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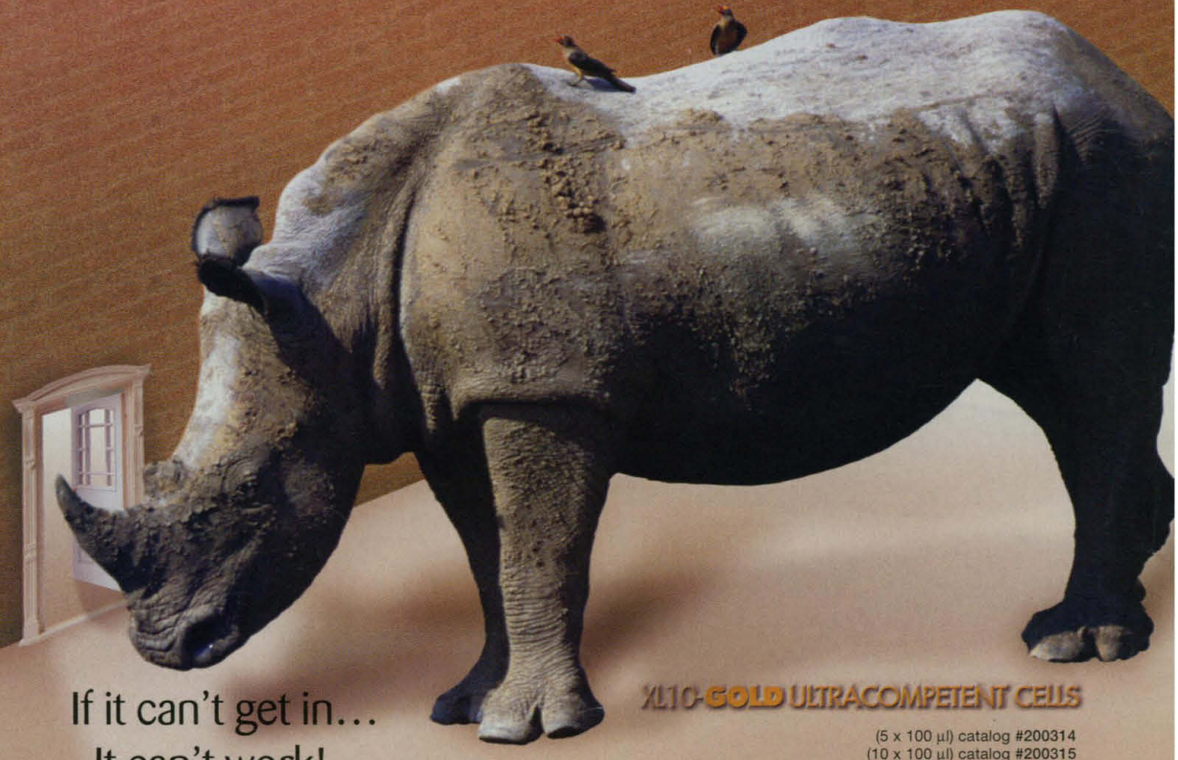

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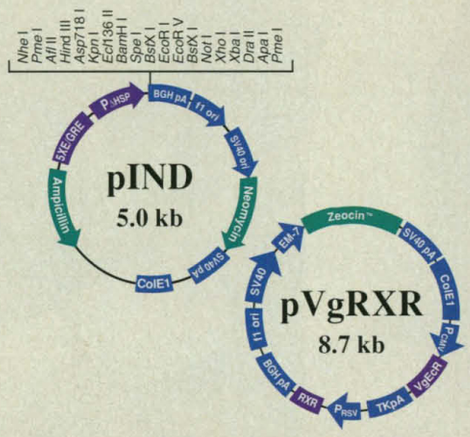

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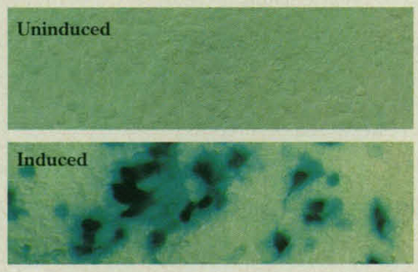

Uninduced and induced transiently transfected 293 cells stained with X-gal.

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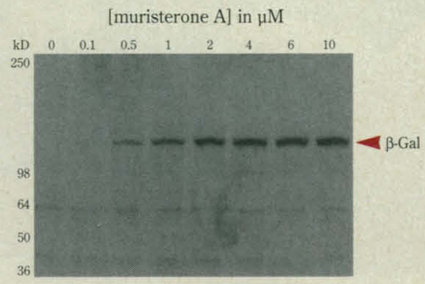

Dose-dependent β-galactosidase Induction. 293 cells stably transfected with pVgRXR and pIND/*lacZ* treated with increasing amounts of muristerone A. Equal amounts of isolated protein were separated by SDS-PAGE, blotted and detected by antibody and chemiluminescence.

