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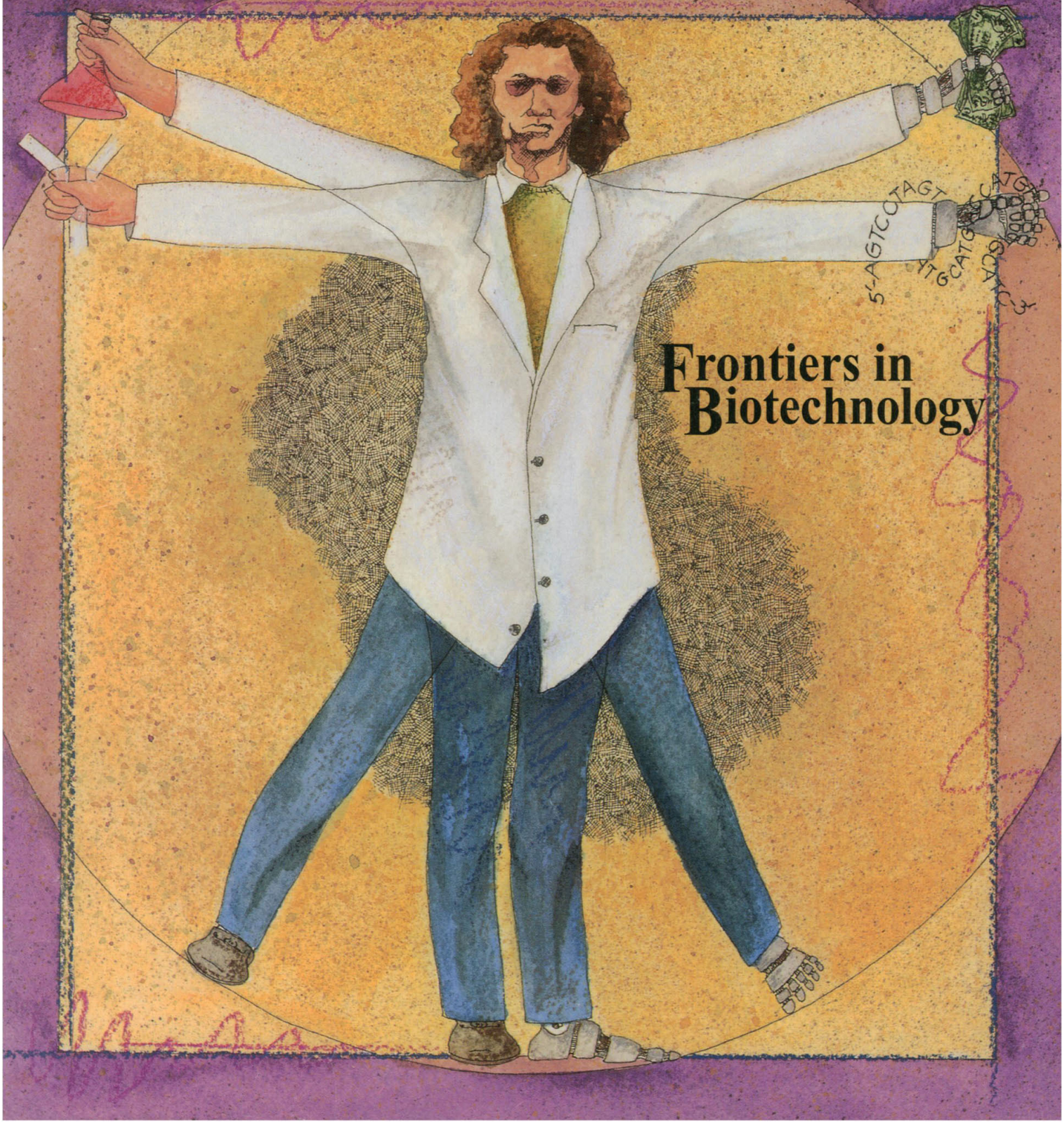

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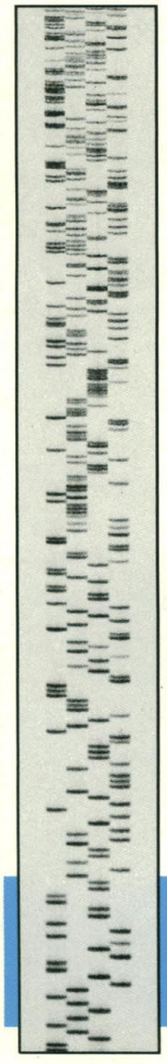

Figure Legend : Autoradiograph of sequencing gel using the BaseAce Sequencer and the FeatherVolt 2000 power supply. 1.0 µg M13 ssDNA was labeled with S-35 ATP and run for 3 hrs at 65 watts on a 6% acrylamide (7M Urea, 1X TBE) gel.

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1. Nielson, K. and Mathur, E.J. (1990) Strategies 3:17-19.
2. Nielson, K. and Mathur, E.J. Manuscript in preparation.
3. Nielson, K. and Mathur E.J. (1989) U.S. patents filed.
4. Mullis, K.B., and Faloona, F.A. (1987) Meth. Enzymol. 155:335-350.

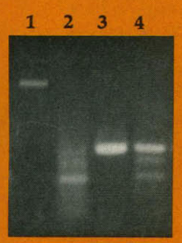

Figure Legend: A photograph of a 1% agarose gel stained with ethidium bromide representing reaction products from PCR amplifications using the GeneAmp™ Kit† from Perkin-Elmer Cetus according to manufacturer's instructions. The reactions were conducted with (lanes 1 and 3) and without (lanes 2 and 4) the inclusion of 1 unit Perfect Match polymerase enhancer. Lanes 1 and 2 represent 100 ng of human genomic DNA amplified with two 26-mer primers separated by 1400 nucleotides. Lanes 3 and 4 represent 100 ng of mouse genomic DNA amplified with two 23-mer primers separated by 550 nucleotides.

Figure 1 shows two examples of *in vitro* amplification reactions that are significantly enhanced by the addition of Perfect Match polymerase enhancer to the polymerase preparation. Note that in lanes 1 and 2, the desired PCR product cannot be detected unless Perfect Match polymerase enhancer is added to the amplification reaction. In lanes 3 and 4, Perfect Match polymerase enhancer not only increases the intensity of the desired amplification products, but dramatically reduces the background artifacts generated by non-specific priming events.

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COVER Inspired by Leonardo da Vinci's "Proportions of the Human Figure According to Vitruvius," the cover image symbolizes that the creativity of scientists is at the center of technological advances. Scientists' curiosity about biological processes has often led to discoveries that proved useful for biotechnology. One-half of the figure's appendages are robot-like, showing that technology is an extension of its creator. The figure holds a flask of microorganisms, an antibody, and oligonucleotide primers, representing some of the tools of biotechnology discussed in this issue; the fistful of dollars signifies the entrepreneurial aspect of biotechnology. See pages 1643 to 1681. [Illustration by Julie Cherry]

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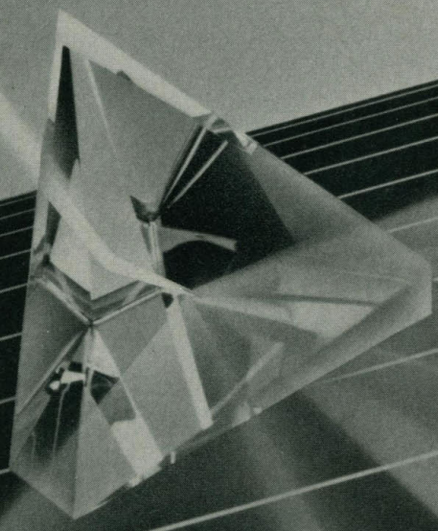

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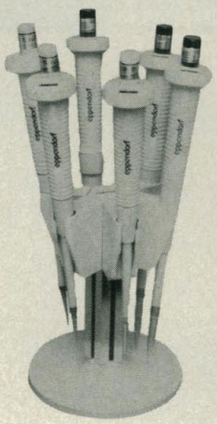

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The big chill

IT seems to be the rule rather than the exception that, professionally, women astronomers and physicists are treated as second class citizens. At meetings and in the workplace, they are subjected to a "chilly climate;" they are often excluded from informal social events, where, as all scientists are aware, much of the inside information of science is passed along. Flam reports on two recent surveys—one conducted by an astronomer and the other performed under the auspices of the American Astronomical Society—that indicate a high level of discontent among women astronomers and physicists (page 1604). In general the complaint is not one of overt discrimination but of forms of discrimination that are more subtle and more difficult to document. In a companion piece, Selvin describes the legal battles of Jenny Harrison, a mathematician who was denied tenure at the University of California at Berkeley in 1986. She is currently suing the university, charging overt sex discrimination in the math department's decision to deny her tenure (page 1606).

Workhorse virus

IN 1980, the World Health Organization declared that smallpox had been eradicated from the earth; the last naturally occurring case had developed in Somalia in 1977. Successful control of the disease was achieved with a vaccine made from a virus (vaccinia) related to but not the same as the smallpox virus (variola). Even though smallpox vaccines are no longer administered, the vaccinia virus is not being consigned to retirement. In one of the 6 articles in this Frontiers in Biotechnology issue (see pages 1643 to 1681 and the editorial on page 1593), Moss describes some of the research projects and clinical trials that are now underway or in the planning stages with this versatile virus (page 1662). One of the most interesting is the proposed use of vaccinia in vaccines for diseases that are unrelated to smallpox. The virus has a large genome and can easily accommodate a dozen or more average-size genes. Thus vaccinia viruses could serve as live vectors, multiplying in hosts and carrying with them the genes for immunogenic substances of one or more pathogens. Perhaps a cocktail of many recombinant vaccinia viruses might one day be used in a multi-pathogen vaccine. Risks from the vaccine were acceptable for smallpox because smallpox was such a serious disease; for future uses, some modifications of vaccinia viruses may be necessary to further reduce side effects of these viral agents.

