



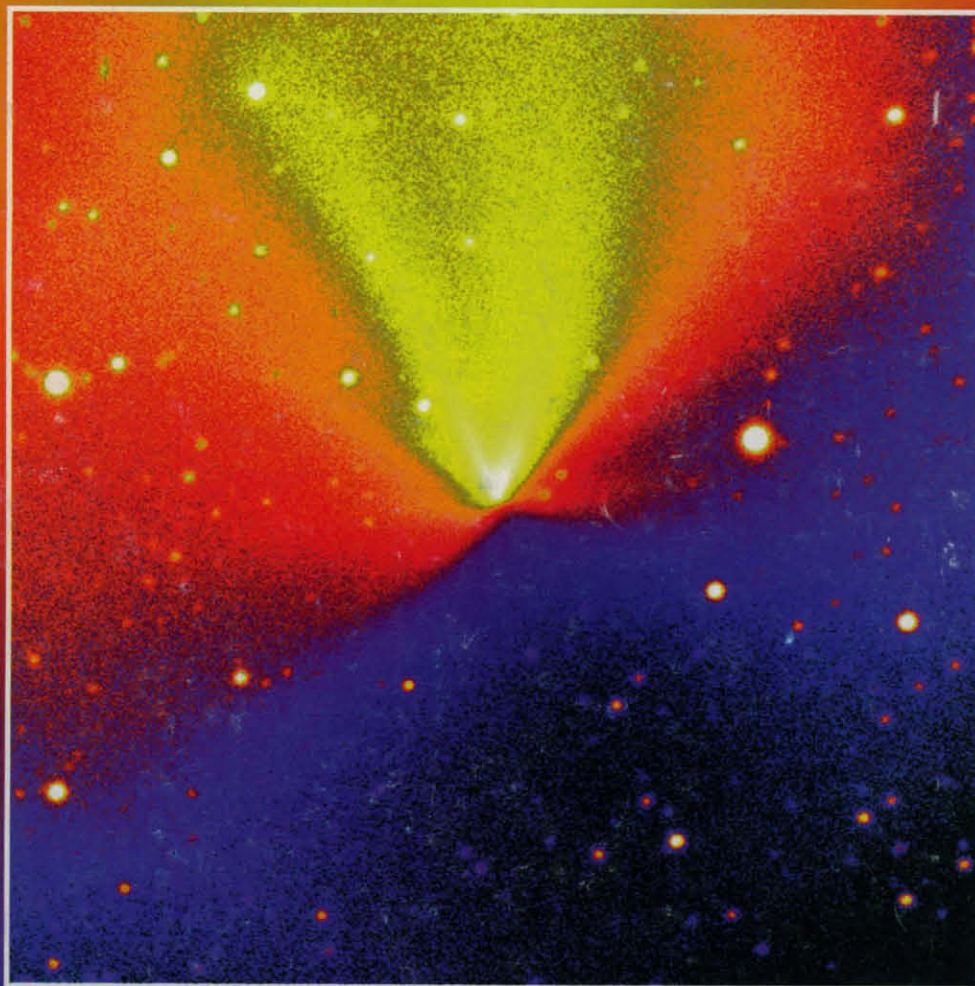
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Comet Hale-Bopp
Before
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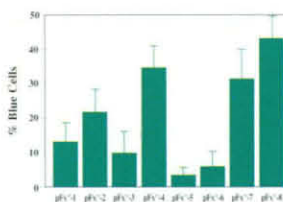


Figure 1: Percent blue cells produced by transfection of CHO cells with a lacZ control vector using PerFect Lipids™ (pFx™ 1 - pFx™ 8).

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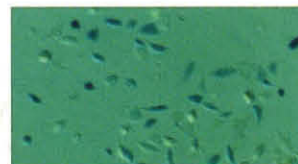


Figure 2: Transfected CHO cells expressing β -galactosidase, stained with X-gal.

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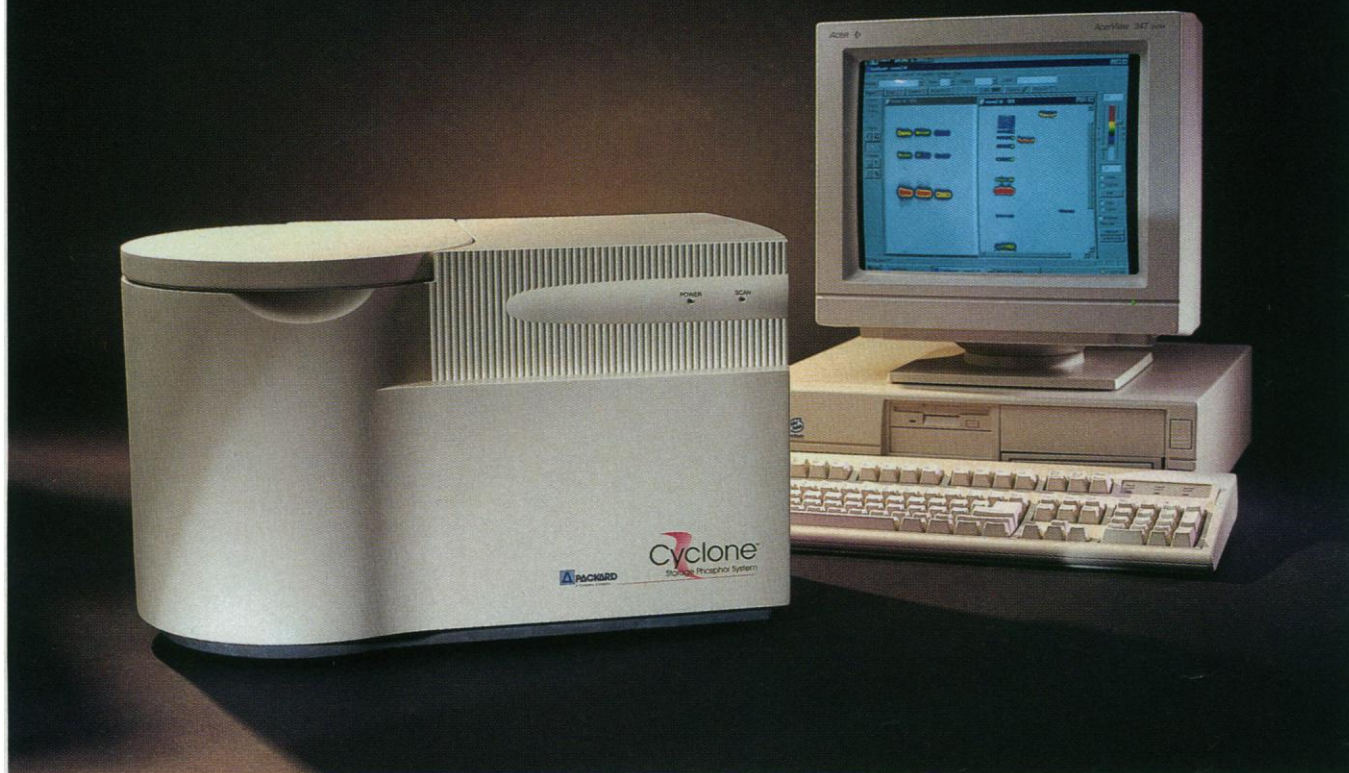
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Terri Davis is a cellular
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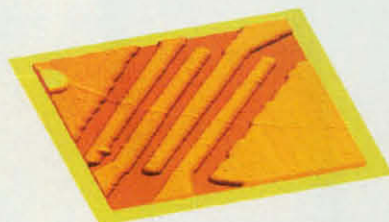
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**1896 &
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- COMET HALE-BOPP** 1900
The Activity and Size of the Nucleus of Comet Hale-Bopp (C/1995 O1)
H. A. Weaver, P. D. Feldman, M. F. A'Hearn, C. Arpigny, J. C. Brandt, M. C. Festou, M. Haken, J. B. McPhate, S. A. Stern, G. P. Tozzi

