

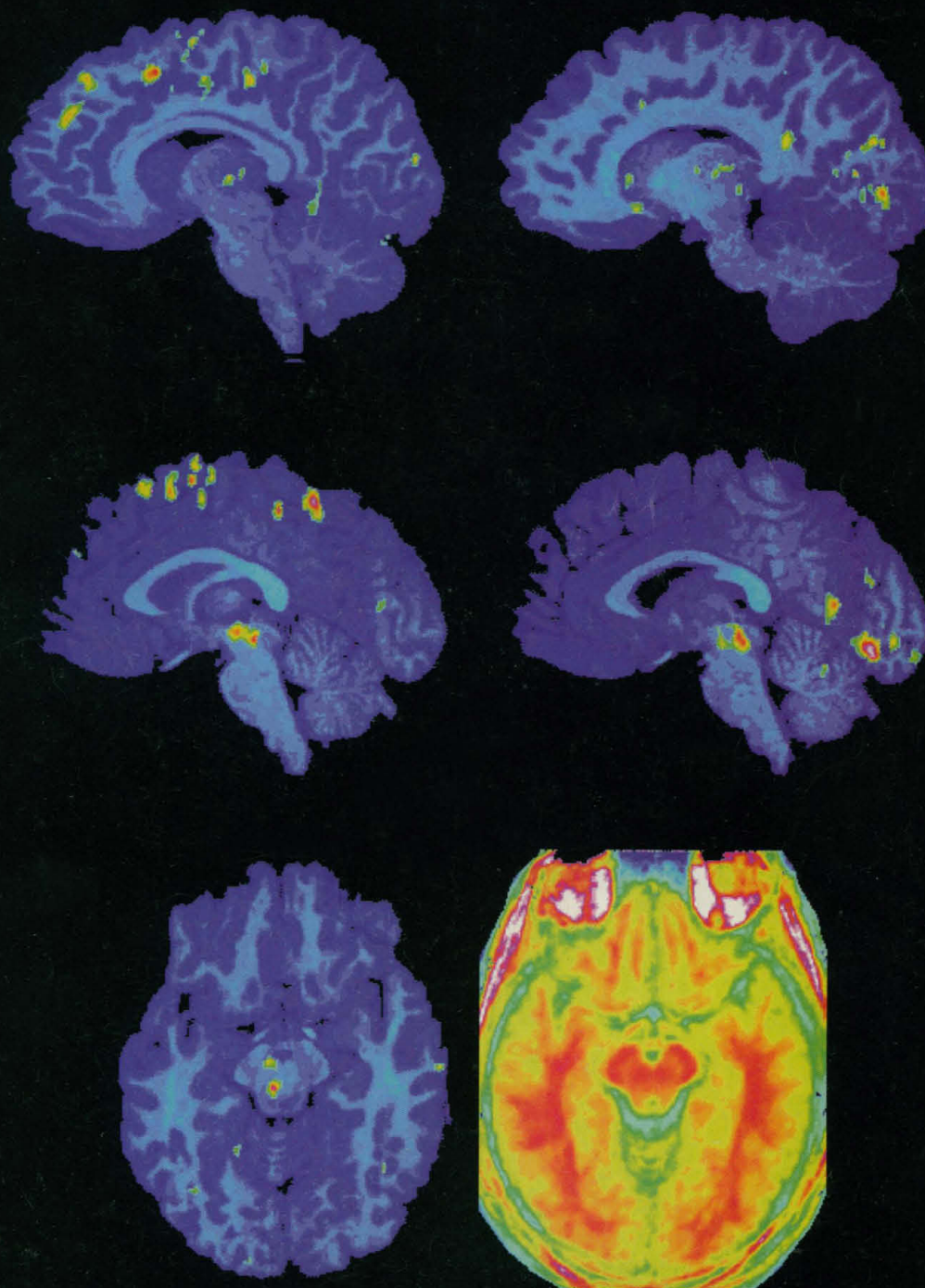


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For drug discovery work, VersaTip will sense small sample volumes in microplates, and handle both ionic and nonionic solutions such as DMSO. With four- and eight-tip MultiPROBE systems, you can stop wasting precious compounds for all solubilization, distribution, and screening applications.

