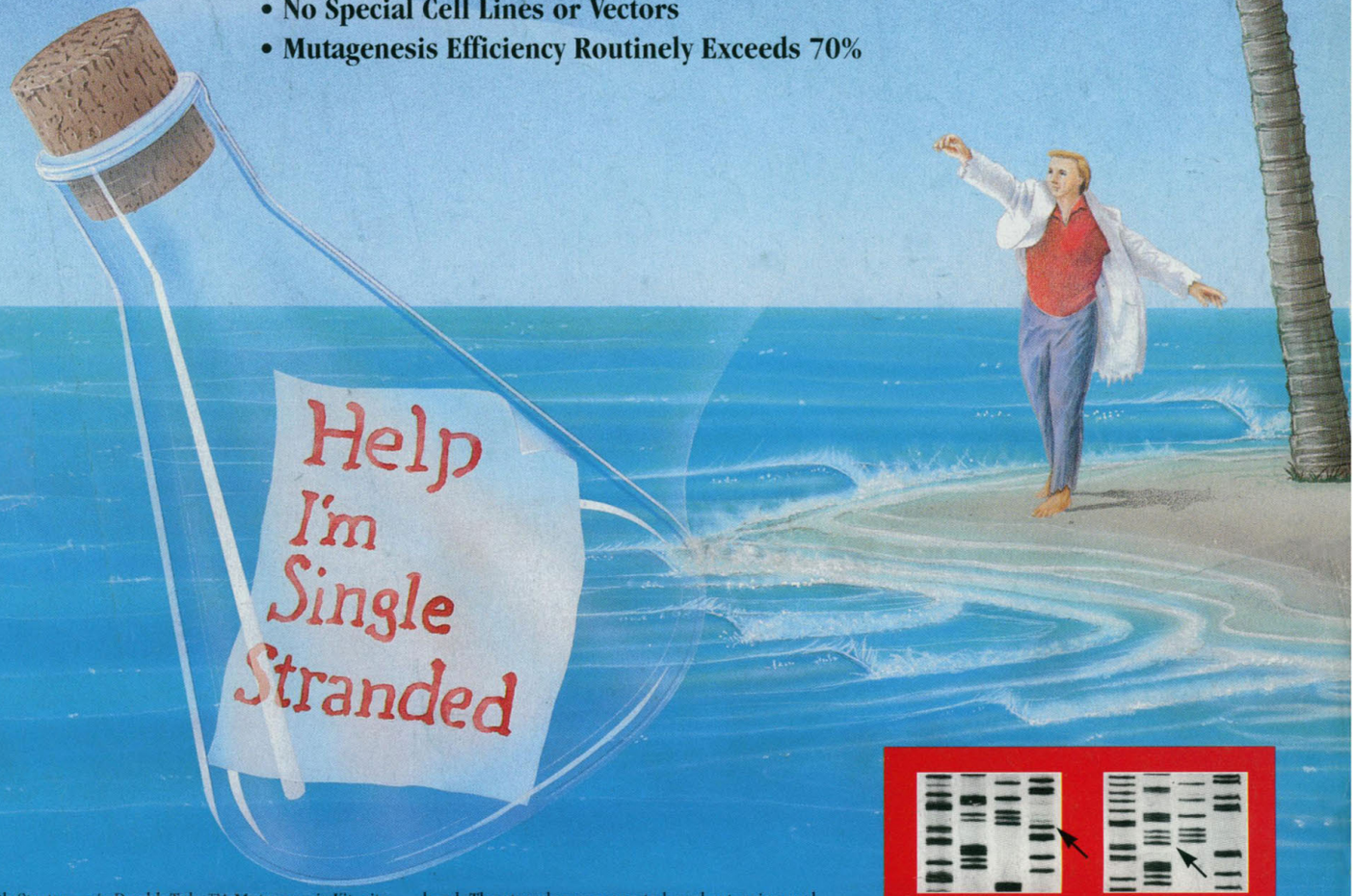
- **No Special Cell Lines or Vectors**
- **Mutagenesis Efficiency Routinely Exceeds 70%**



With Stratagene's DoubleTake™ Mutagenesis Kit, site-directed mutagenesis can now be performed on double-stranded plasmids…in one day. The DoubleTake Mutagenesis Kit eliminates tedious subcloning into filamentous phage and the need to produce single-stranded templates. The method is fast and easy with mutagenesis efficiencies greater than 70%.

