28 August 1998

Science

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VOLUME 281 28 AUGUST 1998 NUMBER 5381

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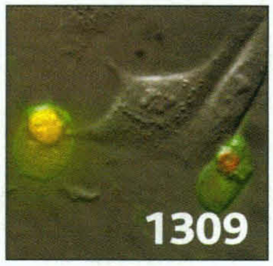
COVER Time-lapse microscopy (over ~1 hour) of human HeLa cells undergoing apoptotic cell death. The green marks a membrane lipid change that occurs during apoptosis, and the red labels DNA after the membrane has lost its integrity, a later apoptotic event. See the Green and Reed Review and the special section beginning on p. 1301. [Images: J. C. Goldstein, La Jolla Institute for Allergy and Immunology]



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New ways to achieve diversity

NEWS

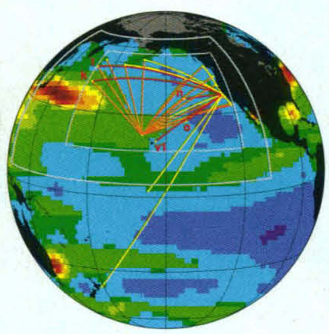
NEWS OF THE WEEK

NEWS FOCUS

RESEARCH

RESEARCH ARTICLE

REPORTS



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Sounding out the ocean heat budget

APOPTOSIS

NEWS

REVIEWS

See related Editorial on p. 1283, Perspective on p. 1298, and Report on p. 1355.

DEPARTMENTS

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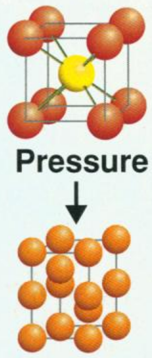
SCIENCE'S COMPASS

1296

Superconductivity, salt, and pressure



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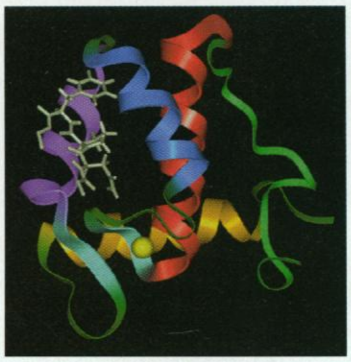

1357

The EH domain clasps the NPF peptide with a pair of EF hands

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SUSTAINABLE GROWTH?

How can a growing world population be sustainably fed while maintaining essential ecosystem inputs, such as water for crops? In a Policy Forum, Daily *et al.* (p. 1291) explore the inextricable links between sustainable food production and environmental health and point out that this is not just a global statistical issue but one that must be addressed at the local level. A longer term view is considered in a book by Hammond (reviewed by Folke, p. 1293), which explores three scenarios for the interplay of social, environmental, and economic factors in the coming century.

LISTENING TO THE OCEAN

Obtaining an accurate measurement of the change in temperature and circulation of the oceans in response to climate change has been difficult in large part because of limited and variable sampling. The ATOC Consortium (p. 1327) presents results from an experiment that obtained such data by measuring the speed of sound across the North Pacific. Comparison with satellite measurements of ocean surface height and modeling studies indicates that large seasonal variations occurred in ocean heat flux during the past several years.

SQUEEZING SALTS INTO METALS

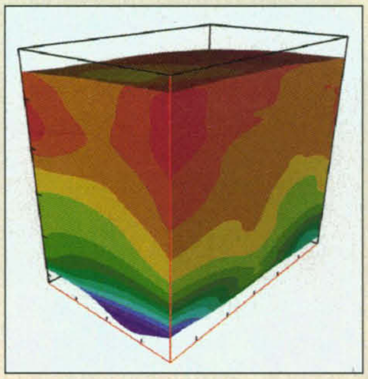
How pressure changes the electrical properties of materials has planetary implications, such as understanding the electromagnetic properties of Earth's core or the formation of giant planets. Eremets *et al.* (p. 1333) measured the resistance of the alkali halide CsI in a diamond anvil cell over a range of temperatures (from 50 millikelvin to 300 K) and pressures [about 45 to 220 gigapascals (GPa)]. At about 115 GPa, CsI converted to a metal, and at 180 GPa and 2 K there was a drop in resistance suggestive of superconductivity. These measurements provide empirical data to improve theoretical models of metallization and superconductivity for a broad range of related materials (see the Perspective by Hemley).