Southern Hemisphere atmosphere pollution

BIOMASS burning in Africa and in southeastern Brazil has caused pollution not only locally in the troposphere but throughout the Southern Hemisphere (page 1693). Evidence of widespread pollution was obtained with satellite data and ozonesonde measurements made at Brazzaville, Congo, and at Ascension Island in the Atlantic Ocean. The ozone that is produced over southern Africa during the dry season (August to October) is transported by low-troposphere easterlies to the eastern South Atlantic Ocean. Some ozone then rises into the upper troposphere where westerlies can transport it long distances, even as far as Australia. In addition to ozone, tropospheric abundances of two other gases—carbon monoxide and methane—vary seasonally. Fishman *et al.* note that these three pollutants typically have been associated with human activities in industrialized countries of the Northern Hemisphere; in the Southern Hemisphere their seasonal variabilities are best explained by the seasonal differences in the amount of biomass that gets burned.

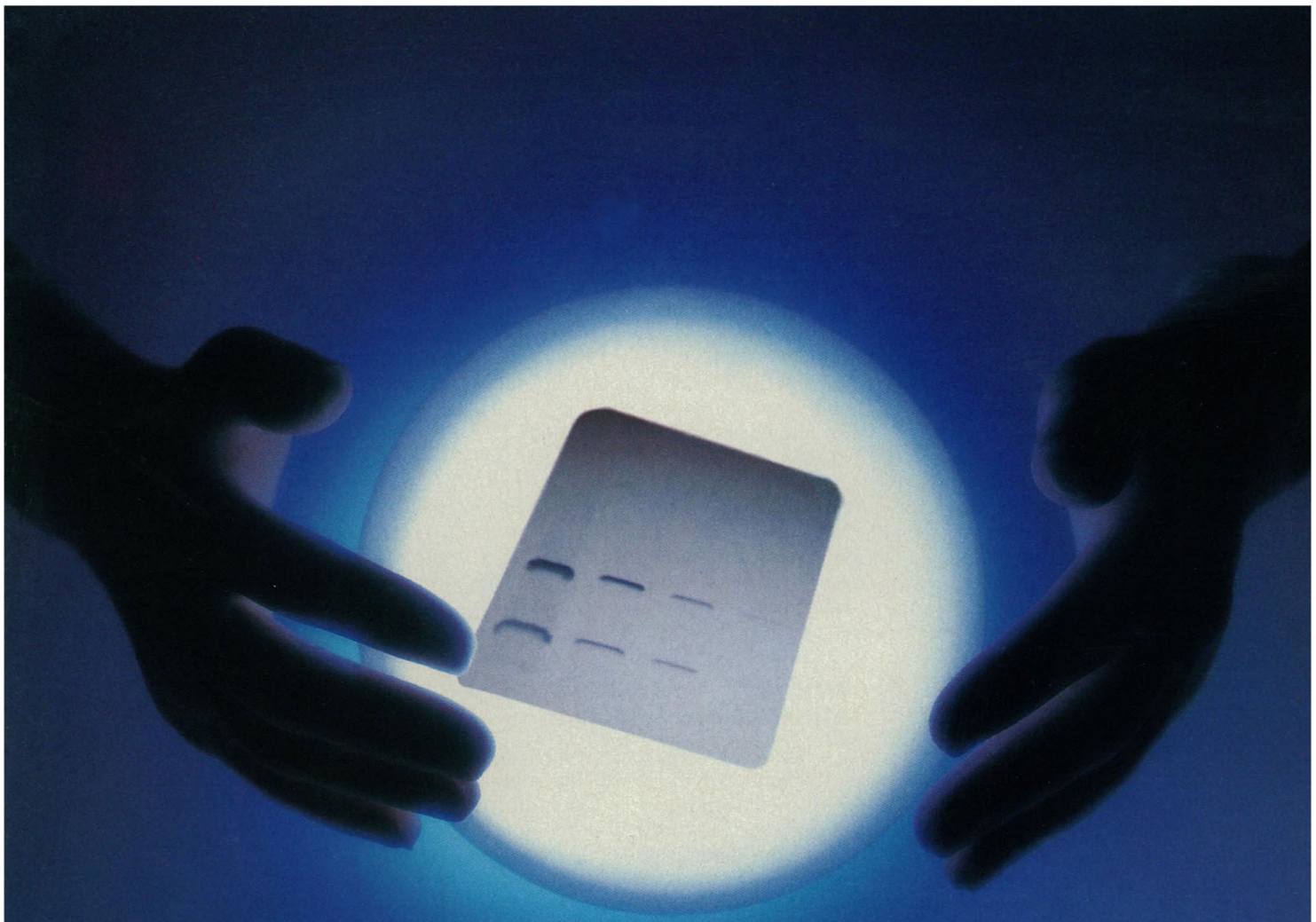
Accepting xenografts

IT is not easy to graft tissue between species (xenografts), because tissue that is so unlike self typically elicits a powerful reaction from the immune system of the graft recipient. One way around this problem is to suppress the immune system of the host, but this leaves the host vulnerable to infections. A different approach is to try to mask the foreignness of the graft such that the immune system is not activated. Faustman and Coe have had a remarkable success with the second approach (page 1700). They report that when human pancreatic islet cells (the cells that were to be grafted) were pretreated with specific antibody fragments, these cells could then be successfully transplanted into mice; survival exceeded 200 days. The antibody fragments were those directed against the cells' surface HLA class I antigens, which are among the target antigens against which the host's immune response is usually directed. This result is surprising and exciting; if it is broadly applicable, it could simplify tissue grafting across many types of transplantation barriers.

Fusion toxin for HIV-1-infected cells

L chimeric molecule has been found to halt the effects of the human immunodeficiency virus type 1 (HIV-1) on lymphoid cells in vitro (page 1703). The fusion toxin consists of the receptor-binding domain of interleukin-2 (IL-2) and portions of the diphtheria toxin. Receptors for IL-2 are expressed on HIV-1-infected cells after the cells are activated. The fusion toxin binds selectively to activated but not quiescent cells and then specifically kills the cells. Finberg *et al.* report that production of viral proteins was blocked by this treatment and thus the proliferation of infectious viruses was inhibited. Because the IL-2 receptors appear on cell surfaces only after the cells have been activated, normal T lymphoid cells are not affected by the treatment. This form of chemotherapy might be valuable not only for the treatment of the early stages of infection with HIV-1 but for other diseases in which the activation of T lymphoid cells also marks the beginning of the disease process.

■ RUTH LEVY GUYER



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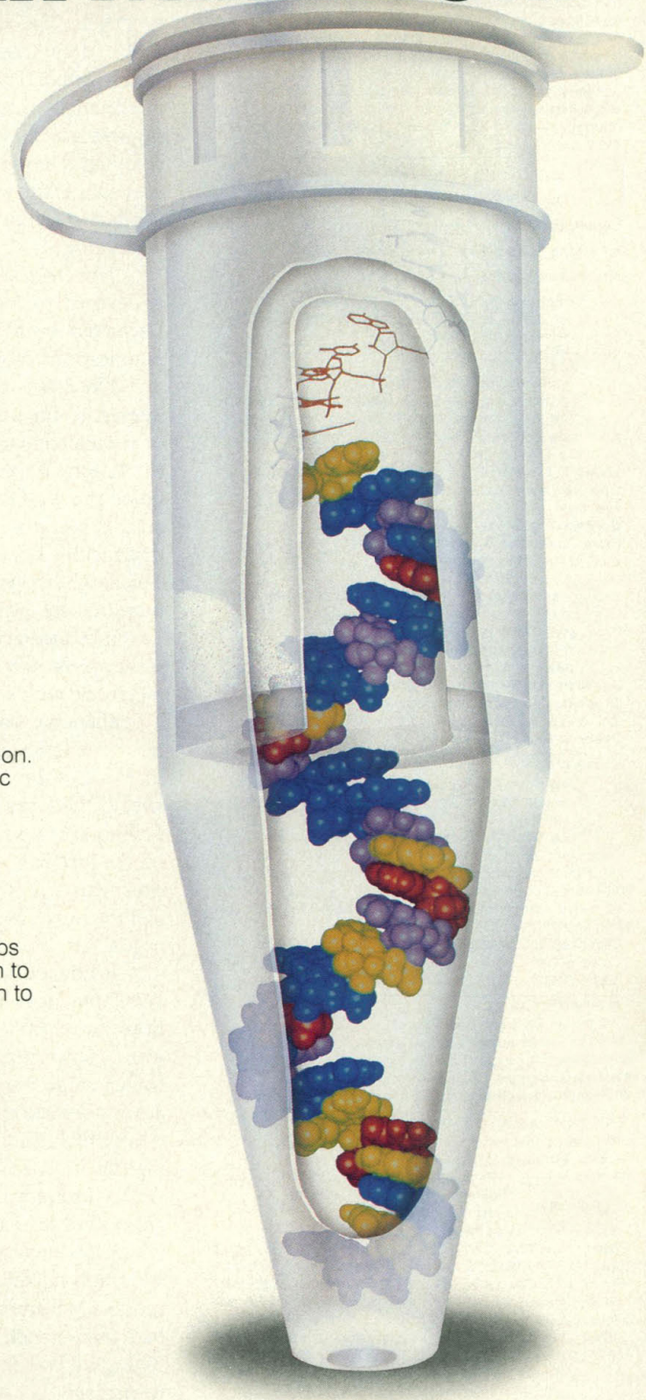