Stratagene's DoubleTake™ Mutagenesis Kit uses a novel solid-phase approach. First, the double-stranded DNA is biotinylated and attached to an avidin bead. The strands are separated, and extension and mutant oligonucleotides are annealed to one of the bound template strands. DNA polymerase is then used to synthesize and incorporate the oligonucleotides. The synthesized complementary strand is melted off of the bead and recircularized. The resulting circular molecules are then transformed into the host.

So do a DoubleTake…and never be single-stranded again!

Figure A Figure B

Sequencing data of a point mutation generated in the pBluescript® II Vector using the DoubleTake™ Mutagenesis Kit.
A) Sequence of unmutated plasmid DNA. The arrow indicates the target adenine residue.
B) Sequence of plasmid DNA isolated after site-directed mutagenesis. The arrow indicates the adenine to guanine transition.

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two

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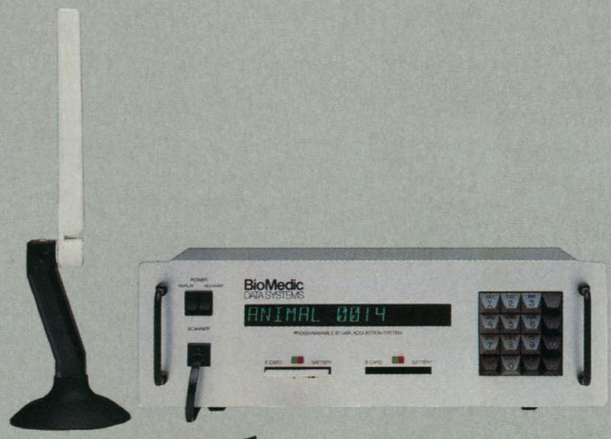

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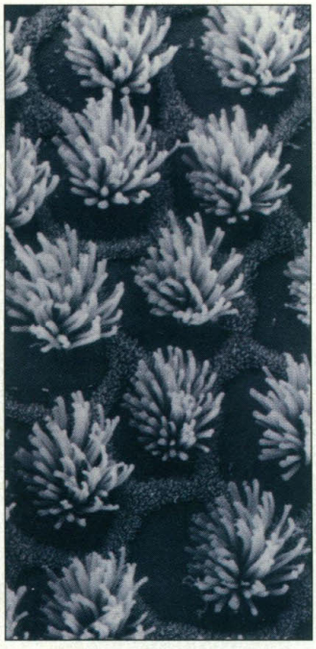

1344
The ear's hair cells can regenerate—in some animals

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PERSPECTIVES

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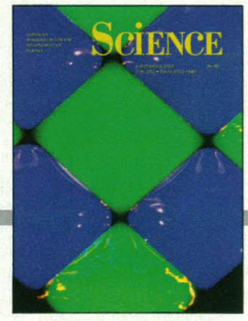
RESEARCH ARTICLE

DEPARTMENTS

COVER

Micrometer-wide lines of a hydrophobic self-assembled monolayer separate square regions of a hydrophilic monolayer; drops of water (with blue and green coloration) wet the square regions but do not contact one another. The lines of separation provide new structures with which to manipulate the shapes of liquid drops. See page 1380. The sides of each square are about 4 millimeters long. The blue drops do not completely wet the corners. [Photograph: F. Frankel]



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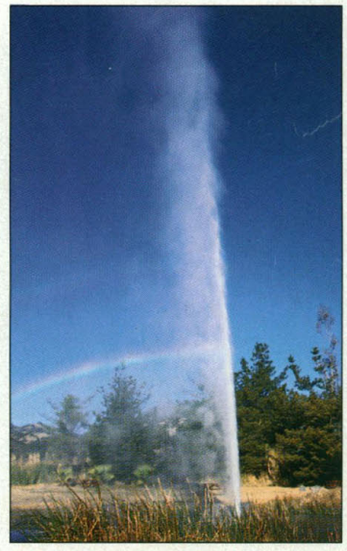
How do we see in three dimensions?



