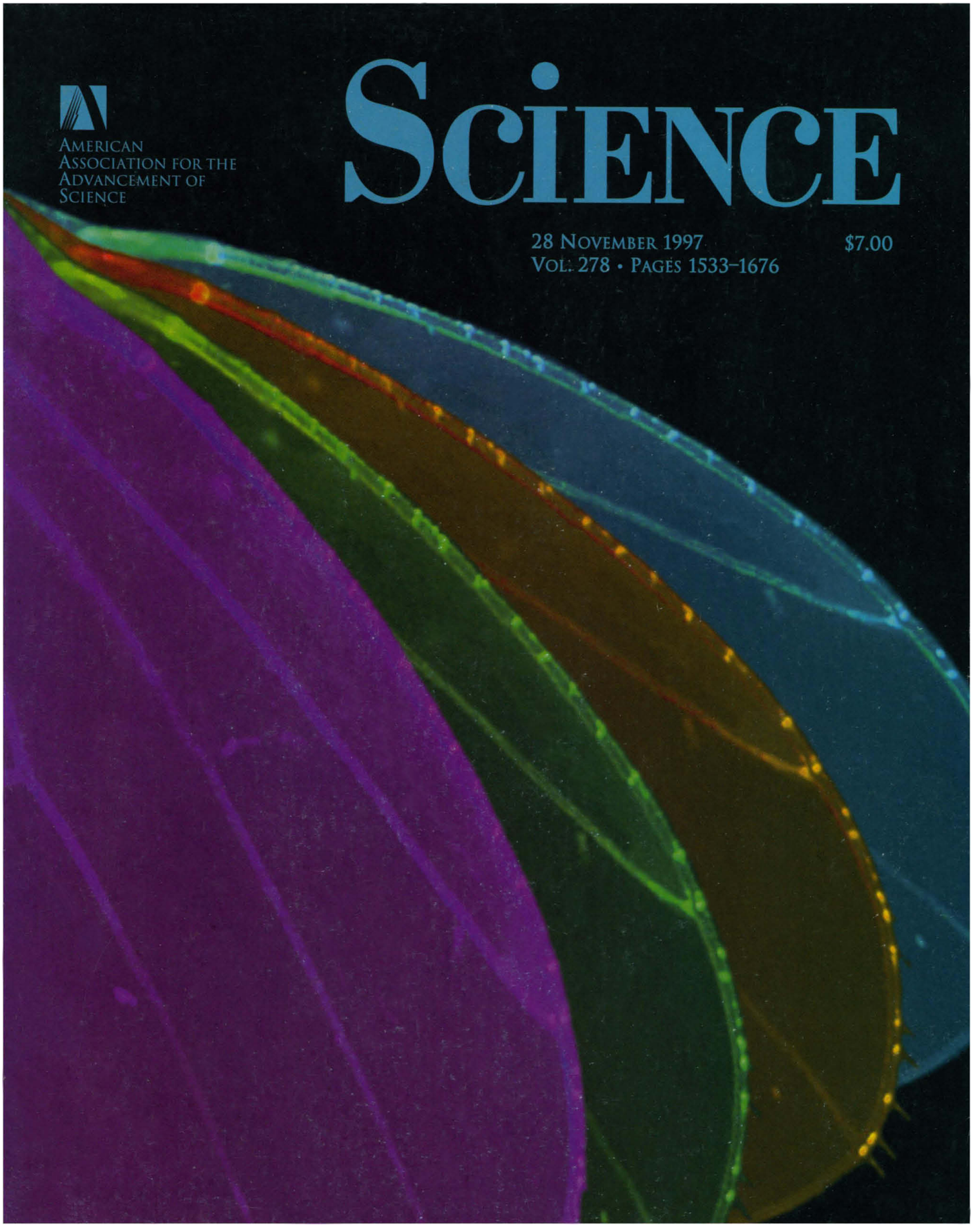
American Association for the Advancement of Science