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COVER

Comet Hale-Bopp on 20 August 1996 observed from the European Southern Observatory, Chile, during the monitoring campaign to study the evolution of its activity. The image was taken through an *R*-filter (wavelength 530 to 950 nanometers) (exposure time of 15 seconds),

and the jet structures have been enhanced. North is at the top, and the field of view is 3.4 arc minutes. See the related papers beginning on page 1900 and the Perspective on page 1895. [Image: H. Boehnhardt, M. Küppers, H. Rauer, K. Rembor, N. Thomas]



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1876 & 1943

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Electron transport in nanotubes

Single electrons represent the ultimate "bit" in computing, and much effort has been devoted to creating structures whose conductance varies for changes in charging of only one electron. Bockrath *et al.* (p. 1922; see the Perspective by Kouwenhoven, p. 1896) measured the transport properties of bundles, or "ropes," of highly ordered single-walled carbon nanotubes that were lithographically attached to metal contacts separated by 200 to 500 nanometers. At temperatures at or below 10 kelvin, there is a region of suppressed conductance for low bias voltages. Large peaks are observed in the conductance as the number of electrons in the bundle changed with changes in a bias voltage. Resonant tunneling of single electrons through individual nanotubes appears to account for these results.

Gut (immune) reaction

The gut is not only the main site of exposure to pathogens, as a mucosal surface it is also a weak barrier to pathogen entry. Wang *et al.* (p. 1937; see the Perspective by Shanahan, p. 1897) add a new component to the known complexity and flexibility of intestinal immune defense. They describe a regulatory interaction between the intestinal epithelial cells and neighboring lymphocytes, mediated by neuroendocrine hormones of the hypothalamus-pituitary-thyroid axis. In the absence of a component of the network, the range of T cell types in the intestinal, but not peripheral, immune system is reduced. The network may be

Comet Hale-Bopp: The shape of things to come

A series of reports focus on comet Hale-Bopp, including its extreme brightness, its increasing activity, and its flair for variable, dusty outbursts as it approaches the sun (see the Perspective by Cruikshank, p. 1895). Detailed images from the Hubble Space Telescope (Weaver *et al.*, p. 1900) indicate that the comet nucleus is very large (between 27 to 42 kilometers in diameter). Thermal infrared observations from the Earth-orbiting Infrared Satellite Observatory (Crovisier *et al.*, p. 1904) and ground-based telescopes (Hayward and Hanner, p. 1907) indicate that the dust grains coming off the nucleus as the comet moved inside of Mars' orbit are probably crystalline and amorphous silicates. Optical observations (Rauer *et al.*, p. 1909, see cover, and Wagner and Schleicher, p. 1918) showed high rates of sublimation of icy, dust grains, dominated by water and cyanide even at large distances from the sun. Photometric observations (Schleicher *et al.*, p. 1913) also indicated that the gas production rates are 20 to 100 times greater than any other comet at any other observed distance. Radio observations (Biver *et al.*, p. 1915) tracked the rates and temporal changes in the gaseous release of molecules as Hale-Bopp approaches the sun and changes from sublimation of its dusty tail to sublimation of its nucleus. Cometary scientists have begun deciphering how this comet physically jets, spins, and chemically differentiates over an unusually long period of observations.

important in gut T cell development findings; it also suggests highly flexible and localized control of immune activity, an important property given the function of the gut.

Brain cancer gene

Glioblastoma is the most lethal form of human brain cancer, yet little is known about its molecular pathogenesis. Li *et al.* (p. 1943; see the news story by Pennisi, p. 1876) have identified a candidate tumor suppressor gene, *PTEN*, that is mutated in about one-third of the glioblastoma cell lines, xenografts, and primary tumors they tested. The *PTEN* protein has sequence homologies to protein tyrosine phosphatases and to tensin, a protein that binds actin filaments at sites of cell surface signaling. Mutations in *PTEN* were also de-

tected at lower frequency in prostate and breast cancer samples.

Getting a GRP

Phosphoinositide (PI) 3-kinases are activated in response to many receptors on the cell surface. The enzyme catalyzes the formation of phosphatidylinositol-3,4,5-trisphosphate [PtdIns(3,4,5)P₃], but subsequent steps in signaling through this pathway have been unclear. Klarlund *et al.* (p. 1927; see the Perspective by Hemmings, p. 1899) identified a protein they call GRP1 that binds to PtdIns(3,4,5)P₃. GRP1 appears to interact with other proteins that mediate the cellular effects of PI 3-kinase. GRP1 may control cell adhesion through interaction with integrins, and interaction of GRP1 with the guanosine tri-

phosphatase ARF may allow regulation of protein sorting and membrane trafficking.

