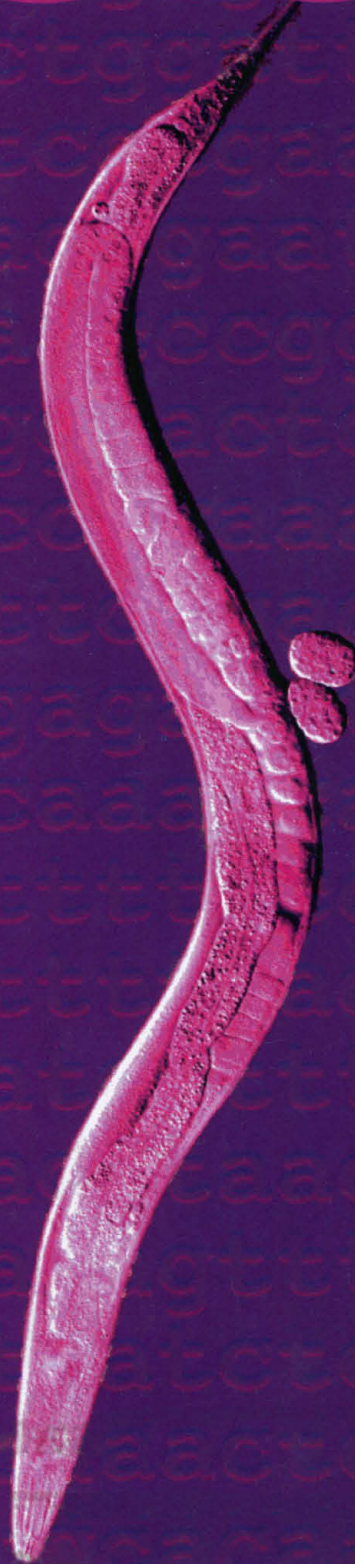


11 December 1998

# Science

Vol. 282 No. 5396  
Pages 1945-2140 \$7



*C. elegans*

Sequence to Biology



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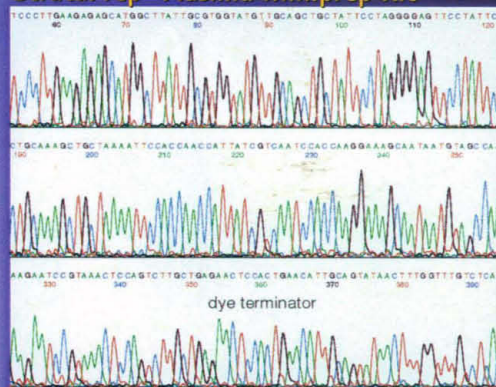
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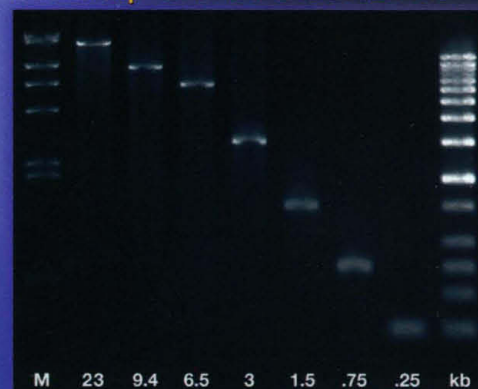
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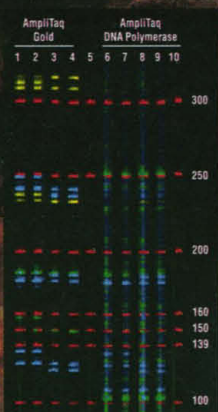


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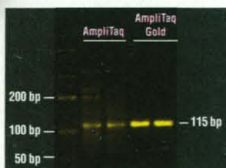


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**COVER** A view of the adult nematode *Caenorhabditis elegans* (~1 millimeter long, with two adjacent embryos) against a background of its sequence. The special section (beginning on p. 2011) commemorates the completion of the genome sequence for *C. elegans* and highlights some of the new insights in biology that are now possible. [Photomicrograph: Maria Gallegos, CMB Program, University of Wisconsin-Madison. Graphic manipulation: Cynthia Faber-Smith]



## 1975

Japan's cloning efforts multiply

## NEWS

### NEWS OF THE WEEK

- 1962 EMBRYOLOGY: Use of Stem Cells Still Legally Murky, But Hearing Offers Hope
- 1963 EXPERT WITNESSES: Scientific Panel Clears Breast Implants
- ▼ 1965 PLANETARY IMPACTS: Argentina, and Perhaps Its Life, Took a Hit  
2061
- ▼ 1966 MATERIALS SCIENCE: Insulator's Baby Steps to Superconductivity  
2067
- 1967 ANIMAL EXPERIMENTATION: India Backs Off on Central Control
- 1967 GERMAN RESEARCH: Extremists Steal Minister's Spotlight
- 1968 AUSTRALIA: Forest Pact Bypasses Computer Model
- 1969 2000 CENSUS: Supreme Court Gets Lesson in Enumeration

- 1969 ASTRONOMY: Sky Survey Racks Up Record-Setting Quasars
- 1971 PEDIATRIC VACCINES: Gates Launches \$100 Million Initiative

### NEWS FOCUS

- 1972 GENOME SEQUENCING: Worming Secrets From the *C. elegans* Genome
- ▼ 1975 ANIMAL CLONING: Bid for Better Beef Gives Japan a Leg Up on Cattle  
2095
- 1976 COMPUTER SCIENCE: From Army of Hackers, an Upstart Operating System
- 1979 RUSSIAN SCIENCE: New Minister Sets Lofty Goals
- 1980 NUCLEAR POWER: New DOE Research Program to Boost Sagging Industry

### C. ELEGANS: SEQUENCE TO BIOLOGY

- 2011 Special Section Introduction

### REVIEWS

- 2012 Genome Sequence of the Nematode *C. elegans*: A Platform for Investigating Biology The *C. elegans* Sequencing Consortium
  - 2018 Zinc Fingers in *Caenorhabditis elegans*: Finding Families and Probing Pathways N. D. Clarke and J. M. Berg
  - 2022 Comparison of the Complete Protein Sets of Worm and Yeast: Orthology and Divergence S. A. Chervitz, L. Aravind, G. Sherlock, C. A. Ball, E. V. Koonin, S. S. Dwight, M. A. Harris, K. Dolinski, S. Mohr, T. Smith, S. Weng, J. M. Cherry, D. Botstein
  - 2028 Neurobiology of the *Caenorhabditis elegans* Genome C. I. Bargmann
  - 2033 The Taxonomy of Developmental Control in *Caenorhabditis elegans* G. Ruvkun and O. Hobert
  - 2041 *Caenorhabditis elegans* Is a Nematode M. Blaxter
- See related Editorial on p. 1989 and News story on p. 1972.
- 2072 Promotion of Trophoblast Stem Cell Proliferation by FGF4 S. Tanaka, T. Kunath, A.-K. Hadjantonakis, A. Nagy, J. Rossant

## RESEARCH

### RESEARCH ARTICLE

- 2053 Observations of the North Polar Region of Mars from the Mars Orbiter Laser Altimeter M. T. Zuber, D. E. Smith, S. C. Solomon, J. B. Abshire, R. S. Afzal, O. Aharonson, K. Fishbaugh, P. G. Ford, H. V. Frey, J. B. Garvin, J. W. Head, A. B. Ivanov, C. L. Johnson, D. O. Muhleman, G. A. Neumann, G. H. Pettengill, R. J. Phillips, X. Sun, H. J. Zwally, W. B. Banerdt, T. C. Duxbury

### REPORTS

- ▼ 2061 A 3.3-Ma Impact in Argentina and Possible Consequences P. H. Schultz, M. Zarate, W. Hames, C. Camili6n, J. King  
1965
- 2063 The Dusty Atmosphere of the Brown Dwarf Gliese 229B C. A. Griffith, R. V. Yelle, M. S. Marley
- ▼ 2067 Photoemission Evidence for a Remnant Fermi Surface and a *d*-Wave-Like Dispersion in Insulating  $\text{Ca}_2\text{CuO}_2\text{Cl}_2$  F. Ronning, C. Kim, D. L. Feng, D. S. Marshall, A. G. Loeser, L. L. Miller, J. N. Eckstein, I. Bozovic, Z.-X. Shen  
1966

### DEPARTMENTS

NETWATCH  
1951

THIS WEEK IN  
SCIENCE  
1953

SCIENCESCOPE  
1965

RANDOM SAMPLES  
1983

ESSAY ON SCIENCE  
AND SOCIETY  
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1985

