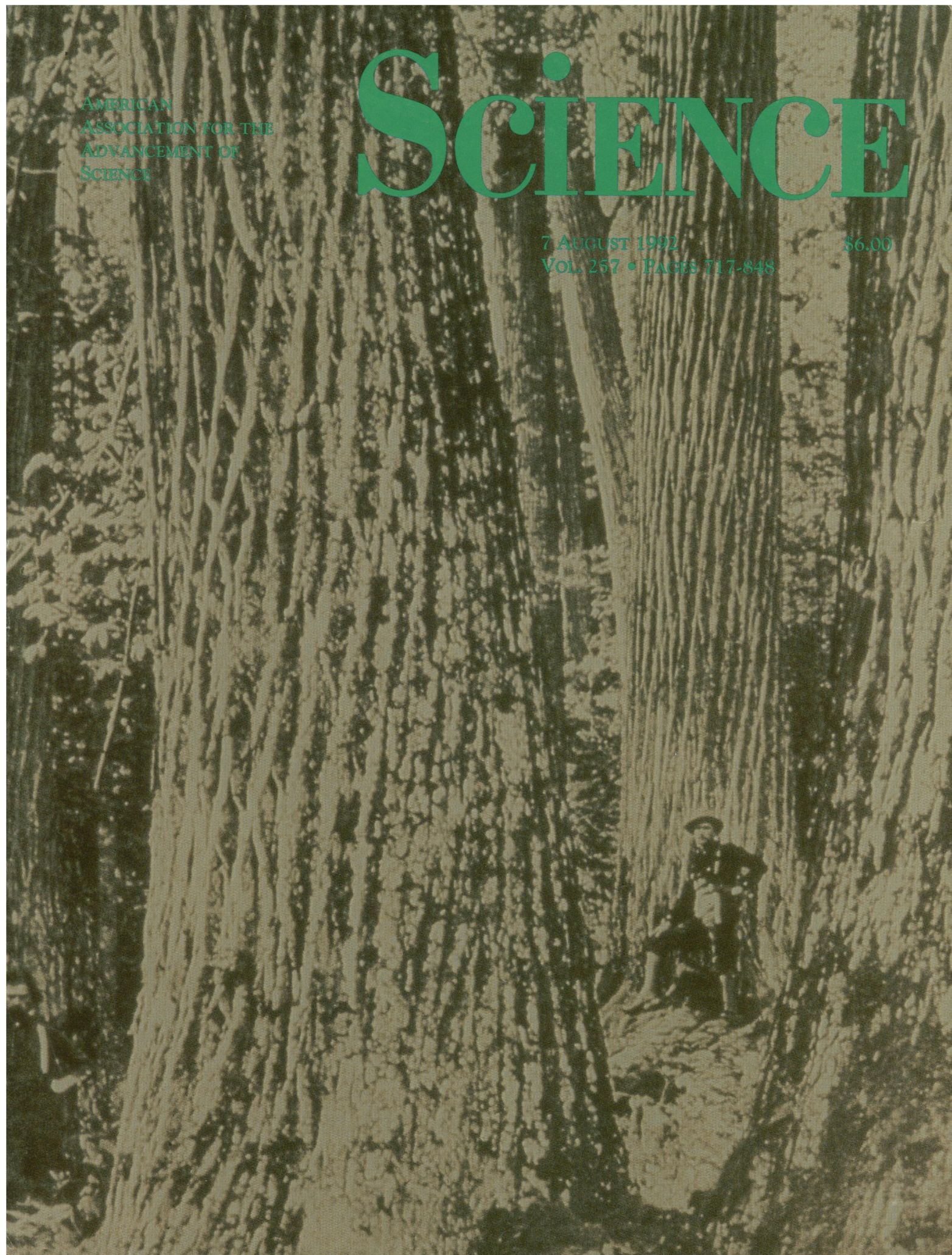


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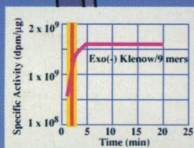
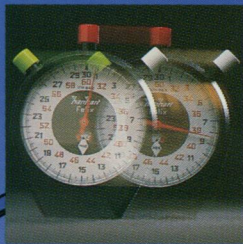