Out of the nucleus

Gene transcription critical for the immune response is regulated by the transcription factor NF-AT. Calcium-dependent dephosphorylation of NF-AT leads to import of the transcription factor into the nucleus. Beals *et al.* (p. 1930) describe another layer of regulation of NF-AT. In this case, NF-AT is phosphorylated by the protein kinase glycogen synthase kinase-3 (GSK-3) and is exported. In this way, GSK-3 opposes the calcium-dependent activation of NF-AT. The effects of GSK-3 in control of pattern formation during development may result, at least in part, from regulation of NF-AT.

Evolving rapidly

How quickly can evolution occur in nature? Reznick *et al.* (p. 1934; see the news story by Morrell, p. 1880) transferred populations of guppies from high-predation environments to new locations, such as upstream of waterfalls, that were



inaccessible to predators. Monitoring life history characters such as body size revealed rapid short-term changes, illustrating that evolution can happen quickly in nature, even outside the framework of human-induced environmental change.



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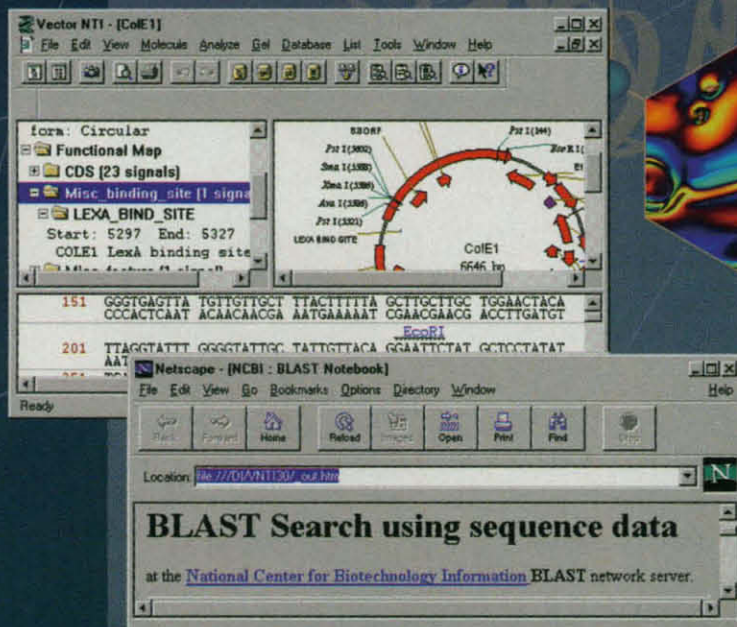
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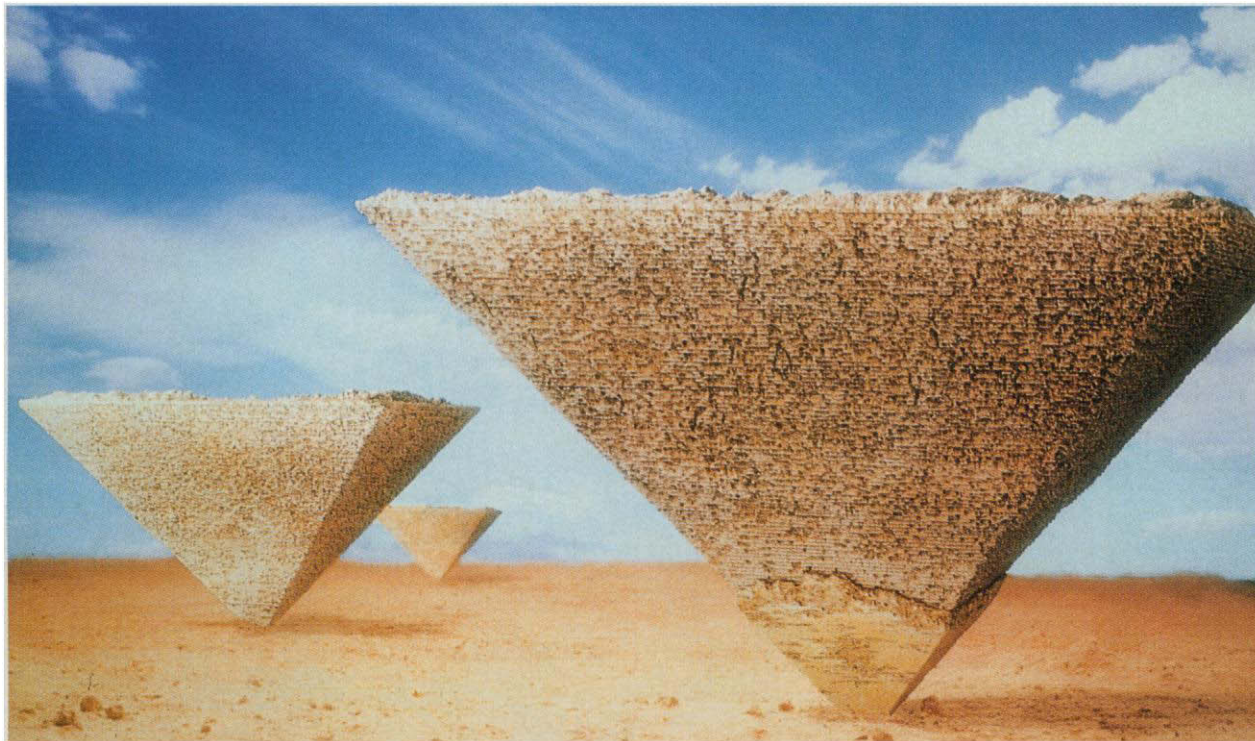
