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SCIENCE

8 September 1989
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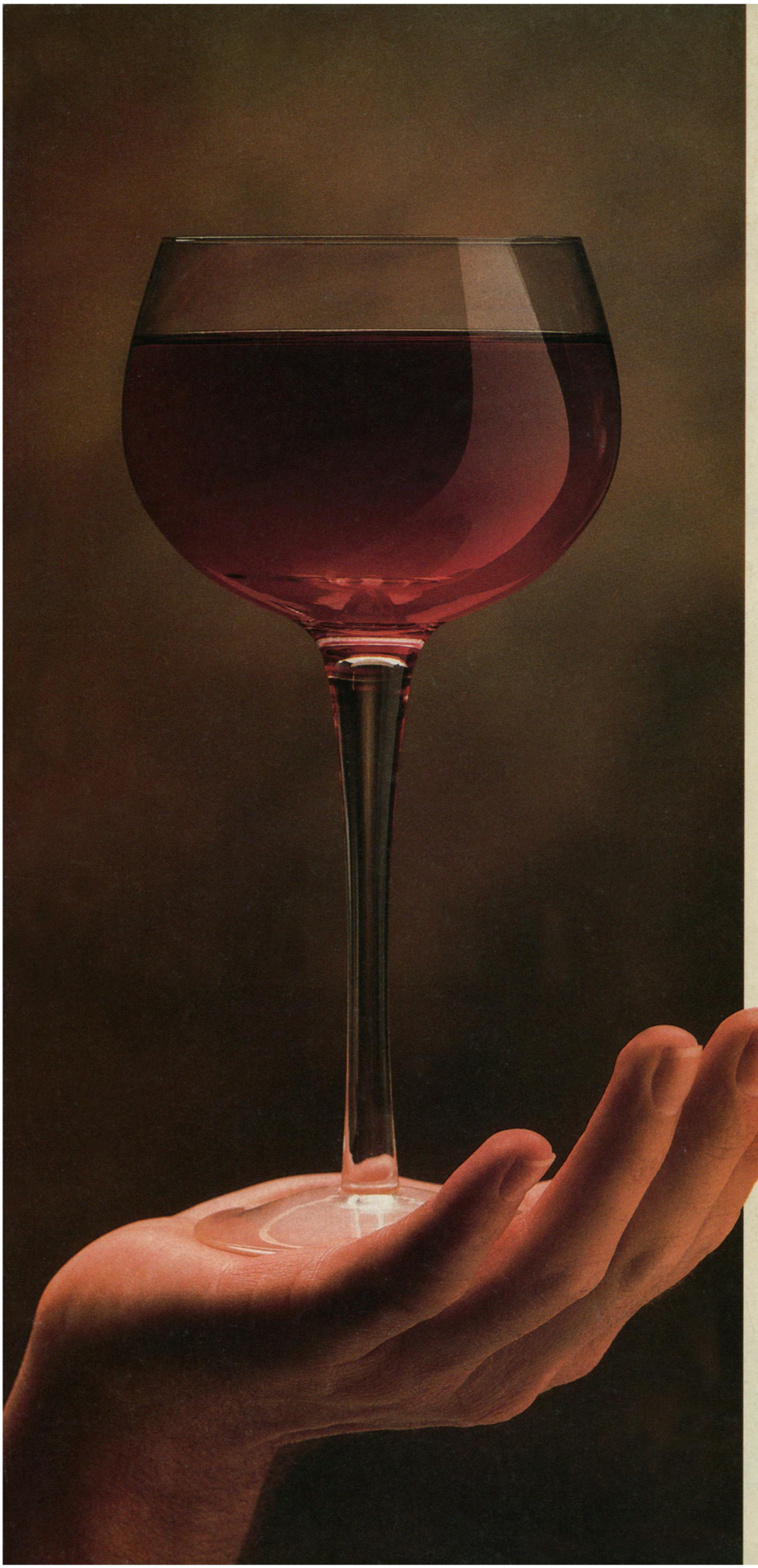
Cystic Fibrosis

Cloning and Genetics



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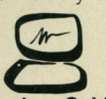

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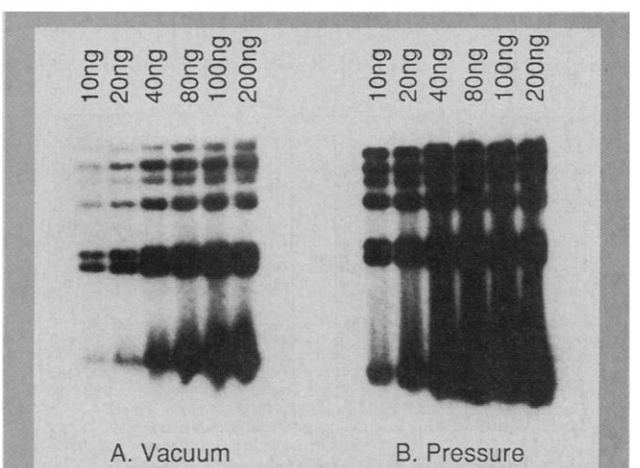

Figure legend: ^{32}P end-labeled lambda Hind III markers were electrophoresed in 0.8% agarose. The DNA was then transferred to a nylon membrane with a vacuum blotter at 30 mm Hg below atmospheric or with the PosiBlot™ pressure blotter at 100 mm Hg above atmospheric. Both transfers were carried out for 15 minutes. As can be seen, pressure blotting transferred significantly more DNA in the same period of time, especially in the higher molecular weight range (largest band is 23 kilobases).

