

1231 This Week in *Science*

Editorial

1233 The Engineering of Species

Letters

1245 The Dingell Investigation: M. O'TOOLE; DON S. DOERING ■ Responsibility: C. H. FOX

News & Comment

1248 Bringing NASA Down to Earth ■ Low-Tech Earth Observation ■ Early Data: Losing Our Memory?

1251 German Biotech Firms Flee Regulatory Climate

1253 EPA Drafts New Research Agenda
Cambridge to Oversee Animal Research

Research News

1254 New Hope on the AIDS Vaccine Front ■ Hecklers and Protesters Liven up a Dull Meeting

1256 Illuminating Jet Lag

1257 New Machine Sparks Rivalries at CERN ■ Acronyms in Search of Particles

1260 Another Piece of 3.14159 . . . ?

Articles

The New Harvest: Genetically Engineered Species

1275 Progress Toward Human Gene Therapy: T. FRIEDMANN

1281 Genetic Engineering of Livestock: V. G. PURSEL, C. A. PINKERT, K. F. MILLER, D. J. BOLT, R. G. CAMPBELL, R. D. PALMITER, R. L. BRINSTER, R. E. HAMMER

1288 Altering the Genome by Homologous Recombination: M. R. CAPECCHI

1293 Genetically Engineering Plants for Crop Improvement: C. S. GASSER AND R. T. FRALEY

1300 Genetic Engineering of Bacteria from Managed and Natural Habitats: S. E. LINDOW, N. J. PANOPOULOS, B. L. MCFARLAND

1307 Construction of Large DNA Segments in *Escherichia coli*: M. O'CONNOR, M. PEIFER, W. BENDER

1313 Genetic Engineering of Filamentous Fungi: W. E. TIMBERLAKE AND M. A. MARSHALL

Reports

1326 Availability of Metabolic Fuels Controls Estrous Cyclicity of Syrian Hamsters: J. E. SCHNEIDER AND G. N. WADE

■ 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 © 1989 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): \$75. Domestic institutional subscription (51 issues): \$120. Foreign postage extra: Canada \$46, other (surface mail) \$46, air mail via Amsterdam \$85. First class, airmail, school-year, and student rates on request. Single copy sales: Current issue, \$3.50; back issues, \$5.00; Biotechnology issue, \$6.00 (for postage and handling, add per copy \$0.50 U.S., \$1.00 all foreign); Guide to Biotechnology Products and Instruments, \$18 (for postage and handling add per copy \$1.00 U.S., \$1.50 Canada, \$2.00 other foreign). Bulk rates on request. Change of address: allow 6 weeks, giving old and new addresses and 11-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, P.O. Box 1722, Riverton, NJ 08077. Science is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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COVER Advances in genetic engineering are bringing new variations of naturally occurring species to the research laboratory and into the field for testing and marketing. This issue of *Science* focuses on the applications of this technology that are already available and the prospects for the future. See page 1275. [Illustration by Donna Williams]

- 1328 Bright Light Induction of Strong (Type 0) Resetting of the Human Circadian Pacemaker: C. A. CZEISLER, R. E. KRONAUER, J. S. ALLAN, J. F. DUFFY, M. E. JEWETT, E. N. BROWN, J. M. RONDA
- 1333 Water-Inserted α -Helical Segments Implicate Reverse Turns as Folding Intermediates: M. SUNDARALINGAM AND Y. C. SEK HARUDU
- 1337 Global Positioning System Measurements for Crustal Deformation: Precision and Accuracy: W. H. PRESCOTT, J. L. DAVIS, J. L. SVARC
- 1340 Novel Sites of Expression of Functional Angiotensin II Receptors in the Late Gestation Fetus: M. A. MILLAN, P. CARVALLO, S.-I. IZUMI, S. ZEMEL, K. J. CATT, G. AGUILERA
- 1342 Recombinant Gene Expression in Vivo Within Endothelial Cells of the Arterial Wall: E. G. NABEL, G. PLAUTZ, F. M. BOYCE, J. C. STANLEY, G. J. NABEL
- 1344 Implantation of Vascular Grafts Lined with Genetically Modified Endothelial Cells: J. M. WILSON, L. K. BIRINYI, R. N. SALOMON, P. LIBBY, A. D. CALLOW, R. C. MULLIGAN
- 1346 Control of Gene Expression by Artificial Introns in *Saccharomyces cerevisiae*: T. YOSHIMATSU AND F. NAGAWA
- 1348 Isolation of Single-Copy Human Genes from a Library of Yeast Artificial Chromosome Clones: B. H. BROWNSTEIN, G. A. SILVERMAN, R. D. LITTLE, D. T. BURKE, S. J. KORSMEYER, D. SCHLESSINGER, M. V. OLSON
- 1351 Cl^- Channels in CF: Lack of Activation by Protein Kinase C and cAMP-Dependent Protein Kinase: T.-C. HWANG, L. LU, P. L. ZEITLIN, D. C. GRUENERT, R. HUGANIR, W. B. GUGGINO
- 1353 Regulation of Chloride Channels by Protein Kinase C in Normal and Cystic Fibrosis Airway Epithelia: M. LI, J. D. MCCANN, M. P. ANDERSON, J. P. CLANCY, C. M. LIEDTKE, A. C. NAIRN, P. GREENGARD, M. J. WELSH
- 1357 The Fc and Not CD4 Receptor Mediates Antibody Enhancement of HIV Infection in Human Cells: J. HOMSY, M. MEYER, M. TATENO, S. CLARKSON, J. A. LEVY
- 1360 Pathological Changes Induced in Cerebrocortical Neurons by Phencyclidine and Related Drugs: J. W. OLNEY, J. LABRUYERE, M. T. PRICE