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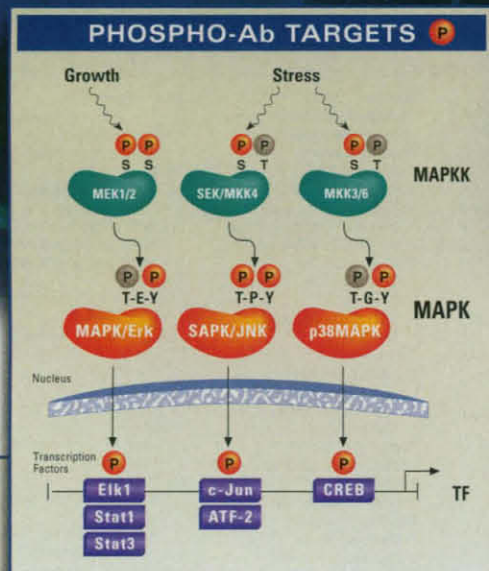
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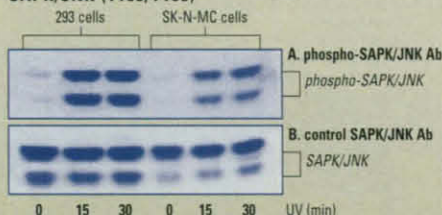
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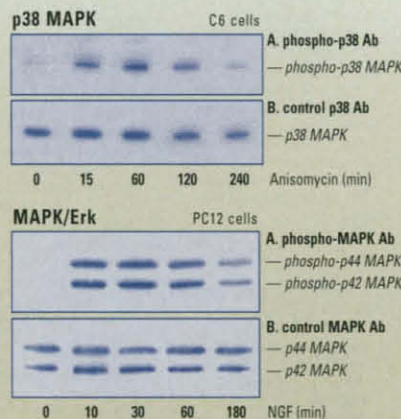
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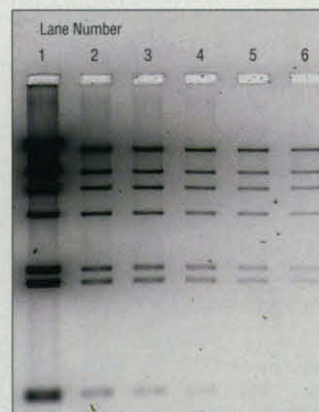
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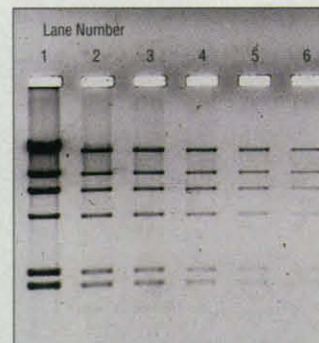
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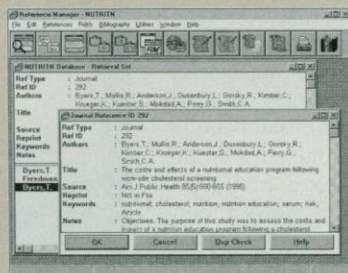
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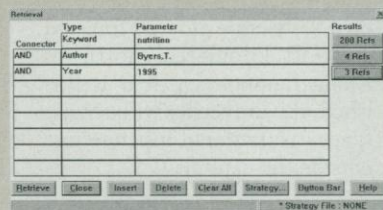
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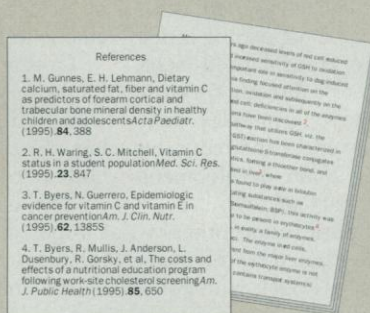
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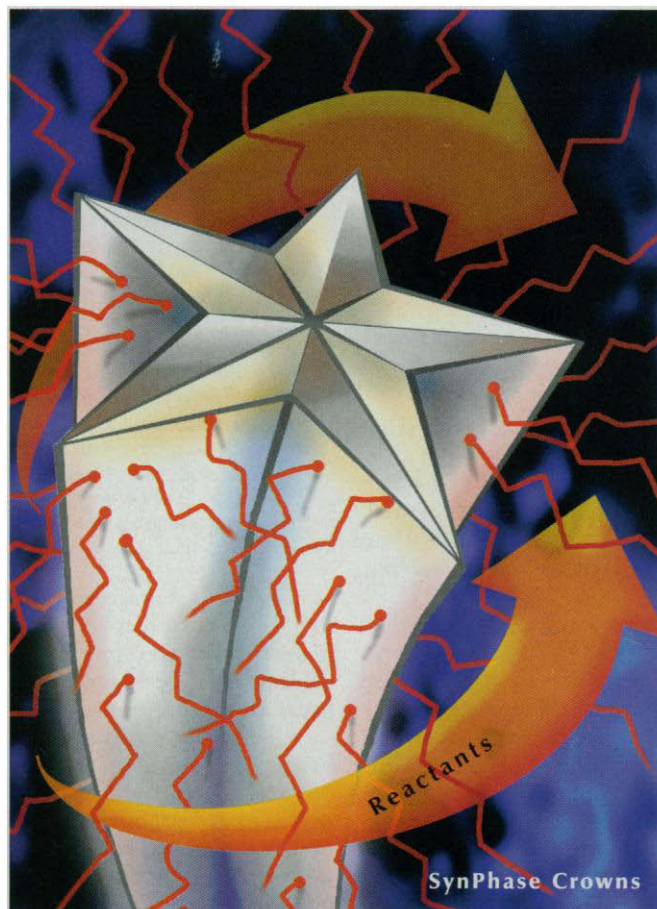
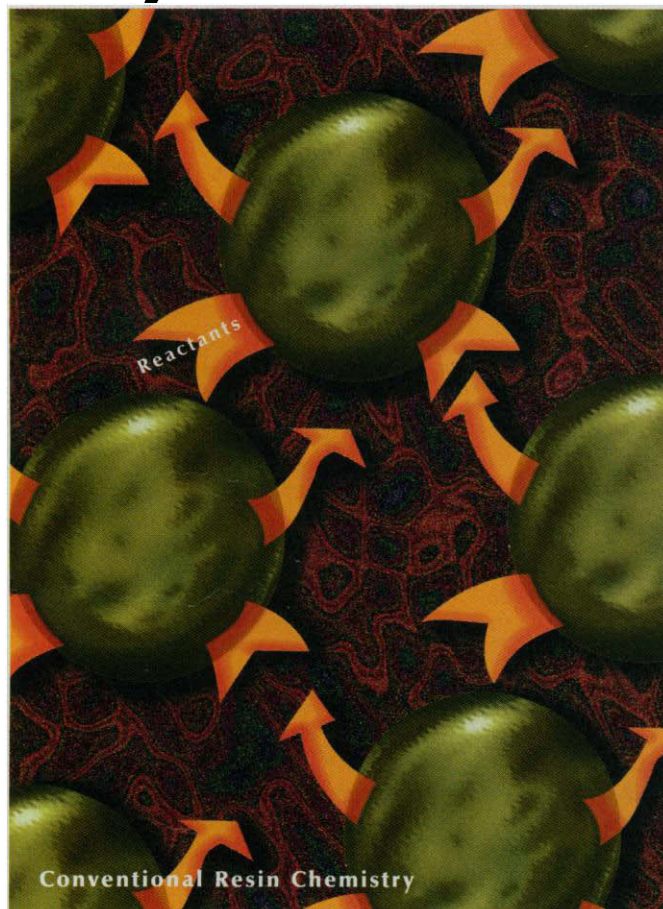
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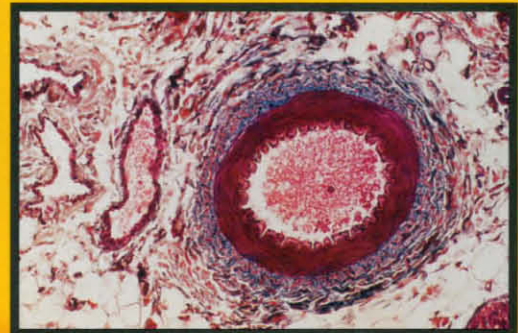
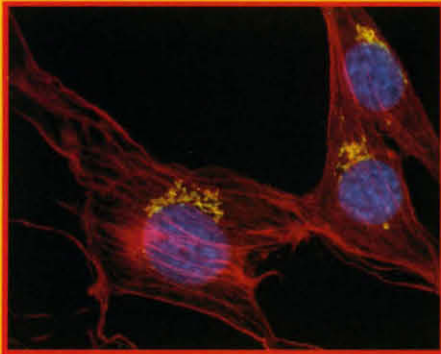
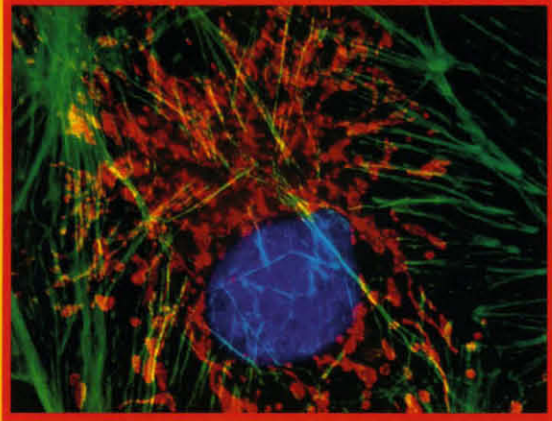
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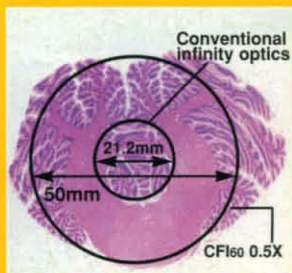
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**Until Nikon redefined infinity,
no infinity optical system
could do all this.**



