

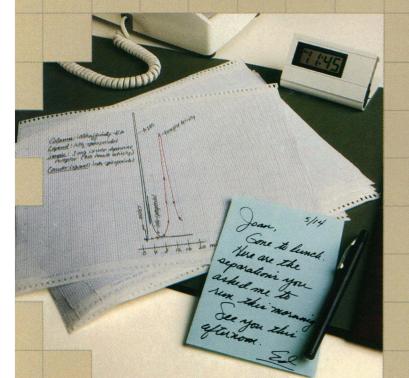


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COVER

Autoregulation of yeast copperthionein gene. Yeast cells were grown on a bromthymol blue galactose indicator plate on which positive cells are yellow and negative cells are white. Both strains contain an episomal fusion gene in which yeast copperthionein regulatory sequences drive the expression of bacterial galactokinase. The cells to the left contain multiple copies of the chromosomal structural gene for copperthionein and are galactose-negative. The cells to the right lack an intact copperthionein gene and are galactosepositive due to increased basal transcription of the fusion gene. See page 685. [Dean H. Hamer, National Institutes of Health, Bethesda, Maryland 20205]

Assembling the immunoglobulin genes

Genes for immunoglobulins are constructed from pieces of DNA scattered on the chromosome. Genetic mechanisms that might contribute to the assembly of the gene for one region of the immunoglobulin molecule (the V-J portion responsible for binding to antigens) have been analyzed in a model system (page 677). The genes for the V and J regions are made contiguous by a sitespecific recombination process, and secondary genetic mechanisms may have a role in the nature of the final gene product. The genetic processes for V-J assembly may prove to be generally applicable for other antigen receptors and for other portions of the immunoglobulin molecule.

Fossil record of soft-bodied organisms

The fossil remains of a group of soft-bodied organisms that lived 400 million years ago have been discovered at a site near Milwaukee, Wisconsin (page 715). Scientists rarely get a chance to see such a collection, and it is thought that some unusual features of the local environment contributed to the preservation of these soft structures. The range of organisms represented in the collection gives an indication of the diversity of biologic forms that lived in Paleozoic times. Compound eyes were found in wormlike and arthropod specimens, and several kinds of appendages were seen on arthropods. One unusual limb suggests an adaptation for seizing prey. Such structures had previously been reported only on organisms that lived 40 million years later. A toothlike formation, probably from a conodont organism, may be only the second such specimen ever described. Although some organisms cannot yet be classified, after further analysis they may help explain gaps in the taxonomic record of Paleozoic organisms. This discovery provides new data for a 100-million-year period from which little information has been available.

Herpes simplex vaccine

Herpes simplex viruses (HSV) cause tremendous suffering. They initially infect the eyes, the lips, or, in the most well-publicized example, the genitalia; they then can travel along nerves and remain latent in the nervous system. Intermittently, they may be reactivated to cause new herpes lesions. A genetically engineered vaccine has now been prepared which successfully protects mice from lethal HSV infections and also seems to be effective in preventing the establishment of latent infections (page 737). The vaccine uses a modified vaccinia virus into which herpes DNA, coding for a herpes glycoprotein, was inserted. Under the control of a strong promoter gene of vaccinia, the HSV glycoprotein was produced and displayed on the vaccinial surface, where it proved to be immunogenic. Vaccinia was chosen for the vaccine because it is known to be a stable virus for immunization. It was the agent used for vaccination against smallpox, a disease that has now been eradicated worldwide. Because vaccinia can accommodate large amounts of foreign DNA, it may be used in the future as the carrier in a polyvalent vaccine containing immunogenic materials from many pathogens.

Golgi apparatus in live cells

A new technique has been developed for labeling the Golgi apparatus, permitting, at last, a study of its dynamics in the live cell (page 745). The Golgi apparatus, a netlike, membranous structure, was first seen inside cells that had been fixed and stained for light microscopic study almost 100 years ago and was later studied in detail in dried cells in the electron microscope. Since similar structures were never detectable in living cells, a slim possibility lingered that the Golgi apparatus was only an artifact. The label, a fluorescent lipid complex, tags membranous components of the cell as its lipid component is metabolized. The experimental conditions were adjusted for preferential accumulation of the label in the Golgi apparatus. With the fluorescent label, structural changes of the Golgi previously seen in cells that had been prepared for microscopy during successive stages of cell division were shown to be the same in live cells. The functions of the Golgi apparatus in assembling and transporting different kinds of molecules in the cell have been known for some time. With the fluorescent label, it may now be possible to correlate these functions with structural changes in this important cellular apparatus.