1363
A geyser that predicts earthquakes?

◩ Indicates accompanying News story or Perspective

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Ask the geyser

Earthquakes can have dramatic effects on the behavior of geysers, which in effect act as sensitive natural strain gauges. The practical value of this effect would be the recognition of consistent changes in geyser response in advance of large earthquakes. Silver and Valette-Silver (p. 1363) discuss such a possibility for the Calistoga Geyser in Northern California using detailed records of the interval between eruptions recorded at the geyser for the past 20 years. The interval changed significantly 1 to 3 days before the three largest earthquakes within 250 kilometers of the geyser, including Loma Prieta.

Magma movements

Magmas may take only a few years to many thousands of years to ascend from a region of melting to near the surface of the crust. Many processes, including ponding and partial crystallization in shallow magma chambers, can alter the composition of the magma during its transit. Gill and Condomines (p. 1368) review how uranium and thorium radioactive decay chains are used to understand these processes. Many of the isotopes that are produced as uranium and thorium decay to lead half-lives that range from a few years to several million years. Fractionation of the isotopes between the magma and residual crystals during the melting and ascent provide information on magma genesis.

RNA and clay

One problem in trying to reconstruct the events of prebiotic synthesis of nucleotides has been to oligomerize RNA nucleotides with the characteristic 3',5'-linkages between phosphates and sugar rings. Ferris and Ertem (p. 1387) report that condensation reactions of an adenosine nucleotide (the 5'-phosphorimidazolide) with itself and with a diadenosine over a montmorillonite clay was highly specific, producing oligomers up to ten nucleotides in length with predominantly 3',5'-linkages. The 2',5'-linkages occurred at the 3'-terminus.

Ring around the sun . . . not

A total solar eclipse permits study of things usually unseen, such as the hot plasma of the solar corona. Interplanetary dust particles around the sun, which should be visible as a circumsolar ring, are another object for study, but observations over the past 25 years have been inconclusive. Lamy *et al.* (p. 1377) used an infrared detector array to study the 11 July 1991 eclipse from the summit of Mauna Kea, Hawaii. The structure of the corona was resolved but no dust ring was found, which suggests that the dynamics of interplanetary are more complicated than previously thought.

Polymerase pieces

Transcription of genes by RNA polymerase II requires several transcription factors. It appears that initiation of transcription or the transition to elongation requires phosphorylation of RNA polymerase II on its carboxyl-terminal repeat domain (CTD). Two research groups show that a subunit of one of the general transcription factors is a CTD kinase. Gileadi *et al.* (p. 1389) cloned a 75-kD subunit from yeast RNA polymerase II initiation factor b. The 75-kD polypeptide was associated with two other polypeptides, and the complex had transcriptional activity and associated CTD kinase activity. Fischer *et al.* (p. 1392) cloned a 62-kD subunit of the HeLa cell transcription factor BTF2 (TFIIH). The sequence of the 62-kD protein is similar to that of the 75-kD subunit of factor b.

Improving the blood supply

Occlusion of coronary arteries that supply the myocardium causes tissue damage that results from insufficient blood supply. This process (a heart attack) creates an area of necrotic tissue, or myocardial infarct. Yanagisawa-Miwa *et al.* (p. 1401) studied the effects of basic fibroblast growth factor (bFGF) on myocardial infarcts produced experimentally in dogs. Injection of bFGF into a coronary artery increased the number of arterioles and capillaries in the infarct. Treatment with bFGF also decreased the size of the infarct and improved cardiac function. Thus bFGF might be useful in therapies designed to salvage infarcted myocardium.

Depends on context

The changes in synaptic response that are assumed to occur during learning have been difficult to study directly because of the problems associated with obtaining intracellular recordings from the neurons of awake animals. Ahissar *et al.* (p. 1412) circumvented these problems by recording the firings from several neurons and then looking for cross-correlations between their firing times that correspond to "functional connections" between interacting neurons. Recordings were taken from two to ten single neurons in the auditory cortex of awake monkeys performing a variety of learning tasks while undergoing conditioning with auditory stimuli. During a successfully performed task, an auditory stimulus was given shortly after one of the neurons of a given pair fired. This paradigm, which the authors call "behavior with conditioning," always yielded stronger modifications of the connections between a pair of neurons than did other paradigms in which no task was performed or in which the delivery of the stimulus was not correlated with neuron firing. These results indicate the dependence of lasting synaptic changes on a behavioral context.

