

503 This Week in *Science*

## Editorial

505 Sequencing the Human Genome

## Letters

507 Women in Science: E. F. KELLER ■ Adolescence and Mental Illness: I. FEINBERG  
■ Bibliographic Databases: T. ROBINSON

## News & Comment

509 Doubt Cast on Laser Weapons  
510 Frederickson Takes Leave from Hughes  
511 California Field Test Goes Forward  
512 U.K. Science: Survival of the Fittest—or Fattest?  
514 Security Council Blocks NSF Grant to IASA  
515 Plutonium by the Ton  
516 *Briefing*: NAS Hopes to Save *Issues* ■ MIT Gets \$3 Million for News Fellowships

## Research News

517 Clinical Promise with New Hormones  
519 On the Benefits of Being Eaten  
521 Statistical Traps Lurk in the Fossil Record  
522 Supernova 1987A: Notes from All Over: A New Limit on the Mass of the Neutrino? ■ Some Neutrino Facts ■ Sanduleak -69 202: Guilty as Charged

## Articles

537 Decision-Making in the Presence of Risk: M. J. MACHINA  
543 Accelerator Mass Spectrometry for Measurement of Long-Lived Radioisotopes:  
D. ELMORE AND F. M. PHILLIPS  
551 The Basis for the Immunoregulatory Role of Macrophages and Other Accessory  
Cells: E. R. UNANUE AND P. M. ALLEN

## Research Articles

558 Assembly of Clathrin-Coated Pits onto Purified Plasma Membranes: M. S. MOORE,  
D. T. MAHAFFEY, F. M. BRODSKY, R. G. W. ANDERSON

## Reports

564 Free Energy Calculations by Computer Simulation: P. A. BASH, U. C. SINGH,  
R. LANGRIDGE, P. A. KOLLMAN  
568 On the Prevalence of Room-Temperature Protein Phosphorescence:  
J. M. VANDERKOOI, D. B. CALHOUN, S. W. ENGLANDER  
570 Mitogens and Oncogenes Can Block the Induction of Specific Voltage-Gated Ion  
Channels: J. M. CAFFREY, A. M. BROWN, M. D. SCHNEIDER  
573 Clustering of Genes Dispensable for Growth in Culture in the S Component of the  
HSV-1 Genome: R. LONGNECKER AND B. ROIZMAN

- **SCIENCE** is published weekly on Friday, except the last week in December, and with an extra issue in February by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005. Second-class postage (publication No. 484460) paid at Washington, DC, and at an additional entry. Now combined with *The Scientific Monthly* © Copyright © 1987 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): \$65. Domestic institutional subscription (51 issues): \$98. Foreign postage extra: Canada \$32, other (surface mail) \$27, air-surface via Amsterdam \$65. First class, airmail, school-year, and student rates on request. Single copies \$2.50 (\$3 by mail); back issues \$4 (\$4.50 by mail); Biotechnology issue, \$5.50 (\$6 by mail); classroom rates on request; Guide to Biotechnology Products and Instruments \$16 (\$17 by mail). **Change of address:** allow 6 weeks, giving old and new addresses and seven-digit account number. Authorization to photocopy material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of \$1 per copy plus \$0.10 per page is paid directly to CCC, 21 Congress Street, Salem, Massachusetts 01970. The identification code for *Science* is 0036-8075/83 \$1 + .10. **Postmaster:** Send Form 3579 to *Science*, 1333 H Street, NW, Washington, DC 20005. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.
- The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objects are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.