Borna virus and psychiatric disorders

Borna disease has been killing horses and sheep in Germany and Switzerland for 150 years. It is a form of encephalitis in which spasms, paralysis, and either excitability or apathy develop; sometimes it is called "crazy disease." The Borna virus from the brains of sick animals can, when injected into many kinds of experimental animals, cause neurologic and behavioral changes. Could this virus account for behavioral abnormalities in humans? Serum samples from almost 1000 psychiatric patients in the United States and Germany and from appropriate controls were tested for antibody to the Borna virus; evidence of exposure to Borna or a related virus was found in 16 patients (page 755). The clinical diagnosis common to those 16 patients was depression, and usually the depression was cyclical. The possible association of the Borna virus with human psychiatric disorders will undoubtedly stimulate research on the characterization of the virus, the identification of antibodies that can react with it, and the morphologic effects of the virus on the brain and on other parts of the nervous system.









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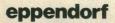
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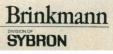
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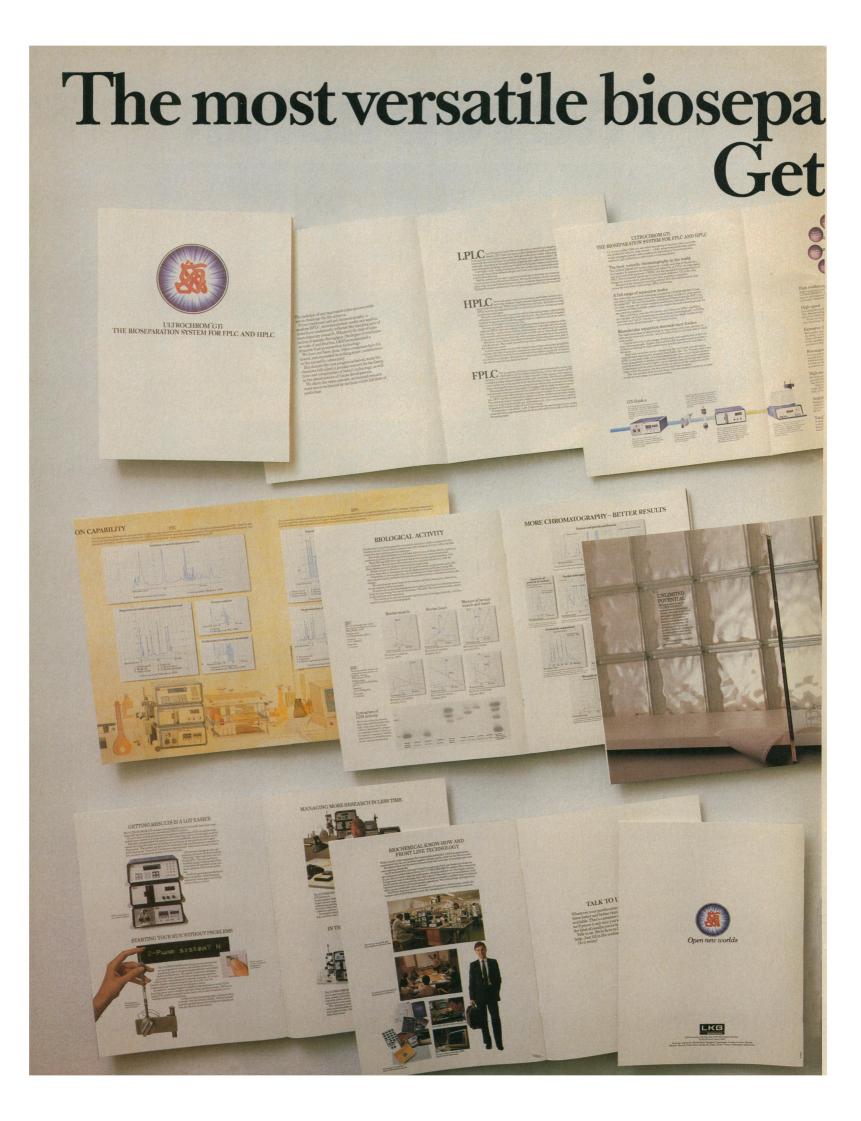
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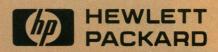
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What are the benefits to the research workers?

