Technical note 3

Violating species barriers

The majority of gene-therapy cases in humans would involve transplanting human DNA from one individual to another. In the forseeable future, research on and application of these techniques (or capabilities) is unlikely to use genes from an animal species to treat human genetic diseases. It is more likely that techniques involving the transplantation of genetic material from one animal species to another would be useful in agricultural or industrial applications; work of this kind has already been performed (involving human genes being moved into certain agricultural animals). The most far- reaching experiments of this sort are designed to increase understanding of mechanisms of genetic control and gene regulation. * This research will enhance scientists' ability to work with the genes of individuals within a species, and thus decrease the need to transfer genetic material between species in future therapeutic endeavors. The question has arisen, though, as to whether such work should be completely avoided or terminated because of an inherent danger or impropriety in "violating species boundaries." A look at nature offers a useful perspective.

A species is a community of organisms that is reproductively isolated from other such groups; that is, within a species there is interbreeding (exchange of genetic material) among individuals and their offspring, but none with individuals of other, different species. The problems with this widely used definition are several, and many of them are quite technical and esoteric. The most significant of these involve the existence and frequency of hybrids, or "crossbreeds" between species.

If species are to be defined on the basis of reproductive isolation, a sort of "genetic quarantine)" then violations of this quarantine, hybrids, should be rare and **unusual. This is emphatically not the case in nature. Hybrids are well known in higher organisms, where admittedly many are sterile (e.g., mules, resulting from a mating between a horse and a donkey). However in some groups hybrids between species are so common that distinct populations of these intermediate forms may exist along the distribution boundaries of neighboring species (Endler, 1977; Mayr, 1963, 1970). In these hybrid populations it is very difficult to assign an individual to either of the parent populations, which might themselves be quite easily distinguished from one another. Hybrids are more common in less advanced vertebrates, such as amphibians or fish, and there are even cases known where new species have been formed by hybridization between two previously existing species (White, 1978). In other situations species "boundaries" are so permeable that relatively widespread movement of genetic material from one species to another exists, a phenomenon called introgression. In plants, hybridization is so common that one leading expert (Raven, 1980) has concluded that it is almost useless to talk of "species" and that the most important reproductive group is the local population, or deme. To complicate matters further, some recent research offers tantalizing hints that horizontal transmission (between individuals of the same generation) very similar to the sort contemplated in some types of gene therapy have probably taken place between distantly related species (felids, or cat-like creatures, and primates) in the past (Benveniste and Todaro, 1982; Lewin, 1984). Specialists today are therefore becoming increasingly interested in factors that keep a species together rather than in mechanisms that may serve to keep them apart (Paterson, 1981, 1982).**

This is a useful approach in considering animal experiments relevant to human gene therapy. The question changes from "When can we justify violating species barriers?" to '(How much transmission of genetic material from one species to another can be tolerated before the integrity or separateness of the recipient species is threatened?" The answer is clear—an enormous amount; far more than would ever be involved in any case of gene therapy.

*The study of oncogenes (genes whose expression is linked to cancer) has involved hundreds of transfers of genes between species. From them we have learned enormous amounts about the mechanisms of carcinogenesis and gene regulation.