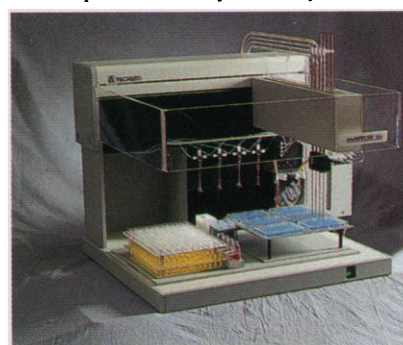
Molecular Biology

For molecular biology applications, VersaTip can automatically pick up micro tips to handle very small volumes, switch to larger

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Clinical Testing

For clinical testing, VersaTip will automatically adapt to the carry-over requirements of your assays. Four-tip systems with Varispan



can switch from disposable to washable tips, and transfer samples from any size test tube or vial, to microplates or other labware — all without user intervention. Combine this versatility with a large deck capacity and a bar code reader that can read 256 tubes in 90

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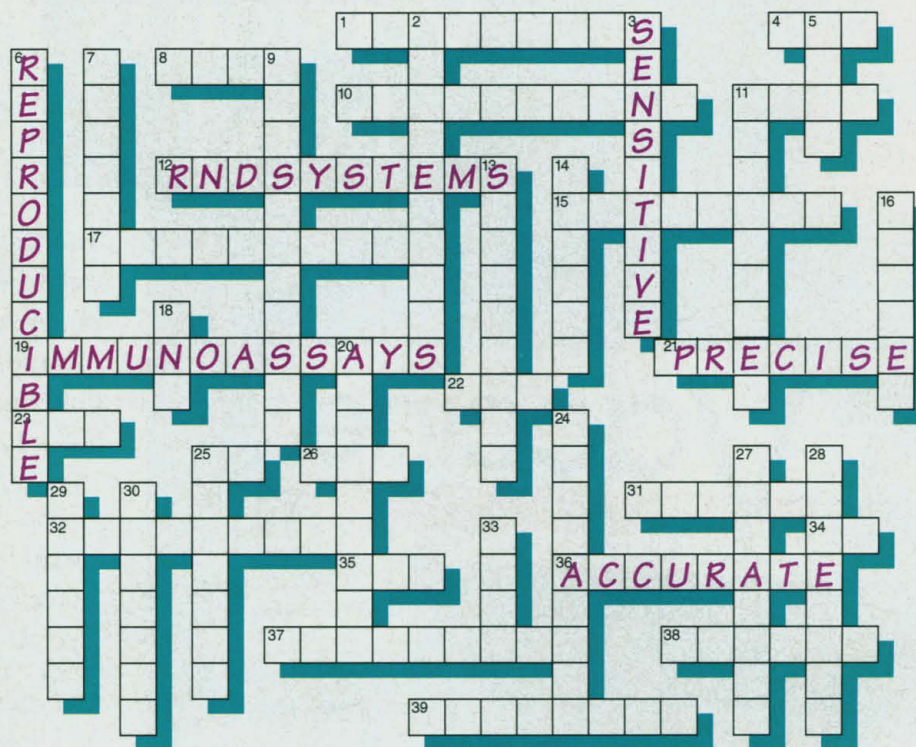
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ACROSS

- 1 1 of 4 specific families of CAMs
4 Abbrev. for biological response modifiers
8 Abbrev. for human anti-mouse antibody
10 R&D Systems' line of immunoassays for the measurement of cytokines
11 Basic structural and functional unit of all organisms
12 R&D Systems URL - http://www.____.com
15 Glycoprotein substance produced by B lymphoid cells in response to stimulation with an immunogen
17 Proteolytic complex with a mass of about 1,000,000
19 Tests that measure antigen or antibody

- 21 Successively reproducible within close specified limits
22 Abbrev. for cell-selective protein that promotes adhesion of cells
23 Abbrev. for gram negative endotoxin
25 Site on DNA lacking either purines or pyrimidines
26 Abbrev. for a detection enzyme
31 Obtained from an affinity column
32 "The Ice Man Cometh" for cells
34 Abbrev. for cluster of differentiation
35 Abbrev. for superoxide dismutase
36 In exact conformity to fact
37 Cross-linked molecules

- 38 Discrete portion of a molecule
39 Region of an antigen that combines with an MHC class II molecule