The Eclipse E800™ with CFI60™ optics redefines research microscopy.

Infinity optics took a quantum leap with Nikon's revolutionary, new CFI60™ technology. Longer working distances, higher numerical apertures and the widest magnification range and documentation field sizes ever achieved through infinity optics give you brilliant images of breathtaking sharpness and clarity, from ultra-low to the highest magnifications.



The new performance standard for every research application.

With Nikon's recent introduction of the Eclipse E800™ and E800M™ microscopes,

you have all the advantages of infinity optics without the limitations of conventional infinity systems. For example, the E800M's exclusive 0.5X objective lets you quickly and easily produce 1:1 specimen documentation while still being able to insert a wide variety of accessories directly into the optical path.

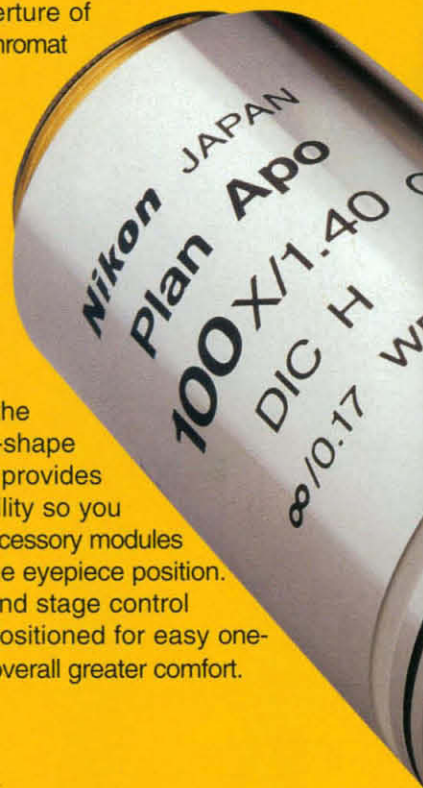


The E800 Micro/Macro System.

You can easily examine even the thickest specimens. The E800's expanded parfocal length of 60mm, increased objective diameter and optimum 200mm focal length tube lens provide you with a working distance up to 210µm at the maximum numerical aperture of 1.4, as with our Plan Apochromat 60X oil objective.

Exceptional ergonomics as well as superb optics.

The Eclipse E800 and E800M offer a full range of exclusive ergonomic features. With the widest base and arm dimensions in the industry and a unique T-shape configuration, the stand provides incomparable stability so you can add different accessory modules without affecting the eyepiece position. In addition, focus and stage control knobs are carefully positioned for easy one-hand operation and overall greater comfort.



The redefinition continues...

Compare the advantages of the Eclipse Series with other infinity microscopes.