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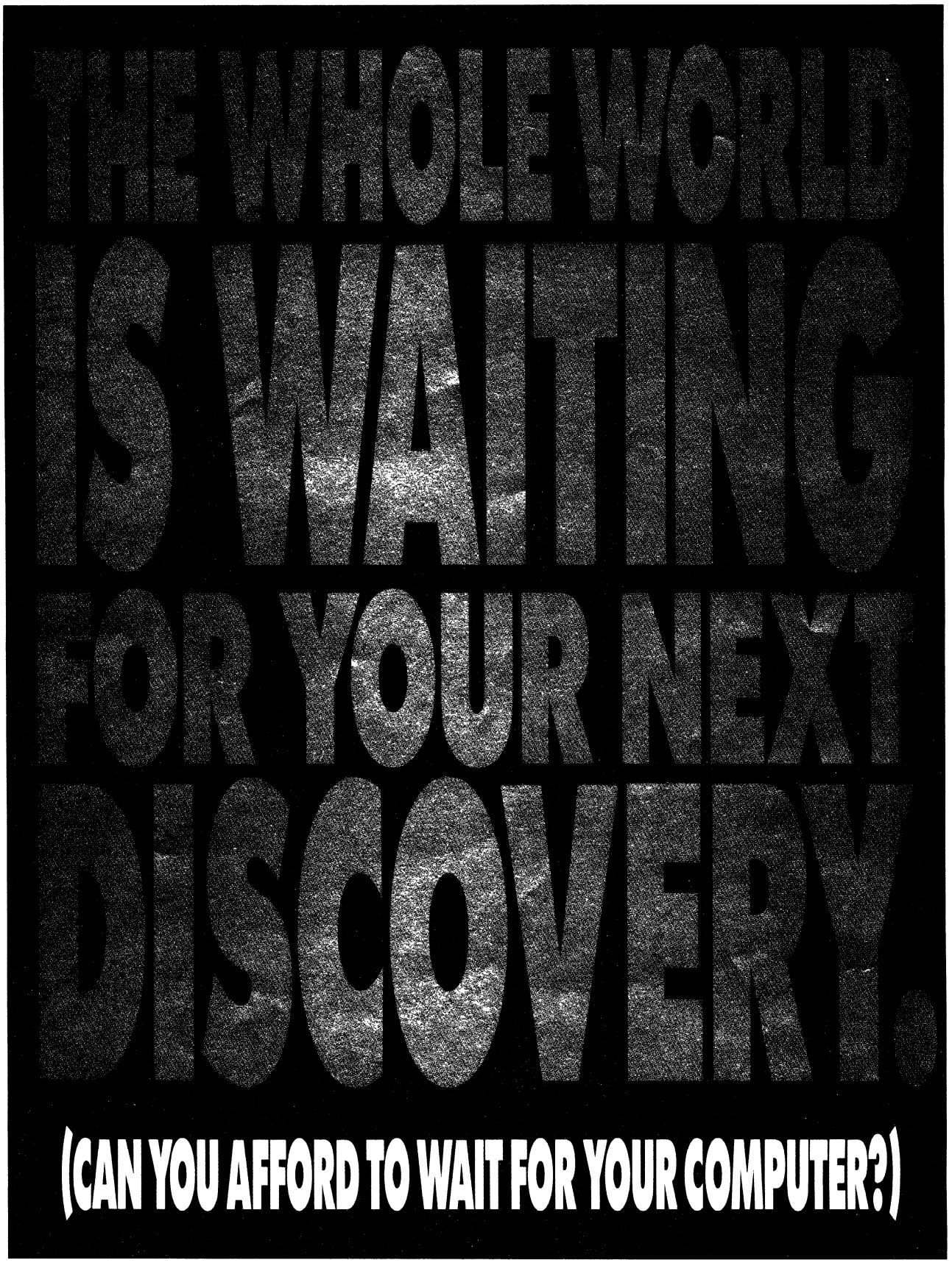

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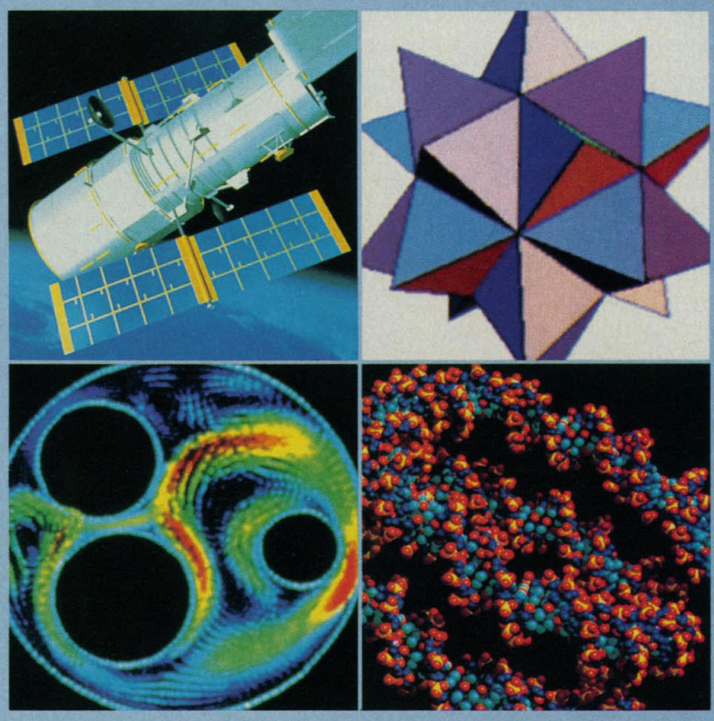

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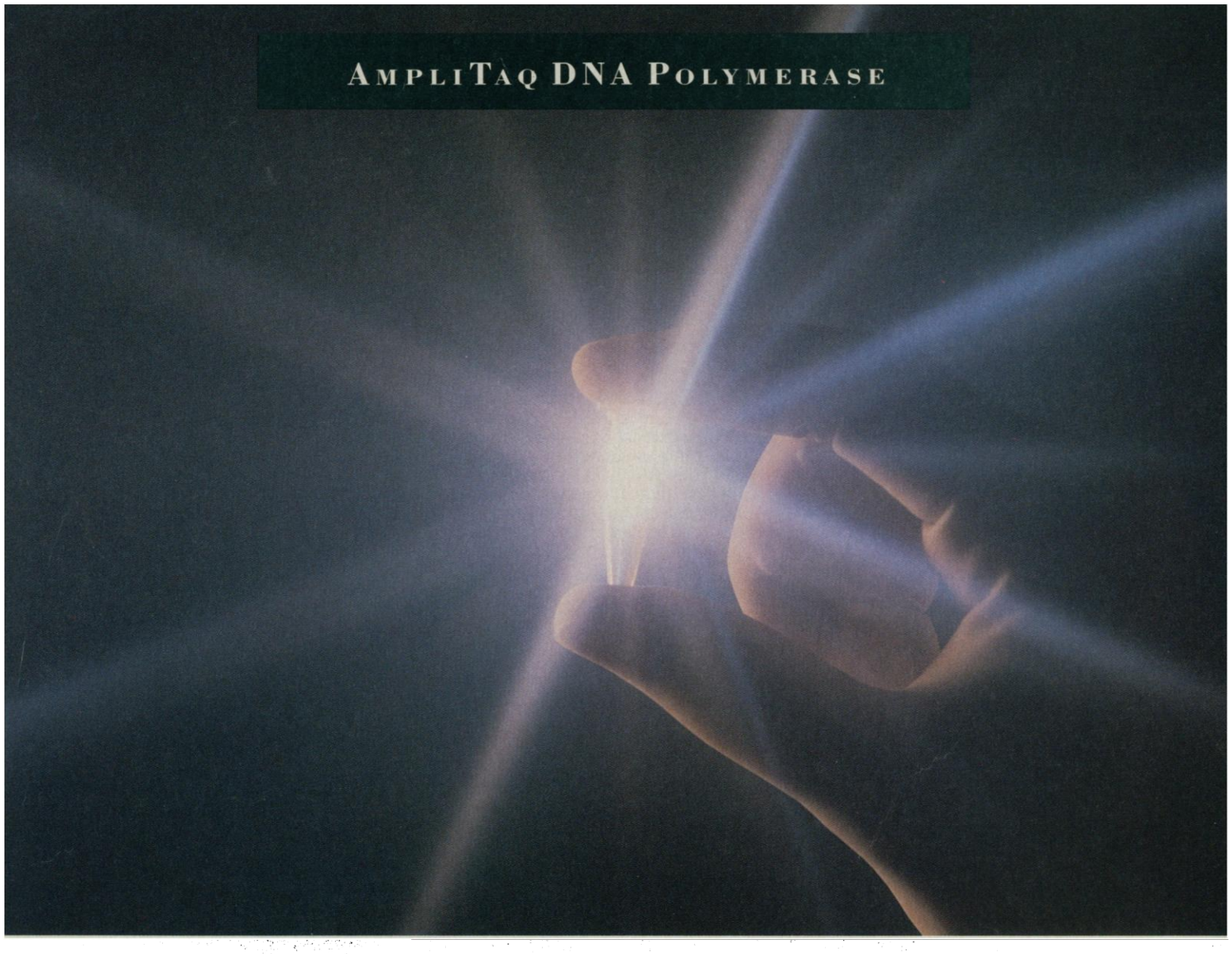

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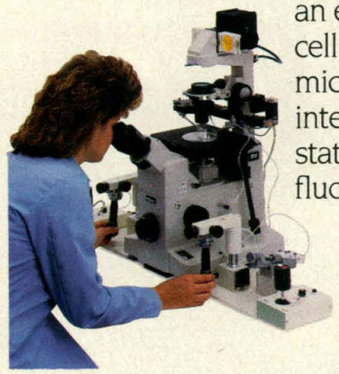