DOWN

- 2 Cell migration from the interior of small vessels into tissue spaces
3 A high level of discrimination; with 21 and 36 across, descriptive of Quantikine kits
5 Evidence ignored by Simpson jury
6 Capable of replication
7 An antigenic determinant
9 An end-to-end union or joining together of blood vessels
11 What R&D Systems is your source for
13 Substance acted upon by enzymes

- 14 The weight of a single hydrogen atom or a member of an outlaw gang
16 Winner who shared 1984 Nobel prize with Milstein
18 Major component of Dawkins' selfish entity
20 A molecule that serves as a homing device
24 Having a single binding site
25 A substance with which an antibody molecule or T cell receptor may bind
27 A defining example
28 Complementary binding site
29 "M" of ECM
30 A specimen of known content used together with an unknown in order that the two may be compared
33 Abbrev. for an anticoagulant that binds divalent cations

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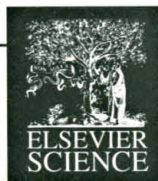
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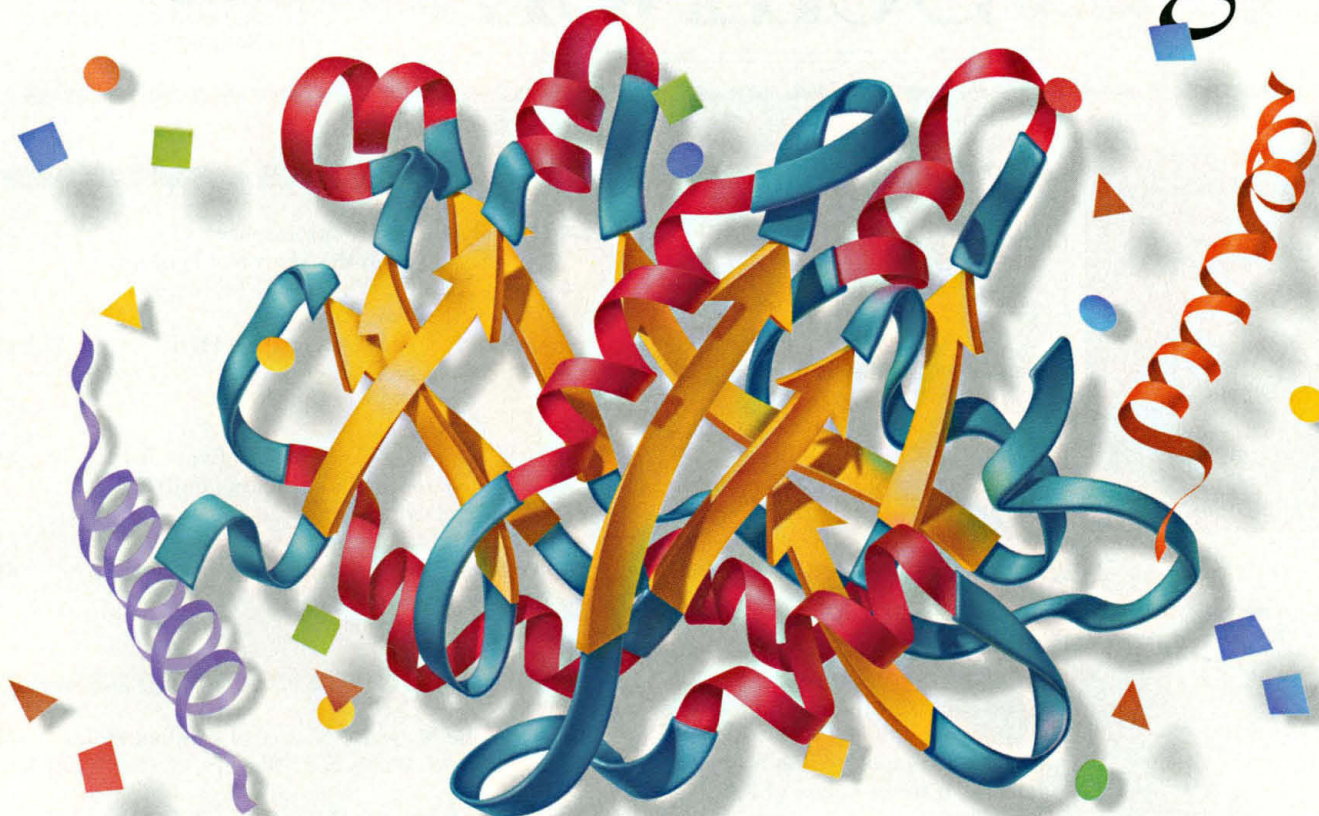