SCIENCE

28 November 1997
Vol. 278 • Pages 1533–1676
$7.00



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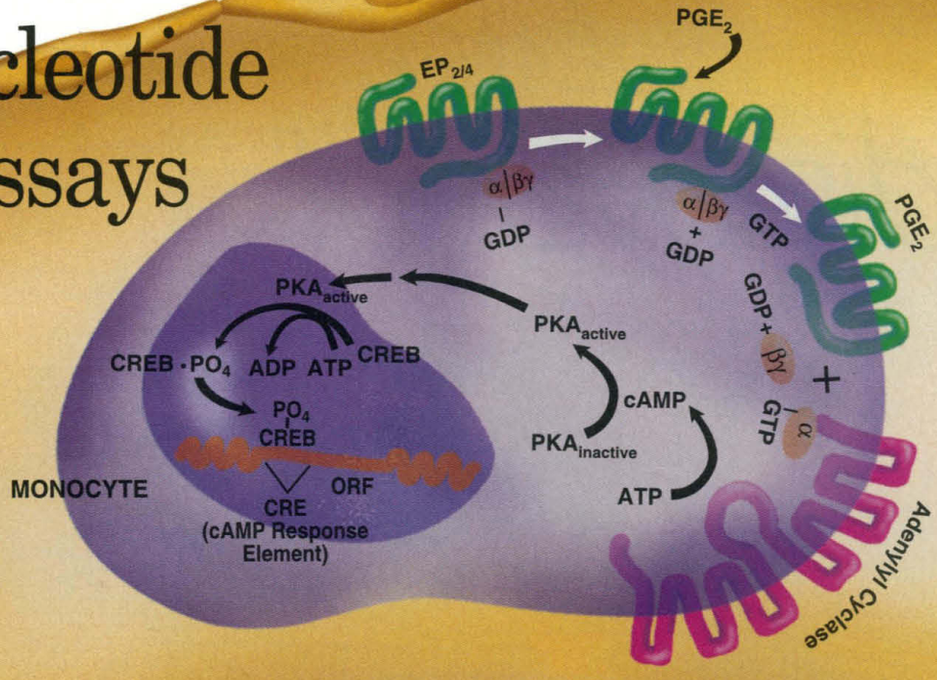

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PGE_1	DE1200	19.5 – 5000	5.95	2.75
PGE_2	DE0100	39 – 5000	36.20	2.75
6-keto-$PGF_{1\alpha}$	DE0800	16 – 50,000	1.40	2.75
$PGF_{2\alpha}$	DE1100	12.2 – 50,000	4.62	2.75
8-iso-$PGF_{2\alpha}$	DE0900	24 – 100,000	12.30	2.75
Total 8-iso-$PGF_{2\alpha}$	DE1000	12.2 – 50,000	11.40	2.75
11β-$PGF_{2\alpha}$	DE1300	32 – 500,000	4.30	2.75

CYCLIC NUCLEOTIDES

FACTOR	CATALOG NO.	RANGE (pmol/mL)	SENSITIVITY (pmol/mL)	TIME (hrs)
cAMP	DE0400	0.5 – 5000	0.38	2.75
cAMP (low pH)	DE0300	0.5 – 5000	0.74	2.75
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cGMP (low pH)	DE0500	0.8 – 500	0.58	2.75

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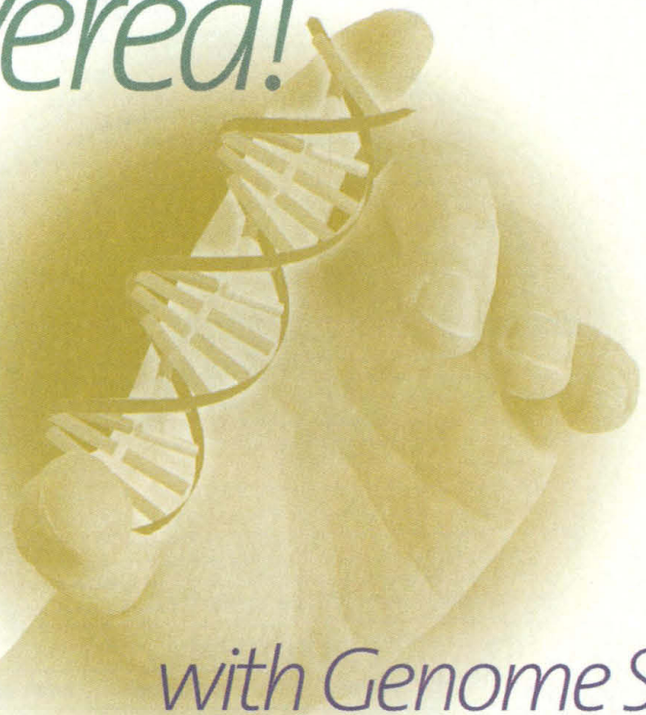

