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The
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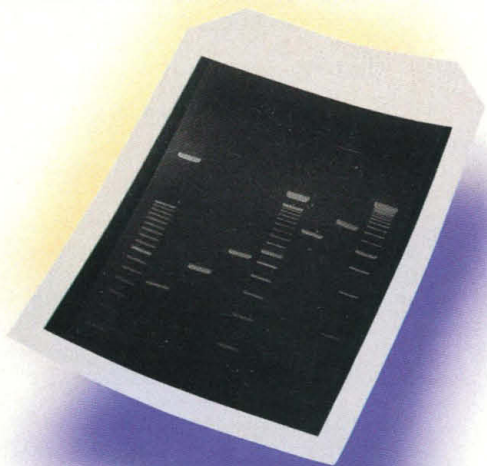
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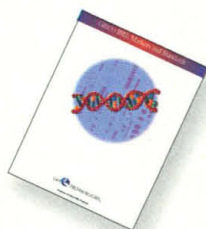
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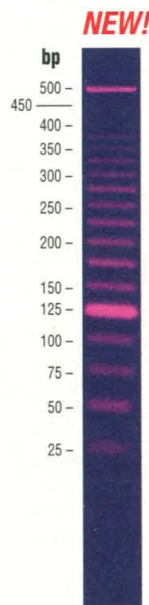
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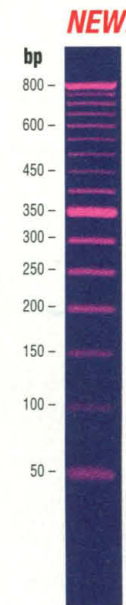
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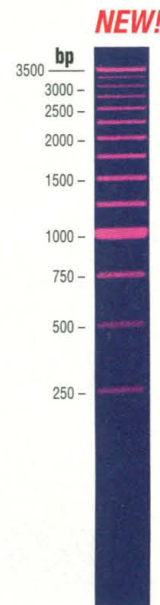
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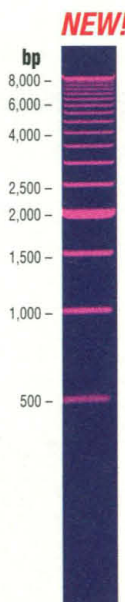
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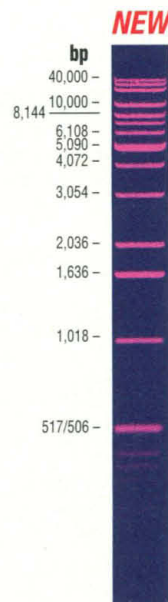
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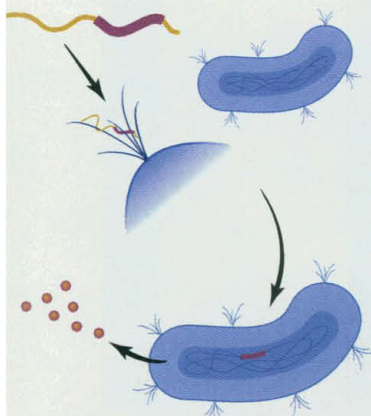
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1869 & 1910

Cholera's toxic guest



1905

Corresponding features

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- Imanishi-Kari Ruling Slams ORI 1864
- Scientists Ponder New Cluster Mission and Uncertain Future 1866
- Italian Space Agency Head Ends Term With a Bang 1867
- National Science Foundation: Awards Mark Research-Learning Links 1868
- Japan: Five-Year Plan to Boost Spending 1868
- Phage Transfer: A New Player Turns Up in Cholera Infection 1869
- Watching the Earth Move 1870
- Divide and Confer: How Worm Embryo Cells Specialize 1871
- Artificial Life Gets Real as Scientists Meet in Japan 1872
- Corn: A Lot of Change From a Little DNA 1873

PERSPECTIVES

- There Is Plenty of Room Between Two Atom Contacts 1901
- C. J. Muller and M. A. Reed
- Glacial Climate in the Tropics 1902
- W. Broecker
- Tickling Memory T Cells 1904
- R. Ahmed

THE NEW FACE OF AIDS

NEWS

- The Changing of the Guard 1876
- The Rebirth of Robert Gallo 1877
- OAR Gets by With a Little Help From New Guard Friends 1878
- The Marketplace of HIV/AIDS 1880
- Protease Inhibitors: A Tale of Two Companies 1882

ARTICLE

- Image Representations for Visual Learning 1905
- D. Beymer and T. Poggio

RESEARCH ARTICLES

- Lysogenic Conversion by a Filamentous Phage Encoding Cholera Toxin 1910
- M. K. Waldor and J. J. Mekalanos
- Minimal Energy Requirements in Communication 1914
- R. Landauer
- Atmospheric, Evolutionary, and Spectral Models of the Brown Dwarf Gliese 229 B 1919
- M. S. Marley, D. Saumon, T. Guillot, R. S. Freedman, W. B. Hubbard, A. Burrows, J. I. Lunine

DEPARTMENTS

- THIS WEEK IN SCIENCE** 1849
- EDITORIAL** 1855
- AIDS: A Global Response
- P. Piot
- LETTERS** 1857
- Hirudo medicinalis* Unplugged: E. L. Bearer • Striving for Creativity: R. J. Sternberg • The Economics of Contraceptives R&D: C. Djerassi • Monbusho and CREST Grants: I. Kanazawa; D. Normile • What Is Holography?: C. Jacobsen • "Natural" Cancer Prevention: P. A. Lachance
- SCIENCESCOPE** 1863
- RANDOM SAMPLES** 1875
- Ice Man Didn't Die Young • Ex-Mobil Scientist Vindicated • Berkeley Gets Chief for Gene Mappers
- BOOK REVIEWS** 1896
- Neotropical Migratory Birds; The Ecology of Migrant Birds; Ecology and Management of Neotropical Migratory Birds*, reviewed by S. A. Temple • *Ocean Acoustic Tomography*, F. Schott • *Optical Coherence and Quantum Optics*, W. P. Schleich • Books Received
- AAAS NEWS & NOTES** 1964
- PRODUCTS & MATERIALS** 1969
- QUARTERLY INDEX** 1974