Since the air in the rack is exhausted into the main exhaust system and does *not* re-enter the animal room itself, research workers are effectively isolated from animal dander or other allergens, odor, pheromones, microorganisms, and food and bedding dust. Even with the doors of the unit open, the direction of air flow tends to be *from* the room and *into* the unit which helps to contain contaminated air *within* the unit. Result: virtual elimination of allergic reactions and generally, a cleaner, safer, odor-free work environment for the research people.

What are the benefits to research programs?

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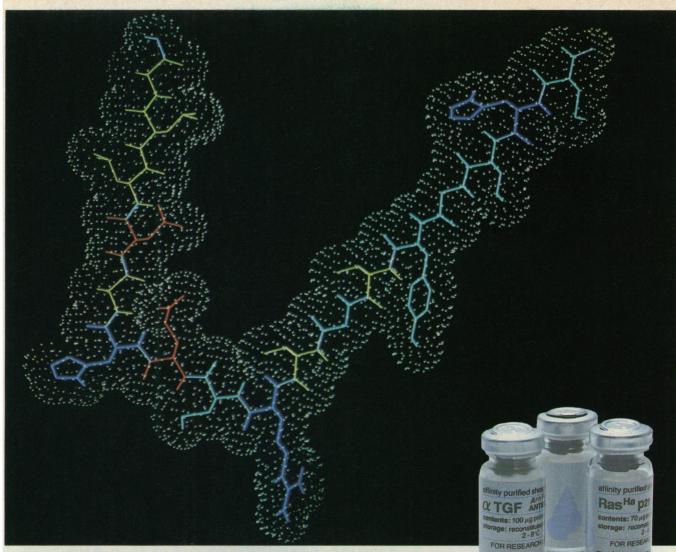
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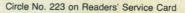
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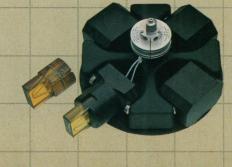
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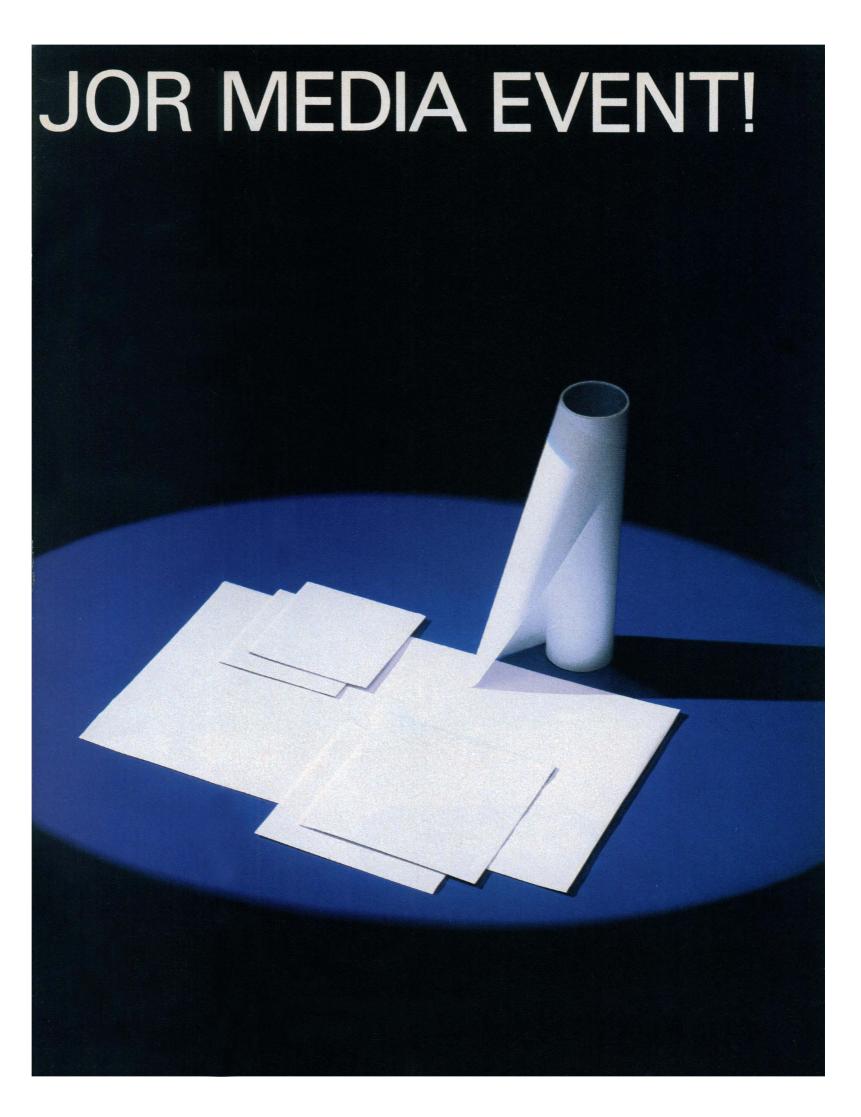
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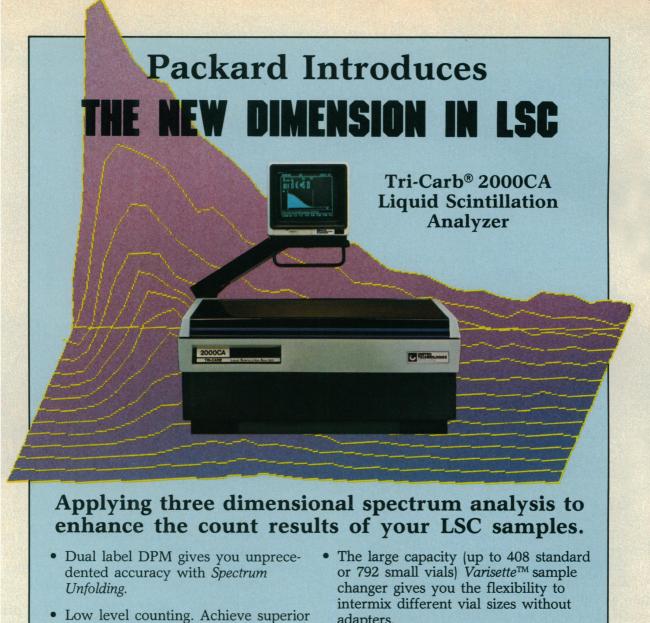
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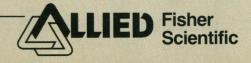
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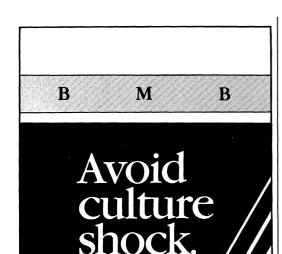
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LETTERS

