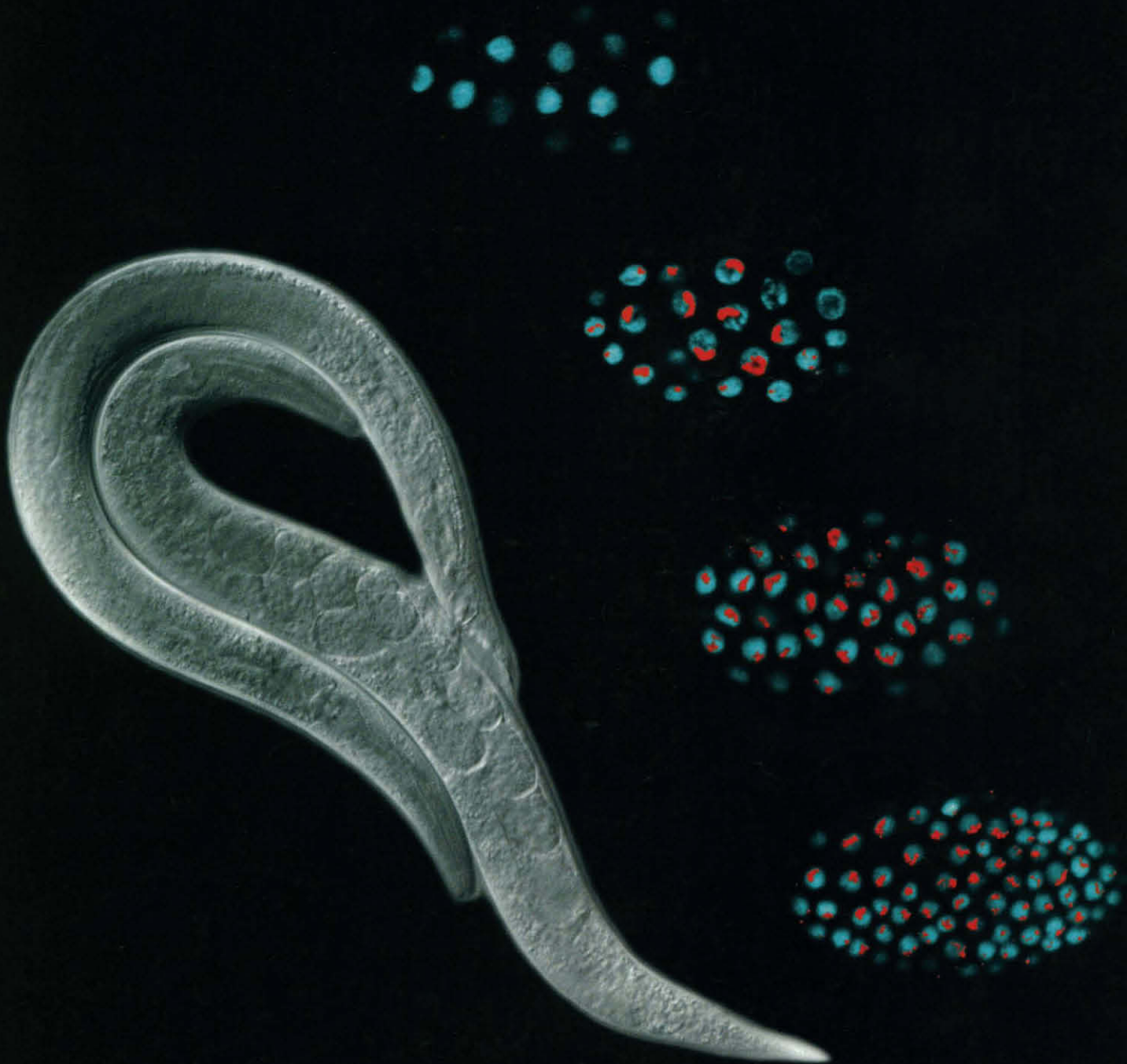


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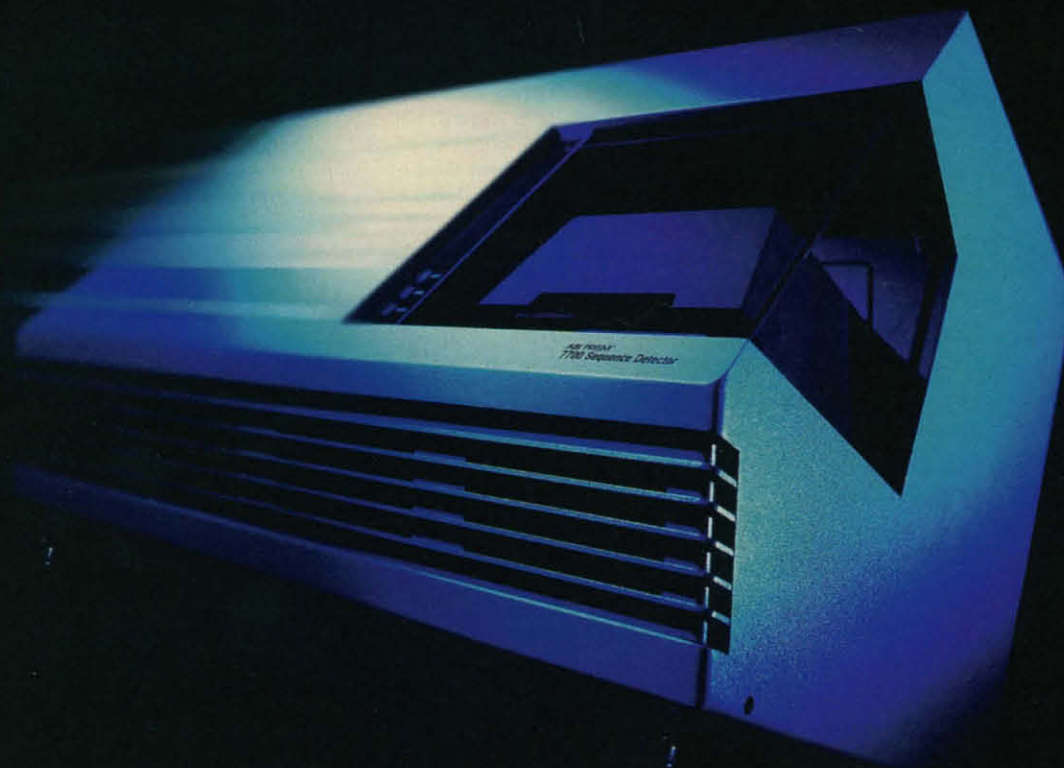
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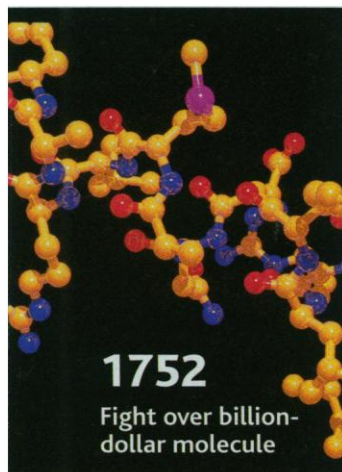
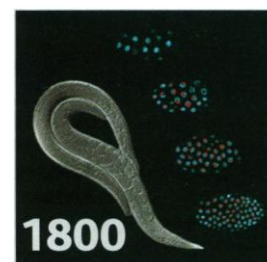
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COVER In mammals, flies, and nematodes, a specialized dosage compensation complex equalizes the expression of genes on the X chromosome between 1X males and 2X females (or hermaphrodites) by modulating transcript levels. In *Caenorhabditis elegans*, SDC-2 protein (red) targets the complex along the X chromosomes of hermaphrodite embryos (~50 μ m long) (DNA in blue) at about the 40-cell stage. A mating pair (~1 mm long) is on the left. [Images: H. Dawes and A. Villeneuve]