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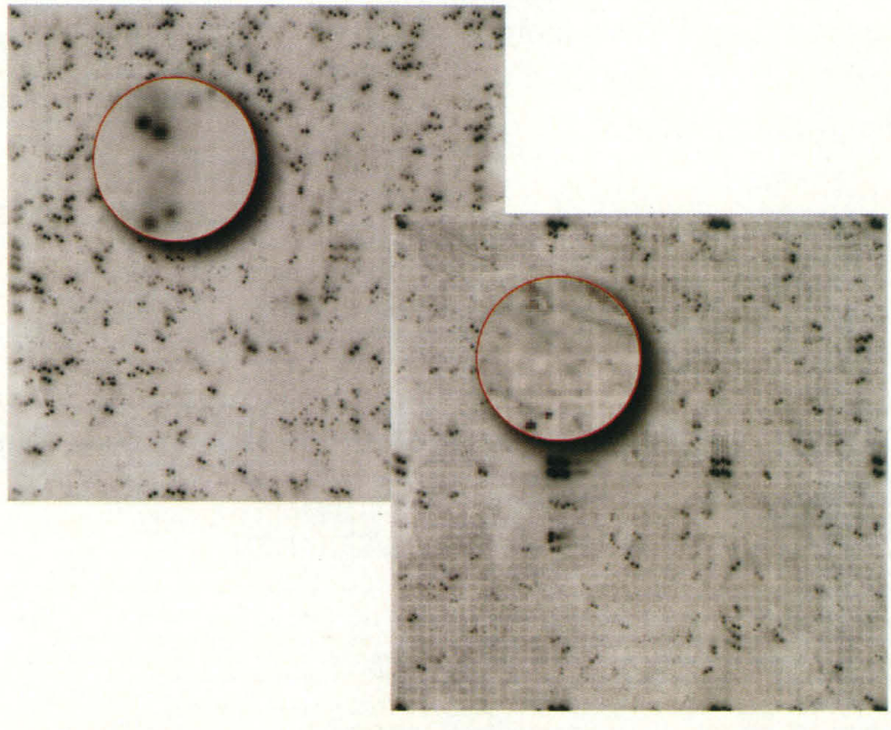

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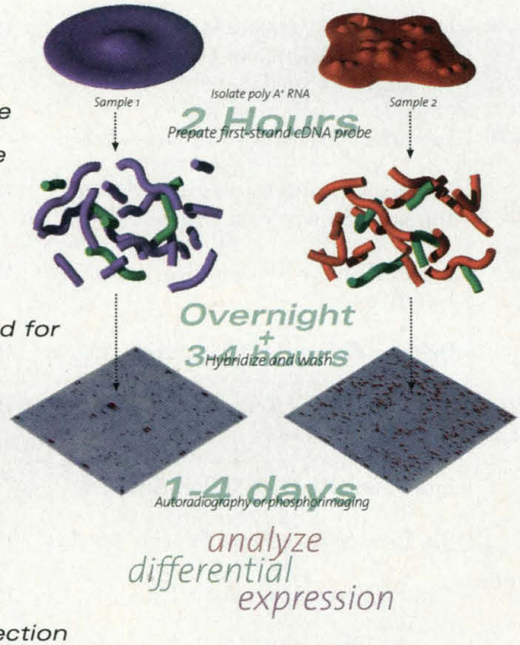

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1. *"The I.M.A.G.E Consortium: An Integrated Molecular Analysis of Genomes and their Expression", Lennon, G.G., Auffray, C., Polymeropoulos, M., and Soares, M.B. [1995] Genomics.*

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ISSN 0036-8075
28 NOVEMBER 1997
VOLUME 278
NUMBER 5343

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

1565
Africa's preeminent AIDS project

1576
Mantle message from space

NEWS

SPECIAL NEWS REPORT

PERSPECTIVES

POLICY FORUM

ARTICLE

DEPARTMENTS

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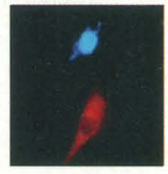
COVER

Chemosensory cells and bristles along the edge of the *Drosophila* wing are marked by a pseudocolored green fluorescent protein signal, driven from the promoter of the circadian clock gene *period*. These cells support independent photoreceptive clocks; multiple tissues (including the wing) throughout the animal display circadian rhythms in culture. See page 1632 and the related News story on page 1560. [Image: Jeffrey Plautz, Steve Kay, Cynthia Faber Smith]

RESEARCH ARTICLE

REPORTS



1638
Transcriptional control by exclusion

Indicates accompanying feature

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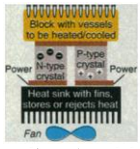
THE MJ RESEARCH NOTEBOOK

Volume VII...No. 1a *A Bulletin of Technological Advance in Molecular Biology* *Autumn 1997*

The Peltier-effect Thermal Cycler That Began A Technological Trend: The MJ RESEARCH PTC-100

Left to right: A PTC-100-96AgV with a speedy silver-gold block that can ramp at up to 2.5°C/sec, a PTC-100HB with improved Hot Bonnet heated lid that applies heat and pressure to the tops of tubes or plates for oil-free reactions, and a PTC-100-16MS that holds 16 slides & 24x0.2ml tubes for *in situ*.