figure 1

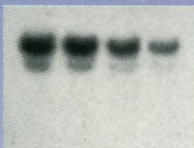
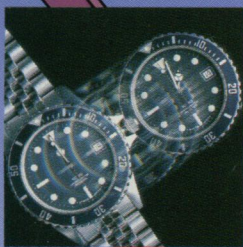


figure 2



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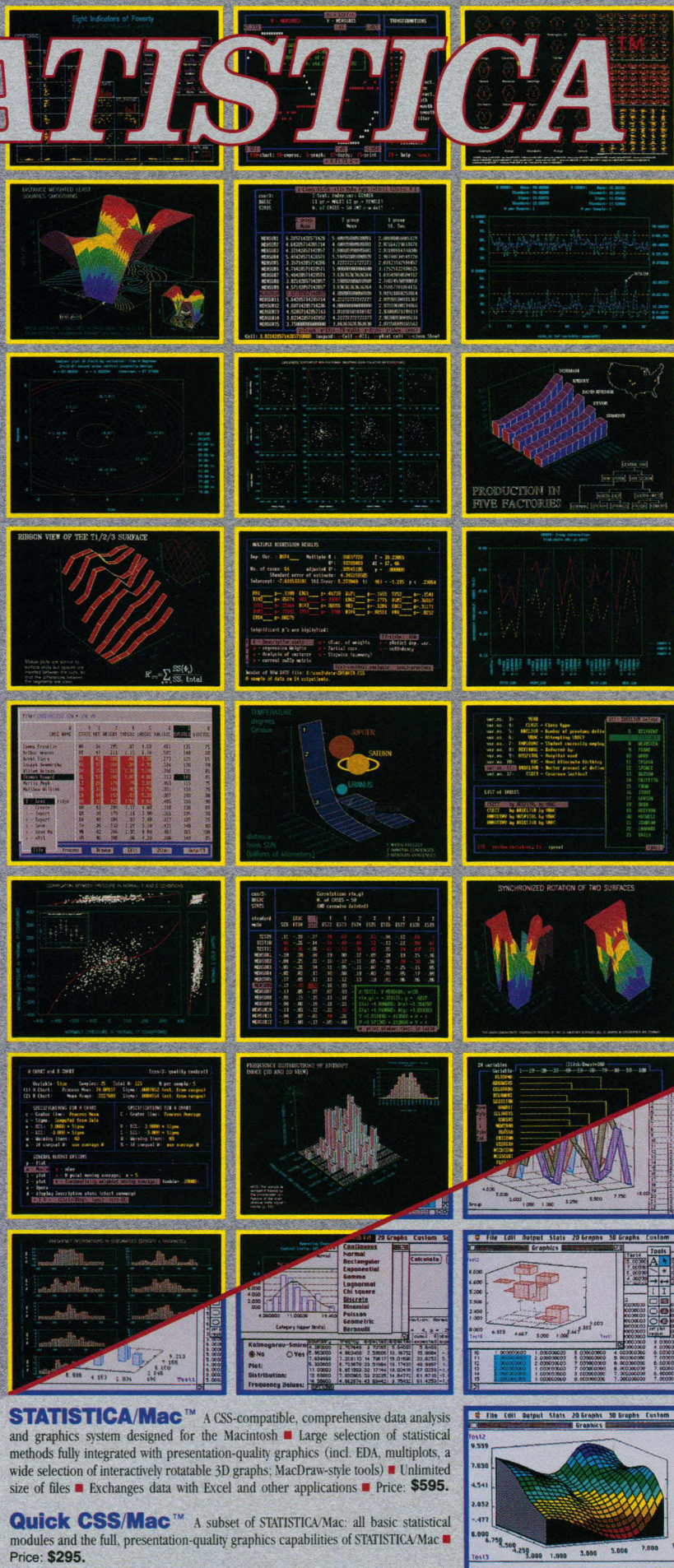


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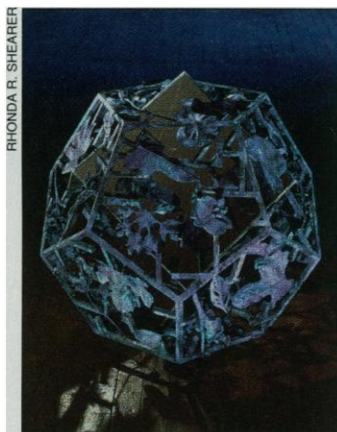
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## NEWS & COMMENT

**Science in Court: A Culture Clash** 732  
Prosecutor v. Scientist: A Cat-and-Mouse Relationship  
Hired Guns or True Believers?