CONTACT SCIENCE  
1989

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## SCIENCE'S COMPASS

### EDITORIAL

- 1989 Staying Afloat on the Seas of Data

### LETTERS

- 1991 **Neandertals: Not So Fast** M. H. Wolpoff.  
**Solving the Acid Rain Problem** G. E. Likens, K. C. Weathers, T. J. Butler, D. C. Buso. **The Context of Molecular Data** B. K. Penney. **Icelandic Health Records** B. Andersen. **Protein Data Bank Deposits** J. L. Sussman. **The Handy-Dandy Kitchen Device** P. R. Abramson and S. D. Pinkerton. **Response** A. M. Welch, R. D. Semlitsch, H. C. Gerhardt. **Proprioception and the McGurk Effect** J. Moody. **Corrections and Clarifications**

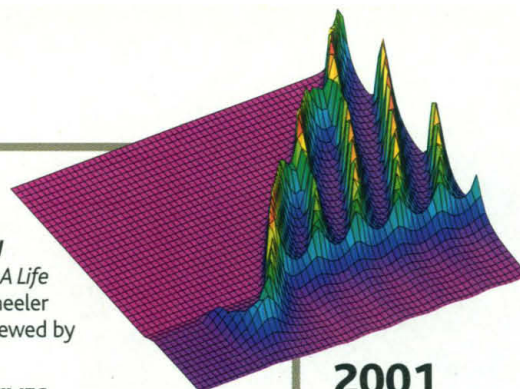
### BOOKS AND NEW MEDIA

- 1997 **HISTORY OF TECHNOLOGY: Edison A Life of Invention** P. Israel, reviewed by B. Holtzmann Kevles

- 1998 **PHYSICS: Geons, Black Holes, and Quantum Foam A Life in Physics** J. A. Wheeler with K. Ford, reviewed by F. Wilczek

### PERSPECTIVES

- ▼ 1999 **MICROBIOLOGY: A Welcome Mat for Leprosy and Lassa Fever** P. G. Spear  
 2076  
 2079  
 2000 **CHEMISTRY: A New Type of Hydrogen Bond** R. H. Crabtree  
 2001 **TRAFFIC THEORY: Jams, Waves, and Clusters** D. Helbing and M. Treiber  
 ▼ 2003 **MOLECULAR BIOLOGY: Nuclear Functions Charge Ahead** A. K. Hopper  
 2082



2001

The physics of traffic

2053

Less and lower ice on Mars



- ▼ 2076 **Role of  $\alpha$ -Dystroglycan as a Schwann Cell Receptor for *Mycobacterium leprae*** A. Rambukkana, H. Yamada, G. Zanazzi, T. Mathus, J. L. Salzer, P. D. Yurchenco, K. P. Campbell, V. A. Fischetti  
 1999  
 2079  
 ▼ 2079 **Identification of  $\alpha$ -Dystroglycan as a Receptor for Lymphocytic Choriomeningitis Virus and Lassa Fever Virus** W. Cao, M. D. Henry, P. Borrow, H. Yamada, J. H. Elder, E. V. Ravkov, S. T. Nichol, R. W. Compans, K. P. Campbell, M. B. A. Oldstone  
 1999  
 2076  
 ▼ 2082 **Proofreading and Aminoacylation of tRNAs Before Export from the Nucleus** E. Lund and J. E. Dahlberg  
 2003  
 2085 **Defective LPS Signaling in C3H/HeJ and C57BL/10ScCr Mice: Mutations in *Tlr4* Gene** A. Poltorak, X. He, I. Smirnova, M.-Y. Liu, C. Van Huffel, X. Du, D. Birdwell, E. Alejos, M. Silva, C. Galanos, M. Freudenberg, P. Ricciardi-Castagnoli, B. Layton, B. Beutler  
 2088 **Exploiting the Basis of Proline Recognition by SH3 and WW Domains: Design of N-Substituted Inhibitors** J. T. Nguyen, C. W. Turck, F. E. Cohen, R. N. Zuckermann, W. A. Lim

- 2092 **Defective T Cell Differentiation in the Absence of *Jnk1*** C. Dong, D. D. Yang, M. Wysk, A. J. Whitmarsh, R. J. Davis, R. A. Flavell  
 ▼ 2095 **Eight Calves Cloned from Somatic Cells of a Single Adult** Y. Kato, T. Tani, Y. Sotomaru, K. Kurokawa, J.-y. Kato, H. Doguchi, H. Yasue, Y. Tsunoda  
 1975  
 2098 **Elevating the Vitamin E Content of Plants Through Metabolic Engineering** D. Shintani and D. DellaPenna

### TECHNICAL COMMENTS

**Pleistocene Speciation and the Mitochondrial DNA Clock** B. S. Arbogast and J. B. Slowinski. **Response** J. Klicka and R. M. Zink

[www.sciencemag.org/cgi/content/full/282/5396/1955a](http://www.sciencemag.org/cgi/content/full/282/5396/1955a)

**Proofreading by Isoleucyl-transfer RNA Synthetase** X. Qiu

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2072

Trophoblast stem cells isolated

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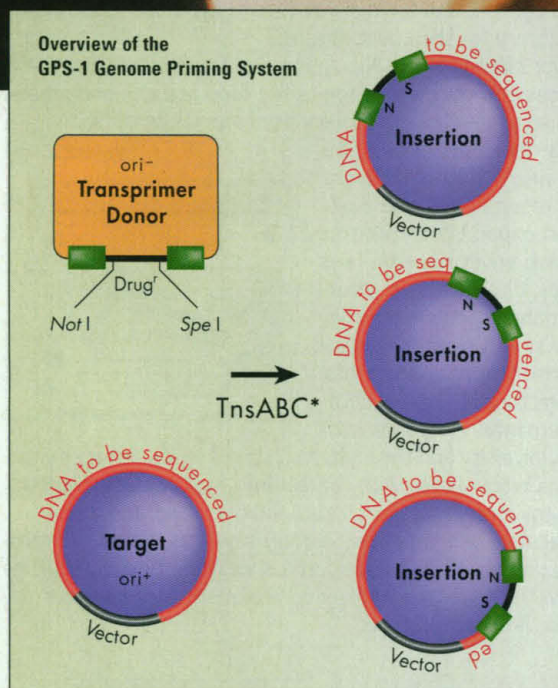
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## SURVEYING THE MARTIAN NORTH POLE

Much of the current visible inventory of volatiles on Mars resides in its polar caps. Understanding the history of water on Mars requires an accurate measure of the size of the north polar cap and the elevation of the polar basin with respect to the elevation of lower latitudes. The Mars Global Surveyor (MGS) has been examining the northern hemisphere of Mars closely, and Zuber *et al.* (p. 2053) now present an analysis of the topography of the north polar region and the ice cap. The data show that the cap is much smaller than previously assumed (about half the size of the Greenland Ice Sheet), is cut by deep fissures, was once somewhat larger, and resides in a topographic basin that is at a lower elevation than low-latitude regions. This result may negate models in which groundwater flows southward from the ice cap toward the equator. MGS also imaged clouds forming above the ice cap.

## A DUSTY, OLD BROWN DWARF

Brown dwarfs are caught in the middle: They are too massive to be planets and not massive enough to be stars. Gliese 229B was the first bona fide brown dwarf identified in 1995 and it remains the coldest brown dwarf (900 Kelvin) that has been studied. Griffith *et al.* (p. 2063) realized that Gliese 229B was too warm to have ice clouds like Jupiter, and too cool to have silicate-rich clouds like some stars. This lack of clouds allowed them to observe Gliese 229B's atmosphere with near-infrared wavelength spectroscopy with the Keck I Telescope. The spectrum suggests the presence of an organic-rich haze in Gliese 229B's atmosphere that probably formed as a result of incident radiation from its primary star, just like the mechanism suggested for the formation of Jupiter's stratosphere. Thus the radiation from a star may cause a brown dwarf to become more planet-like.

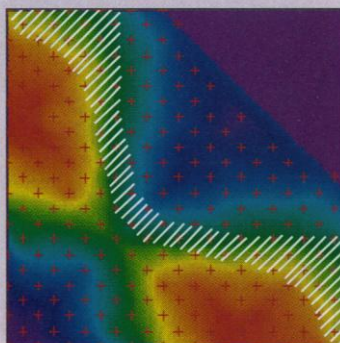
## IMPACT AND EXTINCTION IN ARGENTINA

Evidence for an impact event in the mid-Pliocene (about 3 million years ago) of South America has been found in the Pampean Formation of coastal, central Argentina. Schultz *et al.* (p. 2061) describe centimeter- to meter-sized glass fragments that contain flow structures and vesicles that are indicative of a dynamic fusion process. These textures are similar

to textures seen in impact glasses from known craters. This possible impact event, if it is confirmed by the identification of the impact crater, which should be near to the location of the glassy fragments, seems to be nearly coeval with the regional extinction of endemic fauna in Argentina, as highlighted in a news story by Kerr.