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COVER

Human immunodeficiency virus (HIV) docking onto the CD4 receptor of a T lymphocyte with chemokine receptors (blue) at the ready. The face of acquired immunodeficiency syndrome has changed dramatically over the past few years, as a new generation of researchers comes to

the fore, a new class of drugs shows promise, and scientists gain new insight into how HIV infects a CD4-bearing cell, its primary target. See the special section (pages 1876 to 1890), editorial (page 1855), and related reports (pages 1939 and 1955). [Illustration: Terese Winslow]



**Eradicating HIV From a Patient:
Not Just a Dream?** 1884

VIEWPOINTS

**HIV Receptors and the Pathogenesis
of AIDS** 1885

R. A. Weiss

HIV Therapeutics 1886

D. D. Richman

A Perspective on AIDS Vaccines 1888

B. R. Bloom

**Off-Resonance Conduction Through
Atomic Wires** 1921

A. Yazdani, D. M. Eigler, N. D. Lang

**Shape-Controlled Synthesis of
Colloidal Platinum Nanoparticles** 1924

T. S. Ahmadi, Z. L. Wang, T. C. Green, A. Henglein, M. A. El-Sayed

**A Benzene-Thermal Synthetic Route
to Nanocrystalline GaN** 1926

Y. Xie, Y. Qian, W. Wang, S. Zhang, Y. Zhang

**Experimental Constraints on Recycling
of Potassium from Subducted Oceanic Crust** 1927

M. W. Schmidt

**Pore Fluid Constraints on the
Temperature and Oxygen Isotopic
Composition of the Glacial Ocean** 1930

D. P. Schrag, G. Hampt, D. W. Murray

**Nuclear Encoding of a Chloroplast RNA
Polymerase Sigma Subunit in a Red Alga** 1932

K. Tanaka, K. Oikawa, N. Ohta, H. Kuroiwa, T. Kuroiwa, H. Takahashi

**Requirement for the Adapter Protein
GRB2 in EGF Receptor Endocytosis** 1935

Z. Wang and M. F. Moran

**Antiviral Effect and Ex Vivo CD4⁺
T Cell Proliferation in HIV-Positive
Patients as a Result of CD28 Costimulation** 1939

B. L. Levine, J. D. Mosca, J. L. Riley, R. G. Carroll, M. T. Vahey, L. L. Jagodzinski, K. F. Wagner, D. L. Mayers, D. S. Burke, O. S. Weislow, D. C. St. Louis, C. H. June

**Solution Structure of a Two-Base DNA
Bulge Complexed with an Eneidyne Cleaving Analog** 1943

A. Stassinopoulos, J. Ji, X. Gao, I. H. Goldberg

**Induction of Bystander T Cell
Proliferation by Viruses and Type I
Interferon in Vivo** 1947

D. F. Tough, P. Borrow, J. Sprent

**Nonselective and G_{βγ}-Insensitive
weaver K⁺ Channels** 1950

B. Navarro, M. E. Kennedy, B. Velimirović, D. Bhat, A. S. Peterson, D. E. Clapham

**A Chemoautotrophically Based Cave
Ecosystem** 1953

S. M. Sarbu, T. C. Kane, B. K. Kinkle

**CC CKR5: A RANTES, MIP-1 α ,
MIP-1 β Receptor as a Fusion Cofactor
for Macrophage-Tropic HIV-1** 1955

G. Alkhatib, C. Combadiere, C. C. Broder, Y. Feng, P. E. Kennedy, P. M. Murphy, E. A. Berger

TECHNICAL COMMENTS

**HIV-2 and Natural Protection Against
HIV-1 Infection** 1959

A. E. Greenberg, S. Z. Wiktor, K. M. DeCock, P. Smith, H. W. Jaffe, T. J. Dondero Jr., P. J. Kanki, G. Eisen, K. U. Travers, R. G. Marlink, M. E. Essex, C.-c. Hsieh, S. MBoup

**Modeling HIV Concentration During
Acute AIDS Infection** 1960

S. E. Wilson, J. A. Habeshaw, J. S. Oxford, A. N. Phillips

**Rate of Killing of HIV-Infected
T Cells and Disease Progression** 1962

M. A. Huynen and A. U. Neumann



1943
A wedge into DNA

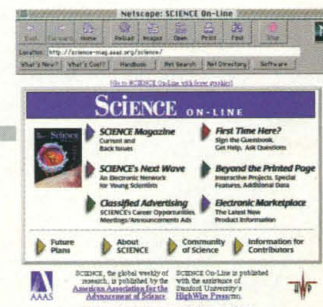
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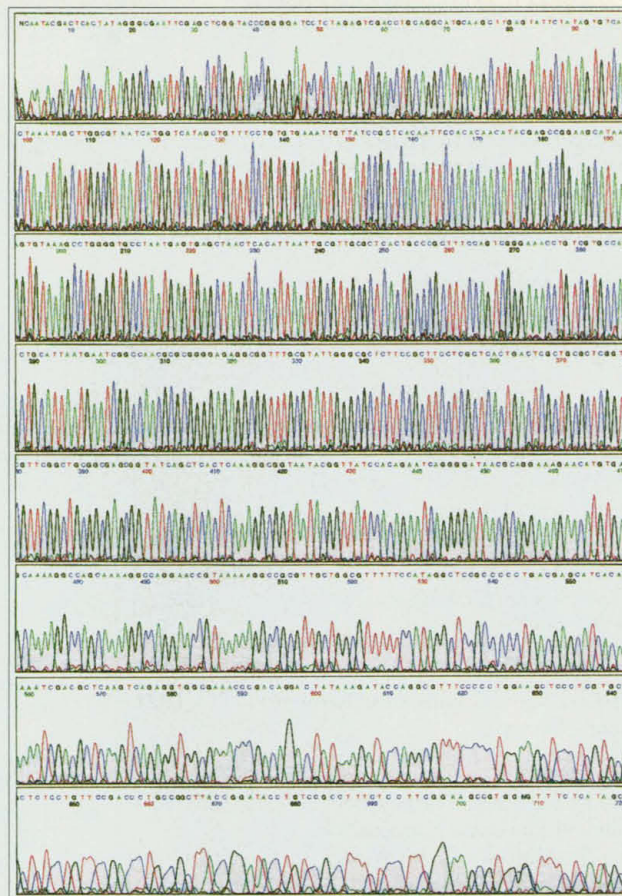
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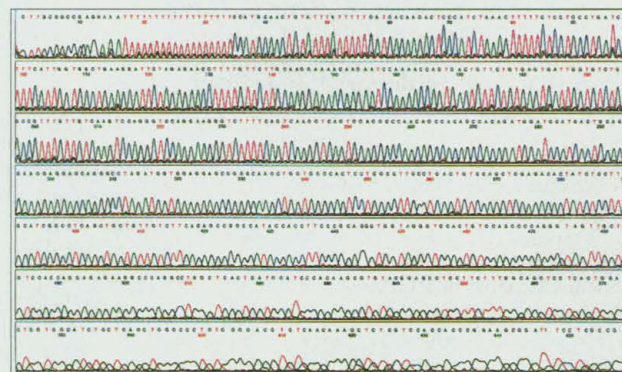
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1. *Proc. Natl. Acad. Sci., USA*, 92(14), pp.6339-6343, (1995).