RAPID STRETCHING

Previous studies of flexible polymers (DNA molecules) in solution experiencing shear forces revealed a complex array of dynamics and conformations that varied greatly from molecule to molecule. Concerns were raised that this heterogeneous response arose from preparation conditions that may have skewed the initial distribution of conformations from equilibrium. Smith and Chu (p. 1335) can now shear DNA molecules starting at rest and stretch them much faster than the polymer relaxation rate (up to 55 times faster). They can now attribute the complex dynamics of this system to the differing evolution of an array of conformations initially present at equilibrium.

INSIDE A GLACIER

Glaciers deform internally as they flow, but mapping the flow and deformation in three dimensions requires placing markers within the glacier. Harper *et al.* (p. 1340) performed this experiment on a section of the Worthington Glacier, Alaska. They drilled



28 bore holes through the glacier and monitored the deformation of points along the holes and at the surface for 6 months. Between 60 and 70% of the glacier's motion was sliding along the bed; internally, the ice flowed both down the glacier and laterally.

RUNAWAY GLACIATION

The most extensive glaciations in Earth's history may have occurred in the Neoproterozoic, about 750 to 550 million years ago, when some evidence suggests that glaciers extended periodically to near the equator. Hoffman *et al.* (p. 1342; see the news story by Kerr) provide data that tests one possible cause of this glaciation: A runaway albedo feedback where growth of sea ice increasingly reflects more sunlight, cooling the Earth. A series of detailed carbon isotope data from a sequence of rocks in Namibia, including a large carbonate deposit that caps an extensive glacial deposit, imply that ocean biological productivity crashed and remained low for millions of years. Volcanic outgassing later provided sufficient CO_2 to warm the Earth, melt the sea ice, and rapidly form carbonate rocks on ocean shelves.

"CHOPPING" MOLECULES IN HALF

Simple pictures of chemical bonding would suggest that when a diatomic molecule photodissociates, the bond "snaps" and the two recoiling atoms depart with no spin (as if hit by a "smash" in tennis). This model fails, however, if the molecule can access two different excited states with different symmetries. The electron cloud of the molecule, instead of oscillating along the bond or perpendicular to it, can oscillate at some intermediate angle, which corresponds to the "chop" shot in tennis. The resulting fragments in this case exit with either topspin or backspin. Rakitzis *et al.* (p. 1346) observed such behavior in the photodissociation of iodine monochloride and attribute it to quantum mechanical interference of the excited states.

FINDING THE RIGHT TARGET

Abnormalities in synaptic transmission mediated by glutamate release have been implicated in schizophrenia, but targeting glutamate receptors that act through ion channels has been considered therapeutically impractical because these receptors mediate fast synaptic transmission throughout the nervous system. Moghaddam and Adams (p. 1349; see the news story by Wickelgren) have targeted metabotropic glutamate receptors, which act through G proteins. Agonists acting on a specific subpopulation of these receptors reversed symptoms in the phencyclidine animal model of schizophrenia without interfering with normal glutamateric synaptic transmission.

CELL DEATH SQUADS

Both the CED-4 and CED-3 proteins are required for developmental cell death in the worm *Caenorhabditis elegans*, but the mechanism by which CED-4 activates CED-3 (a member of the proteolytic "caspase" family) or how the inhibitory protein CED-9 prevents this activation is not known. Yang *et al.* (p. 1355; see the Perspective by Hengartner) found that only oligomerized CED-4 bound to CED-3, which forced the clustering of CED-3 proteins and seemed essential for their activation. CED-9 prevented CED-3 activation by binding to CED-4, thereby blocking the dimerization of CED-4 and CED-4's ability to cluster and activate CED-3.