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1. No, D. *et al.* (1996) *Proc. Natl. Acad. Sci. USA* **93**: 3346-3351.

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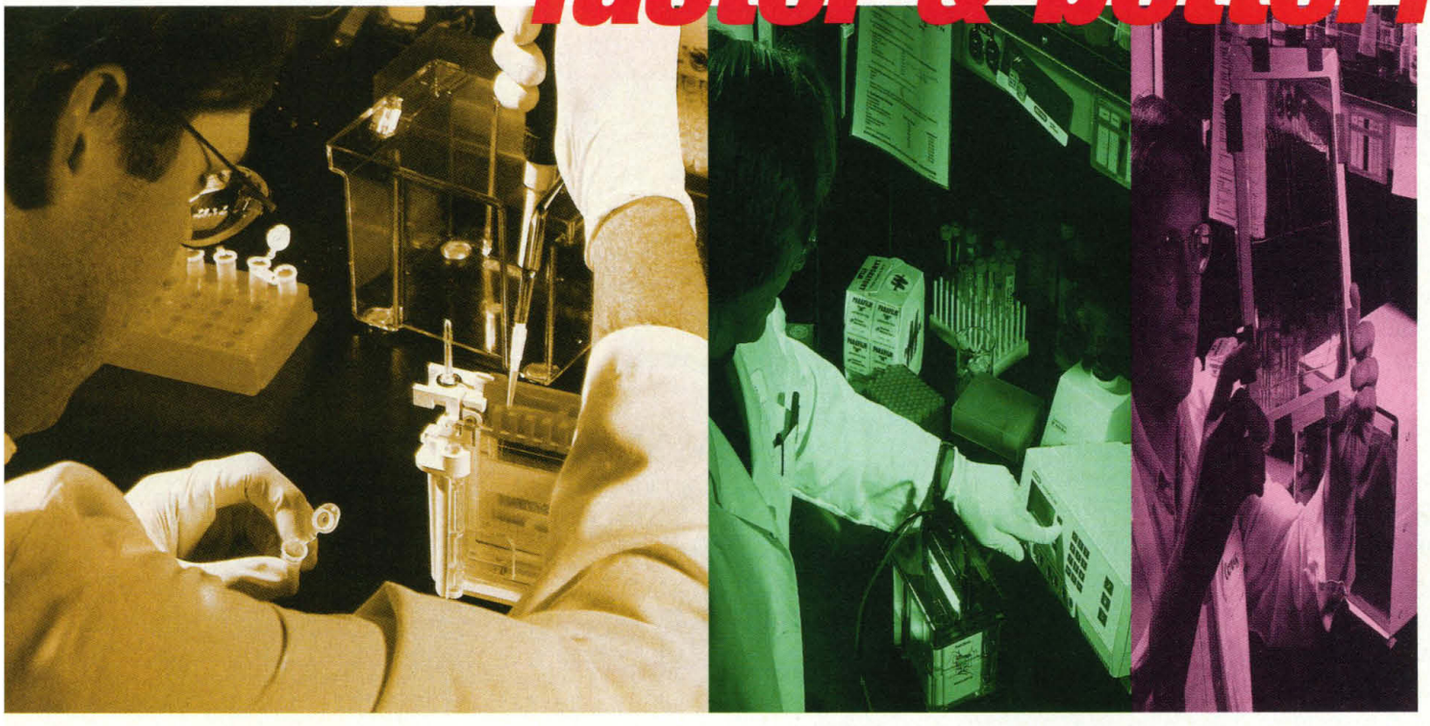

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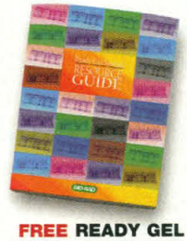

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SCIENCE

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150 YEARS • 1848-1998

178
One way to avoid grantsmanship

217
Closing up cracks at Landers

NEWS

SPECIAL NEWS REPORT

SCIENCE'S COMPASS

Policy

Books and New Media

Research

Review

REPORTS

DEPARTMENTS

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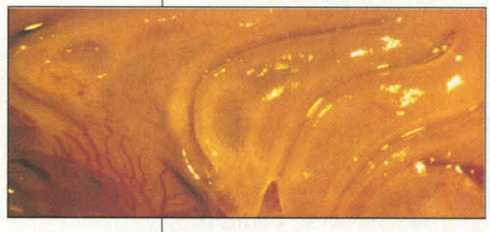
COVER