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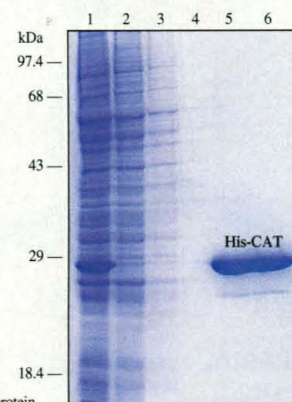
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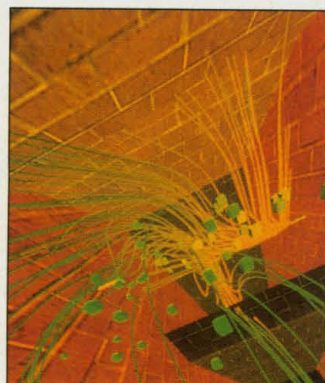
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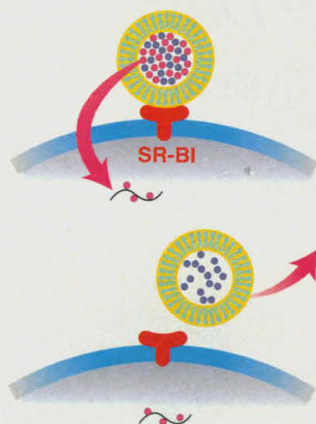
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COVER

Regions deep within the brain control alertness in humans. The midbrain reticular formation and the intralaminar thalamic nuclei are activated (red and yellow) in normal individuals when they change from a relaxed awake state into a state of high alertness and

attention, demonstrating that these structures are active in changing levels of consciousness in the awake state. Lower right: brain structure data from 10 individuals. See page 512. [Image: P. E. Roland]



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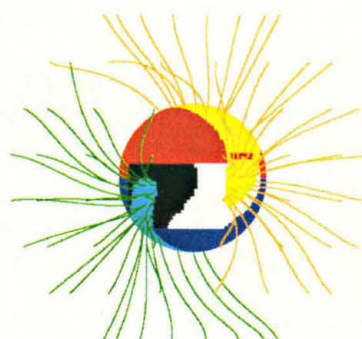
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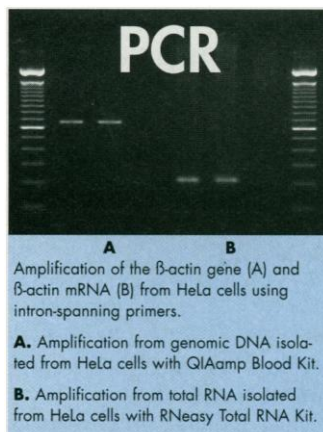
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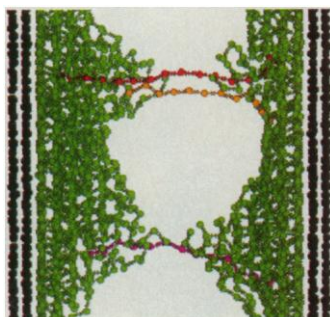
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Torn apart

What happens at the molecular level when two surfaces, held together by an adhesive film, are pulled apart? The answer depends on the type and state of the adhesive, the temperature,



the speed at which the surfaces are pulled apart, and the strength of bonding between the surfaces and the adhesive. Entangled adhesive molecules resist rupture, leading to a buildup of energy that is dissipated differently, depending on the state of the polymer. Baljon and Robbins (p. 482) performed molecular dynamics calculations to follow individual polymer changes during this process, and have identified three mechanisms of energy dissipation during rupture that have parallels to macroscopic phenomena observed in commercial adhesives.