Book Reviews

- 1385 In Sickness and in Wealth, reviewed by D. MECHANIC ■ Mechanical Man, J. REED ■ Books Received

Products & Materials

- 1388 Solar-Powered pH Meter ■ Software for Mathematical Surfaces, Vector Fields ■ Densitometry Software ■ Computer Interruption-Protection Hardware ■ IgG Purification Kit ■ Desktop RISC Workstation ■ Literature

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The Engineering of Species

Somewhere in the vast pantheon of science a molecular biologist is saying, "I'd like to engineer a wolf into a dog." Somewhere else, the sepulchral voice of a geneticist will reply, "It's been done." For in fact, over evolutionary time, the friendliest of wolves (and possibly the most intelligent) learned that wagging their tails and delivering slippers was an easier way to earn a living than hunting caribou in the wilds. In modern times, scientists have accelerated evolution for the benefit of humans by deliberate selection techniques to improve livestock, crops, and other life forms. The difference between these techniques and the use of recombinant DNA is that direct gene alteration removes some chanciness and accelerates the pace at which new variants can be produced. This issue of *Science*, assembled with the insight and editing skills of Barbara Jasny, shows how various species are being genetically engineered.

The most controversial genetic engineering involves humans and Friedmann covers the latest exciting advances in the development of gene therapies. Gene transfer techniques that produce somatic mutations, such as by the introduction of viral vectors into bone marrow, have great potential for curing patients without affecting succeeding generations. Homologous recombination, as described in the article by Capecchi, allows the surgical removal of a single deficient gene and its replacement by a normal gene, the crucial step needed for efficient alteration of a germ line. It can reverse history in ending the progress of a deficient gene into new generations.

Even the best intentioned genetic engineering can have bad effects as illustrated in the article by Pursel *et al.*, in which the genetic engineering of livestock has been carried on for several generations. Two successive generations of pigs engineered to produce elevated levels of bovine growth hormone showed significant improvements in weight gain and feed efficiency and marked reduction in fat. However, these beneficial effects were offset by a high incidence of gastric ulcers, arthritis, cardiomegaly, dermatitis, and renal disease.

Plant research, as discussed by Gasser and Fraley, is one of the triumphs of modern genetic engineering; plants are being produced that are resistant to infectious agents or weed-control agents and can produce more and better food. As pesticides come under continual attack, the development of plants that naturally resist predators will become increasingly useful. An ironic feature is that some plant defenses involve synthesis of natural carcinogens. It is thus conceivable to get a plant that can be grown without pesticides but is deadly poisonous.

One alternative to pesticides is the use of biocontrol, a subject that is illustrated in the article by Lindow, Panopoulos, and McFarland. The famous "Ice" bacterium is a classic case in which genetic engineering of a bacterial species results in an organism that protects plants against damage from freezing. The importance of microorganisms is further illustrated by the genetic engineering of *Rhizobium* to improve nitrogen fixation, a development that could increase plant yields and diminish the need for agricultural chemicals. Additionally, engineered bacteria are being used to improve the cleanup of hazardous waste sites. Techniques described by O'Connor, Peifer, and Bender can accelerate the ease and efficiency of genetic engineering, not only on bacteria, but possibly on other organisms as well. Finally, Timberlake and Marshall discuss genetic engineering of fungi, which have great relevance, not only because they are serious pathogens in many diseases, but also because they have potential applications for the industrial production of antibiotics and other important chemicals.

This issue reminds us that we must proceed cautiously in introducing new genes or new combinations of genes into species, and long-term experiments are needed to study detrimental effects. We are nowhere near the knowledge needed to genetically engineer the complex behavior of a wolf or a dog. An original wolf might say to the dog, "You have lost your freedom. Your obsequiousness is humiliating to the family Canidae." The dog could reply, "I am much less warlike, far more altruistic, and besides, it's a wonderful standard of living." Whether society prefers to have wolves or dogs remains to be seen.

—DANIEL E. KOSHLAND, JR.