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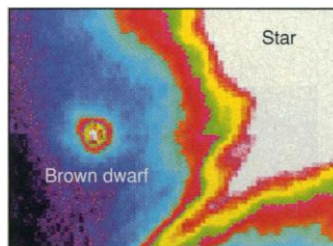
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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Not quite a star

Now that astronomers have clearly identified a brown dwarf, Gliese 229 B, there is great interest in determining what makes this intermediate between a star and a planet tick. Marley *et al.* (p. 1919) used the methane spectrum of Gliese 229 B



and a jovian atmospheric evolution model to estimate this body's mass and age. In addition, their model suggests that there is a flux enhancement in the 4- to 5-micrometer region that observers might use in their search for other cool objects.

Atomic conductors

Future device applications will require an understanding of electron transport through nanostructures or even atomic structures. Yazdani *et al.* (p. 1921; see the Perspective by Muller and Reed, p. 1901) measured the electrical resistance of a single xenon atom or a pair of xenon atoms held between a scanning tunneling microscope tip and a nickel surface. Theoretical calculations accurately predict the observed resistivity and show that off-resonant conduction occurs through the tail of the 6s electronic level.

Cluster creation

Two reports focus on new methods for synthesizing nanoclusters. Ahmadi *et al.* (p. 1924) show that the morphology of plati-

Role of bacteriophage in cholera

A filamentous phage has been shown to encode a virulence factor. Waldor and Mekalanos (p. 1910; see the news story by Williams, p. 1869) show that a phage encodes the structural genes for cholera toxin. Transmission of the phage occurs in the gastrointestinal tract. The receptor is an intestinal colonization factor called the toxin-coregulated pili. Because phage focuses in on those strains that can colonize the gut, it may prove useful as a gene therapy vector. Many clinically relevant pathogens express similar pili, raising the possibility that these may also serve as receptors for virulence-related phages.

num particles can be controlled in colloidal synthesis by changing the concentration of a capping material, sodium polyacrylate. Xie *et al.* (p. 1926) have synthesized nanocrystalline gallium nitride, which has applications in blue-green laser diodes, by a method analogous to hydrothermal synthesis except that benzene is used instead of water. In addition to the hexagonal phase, they also make the rocksalt phase normally seen only at high pressure for bulk samples.

Speaking volumes

The oxygen isotope value of plankton preserved in sediments reflects both the water temperature and the amount of water stored in ice sheets, which affects the isotopic composition of the ocean. Schrag *et al.* (p. 1930; see the Perspective by Broecker, p. 1902) now have analyzed pore waters in sediments from a deep sea core to extract the ice-volume part of the signal, as no temperature-dependent fractionation occurred. The results imply that the deep water in the Atlantic Ocean was 4°C cooler during the last glacial maximum than it is today and that the ice sheet growth modified the ocean isotopic values by 1 per mil.

CD28 and HIV-1 infection of T cells

Although CD4⁺ T cells are the main site of infection for human immunodeficiency virus-type 1 (HIV-1), not all of these cells are necessarily infected. Attempts to stimulate polyclonal proliferation of the uninfected cells for immune reconstitution or gene therapy are usually hampered by simultaneous stimulation of infected cells. Levine *et al.* (p. 1939) now show that costimulation of T cells from infected individuals with immobilized monoclonal antibodies to CD28 decreased HIV-1 viral load. Similar stimulation of T cells from uninfected donors rendered the cells resistant to HIV-1 infection.

Macrophages and HIV-1

Different HIV-1 isolates vary in their ability to infect different CD4⁺ cells because of differences in their envelope glycoprotein, which interact with specific fusion cofactors. Recently, the T cell cofactor was identified as fusin. Alkhatib *et al.* (p. 1955; see the news story in last week's issue by Balter, p. 1740) have now shown that the cofactor for macrophages is CCCKR5, a G protein-coupled receptor for the chemokines RANTES, MIP-1 α , and MIP-

1 β . The identification of these cofactors suggests that varying levels of expression of CCCKR5 may explain why some individuals remain uninfected after repeated HIV exposure and may allow for the development of therapeutic strategies and small animal infection models.

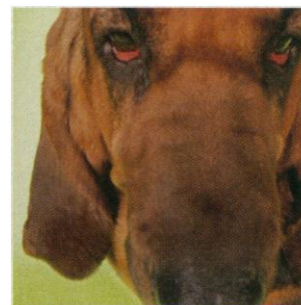
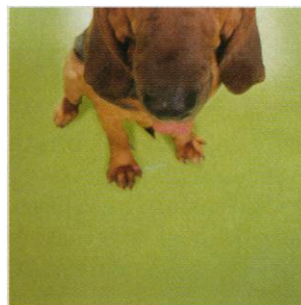
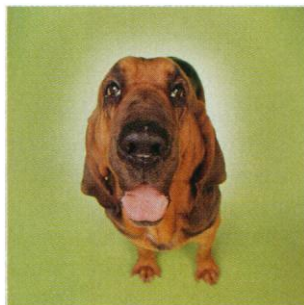
Cave dwellers

Ecosystems based on organisms that derive their energy from hydrogen sulfide rather than from the familiar photoautotrophic processes have been described in deep sea thermal vents, in deep freshwater lake thermal vents, and in surface hot springs. Sarbu *et al.* (p. 1953) have added a fourth chemoautotrophic system, a small terrestrial ecosystem discovered in a cave in Romania. In this karstic system, a diverse fauna, many of which are endemic to the system, subsists on grazing chemoautotrophic primary producers.