Random magnetism

Materials that contain chain structures can approximate one-dimensional systems, whose properties, such as the magnetic coupling between electrons, can be quite different from that seen in three-dimensional systems. Nguyen *et al.* (p. 489) describe a compound, $\text{Sr}_3\text{CuPt}_{0.5}\text{Ir}_{0.5}\text{O}_6$, that is a solid solution of ferromagnetic $\text{Sr}_3\text{CuPtO}_6$ and antiferromagnetic $\text{Sr}_3\text{CuIrO}_6$. This intermediate compound forms a random quantum spin chain paramagnet—the coupling of spins along the chain through

Linking atmospheric oxygen and phosphorus

Oxygen levels in Earth's atmosphere evidently have been maintained at levels that allow life to persist for billions of years. The controls that essentially buffer the system have been uncertain. Van Cappellen and Ingall (p. 493; see the Perspective by Kump and Mackenzie, p. 459) suggest that the key is the phosphorus cycle; phosphorus is a key nutrient driving oceanic production and respiration, is a minor component of the atmosphere, and its burial is extremely sensitive to the oxidation state of the oceans. Analysis of phosphorus burial in the past shows that when waters are low in oxygen, less phosphorus is buried.

exchange interactions can be randomly ferromagnetic or antiferromagnetic.

Enzyme clocks for kingdom divergence

Most mutations in proteins occur as random events over time, so, in principle, one can estimate when divergence occurred from a common ancestor by analyzing sequences of the same protein from different organisms. In practice, proteins mutate at different rates, and functionally similar proteins may in fact have different origins. Doolittle *et al.* (p. 470; see the news story by Morrell, p. 448) analyzed divergence times for 57 different enzymes from organisms from all of the major biological groups. The analysis of this large data set indicates that eukaryotes and eubacteria had a common ancestor about 2 billion years ago, or about twice as long ago as the plant-animal divergence.

HIV dynamics

During the first few weeks of HIV infection, the concentration of virus in plasma rises but then drops off. Phillips (p. 497) has modeled the course of early HIV infection and suggests that the drop-off is not an HIV-specific immune response but is

actually due to population dynamics in HIV replication. The supply of uninfected cells is quickly depleted, thus decreasing virus production.

Ancient enzymes

Although the DNA sequence of an ancestral gene may be predictable, the enzymatic function of the protein product may not be. Chandrasekharan *et al.* (p. 502) used extant chymase gene sequences to predict the ancestral form of the enzyme, and then expressed the enzyme and characterized its kinetics for converting angiotensin I to angiotensin II. The ancestral form is very specific and efficient for this reaction, and some modern chymases actually have less substrate specificity than this ancestral form.

Hepatitis G virus

In some hepatitis cases, the causative agent is unknown, which suggests that some hepatitis viruses are still unidentified. Linnen *et al.* (p. 505) identified an RNA virus, hepatitis G virus (HGV), by analyzing immunoreactive complementary DNA clones from a patient who was also infected with hepatitis C virus. Although the pathogenesis of HGV remains to be

determined, it is associated with both acute and chronic hepatitis and is present in the blood-donor population.