Control the flow

Transmission of excitatory signals in the central nervous systems of vertebrates is mediated by glutamate receptors, the NMDA (*N*-methyl-D-aspartate) receptors, which mediate slow currents, and the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors, which mediate fast currents. The NMDA receptors are highly permeable to calcium ions and are easily blocked by magnesium ions. The NR1 and NR2 subunits of NMDA receptor both contain an asparagine residue in the putative channel-forming region that is homologous to the Q/R site in the AMPA receptor. Burnashev *et al.* (p. 1415) found that replacement of this residue with glutamine in the NR1 subunit decreases calcium permeability and slightly reduces magnesium block, whereas in the NR2 subunit this change has little effect on calcium permeability but strongly reduces magnesium block.

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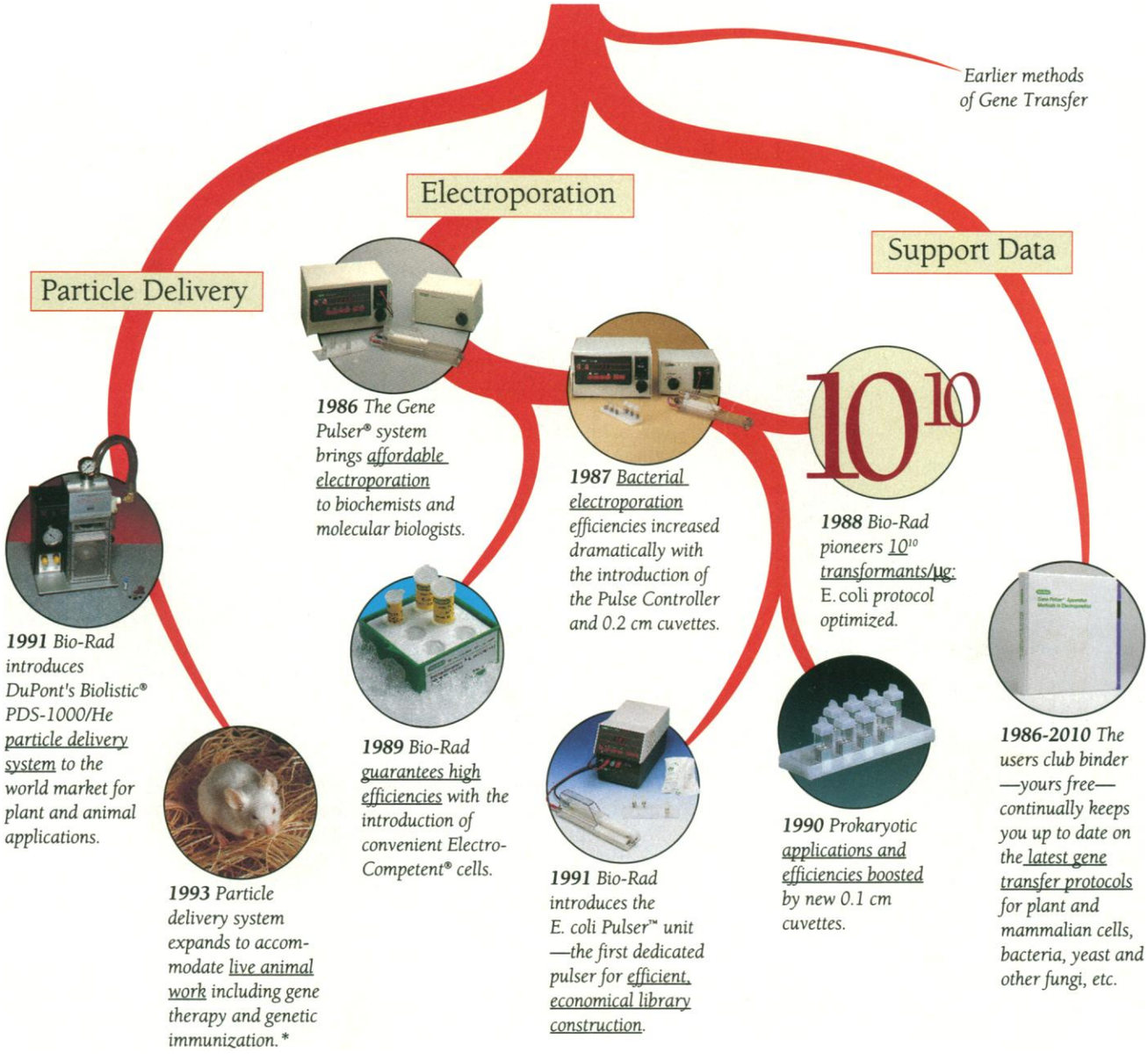