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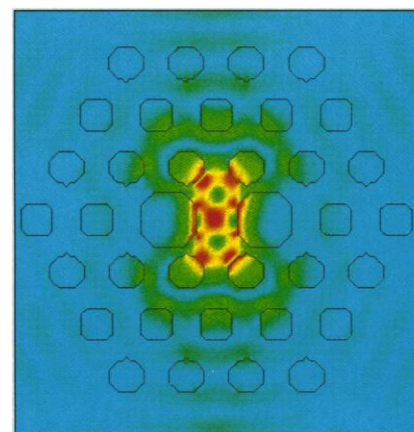
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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 1999 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$110 (\$62 allocated to subscription). Domestic institutional subscription (51 issues): \$325; Foreign postage extra: Mexico, Caribbean (surface mail) \$55; other countries (air assist delivery) \$90. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. Printed in the U.S.A.

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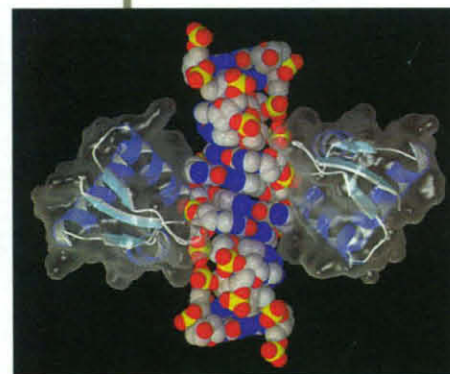
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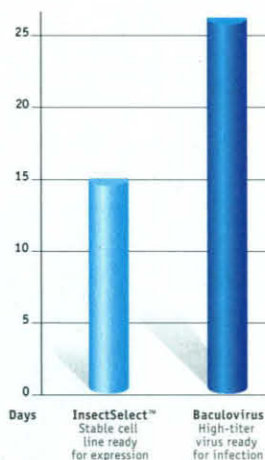
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FIXING THE FOSSIL TREE

Much of the tree of evolution, and particularly the important details relating to genus and species, has been constructed by cladistics, the analysis of a variety of morphological traits of fossils. Consideration of the temporal occurrence of fossils has been problematic because there may be many gaps in the fossil record and because "living fossils" that preserve primitive traits may persist; often, the temporal data are not weighted or included in the analysis. Fox *et al.* (p. 1816) constructed a computer model of evolution of several character traits and show that inclusion of the temporal occurrences of fossils greatly improves the likelihood of capturing the correct or a reasonable phylogeny.

SMALL, COHERENT, AND BRIGHT

Smaller optical devices could lead to "all-optical" computing and also find applications in communications and in near-field (subwavelength) optics. Painter *et al.* (p. 1819) introduce a cavity laser that is only 0.03 cubic micrometer in size. Its operation combines a laser cavity, which consists of a gap between two reflectors in which the photons can build up, and a photonic crystal that has an intentionally placed defect. The defect, a single departure from the otherwise periodic array of holes etched into the material, effectively "locks" or localizes the light output to that particular point.

ASSAYING ANCIENT ATMOSPHERES

Earth's climate was warmer during the middle Eocene, possibly because atmospheric CO₂ concentrations were considerably greater than they are today or possibly because of differences in ocean circulation. Pearson and Palmer (p. 1824; see the news story by Kerr) evaluated this hypothesis by constructing a pH profile of the Eocene ocean from boron isotopes in several species of fossil plankton—ocean pH reflects the amount of CO₂ dissolved in seawater, which in turn depends on atmospheric CO₂. The data imply that atmospheric CO₂ concentrations during the middle Eocene were similar to or only slightly greater than modern values.

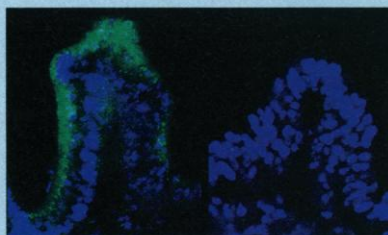
DIRECTING HERMAPHRODITE DEVELOPMENT

For the specification of sexual development, many organisms require the action of two different mechanisms, one that determines overt sexual characteristics (sex determination) and one that equalizes

gene expression from the sex chromosomes despite the difference in sex chromosome dose (dosage compensation). Dawes *et al.* (p. 1800; see the cover and the Perspective by Kuroda and Kelley) now demonstrate that a single factor in the nematode *Caenorhabditis elegans* acts as a "switch" to direct hermaphrodite development. This factor, SDC-2, coordinately regulates both sex determination and dosage compensation by acting as a repressor of the male-specific gene *her-1* and by initiating complex formation on the X chromosome to reduce the chromosome's overall expression, respectively. The dual repression functions of SDC-2 in regulating sex determination and dosage compensation in *C. elegans* exemplifies the elaborate control mechanism necessary for such a complex developmental program.

THE CELLULAR CONNECTION IN HEARING

Hair cells in the inner ear are the crucial first link in a long chain of elements that participate in the hearing process, and the destruction of hair cells is one of the most important causes of hearing loss and deafness.



How these cells develop and differentiate during embryogenesis has been largely unknown. Bermingham *et al.* (p. 1837) now identify a proneural gene, *Math1*, that is required for the production of hair cells. This homolog of the *Drosophila* proneural gene *atonal* is expressed in developing sensory patches. In mutant mice that lacked *Math1*, no hair cells developed in the embryo.

HOLDING BOTH LEFT AND RIGHT

Although DNA is usually found in a form known as B-DNA, which is a right-handed double helix—meaning that the spiraling directionality of the sugar-phosphate backbone can be mimicked by the thumb and fingers of the right hand—it does transiently adopt a left-handed form, called Z-DNA, in the wake of an actively transcribing

RNA polymerase. Schwartz *et al.* (p. 1841) describe the structure of a complex between Z-DNA and the Z-DNA binding domain of an RNA editing enzyme. They find a familiar motif in DNA-protein interactions, the helix-turn-helix fold used by many proteins in binding to B-DNA. The versatility of this fold is revealed by how the second helix, which normally recognizes specific bases within the major groove when bound to right-handed B-DNA, instead makes polar contacts with the sugar-phosphate backbone of Z-DNA.

