

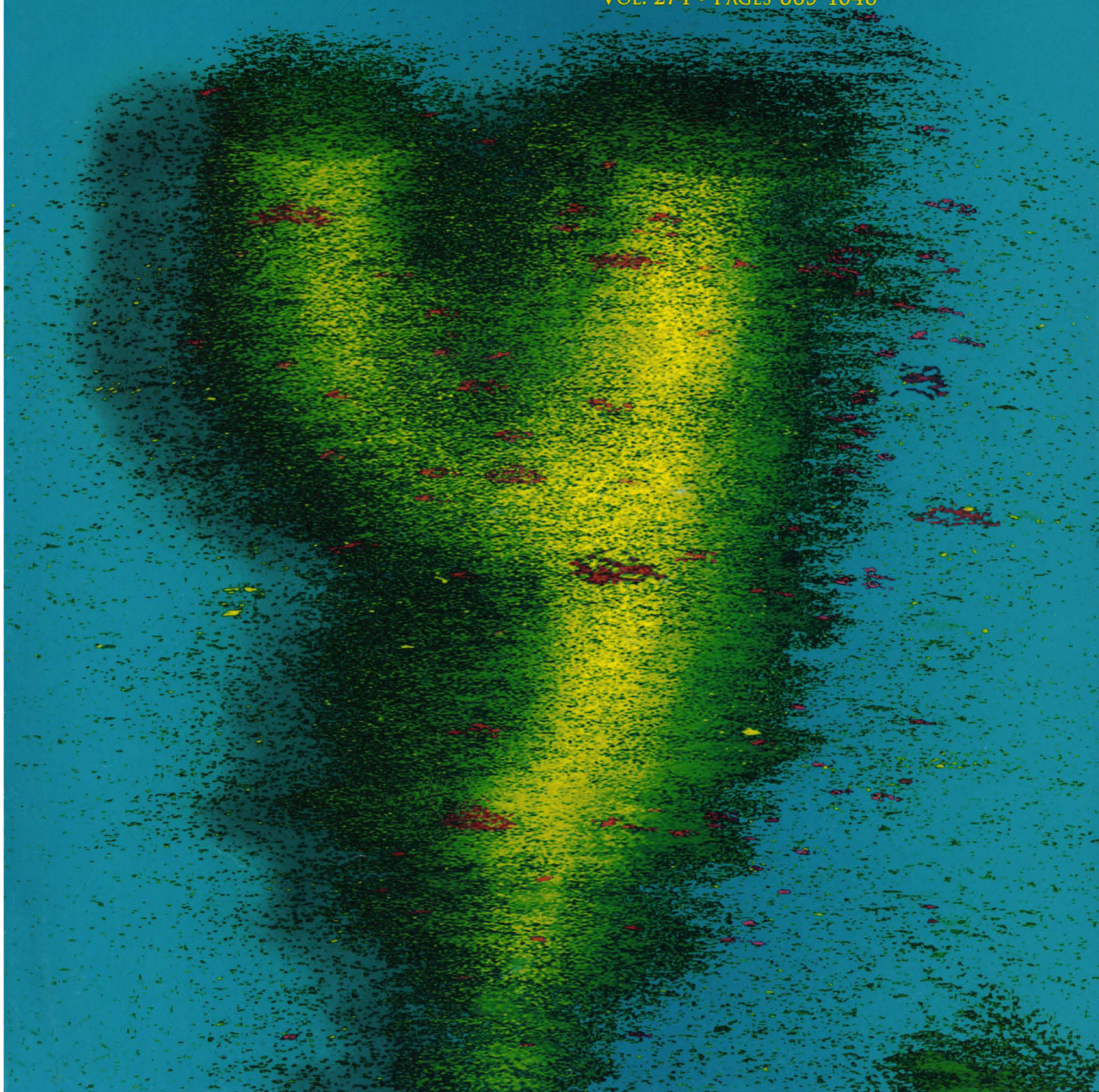


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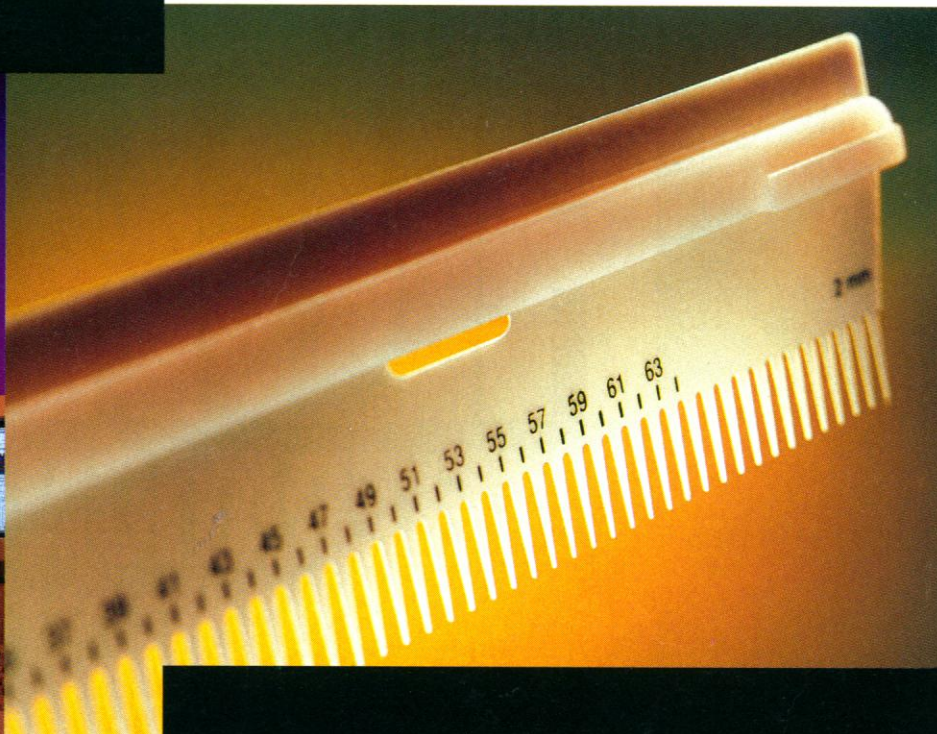
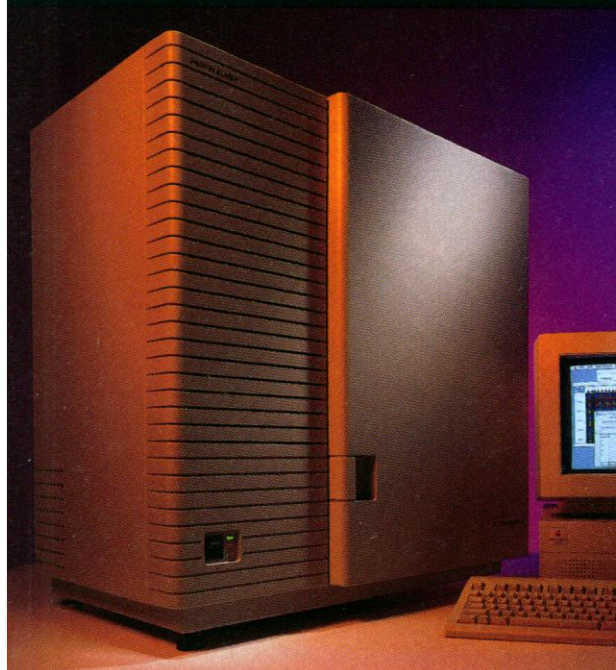
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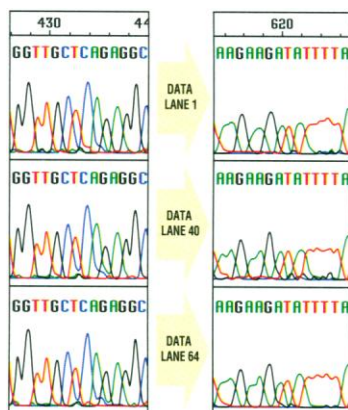
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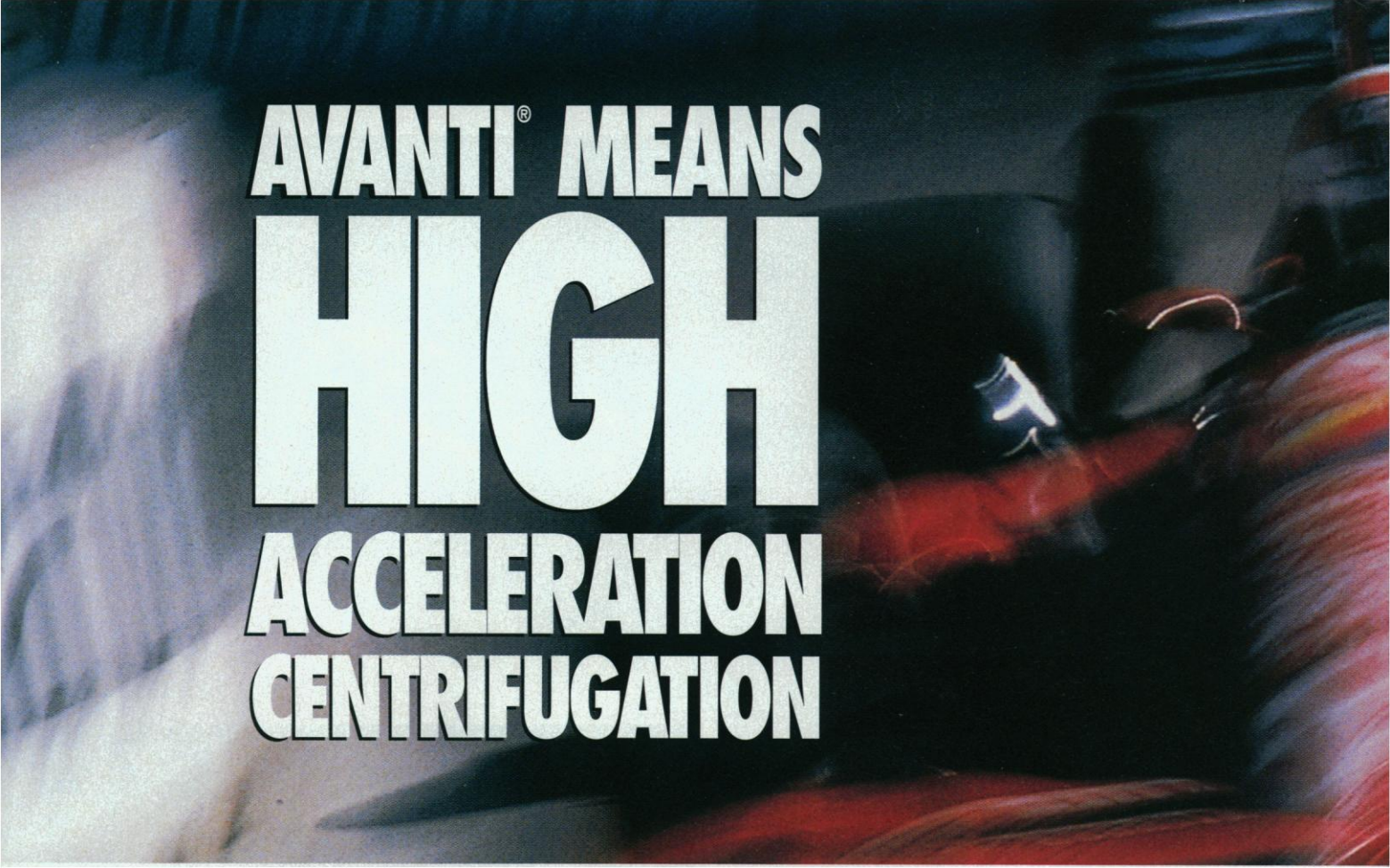