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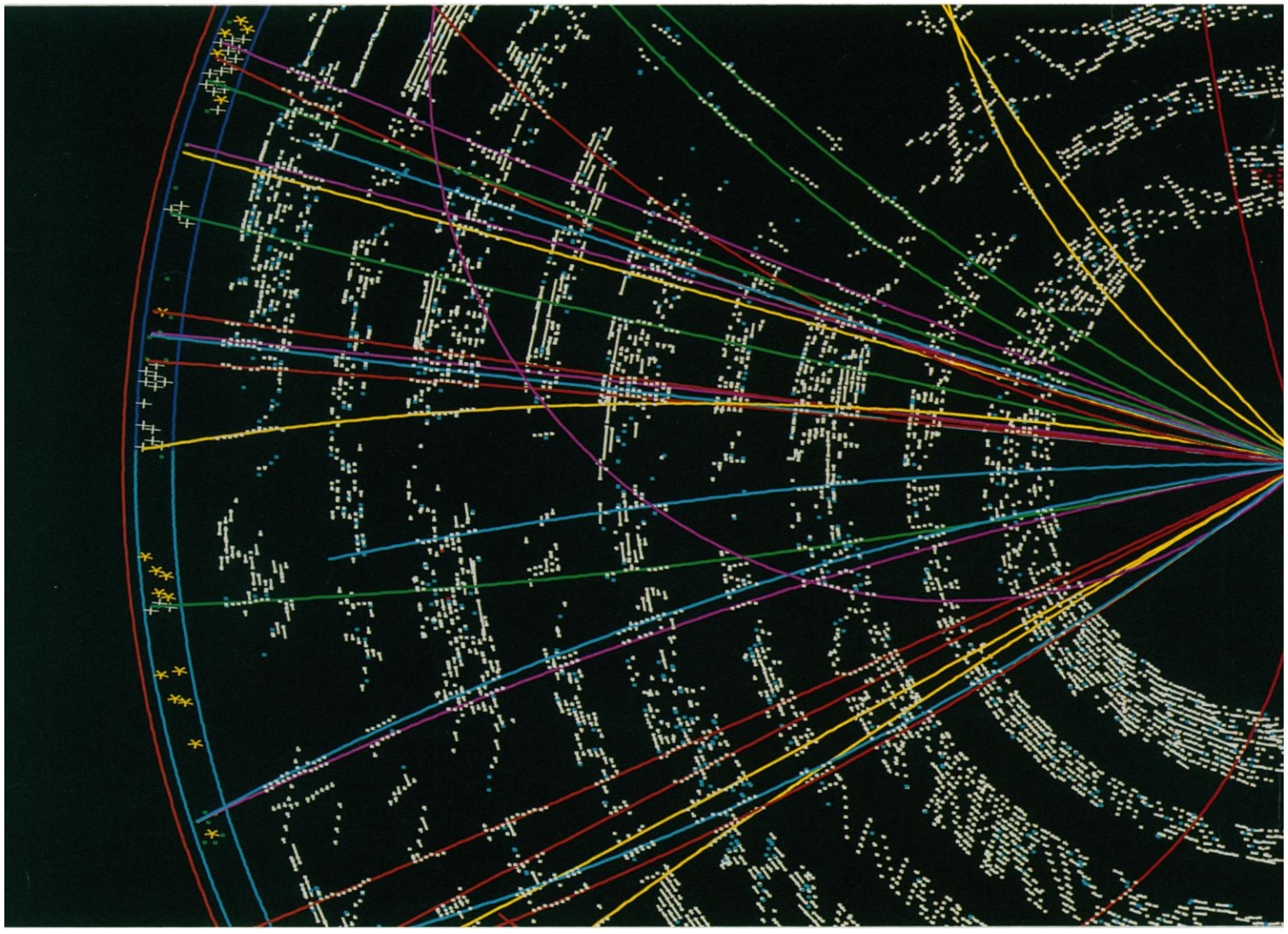