"Nuclear Winter" Calculations

The description by Turco et al. of the possible global consequences of multiple nuclear explosions" (23 Dec 1983, p. 1283), represents an important attempt to quantify the effects of a nuclear war on global climate. In common with other preliminary studies (1), the numerical model simulations of Turco et al. suggest that heating of the earth's surface by solar radiation might be drastically reduced by the dust raised in high-yield nuclear blasts and by smoke from city and forest fires ignited by the blasts. However, in view of uncertainties in important inputs to the models and in many of the physical processes involved, as well as inadequacies in the models themselves, the predictions of a nuclear winter must be viewed as a possible, rather than the definite, outcome of a nuclear war. While this caveat has generally been made in scientific articles on the subject, and has been reemphasized in an excellent report by the National Academy of Sciences (2), it is often neglected in communications with the general public.

To further underscore the tentative nature of the nuclear winter predictions, I list below some of the scientific uncertainties associated with the numerical model calculations (3).

1) The amounts of material that would burn are not well quantified (for example. How widespread will forest fires be in winter?).

2) There are large uncertainties about the quantities of smoke particles that would be emitted into the atmosphere from various types of fires. On the basis of limited field data available (4), it appears that Turco et al. may have overestimated these emissions.

3) Clouds generally form above large fires, and these clouds often produce rain. This provides a mechanism for the prompt removal of some of the smoke particles, which would further reduce the effective (widespread) emissions of smoke.

4) The radiative properties of smoke particles are not well known. In view of the complex nature of smokes, these properties need to be established by field studies of the plumes from large fires.

5) Widespread smoke will change the radiative properties of clouds. Possible effects include enhanced absorption of terrestrial (long-wave) radiation by smoke particles when they are covered with water, decreases in the average size of cloud droplets (5), and decreases in

the ice content of clouds (6). In view of the profound effects that clouds have on the radiative balance of the earth, these effects should be included in numerical simulations of the effects of smoke particles on atmospheric temperatures.