**Gain for Space Station; Pain for NSF** 737

**SSC: Senate Issues a Stay of Execution** 737

**Researchers Call for Time Out on Cell-Transplant Research** 738

**NIH Wrestles With Furor Over Conference** 739

**NIH to Size Up Growth Hormone Trials** 739

**Contracting Practices at EPA Labs Go Under the Microscope** 740

**HHS Starts Audit of Grant Fund Use** 741

## RESEARCH NEWS

**Taking a Direct Path to the Genes** 744

**At the Galactic Center, a Nest of Stellar Oldsters** 746

**DNA Shows Unexplained Patterns Writ Large** 747

**Cross-Disciplinary Artists Know Good Math When They See It...** 748

**Innovation in San Francisco** 750

**Mounting a Targeted Strike on Unwanted Immune Responses** 751

## PERSPECTIVE

**Quantum Cryptography: Uncertainty in the Service of Privacy** 752  
C. H. Bennett

## ARTICLES

**Chaos, Symmetry, and Self-Similarity: Exploiting Order and Disorder in Mixing Processes** 754  
J. M. Ottino, F. J. Muzzio, M. Tjahjadi, J. G. Franjione, S. C. Jana, H. A. Kusch

**Stagnation in the Decline of the World Population Growth Rate During the 1980s** 761  
S. Horiuchi

## RESEARCH ARTICLES

**Evidence for Retrograde Lithospheric Subduction on Venus** 766  
D. T. Sandwell and G. Schubert

## DEPARTMENTS

**THIS WEEK IN SCIENCE** 723

**EDITORIAL** 725  
Fifty Years of National Service

**LETTERS** 727  
Stratospheric Ozone Trends: K. M. Towe; R. Stolarski • Appraising the Evidence: A. Wildavsky; A. Schnaiberg

**SCIENCESCOPE** 731

**RANDOM SAMPLES** 742

Uganda to Host AIDS Vaccine Therapy Trials • Physics Organizations to Shack Up Together, etc.

**BOOK REVIEWS** 819

*Hans Krebs*, reviewed by J. W. Servos • *To the Ends of the Earth*, R. A. Nye • *Ten Lectures on Wavelets* and *An Introduction to Wavelets*, F. A. Grünbaum • Recent Collections on Wavelets • Books Received

**PRODUCTS & MATERIALS** 824

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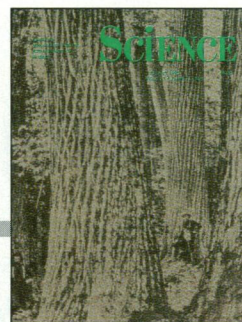
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## COVER

American chestnut trees in the Great Smoky Mountains, North Carolina, before a blight epidemic that destroyed several billion mature trees when the Asian fungus *Cryphonectria parasitica* was unintentionally introduced early this century. The cloning of an endog-

enous virus that infects the fungus provides the potential for effective biological control of chestnut blight and the restoration of this once valuable forest tree. See page 800. [Photograph: Museum of North Idaho]



## Analysis of the *Escherichia coli* Genome: DNA Sequence of the Region from 84.5 to 86.5 Minutes

D. L. Daniels, G. Plunkett III, V. Burland, F. R. Blattner

## REPORTS

### Origins for the Near-Earth Asteroids

R. P. Binzel, S. Xu, S. J. Bus, E. Howell

### Uranium Bioaccumulation by a *Citrobacter* sp. as a Result of Enzymically Mediated Growth of Polycrystalline $\text{HUO}_2\text{PO}_4$