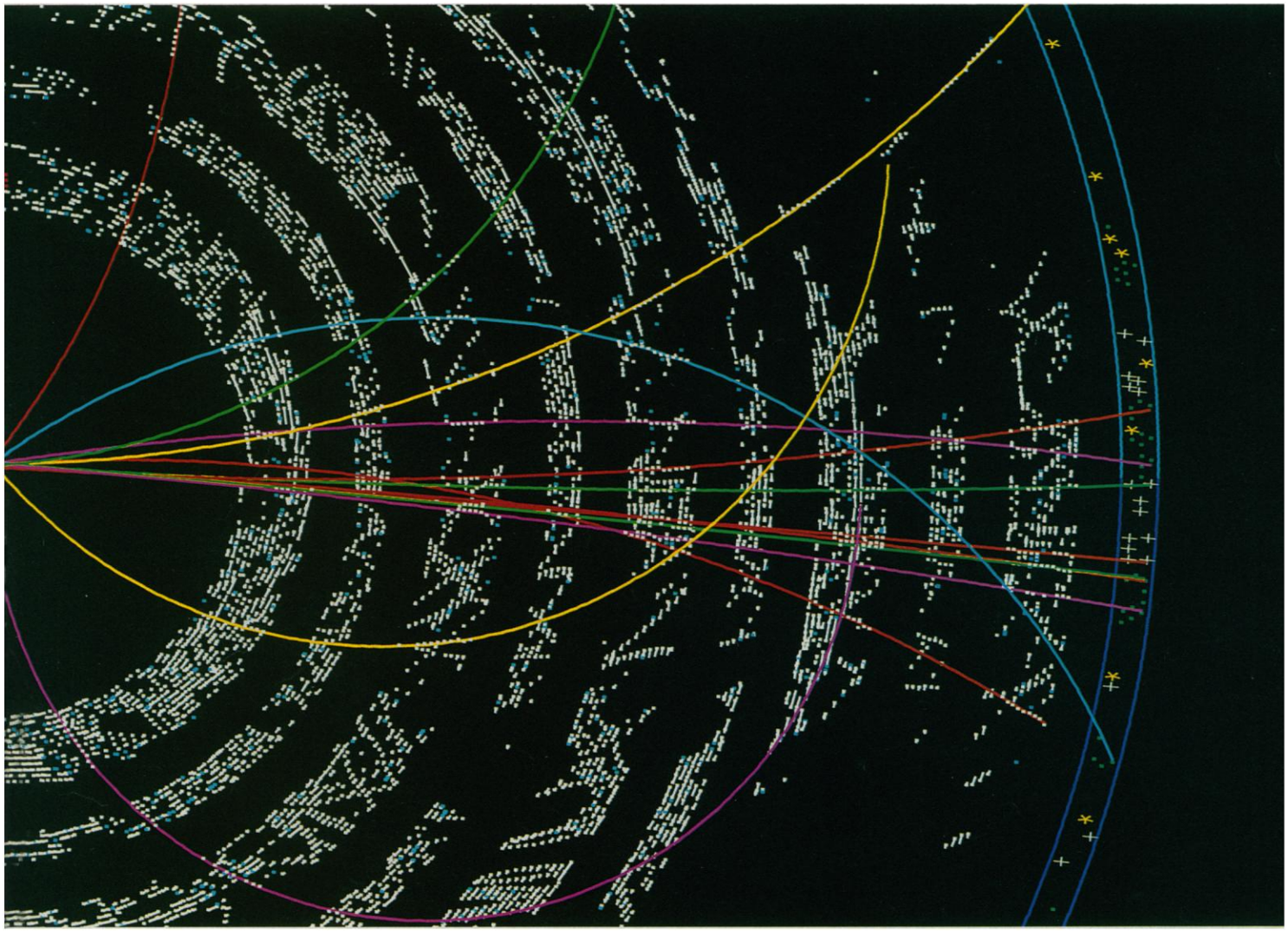
Fermilab is tapping a new

If there's one thing you can count on in science, it's that your data will increase exponentially but your funding won't.

The scientists at Fermi National Accelerator Laboratory (Fermilab) have encountered this problem in a very big way. The data Fermilab processes for subnuclear event reconstruction and modeling has reached 40 terabytes a year. And they've developed an innovative solution to meet their needs.

Instead of relying on supercomputers, Fermilab has distributed a significant part of the workload to clustered IBM RISC System/6000™ workstations. They've combined 108 of them, at latest count, in a LAN-connected

Computer reconstruction of proton/anti-proton collision at Fermilab.



source of power.

processor farm. This farm gives Fermilab a full 3,000 MIPS that can be dedicated to a single parallel processing application.