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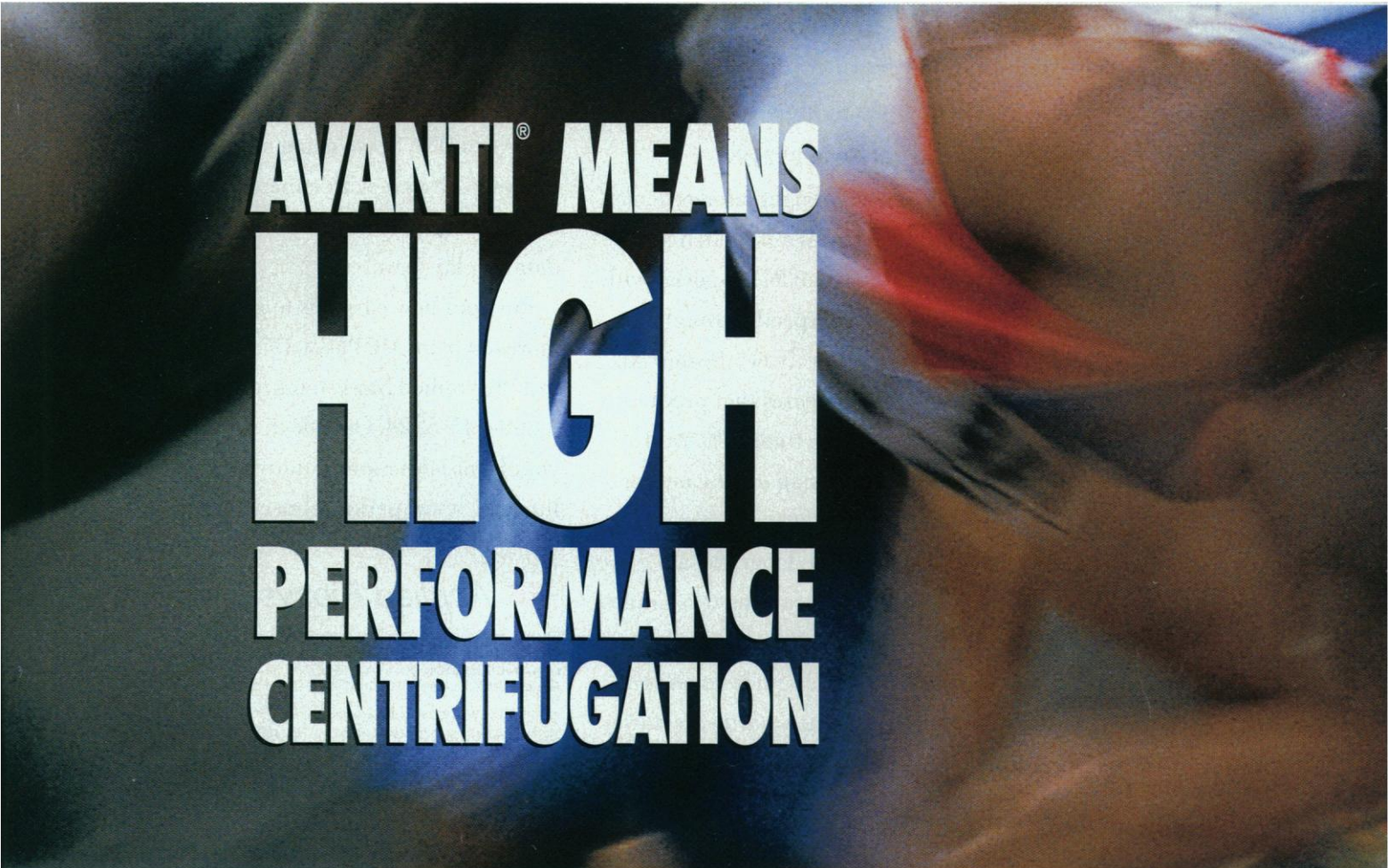