STIMULATING SYNAPSES

The underlying mechanisms of the changes in synaptic activity induced by high-frequency stimulation of neurons, such as long-term potentiation (LTP), and their implications for memory, have been controversial; two research articles address these topics (see the news story by Barinaga). The changes induced in AMPA-type glutamate receptor function during repetitive stimulation could be due to greater intrinsic activity or to their recruitment to synapses. Shi *et al.* (p. 1811) were able to count AMPA receptors in hippocampal slice cultures by tagging a subunit with green fluorescent protein. After tetanic stimulation, a large intracellular pool of AMPA receptors was redistributed into dendritic spines or clustered in dendrites. This phenomenon could be prevented by blockade of NMDA receptors in a manner analogous to synaptic potentiation. How does LTP, an electrophysiological phenomenon, relate to memory? Zamanillo *et al.* (p. 1805) show that LTP is essentially absent in mutant mice that lack an important glutamate receptor subunit. However, their spatial learning performance in the water maze test is unchanged. These findings indicate that there is a dissociation between LTP and certain forms of spatial memory. The interplay between events on the cellular and synaptic level and the behavior of the organism is more sophisticated than earlier simplistic models assumed.

VIRAL VIGILANTES

The first response by a mammal to viral infection is to produce the cell-protective type 1 interferons α and β . The major source of the interferon is not known, but natural interferon-producing cells (IPCs) are known to express CD4 and major histocompatibility complex class II proteins. Siegal *et al.* (p. 1835; see the news story by Hagmann) have now determined that these cells are the same as the recently

CONTINUED ON PAGE 1735

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1733

identified precursors of type 2 dendritic cells (pDC2s), which can induce a cell-mediated T helper cell response. As these cells mature, they work on various levels to quell viral attacks and they may provide an interesting therapeutic target for boosting antiviral responses.

FIRE AND ECOSYSTEMS

Fire has a well-recognized nature role in shaping ecosystems, but the impact of human activity on fire dynamics needs to be better understood (see the Perspective by Goldammer). Cochrane *et al.* (p. 1832) report that in tropical forests, fires caused accidentally by humans have become much more common. A positive feedback occurs that results in the accumulation of combustible biomass, which leads both to an increased incidence and an increased severity of re-burning. Using the location and patterns of fires and subsequent land use as a guide, the authors estimate that these accidental fires are currently responsible for more Amazon deforestation than intentional timber harvesting and agricultural clearing. Keeley *et al.* (p. 1829) analyzed fire frequency in California brushland using almost a cen-

tury's worth of data. It has been widely believed that brushlands are similar to woodlands—fire suppression management is needed because fuel accumulation leads to less frequent but more catastrophic fires. In fact, no Californian brushland county appears to have suffered an increase in fire size since 1910; instead, fire frequency is positively correlated with human population density. These results have implications for other fire-prone shrublands in areas of high human population density.

PSD-95 AND NEURONAL CELL DEATH

Excessive Ca^{2+} influx causes cell death in neurons, but the underlying molecular mechanisms are not fully understood. Sattler *et al.* (p. 1835) investigated the specific link between NMDA receptor signaling and the intracellular scaffolding molecule PSD-95. They showed that PSD-95 links NMDA neurotoxicity to the production of nitric oxide (NO). Suppressing PSD-95 by antisense oligodeoxynucleotides selectively blocked Ca^{2+} -activated NO generation by NMDA receptors but not by other glutamate or Ca^{2+} channels.

TECHNICAL COMMENT SUMMARIES

Heat Content Changes in the Pacific Ocean

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5421/1735a

The Acoustic Thermometry of Ocean Climate (ATOC) Consortium (Reports, 28 Aug., p. 1327) compared measurements of the heat content of the Pacific Ocean and sea surface height with results from a general circulation model. They concluded that only about half of the changes in sea level "are attributable to thermal expansion."

K. A. Kelly *et al.* comment "that the ATOC estimates [of heat content changes as made by the numerical model] are too small by a factor of two." Estimates of seasonal heat flux can be reconciled with temperature and sea-level data "after accounting for adiabatic terms, without resorting to large advective contributions."

In response, ATOC agrees "that the model may be underestimating the annual cycle of the heat flux" and states that ATOC has "no conflict with the numbers provided by Kelly *et al.*"

Regional Carbon Imbalances in the Oceans

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/284/5421/1735b

C. M. Duarte and S. Agustí (Reports, 10 July, p. 234) compiled data from many studies to model the relation between "community respiration" and "gross primary production" of ocean ecosystems. They found that, in total, the ocean "biota can act as CO_2 sinks at the global scale."

P. J. le B. Williams and D. G. Bowers comment that the apparent CO_2 deficit calculated in the report is a result of "the form of analysis." They conclude that there is insufficient evidence to suggest "that the open oceans, either as a whole or regionally, are substantially out of organic balance."

In response, Duarte and Agustí discuss choices of data sets and analysis and the challenges of making comparisons across scales and studies. They maintain that "the bulk of available empirical evidence" shows a "pattern toward heterotrophy in the oligotrophic ocean...."