L. E. Macaskie, R. M. Empson, A. K. Cheetham, C. P. Grey, A. J. Skarnulis

### Increasing Rates of Atmospheric Mercury Deposition in Midcontinental North America

E. B. Swain, D. R. Engstrom, M. E. Brigham, T. A. Henning, P. L. Brezonik

### Evidence from 18S Ribosomal RNA Sequences That Lampreys and Hagfishes Form a Natural Group

D. W. Stock and G. S. Whitt

### Long-Term Survival of Xenogeneic Pancreatic Islet Grafts Induced by CTLA4Ig

D. J. Lenschow, Y. Zeng, J. R. Thistlethwaite, A. Montag, W. Brady, M. G. Gibson, P. S. Linsley, J. A. Bluestone

### Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule

P. S. Linsley, P. M. Wallace, J. Johnson, M. G. Gibson, J. L. Greene, J. A. Ledbetter, C. Singh, M. A. Tepper

### Activation-Induced Ubiquitination of the T Cell Antigen Receptor

C. Cenciarelli, D. Hou, K.-C. Hsu, B. L. Rellahan, D. L. Wiest, H. T. Smith, V. A. Fried, A. M. Weissman

### The Skeletal Muscle Chloride Channel in Dominant and Recessive Human Myotonia

M. C. Koch, K. Steinmeyer, C. Lorenz, K. Ricker, F. Wolf, M. Otto, B. Zoll, F. Lehmann-Horn, K.-H. Grzeschik, T. J. Jentsch

### Hypovirulence of Chestnut Blight Fungus Conferred by an Infectious Viral cDNA

G. H. Choi and D. L. Nuss

### Identification of a Protein That Binds to the SH3 Region of Abl and Is Similar to Bcr and GAP-rho

P. Cicchetti, B. J. Mayer, G. Thiel, D. Baltimore

### Selective Role of N-Type Calcium Channels in Neuronal Migration

H. Komuro and P. Rakic

### Interferon-Dependent Tyrosine Phosphorylation of a Latent Cytoplasmic Transcription Factor

C. Schindler, K. Shuai, V. R. Prezioso, J. E. Darnell, Jr.

### Activation of Transcription Factors by Interferon-alpha in a Cell-Free System

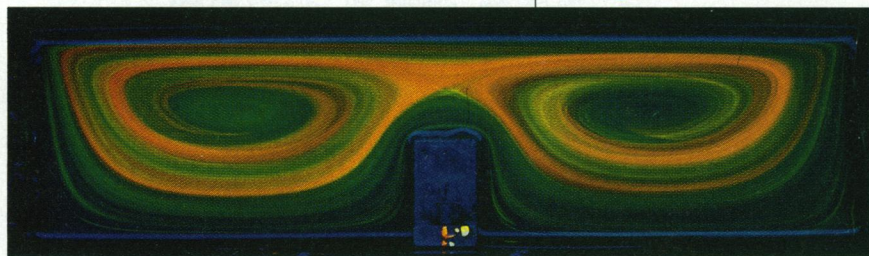
M. David and A. C. Lerner

### $\text{IP}_3$ Receptor: Localization to Plasma Membrane of T Cells and Cocapping with the T Cell Receptor

A. A. Khan, J. P. Steiner, M. G. Klein, M. F. Schneider, S. H. Snyder

**815**  
Calcium and surface  $\text{IP}_3$  receptors

**754**  
Mixing and chaos in fluids



■ Indicates accompanying feature

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## Venusian tectonics

Venus is the planet that is most like Earth, but its tectonic style and the relation of crustal deformation to mantle processes has been uncertain. Sandwell and Schubert (p. 766) compare the topography of coronae on Venus, which are large elevated circular structures that are commonly surrounded by a moat and an outer rise, to the topography of subduction zones on Earth. They show that as for subduction zones, the topography surrounding Venus' coronae can be explained with a lithospheric flexure model in which bending of the surrounding crust beneath the coronae leads to the trench and outer rise. Subduction of the crust by 100 kilometers or more may be occurring around the largest coronae.

□

## Strategic sequencing

Complete sequencing of the *Escherichia coli* genome would yield all of the information necessary to define a life form. Daniels *et al.* (p. 771) describe and analyze the DNA sequence from a 91.4-kilobase segment from an *E. coli* K-12 strain (about 2 percent of the genome). They show how a variety of strategies, from sequencing clones picked at random from libraries to directed approaches that target known genome positions, can be combined to sequence efficiently and accurately an entire stretch of a chromosome.