While some of these effects would tend to diminish the predicted decreases in temperature at the earth's surface, others would tend to enhance the lowering in surface temperatures. Clearly, at this juncture, there are too many uncertainties and simplifications in the numerical simulations of the effects on climate of a nuclear war to place much reliance on their predictions. Reduction of these uncertainties will require dedicated research efforts to better quantify the amounts and nature of the smoke particles from various types of fires, the rates of removal of smoke particles from the atmosphere (particularly prompt removal), and the radiative properties of smokes and clouds affected by smoke, as well as to improve numerical models of global climate. The importance and urgency of the problem dictates that these research tasks be given top priority. PETER V. HOBBS

Cloud and Aerosol Research Group, Department of Atmospheric Sciences, University of Washington. Seattle 98195

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- A more detailed discussion of the scientific uncertainties is given in P. V. Hobbs, L. F. Radke, D. A. Hegg, ICSU-SCOPE Workshop on the Nuclear Winter Scenario, Proc. 9th In-tern. Cloud Physics Conf. (1984), Tallinn, Esto-
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 I thank L. F. Radke, D. A. Hegg, C. Leovy, and S. Warren for helpful discussions.

S. Warren for helpful discussions.

Diagnostic Ultrasound

Our initial report on increased frequency of sister chromatid exchanges (SCE's) after in vitro exposure of human lymphocytes to pulsed diagnostic level ultrasound (1) has been confirmed and extended in publications from five laboratories in the United States and elsewhere (2-4). The increase has now been detected after continuous wave insonation and after in vivo exposure (4). The

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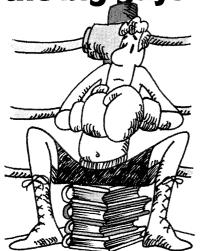
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frequency of SCE's increased with acoustic power in a critical range (3).

Free radicals are generated in aqueous solutions by pulsed ultrasound (5); their products have also been identified in the DNA thymidine of animal cells exposed to continuous wave insonation (6). The bioeffects of ultrasound responsible for the increased SCE frequency and some of the other findings described in more than 700 publications since 1950 (7) may well be the result of free radical release.

The failure of Ciaravino et al. to confirm our results (15 Mar., p. 1349) might be accounted for by many factors. Among these are the high degree of interobserver variation in their SCE scoring, their high SCE baseline values, and the fact that their critical acoustical power range was not verified and was not systematically varied. These and other variables may account for the failure of some laboratories to reproduce results of others, leading to the confusion in this field. **ROBERT BASES**

Department of Radiology Albert Einstein College of Medicine, Yeshiva University, Bronx, New York 10461

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The following points are pertinent to Bases' letter.

1) Interobserver variation in SCE scores is expected and is the reason why controls were included. The SCE rate in our experiments did not increase above control values for any of the three independent scorers.

2) SCE baseline values vary considerably from laboratory to laboratory; for example, they were 3.28 for Kakati et al. (1), 16.3 for Lambert et al. (2), and 27.33 for Dutrillaux et al. (3). Our SCE baseline values were well within this range.

3) The dosimetry for our experiments was accomplished by Paul Goodwin, staff physicist at Albert Einstein College of Medicine, who also was involved in making dosimetric determinations for Liebeskind et al. (4). The intent of our experiments (5) was to duplicate exactly the experimental conditions of the Liebeskind et al. study (4) with a welldefined, nonvarying field from a specific diagnostic ultrasound device. Our earlier attempts to verify their results with our equipment had been unsuccessful (6).

4) The Albert Einstein group declined to score the slides that we made on their premises with their equipment.

5) Bases suggested that we undertake "independent double-blind scoring by recognized experts . . ." of our slides (7). The coded slides were sent to William Morgan (at the University of California Medical Center, San Francisco); his evaluation agreed with ours.

6) Bases then suggested (8) that we send the slides to David Jacobson-Kram (George Washington University) for evaluation. His scoring agreed with ours.

7) The results of Martin et al. (9) are negative [" χ^2 tests . . . were not significant. . . ." (9, p. 993)], as are the results of most of the studies in this area (10).

8) Makino et al. (11) used a Bransonic 12 cell disrupter that produces a continuous sound wave at a frequency of 20 kilohertz; their study thus has little relevance to diagnostic ultrasound.

> MORTON W. MILLER VICTOR CIARAVINO

Department of Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, New York 14642

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Murine Retroviral Vectors and Human Gene Therapy

In his excellent and timely article, "Prospects for human gene therapy" (26 Oct. 1984, p. 401), W. F. Anderson discusses some of the possible difficulties surrounding the envisaged future use of retroviral vectors in attempts to correct human genetic defects. Such vectors unfortunately appear to have a strong propensity for deleting or rearranging their own sequences. One way in which such structural alterations might arise is through recombination events with homologous endogenous viruses already present in the cellular genome. In addition to the possible loss of vector-born



1. Co-culture of human diploid fibroblasts and Madin Darby Canine Kidney (MDCK) cells treated with fluorescein labelled monoclonal antibodies to MDCK cells!