## REMNAANT FERMI SURFACES IN INSULATORS

High-temperature superconductors (HTSs) exhibit an unusual "d-wave" symmetry in the energy gap that separates the superconducting and insulating states. Whether a gap exists depends on the momentum of the elec-



trons, and this behavior is not readily accounted for theoretically. Ronning *et al.* (p. 2067; see the news story by Service) suggest a possible origin for this gap symmetry—it may already be present in the parent insulating state. Photoemission spectra of a Mott insulator related to HTSs,  $\text{Ca}_2\text{CuO}_2\text{Cl}_2$ , show that a remnant Fermi surface is present (defined in this case as a sharp drop in electron occupancy probability as a function of momentum) and that the d-wave shape is similar to that of the HTS superconducting gap.

## PLACENTA ORIGINS

In early mammalian development, the blastocyst contains an inner cell mass (ICM), which becomes the embryo proper; and the trophectoderm, a layer of surrounding epithelial cells that specifies the fetal portion of the placenta. An unknown signal from the ICM is required for the maintenance of the trophectoderm. Tanaka *et al.* (p. 2072) have now identified the growth factor FGF4 as this embryo-derived signal. Cell culture conditions that included FGF4 allowed a trophoblast stem

cell line to be isolated. This cell line can be used to understand better placental development and placental insufficiencies.

## CONNECTING MUSCULAR DYSTROPHY AND LEPROSY

The mechanism of infection by *Mycobacterium leprae*, the bacterium responsible for leprosy, and for a class of viruses known as arenaviruses have been unexpectedly linked to muscular dystrophy (see Perspective by Spear). Rambukkana *et al.* (p. 2076) showed that *M. leprae* uses  $\alpha$ -dystroglycan—a protein of the dystrophin complex implicated in muscular dystrophy—to mediate its internalization by its target Schwann cells. Cao *et al.* (p. 2079) demonstrate that arenaviruses, including lassa fever virus, use the same protein as their host cell receptor.

## NUCLEAR PROCESSING OF TRANSFER RNA

In protein synthesis, it is important that only mature and functional transfer RNAs (tRNAs) are used; otherwise, the translation process would be defective. Maturation of tRNA includes base modification, processing of the 5' and 3' ends, and splicing. Lund and Dahlberg (p. 2082; see also the Perspective by Hopper) now show that correct folding and end maturation of tRNA are required for efficient export from the nucleus, and they suggest that aminoacylation serves to proofread these tRNAs prior to export. These findings counter the prevailing viewpoint that RNA is transcribed and processed in the nucleus and then aminoacylated in the cytoplasm. The nucleus plays a bigger role than was previously thought.

## MEDIATING TOXIC SHOCK

Recognition of lipopolysaccharide (LPS), a product of Gram-negative bacteria, can lead to toxic shock, but animals without a response to LPS cannot effectively clear Gram-negative infections. The protein responsible for transmitting signals from LPS to the cell has been found by Poltorak *et al.* (p. 2085). Two mouse strains known to be defective in their response to LPS had mutations in the toll-like receptor-4 (*Tlr-4*) gene—one strain had a mutation in the coding region and the other lacked transcripts from the gene entirely. *Tlr-4* is thus necessary for LPS signaling in mice; the endogenous *Tlr-2* gene, which in humans can transmit signals from LPS, does not replace *Tlr-4* function in mice.

CONTINUED ON PAGE 1955



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## THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1953

### SHAPELESS SIGNALING

Many cellular signaling pathways require specific protein-protein interactions mediated by SH3 (Src homology 3) or WW domains (so called because they usually contain two tryptophan or W residues). These domains bind to proline-rich sequences in other proteins. Nguyen *et al.* (p. 2088) explored the requirement for proline in the target binding site and found that the critical requirement is the presence of an N-substituted amino acid, not the side chain shape. This property allows interactions of high specificity but low affinity, which are critical for the transient interactions of signaling proteins. By substituting nonnatural N-substituted amino acids, Nguyen *et al.* could also create ligands that bound selectively to an SH3 domain with 100 times greater affinity than the that of the normal interaction. These results may facilitate drug design strategies directed at protein interactions mediated by SH3 and WW domains.

### JNK1 AND T HELPER CELL DIFFERENTIATION

When an antigen initially activates helper T cells of the immune system, the cells differentiate into either type 1 ( $T_H1$ ) or type 2 ( $T_H2$ ) cells. The specific choice is influenced by the cytokine milieu. When Dong *et al.* (p. 2092) constructed mice that lacked the kinase Jnk1, their T cells preferentially differentiated into  $T_H2$  cells and had enhanced proliferation. The cells could produce the cytokines that were necessary for  $T_H1$  de-

velopment but could not down-regulate the production of the  $T_H2$  cytokines, such as interleukin 4 (IL-4), which skewed differentiation. T cells with no Jnk1 selectively accumulated in their nuclei the transcription factor NFATc, which is required for IL-4 transcription and  $T_H2$  differentiation. Thus, Jnk1 may normally function to regulate cell growth and to turn down  $T_H2$  differentiation signals after T cell activation.

### INCREASING VITAMINS IN PLANTS

The vitamins and nutrients critical to a healthy diet are not always easily available in the foods that habitually show up on our dinner tables. Shintani and DellaPenna (p. 2098) show how molecular tools can be used to revise a plant's metabolism and dramatically shift its production of important nutrients. The specific case presented results in ninefold increase in vitamin E activity, a nutrient often undersupplied in average diets, in the seed oil of the model plant *Arabidopsis*.

### CLONING MANY COWS

The most immediate application of recent advances in cloning technology may well be the application of the procedure to the production of identical herds of animals. Kato *et al.* (p. 2095; see the news story by Normile) report high success rates in production of calves derived from nuclei of single, adult somatic cells. Epithelial cells from the oviduct and cumulus cells from ovarian oocytes were used as sources of nuclei.

### TECHNICAL COMMENT SUMMARIES

#### Pleistocene Speciation and the Mitochondrial DNA Clock

The full text of these comments can be seen at [www.sciencemag.org/cgi/content/full/282/5396/1955a](http://www.sciencemag.org/cgi/content/full/282/5396/1955a)

J. A. Klinka and R. M. Zink (Reports, 12 Sept. 1997, p. 1666) found that "molecular data suggest a relatively protracted history of speciation events among North American songbirds over the past 5 million years," contrary to that suggested by the "Late Pleistocene Origins (LPO) model."

B. S. Arbogast and J. B. Slowinski comment that the report contains invalid assumptions about estimating "dates of divergence," no measures of error, and no test of whether "a molecular clock holds for their data"—which Arbogast and Slowinski find it does not.

In response, Klicka and Zink discuss the assumptions made in the report (finding that a molecular clock "is valid for this data set"), provide details of their analyses, and maintain that the LPO model of speciation has been falsified.

#### Proofreading by Isoleucyl-transfer RNA Synthetase

The full text of these comments can be seen at [www.sciencemag.org/cgi/content/full/282/5396/1955b](http://www.sciencemag.org/cgi/content/full/282/5396/1955b)

O. Nureki *et al.* (Reports, 24 Apr. 1998, p. 578) described the crystal structure of isoleucyl-transfer RNA synthetase (IleRS), "an enzyme with editing activity in translation." Figure 4 of the report was a "stereoview of the IleRS editing site as a ball-and-stick representation."

X. Qiu comments that, "although this is an excellent study, fig. 4 and the discussion of it on the same page (p. 581) do not seem to build a reasonable argument." Qiu cites three reasons why the scenario depicted seems "unlikely."