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COVER The discovery of the gene that is defective in the childhood disease cystic fibrosis has generated hope and excitement in the scientific and medical communities. See page 1059. The colored bars represent chromosomes from different patients with cystic fibrosis. Original data are from B. Kerem *et al.*, Table 3, page 1076. [Photograph by Carol Clayton of a child from the Cystic Fibrosis Foundation]

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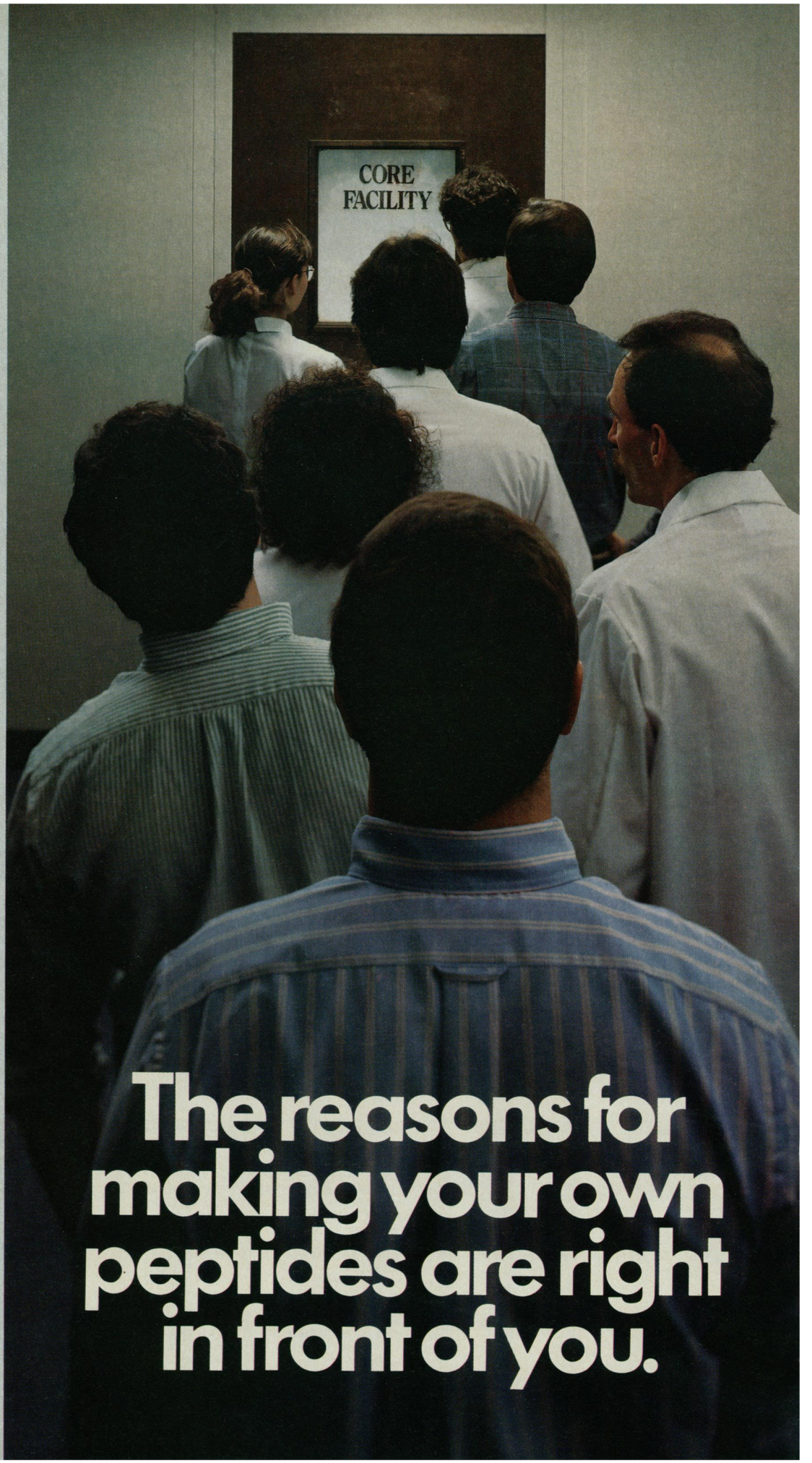

The reasons for making your own peptides are right in front of you.

Cystic fibrosis

A milestone has been reached in cystic fibrosis research: the gene that is defective in individuals with the disease has been identified. This discovery has made it possible to predict a likely structure and function for the protein that the gene encodes. In diseased individuals, only one of 1480 amino acids is missing in the predicted protein, the "cystic fibrosis transmembrane conductance regulator," yet this slight structural change apparently radically disrupts normal functioning of the lungs, sweat glands, and pancreas. The first payoffs from identification of the molecular defect are expected to include improved methods both for screening for carriers of the gene in the general population and for prenatal diagnosis. Farther down the road, knowledge of the responsible gene could lead to more effective therapies and perhaps to a cure. The experimental findings are reported in three Research Articles (pages 1059, 1066, and 1073) and are discussed both in this week's editorial (page 1029) and in a news story in last week's issue of *Science* (page 923). The Cystic Fibrosis Foundation has announced new grants in conjunction with the discovery and an upcoming meeting (pages 1084 and 1085).

All-carbon species

Some of the products of combustion are composed of carbon and nothing else (C_n); similar all-carbon molecules are also believed to be constituents of interstellar dust. Those with $4n + 2$ carbon atoms are considered to be especially stable, and by the time 60 carbon atoms are assembled into geodesic dome-like "buckminsterfullerenes," exceptionally stable molecules are generated. What is key to elucidation of the properties of all-carbon molecules is the ability to synthesize compounds of a single size; the laser vaporization of graphite, which has been used to produce all-carbon molecules, is believed to yield a mixture of linear and cyclic molecules having from 2 to more than 600 carbon atoms. Diederich *et al.* have designed a synthetic pathway for the production of one of the smaller closed-shell species, C_{18} (page 1088). They describe a direct precursor of C_{18}, verify its precursor status, and analyze its structure. Theoretical calculations suggest that the C_{18} compound has alternating single and triple bonds and two perpendicular aromatic systems of π electrons.