Alzheimer's is characterized by short-term memory loss and plaques and tangles in the cerebral cortex. Aberrant ubiquitin protein, likely resulting from an RNA mutation, is detectable in plaques (vague spots) and tangles (flame shapes, ~40 μm long) in the hippocampus (a region involved in short-term memory) from an Alzheimer's patient. This mutation mechanism is likely a factor in non-familial Alzheimer's and other neurodegenerative pathologies. See p. 242 and the News story on p. 174. [Image: F. W. van Leeuwen and G. van der Meulen]

TECHNICAL COMMENTS

193 & 237
Navigating odor space



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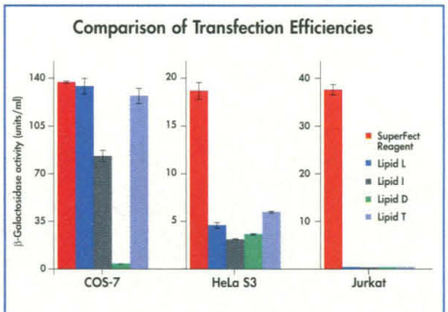

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edited by PHIL SZUROMI

Blackbody chemistry

Unimolecular decay is the most basic chemical reaction; a molecule A is activated and dissociates to form B and C. An early hypothesis was that, for a thermal reaction, blackbody radiation could energize the molecule, but it has been long accepted that A is actually energized by collisions with another molecule M (the Lindemann-Christiansen hypothesis). Dunbar and McMahon (p. 194) review evidence from Fourier transform ion cyclotron resonance experiments which shows that for certain reactions, such as the dissociation of weakly bound clusters, the blackbody radiation field is the source of activation energy. The reaction conditions avoid collisions between cluster species such as $F^-(CH_3OH)_3$. Detailed kinetic modeling of such data can reveal binding energies for the parent cluster ions.

■

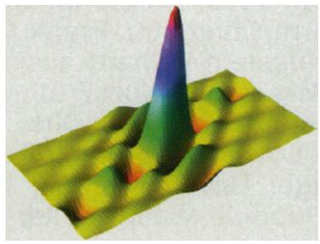
More accepting

Antibiotics such as erythromycin are synthesized by large multienzyme complexes, the polyketide synthases. Variants of these antibiotics, which are useful in combating antibiotic resistance, could be produced if these enzyme complexes could be induced to accept different substrates as starting materials. Marsden *et al.* (p. 199) show that by grafting the avermectin-producing polyketide synthase onto the first module of the erythromycin-producing enzyme, a wide variety of erythromycin derivatives could be produced from different carboxylic acids.

■

Trapping electrons

The dynamics of charge carriers at or near interfaces (such as those between a metal and a dielectric) are complex and involve polarization and localization or delocalization of the charge carriers. Such processes occur on a femtosecond time scale and have only recently become accessible to detailed experimental characterization. Ge *et al.* (p. 202; see the commentary by Höfer, p. 190) found that optical excitation at the alkane-silver interface first creates interfacial electrons that can



freely move parallel to the interface. Within a few hundred femtoseconds, they become trapped into a localized state, and within picoseconds they decay back into the metal. A theoretical description analogous to electron transfer theory was applied successfully to these results.

■

Photonic channeling

Information transfer over networks is plagued by a host of security problems. Quantum mechanics offers a possible solution; because of the special nature of quantum states, it is impossible for a third party to intercept and copy a quantum signal without the recipient knowing about it. Van Enk *et al.* (p. 205) describe a theoretical approach to implementing a quantum network for communicating through photons. Physical implementation of quantum information processing poses huge practical obstacles, but such theoretical efforts are adding fundamentally to our understanding of information storage and error correction in quantum systems.

■

Frameshift mutations andneurodegeneration

An unanticipated set of aberrant proteins in the neurodegenerating brains of Alzheimer's disease and Down syndrome patients has been discovered by van Leeuwen *et al.* (p. 242; see the cover and the news story by Vogel, p. 174). Proteins are produced that have a frameshift mutation caused by the deletion of a dinucleotide from the encoding RNA. The so-called +1 proteins include a form of ubiquitin and a form of the β-amyloid precursor protein that were shown to accumulate in the neuritic plaques characteristic of these patients. A form of the ubiquitin protein was found in elderly control group patients.

Time strengthens all ruptures

Fault zones, where earthquakes repeatedly occur, must strengthen themselves between events in order to build up enough stress to produce a new rupture. Li *et al.* (p. 217) monitored the recovery of the Johnson Valley fault zone, one of three faults ruptured in 1992 by the magnitude 7.5 Landers, California, earthquake, with two borehole explosions and an array of three-component seismometers. The velocities of the sound waves within the narrow zone of the fault increased from 1994 to 1996 through a decrease in crack density of about 1 percent. These results provide a highly detailed observational study of the closing of mainly dry cracks along the Johnson Valley fault over a 2-year period that will help seismologists understand how fault zones regain their strength for the next rupture.