CONTINUED ON PAGE 1251

THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1249

ONE ALLELE IS ENOUGH

The regulation of gene expression can occur through many mechanisms, but only rarely by shutting down one allele entirely. Bix and Locksley (p. 1352) have evidence that the cytokine interleukin-4 (IL-4) can be expressed in a monoallelic fashion in T cell clones. Parental imprinting does not seem to play a role in determining which allele is expressed, but the choice of allele is passed on to successive generations of the clone. This is the second such cytokine to be reported (the first was IL-2) that can be monoallelically expressed and raises questions about the generality of the phenomenon and its biologic consequences.

PEPTIDE RECOGNITION

The reversible interaction of proteins is a recurring feature of many cellular processes such as signal transduction and membrane trafficking. The modes of interaction often are governed by structural domains that recognize short peptide sequences in a variety of partners. De Beer *et al.* (p. 1357) present the nuclear magnetic resonance structure of the Eps15 homology (EH) domain and characterize its interactions with the target sequence Asn-Pro-Phe. Tandem repeats of EH domains are likely to have their peptide binding sites next to each other, which facilitates multivalent interactions. A tryptophan residue in the middle of the hydrophobic binding pocket is critical for recognition.

CONTROLLING NF-κB

NF-κB is a transcriptional activator that participates in control of diverse biological processes, including immune function, growth control, and cell death. Activity of NF-κB is held in check by the inhibitory proteins IκBα and IκBβ, and such inhibition is relieved by phosphorylation and consequent degradation of the IκB proteins. Zandi *et al.* (p. 1360) report that the IκB proteins are directly phosphorylated by the IκB kinases, IKKα and IKKβ, and that the IKK proteins can function either as homo- or heterodimers. They also find that the IκB proteins are better substrates for the IKKs when they are bound to NF-κB. This property would allow the IκB proteins to accumulate in cells even if IKK was still active and thus helps explain how tight control of NF-κB activity is maintained.

ROLL YOUR EYES

We can roll our eyes left and right and up and down, but how about rotating them clockwise? Tweed *et al.* (p. 1363) show that indeed we can. Subjects were asked to follow a fast-moving laser spot while their eye movements were recorded. They exhibited strong torsional eye movements that compensated for the relative slowness of the head that helped keep the retinal image stabilized. The neuronal system for controlling this sophisticated eye and head movement coordination is highly differentiated, which suggests some evolutionary pressure to develop such a system.

WHAT'S THE LOGGING PROBLEM?

The diversity of tree species in tropical forests is the foundation for the most diverse ecosystems on the planet. What sort of long-term impact should be expected for the selective commercial logging of the dominant tree species? A case study by Cannon *et al.* (p. 1366; see the Perspective by Chazdon) concludes, surprisingly, that 8 years after a widespread commercial logging operation, a high level of species richness is retained in the exploited forests. This study in Southeast Asia may or may not be generalizable to all tropical forests, but it should offer some encouragement to conservationists.