How Peltier-effect Heat Pumps Actually Work



The Peltier effect is a solid-state physical phenomenon that was first described by Jean Peltier in the *Annales de chimie* in 1834. Peltier observed that when current passes through a bimetallic junction, one side gets hot and the other gets cold. In the 20th century, this "effect" has been combined with semiconductor technology to construct small, bi-directional heat pumps that are electronic in nature. These pumps are extremely precise and reliable, and they are the basis of MJ cyclers.

RIGHT WAY TO USE PELTIER

It is now widely accepted that Peltier heat pumps are the best technology for thermal cyclers—but exactly how these pumps are applied is critical. A design was pioneered with the PTC-100 where the pumps are mounted between a low-mass sample block and a large, efficient heat sink. Permanent mounting allows fast, efficient heat flow between the pumps and the block. The heat sink can store heat to be later pumped back into the sample block, or it can disperse the heat to outside air—this depends upon the action of a computer-controlled fan.

The Cycler That Went To War in the Persian Gulf and Battled Plague in India

When adversity flared in the Persian Gulf six years ago, the tools of molecular biology were brought to the front. Biological weapons were threatening; means to detect their use were needed. PTC-100s were there—and they did their duty.

In 1994, unsettling reports were circulating that plague had erupted in Surat, India. Indian authorities were addressing the problem as best they could, but the skills to detect *Y. pestis* had atrophied over time. Working with the WHO, MJ RESEARCH donated several PTC-100s, allowing Indian scientists to use molecular methods to battle the disease. In the final analysis, *only* these molecular tests* proved that the plague pathogen was ever present (see *Nature Med* 1:1237-9).

* PCR is covered by patents owned by Hoffmann-La Roche, Inc. & F. Hoffmann-La Roche Ltd. Users should obtain license to perform the reaction.

MJ Engineer Paul Titcomb in 1990, with a PTC-100 that was camouflaged by the U.S. Marine Corps for field use in *Operation Desert Storm*.

A MUCH-COPIED DESIGN

First Introduced in 1988 and Improved Over Time—It Still Outperforms Most Cyclers

WATERTOWN, Mass.—In 1986 and 1987, much "buzz" was circulating in the biology community about a new method for identifying and amplifying sequences of DNA that was being developed by the Cetus Corporation. A tantalizing paper describing an early form of PCR* had appeared in *Science* in late '85, but a critical refinement—the use of thermostable polymerase enzyme—was not described officially until '88. At that time, the need for significant numbers of instruments to thermally cycle tiny aliquots of biological reagent first became apparent.

The partner of the Cetus Corporation, The Perkin-Elmer Corporation, concentrated on the development of a thermal cycler based upon mechanical vapor compression technology. MJ RESEARCH, INC.—then a year-old start-up company—recognized the opportunity and began development of instrument based upon the more promising Peltier-effect heat pump. Several other companies in the U.S. and England also began development of thermal cyclers—mostly based upon resistive heating and passive air or water cooling (though one other US firm also developed a variant of the Peltier cycler).

In late '88, MJ RESEARCH introduced the world's first Peltier thermal cycler—the PTC-100. Since that time, the instrument's design has been modified, crafted, tweaked—and perfected. To this day, the PTC-100 outperforms most competing cyclers in uniformity, speed, accuracy, and capacity—even though at least twenty other manufacturers have since entered the market. MJ has introduced newer designs—the Mini-Cycler, DNA Engine, and Tetrad—yet the PTC-100 remains a respected workhorse of science.

But perhaps the greatest compliment to this pioneering design is the ubiquitous imitation. Though it was scorned at first by some, the PTC-100's configuration is now mimicked by virtually every manufacturer in every new introduction.

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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Reversible polymers

Polymers that form through hydrogen bonding could have interesting properties, such as reversibility of the polymerization through heating or concentration change. However, insufficient strength and directionality of the bonding between the monomer units have hampered progress. Sijbesma *et al.* (p. 1601; see the Perspective by McLeish, p. 1577) found that highly directional polymerization resulted for monomer units bearing a self-complimentary array of four hydrogen bonds. Viscosity, chain length, and composition can be tuned by changing conditions.

■

Current events

Ocean currents are now dominated by thermohaline circulation, the sinking of dense, cool, salty water at high latitudes. Today, approximately equal amounts of deep water are formed in the Arctic and Antarctic. Changes in this pattern are thought to have affected climate greatly in the recent past. Broecker (p. 1582) reviews our present understanding of this circulation pattern and its evolution through time. A critical question is whether increases in greenhouse gases in the atmosphere might disturb this balance and flow pattern.