■

Silicon and germanium nanotubes

Although several varieties of carbon and boron nitride nanotubes are now known, it has proven more difficult to readily synthesize crystalline silicon and germanium in nanotube form. Morales and Lieber (p. 208) have combined vapor-liquid-solid synthesis methods used to make larger tubular structures with the laser-ablation methods of carbon nanotube synthesis to produce nanotubes of these semiconductors. This morphology may lead to improved materials for electronic and optical applications.

■

Atmospheric NO source

Nitric oxide (and other reactive nitrogen oxides) plays a key role in the stratospheric destruction of ozone. Most NO is thought to form from oxidation of N_2O. Zipf and Prasad (p. 211), however, present a series of experiments showing that significant amounts of NO may also form photochemically in the stratosphere from a reaction involving N_2, O_2, and the N_2:O_2 dimer. In this reaction, the nitrogen-15/nitrogen-14 ratio in the resulting NO is very low and might be used as a tracer in the stratosphere.

■

Atmospheric CO_2 source

The large boreal forests of the Northern Hemisphere have generally been thought to be one of the major sinks for CO_2 in the Earth's atmosphere. Using a variety of measures, Goulden *et al.* (p. 214) show that recent climate warming has at least locally increased emissions of CO_2 from the boreal forest such that it has acted as a carbon source. As a result of warming, thawing at high latitudes extended deeper into the soil, where decomposition released old carbon buried in organic matter.

■

Language locations

One of the brain areas involved in language is the planum temporale, notable for being larger on

(Continued on page 151)

NOMINATIONS FOR THE 1999 LOUIS-JEANTET PRIZE FOR MEDICINE

Nominations are being sought for the 1999 Louis-Jeantet Prize for medicine. One to three prizes will be awarded. They will amount to a maximum of 2 million Swiss Francs (approximately 1.4 million US Dollars) in 1999. These prizes will provide substantial funds for the support of biomedical research projects (fundamental or clinical) of the highest quality. Candidacies in clinical research are strongly encouraged.

Candidates (either individuals or research groups) must be nominated by scientists, physicians or institutions having detailed knowledge of the candidates' research. The Louis-Jeantet Prize for medicine is not intended to honour past accomplishments but to help and encourage the winners' continued research activity. Candidates shortlisted for the final selection will therefore be asked to provide a research project to which the financial support of the Prize could give decisive impetus.

The winners of the ten previous Louis-Jeantet Prizes for medicine have been **Roberto Poljak, Walter Schaffner** and **Greg Winter** in 1989, **Nicole Le Douarin, Harald Von Boehmer** and **Gottfried Schatz** in 1990, **Pierre Chambon, Frank Grosveld** and **Hugh Pelham** in 1991, **Paul Nurse, Christiane Nüsslein-Volhard** and **Alain Townsend** in 1992, **Jean-Pierre Changeux, Richard Henderson and Kurt Wüthrich** in 1993, **Thierry Boon, Jan Holmgren** and **Philippe Sansonetti** in 1994, **Dirk Bootsma** and **Jan Hoeijmakers, Peter Goodfellow** and **Robin Lovell-Badge**, and **Peter Gruss** in 1995, **Björn Dahlbäck, Ulrich Laemmli** and **Nigel Unwin** in 1996, **Philip Cohen, Kim Nasmyth** and **Richard Peto** in 1997, **Denis Duboule, Walter Keller** and **Ronald Laskey** in 1998.

The following general points should be noted:

1. The Prize is intended for researchers working in European countries, members of the Council of Europe. The candidates need not, however, be themselves nationals of any of these countries.

2. Applications must be submitted, confidentially, on the official forms only. These are obtainable from:

   The Secretary of the Science Committee
   The Louis-Jeantet Foundation for medicine
   P.O. Box 277
   CH-1211 GENEVA 17
   Switzerland

   Further information will be sent with the nomination form.

3. The deadline for applications is February 15, 1998.

The name(s) of the winner(s) of the 1999 Louis-Jeantet Prize for medicine will be announced in January 1999. The Prize Ceremony will take place in Geneva (Switzerland) in April 1999.

(Continued from page 149)

the left side than the right in humans and for being evenly sized in the brains of other primates. Gannon *et al.* (p. 220) now present quantitative morphological evidence of a similar asymmetry of the planum temporale in chimpanzees and discuss how this finding relates to the known predominance of the left hemisphere for language functions in the human.