Nonmarine evaporites

Evaporites are sedimentary rocks that form where lakes or oceans once stood; they consist of salts and minerals that have precipitated out of the aqueous solution. Evaporites have been useful for making inferences about the compositions of ancient waters through time. In Qaidam Basin in western China, large potash-bearing evaporites are forming from nonmarine waters (page 1090). The Basin has vast salt deposits, a number of shallow saline lakes from which precipitation is occurring, and a permanent ground water brine below the surface. The lakes are fed by rivers and calcium chloride springs; there is no input from marine water as the Basin is thousands of meters above the sea. Lowenstein *et al.* conclude that many of the ancient "anomalous" potash evaporites—those deficient in the magnesium sulfate salts that would be expected to be there had mineral precipitation occurred from seawater—can now be understood as forming, as in Qaidam Basin, from nonmarine source waters.

Ozone losses

In spring in the Southern Hemisphere, ozone is destroyed in the stratosphere and an "ozone hole" widens over Antarctica. How well do the chemical reactions that have been proposed for the conversion of ozone to oxygen account for the ozone losses? In experiments described by Sander *et al.*, the temperatures and pressures that would pertain in the polar stratosphere were simulated and measurements made of the rates at which dimers of gaseous chlorine monoxide formed (page 1095); this dimerization is considered to be the rate-limiting step in the catalytic destruction of ozone. Reaction rates were slower than had been indicated in previous studies, yet quantitative computations with a one-dimensional photochemical model showed that such rates accounted for 100% of the late spring ozone losses. In contrast, qualitative assessments indicated that less than one-half of observed early spring losses of ozone could be accounted for, implying that in early springtime other catalytic destruction mechanisms may be operating.

Circadian rhythm to sperm release

The release of sperm from the testes into the seminal ducts of male gypsy moths occurs rhythmically. During a standard cycle of 16 hours of light and 8 hours of dark, clones of sperm cells develop and are released in bundles into the upper vas deferens shortly before the end of the light period. They remain there through the dark period and, within 2 to 4 hours of reexposure to light, move en masse into the seminal vesicle. Eventually the sperm move asynchronously into the duplex where they mix with sperm that were produced during other cycles. Giebultowicz *et al.* found that this rhythmic pattern continued in complexes of testis, upper vas deferens, and seminal vesicles placed in culture (page 1098). The rhythm held whether the cultured complexes were exposed to the standard light-dark cycle or to total darkness. If the light-dark cycle was shifted to a new phase, the rhythm also shifted and then was sustained even after complete darkness was later imposed. The complexes thus contained an internal light-sensitive pacemaker. If the normal and proper maturation of sperm is dependent on rhythmic release of sperm, disruption of the rhythm might prove to be an effective strategy for pest control.

■ RUTH LEVY GUYER

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SCIENCE

8 SEPTEMBER 1989
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The Cystic Fibrosis Gene Story

In this issue of *Science*, there is a story that does not begin at the beginning or end at the end, but has a very happy middle. The beginning is the basic research that made it possible to search for a genetic needle in a haystack of DNA bases. The end is a cure for a fatal disease. The middle is the finding of the cystic fibrosis gene, a milestone of major importance.

The middle of the story, the three papers published in this issue on the cystic fibrosis gene (pp. 1059–1080), is an event of great scientific achievement that brings credit to the investigators whose dedication and ingenuity made it possible (see the news story by Jean Marx, *Science*, 1 September, p. 923). Until now cystic fibrosis could not be studied in animals, and clues to the actual defect are circumstantial. The discovery of the gene makes possible its manipulation and insertion into experimental systems, thus bringing the day of therapy and cure much closer. This advance immediately increases the accuracy of diagnosis, both in the born and the unborn. It also has provided strategies that will be useful in searching for other disease-causing genes.

The beginning of the story explains why scientists believe in the importance of basic research. The tools that made this finding possible arose from a background of basic research into such apparently esoteric and academic subjects as the understanding of the genetic code, the recognition that enzymes from soil bacteria are able to cut DNA at specific locations, a solid familiarity with the structure of chromosomes, classical genetics, and the use of statistical probability. Much of the early basic research did not seem relevant to the cystic fibrosis problem, and was pursued in the quest for extended knowledge, not practical application. At times, legislators get impatient with scientists who emphasize such research, implying that while scientists may prefer it, society does not need it. Scientists have learned, however, that basic research often turns out to be practical, but the time scale for its application differs from that of applied research. There is a time when the search for basic knowledge is essential because there are no tools available for a direct application. Once the tools have been obtained, often by investigations that were primarily directed toward another goal, the clever and prepared investigator will apply them to the problem at hand. Thus the apparently arcane interests of ivory-tower scientists are essential and inexorable steps along the path to the triumphs of today.

Another happy feature of the present story is the combination of private philanthropy and public funding that made this research possible. The thousands of individuals who contributed to the Cystic Fibrosis Foundation, the brilliant and eccentric man who created the Howard Hughes Foundation, the supporters of the Hospital for Sick Children in Canada, the sensible managers of those charities, and the farsighted government officials who also provided funds, all deserve credit. In a world in which terrorists, embezzlers, prevaricators, and self-indulgers seem to grab the daily headlines, a story in which thousands of people directly or indirectly provided funds to attack a disease that would not affect them personally provides a warm glow.

Finally, the story illustrates another angle on that frequently maligned phenomenon, competition. There is a great deal of discussion these days that the "publish or perish" pressure creates the occasion for misconduct, and certainly the race for the cystic fibrosis gene had elements of competitive pressure. What those standing on the sidelines, who sometimes seem to want a competition-free world, fail to say is that the same competition that attracts Olympic sprinters and mountain climbers impels scientists to work with intensity and dedication. The personal satisfaction of knowing one has contributed to the solution of a difficult problem, the excitement of doing one's best in an all-out effort, and the lure of fame and fortune, in whatever proportion, all combine to ensure that the jobs of science get done faster than would be accomplished in a leisurely 9 to 5 schedule. In the case of cystic fibrosis, honorable competition led to cooperation, when three of the laboratories racing toward the same goal decided to join forces and share information. That cooperation and intensity means that the one in 2000 children born each year with a fatal defect now has a greater chance for a happy future.—DANIEL E. KOSHLAND, JR.