■

Melting in 2D

The physics of phase transitions, such as melting, in two-dimensional (2D) systems can differ from that in bulk; theory suggests that a hexagonal crystal, a typical packing, will show an intermediate hexatic phase before melting, but this phase has been difficult to observe. One problem is that defects will distort the packing to orthorhombic, in which case theory predicts that a smectic phase will precede the hexatic phase. Sikes and Schwartz (p. 1604), using high-temperature atomic force microscopy, present evidence for such a smectic phase in supported Langmuir-Blodgett films of fatty acids.

■

Climate and human evolution

It has recently been suggested that a change to a drier climate in Africa about 2.5 million years ago spurred early human evolution and led to a turnover in mammalian fauna. Behrensmeyer *et al.* (p. 1589) analyzed a large collection of mammalian fossils dating from 3 to 1.8 million years ago from the Turkana Basin in Kenya and Ethiopia. Although the data show that perhaps up to 78 percent of the mammalian fauna turned over during this time, the major change in fauna was not at 2.5 million years ago, but occurred continually afterward.

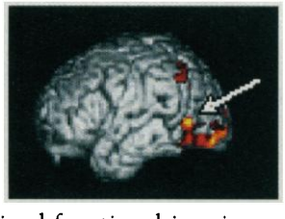
Stormy weather

Several times a year, large stable weather patterns form and persist for weeks to up to a month or so. Weeks *et al.* (p. 1598) performed an experiment with a rotating annulus to show that this pattern, and the transition to more normal eastward atmospheric flow, reflects interactions of the rotating atmosphere with topography.

■

Types of attention

Two opposing views of neural implementations of attention are a top-down (or roving spotlight) mechanism or a bottom-up (or competitive inputs) mechanism. Both views are supported by studies of neurological patients, primate experiments, and functional imaging of normal humans. Rees *et al.* (p. 1616) describe a combined functional imaging and psychophysical study of how the degree of visual perception is influenced by the difficulty of simultaneously performing a word-based task. Irrelevant visual stimuli were not perceived only when the task commands large processing resources.



Experiments in space

The spatial aspect of population ecology can be more readily modeled than it can be tested and studied in the field. Two reports help redress the balance. Maron and Harrison (p. 1619) demonstrate experimentally how a host-parasitoid interaction can result in the patchy distribution of a population within a continuous habitat, a result predicted theoretically. Ranta *et al.* (p. 1621) used a 68-year record of the population size of Canadian lynx from eight provinces of Canada to investigate the dynamics of populations in time and space. Notable, but unstable, synchronicities occur, particularly among neighboring populations. These dynamics can be captured by a straightforward model of population dynamics, which suggests that there may be a simple explanation for the phenomenon.

■

Clocks all over

Most animals are thought to contain central circadian clocks in the brain—mammals in the superchiasmatic nucleus, and birds and fish in the pineal. Plautz *et al.* (p. 1632; see the cover and the news story by Pennisi, p. 1560) have visualized the expression of the key clock component PER by engineering the protein luciferase together with PER to form a fusion protein. This construct revealed that the fly *Drosophila* contains multiple independent oscillators in peripheral tissues, notably in the chemosensory cells of the wing margin. Each independent clock can be reset directly by light, likely through as yet undefined photoreceptors.