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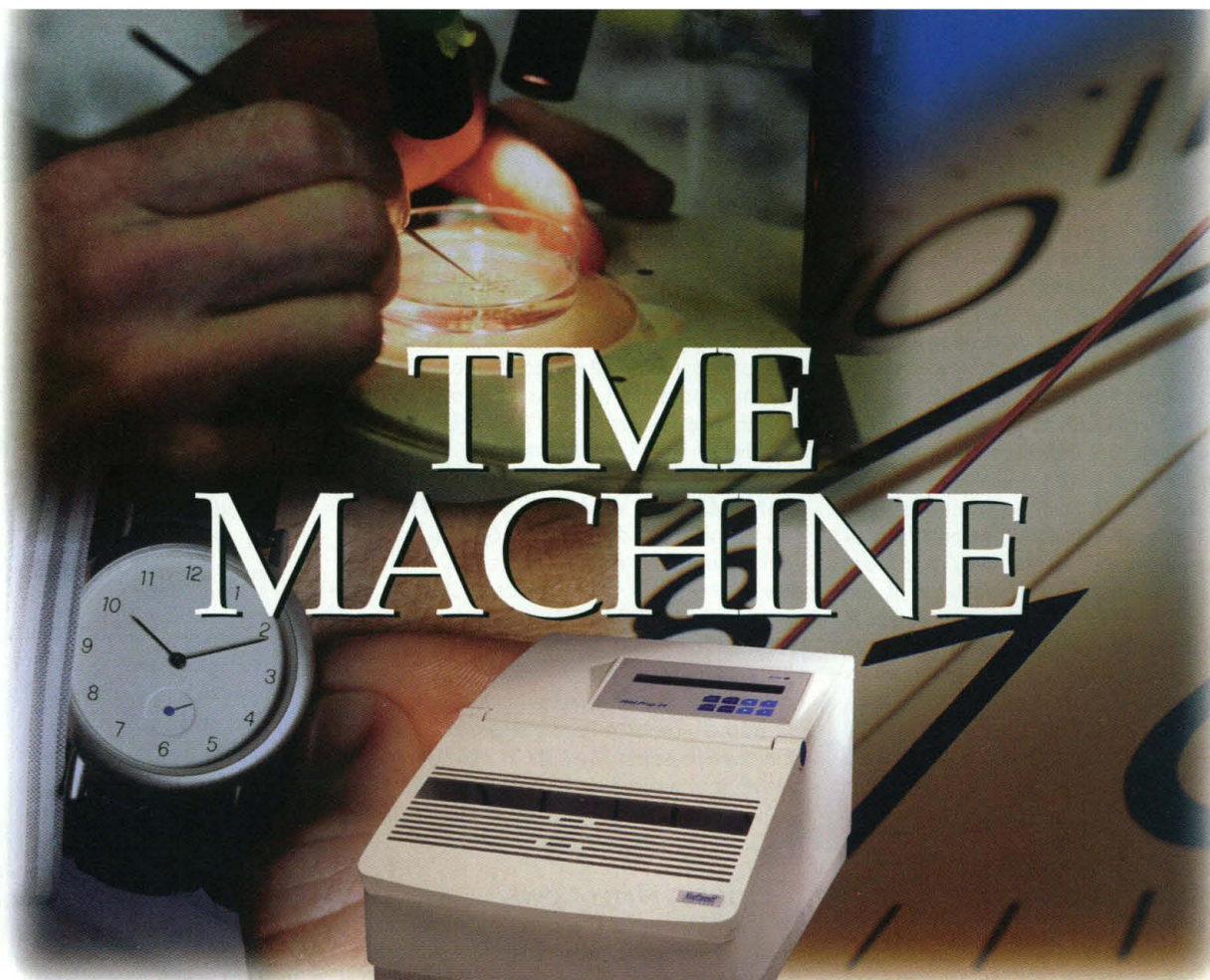
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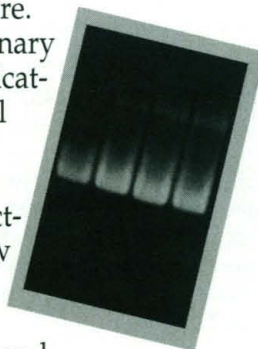
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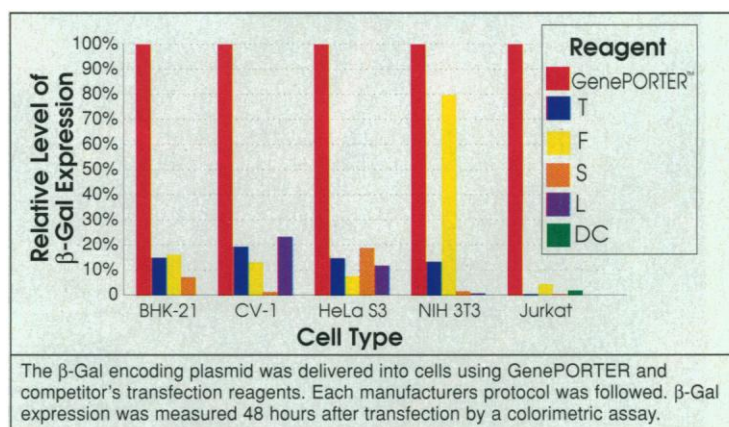
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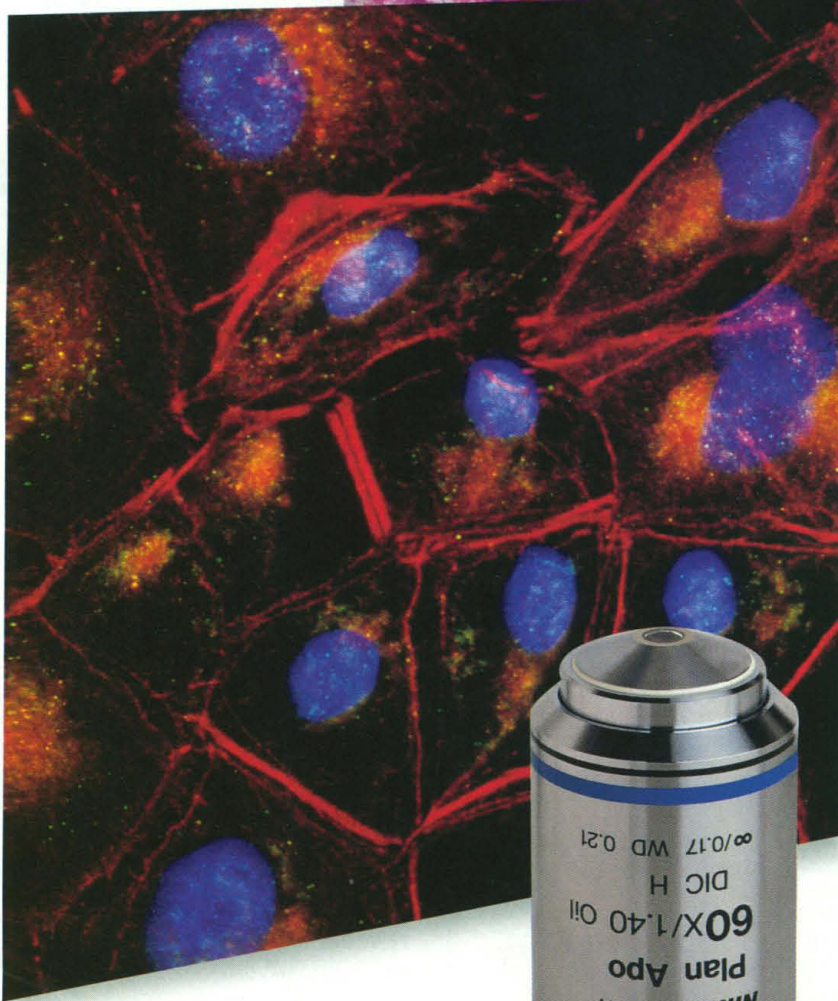
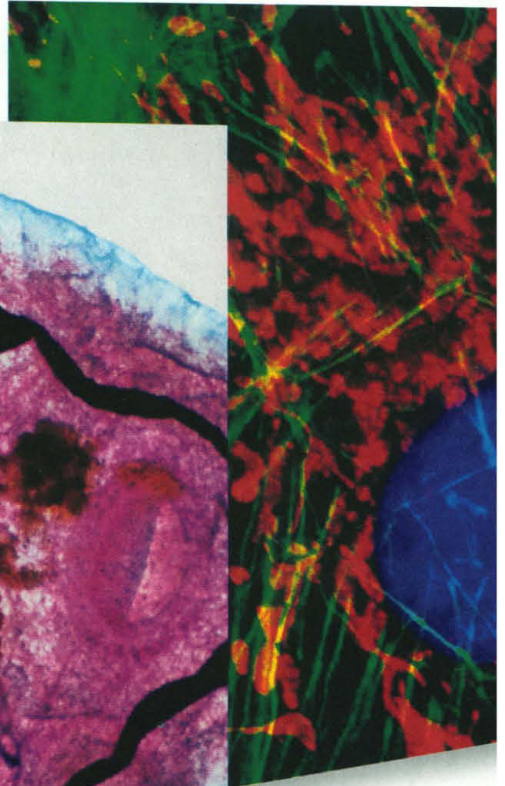