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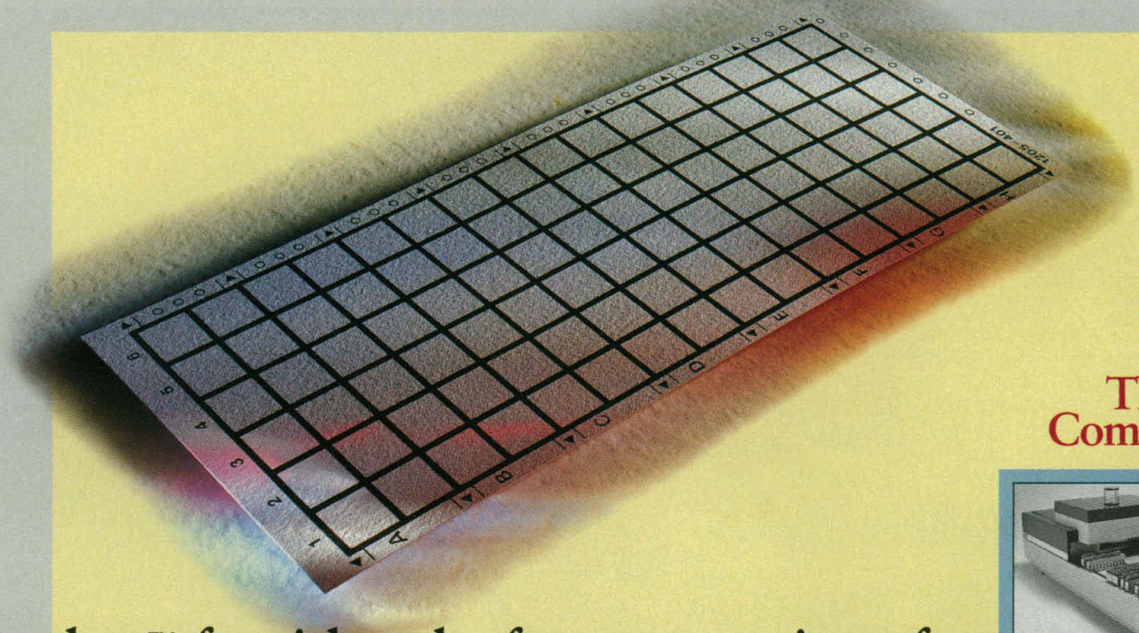
The Mat.



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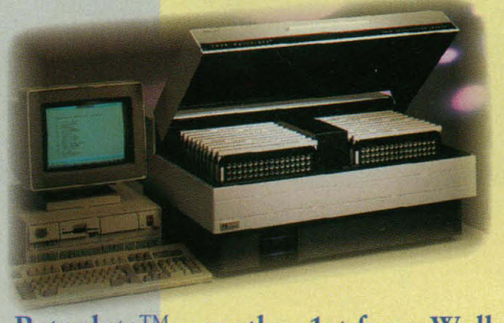

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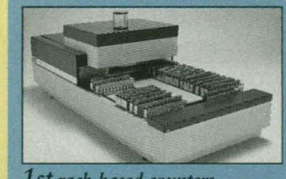

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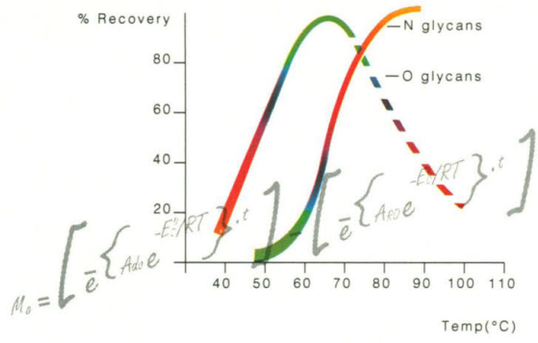