Outstanding Optics

	<u>CFI60</u>	<u>Others</u>
Largest magnification range for both observation and documentation.	Yes	No
Highest numerical apertures and longest working distances for sharper images and thicker specimens.	Yes	No
60mm infinity objective design for superior performance characteristics.	Yes	No
CFI chromatic aberration corrected infinity objectives.	Yes	No
Widest viewfield at 1X for maximum specimen viewing area.	Yes	No
Plan Fluor objectives with the brightest UV transmission for superior fluorescence.	Yes	No
60X Plan Fluor 0.85 dry and 60X Plan Apo 0.95 dry.	Yes	No
"Fast focus" correction collar design with minimum focus shift for easy use.	Yes	No

Superior Epi-Fluorescence

	<u>Eclipse</u>	<u>Others</u>
4 filter cube linear slider for fastest switching between wavelengths.	Yes	No
Front-mounted shutter for maximum ergonomics.	Yes	No
CF corrected collector lens for even illumination at all visible wavelengths.	Yes	No
Upfront labels with filter cube specifications for easy identification.	Yes	No
3 built-in neutral density filters for precise illumination control.	Yes	No
UL/CE listed fluorescence illuminator for safety assurance.	Yes	No

Which Nikon Eclipse is right for you?

Regardless of your research area or what applications you are pursuing, there is an Eclipse microscope for your requirements. See for yourself the dramatic advances in optics, modularity and ergonomics that Eclipse CFI60 offers. Whether you choose the remarkable E800/E800M for advanced research, the versatile E600 with its superior epi-fluorescence, the powerful TE300/TE200 for inverted microscopy applications, or the economical E400 for basic research and clinical examination, there is an Eclipse model that's just right for your lab.

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The new Eclipse TE300/200™ redefines inverted microscopy.

Imagine Nikon's renowned Diaphot inverted microscopes with even greater flexibility, improved ergonomics, more stability plus the unparalleled performance of CFI60 optics. That's exactly what you get in the Eclipse TE300™ and TE200™ microscopes. Both feature the highest numerical apertures and longest working distances in their categories. Both come with standard 100-watt or optional 30-watt illuminators. And, whether you select the Eclipse TE300 with its full complement of features or the economical Eclipse TE200, each represents the highest magnitude of stability and functionality in inverted microscopy.

Maximum control of light for the brightest, most precise images.

The Eclipse TE300's exclusive 4-position beam-splitter lets you select the amount of light distributed to the eyepieces, side imaging port and the built-in, front-mounted 35mm SLR port. The TE200 offers a simpler 2-way light path, so you can choose to send light to the eyepiece, or to both the eyepiece and side-mounted port.

The Eclipse TE300 offers a bottom-mounted image port option for the highest light throughput possible, while the Eclipse TE200 offers an optional 100% side port. Both models feature shorter optical paths with less glass, and the ability to accept our exclusive 0.8X side port

for the brightest and widest fields in the industry. The newly designed high efficiency epi-fluorescence attachment, which can hold up to four filter cubes, utilizes a quick-change linear slider rather than the slower turret type of most competitive models.

The widest choice in objectives for the most flexible upgrade path.

Start with our basic level Achromat series, including LWD versions for brightfield and phase microscopy. Or select our incomparable high transmission Plan Fluor objectives.

Our newly designed ELWD Plan Fluors—with extra long working distances and higher numerical apertures—will outperform anything on the market.

The 60X water-immersion Plan Apo objective and 20X multi-immersion objective for water or oil offer sophisticated approaches to high NA requirements and top

spherical correction.

This extensive multi-imaging capability and flexibility, along with so much more comfort and ease of use, make the TE300/200 series ideal for everything from tissue culture to UV fluorescence, *in-vitro* fertilization, high resolution video microscopy, patch clamp techniques, microphotometry and confocal laser scanning microscopy.



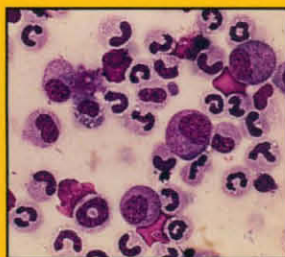
The epi-fluorescence module has the brightest illumination and 4 filter cube capability.



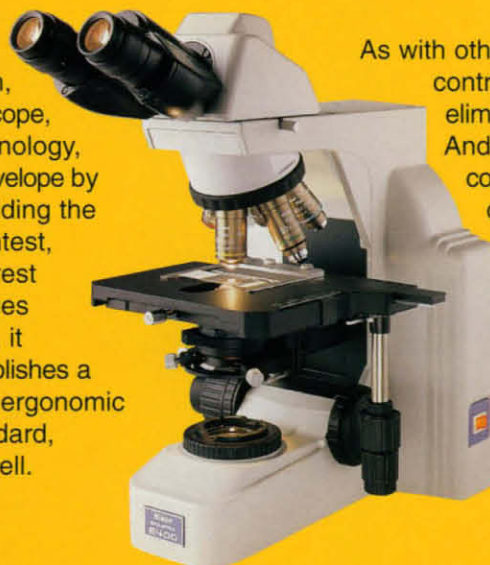
Eclipse inverted microscopes offer the most extensive line of objectives available.

The new Eclipse E400™ redefines comfort and performance.

When it comes to basic research or clinical evaluation, the new Eclipse E400™ microscope, with breakthrough CFI60 technology, not only pushes the optical envelope by



providing the brightest, clearest images ever, it establishes a new ergonomic standard, as well.



As with other Eclipse models, all basic controls are located up front to eliminate uncomfortable reaching. And the fine focus and stage control knobs permit one-hand operation. The stage is 20mm lower and eyepieces are inclined at the new 25° ergonomic standard for the most comfortable viewing experience ever. A unique variable angle tilting binocular body tube, with adjustable eyetube position, will be available soon.

Nikon advances photomicrography.

Nikon's powerful, new H-III camera, or the more advanced U-III, will give you the best photos ever. And they'll do it faster, easier and less expensively, without the long learning curve other cameras require. Among the U-III's full complement of features which, along with your photographic data, can be accessed from your PC are:

- 5 exposure metering modes, including 2 scanning types.
- LCD prompting display.
- An auto bright viewfinder that minimizes the effect of room light during composition.