■

NKT cells and tumors

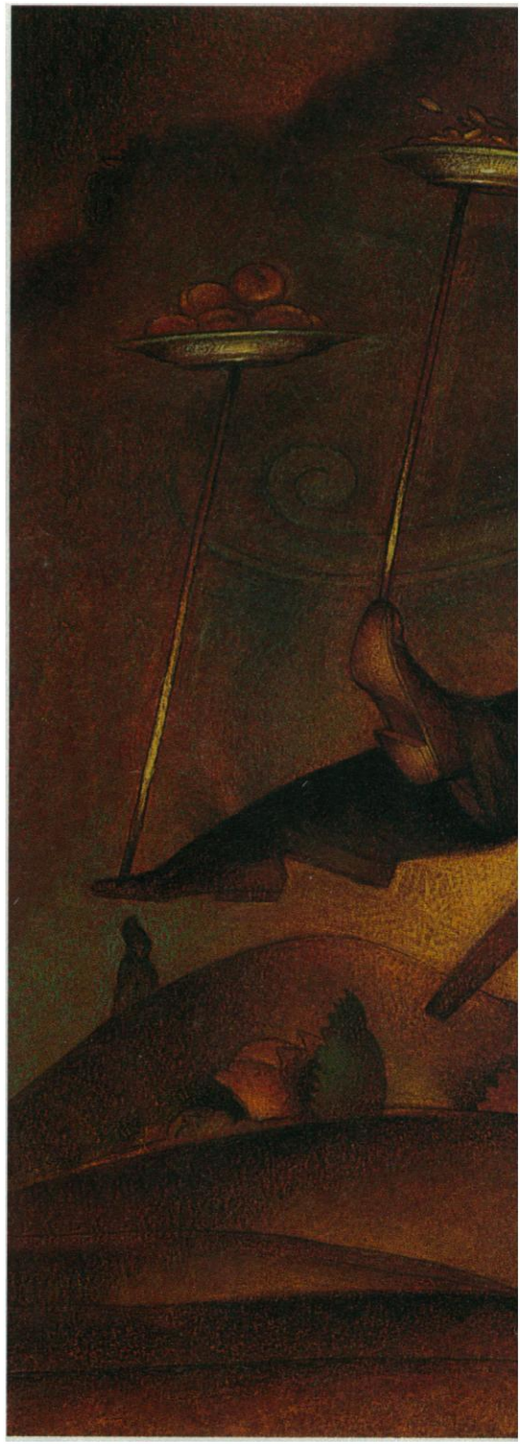
An unusual subset of T cells, natural killer T (NKT) cells, all have the same T cell receptor and all bear some NK cell markers; two reports show that they play a role in fighting tumors. Cui *et al.* (p. 1623) now show that these cells seem to be indispensable for the control of syngenic tumors mediated by interleukin-12. The mechanism involves the production of interferon γ by these cells. Kawano *et al.* (p. 1626) found that NKT cells recognize a galactosylceramide lipid found in marine sponges in the context of CD1d; an analog of this lipid may be the natural ligand for antigen recognition. Addition of galactosylceramide in a model of tumor metastasis activated these cells and inhibited development of tumor metastases. Activation of the NKT cells is similar to T cells, but their effector function is more like NK cells.

■

Ice role for STATs

STATs (signal transducers and activators of transcription) are important mediators of regulated transcription induced by exposure of cells to various cytokines and growth factors. Kumar *et al.* (p. 1630; see the Perspective by Hoey, p. 1541) describe a different role for these transcription factors—constitutive activation of transcription of Ice-family proteases. These proteases function in apoptosis (programmed cell death), and cells that lack STAT1 failed to undergo apoptosis in response to tumor necrosis factor–α. The constitutive transcription of the protease genes is distinct from the regulated transcriptional activation mediated by STAT1 in that dimerization is apparently not required for the former.

DOCTORS HAVE TO BALANCE A MULTITUDE OF VARIABLES IN TREATMENTS. WE MAY BE ABLE TO BRING SOME CERTITUDE TO THE PROCESS.



Every small advance adds yet another tool to medicine. And yet another factor the physician has to store away in his brain, to weigh against hundreds of others in virtually every treatment.

Now add to that the inexorable pressure from healthcare providers to contain costs and increase efficiency.

This is the backdrop for a dramatic new medical technology that may let physicians destroy diseased or target cells with high selectivity, minimal invasiveness, and minimal effect on healthy cells.

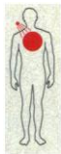
PhotoPoint,™ being developed by Miravant, utilizes highly-purified synthetic drugs which are activated by a special non-thermal light. Applications as diverse as cancer and eye disease are being examined, most of them likely to be handled on an outpatient basis.

Certain of these drugs appear to naturally collect in rapidly reproducing cells, and by exposing them to a different wavelength of light it may also be possible to make the diseased cells fluoresce, thus creating a completely new diagnostic tool.

In short, this may be one advance which ultimately simplifies the doctor's treatment selection.

PhotoPoint has potential to selectively target a range of abnormal tissues in the body, such as diseases like cancer or retinal abnormalities.

In clinical studies, the PhotoPoint drug is injected and is subsequently retained by target cells. It remains inactive until exposed to a specific wavelength of non-thermal red light.



Light is directed at the target area. A small diode-based system generates the light, and special devices deliver it within the body or on its surface.

Targeted cells are destroyed by an interaction between the drug and the light, with minimal known side effects. PhotoPoint, now in clinical trials, is being developed as an outpatient procedure.

Learn more about PhotoPoint™ and Miravant (Nasdaq: MRVT) at www.miravant.com, or call toll-free at 888-685-6788. The company's products require U.S. Food and Drug Administration approval before marketing.