TECHNICAL COMMENT SUMMARIES

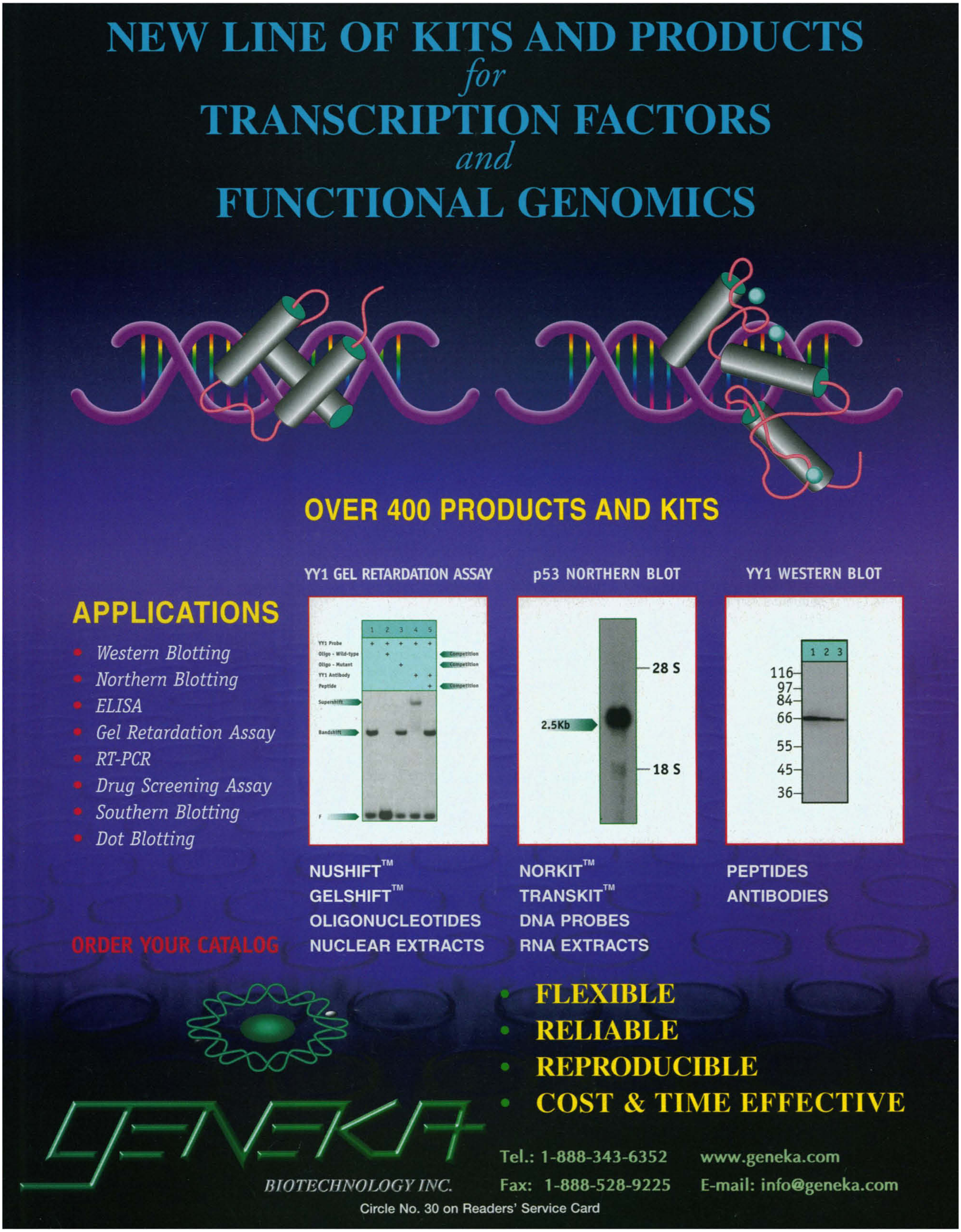
Growth of the Southern Greenland Ice Sheet

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/281/5381/1251a

C. H. Davis *et al.* (Reports, 27 Mar., p. 2086) studied "satellite altimeter measurements" and calculated that "the average growth rate [of ice] is too small to determine [whether] the Greenland ice sheet is undergoing a long-term change [as a result of] a warmer polar climate."