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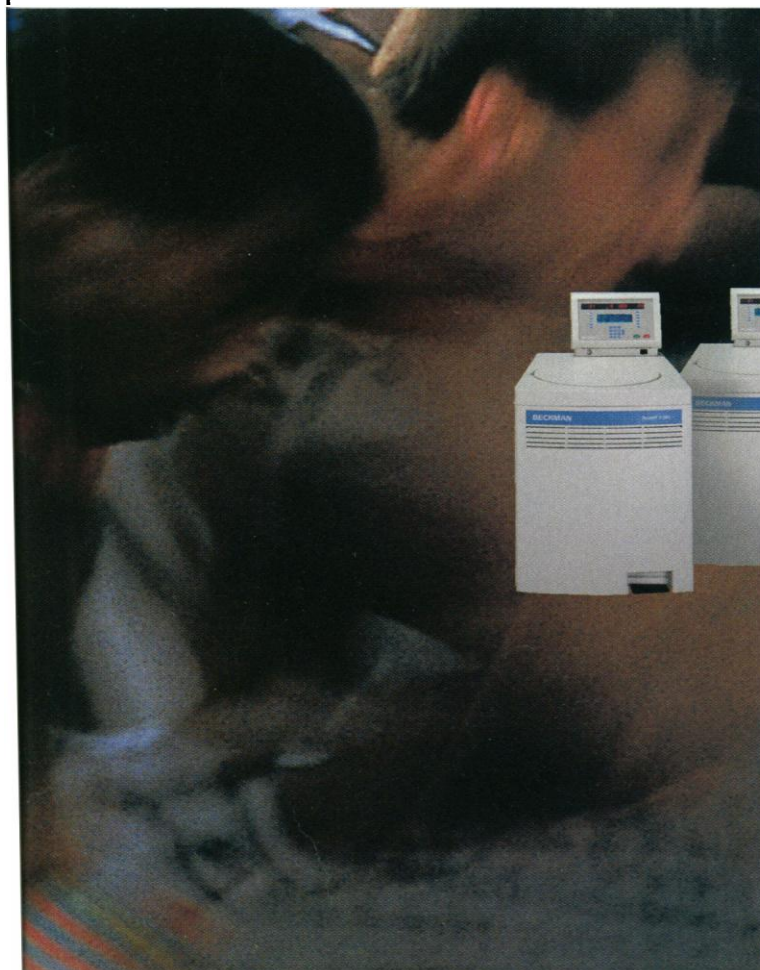
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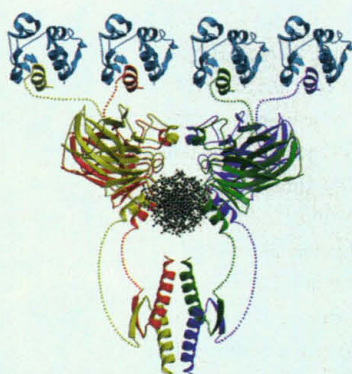
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916

Not an ecological desert



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p53 and its molecular  
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## COVER

Sites of production and storage of human immunodeficiency virus (HIV) in lymphoid tissue, reconstructed in three dimensions from images of HIV RNA in 66 tissue sections. Red-colored infected cells surround, or are enmeshed, in a yellowish cloud representing viral par-

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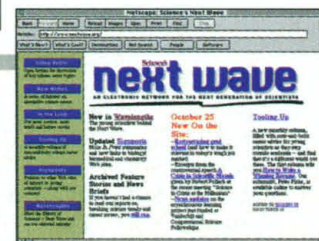
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# THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

## Tighter orbits

The detection of Jupiter-sized planets orbiting very close to a central star in other solar systems has sparked a flurry of modeling to explain how a planet could have evolved to such a tight yet apparently stable orbit. Rasio and Ford (p. 954) present the results of simulations that start with two Jupiter-sized planets orbiting far from the central star. They find that in some cases one planet will be ejected from the system while the other planet will decrease and circularize its orbit by tidal dissipation.

## Inner core convection

Seismic observations have indicated that sound waves travel faster through the inner core if they travel along a path parallel to the rotation axis of the Earth. The reason for this inner core anisotropy remains a mystery. Romanowicz *et al.* (p. 963) used compressional wave velocities and free oscillations at the Earth's surface that are sensitive to the structure of the inner core to derive a model for the inner core anisotropy. They suggest that large-scale convection cells may be producing the anisotropy.

## Soft landings

One approach for constructing nanoscale structures would be to deposit them onto surfaces from the gas phase. However, the impact with the surface may fragment the deposited structures into smaller species and may damage the surface. Bromann *et al.* (p. 956) used variable-temperature scanning tunneling microscopy to study the effects of impact energy on

## Thermally activated optical switches

Just as the arrangement of atoms in a crystal scatters x-rays, larger colloidal particles in a crystalline array can scatter visible light. Weissman *et al.* (p. 959) have developed polymeric colloidal arrays whose periodicity responds to changes in temperature. In one case, the degree of ordering, and hence scattering efficiency, was changed, and in another the periodicity, and hence the scattering wavelength, was changed. Such materials could find use as tunable optical filters.

the deposition of silver clusters on a platinum surface and looked at ways to minimize destructive effects. Fragmentation and substrate damage occurred at impact energies above 1 electron volt, but clusters with higher impact energies could be adsorbed intact if a buffer layer of argon, an inert gas, was adsorbed first. The buffer layer efficiently transferred kinetic energy from the hot cluster before it could fragment.

## Molecular motion

Imaging single molecules often requires immobilizing the molecules in solids or at surfaces or at low temperatures to slow down molecular motion. Application of such methods to biological molecules, however, would require imaging in aqueous solution if the results are to be meaningful. Dickson *et al.* (p. 966) used the water-filled pores present in a polyacrylamide gel, whose pore size can be tuned by changing the concentration of the gel, to restrict the Brownian motion of molecules. Laser excitation was performed in a thin plane so that the lateral motion of a molecule could be followed for about 1 second. For example, a dye molecule, Nile Red, could be imaged in a gel with 2-nanometer pores. Larger molecules, such as fluorescently tagged

antibodies, were imaged in the same manner by using less concentrated gels with larger pores.

## Form and function

The visual systems of the *Xenopus* tadpole process information even as they continue through development. Neurons in the tadpole's optic tectum represent a range of developmental maturation states. Wu *et al.* (p. 972), after analyzing the synaptic transmission characteristics of these neurons, suggest that function directs concurrent development. Immature neurons can signal with *N*-methyl-D-aspartate but do not contribute to functional visual processing. With maturity, promoted by feedback signaling from an active synapse, comes the shift to signaling with  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid in a manner that contributes to visual processing.

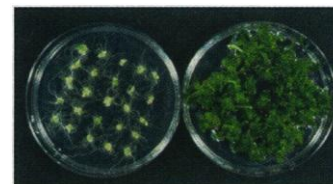
## HIV-1 reservoirs

Human immunodeficiency virus-type 1 is produced and persists in lymphoid tissue, but quantitating the viral burden in these organs is much more difficult than doing so for a blood sample. Haase *et al.* (p. 985; see cover) used *in situ* RNA hybridization and image

analysis to analyze HIV-1 load of several presymptomatic individuals, most of whom were receiving antiretroviral therapies. Large, stable pools of virus were found in follicular dendritic cells that were 100 to 10,000 times greater in number than those found in plasma. Such analysis will allow monitoring of the effects of therapies on overall viral burden.