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Number 2

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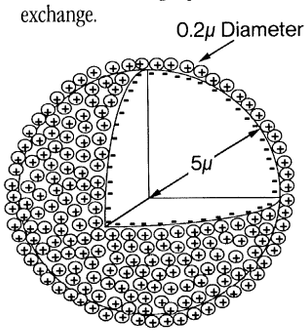

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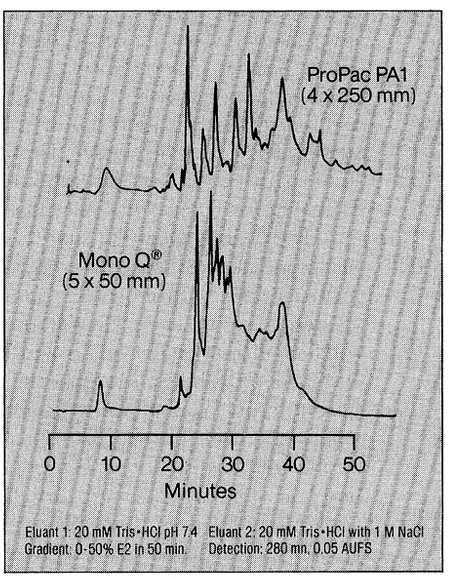

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Cytochrome C	12.4	10.7	0.8–66
Lysozyme	14.1	11.1	0.8–200
BSA	67.1	4.9	0.8–200
Myoglobin	16.9	7.1	0.8–66
Ovalbumin	43.1	4.6	0.8–66
Carbonic Anhydrase	31.1	6.2	5.0–125
Apoferritin	669.0	—	3.0–200

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mined statistically by noting an increase in the expected incidence rate for that particular cancer. Even when such an increased incidence rate is observed, we cannot distinguish between those cancers that would have normally occurred and those that were due to exposure to the carcinogen.

HERMAN CEMBER
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Balance in *Science*

I disagree with Daniel E. Koshland, Jr.'s, statement that "the chance of being published in *Science* is approximately the same for all fields of research" (Editorial, 28 July, p. 341).

To favor papers in physics and social sciences over those in biology does help represent the former two disciplines. But a definition of "biology" based on the contents of *Science* excludes many fields of biology. So many of the papers in *Science* are concerned with molecular, cell, and biochemical biology, especially those with human applications, that the journal's name might be changed to "*Biomedical Science.*" One has to be in one of those specialized fields to even understand the titles! *Science* publishes so few papers on organismal biology (in such fields as ecology, zoology, or vertebrate morphology—which is the major division of the American Society of Zoologists), that it is no wonder authors from these fields do not bother to submit their papers to *Science.*

I think that *Science* has a long way to go before it "publish[es] the cutting edge of research in every branch of science as well as present[s] research that will interest readers ranging from physicists to social scientists."

STEPHEN M. REILLY
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Response: Physicists will find it hard to believe that a biologist feels discriminated against by *Science*, but reader Reilly illustrates the point I was trying to make. Within each major field (physics, biology, and so forth), there are subdivisions (organismal, AIDS, crystallography, cell, and so forth in biology), each of which thinks their own area is underrepresented. What appears in *Science* is to a first approximation a constant fraction of what we receive in each area. That distribution is affected by funding and fashions that control the number of workers in a field, but we do not want it to be further influenced by the preconceptions of authors. We try to judge all papers equally but, if anything, give a slight edge to underrepresented areas—DANIEL E. KOSHLAND, JR.

Correction

We wish to make a correction concerning our 9 September 1988 report "Selection of variable-joining [VJ] region combinations in the α chain of the T cell receptor" (*1*). We have discovered that the $V_{58}J_3$ isolates actually contain part of the 3′ heptamer-spacer sequence from the V_{58} germline (*2*) and thus these do not, in fact, contain a joining segment. Because these isolates exhibit diversity at the coding-signal junction, we incorrectly assumed that they were bona fide VJ transcripts. At this time we do not know whether the junctional bases are nongermline elements introduced at the coding-signal joints, or whether transcripts from such nonrearranged V_α genes might serve some function. Transcripts from nonrearranged gamma genes have recently been reported, and these are inducible by interleukin-3 (*3*).

We would also like to comment on the observation that the $V_{58}J_{58}$ isolates do not contain diversity at the VJ joint. This lack of diversity, in contrast to that of all other VJ isolates from our laboratory, has raised the question of whether these may have been derived, as a polymerase chain reaction contaminant (*4*), from the α chain gene isolated from CTL 2C. At this time we do not have a definitive answer.

Despite the error in our analysis of the $V_{58}J_3$ isolates, the main tenet of our report (that is, the preferential association and expression of particular VJ combinations) holds true. Thus, the J_1 and J_2 isolates (figures 1 and 3) and only a few other J segments (*5*) have been found to be expressed as the predominant V_{58} transcripts.

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REFERENCES

1. M. E. Roth, M. J. Lacy, L. Klis McNeil, D. M. Kranz, *Science* **241**, 1354 (1988).
2. A. C. Hayday *et al.*, *Nature* **316**, 828 (1985).
3. Y. Weinstein, K. Morishita, J. L. Cleveland, J. N. Ihle, *J. Exp. Med.* **169**, 2059 (1989).
4. S. Kwok and R. Higuchi, *Nature* **339**, 237 (1989).
5. M. E. Roth, M. J. Lacy, L. Klis McNeil, D. M. Kranz, unpublished observations.