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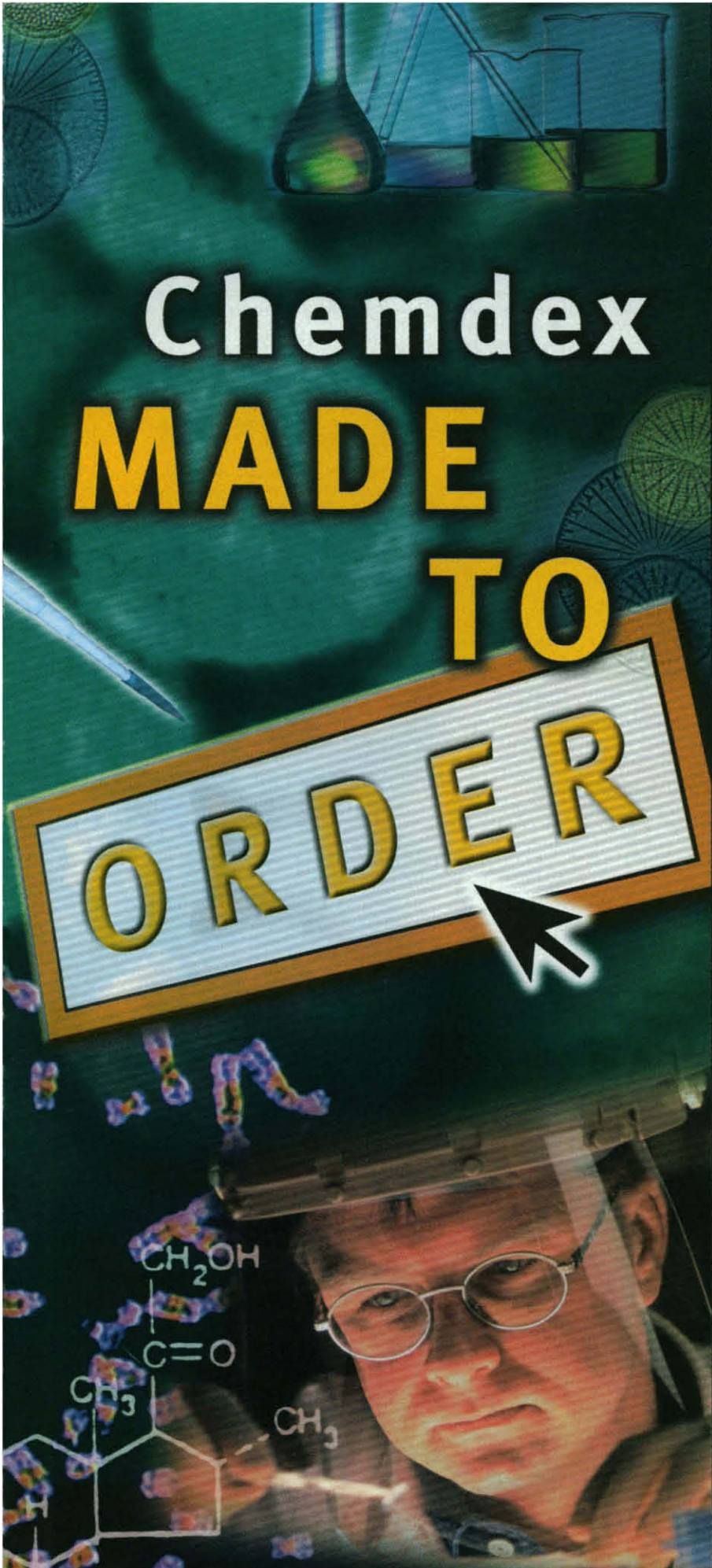
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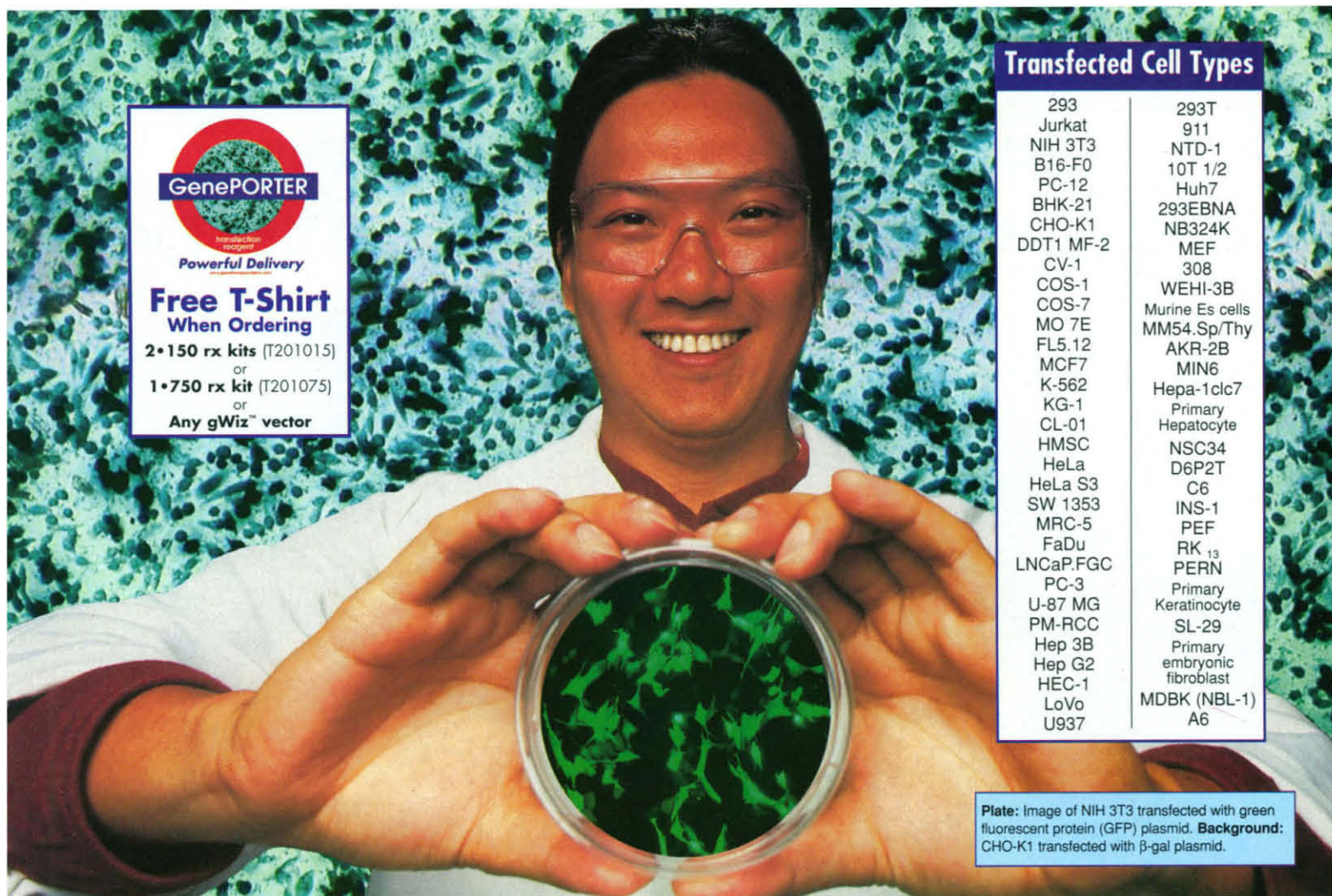
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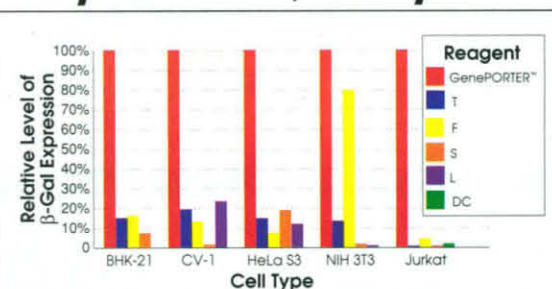
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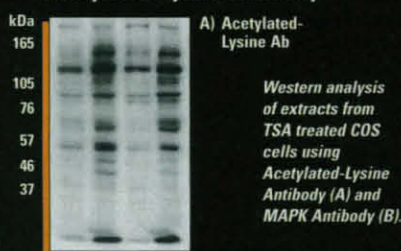
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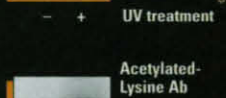
Acetylated-Lysine Antibody



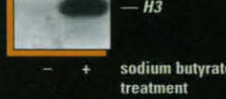
**Western analysis
of extracts from
TSA treated COS
cells using
Acetylated-Lysine
Antibody (A) and
MAPK Antibody (B)**



Increase in p53 acetylation of UV treated 293 cells detected by IP using p53 Antibody followed by Western blotting using Acetylated-Lysine (A) and p53 Antibodies (B).



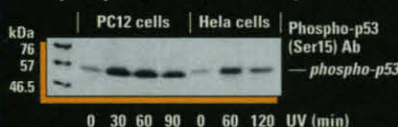
Increase in Histone acetylation of NIH/3T3 cells treated with 5 mM sodium butyrate for 24 hours detected by Western blotting using Acetylated-Lysine Antibody.