NT-88 Micromanipulation Workstation

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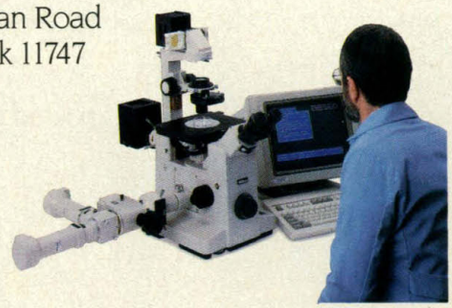

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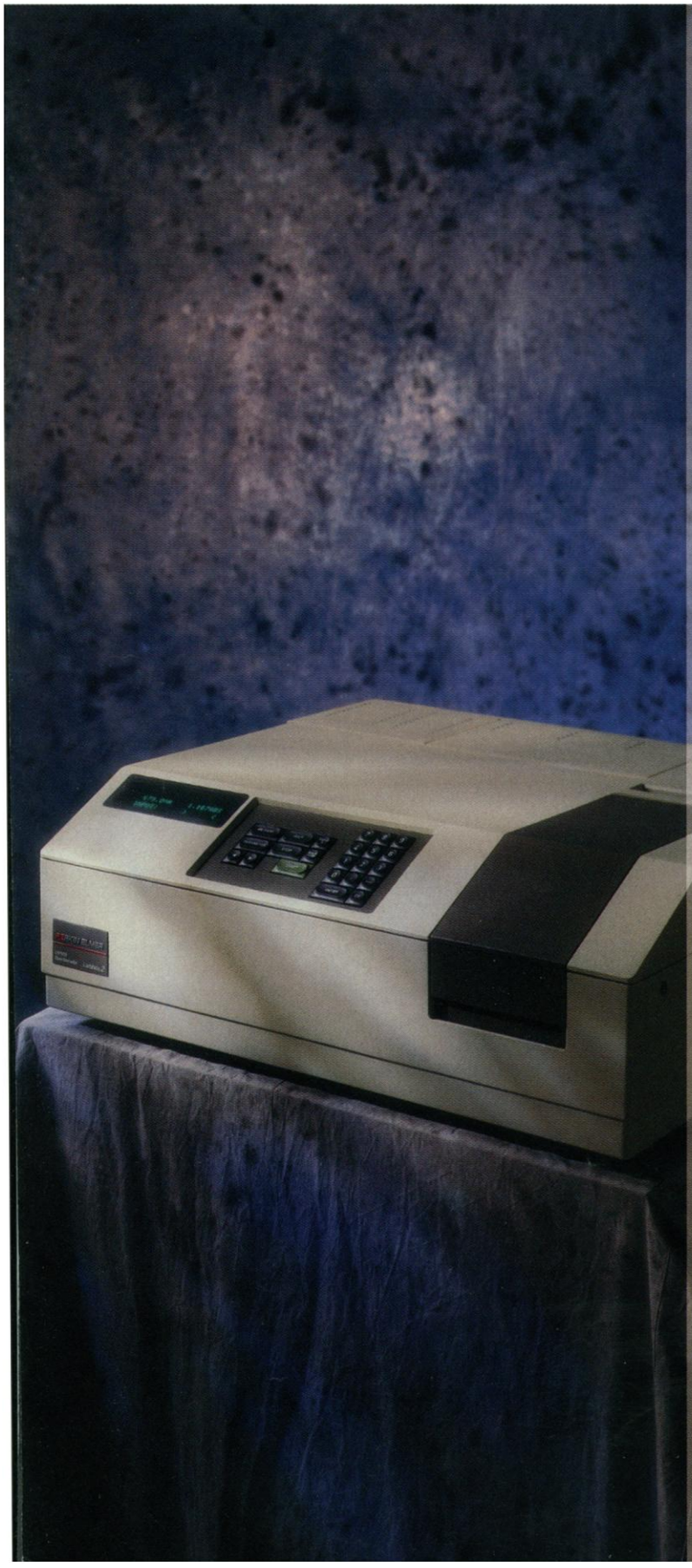

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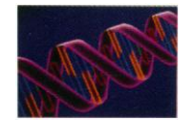

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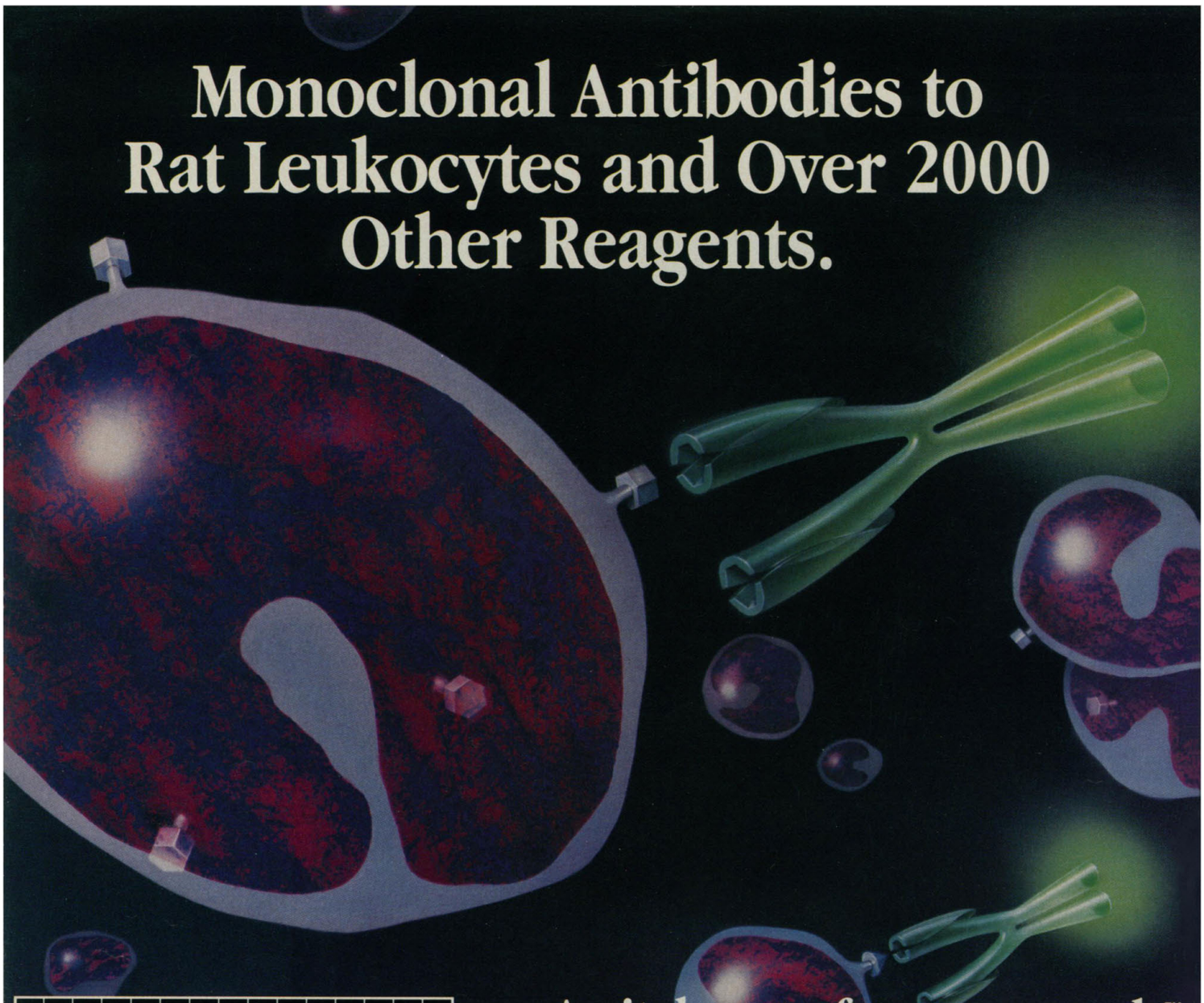