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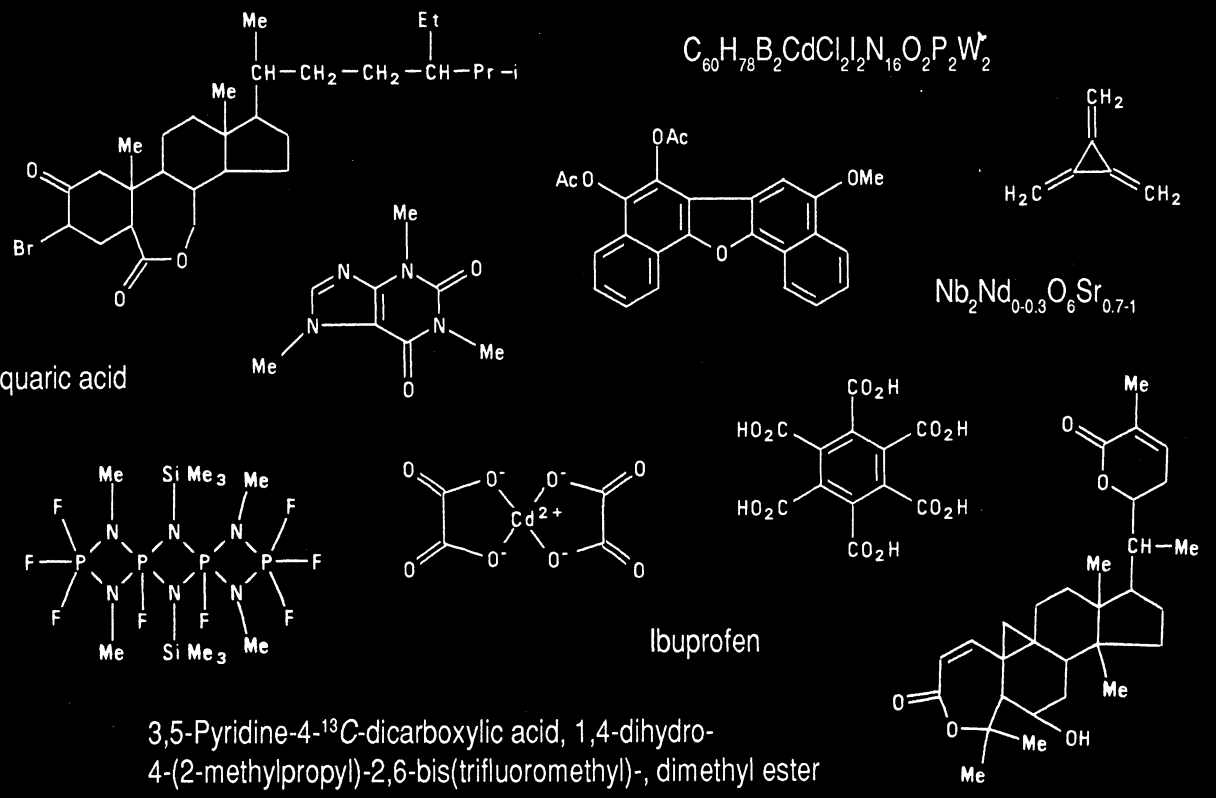

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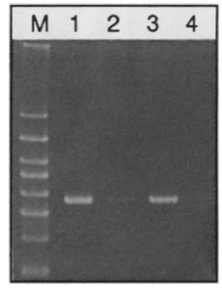

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- Ideal band sizes
- Accurate determination of product size
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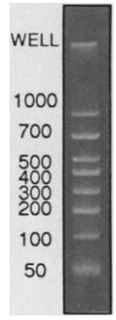

BioMarker™ Low 50 Assay size Catalog No. M-1 **Circle Reader No. 25**

10 Minutes to Protein Free DNA with *EnZap™*

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- Rapid removal of proteins
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Alkaline Phosphatase removal Units AP per 100μl	After EnZap O.D. 405nm	% Removal
5 Units	.010	~ 100%
2.5 Units	.010	~ 100%
1.2 Units	.010	~ 100%
0 Units	.010	NA

EnZap™ 5, 25 and 100 Assays Catalog No.'s EZ-5; EZ-25; EZ-100 **Circle Reader No. 26**

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FAX: 1-615-896-4837
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† The PCR process is owned by Hoffmann-La Roche, Inc.

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GenPharm PIM mice, with an additional copy of the *pim*-1 oncogene, develop T-cell lymphomas in response to a carcinogen in significantly less time than non-transgenic mice.

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1. *Cell* **56**, 673-682 (1989). 2. *Nature* **340**, 61-63 (1989). 3. *Cancer Research* **51**, 958-963 (1991).