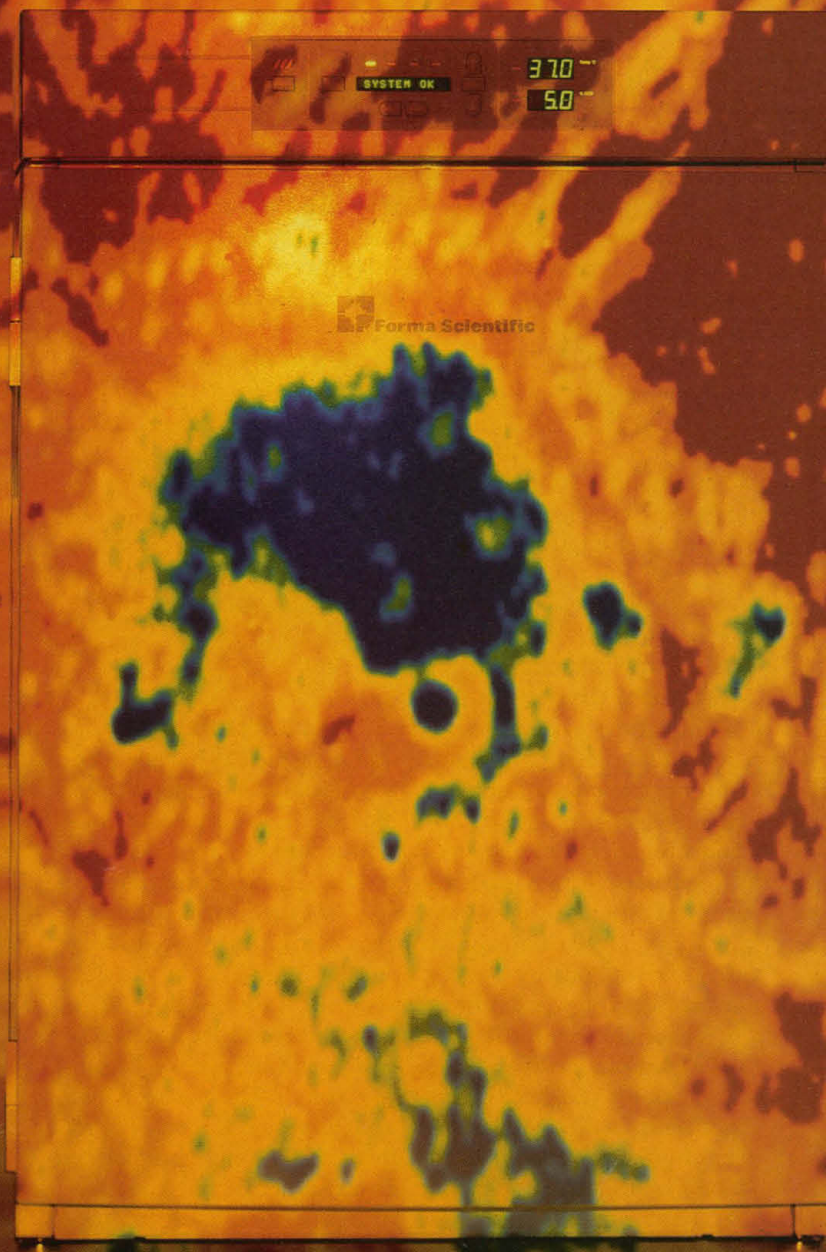
Overactive enzyme

About 20 to 25% of patients with familial amyotrophic lateral sclerosis (FALS) have mutations in the gene encoding copper-zinc superoxide dismutase (CuZnSOD). Wiedau-Pazos *et al.* (p. 515; see the news story by Marx, p. 446) show that the mutant CuZnSOD is more active than wild type in catalyzing oxidation of a model substrate, and that this enhanced activity can be inhibited by copper chelators. In a cell culture model of FALS, copper chelators inhibited the cell death induced by mutant CuZnSOD. Aberrant oxidative reactions catalyzed by mutant CuZnSOD may underlie the neuropathologic changes in FALS, and copper chelators may have therapeutic value for some FALS patients.

Apoptosis links

Programmed cell death (PCD), which typically occurs through apoptosis, is a normal function in multicellular organisms. Dysregulated PCD, however, can cause numerous disorders, including neurodegenerative diseases and cancer. Several studies indicate that Ca^{2+} plays a role in apoptosis; Vito *et al.* (p. 521) developed a selection system which allowed them to identify two genes, ALG-2 and ALG-3, that mediate apoptosis. The ALG-2 gene encodes a Ca^{2+} -binding protein required for several apoptotic pathways, and the ALG-3 gene is homologous to the Alzheimer's disease gene STM2.

