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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]

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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.