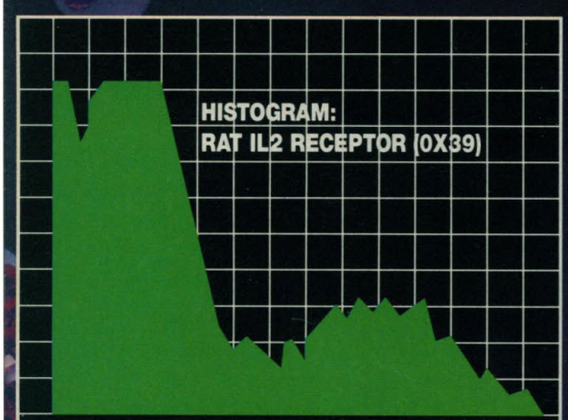

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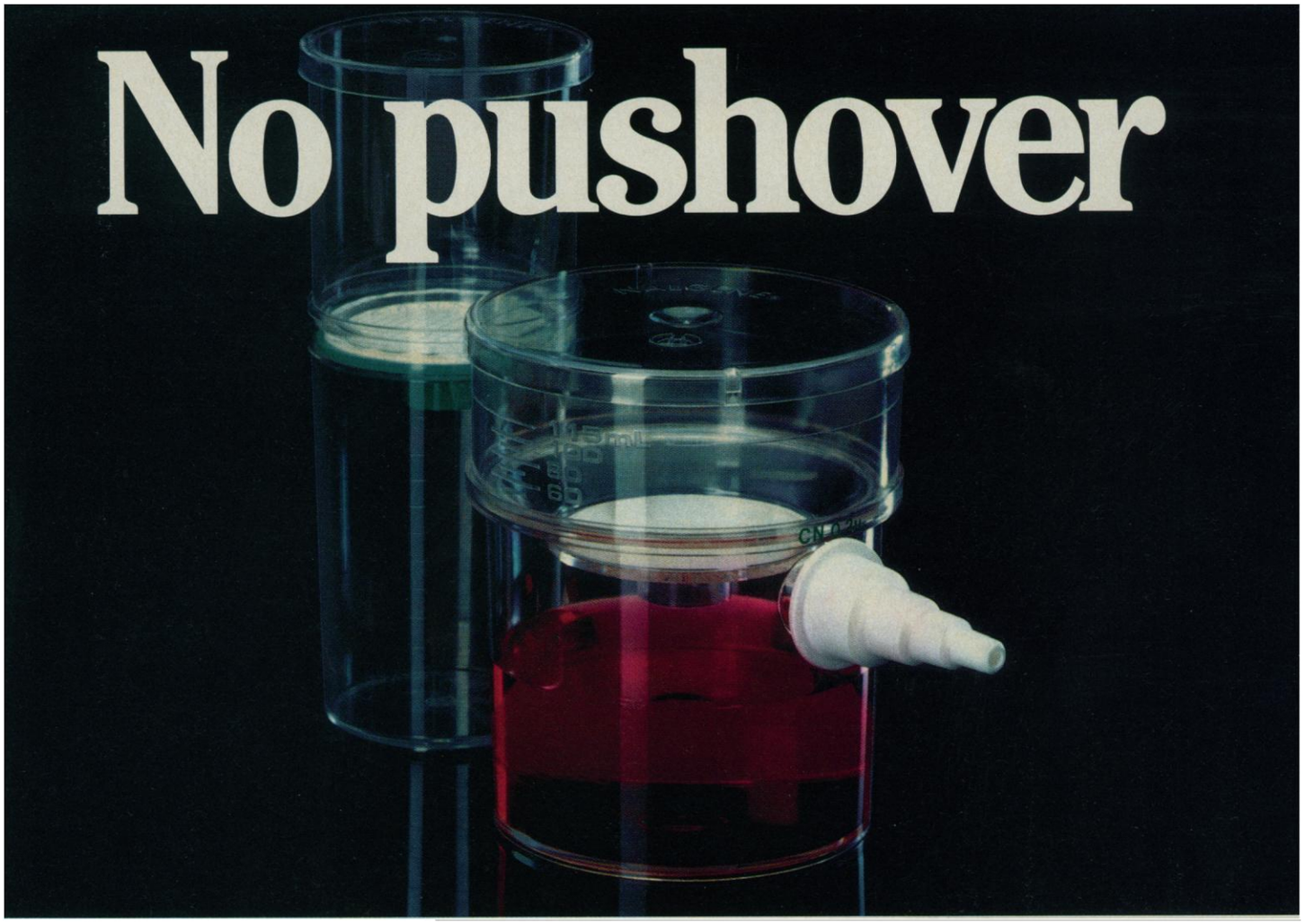

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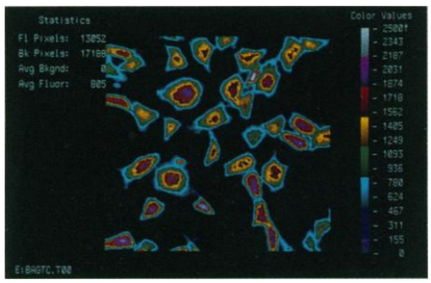
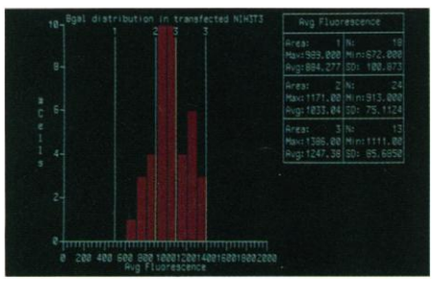
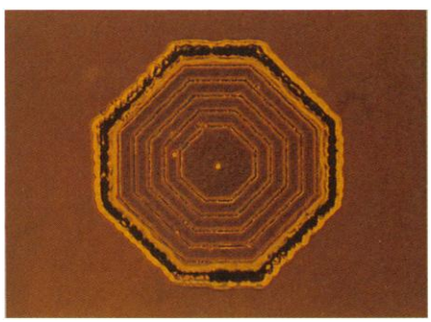


Two-dimensional, pseudo-color fluorescence image of FDG-labeled, lacZ⁺, NIH3T3 cells.



Histogram display of ß-galactosidase positive, NIH3T3 cells.



An example of ACAS cell sorting using the "Cookie-Cutter"™ technique to isolate single cells in culture while preserving their normal anchorage dependent growth state.

The ACAS is *the* pioneer instrument for Interactive Laser Cytometry, giving you new techniques for quantitative fluorescence analysis and adherent cell sorting.

It is the only instrument you can use for the automated selection and cloning of adherent cells in culture. With the ACAS you can:

- Screen cells,
- Sort cells in culture based on physical and biochemical measurements,
- Select mutant cells at frequencies of one in a million,
- Clone cells without altering morphology, phenotype, or viability,
- Isolate sub-populations of cells for quantitative fluorescence analysis and,
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Meridian Instruments Inc., introduces a major breakthrough in cloning transfected cells with the ACAS 570. The ACAS was used for the screening, selection, and cloning of transfected mammalian cells carrying the E.coli *lacZ* gene.[1] The product of expression of the *lacZ* gene, ß-galactosidase, was measured using the fluorescent probe fluorescein di-ß-D-galactopyranoside (FDG).[2] Selected cells were easily isolated and cloned using the patented ACAS "Cookie-Cutter"™ technique. The ACAS provided quantitative criteria to select $lacZ^+$ and $lacZ^-$ cells, and to distinguish between high and low expressers for cloning.

You can use this powerful interactive technique for the automated sorting and cloning of:

- Mutant cells
- Transfected cells
- Hybridomas
- Rare cells

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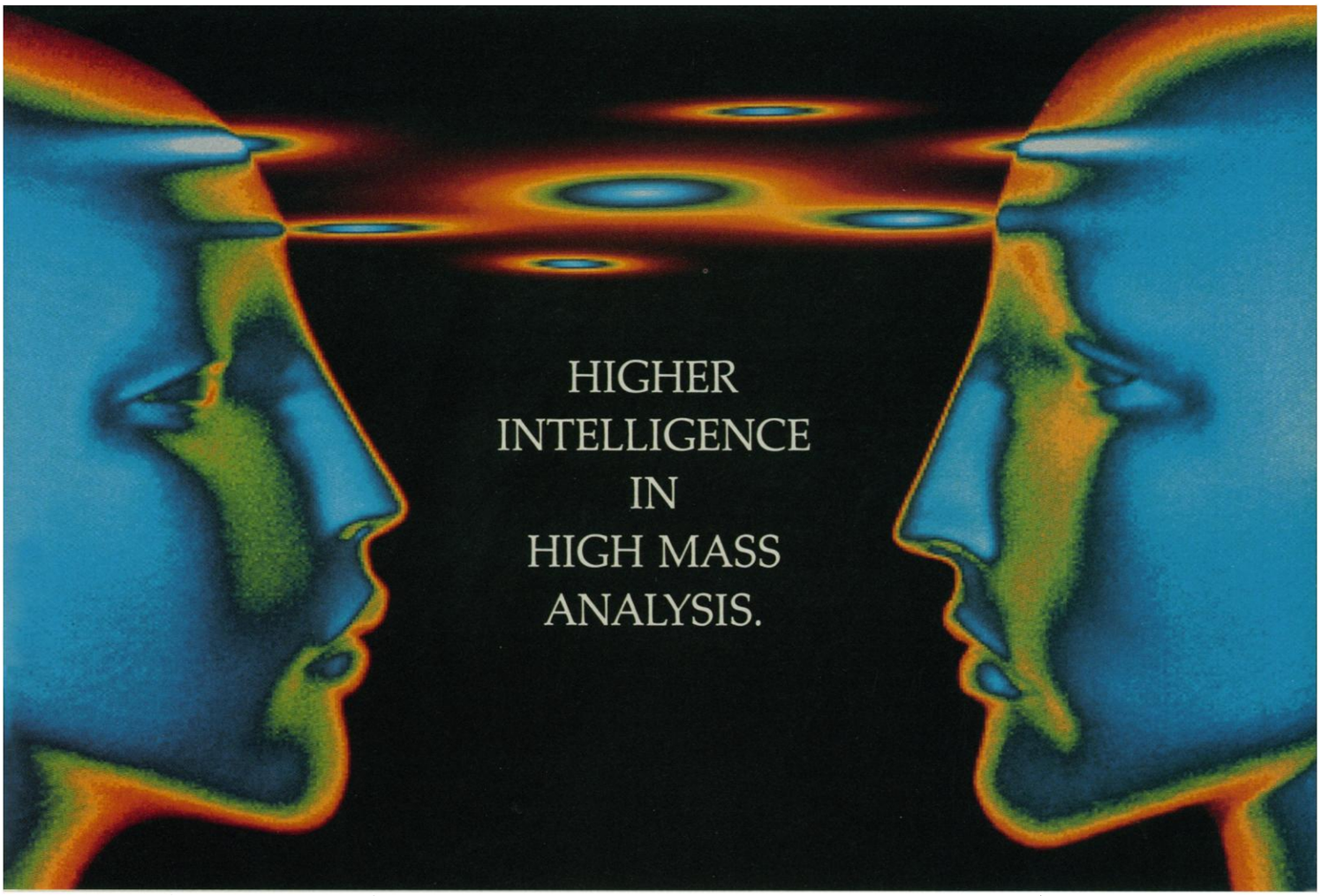
[1]Courtesy of James M. Wilson, Howard Hughes Medical Institute, University of Michigan, and Asmina H. Jiwa, Meridian Instruments, Inc.
[2]Molecular Probes, Inc.