**COVER** Distribution of human cone photoreceptors revealed by computer reconstruction of a whole mounted retina. Black oval represents optic disk in nasal retina. Warm colors indicate high cone density, and cool colors low cone density. Foveal density (white) is so high it is off scale. Isodensity contours are elongated horizontally and shifted nasally in peripheral retina. See page 579. [Computer graphics and photography by Kenneth R. Sloan, Jr., University of Washington, Seattle, WA 98195]

- 576 Rapid Identification of Nonessential Genes of Herpes Simplex Virus Type 1 by Tn5 Mutagenesis: P. C. WEBER, M. LEVINE, J. C. GLORIOSO
- 579 Distribution of Cones in Human and Monkey Retina: Individual Variability and Radial Asymmetry: C. A. CURCIO, K. R. SLOAN, JR., O. PACKER, A. E. HENDRICKSON, R. E. KALINA
- 582  $\beta$ 1-6 Branching of Asn-Linked Oligosaccharides Is Directly Associated with Metastasis: J. W. DENNIS, S. LAFERTÉ, C. WAGHORNE, M. L. BREITMAN, R. S. KERBEL
- 586 Insulin Rapidly Increases Diacylglycerol by Activating De Novo Phosphatidic Acid Synthesis: R. V. FARESE, T. S. KONDA, J. S. DAVIS, M. L. STANDAERT, R. J. POLLET, D. R. COOPER
- 589 Zinc Selectively Blocks the Action of *N*-Methyl-D-Aspartate on Cortical Neurons: S. PETERS, J. KOH, D. W. CHOI
- 593 A Chicken Transferrin Gene in Transgenic Mice Escapes X-Chromosome Inactivation: M. A. GOLDMAN, K. R. STOKES, R. L. IDZERDA, G. S. MCKNIGHT, R. E. HAMMER, R. L. BRINSTER, S. M. GARTLER
- 595 Asymmetries in Mating Preferences Between Species: Female Swordtails Prefer Heterospecific Males: M. J. RYAN AND W. E. WAGNER, JR.
- 597 Cloning of Complementary DNA for GAP-43, a Neuronal Growth-Related Protein: L. R. KARNS, S.-C. NG, J. A. FREEMAN, M. C. FISHMAN
- 600 Primary Structure and Biochemical Properties of an  $M_2$  Muscarinic Receptor: E. G. PERALTA, J. W. WINSLOW, G. L. PETERSON, D. H. SMITH, A. ASHKENAZI, J. RAMACHANDRAN, M. I. SCHIMERLIK, D. J. CAPON

## AAAS News

- 610 Project on Liberal Education and the Sciences Receives Funding: B. G. WALTHALL  
 ■ Reminder for Members ■ Pacific Division Meets in San Diego, 14–18 June ■ SB&F Focuses on Science in the Middle Grades ■ Section Y Adopts Statement of Membership and Purpose ■ Obituaries

## Book Reviews

- 617 Gene Banks and the World's Food, *reviewed by* W. L. BROWN ■ Insect Flight, D. ROFF ■ The Galaxy and the Solar System, M. E. BAILEY ■ North Atlantic Palaeoceanography, W. A. BERGGREN ■ Books Received

## Products & Materials

- 621 Centrifuge for Cell Culture ■ Cold Stage for SEM ■ Low-Grain, High-Speed Film ■ Molecule-Drawing Software ■ Remote Sensing for PCs ■ Disposable Microplate Sections ■ Titrator ■ Literature

### Board of Directors

Lawrence Bogorad  
Retiring President,  
Chairman

Sheila E. Widnall  
President

Walter E. Massey  
President-elect

Robert McC. Adams  
Floyd E. Bloom  
Mary E. Clutter  
Mildred S. Dresselhaus  
Beatrix A. Hamburg  
Donald N. Langenberg  
Frank von Hippel  
Linda S. Wilson

William T. Golden  
Treasurer  
Alvin W. Trivelpiece  
Executive Officer

### Editorial Board

Elizabeth E. Bailey  
David Baltimore  
William F. Brinkman  
Philip E. Converse  
Joseph L. Goldstein  
James D. Idol, Jr.  
Leon Knopoff  
Seymour Lipset  
Oliver E. Nelson  
David V. Ragone  
David M. Raup  
Vera C. Rubin  
Larry L. Smarr  
Solomon H. Snyder  
Robert M. Solow  
James D. Watson