□

## Mercury rising

Although mercury contamination of remote watersheds has generally been attributed to atmospheric deposition, the amount of recent inputs and sig-

## Costimulation and immunosuppression

A number of immune system responses, such as the proliferation of killer T cells and B cell differentiation, can be brought about through the activation of the helper T cells by antigen-presenting cells (APCs). To become activated, T cells need stimulation not only through their antigen receptors but also through other cell surface molecules. This "costimulation" can occur in vitro through the CD28 molecule. Unwanted immune responses should in theory be thwarted by blockade of this costimulatory pathway. A soluble molecule, CTLA4Ig, was engineered to bind to the CD28 ligand and prevent interaction with the T cell. Lenschow *et al.* (p. 789) found that injection of such a construct into mice that received human pancreatic islet transplants resulted in prolonged unresponsiveness to the donor islets and long-term survival. Linsley *et al.* (p. 792) showed that T cell-dependent production of antibodies by B cells could be specifically suppressed in mice that received CTLA4 constructs (see news story by Cohen, p. 751).

nificance of geologic sources have been uncertain. Swain *et al.* (p. 784) analyzed cores from seven remote lakes in Minnesota and Wisconsin. Analysis of the cores, which provide records back to A.D. 1700, show that mercury deposition has more than tripled from earlier rates since about 1850.

□

## Still a natural

Lampreys and hagfishes lack a hinged jaw, and as the surviving members of the jawless vertebrates, their phylogenetic relation to other organisms has been studied extensively. Traditionally considered a natural, or monophyletic group, recent morphological analyses have suggested that the hagfishes are even more primitive than the lampreys and that the lampreys are more closely related to jawed vertebrates. Stock and Whitt (p. 787) analyzed RNA sequences from the small subunit of the ribosome from two hagfishes and two lampreys and compared them with sequences for chordate invertebrates (a tunicate and a lancelet) as well as with jawed vertebrates. The

analysis supports the traditional monophyletic grouping of the hagfishes and the lampreys.

□

## Ubiquitin tag

The T cell antigen receptor (TCR) contains several subunits. The  $\zeta$  subunit functions in signal transduction from the receptor. Cenciarelli *et al.* (p. 795) report that when the TCR is activated, the  $\zeta$  chain is modified by the addition of one or more molecules of ubiquitin, a neutral protein of 8 kilodaltons. The effect of ubiquitination on the  $\zeta$  chain is not yet known, but it might mark the TCR as a target for degradation or otherwise influence the function of the receptor.

□

## Chloride channels and human myotonia

Generalized myotonia (GM), an autosomal recessive disease, and myotonia congenita (MC), which is autosomal dominant, are muscle disorders whose symptoms appear in early childhood. Muscle stiffness is caused by repetitive excitation of the

muscles, which could be caused by defects in ion channel activity that slow the rate of membrane repolarization. Koch *et al.* (p. 797) have partially cloned a chloride channel from human skeletal muscle (CLC-1) from chromosome 7 that shows tight linkage to the T cell receptor locus. These loci were tightly linked to GM and MC in family studies. In two GM families, a mutation from phenylalanine to cysteine was found. Although no mutations were identified linking CLC-1 to MC, these findings and the greater severity of the recessive disease suggest that different mutations in a multimeric chloride channel give rise to these diseases.