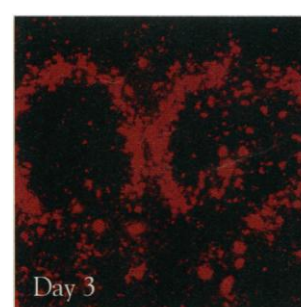
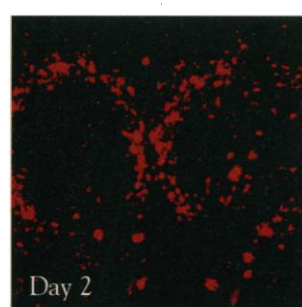
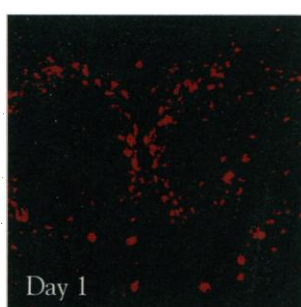
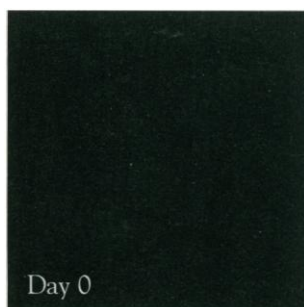
Chloroplast import of sigma factor

Chloroplast genomes encode all of the various proteins that make up the RNA transcription machinery except for the sigma factor, which affects promoter selectivity. Tanaka *et al.* (p. 1932) found that the missing gene is not in the chloroplast but is found in the nuclear genome. The nuclear gene product shows sequence similarity to cyanobacterial sigma factors and is imported into the chloroplast. This unusual distribution of genes may represent transfer of a gene from the primitive endosymbiont to the host nuclear genome during the evolution of eukaryotic cells.

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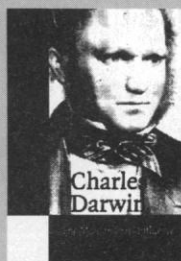
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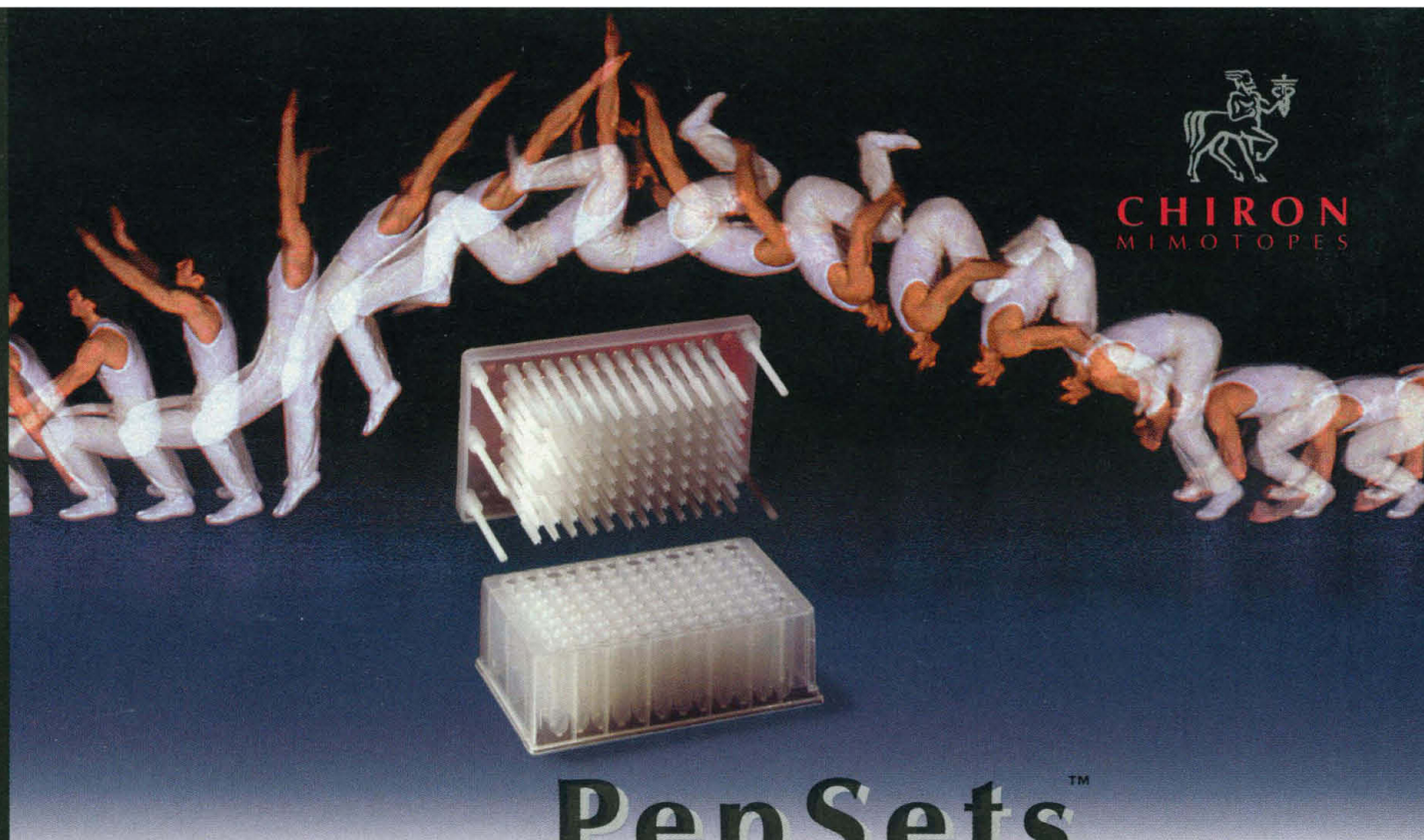
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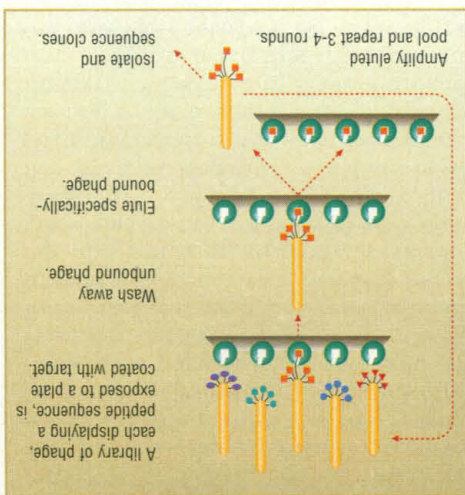
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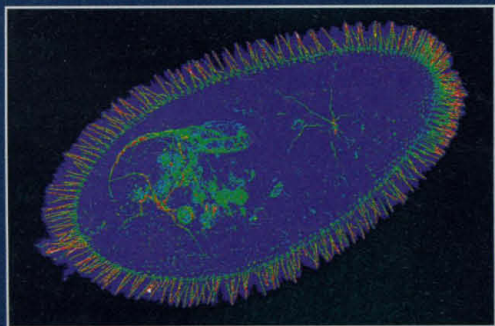
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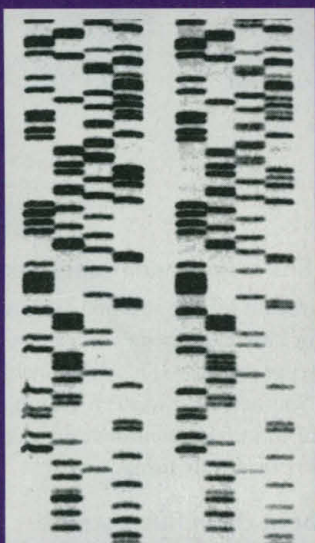