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1836 153 (25 Mini tablets)	10 ml
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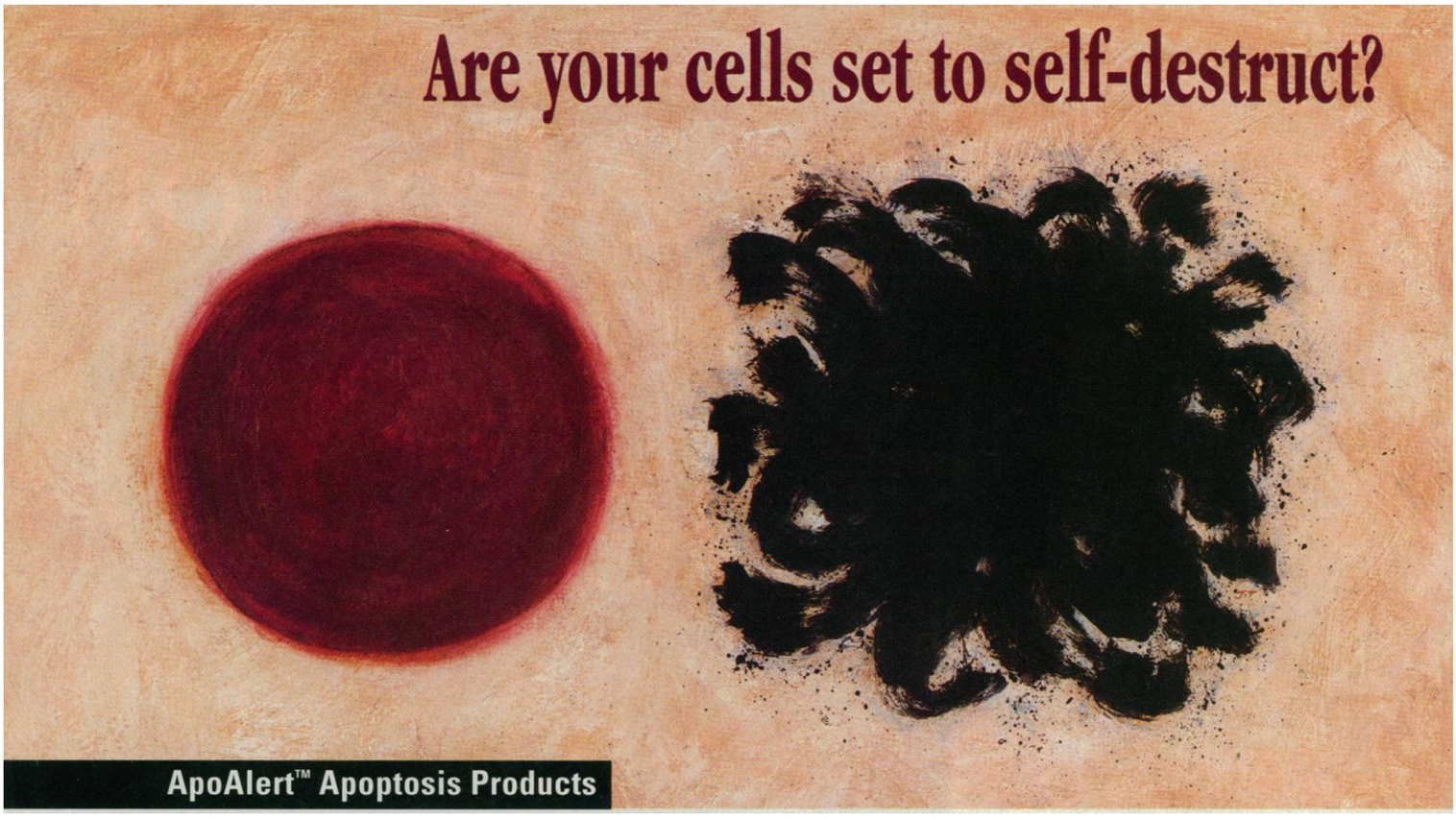
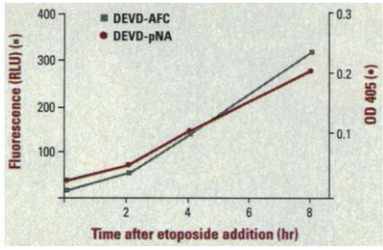
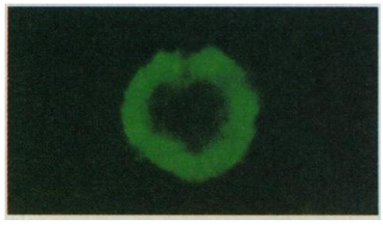


ApoAlert™ Apoptosis Products



ApoAlert CPP32 Protease assay detects CPP32 activity soon after induction of apoptosis.



ApoAlert Annexin V assay detects early-stage apoptosis by flow cytometry or fluorescence microscopy.

The **ApoAlert CPP32 Fluorescent and Colorimetric Protease Assay Kits** (#K2026-1, -2, #K2027-1, -2) provide convenient means of detecting CPP32 activity. CPP32 is an ICE-family protease implicated in initiating apoptosis in a variety of systems.