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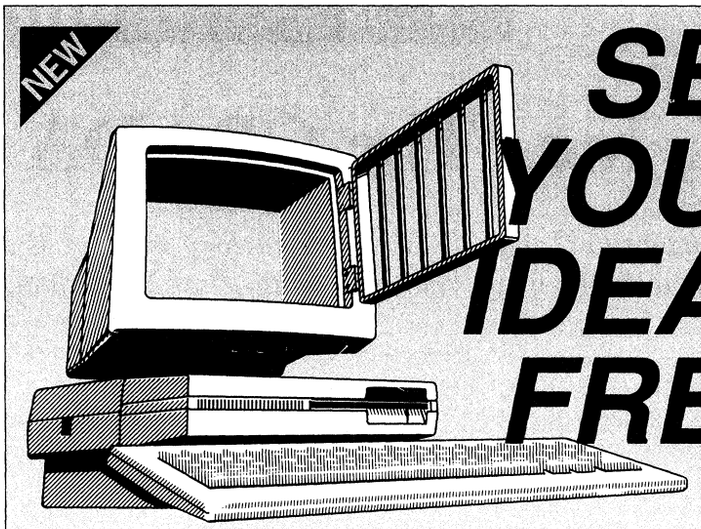

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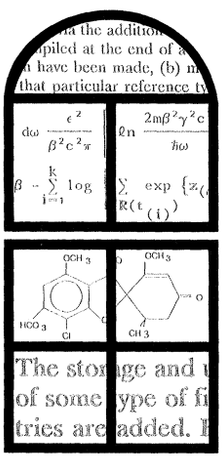

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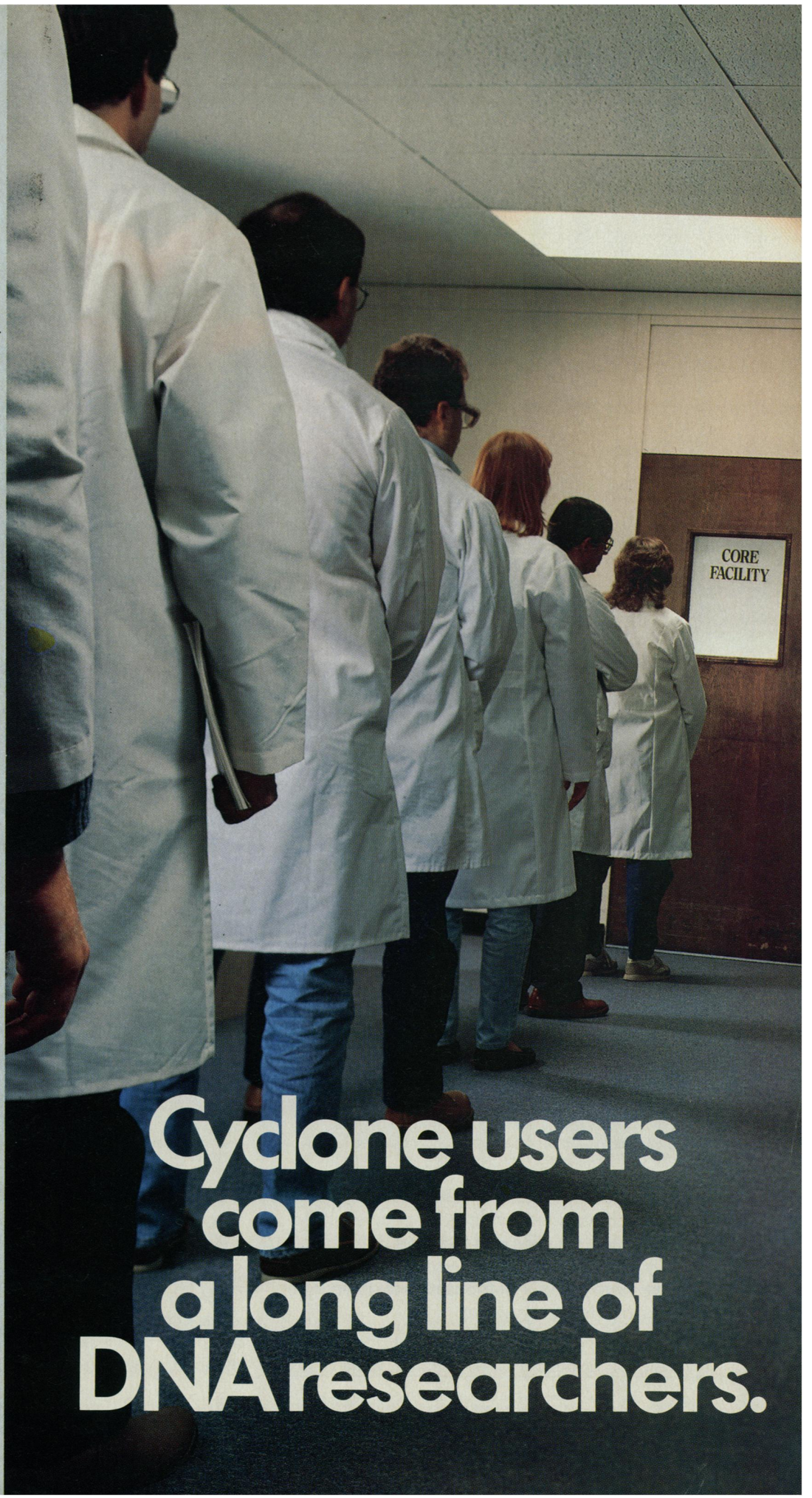