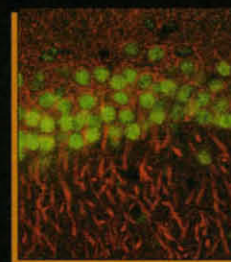
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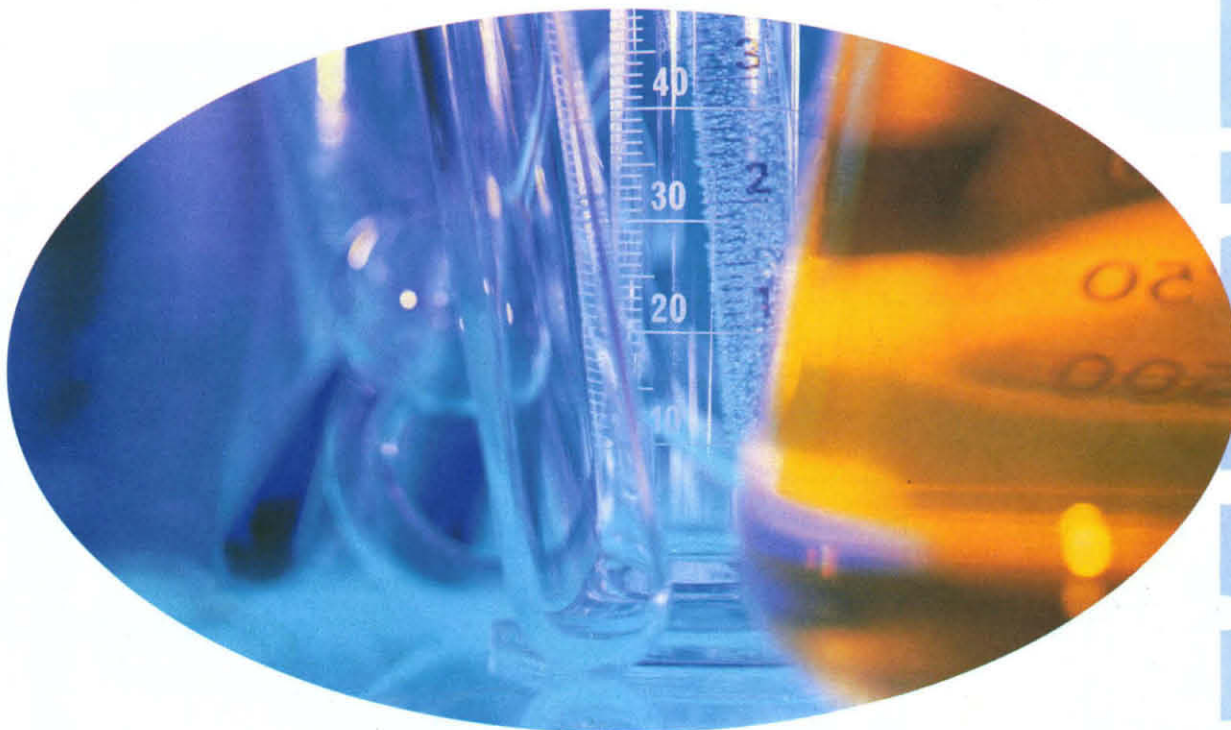
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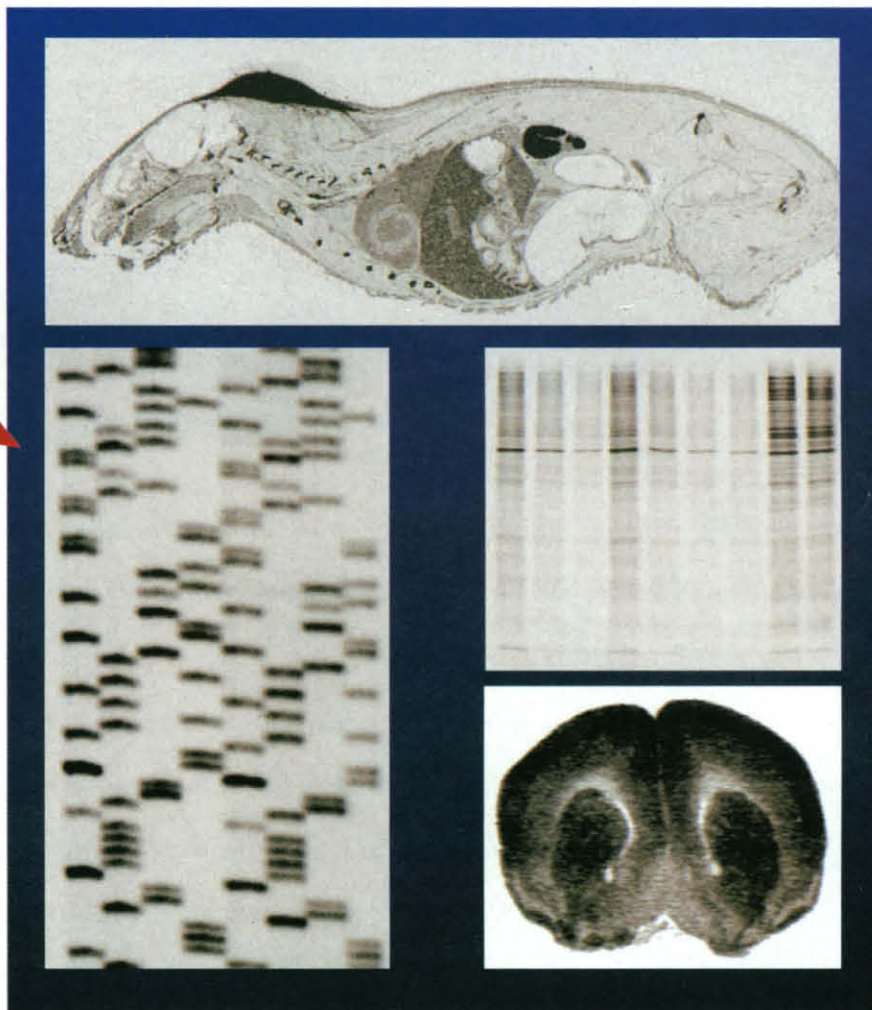