■

Receptors that make scents

Several years ago, a family of putative odorant receptors was identified, but direct evidence that these receptors really were mammalian odorant receptors has been lacking. Zhao *et al.* (p. 237; see the commentary by Reed, p. 193) now provide such evidence by showing that the expression of particular putative receptors in a rat's nose increased the responsiveness of the rat's olfactory neurons to specific odors.

■

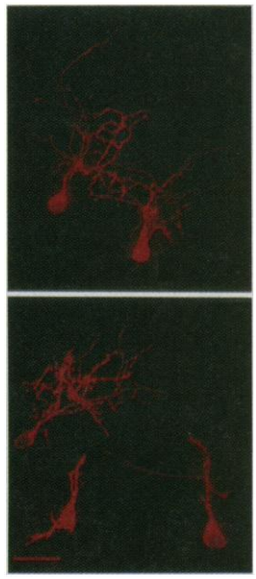
AM and FM calcium signals

Intracellular calcium concentrations ($[Ca^{2+}]_i$) are tightly controlled and are a critical regulator of cell function. Not only does the overall $[Ca^{2+}]_i$ change in response to various stimuli, but oscillations in $[Ca^{2+}]_i$ occur that can vary in frequency, amplitude, duration, or number. Most attention has been focused on the amplitude of changes in $[Ca^{2+}]_i$, partly because no mechanism was known to detect or decode changes in frequency. De Koninck and Schulman (p. 227; see the commentary by Putney, p. 191) now show that in vitro, a single enzyme, the Ca^{2+}/calmodulin–dependent protein kinase II (CaM kinase II), can respond to changes in frequency of Ca^{2+} oscillations with changes in its autonomous (Ca^{2+}-independent) activity. Modulation of the response of CaM kinase II by the amplitude and duration of the oscillations indicate that fine tuning of the kinase's activity may occur as it participates in control of diverse cellular activities.

■

Slowing their search

Young neurons, as they search and form their mature connections, extend more dendrites than do more mature neurons that already have connections in place. As neurons mature in the *Xenopus* optic tectum, the rate at which they extend new dendrites slows down. Wu and Cline (p. 222) showed that this change in



cellular activity correlates with an onset of expression of α-calcium-calmodulin–dependent kinase II (CaMKII). By over- or underexpressing CaMKII activity, they were able to diminish or enhance the rate of dendrite extension, respectively.

■

A near-death experience

Caspases are proteases known for their role in killing a cell from the inside out. However, caspase activation does not inevitably lead to cell death. McCall and Steller (p. 230) found that during oogenesis in fruit flies, the DCP-1 caspase was crucial for oocyte development. Normally, the oocyte is fed cytoplasm from the surrounding nurse cells, which eventually die. This process of "cytoplasmic dumping" relies on the activation of caspases in the nurse cell cytoplasm to initiate cytoskeletal and nuclear changes. These activated caspases are probably transported along with other cytoplasmic proteins from the nurse cells into the oocyte, and yet the oocyte not only does not die but actually requires this step for maturation. Thus, the effector end of the death pathway can be usurped for what is a related, but quite distinct, function.

■

NO control via nitrosylation

Controlled release of calcium from intracellular stores is the primary regulatory mechanism governing the force of contraction of cardiac muscle cells. Such calcium release occurs through channels on the sarcoplasmic reticulum that are known as ryanodine receptors. Xu *et al.* (p. 234) have explored the molecular mechanism by which nitric oxide, which is generated in stimulated cardiac cells, might influence such a control mechanism. They found that the effects of NO were not the result of a general change in redox potential. Rather, NO appeared to cause specific covalent modification by S-nitrosylation of certain thiol groups on the ryanodine receptor. These increases in S-nitrosylation led to increased opening of the channel. Such nitrosylation had a distinct effect from that of oxidation of thiols to disulfides. Thus, NO and related compounds may regulate the calcium release channel through particular chemical modifications that allow specific control of various channel functions rather than through a general change in cell redox potential.

Technical Comment Summaries

Paleosols and Devonian Forests

The Rosemary pedotype is a soil profile from Victoria Land, Antarctica. G. J. Retallack described (Reports, 25 Apr., p. 583) this "geologically most ancient paleosol thought to have supported well-drained forest" and evaluated "its importance within the context of other Paleozoic paleosols."

D. Dahms *et al.* "question the horizon designations, the interpretations of the profile descriptions and data, and the inference that these horizons characteristics are diagnostic of soils developed beneath a Devonian forest."