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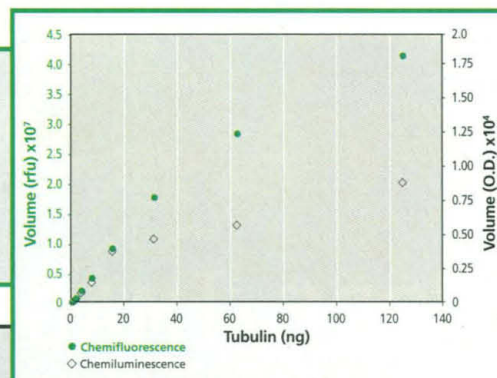
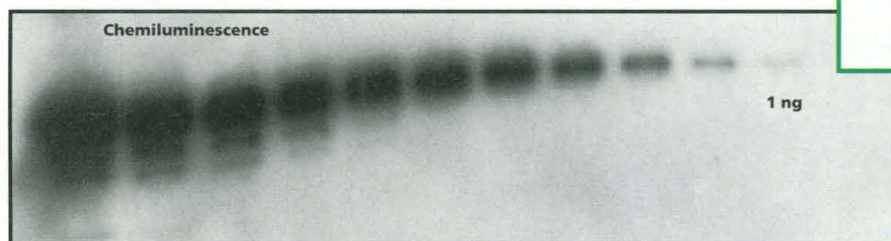
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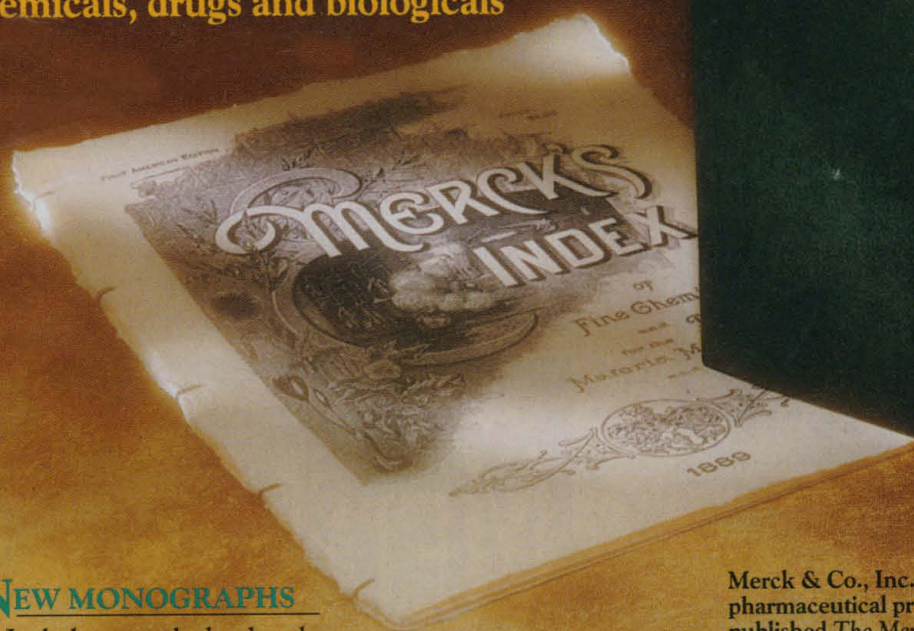
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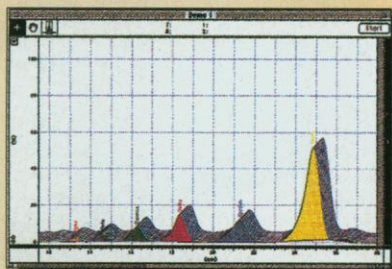
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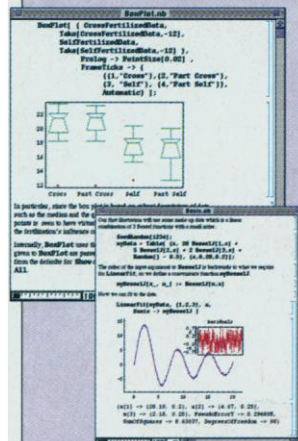
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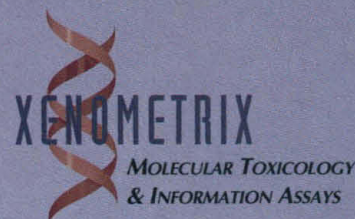
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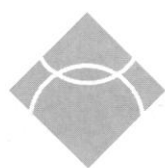
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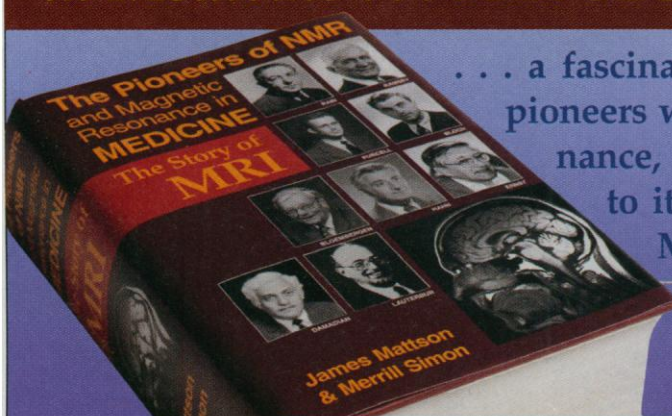
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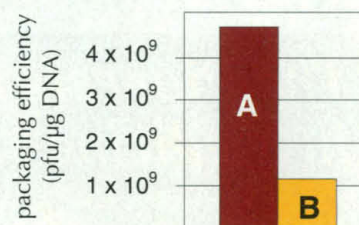
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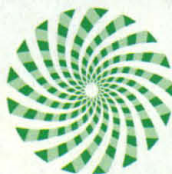