The **ApoAlert Annexin V Apoptosis Kit** (#K2025-1, -2) quickly and easily detects an early apoptosis indicator—the translocation of phosphatidylserine to the outer leaflet of the plasma membrane.

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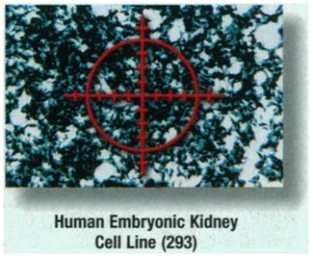
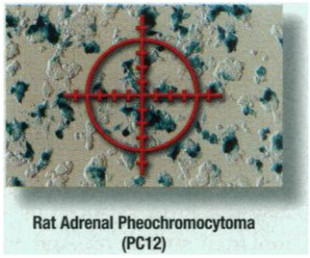
Now it's even easier to hit your target,

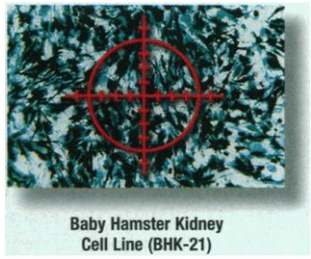
Human Primary Passaged Fibroblasts



Human Embryonic Kidney Cell Line (293)

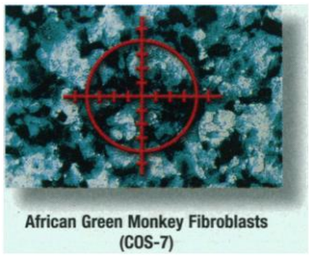


Rat Adrenal Pheochromocytoma (PC12)

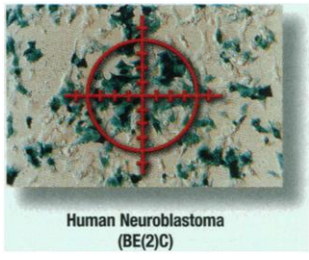


Baby Hamster Kidney Cell Line (BHK-21)

Human Breast Carcinoma (SK-BR-3)



African Green Monkey Fibroblasts (COS-7)



Human Neuroblastoma (BE(2)C)

with LIPOFECTAMINE PLUS Reagent.

Aim for better transfection with the newest addition to Life Technologies' broad spectrum of established, dependable GIBCO BRL™ products for transfection, an integral part of your state-of-the-art gene expression studies.

Enhance your protocols with our media, serum, selective antibiotics and lipid reagents, and further increase transfection of your cells, including those that are hard to transfect, with LIPOFECTAMINE PLUS™ Reagent.

Cell lines successfully transfected with LIPOFECTAMINE PLUS Reagent:	
NIH 3T3	HT-29
MRC5	COS-7
HeLa S3	CHO-DXB11
SK-BR-3	BHK-21
Hep G2	MCDK
PC12	293
CHO-K1	HT1080
BE(2)C	Human Fibroblast

LIPOFECTAMINE PLUS Reagent consists of LIPOFECTAMINE™ Reagent, the most efficient and popular cationic lipid reagent for transfecting DNA, and the proprietary PLUS Reagent for precomplexing the DNA. When used together, the LIPOFECTAMINE PLUS Reagent results in unparalleled performance in a wide variety of adherent eukaryotic cell types.

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- Two to more than five times higher peak efficiencies than with other commercially available transfection reagents and methods.
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Less Optimization Required

- Broad range of activity improves reproducibility and eliminates need for exhaustive optimization experiments, saving time and materials.

Less DNA Required

- Half as much precious DNA is needed per transfection as before, so you can actually do more experiments with less material.

Use With or Without Serum

- Outstanding performance in the presence or absence of serum, permitting use with cell types of differing sensitivity.

Product	Cat. No.	Size
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The Ares-Serono Foundation Fellowships in Biomedicine

1998 Award Announcement

FELLOWSHIPS IN REPRODUCTIVE ENDOCRINOLOGY

Two Fellowships will be awarded by The Ares-Serono Foundation for postdoctoral training pertaining to studies in the field of reproductive endocrinology, based on an international competition.

Fellowship Terms

- Full-time postdoctoral training
- 2 years of support
- USD 40,000 annual grant towards salary and expenses for postdoctoral training

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Eligibility

- Applicants must have completed a PhD/MD or equivalent academic degree within 3 years from the start date of the fellowship
- Ability to communicate fluently in English (verbal and written)
- Preference will be given to candidates applying for a postdoctoral training in an Institute other than the one where their final academic degree was obtained.

Schedule

Application deadline:	February 28th, 1998
Grants announced:	July 15th, 1998
Fellowships start:	October 1998

For the Application Form and Eligibility Guidelines, please contact:

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