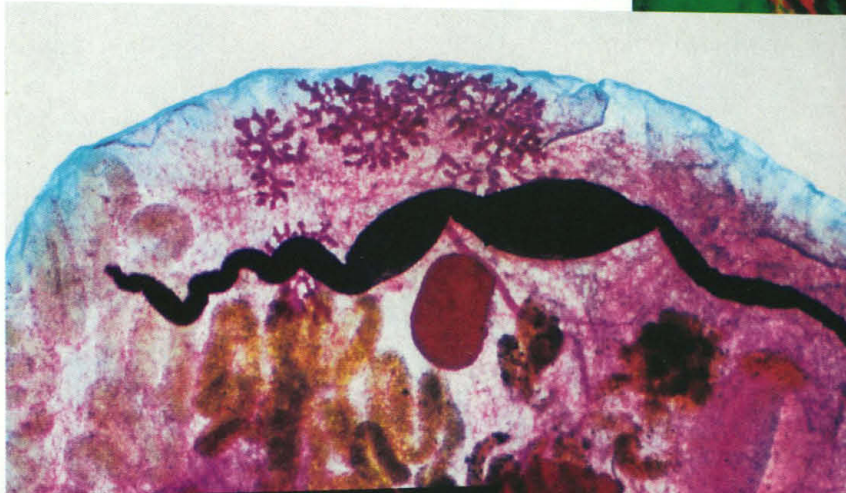
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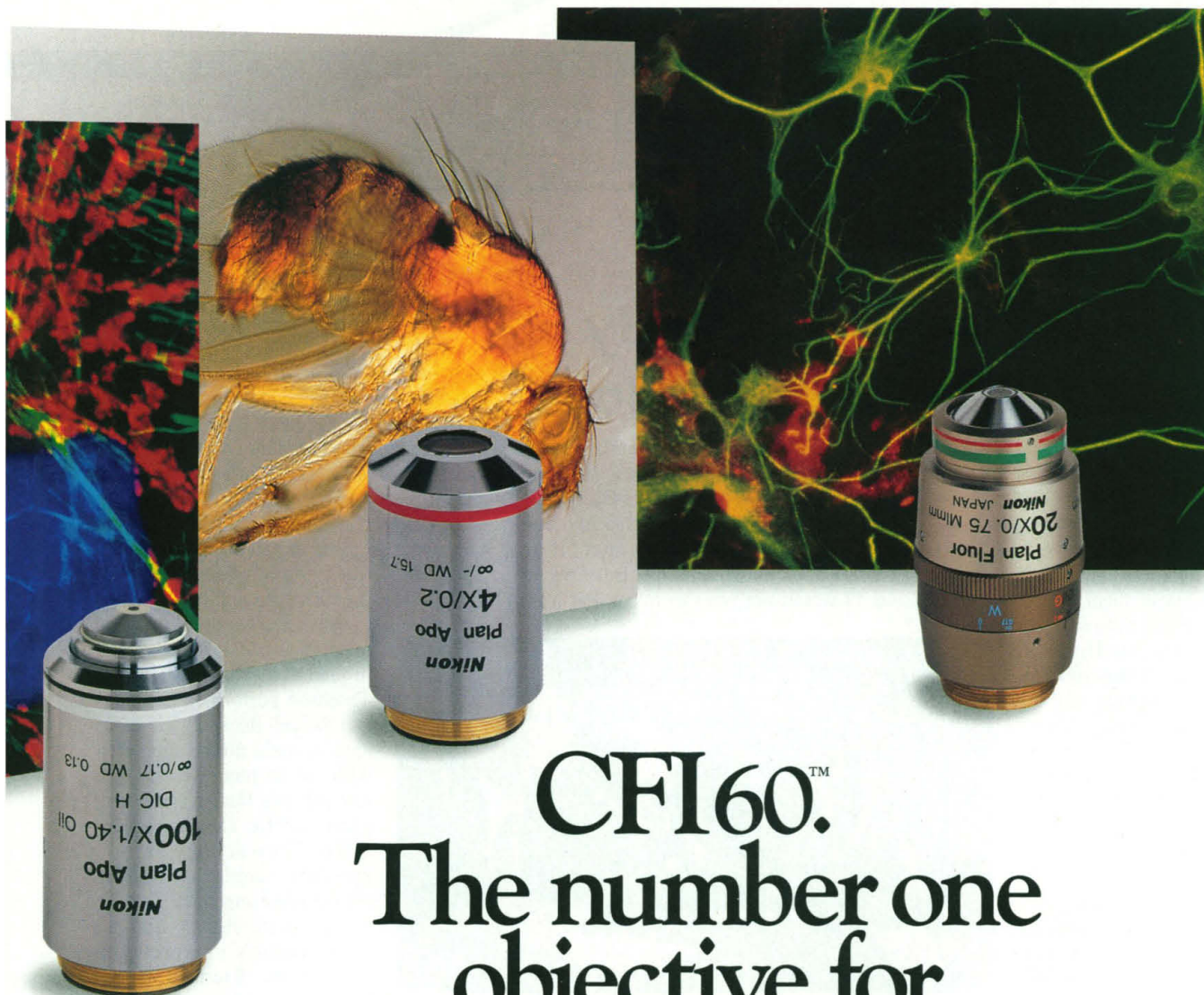
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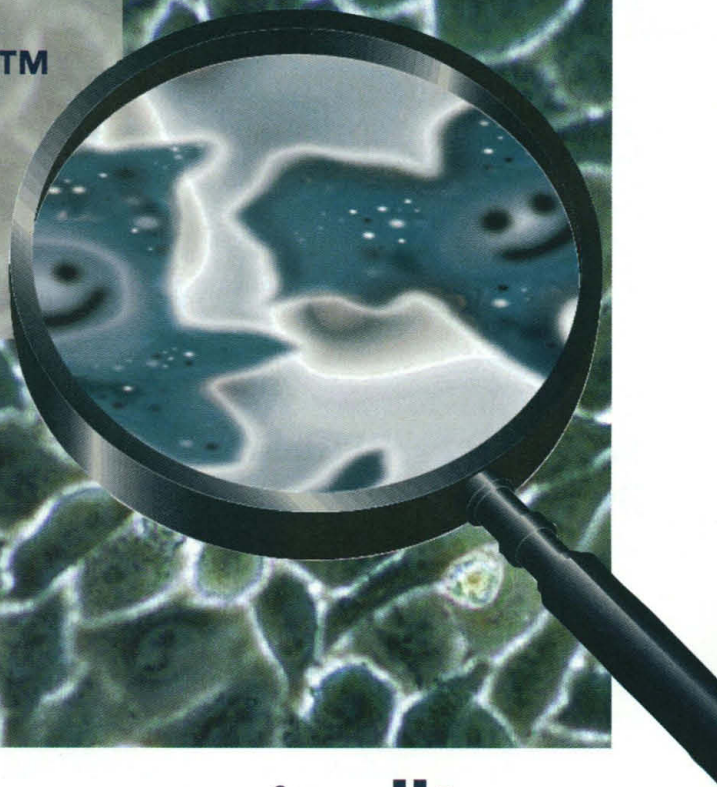
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\*Based on the Opto-Precision Instruments Association's (OPIA) Fourth Qtr. 1997, U.S.A. Microscope Survey