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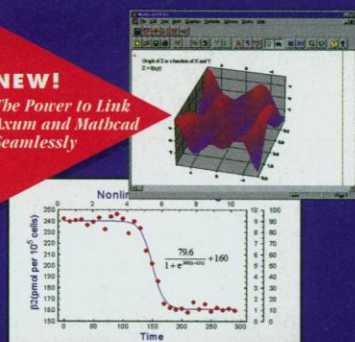
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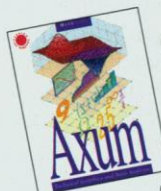
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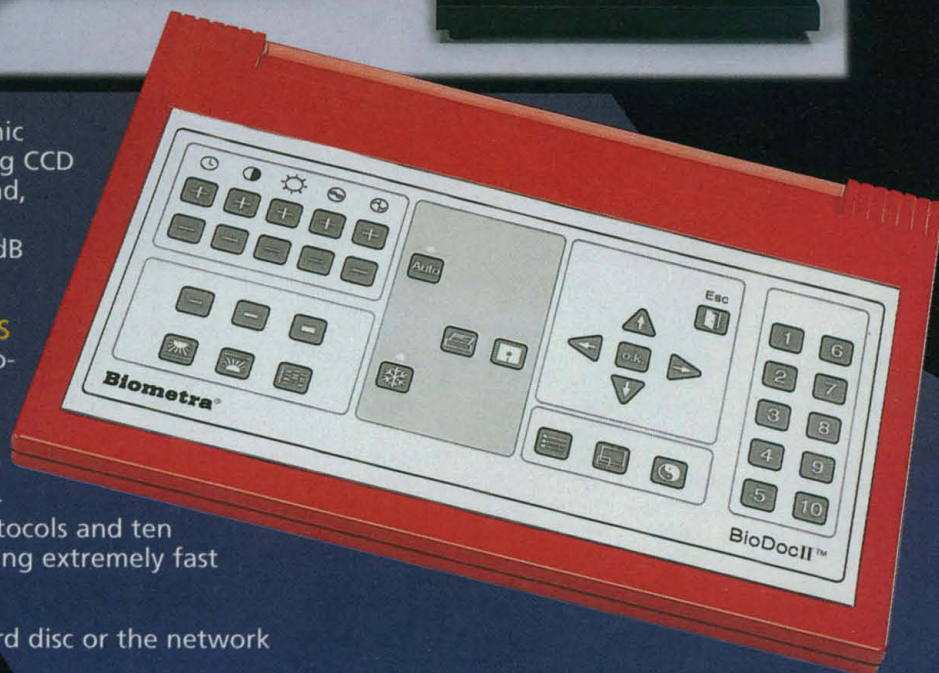
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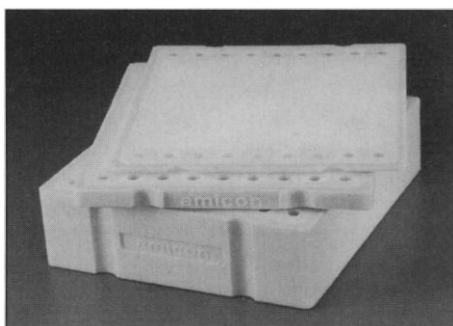
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PRODUCTS & MATERIALS

Cassette Filtration Cartridges

Tangential-flow, membrane filtration cassette cartridges offer fast throughput, consistent retention, and minimal protein binding. They fit all standard cassette holders and allow parallel scale-up from milliliters to thousands of liters. They are designed for clarification, concentration, diafiltration, buffer exchange, and depyrogenation in the biopharmaceutical laboratory, pilot plant, or production facility.



They are available with ultra low-binding, regenerated cellulose membranes for applications where high recovery of proteins, viruses, and hormones is important. They are also offered with a specially formulated, low-protein binding polyethersulfone membrane for use with antibiotics, enzymes, immunoglobulin M desalting, depyrogenation, or vaccines. **Amicon. Circle 135.**

Antibodies

An antibody to *Helicobacter pylori* is available unlabeled or labeled with peroxidase or fluorescein. **Kirkegaard and Perry Laboratories. Circle 136.**

A polyclonal antibody to leptin is available. Leptin is a small protein presumably secreted by adipocytes that appears to play a key role in regulating body weight and composition. **Affinity BioReagents. Circle 137.**

An antibody to retinoblastoma gene product works on formalin-fixed, paraffin-embedded tissues, frozen sections, cell smears,

and protein immunoblots. Retinoblastoma gene product is widely expressed in human tissues and plays a key role in cell cycle control. **Dako Corp. Circle 138.**