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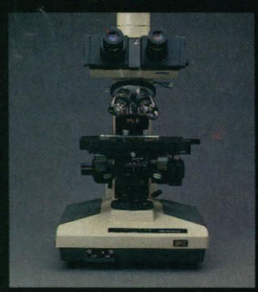

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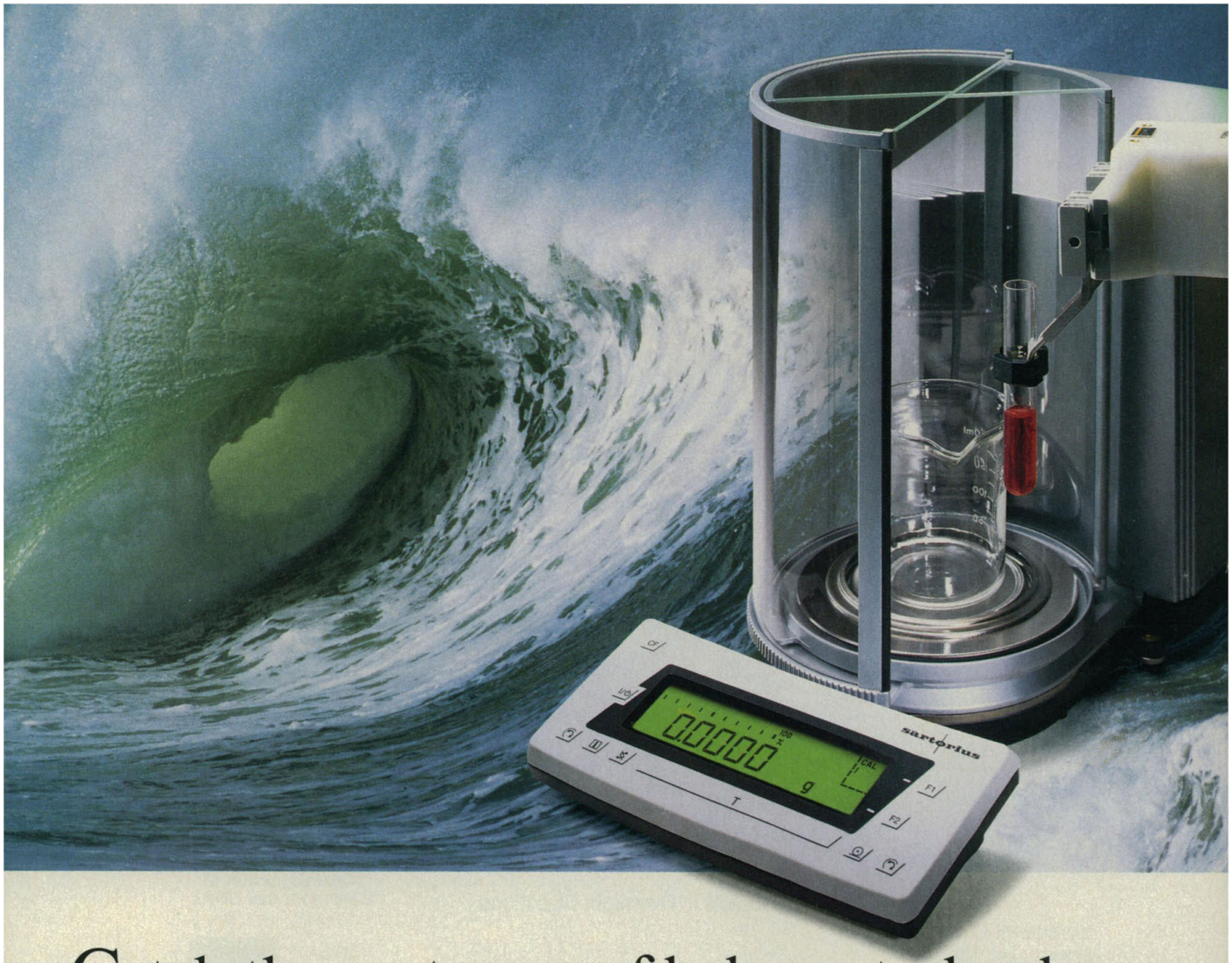

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The Boston Digest

FRIDAY, MARCH 15, 1991

WEATHER REPORT
Today: Clouding up, mid 40's
Saturday: Partly Sunny, 45-50
High Tide: 7:24 am 7:54 pm
Full report: Page 54

NEW ENGLAND BIOLABS DISCOVERS *Asc* I, A NEW 8-BASE CUTTER

Wetland Yields New Endonuclease

GG▼CGCGCC
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BOSTON - An exciting new restriction endonuclease has been found in an *Arthrobacter* species isolated from a Midwestern wetland. The researcher, Rick Morgan of New England Biolabs, reports that the bacteria was isolated from a small pond, dug nine years ago behind his brother's house. A recent family visit gave Morgan the opportunity to collect a water sample from the mature pond.

In Boston, NEB scientists isolated several bacterial strains from the "swamp" water. A number of endonucleases were identified, including isoschizomers for *SnaB* I, *Stu* I and

Scientists confirm global warming trend

By Judy Kramer
DIGEST STAFF

1990 set a record as the warmest year for the earth as a whole according to three out of four research teams monitoring global temperature trends. More significant, however, is the marked warming trend over the past decade which is leading some researchers to conclude that rising temperatures are caused in part by the greenhouse effect.

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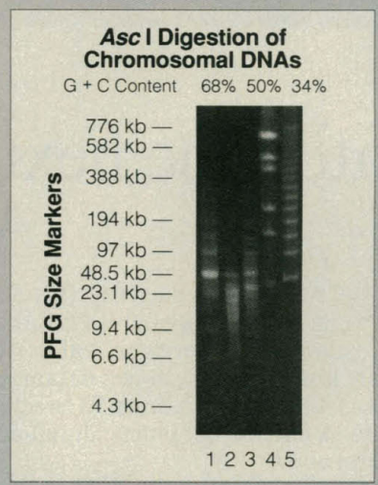

Agarose-embedded chromosomal DNAs of varying G+C content were digested with Asc I and then electrophoresed on a PFG for 29 hrs. Low range PFG marker (lane 1); Asc I digested R. sphaeroides DNA, 68% G+C (lane 2); Asc I digested E. coli DNA, 50% G+C (Lane 3); Asc I digested S. aureus DNA 34% G+C (lane 4); and Lambda ladder PFG Marker (lane 5).

Microscopy from Carl Zeiss

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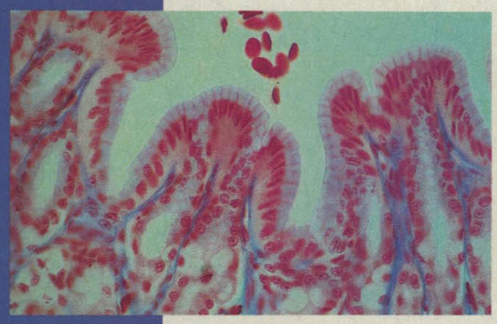

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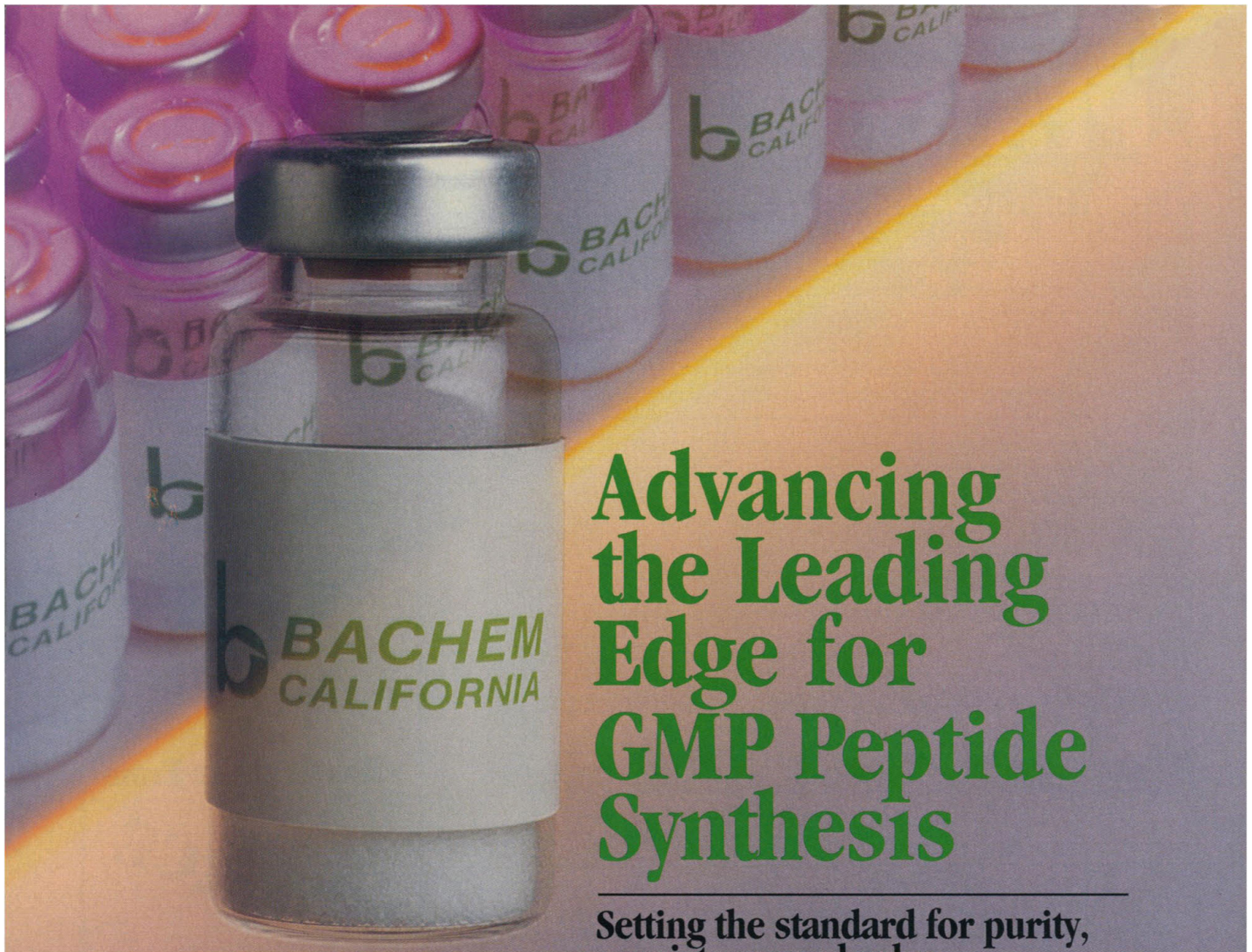