In response, Retallack provides more details about "the soil texture and chemical data" and the "graphical notation" used in the report. He refers to more lengthy studies of such paleosols and hopes "for continued testing of this simple yet important" site.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/279/5348/151a

Nucleotide Sequence: Correction

D. Mathis and C. Benoist state that, in their report of 31 January 1997 (N. Nakano *et al.*, p. 678), there were several mistakes in the nucleotide sequence shown in figure 5 (p. 682). These mistakes were the result of clerical error and do not alter the substance of the report or its conclusions. The correct figure can be seen at www.sciencemag.org/cgi/content/full/279/5348/151b

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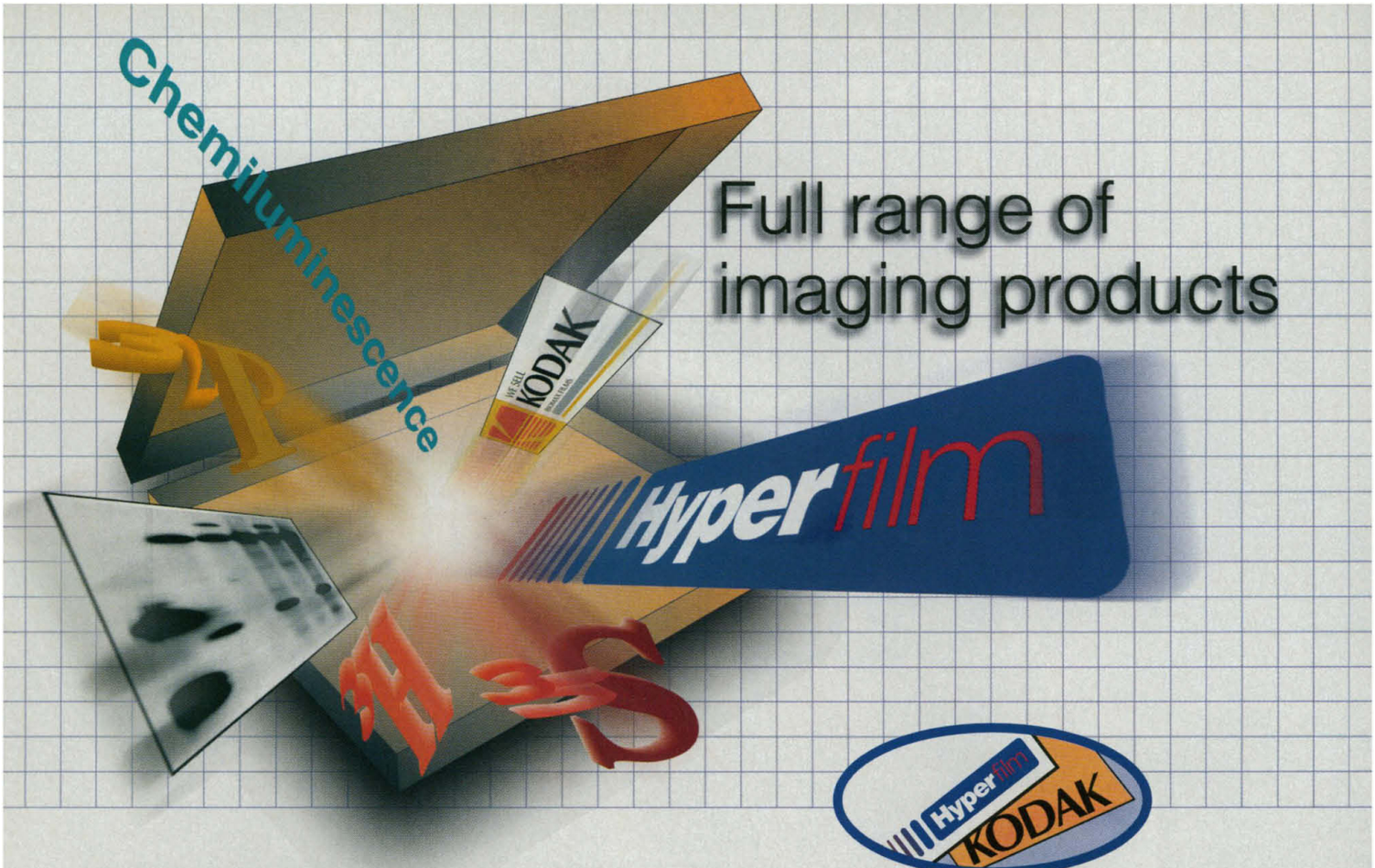

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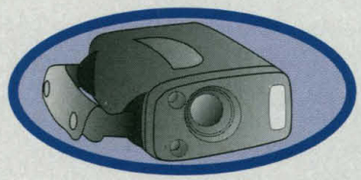