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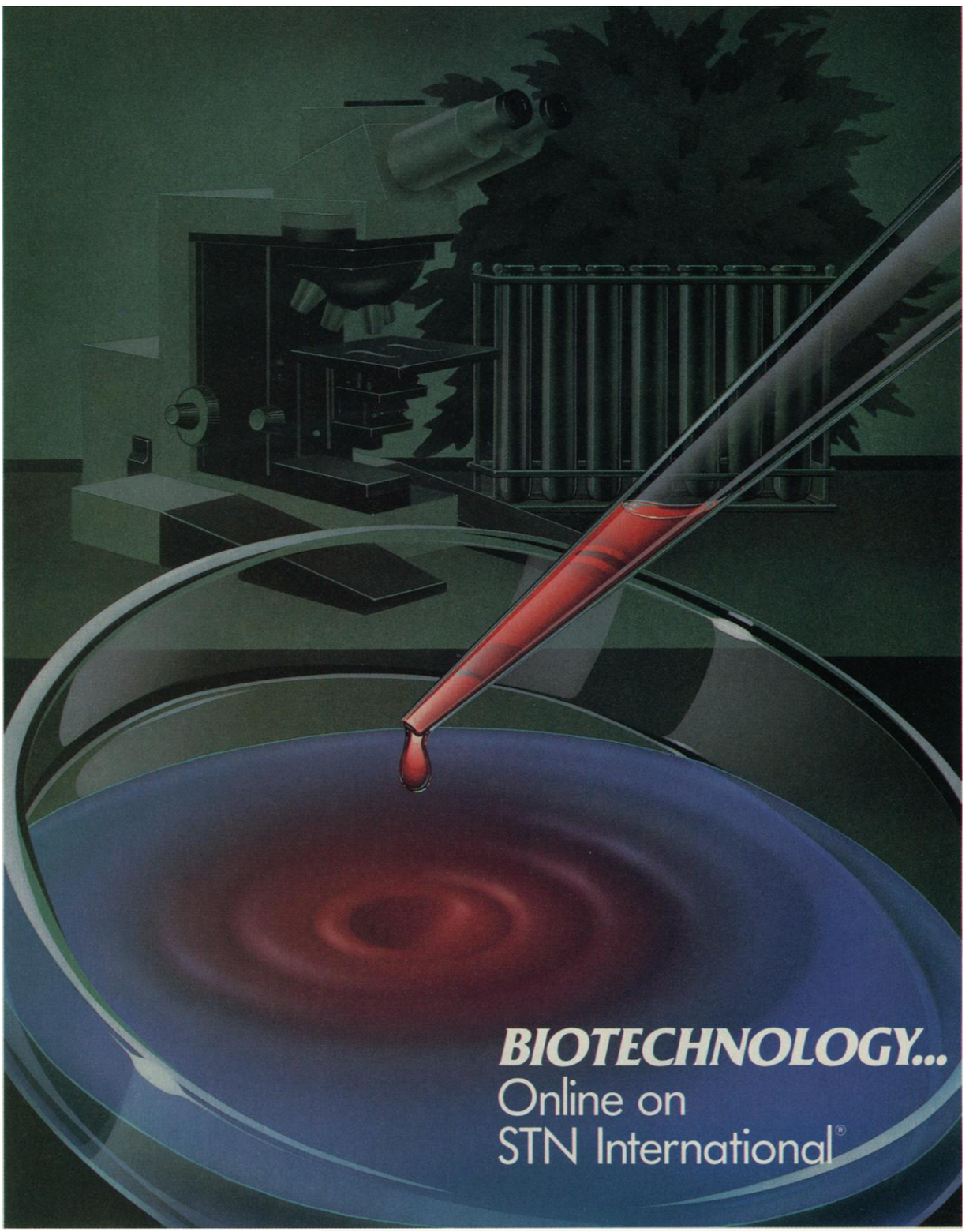

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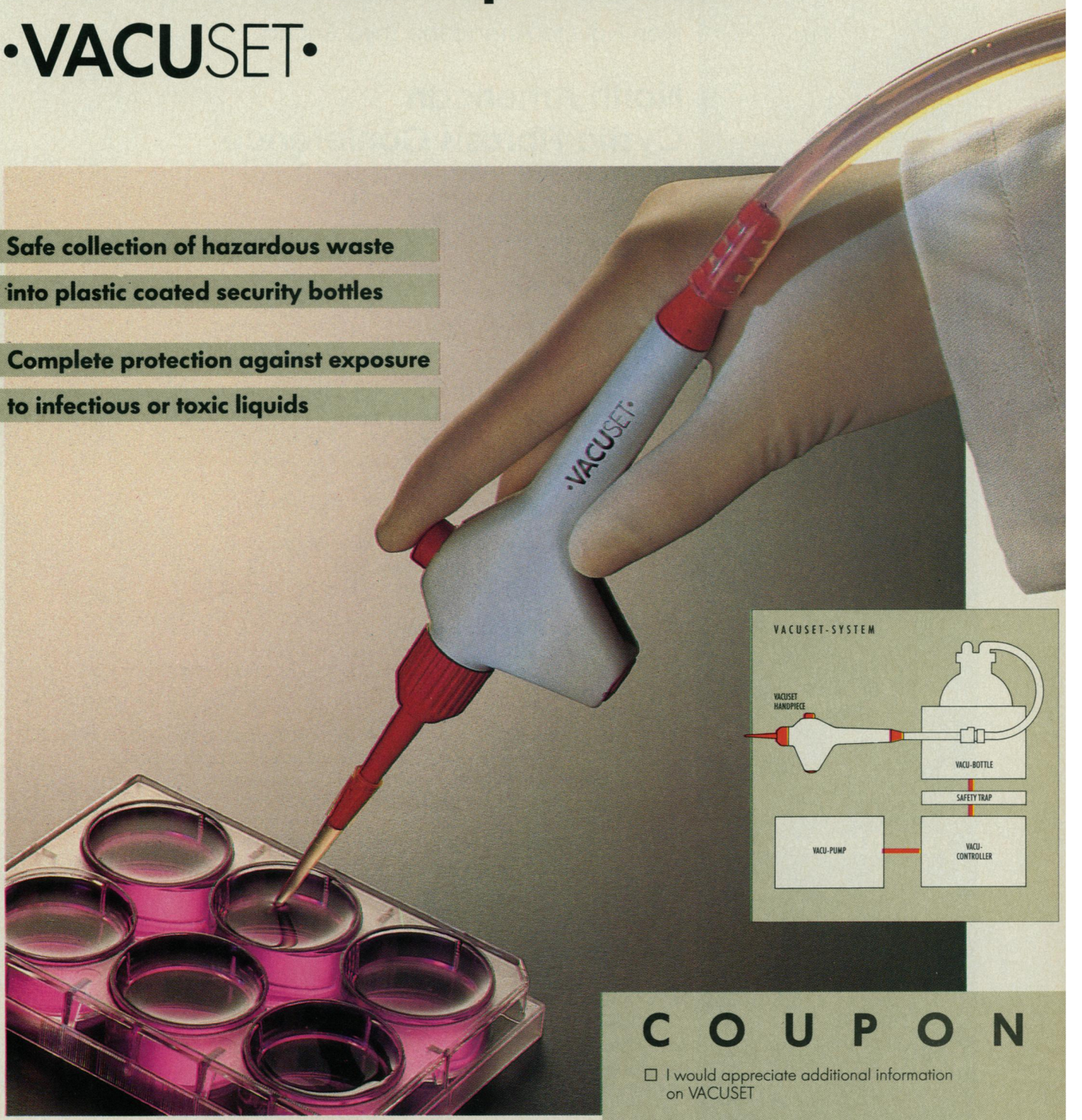