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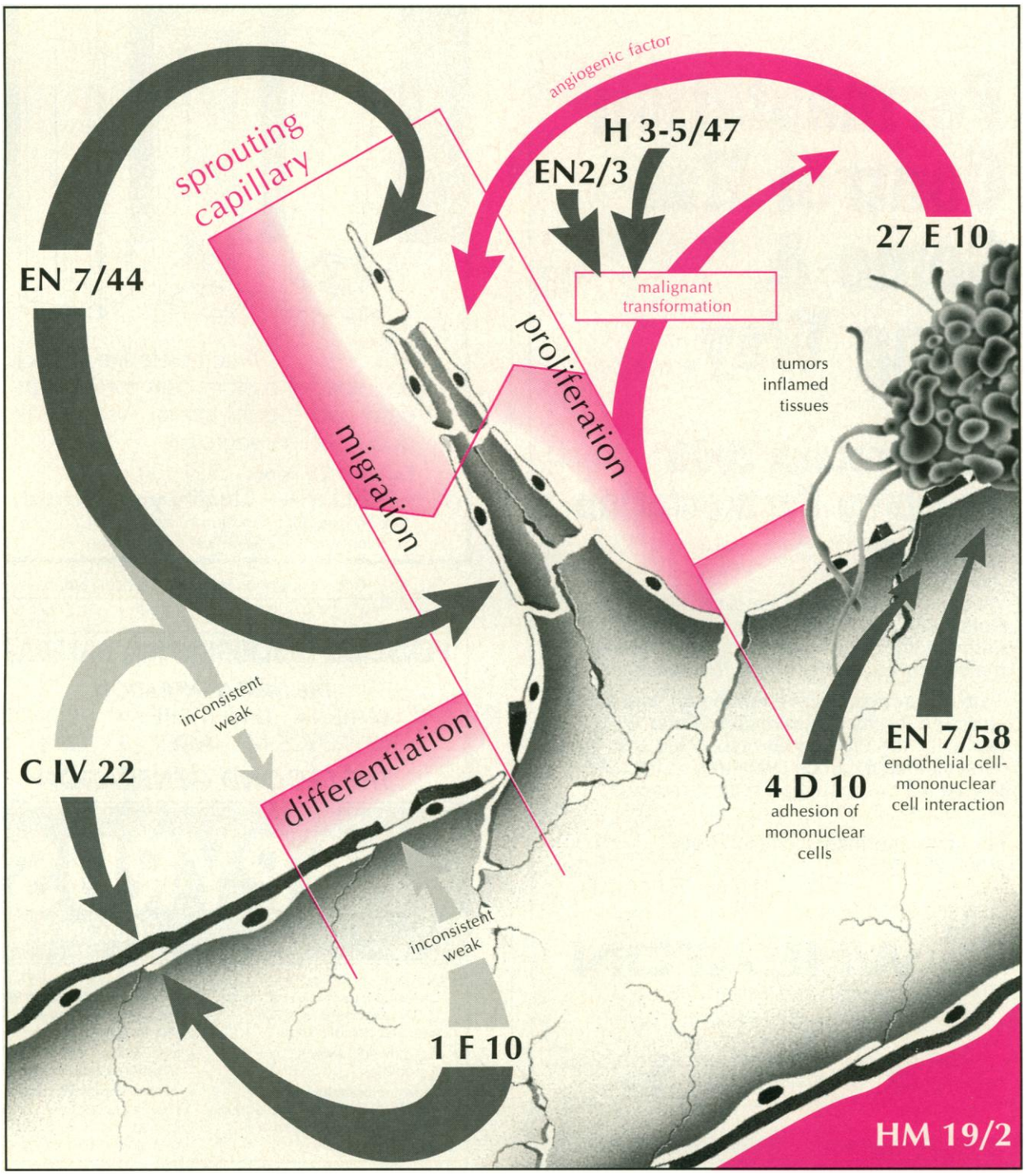
Characterization of the vascularization status with monoclonal antibodies from BMA



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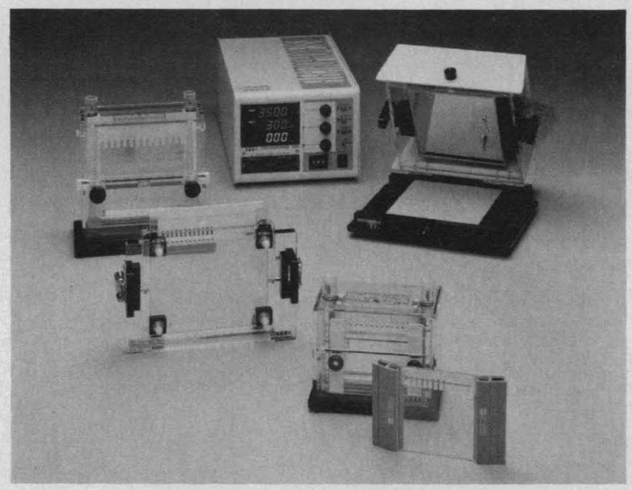

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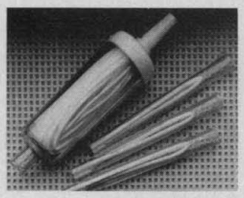

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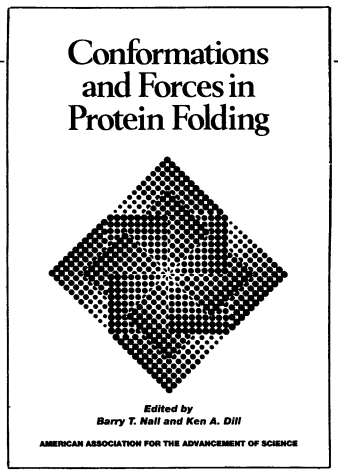
Conformations and Forces in Protein Folding



Barry T. Nall and Ken A. Dill, editors

Protein folding, the self-directed transition from disorganized chains to highly ordered and functional biological structures, is of increasing practical concern for the biotechnology industry and for interpreting DNA sequences. In the biological sciences folding is of major importance in the "self-assembly" process that produces the protein catalysts that facilitate and regulate cellular chemistry. Folding plays a role in such diverse cellular processes as macromolecular transport and assembly, targeting of proteins to intra- or extracellular locations, and in vivo stability of proteins.

Several aspects of folding addressed include forces and interactions important to protein stability and function, methods for determining proteins, studies of alterations in structure in mutant proteins, mechanistic investigations of the folding process, and analyses of auxiliary factors that modify or catalyze protein folding.

1991; ca. 272 pp.; indexed and illustrated; #91-05S — softcover; $34.95 (members $27.95); ISBN 0-81768-394-6

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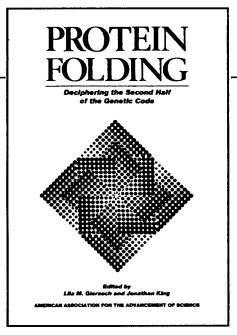

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Lila M. Gierasch and Jonathan King, editors

1990; 342 pp.; indexed and illustrated; color plates #89-18S — softcover; $39.95 (members $31.95); ISBN 0-87168-353-9

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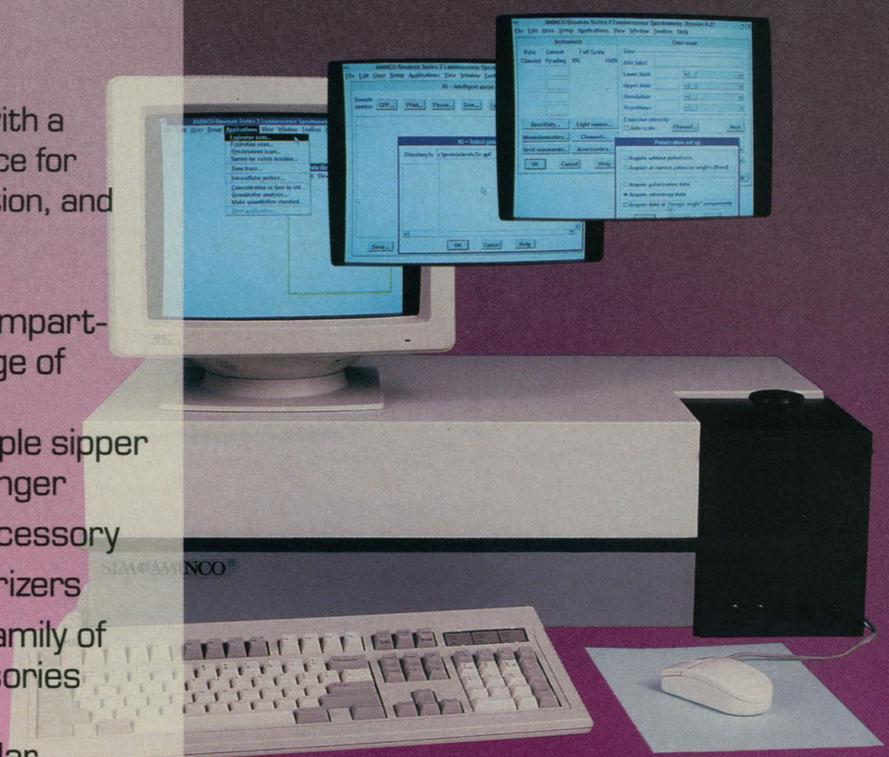