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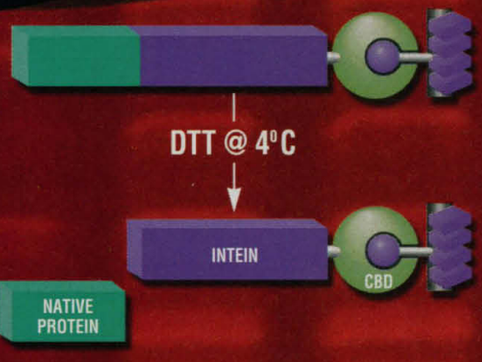

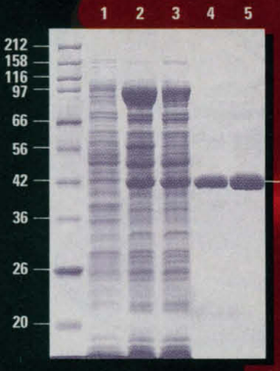

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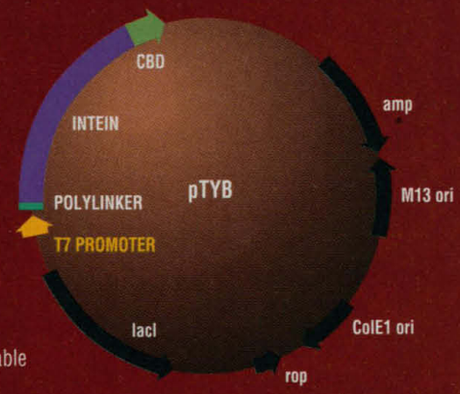

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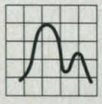

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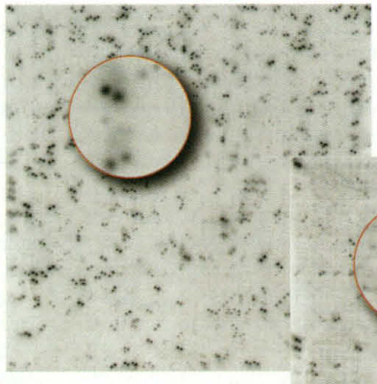

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1. "The I.M.A.G.E Consortium: An Integrated Molecular Analysis of Genomes and their Expression", Lennon, G.G., Auffray, C., Polymeropoulos, M., and Soares, M.B. [1995] Genomics.

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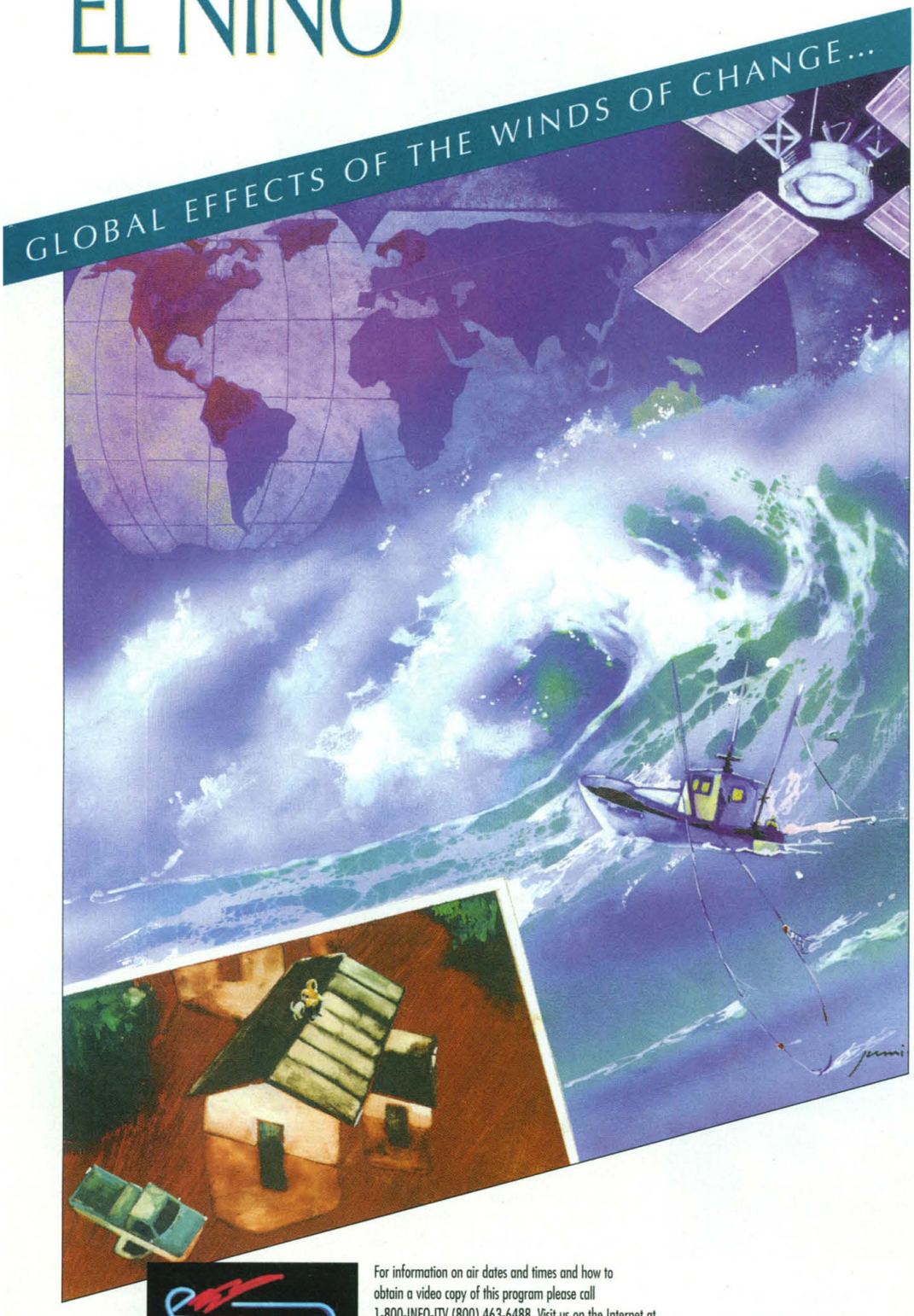