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# Why do these cells prefer SuperFect™ for transfection?

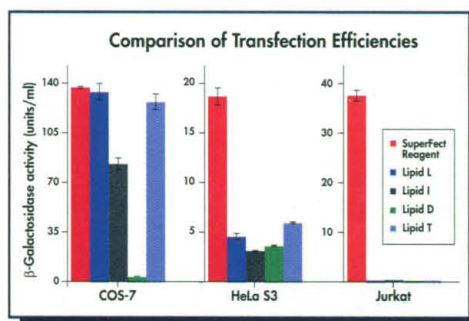


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Comparison of transfection efficiencies obtained using SuperFect Reagent and four of the most commonly used liposome reagents. COS-7, HeLa S3, and Jurkat cells as indicated were transfected in 96-well format using 0.5 µg pCMVβ. 2 x 10<sup>4</sup> cells were seeded per well one day prior to transfection. Transfection efficiencies are given as β-galactosidase units per ml. Each bar represents the average transfection efficiency from four replicates.

**Decreased cytotoxicity** in comparison to liposome reagents.

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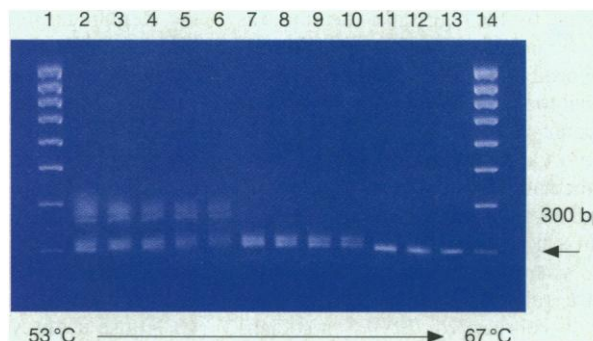
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Of course, both Mastercyclers are licensed and authorized for PCR.



● Experimental determination of optimal annealing temperature.

The calculated primer annealing temperature was 56.5 °C, the actual annealing temperature is 63.5 °C. The ribosomal spacer region of mycoplasmas from H9 cell cultures was amplified.

\*PCR (Polymerase Chain Reaction) is protected by patent. The patent is held by Hoffmann-La Roche. Practice of the patented Polymerase Chain Reaction (PCR) process requires a license. The Eppendorf Thermal Cyclers are Authorized Thermal Cyclers and may be used with PCR licenses available from the Perkin-Elmer Corporation. Their use with Authorized Reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents.

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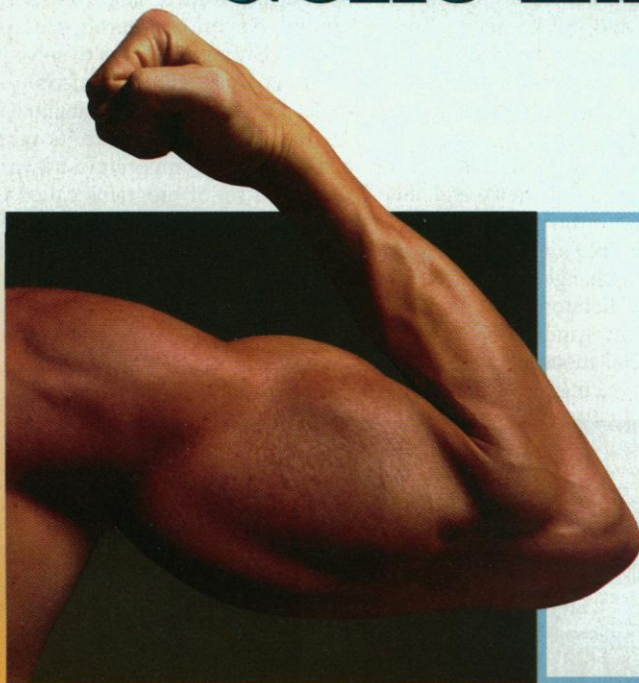
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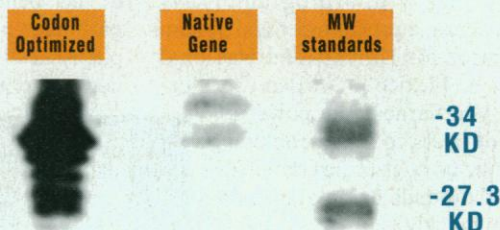
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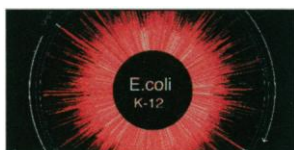
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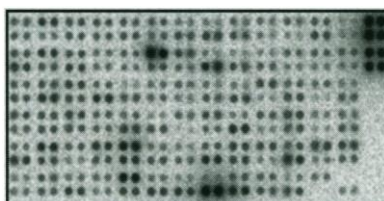
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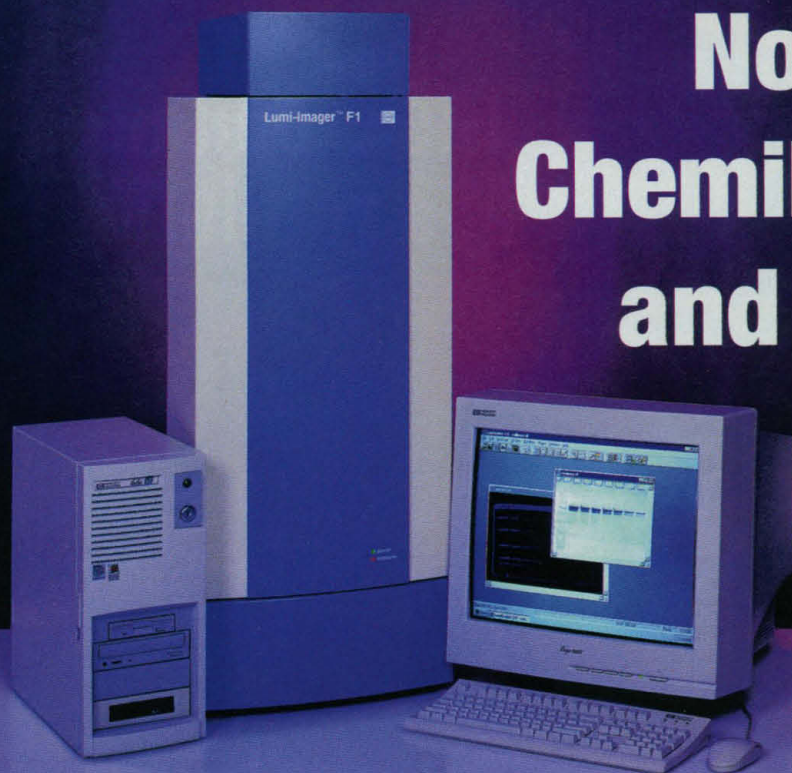
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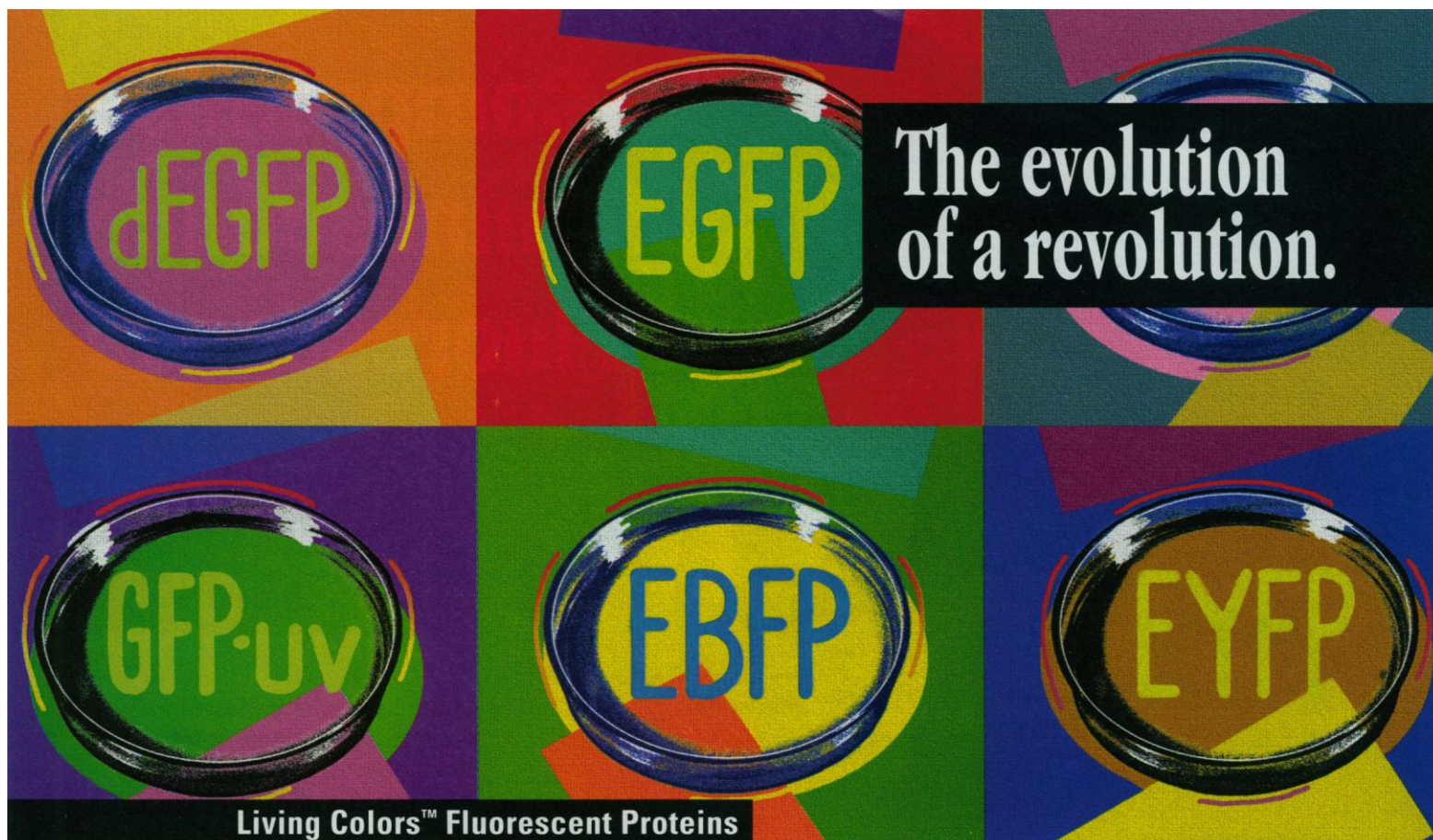