3. Same as Figure 1. Selective irradiation of non-fluorescently labelled cells with a high intensity laser beam.



5. Growth of MDCK cells several days after exposing fibroblasts to laser irradiation.

¹Courtesy of Dr. William Smith, Michigan State University.



2. Computer-generated pseudo-color fluorescent image of labelled cells.

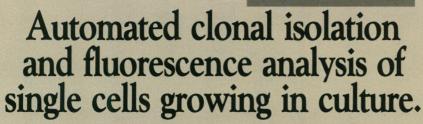


4. Same as Figure 2. Lines indicate the path of the laser beam, selectively leaving the MDCK cells untouched.



6. Same as Figure 5. Fluorescent image of MDCK cells after retreatment with monoclonal antibody

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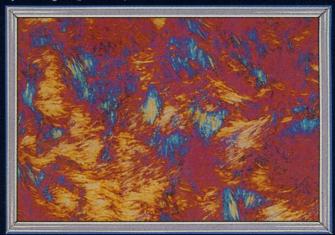
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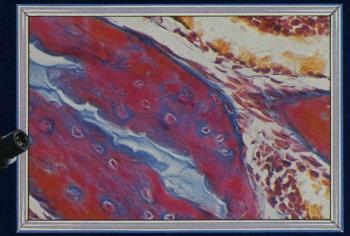
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sequences, such events could lead to the potentially harmful production of packageable infectious recombinant virus. Since avoidance of any homology with endogenous retroviruses is thus desirable, Anderson suggests using mouse retroviral vectors as a delivery system. However, quite apart from the putative inherent instability of recombinant retroviruses, this proposal is probably insufficient to overcome the recombination problem. This is because sequences with homology to mouse mammary tumor virus (1), Moloney murine sarcoma virus (2), Abelson murine leukemia virus (3), and Moloney murine leukemia virus (4) have recently been found in the human genome. Indeed, sequences containing murine retrovirus long terminal repeats (LTR's) have been employed in the screening of human genomic libraries (5).

There would appear to be two alternative means of circumventing this problem which would eventually enable murine vectors to be used in human gene therapy. Every such attempt would have to be preceded by a search for vectorhomologous sequences in the patient's genome by Southern blotting. If sequences homologous to murine retroviral vectors currently in use are indeed found to be common in human genomes. as suggested by the work of Repaske et al. (4), alternative vectors derived from more distantly related species would have to be considered. Clearly, considerable attention will have to be directed toward the construction and experimental trial of appropriate retroviral vectors in order to optimize any future gene delivery system for use in humans.

DAVID N. COOPER

Institut de Biologie Animale, Université de Lausanne, CH-1015 Lausanne, Switzerland

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David Cooper raises a legitimate concern regarding possible recombination between murine leukemia virus (MuLV)-based viral vectors and endogenous retroviral sequences present in the human genome. In fact, recombination between a deletion mutant of Moloney MuLV and homologous sequences in mouse DNA involving a 400-base-pair segment that was 78 percent homologous

has recently been demonstrated (1). To evaluate possible recombination between MuLV's and human endogenous retroviral sequences, mouse cells have been cotransfected with defined gag and pol deletion mutants of Moloney MuLV (2) and cloned gag and pol segments of endogenous human retroviral DNA's. In no case could recombination be demonstrated. Although the deduced amino acid sequences comprising the gag and pol regions of endogenous human retroviral sequences are evolutionarily related to comparable segments of MuLV's (3), the extent of polynucleotide sequence identity may be too low for homologous recombination. For example, the gag and pol regions of human endogenous MuLV sequences are only 35 percent and 44 percent, respectively, related to analogous segments of MuLV. Furthermore, nucleotide sequencing of several different human endogenous retroviral clones (4) has indicated the presence of point mutations, inappropriate terminator codons, and deletions of various sizes, any one of which could render recombinants that might be generated replication defective.

MALCOLM A. MARTIN

Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20205

STEPHEN P. GOFF Department of Biochemistry and Institute for Cancer Research, Columbia University, College of Physicians and Surgeons, New York 10032

W. FRENCH ANDERSON Laboratory of Molecular Hematology, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland 20205

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- 4. R. Repaske et al., J. Virol., in press.