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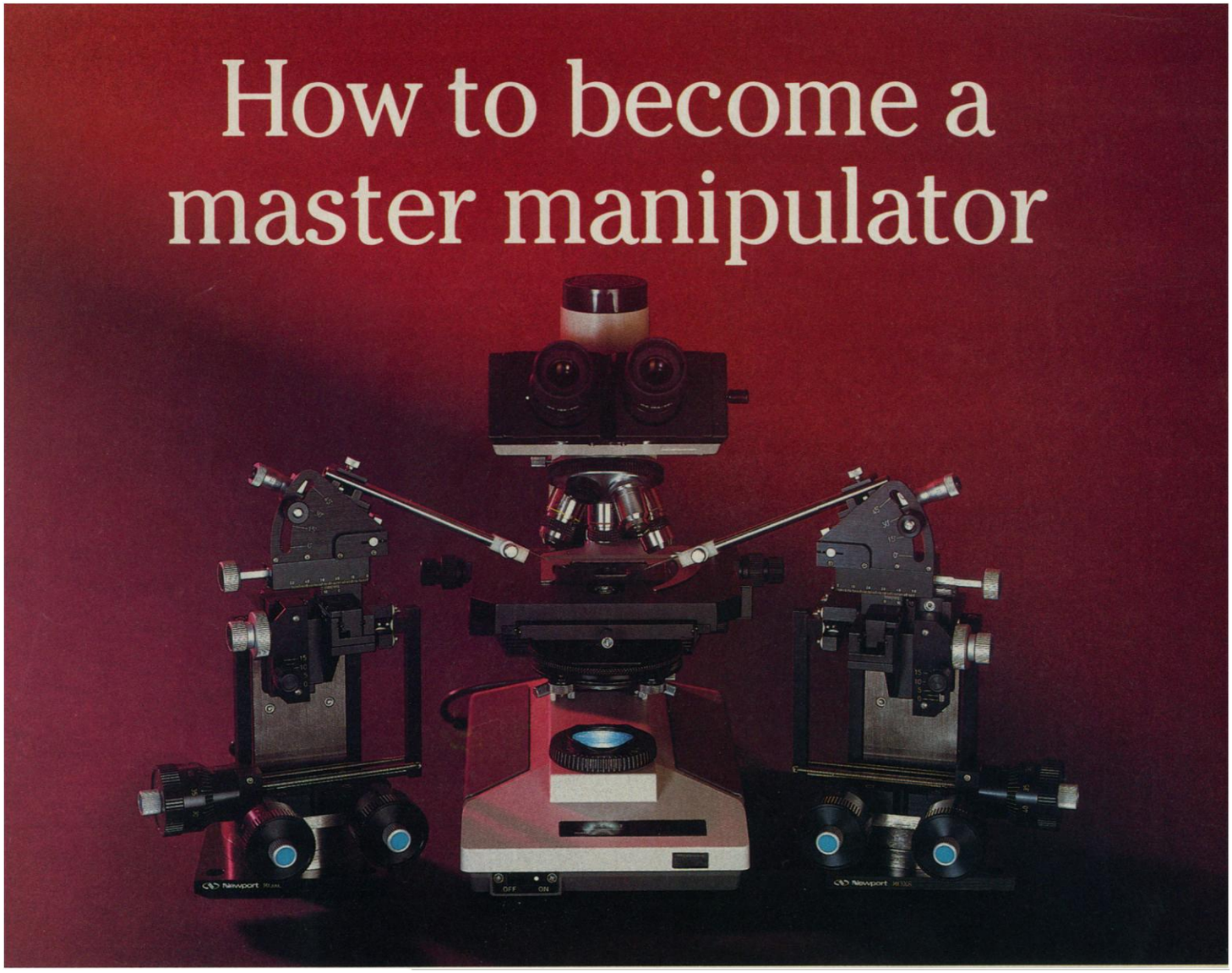

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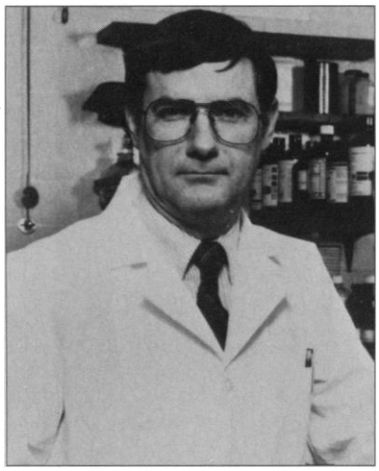
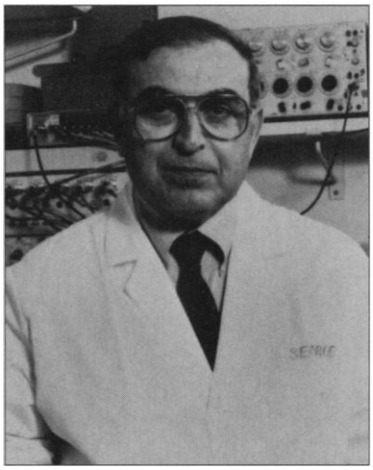
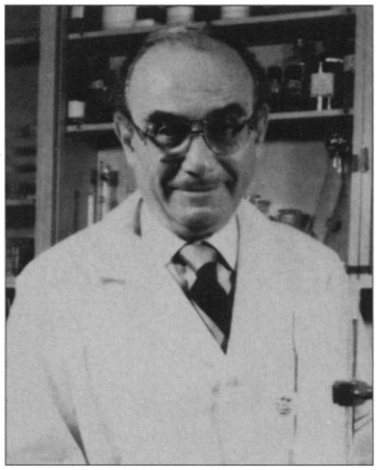
Three who mastered science for better medicine







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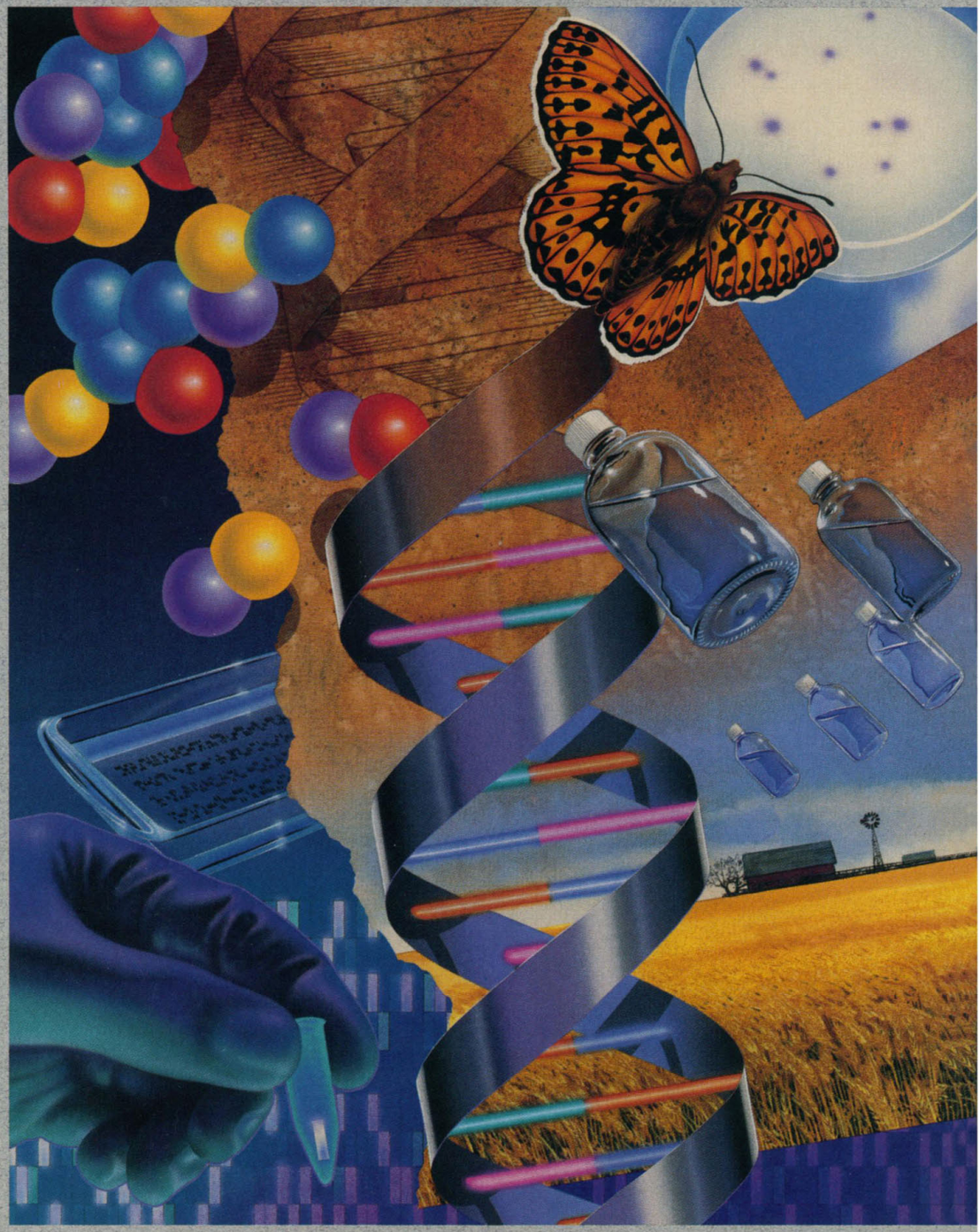

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