### Board of Reviewing Editors

John Abelson  
Qais Al-Awqati  
James P. Allison  
Don L. Anderson  
Elizabeth H. Blackburn  
Floyd E. Bloom  
Charles R. Cantor  
James H. Clark  
Bruce F. Eldridge  
Stanley Falkow  
Theodore H. Geballe  
Roger I. M. Glass  
Stephen P. Goff  
Robert B. Goldberg

Corey S. Goodman  
Stephen J. Gould  
Richard M. Held  
Gloria Heppner  
Eric F. Johnson  
Konrad B. Krauskopf  
I. Robert Lehman  
Karl L. Magleby  
Joseph B. Martin  
John C. McGiff  
Alton Meister  
Mortimer Mishkin  
Peter Olson  
Gordon H. Orians  
John S. Pearce

Yeshayau Pocker  
Jean Paul Revel  
James E. Rothman  
Thomas C. Schelling  
Ronald H. Schwartz  
Stephen M. Schwartz  
Otto T. Solbrig  
Robert T. N. Tjian  
Virginia Trimble  
Geerat J. Vermeij  
Martin G. Weigert  
Harold Weintraub  
Irving L. Weissman  
George M. Whitesides  
Owen N. Witte  
William B. Wood

**American Association for the Advancement of Science**  
*Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

**Publisher:** Alvin W. Trivelpiece

**Editor:** Daniel E. Koshland, Jr.

**Deputy Editors:** Philip H. Abelson (*Engineering and Applied Sciences*); John I. Brauman (*Physical Sciences*)

#### EDITORIAL STAFF

**Managing Editor:** Patricia A. Morgan

**Assistant Managing Editors:** Nancy J. Hartnagel, John E. Ringle

**Senior Editors:** Eleanore Butz, Ruth Kulstad

**Associate Editors:** Martha Collins, Barbara Jasny, Katrina L. Kelnar, Edith Meyers, Phillip D. Szuroni, David F. Voss

**Letters Editor:** Christine Gilbert

**Book Reviews:** Katherine Livingston, *editor*; Deborah F. Washburn

**This Week in Science:** Ruth Levy Guyer

**Chief Production Editor:** Ellen E. Murphy

**Editing Department:** Lois Schmitt, *head*; Mary McDaniel, Barbara E. Patterson

**Copy Desk:** Lyle L. Green, Sharon Ryan, Beverly Shields, Anna Victoreen

**Production Manager:** Karen Schools

**Assistant Production Manager:** James Landry

**Graphics and Production:** Holly Bishop, Kathleen Cosimano, Eleanor Warner

**Covers Editor:** Grayce Finger

**Manuscript Systems Analyst:** William Carter

#### NEWS STAFF

**News Editor:** Barbara J. Culliton

**News and Comment:** Colin Norman, *deputy editor*; Mark H. Crawford, Constance Holden, Eliot Marshall, Marjorie Sun, John Walsh

**Research News:** Roger Lewin, *deputy editor*; Deborah M. Barnes, Richard A. Kerr, Gina Kolata, Jean L. Marx, Arthur L. Robinson, M. Mitchell Waldrop

**European Correspondent:** David Dickson

#### BUSINESS STAFF

**Associate Publisher:** William M. Miller, III

**Business Staff Manager:** Deborah Rivera-Wienhold

**Membership Recruitment:** Gwendolyn Huddle

**Member and Subscription Records:** Ann Ragland

**Guide to Biotechnology Products and Instruments:**

Shauna S. Roberts

#### ADVERTISING REPRESENTATIVES

**Director:** Earl J. Scherago

**Production Manager:** Donna Rivera

**Advertising Sales Manager:** Richard L. Charles

**Marketing Manager:** Herbert L. Burklund

**Sales:** New York, NY 10036: J. Kevin Henebry, 1515 Broadway (212-730-1050); Scotch Plains, NJ 07076: C. Richard Callis, 12 Unami Lane (201-889-4873); Chicago, IL 60611: Jack Ryan, Room 2107, 919 N. Michigan Ave. (312-337-4973); San Jose, CA 95112: Bob Brindley, 310 S. 16 St. (408-998-4690); Dorset, VT 05251: Fred W. Dieffenbach, Kent Hill Rd. (802-867-5581); Damascus, MD 20872: Rick Sommer, 24808 Shrubbery Hill Ct. (301-972-9270); U.K., Europe: Nick Jones, +44(0647)52918; Telex 42513; FAX (0392) 31645.