□

## Interferon- $\alpha$ signals

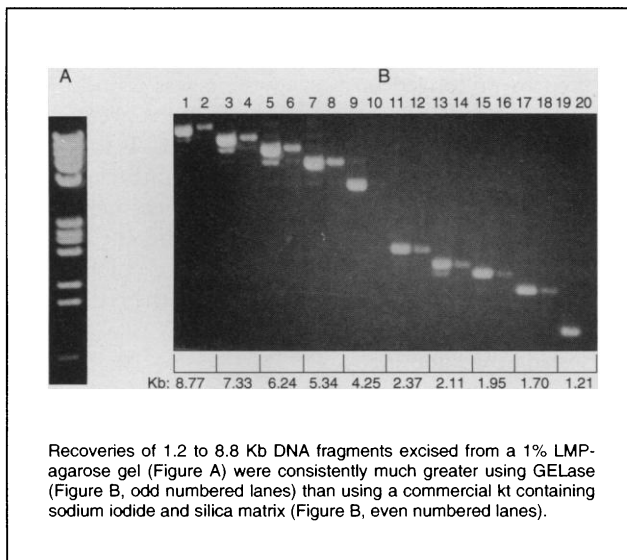
Binding of interferon- $\alpha$  (IFN- $\alpha$ ) to its receptor on the cell surface activates transcription of specific genes. The increase in transcription results in part from regulation of a transcriptional activator, ISGF3 (interferon- $\alpha$ -stimulated gene factor 3), which consists of three subunits. Schindler *et al.* (p. 809) found that in cells treated with IFN- $\alpha$ , the ISGF3 subunits were phosphorylated on tyrosine and that they formed a complex that was translocated to the nucleus. In a related report, David and Larner (p. 813) describe a cell-free system in which they have studied activation of ISGF3. Treatment of a membrane fraction with IFN- $\alpha$  was sufficient to allow activation of ISGF3 when the membrane fraction was subsequently mixed with the supernatant fraction from the same cells. These results help to explain how binding of IFN- $\alpha$  at the cell surface can lead to the transcription of certain genes in the nucleus (see news story by Marx, p. 744).

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NaI/glass bead kits give about 50% recovery for 2–15 Kb DNA (see figure) and much less outside of that size range.



## **2. High molecular weight DNA, even megabase DNA, is not damaged using GELase.**

DNA larger than 15 Kb is sheared using NaI/glass bead kits.

## **3. GELase is easy to use.**

Just melt the gel slice with GELase Buffer, add GELase and incubate at 45°C to digest. To concentrate the DNA, add ethanol. The gel digestion products are soluble and won't precipitate with the DNA.

## **4. GELase is inexpensive.**

One unit of GELase digests 600 mg of a 1% LMP-agarose gel in 1 hour in GELase Buffer. With a 10-hour incubation instead of 1 hour, the 200-unit size of GELase is enough to digest more than a KILOGRAM of a 1% gel.

## **5. DNA purified using GELase is ready to use and biologically active.**

Some companies recommend two rounds of purification with a NaI/glass bead kit to obtain DNA for cloning. That's not necessary with GELase. DNA recovered using GELase is ready for use in restriction mapping, cloning, labeling, sequencing or other molecular biological experiments.

## **6. GELase is active in electrophoresis buffers.**

It digests gels in TAE, TBE, MOPS and phosphate buffers. Special NaI/glass bead kits are needed for gels in TBE buffer.

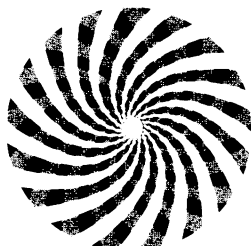
## **7. Protocols for using GELase are the same for RNA as for DNA.**

GELase is RNase-free and active in MOPS or phosphate buffers that are used for RNA gels. In contrast, a special version of NaI/glass bead kit is needed for purification of RNA.

### **What is GELase?**

GELase is a novel enzyme preparation that digests the carbohydrate backbone of agarose into small soluble oligosaccharides, yielding a clear liquid that will not become viscous or gel even on cooling in an ice bath. It permits simple and quantitative recovery of intact DNA or RNA from low melting point (LMP) agarose gels. GELase contains no contaminating DNase, RNase or phosphatase.

\*GELase is a trademark of EPICENTRE TECHNOLOGIES, Madison, WI.



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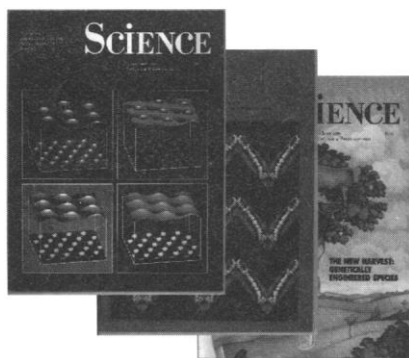
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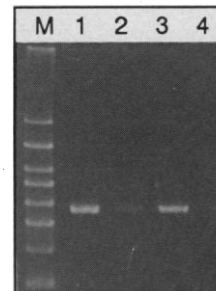
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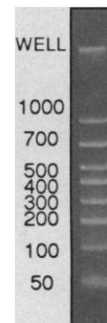


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