H. J. Zwally *et al.* comment that they agree with the "principal conclusion" of the report, but that the average calculated in the report "included only 70% of the area above 2000 meters." They present results from an analysis that uses new data "from the first 18 months of the Geosat mission." The results show values of ice thickening "larger (×3) than those given by Davis *et al.*"

In response, Davis *et al.* "recognize that approximately 30%" of the ice sheet "was not covered" in their original calculations. They go on to present new results that are also based on the new 18-month Geosat data set. These results, they state, are "consistent with the corresponding estimate" that was given in the report.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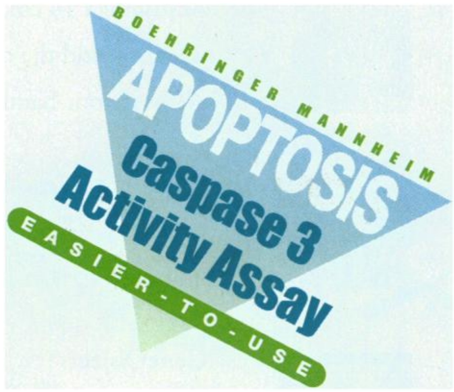

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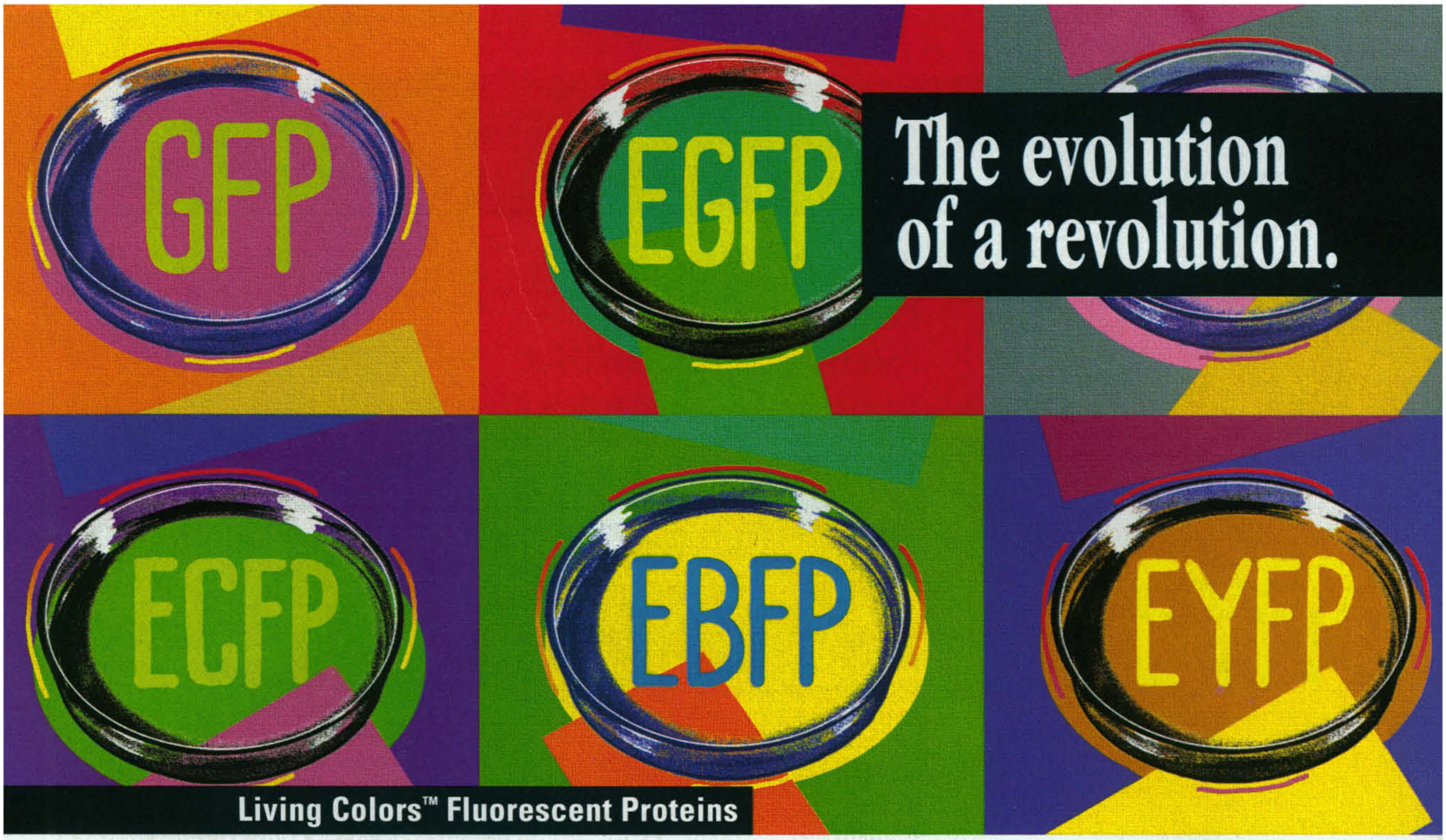
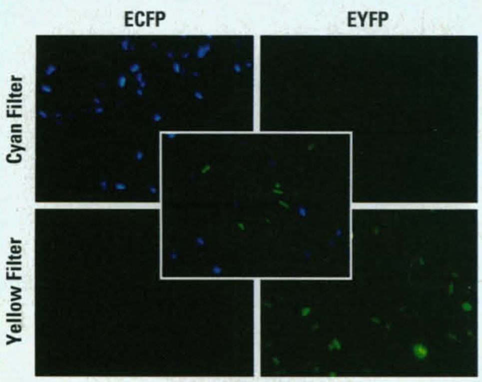