The new U-III and H-III photo systems offer an array of advanced features to enhance documentation.

- Advanced auto bracketing and manual exposure systems.
- Simple macro programming capability.
- Data printing on photos.

The choice is obvious.

Spend your time perfecting your technique with other cameras, or document your work faster, more easily, more effectively, and at lower costs with Nikon's U-III or H-III cameras.



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Redefining Infinity

The new Eclipse E600™ redefines research versatility.

The unprecedented acceptance of the E800 underscores the enormous benefits of CFI60



Unique 4-filter linear slider features a front-mounted shutter.

technology. For those who don't require the advanced features of the Eclipse E800, but want maximum flexibility in configuring a microscope for a multitude of research applications, Nikon introduces the Eclipse E600™ microscope.

This mid-sized, fully featured microscope offers a full array of accessories to support all optical techniques including DIC, dual-viewing, multi-viewing, double port, drawing tube, magnification changer, and the brightest epi-fluorescence available.

Furthermore, it's so versatile you can virtually custom design it to meet both your current and future needs...simply, easily and economically.

Chromatic- aberration-free optics.

The superiority of CFI60 optical technology provides extreme sharpness and color focus over the entire field of view, and you can utilize multiple contrast techniques both individually and in combined applications with new universal Plan Fluor objectives.



A microscope that grows as your needs grow.

Start with the Eclipse E600 main body, which establishes a new standard for ergonomics and mechanical/thermal stability. Next, choose from over 60 new CFI60 objectives, including Plan Apochromats, Plan Fluors, Plan Achromats and super Flat Field Achromats, as well as specialty objectives, such as water immersion or the only 1X objective available in the industry.

Then add the options you need, most of which are compatible with all other Eclipse models.

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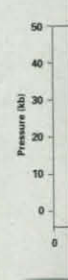
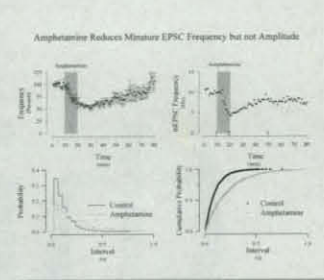
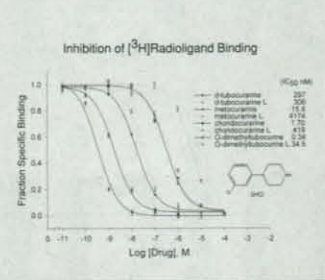
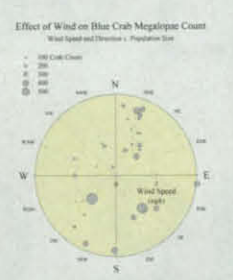
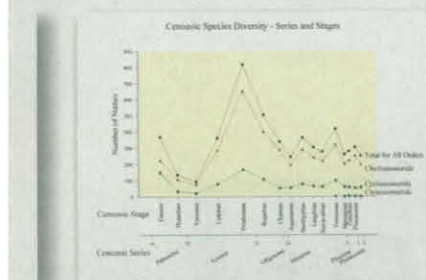
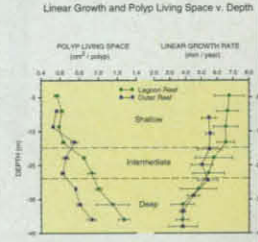
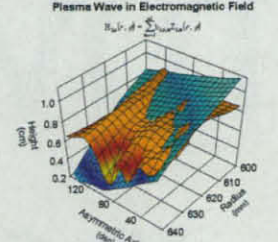
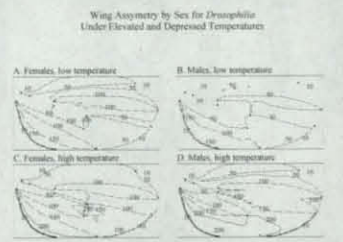
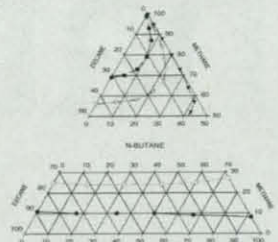
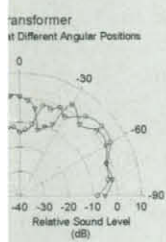
Before you consider any research microscope, compare it—feature for feature, benefit for benefit—with the remarkable Eclipse E600:

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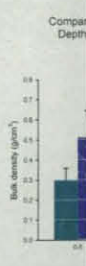
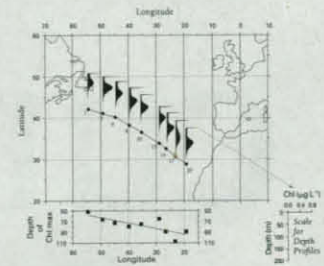
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* The cationic lipid component of the TfxTM Reagents is covered by U.S. Patent No. 5,527,928 assigned to The Regents of the University of California, and pending foreign patents. Tfx is a trademark of Promega Corporation.



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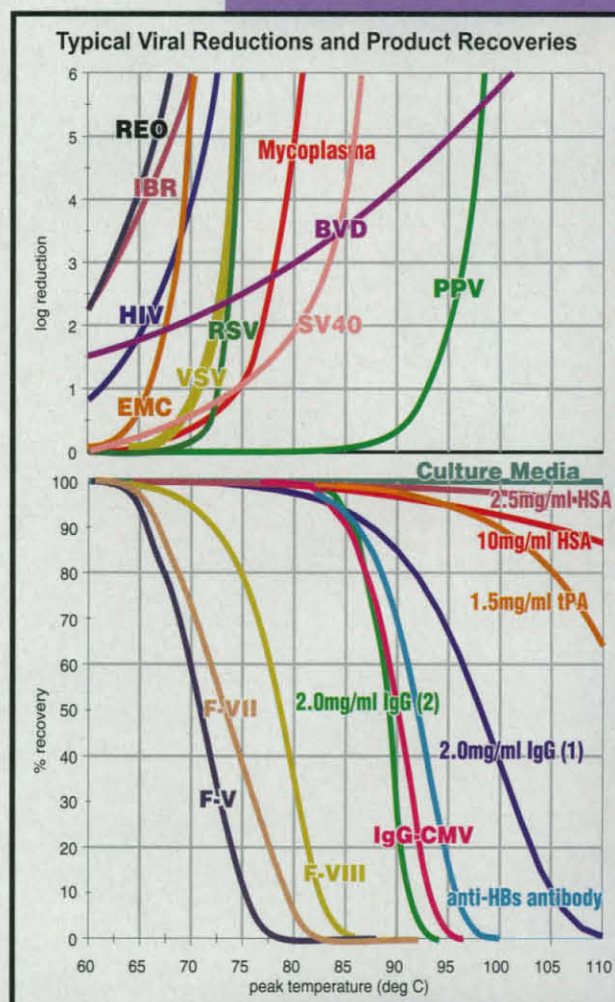


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Fig. 1. Multicolor detection using TSA-Direct.
Courtesy of Kevin Roth, M.D., Washington University
School of Medicine, St. Louis, Missouri.