## Plant signals

The hormone cytokinin regulates a variety of aspects of plant growth and physiology. Kikimoto (p. 983) identified a gene affected in cytokinin-indepen-



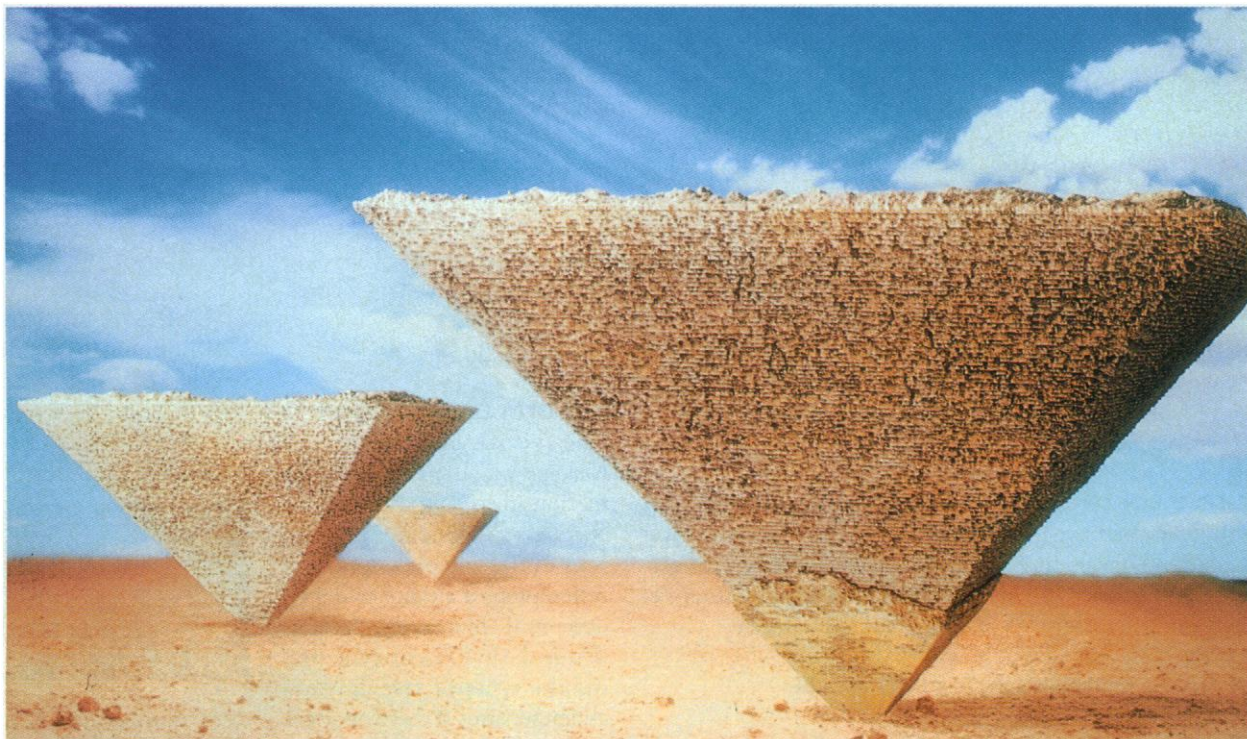
dent mutants of *Arabidopsis*. The gene *CK11* encodes a protein similar to those in the two-component signal transduction systems of bacteria that may act in cytokinin recognition or regulation.

## Clean capture

Many studies in cell biology and biomedicine require the isolation of specific cell populations from heterogeneous tissue sections. Emmert-Buck *et al.* (p. 998) developed a rapid one-step method for this purpose. In laser capture microdissection, a focused laser beam is used to transfer cells of interest within a microscopic field to a thermoplastic film. The cellular material is then readily removed from the film and can be subjected to standard nucleic acid and enzyme assays.



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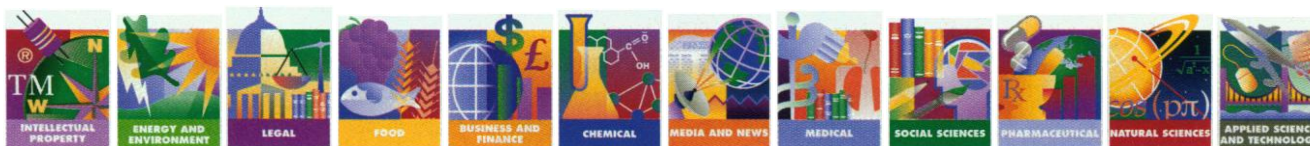
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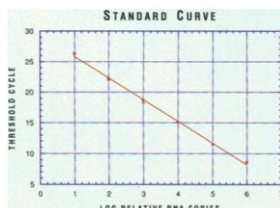
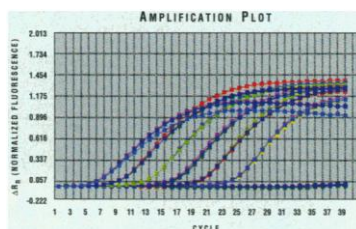
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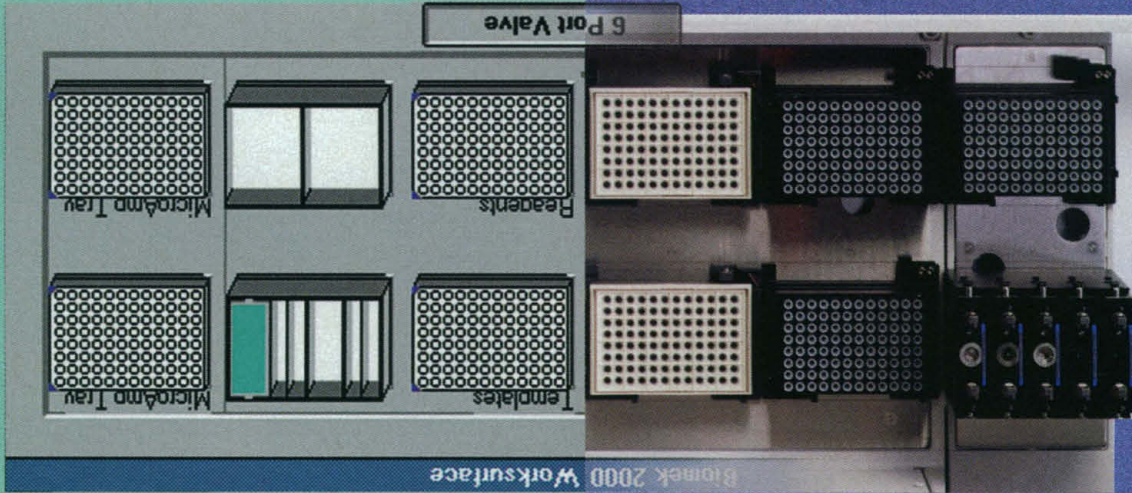
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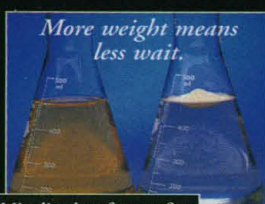


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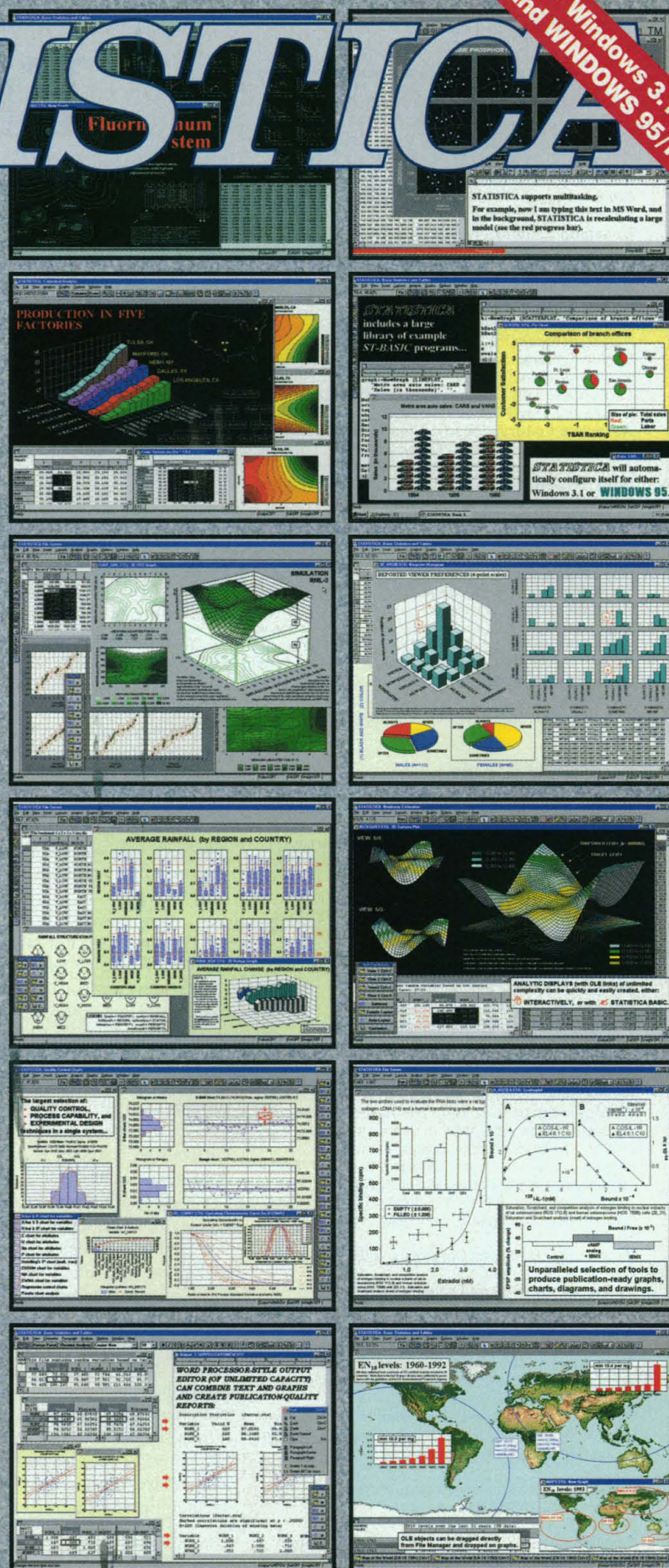