Illustration inspired by the art of Andy Warhol (1925–1987).



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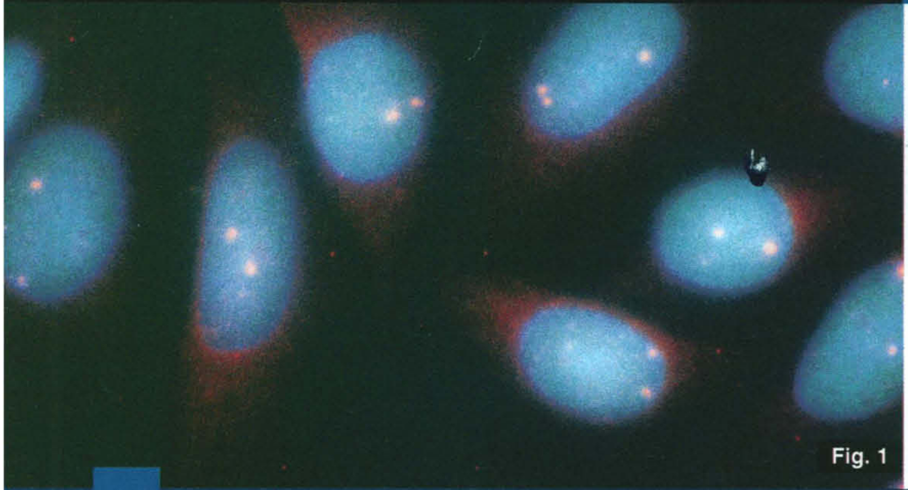

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Fig. 1. Sensitive detection of integrated HPV in SiHa cells using TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe (1000 bp) hybridized to cultured SiHa cells. TSA fluorescence detection used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slide counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using separate tetramethylrhodamine and DAPI filters. Photo taken on KODAK 1000 speed film with 5 second (Cyanine 3 Tyramide) and 0.5 second (Hoechst 33342) double exposure using a 100X objective.

How Does TSA Work?

This technology uses HRP to catalyze the deposition of biotinyl or fluorescent tyramide onto tissue sections or cell preparation surfaces that were previously blocked with protein. This reaction is quick (less than 10 minutes) and results in the deposition of numerous biotin or fluorochrome labels. Deposition occurs right at the enzyme site, resulting in minimal loss of resolution.