Erratum: The name of M. Wallroth was omitted as the fourth author of the report "A simple and general method for transferring genes into plants" by R. B. Horsch *et al.* (8 Mar., p. 1229). *Erratum*: In the legend for figure 2 of the report "*Plasmodium falciparum* malaria: Band 3 as a possi-ble receptor during invasion of human erythrocytes" by V. C. N. Okoye and V. Bennett (11 Jan., p. 169), a reference for the use of metrizamide to purify schizonts was inadvertently omitted after the fifth schizonts was inadvertently omitted after the fifth sentence. It should have read, "Following the meth-od of C. S. Pavia *et al.* [*Am. J. Trop. Med. Hyg.* 32, 675 (1983)], as modified by Lyons."

Erratum: In figure 1 of the report "How bees remember flower shapes" by J. L. Gould (22 Mar., p. 1492), the results shown for the 24-element patterns (K_1 and K_2) should have been P > 0.05.

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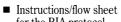
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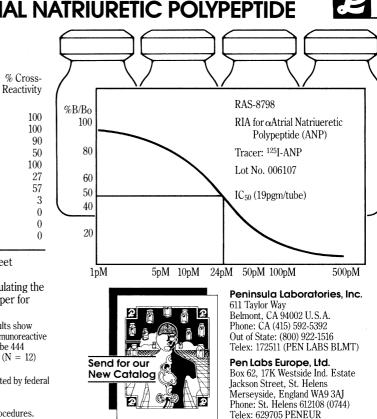
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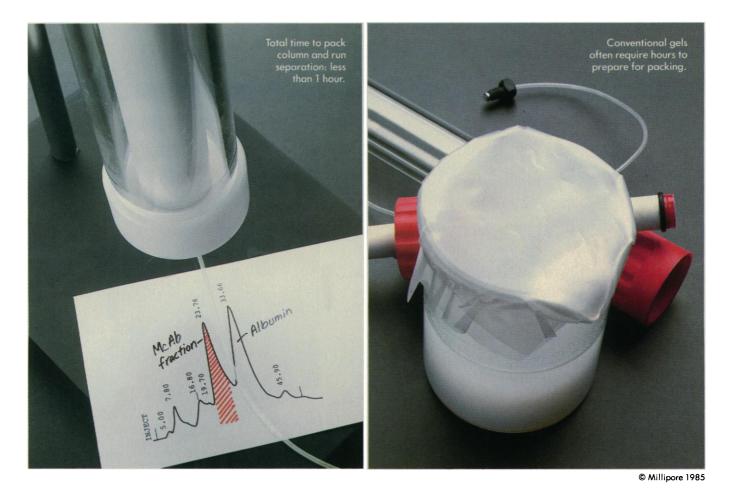
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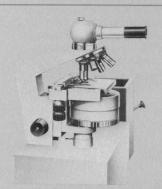
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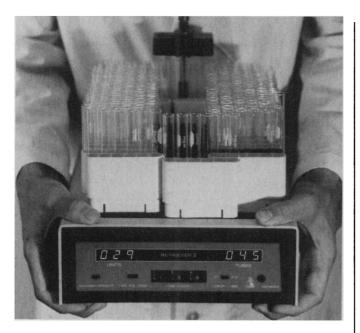


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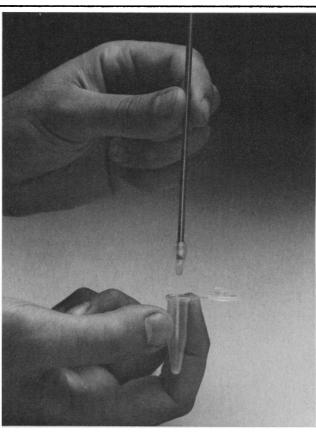
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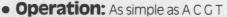
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Modern scientists are accused of being specialists. This is a bum rap; it is also true. It is a bum rap when it implies that Newton knew all of science in his day whereas modern scientists are merely nuclear physicists, steroid chemists, or oil economists. The truth is that each of these specialties alone encompasses far more knowledge than did all of science in Newton's day. The range of facts, theories, and technologies that modern scientists must know is usually very broad, even within what outsiders might consider a specialty. Individual scientists may appear to be narrow because of the ever increasing accumulation of knowledge. Actually they know more, but it is a smaller fraction of total knowledge.