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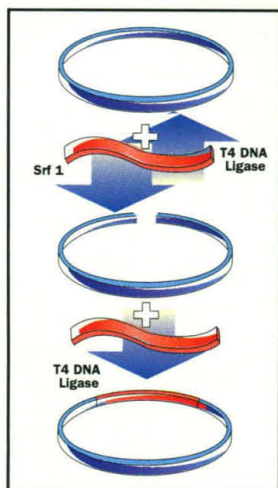
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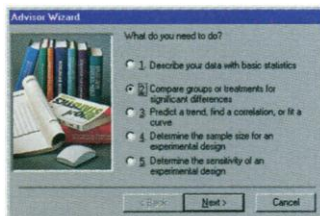
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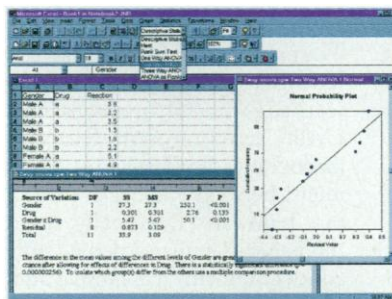
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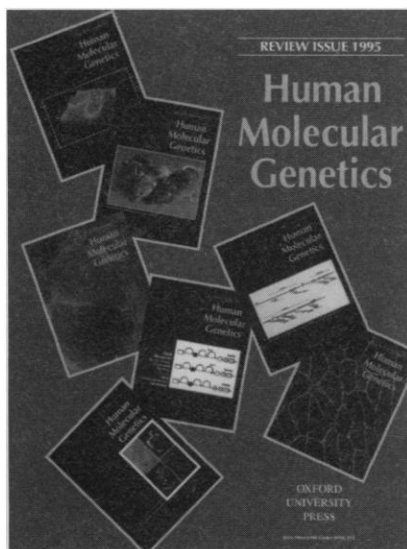
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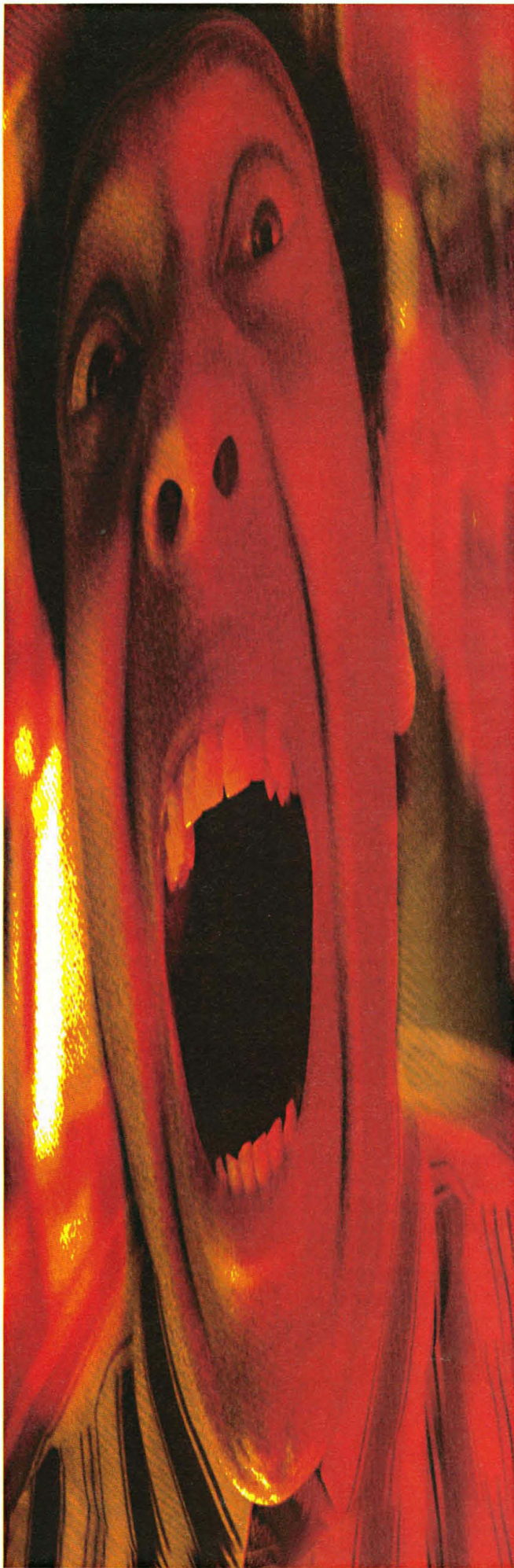
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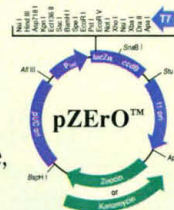
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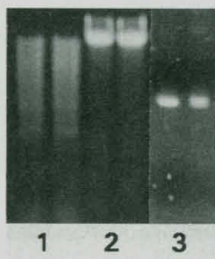
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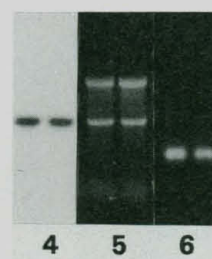
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