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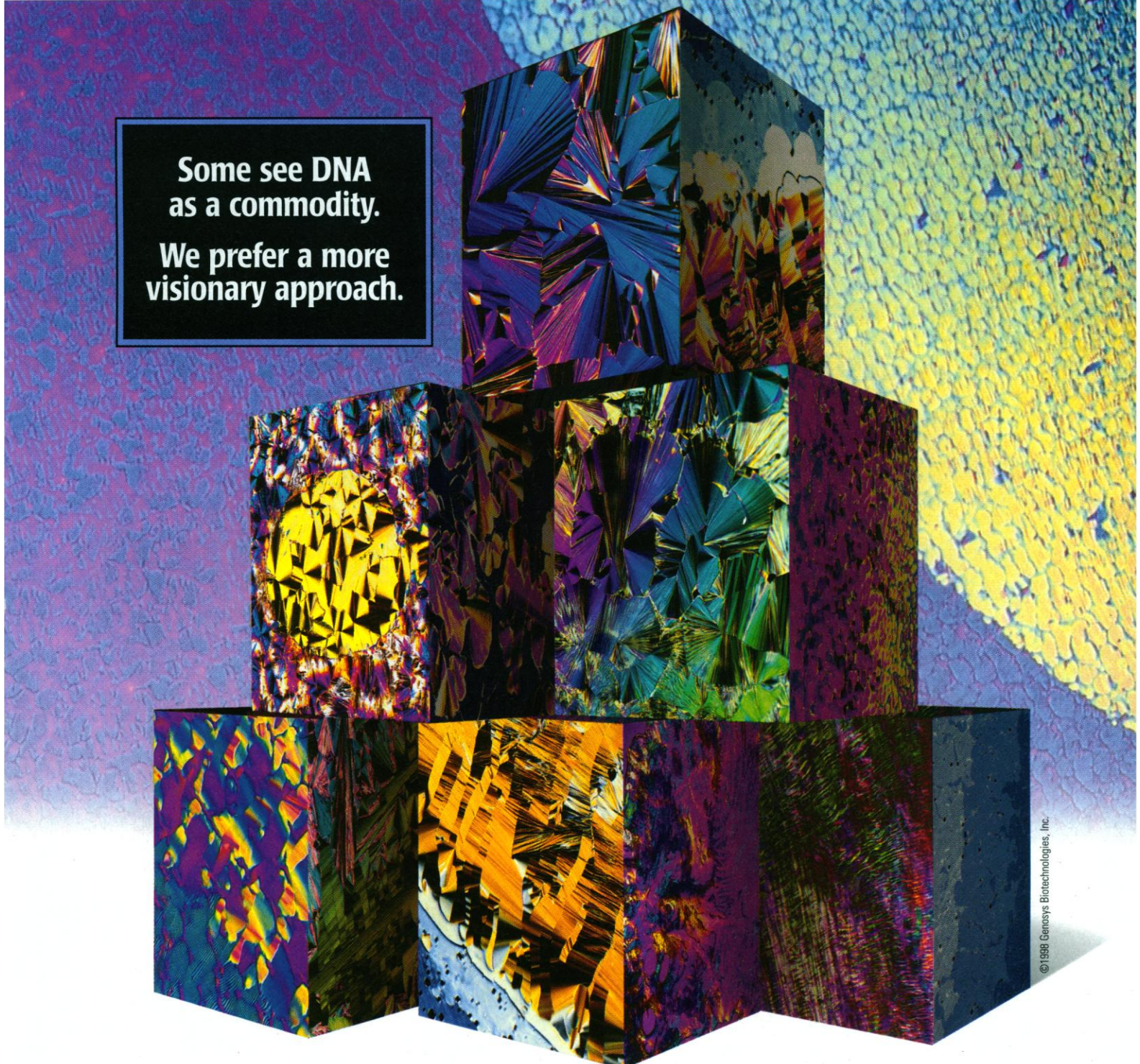
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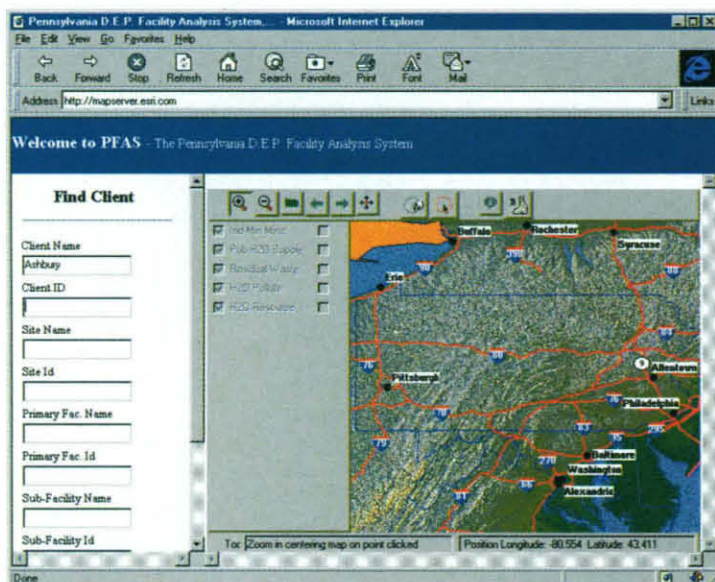
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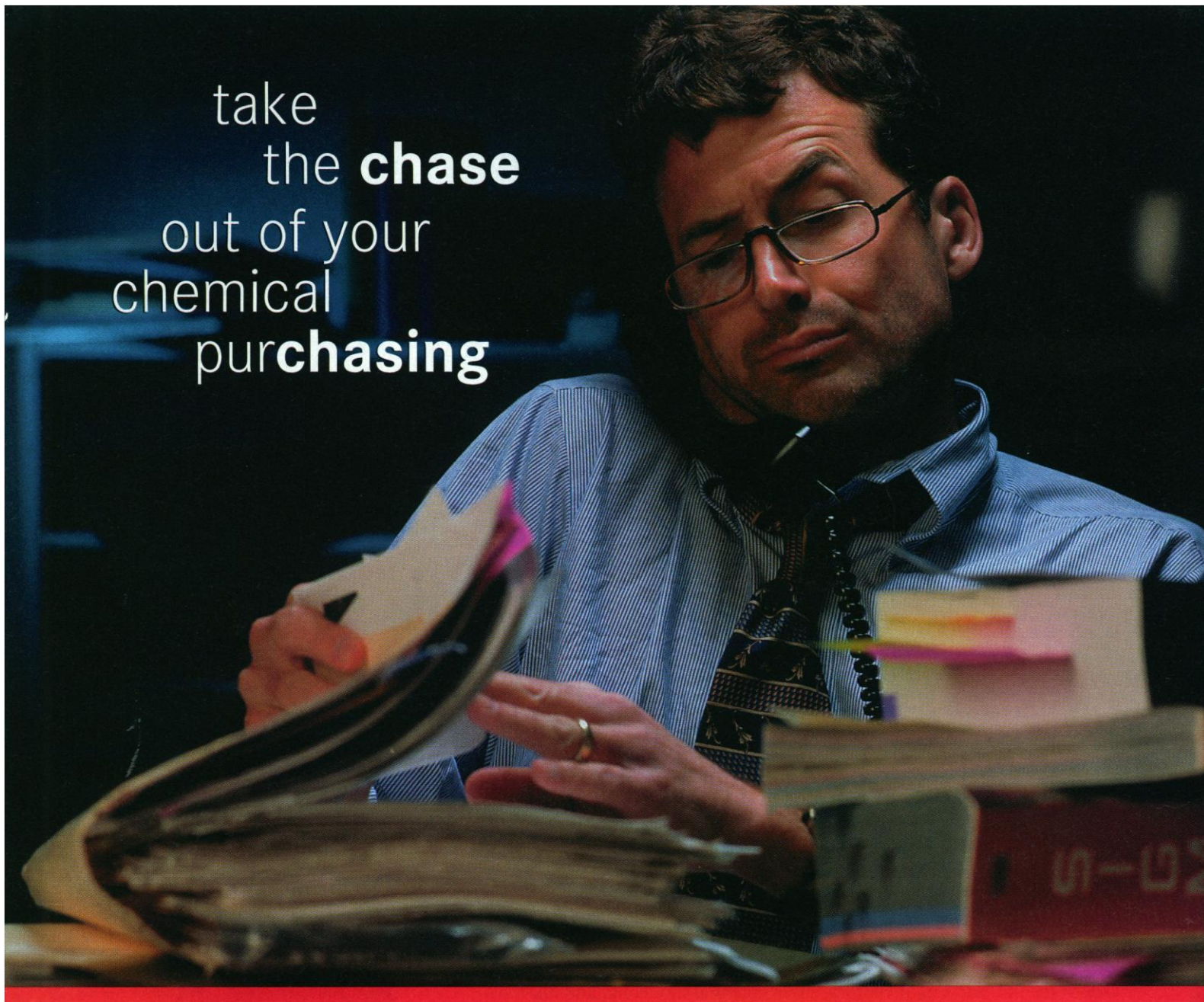
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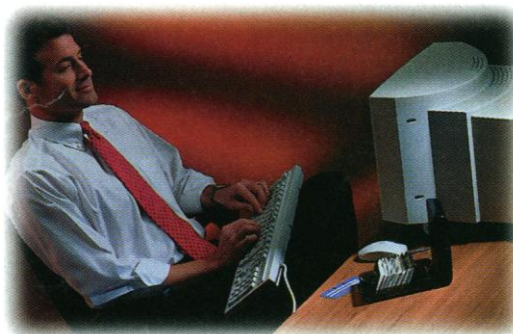
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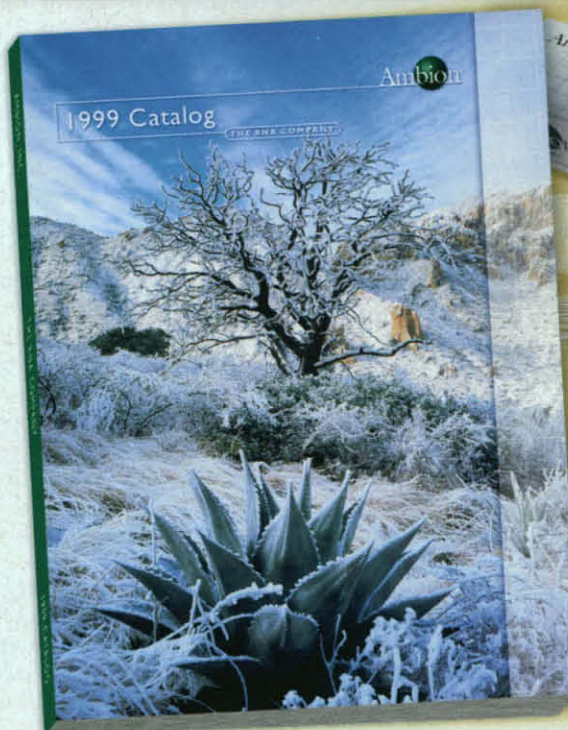
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3. Molecular Recognition & Responses
4. Energy Conversion