ImmunoGold Reagents

Aurion is a line of ImmunoGold reagents and accessories prepared using the highest quality antibodies and binding agents available. All the antibodies and antibody fragments have been immuno-affinity-purified and immuno-cross-adsorbed to reduce non-specific reactions to the greatest extent possible. The performance of the reagent is measured using a dot-spot test, and the size and size distribution are checked by electron microscopy. The reagents have a guaranteed 18-month shelf life. **Electron Microscopy Sciences. Circle 139.**

Graphing and Data Analysis Software

KaleidaGraph is a data analysis and graphing application with versions available for both Windows and Macintosh operating systems. The software's interactive process develops publication quality graphs that mathematically transform even the most complex data into attractive yet meaningful visual displays. KaleidaGraph distinguishes itself with its speed, ability to handle large data sets, robust curve fitting, and a myriad of powerful features that give the user full control over the plot. Windows versions can fully interchange data with the Macintosh version. **Synergy Software. Circle 140.**

Molecular Rendering Software

SymApps is a new three-dimensional molecular rendering program designed for desktop visualization and publishing. The software produces high-quality graphics that

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support perspective views, colors, smoothing, and light source adjustments. The drawings can be used for handouts, presentations, and publishing. SymApps can calculate symmetry point groups and display symmetry elements on the screen. Point groups can be calculated over a range of tolerances, allowing the user to quickly identify distortions in molecular coordinates. **Softshell International.** Circle 141.

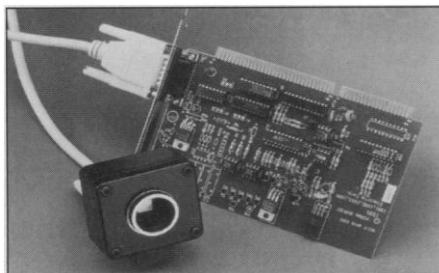
DNA Synthesis Support

The Universal CPG Support for DNA synthesis can be used for all syntheses, irrespective of the first (3') base in the sequence. Its use requires no modification of the standard synthesis protocols and only a minor modification of the deprotection protocol (introduction of 1 to 2% lithium chloride). Deprotection and cleavage of the oligonucleotide can be done using fast or normal synthesis chemistries. **BioGenex.** Circle 142.

Digital Imaging Cameras

Digital imaging cameras offer an affordable shortcut to digitizing images for computer use. Making use of a solid-state charge-

coupled device, these tiny cameras dispense with conventional photo processing and eliminate the need for expensive television camera and digital frame grabber combina-



tions. Users can readily obtain still or moving images through a microscope. Standard photographic lenses are available for non-microscopic images. **World Precision Instruments.** Circle 143.

Multichannel Blood Flow Monitor

The Oxford Array is a device that makes use of the laser Doppler technique to perform continuous, real-time mapping of microvascular blood perfusion from up to 12 different sites with the use of a huge variety of experimental and clinical probes. In addition, the

system can simultaneously record and display eight temperature and two auxiliary inputs (such as pO_2 or blood pressure). It includes extensive record, playback, and print facilities. The system is available in any number of channels from 2 to 12 and is fully upgradeable. **Eppendorf Scientific.** Circle 144.

Baculovirus Expression System

The Bac-to-Bac HT System for expression of recombinant protein in baculovirus is faster than conventional homologous recombination methods. The entire process takes 9 days instead of 4 to 6 weeks. The system yields large amounts of recombinant protein (up to 25% of cell protein with accurate post-translational modifications). It allows one-step affinity purification of recombinant proteins. **Life Technologies.** Circle 145.

Literature

Chirobiotic Handbook is a 22-page publication that describes the use of bonded macrocyclic antibiotic high-performance liquid chromatography phases for analytical and preparative chiral separations. **Advanced Separation Technologies.** Circle 146.

Analytical Standards and Chemicals in Small Quantities is a catalog of more than 7000 chemicals, all available in neat, solution, mixture, and kit formats. It includes environmental standards, pesticide and metabolite standards, inorganic solution standards, analytical and reference standards, and custom solutions. **Chem Service.** Circle 147.

Cortex Biochem Product Reference Manual, a catalog with more than 785 new products, including affinity-purified secondary antibodies and a comprehensive line of magnetizable particles, provides a single source for immunoreagent needs. **Cortex Biochem.** Circle 148.

Biosynth Substrates and Reagents is a catalog that includes more than 30 enzyme substrates, enzyme inducers, and culture media additives. It includes applications highlights, enzyme substrate reaction mechanisms, and a cross-reference section. **Biosynth International.** Circle 149.

Laminar Airflow Equipment describes bench and console model workstations available in 3-, 4-, 5-, and 6-foot-wide configurations. Work surfaces and side walls are constructed of stainless steel. The high-efficiency particulate air filter is rated at 99.99% efficiency for 0.3- μm particulates. **Forma Scientific.** Circle 150.

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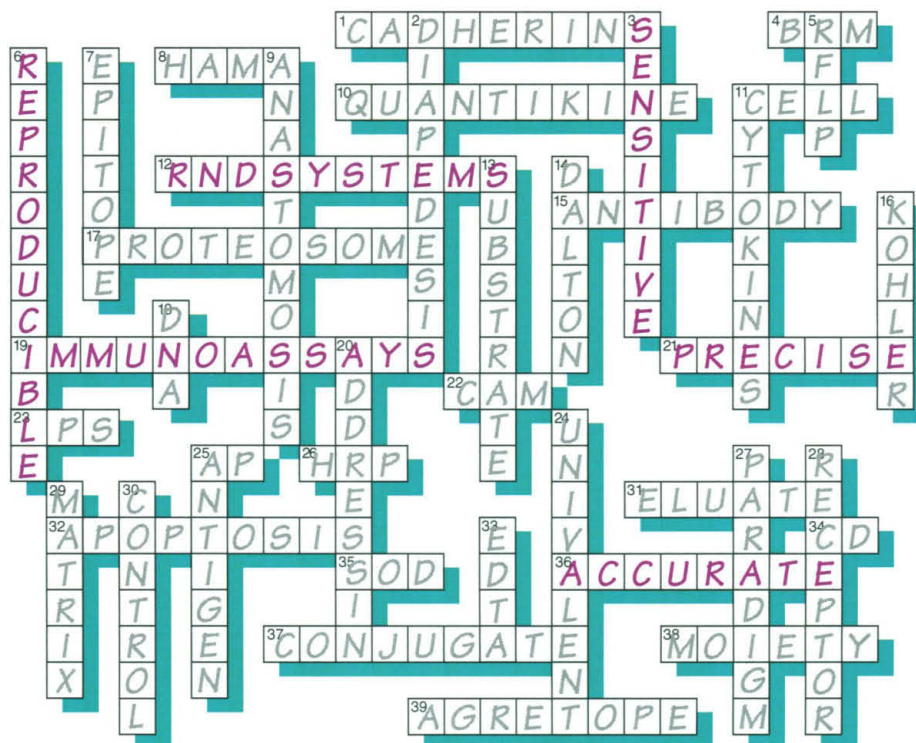