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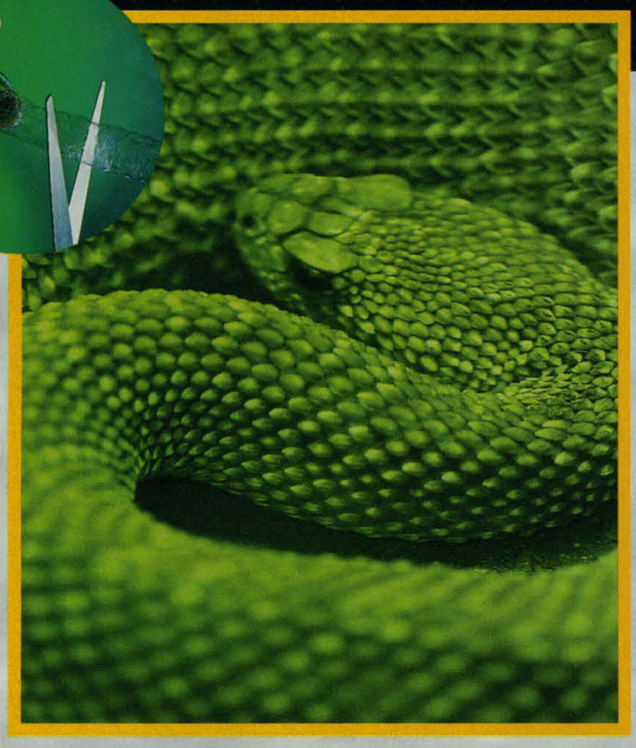

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SnakeSkin™ Pleated Dialysis Tubing – easy, fast and economical. Once you try it, you'll never go back to those flat tubing hassles!

SnakeSkin™ Dialysis Tubing

Product #	MWCO	Pkg. Size
68035CH	3,500	22 mm dry I.D. x 35 feet*
68700CH	7,000	22 mm dry I.D. x 35 feet*
68100CH	10,000	22 mm dry I.D. x 35 feet*

**Equivalent to 10.5 meters of 34 mm dry flat width*

SnakeSkin™ Dialysis Tubing Accessory

Product #	Description	Pkg. Size
68011CH	SnakeSkin™ Dialysis Clips	6 clips/pkg.

ISO 9001 QUALITY SYSTEM CERTIFIED

Call 800-874-3723 for product information. Outside the U.S. call 815-968-0747 for the name of your local distributor.

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R&D Magazine recently recognized the significance of the DLR™ Assay System by presenting Promega with a prestigious R&D 100 Award, given to the 100 most significant and innovative new products in the previous year.

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* U.S. Pat. Nos. 5,283,179, 5,641,641 and 5,650,289 have been issued to Promega Corporation for a firefly luciferase assay method which affords greater light output with improved kinetics as compared to the conventional assay.

** The cDNA encoding luciferase from *Renilla reniformis* is covered by U.S. Pat. No. 5,292,658 assigned to the University of Georgia Research Foundation and sublicensed from SeaLite Sciences, Inc., Norcross GA.

† Patent pending.

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