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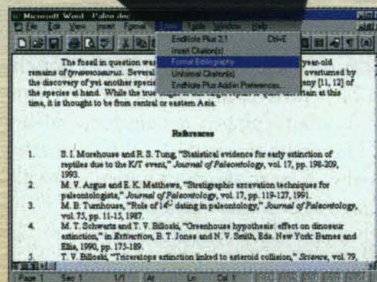
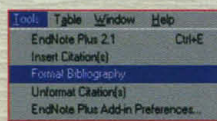
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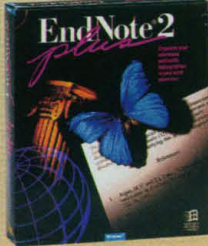
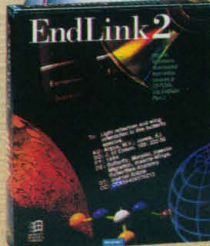
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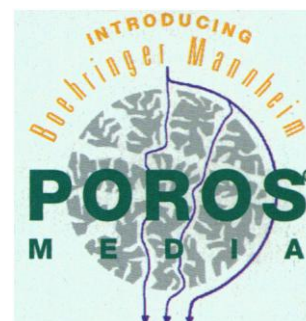
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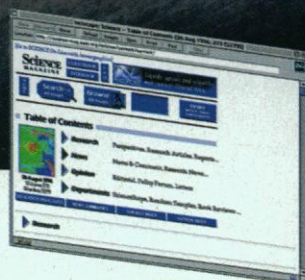
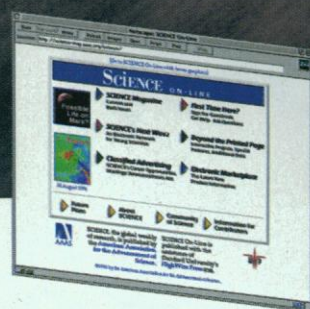


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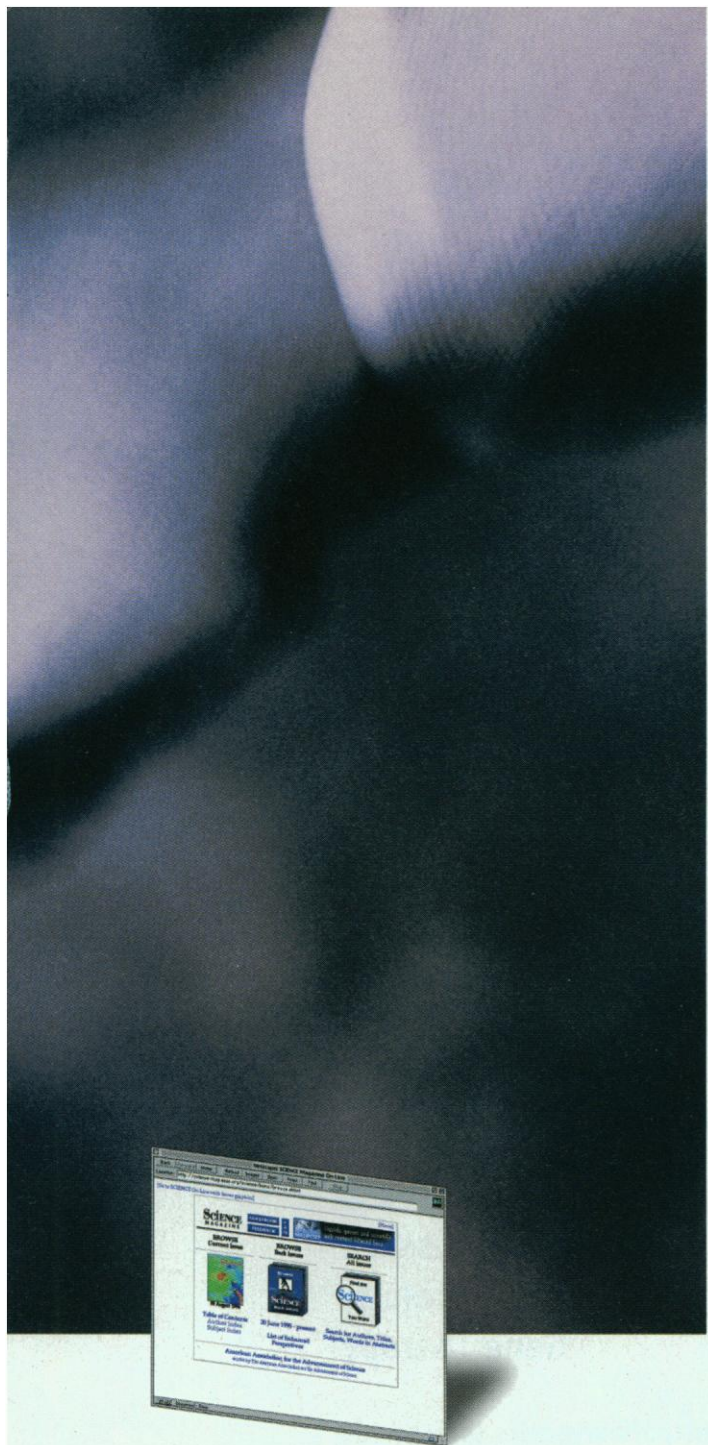


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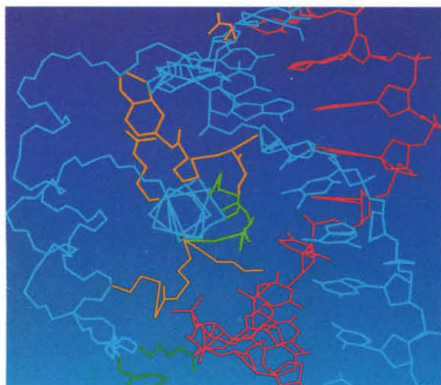