Fig. 1.

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Fig. 2

a. Standard fluorescent detection.

b. TSA-Enhanced fluorescent detection.

c. Standard chromogenic ISH.

d. TSA-Enhanced chromogenic ISH.

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Figs. 2 a-b. Fluorescent detection of chromosome centromere probes in metaphase spreads.
Figs. 2 c-d. In situ chromogenic detection of oxytocin in rat brain tissue sections.

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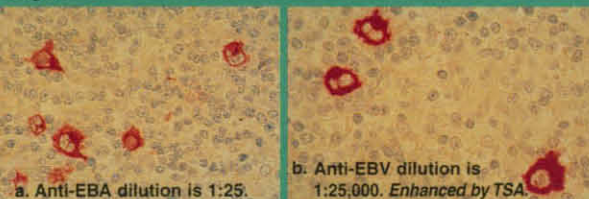
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Fig. 3



a. Anti-EBA dilution is 1:25.

b. Anti-EBV dilution is 1:25,000. Enhanced by TSA.

Figs. 3 a-b. IHC of EBV antigen in Hodgkin's Lymphoma of mixed cellularity.
Courtesy of R. Von Wasielewski and S. Gignac, Pathologisches Institut der
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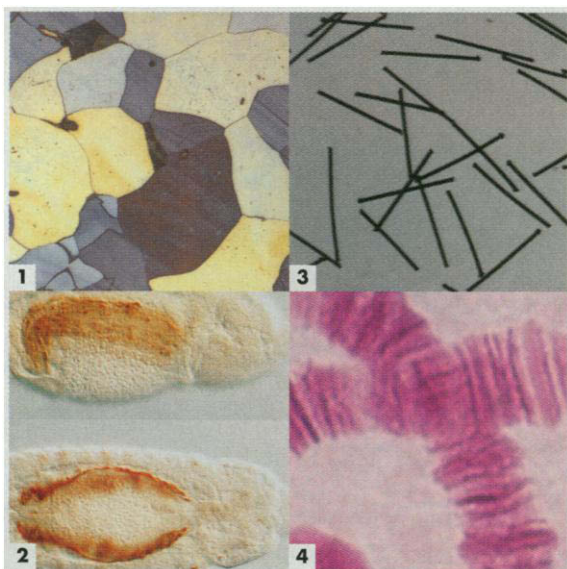
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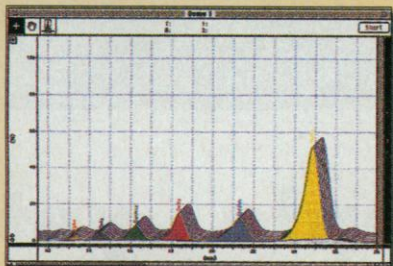
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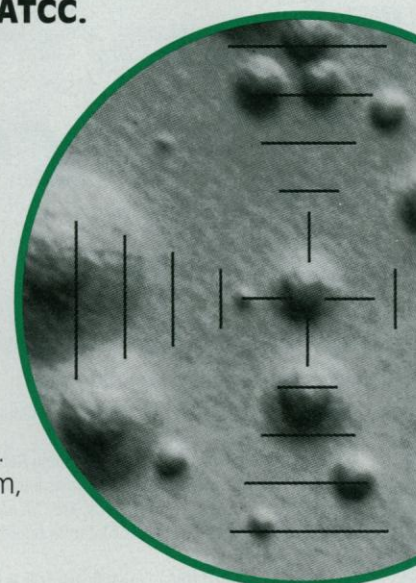
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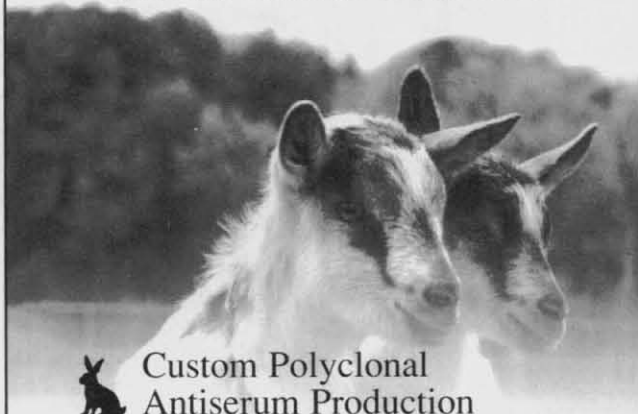
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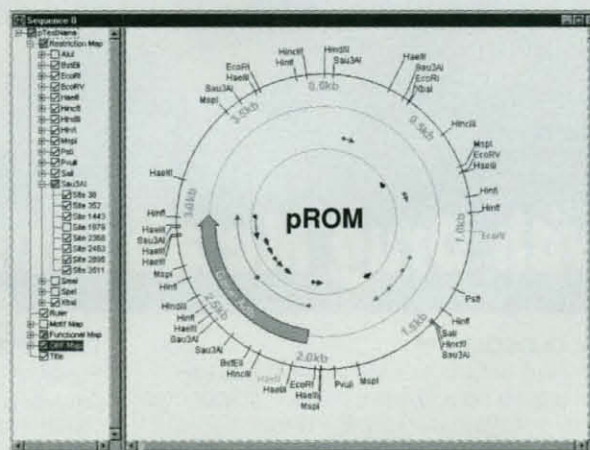
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