Scientists become increasingly isolated because of the jargon used in each specialty. New terms are introduced to describe concepts unknown in Newton's day. The replicons, cistrons, and liposomes of the biologist are foreign phrases to the physicist. The quarks, bosons, and GUT of the physicists are an undeciphered code to the economist. Yet there is both a desire and a need for different disciplines to understand each other. One institution that can contribute to a translating service is a multidisciplinary journal like Science. The question is how. We already publish important findings from many disciplines in the same journal. But just as we see that a giraffe tends to fall in love with another giraffe, we suspect that chemists love to read chemistry, archeologists archeology, and so forth. Moreover, adventurous readers who venture outside their areas of expertise soon run into the language barrier. The arcane terminology of a different field is denounced, whereas the jargon in one's own field is defended as the only way to express complicated concepts succinctly.

We have therefore decided to contribute to interdisciplinary communication by starting a new feature, "This Week in Science." On this new page, Ruth Guyer will summarize four to eight papers that appear in the current issue of the magazine. The purpose of these brief summaries is to allow the mathematician to understand the purpose and basic content of an article in medicine or a sociologist to understand an article in solid-state physics. We are deliberately picking papers to illustrate diverse developments, not to confer honors on a select few. Any scientist knows that what is immediately trendy may turn out in the light of history to be less important than some unheralded work that was far ahead of its time. In addition, a magazine like Science operates in loco parentis-all its authors are valued and cherished. Any article or report that survives our reviewing process is deemed to be of widespread interest. However, it would be physically impossible to give a special accounting of every paper in our weekly issue. We will select only a few so that the page can be read quickly. Over the long run, the subjects will cover a wide spectrum of disciplines even though the selections from one issue will be limited. Thus, over time, the reader of this page should get a good sense of the trends and accomplishments in other fields. This service complements the role played by our Research News and News and Comment writers in reporting the developments in various fields of research. The difference is that the new summaries will be briefer and even less specialist-oriented. An advantage is that those whose curiosity for more is aroused can read the original paper in the same magazine.

Wisdom is sometimes characterized as the ability to learn a little bit about a lot of subjects and a lot about one. We hope that the Renaissance women and men who read our journal will enjoy this new feature.

-DANIEL E. KOSHLAND, JR.

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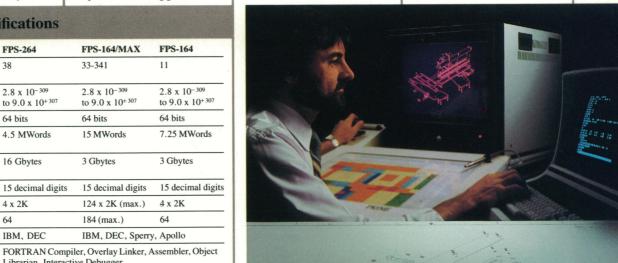
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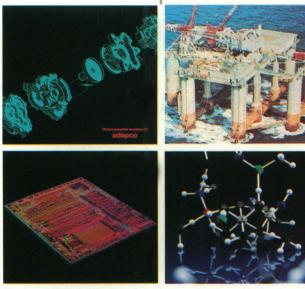
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AAAS members are invited to submit symposium proposals for the next Annual Meeting in Philadelphia, 25-30 May 1986. Please complete the form below, attach a "Synopsis of Objectives" (about 200 words), and send it to us **not later than 1 August 1985**.

We are particularly interested in symposia dealing with the latest developments in science and technology, and the implications of these developments for society.

All symposium proposals are subject to review. If the information submitted is inadequate for reviewing, the proposal will be returned. Endorsement (sponsorship) by a AAAS Section Committee expedites the review process. It is therefore in the interest of the proposer to send a *copy* of the proposal to the appropriate Section Secretary (see table of contents page of Science for names) for endorsement at the same time the *original* is sent to the AAAS Meetings Office.

Speakers should *not* be confirmed at this time; however, sufficient information about probable speakers and their topics should be provided to allow for evaluation of the proposal. Please note that AAAS does not pay honoraria to speakers.

Some Deadlines

October: You will be notified about acceptance, conditional acceptance, or non-acceptance of your proposal. Further information will be provided at that time.

November: Preliminary programs with confirmed speakers are due.

January: Final program copy, suitable for publication, is due.

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Philadelphia, 25–30 May	Submit not later than 1 August 1985	Washington, D.C. 20005		
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Affiliation	Affiliation			
Topic				
2. Speaker	5. Speaker			
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