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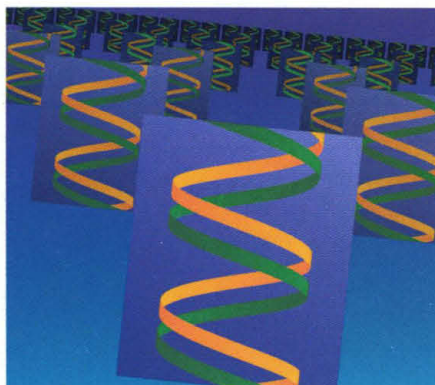
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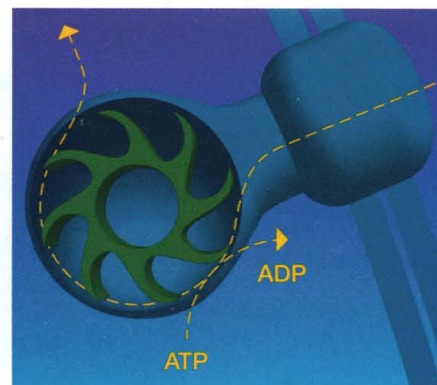
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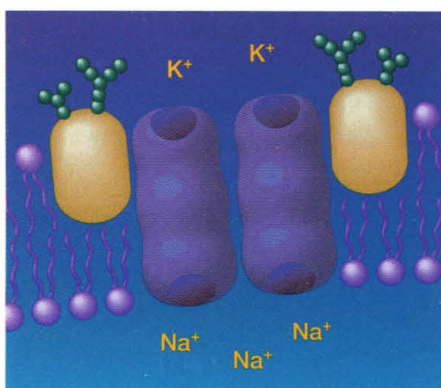
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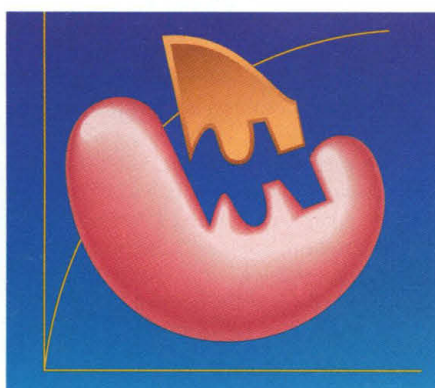
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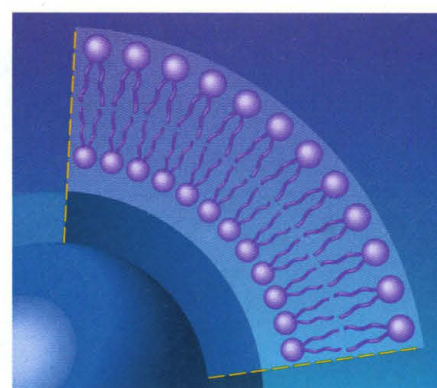
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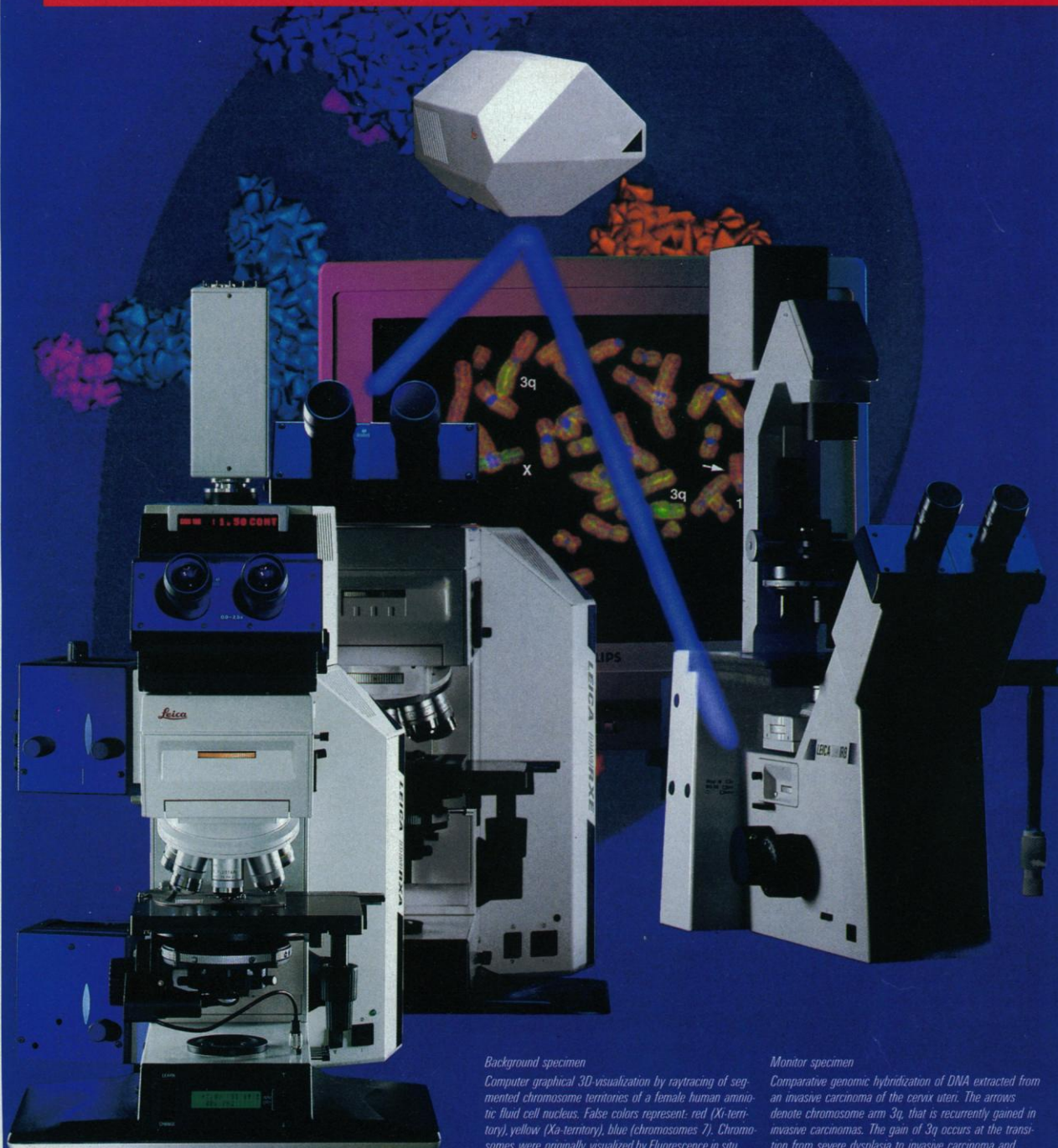
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Courtesy of R. Eils, S. Dietzel, E. Schröck, T. Cremer.

#### Monitor specimen

Comparative genomic hybridization of DNA extracted from an invasive carcinoma of the cervix uteri. The arrows denote chromosome arm 3q, that is recurrently gained in invasive carcinomas. The gain of 3q occurs at the transition from severe dysplasia to invasive carcinoma and serves as a genetic marker of tumor progression.

Courtesy of E. Schröck and T. Ried, National Center for Human Genome Research/NIH.