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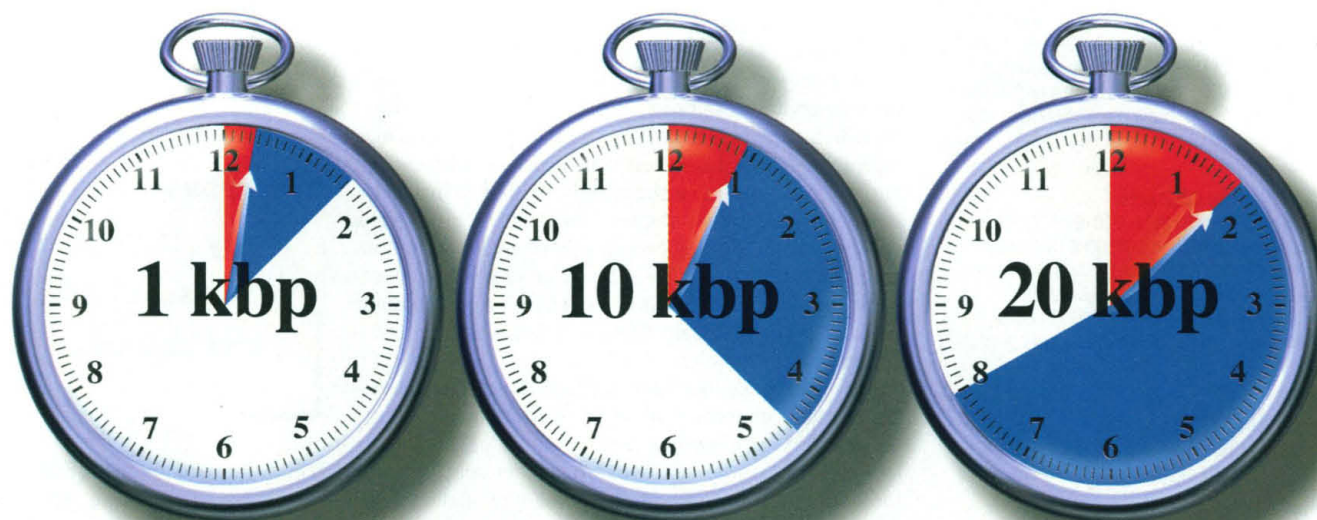
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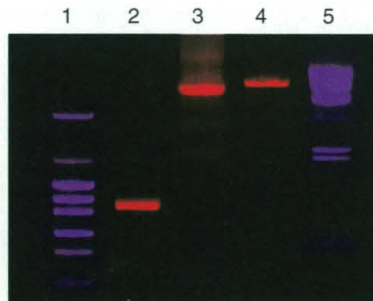
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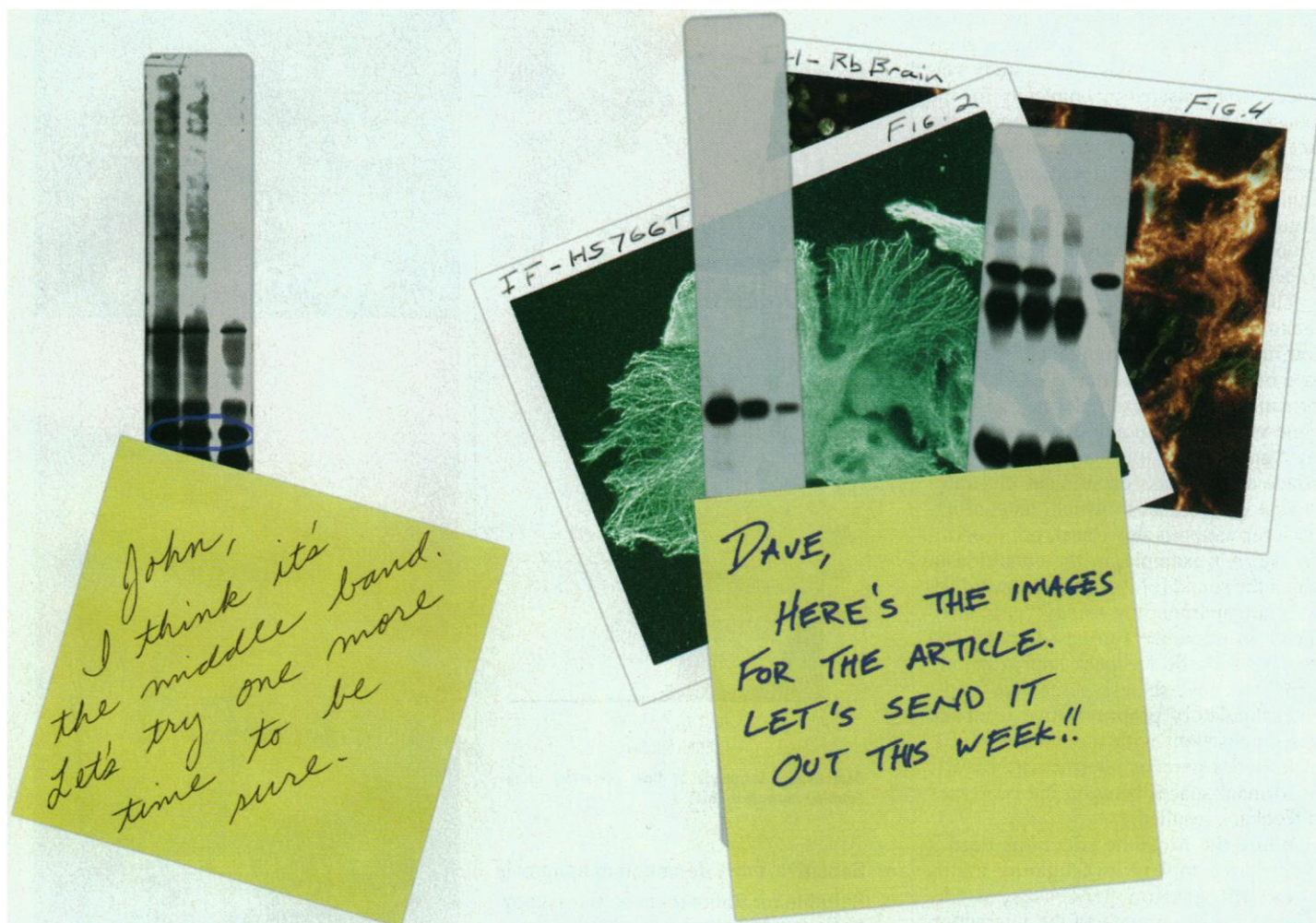
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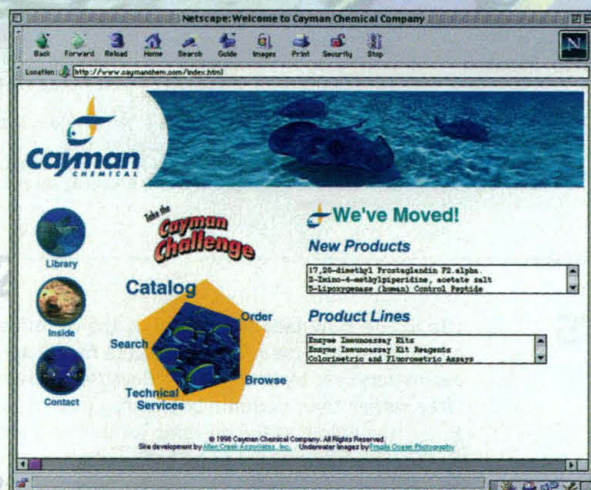
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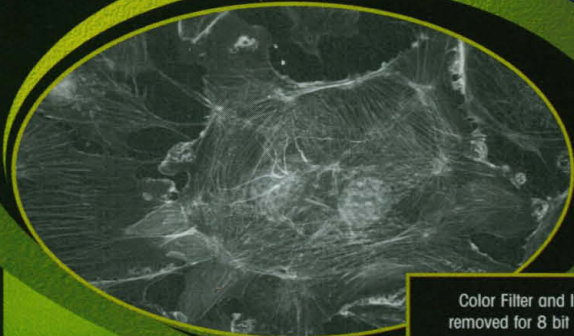
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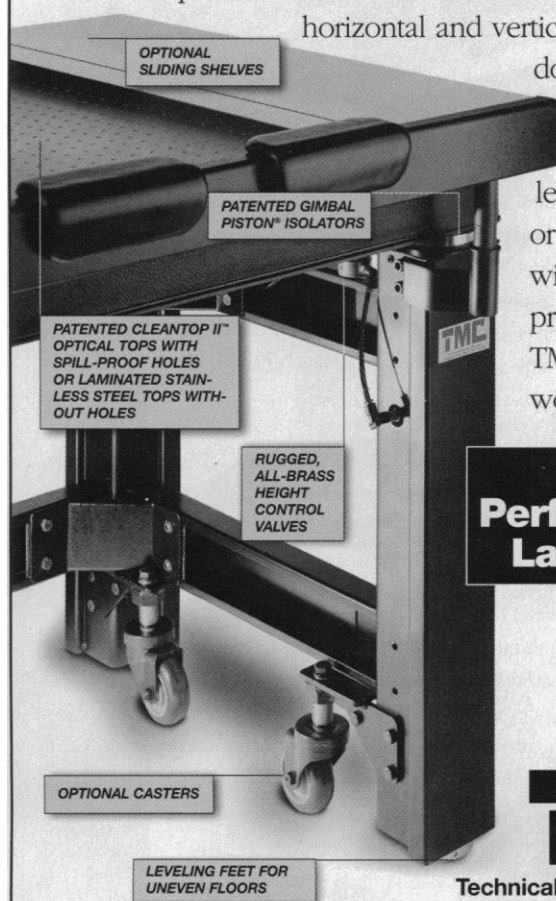
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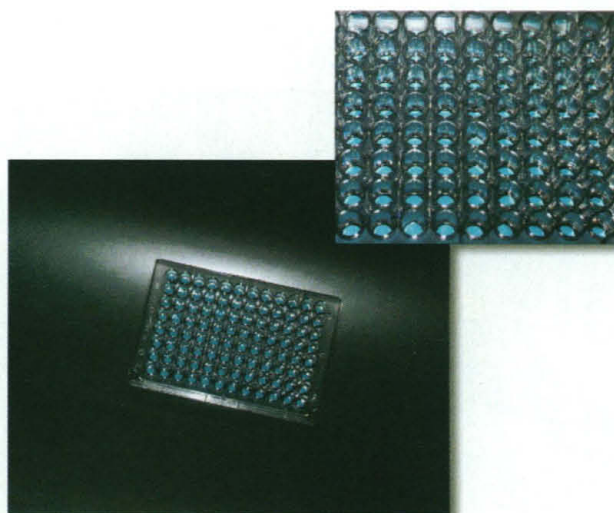