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ACROSS

- 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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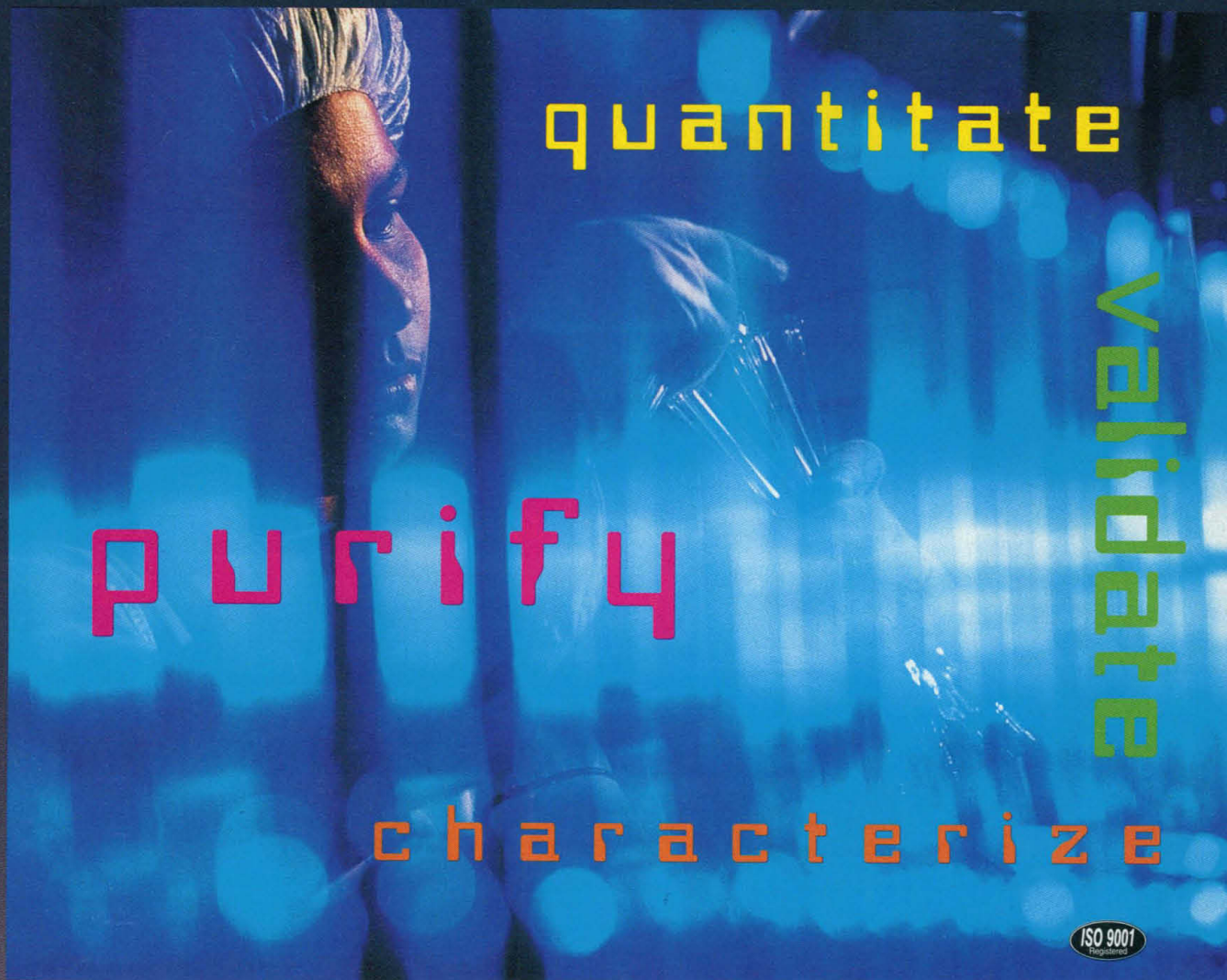
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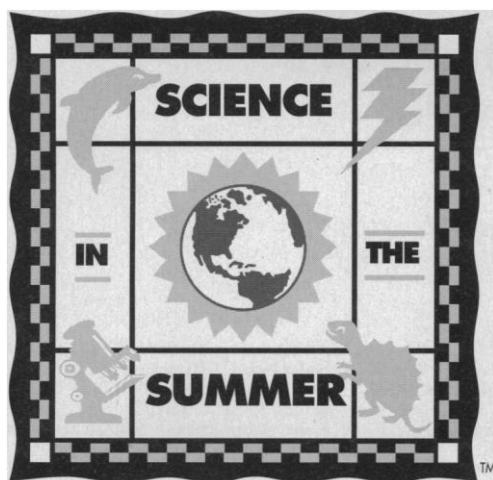
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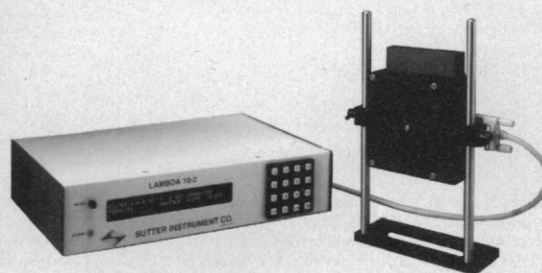
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