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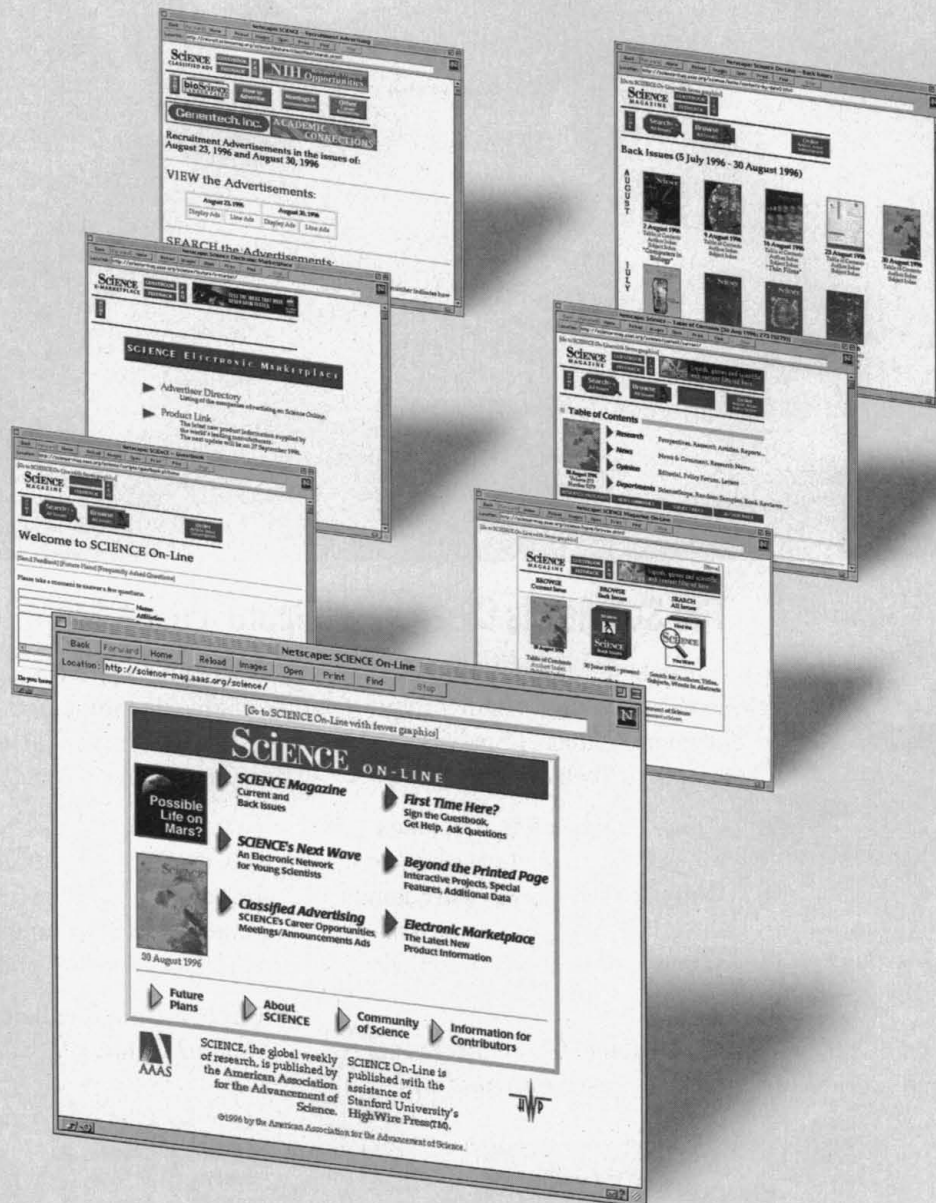


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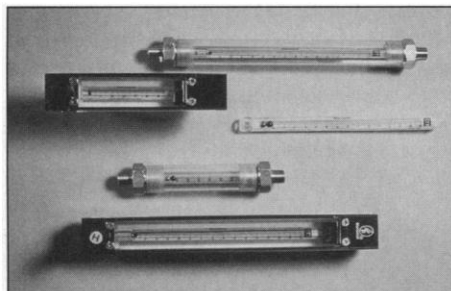
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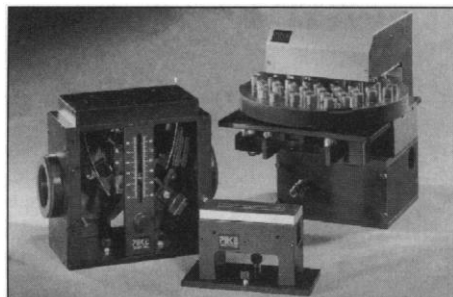
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Numerous enzymes are available for research on the extracellular matrix. These enzymes degrade histological barriers such as the basement membrane, basal laminae, and interstitial stroma that are made up of collagen, non-collagenous glycoproteins, and proteoglycans. The collection includes high purity collagenases, leukocyte elastases, dispase, hyaluronidase, tissue plasminogen activator, and cath-  
**epsin G. Sigma Chemical. Circle 146.**

### Pure Organelles Isolator

The Dynabeads M-500 Subcellular product for direct magnetic immuno-isolation of pure subcellular organelles from crude cellular fractions rapidly isolates more than 99% of target organelles without inefficient and labor-intensive density gradient centrifugation. In addition, the technique can isolate pure target organelles from a cellular fraction of common density. Dynabeads M-500 subcellular product is composed of specially designed, smooth-surfaced superparamagnetic polystyrene beads that can be easily coated with antibodies specific for the user's target organelle. Organelles isolated using the Dynabeads can be assayed by all conventional techniques including chemical, radiolabeling, enzyme immunoassays,

or SDS-polyacrylamide gel electrophoresis analysis. Target organelles can also be fixed for electron microscopy. **Dynal. Circle 147.**

### Literature

*Update* is a newsletter that provides information on Perkin-Elmer's atomic absorption (AA), inductively coupled plasma optical emission spectroscopy (ICP-OES), and ICP mass spectrometry products. Among other articles, the premiere issue introduces AA WinLab and ICP WinLab software and the Optima 3000 SC ICP-OES. **Perkin-Elmer. Circle 148.**

*Peptide Analysis by Capillary Electrophoresis-Mass Spectrometry* is an application note on analysis of a standard peptide mixture. *Protein Digest Analysis using a Nanobore HPLC-Nanoflow Electrospray Interface* is an application note on high-performance liquid chromatography. **Micromass. Circle 149.**

*AstroDAQ Data Acquisition System* is a brochure on a complete system for acquiring, conditioning, and analyzing up to 30 channels of data. The user can select from a wide range of interchangeable signal input modules for voltage, current, strain, bridge, temperature, pressure, and more. **Astro-Med. Circle 150.**

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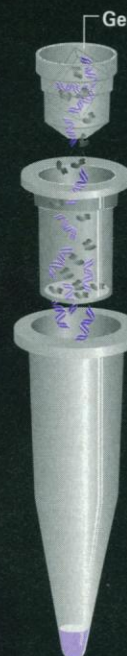
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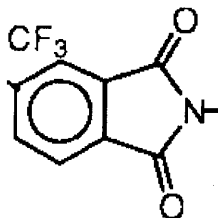
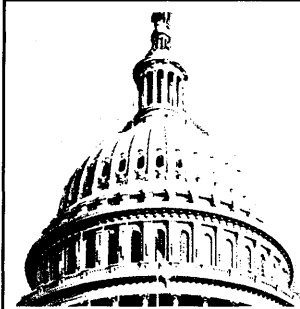
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1997-98

## AAAS FELLOWSHIPS FOR SCIENTISTS AND ENGINEERS

**A**pplicants must have a Ph.D. or equivalent doctoral level degree at the time of application (January 1997). Persons with a master's degree in engineering and at least three years of post-degree experience may also apply. All applicants must be U.S. citizens. The programs are designed to provide each

Fellow with a unique public policy learning experience; to make practical contributions to the more effective use of scientific and technical knowledge in the U.S. government; and to demonstrate the value of science and technology in solving important societal problems. All

Fellows participate in a rigorous orientation on the relevant congressional and executive branch operations and foreign affairs plus a year-long seminar series on issues involving science, technology, and public policy. The Congressional, Diplomacy, Risk Assessment, and Technology Policy programs begin in September 1997, and the summer Environmental program begins in June 1997. All grant-funded programs are subject to continued support.

**All applications must be post-marked by January 15, 1997.**

For additional information and application instructions, write:  
AAAS Fellowship Programs  
1200 New York Avenue, NW  
Washington, DC 20005  
202/326-6600 Fax: 202/289-4950  
Internet: [science\\_policy@aaas.org](mailto:science_policy@aaas.org)  
Minorities and persons with disabilities are especially encouraged to apply.

### CONGRESSIONAL

#### AAAS CONGRESSIONAL SCIENCE & ENGINEERING FELLOWS PROGRAM

Fellows spend one year on Capitol Hill working with Members of Congress or congressional committees as special assistants in legislative and policy areas requiring scientific and technical input. Two fellowships will be offered, with annual stipends of \$43,000.

### DIPLOMACY

#### AAAS SCIENCE, ENGINEERING, & DIPLOMACY FELLOWS PROGRAM

Fellows work in international affairs on scientific and technical subjects for one year, either in foreign policy at the U.S. Department of State or in international development for the U.S. Agency for International Development. One Fellow will be selected at State and approximately twelve Fellows will be selected at USAID. The annual stipend varies with experience, starting at approximately \$46,000.