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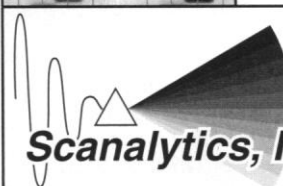
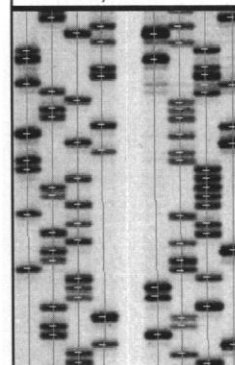
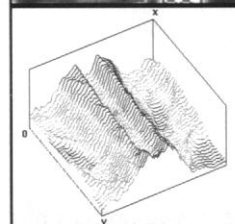
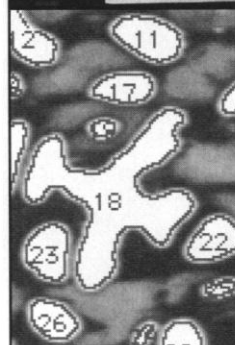
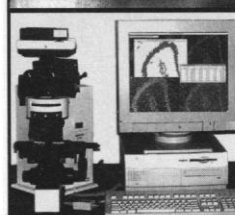
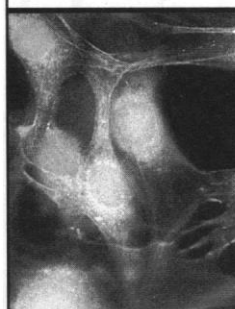
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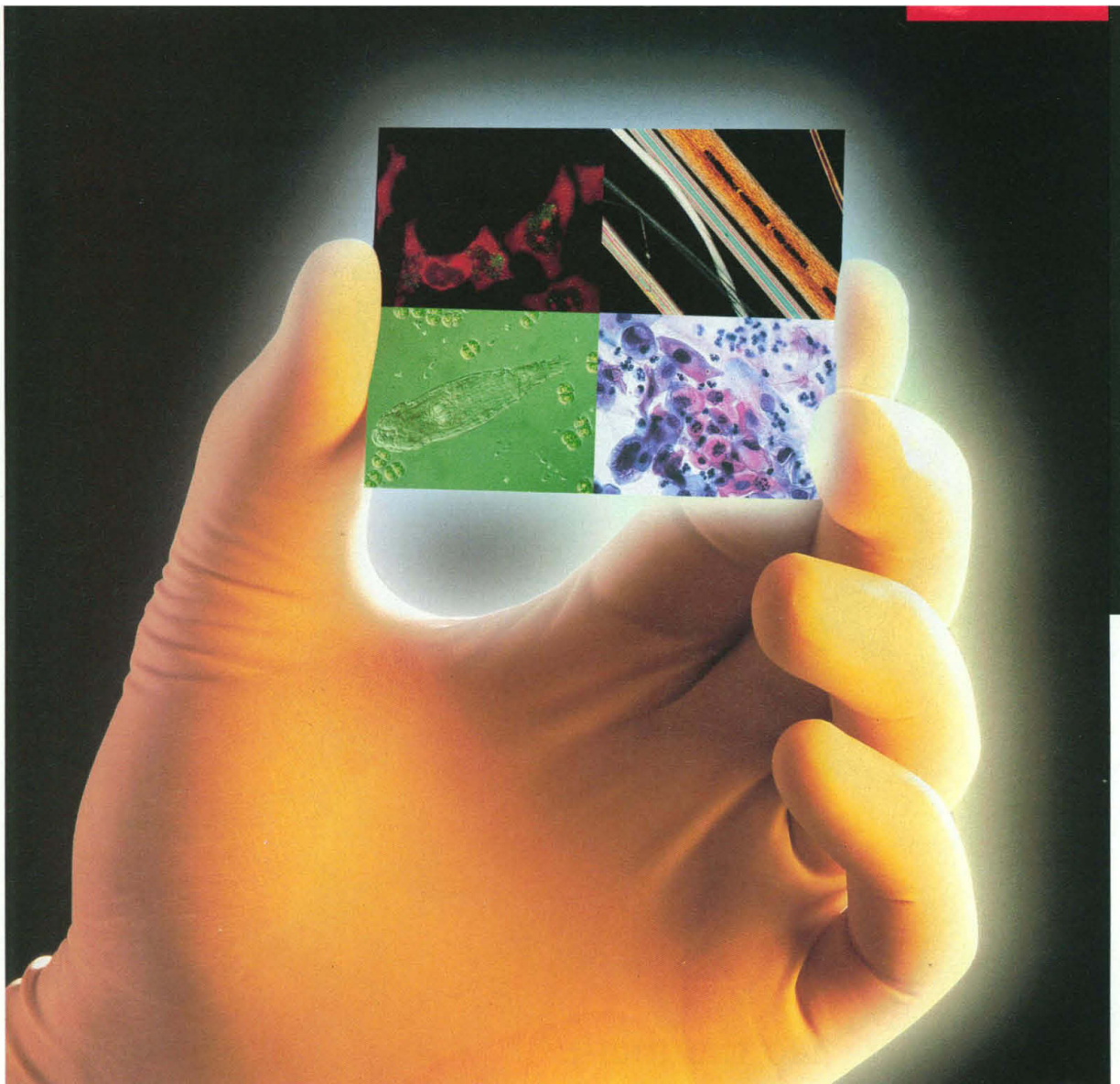
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