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- ***PLENARY SESSIONS***

  - **The CF Gene : Where We Stand**
    Francis S. Collins, M.D., Ph.D.
    University of Michigan, Ann Arbor
    Lap-Chee Tsui, Ph.D.
    Hospital for Sick Children, Toronto

  - **Advances in Medical Treatment of CF**
    Beryl J. Rosenstein, M.D.
    The Johns Hopkins University Hospital

  - **A Look Toward the Future**
    Richard C. Boucher, Jr., M.D.
    University of North Carolina at Chapel Hill

- ***SYMPOSIA***
  - Current Applications of DNA Technology to Clinical Practice in CF
  - The CF Gene: Molecular and Biochemical Approaches
  - Diagnosis and Management of Liver Disease in CF
  - Successful Strategies for Living With CF
  - Nutrition in CF
  - Lung and Heart-Lung Transplantation in CF Patients
  - Evaluation and Management of CF Lung Disease in the First Two Years of Life
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- *Development of appropriate model systems for studying the regulation of defective cellular processes;*
- *Development of pharmacological agents or other therapies to reverse the abnormal phenotype observed in CF cells.*

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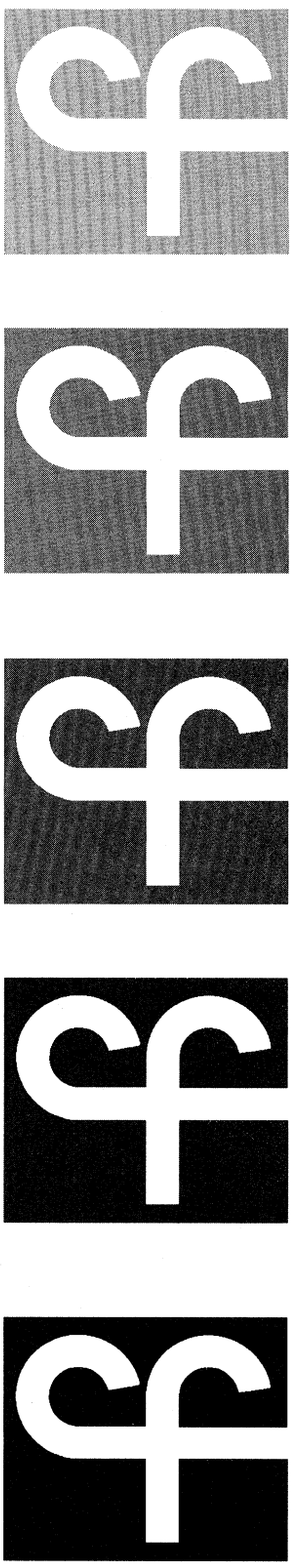
The deadline for receipt of applications is December 1, 1989. For further information and applications, interested individuals are urged to contact Dr. Robert J. Beall or Ms. Dale Glass at the Cystic Fibrosis Foundation.