TYPES OF SUPPORT

The program will only support research that **transcends national boundaries**. Thus, **research grants** will be awarded for programs that involve collaboration between teams in different countries; **fellowships** are available to young post-doctoral scientists who wish to work in a different country; **international workshops** are organized in Strasbourg.

RESEARCH GRANTS Grants for basic research (up to 3 years) carried out jointly by research teams in different countries. The principal applicant must be from one of the eligible countries*.

FELLOWSHIPS **Long Term** (1- 2 years) and **Short-Term** (up to 3 months) Fellowships for researchers early in their careers and from the eligible countries* who wish to do post-doctoral research in foreign countries, or for researchers from outside the eligible countries who wish to do research in one of the eligible countries*.

WORKSHOPS International workshops can be organized by researchers from the eligible countries*.

*Current eligible countries are Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Italy, Japan, Luxembourg, the Netherlands, Portugal, the Republic of Ireland, Spain, Sweden, Switzerland, the United Kingdom and the United States.

RESEARCH GRANTS AND LONG-TERM FELLOWSHIPS : APPLICATION DEADLINE IS 1 SEPTEMBER 1999

(awards to be announced in April 2000)

Applications for **Short-Term Fellowships** and **Workshops** can be submitted throughout the year

Scientists interested in organizing a workshop should contact the Secretariat about possible dates

Guidebooks and application forms will be available in mid-April 1999 and may be obtained upon written request by addressing the form below to the HFSP or by E-mail. Applications using previous year's forms are not accepted. You can retrieve copies of our guidebooks and application forms from our World Wide Web site at <http://www.hfsp.org>