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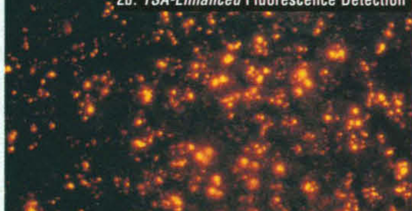
Use conventional filters

2a. Standard Fluorescence Detection

2b. *TSA-Enhanced* Fluorescence Detection



Tetramethylrhodamine filter

2c. Standard Fluorescence Detection.

2d. *TSA-Enhanced* Fluorescence Detection.

Multiband pass filter

Figs. 2a-d. Comparison of HPV fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3 FISH). Biotinylated HPV-16 E6 DNA probe hybridized to cultured CaSki cells.

2a-b. Standard fluorescence detection carried out with Cy™3-conjugated Streptavidin (Jackson ImmunoResearch Laboratories, Inc.). TSA-enhanced fluorescence used Streptavidin-HRP followed by Cyanine 3 Tyramide. Slides counterstained with Hoechst 33342 (Molecular Probes, Inc.) and evaluated using a tetramethylrhodamine filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

2c-d. Protocol same as above but counterstained slides evaluated using a multiband pass filter. Photos taken using KODAK 1000 speed film with a 1 second exposure using a 40X objective.

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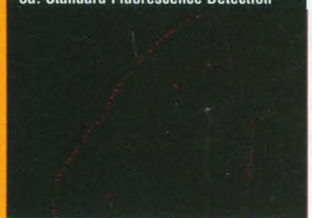
Enhance signals up to 1000-fold with TSA

3a. Standard Fluorescence Detection



3b. *TSA-Enhanced* Fluorescence Detection

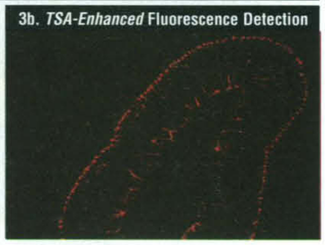


Fig. 3a-b. Comparison of standard fluorescence detection using Cy™3-conjugated Streptavidin versus TSA-Direct (Cyanine 3). Courtesy of *Kevin Roth, M.D., Ph.D., Washington University School of Medicine, St. Louis, MO.* Bouin's fixed, paraffin embedded mouse intestinal tissue, deparaffinized and incubated with biotinylated wheat germ agglutinin. Sections incubated with Cy3-conjugated Streptavidin (3a) or with Streptavidin-HRP followed by Cyanine 3 Tyramide (3b). Wheat Germ Agglutinin labels intestinal epithelial cells at the base of the crypts.

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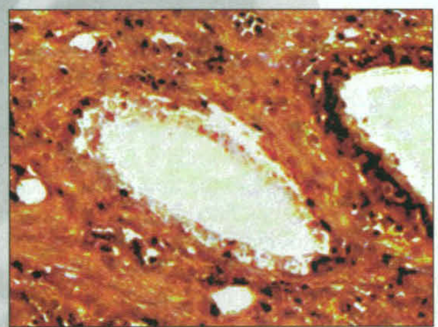

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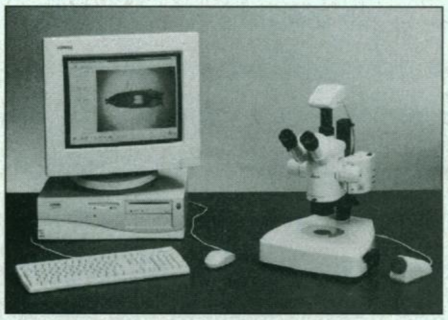

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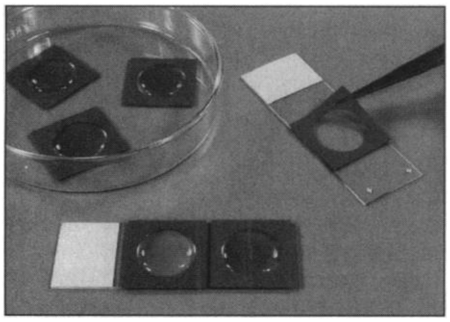

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