**Information for contributors** appears on page xi of the 27 March 1987 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005. Telephone: 202-326-6500.

Advertising correspondence should be sent to Tenth Floor, 1515 Broadway, NY 10036. Telephone 212-730-1050 or WU Telex 968082 SCHERAGO.

## Sequencing the Human Genome

A molecular biologist might say, "The proper study of mankind is the bacterium." The developmental biologist would say, "The proper study of mankind is the fruit fly." The cancer expert says, "The proper study of mankind is the rat." The poet said, "The proper study of mankind is man." All are, of course, partly right and partly wrong. The universality of the genetic code and of metabolic systems means that very different forms of life reveal principles and facts that are relevant to human health and illness. Although each species is interesting in itself, the major reason that research in other species is so strongly supported by Congress is its applicability to human beings. Therefore, the obvious answer as to whether the human genome should be sequenced is, "Yes. Why do you ask?"

The more pertinent question about sequencing is how fast and how much. Major portions of the human genome will be uncovered in bits and pieces with laboratories operating in conventional ways. Yet this sequencing is being done inefficiently because each laboratory must learn the methods, develop its own cloning libraries, and operate with techniques and equipment that could be vastly improved. A massive assault—developing new techniques, creating systematic libraries, coordinating data—would inevitably produce the answer sooner. Large segments of repetitive and "junk" DNA, which may have little use according to current concepts, would be sequenced, but even so the gains in new techniques would more than compensate for the delays of uninteresting stretches.

The next question is who should do the job. The National Institutes of Health has funded most of the scientists who have made the project possible, but it would be in danger of a Big Science–Little Science conflict. The Department of Energy has only a few scientists in the proper leadership area, but has had experience with large projects and offers a political arrangement that could ensure that the program is an add-on, not a subtraction from Little Science.

For this project to command the respect and support of the biological community, acknowledged experts are needed on the governing board of the project. (A National Academy of Sciences committee now studying the whole problem is a blue-ribbon list for selection of such a board.) The program and individual grant requests should be peer reviewed continuously, following the excellent procedures of NIH and the National Science Foundation. Leaders from NIH, NSF, the Howard Hughes Medical Institute, and foreign scientists should play prominent roles in the organization. A DOE program should be expected to use national laboratory personnel for some of the work but to act more as a nerve center, both monitoring and administering a large number of smaller grants to investigators located all over the world. This effort should be international with contributions from different countries in terms of grants, investigators, and leadership advice. A plan in which DOE recognizes the importance of peer review and decentralized administration would thus be a compromise, but it would ensure proper quality and avoid a budget situation that placed Big Science and Little Science in dangerously direct financial competition. An alternative would be to try to set up within NIH a special institute for sequencing. Political memories are short, however, and soon that allocation would be thought of as "NIH funds," creating the unwanted competition between "big" applied and "little" investigator-initiated research. It would appear that DOE could find the leadership excellence more easily than NIH could provide the budgetary insulation.

The implications of sequencing the human genome are staggering. The recent discoveries of genes identified with muscular dystrophy, manic depression, cystic fibrosis, and Alzheimer's disease are illustrative aspects of the potential. Human subjects have been a source of information, medically, psychologically, and evolutionarily for centuries. They offer a wealth of information in regard to basic biology that is not duplicated by any other species. Hereditary defects may be able to be diagnosed more efficiently and eventually eliminated. Moreover, developing the successful methodology for sequencing the human genome means that understanding other species will also be accelerated. The opportunities are enormous. We have been "walking along the chromosomes" long enough. It is time to start running.—DANIEL E. KOSHLAND, JR.