### RISK ASSESSMENT

#### AAAS RISK ASSESSMENT SCIENCE & ENGINEERING FELLOWS PROGRAM

Fellows work for one year at either the U.S. Environmental Protection Agency or the U.S. Department of Agriculture as special research consultants, assessing the significance of environmental and/or human health problems through application of risk assessment. Five fellowships will be offered at EPA and at least one at USDA. The annual stipend will be \$41,000.

### TECHNOLOGY POLICY

#### AAAS/CTI SCIENCE & ENGINEERING FELLOWS PROGRAM

Fellows spend one year working at the RAND Critical Technologies Institute, providing expertise in research and development, technology transfer, international competitiveness, and related issues. At least one Fellow will be selected. Applicants must have a minimum of five years industrial experience, as midlevel or senior executives. Stipends are negotiable, depending on qualifications and experience.

### ENVIRONMENTAL

#### AAAS/EPA ENVIRONMENTAL SCIENCE & ENGINEERING FELLOWS PROGRAM

Fellows work for one year as special research consultants with the U.S. Environmental Protection Agency for ten weeks in the summer. The detailed, future-oriented research assists EPA in assessing the significance of long-range environmental problems. Ten fellowships will be offered with a weekly stipend of \$950.

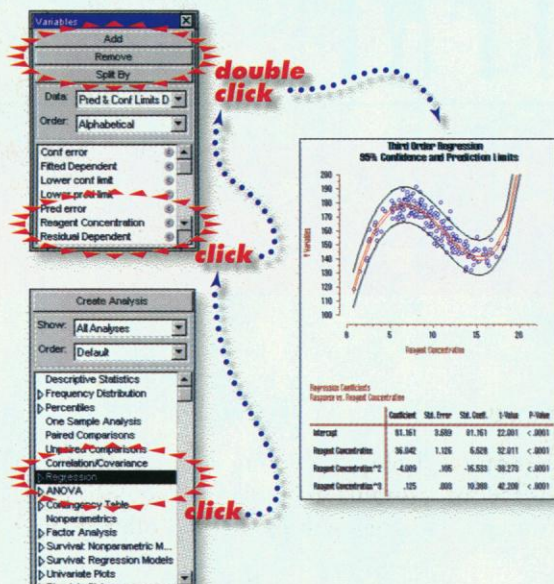


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Wang, X, et al. Matrix metalloproteinase inhibitor BB-94 inhibits human colon tumor growth and spread in a patient like orthotopic model in nude mice. *Cancer Res.* 54, 4726-28 1994

Hoffman, R., Orthotopic is orthodox: why orthotopic transplant metastatic models are different from all other models? *J. Cellular Biochem.* 56, 1-4, 1994

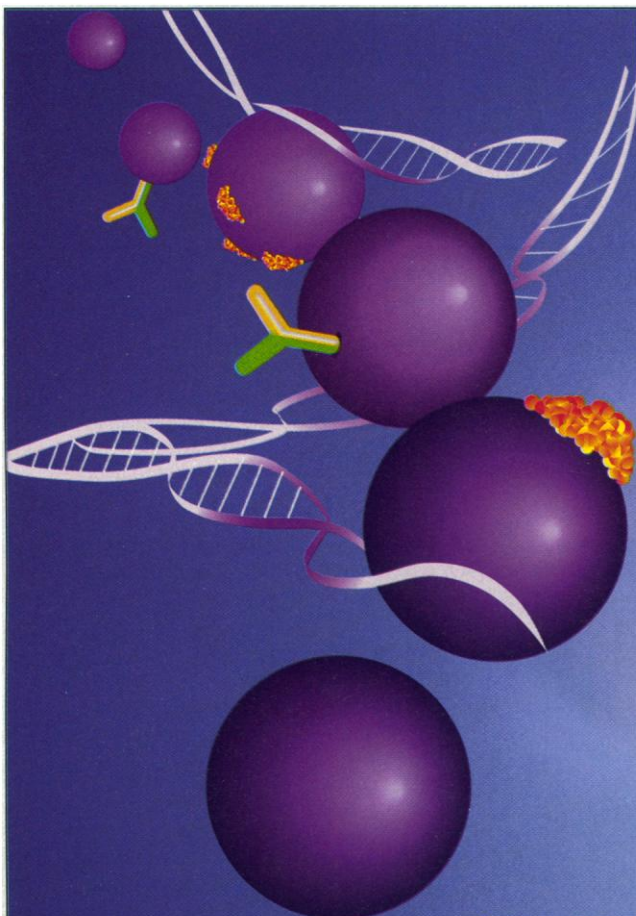


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# Research Opportunities

Headquartered in a new 66,000 square foot, state of the art research facility in the San Francisco Bay Area, **Tularik Inc.** is a privately held biotechnology company focused on the discovery and development of novel small molecule drugs that act through the regulation of gene expression. Tularik has projects in the areas of viral diseases, inflammation, hypercholesterolemia, immune disorders, obesity and bacterial diseases. Tularik's continued growth and outstanding research culture have created a rare opportunity for a handful of dedicated scientists to help us shape the future of human therapeutics.

**SCIENTIST Molecular Virology** • We're looking for a creative molecular Virologist to join our viral diseases project team. The successful candidate will have a strong background in herpesvirus genetics and a strong desire to discover drugs that inhibit CMV and HSV by novel mechanisms. This position requires a Ph.D. and at least two years of postdoctoral experience.

**SCIENTIST Bacterial Genetics** • We also seek an innovative Bacterial Geneticist to join our bacterial diseases project. The successful candidate will be responsible for identifying novel antibacterial targets and designing high throughput assays to discover compounds that modulate their activity. This position requires a Ph.D. and at least two years of postdoctoral experience.

**SCIENTIST Medicinal Chemistry** • This position requires a Ph.D. in synthetic organic chemistry with a minimum of two years of postdoctoral work. Candidates with experience in the pharmaceutical industry and an interest in either medicinal or combinatorial chemistry are strongly encouraged to apply.

**SCIENTIST Obesity** • This position requires a Ph.D. with postdoctoral experience in molecular biology and biochemistry. A background in the area of nuclear hormone receptors, adipocyte biology or regulation of energy homeostasis is advantageous. The successful candidate will play a key role in Tularik's cell-based and biochemical anti-obesity drug discovery screening program.

**SCIENTIST Pharmacology** • We are looking for an experienced pharmacologist to join our growing preclinical development group. This position requires a Ph.D. in pharmacology and a minimum of 5 years of industry experience. The successful candidate will have experience in designing and implementing animal experiments relevant to cancer, inflammation and infectious diseases.

**SENIOR RESEARCH ASSOCIATE Screening Automation** • A B.S. or M.S. in a relevant discipline is required. Essential for this position is extensive professional experience in automation, high throughput screening and biochemical assay development. The successful candidate will be responsible for implementation and operation of robotic systems for novel drug discovery assays.

**RESEARCH ASSISTANT Biochemistry, Molecular Biology and Cell Biology** • Our molecular biology and cell biology groups have openings for individuals to work on the identification of new drug targets or the development and operation of novel high throughput screens. The successful candidate will have a B.S. or M.S. in molecular biology, biochemistry or a related field, with at least two years of relevant laboratory experience.

**RESEARCH ASSISTANT Medicinal Chemistry** • This position requires a B.S. or M.S. degree in chemistry with at least two years of practical experience in organic synthesis and a high level of proficiency in standard laboratory, modern analytical and spectroscopic techniques.

**POSTDOCTORAL FELLOW Immune Regulation & Hypercholesterolemia** • The Tularik postdoctoral program provides outstanding opportunities to perform exciting, publishable science that is focused on drug discovery. We currently have postdoctoral openings in our Immune Regulation & Hypercholesterolemia programs for Ph.D.s in biochemistry or molecular biology. These scientists will work on identifying novel proteins involved in gene regulatory pathways. One researcher, in the laboratory of Dr. Tim Hoey, will investigate mechanisms of signal transduction and transcriptional regulation of the immune response. A second postdoctoral scientist, in the laboratory of Dr. Bei Shan, will study gene regulation as it relates to cholesterol homeostasis.

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