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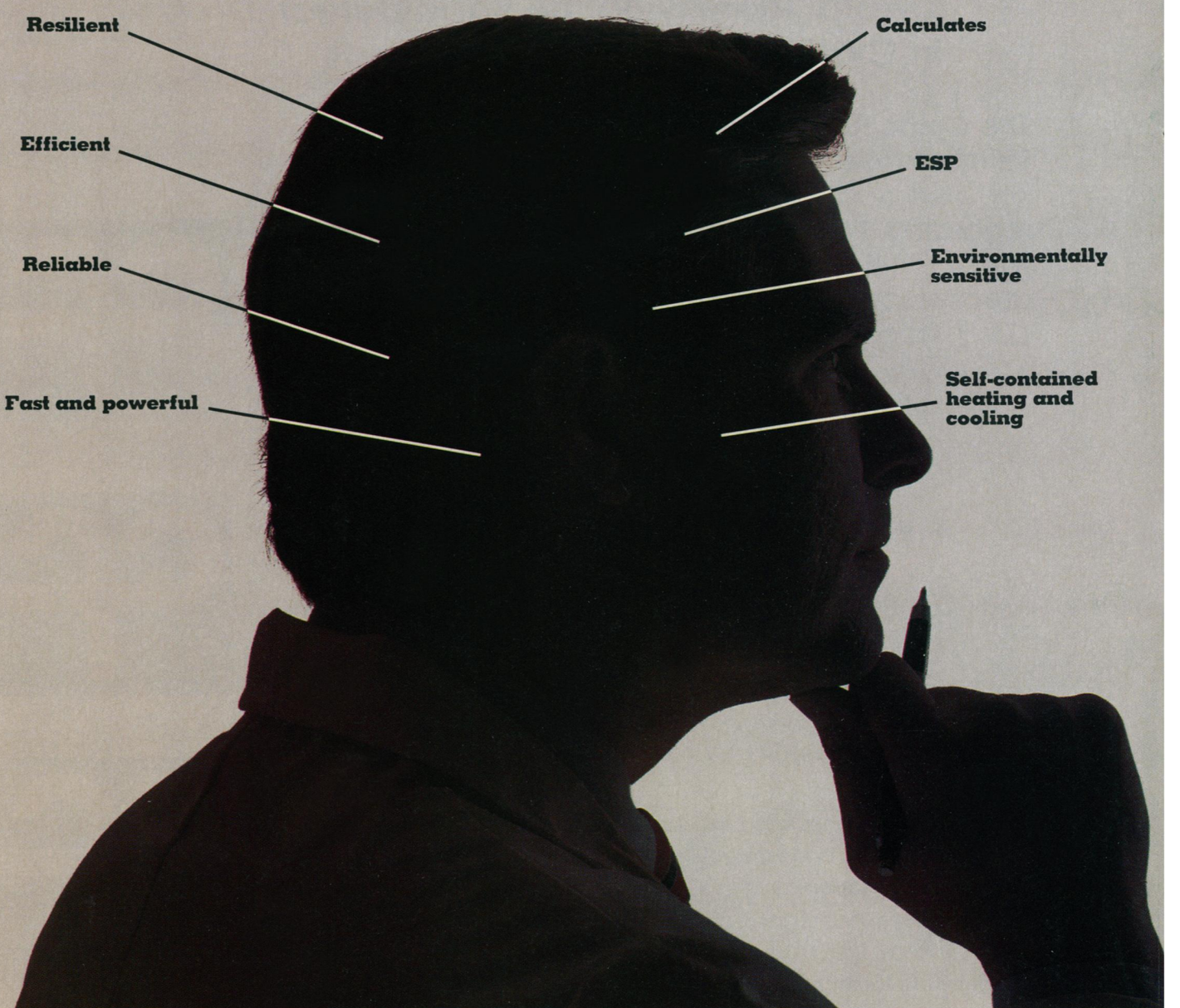

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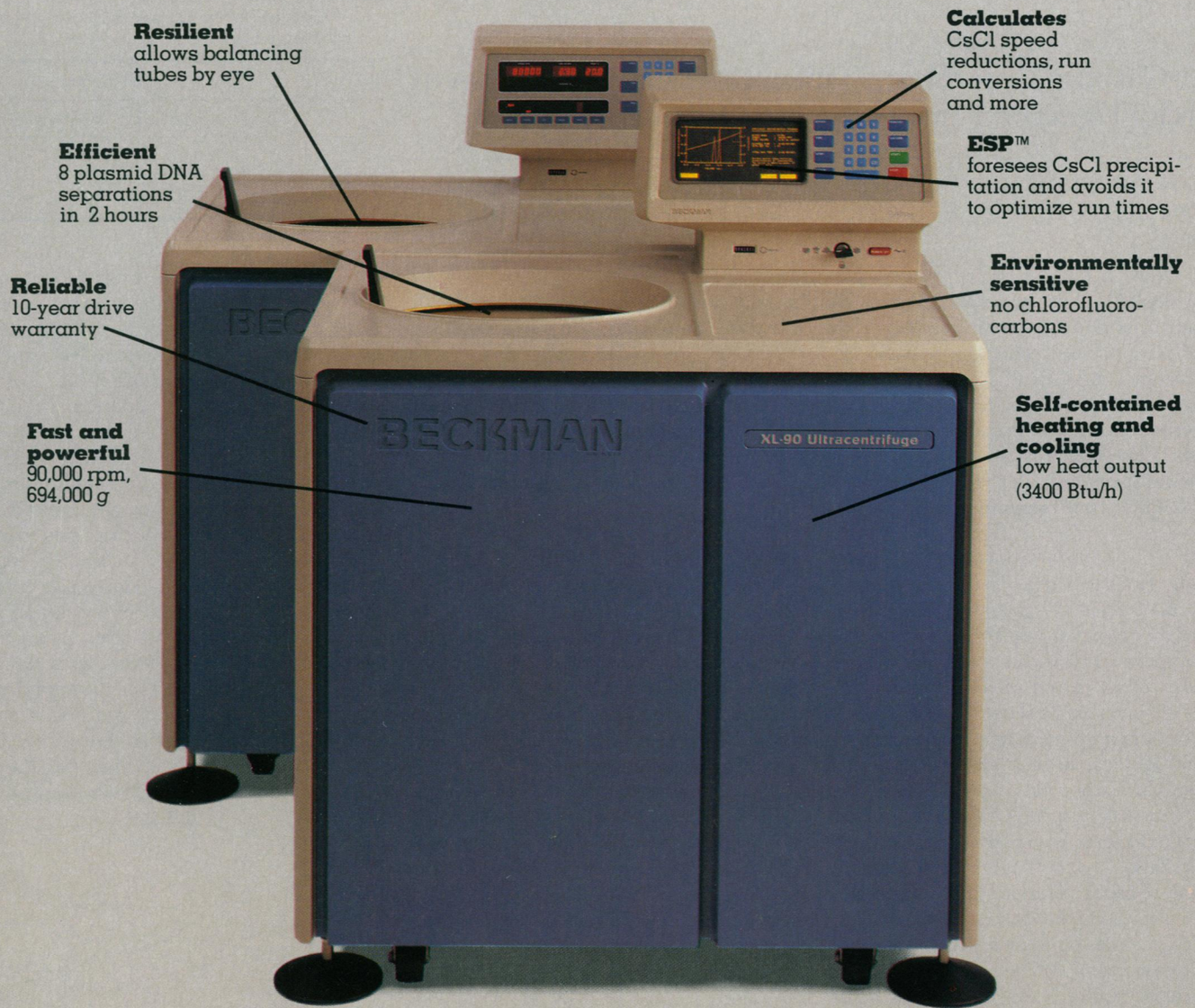

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