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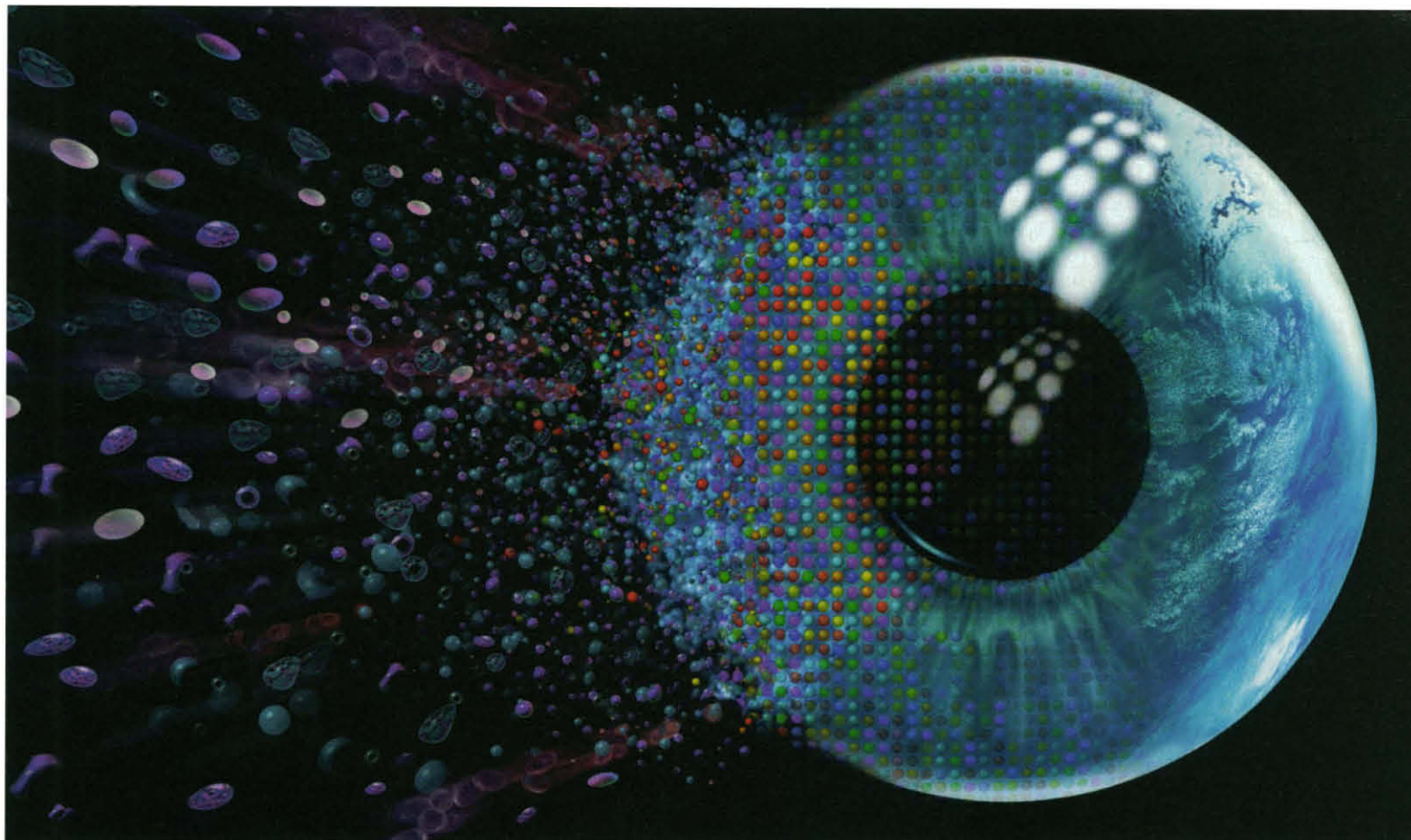
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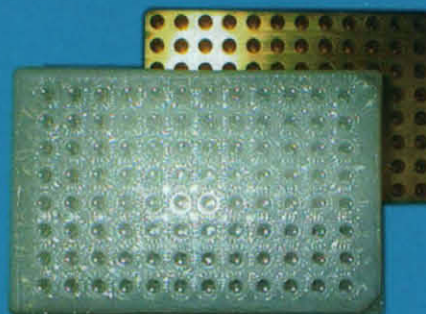
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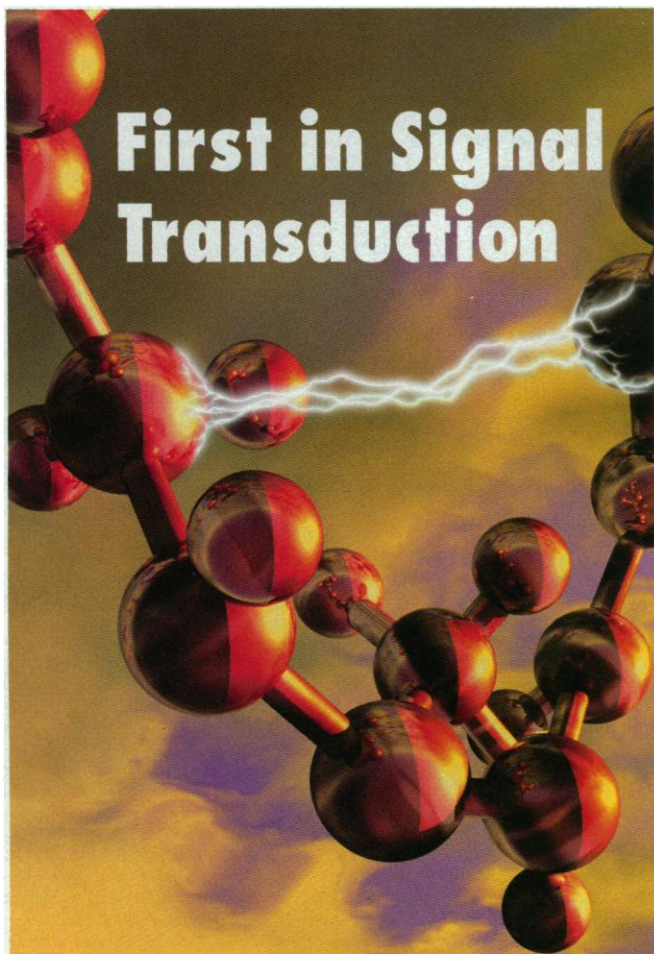
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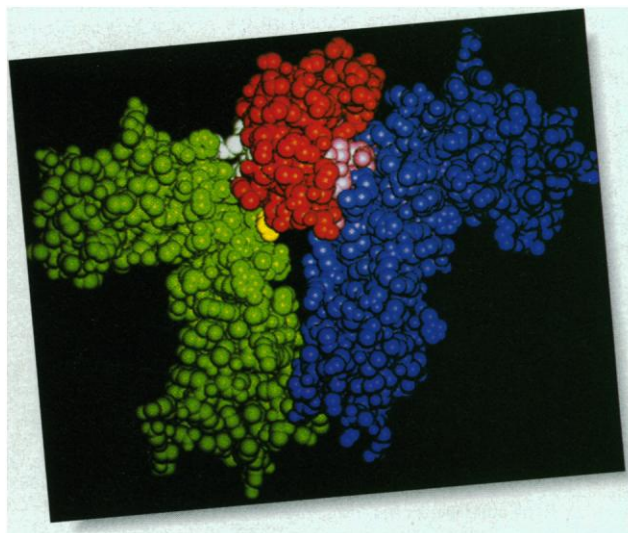
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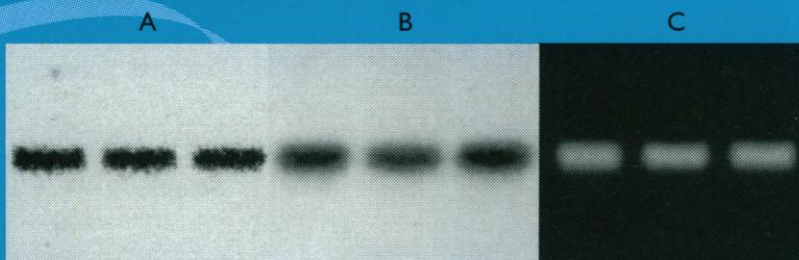
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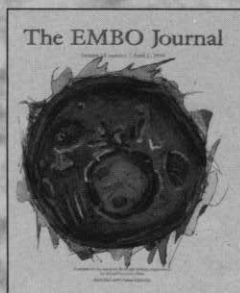
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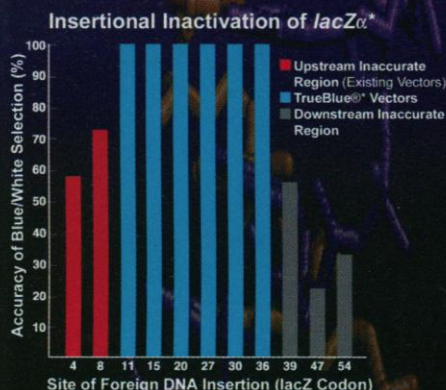
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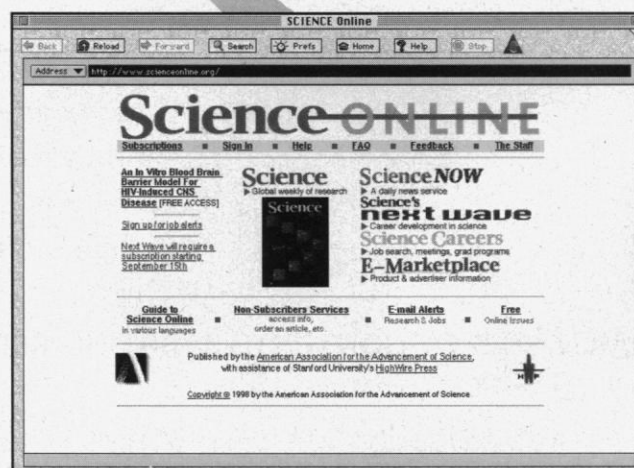
*Sillat, S.N. and Lebel, S. (1998) *Gene* 213:83-91
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