



Parliamentary Research Branch  
Library of Parliament

# IN BRIEF

Sonya Norris 17 November 2000

## Gene Therapy, Genetic Alteration and Cloning

### Introduction

This paper provides a brief overview of gene therapy, genetic alteration and cloning. To the best of our knowledge, of the three practices, only gene therapy has been attempted on humans. However, genetic alteration and cloning have been extensively researched in animals. A fundamental difference between these practices is that although both gene therapy and genetic alteration in humans are primarily for therapeutic purposes, human cloning is not.

### Gene Therapy And Genetic Alteration

Biotechnology in the agricultural and pharmaceutical industries has made use of the procedures for isolating single, identifiable genes and inserting those genes into foreign chromosomes. Applying these and similar procedures in animals and humans is referred to as genetic alteration, which has two approaches:

- *somatic cell gene therapy*: somatic cells are all cells within the body with the sole exception of the germ, or sex, cells. Somatic cell gene therapy is the portion of genetic alteration concerned with treating severe genetic disorders and affects only the individual being treated. The first clinical trials involving human gene therapy began in 1990. Although it has moved rapidly since that time, it is still considered experimental.
- *germ-line genetic alteration*: includes those manipulations that affect not only the individual receiving treatment, but also their subsequent generations. This manner of genetic alteration could theoretically be performed for therapeutic or enhancement purposes.

### 1. Somatic Cell Gene Therapy

This area of study involves the manipulation of any cells in the body with the sole exception of the reproductive cells. This sort of gene therapy is not passed on to the subsequent generation, and therefore would not contribute to the eradication of the disease.

In this type of therapy, it may be sufficient to “insert” a healthy gene somewhere in the chromosomes of an affected individual, which is not yet possible, or to introduce it within a vector for gene expression. Recessive diseases<sup>(1)</sup> may be treated this way. Altering viruses to contain the genes required for therapy produces vectors. The vector is then introduced into those cells of the affected individual where the disease manifests itself. An example of this approach would be for cystic fibrosis. The expression of the healthy gene in the respiratory tract would relieve the symptoms of the disease.

For dominant diseases,<sup>(2)</sup> it may be necessary to excise the gene from the chromosome and replace it with a healthy one. At this point in our biotechnological evolution, only gene insertion via vectors is feasible in humans.

Although somatic cell gene therapy is still at an early experimental stage, it is not expected to be an effective means of therapy. Technical problems include the method of insertion, accessibility of the tissue, and regulation of the gene product (i.e., how much should be produced, how its expression can be turned off, etc.).

### 2. Germ-line Genetic Alteration

The second approach to gene alteration, referred to as germ-line genetic alteration, is technically more difficult. In fact, some believe it is impossible. This approach involves the direct manipulation of the reproductive cells or, more likely, of the zygote or embryo. The affected cells or structures are

(1) Recessive diseases result from an aberrant gene being present on both chromosomes. Carriers of recessive disorders have one aberrant gene and one healthy gene.

(2) Dominant diseases result when only one aberrant gene is present, despite its healthy counterpart being present on the other chromosome.

manipulated *in vitro* (outside of the body) to remove the unwanted gene and to introduce the desired gene into the DNA. The altered zygote or embryo, which is now considered healthy (or not diseased), is transferred to the woman's uterus. The developing embryo would contain the altered genetic make-up in all of its cells, including its own reproductive cells. In this way, the alteration will be passed on to subsequent generations.

Germ-line alteration is considerably more complicated than somatic cell gene therapy. As previously mentioned, somatic cell gene therapy can be accomplished theoretically through either gene insertion or gene replacement. Germ-line genetic alteration could be performed only using gene replacement, which as noted previously is not feasible in human beings at present. Without removing the affected gene, the disease would still be passed on to subsequent generations.

Germ-line genetic alteration has been performed in animals. However, the goal of this technological advance has not been the production of similar results in humans. Animal germ-line alteration has been done either to produce "transgenic" breeds that provide an animal model of a human disease, or to produce animals that make commercially valuable proteins. These are not purposes that apply to humans. Moreover, the failure rate of insertion and transmission is high.

At present, genetic alteration in human beings that affects the germ line is a wholly untested procedure. There is an easy alternative to the risky practice of germ-line alteration that would produce the same desired effect, i.e., reducing the expression of a given genetic disorder in the general public. It is understood that genetic alteration of germ cells, zygotes and embryos would occur only, were it possible, once a genetic abnormality was identified. It would be considerably less risky to eliminate those cells, zygotes or embryos that are affected while allowing those that are genetically healthy to develop.

The argument has been made that all germ-line genetic alteration must be prohibited in order to prevent what is referred to as genetic enhancement. This would be a non-therapeutic use of genetic alteration. Genetic enhancement is enhancing or improving an already genetically healthy organism.

## **Cloning**

Cloning refers to the production of an organism with the exact same genetic makeup of another, living or dead. This happens in nature all the time. The most

commonly offered example is that of identical twins. Identical twins are the result of an embryo splitting into two shortly after fertilization, a fairly rare event. Theoretically any number of clones can be produced this way. The other natural example of cloning is asexual reproduction. Many organisms reproduce simply by splitting in two, such as the single-celled organisms. Others, such as plants, can fertilize themselves.

Artificial cloning is a product of biotechnology. In 1997, a sheep was cloned; in 1999, it was announced that cattle had been cloned. This cloning produced females only by necessity, as it had been believed that only cells from female reproductive tissue could be used. It has been shown, however, that males can also be cloned. Male mice have been successfully cloned using cells from their tails.

The current cloning process involves removing the nucleus from an egg cell and replacing it with the nucleus from a cell of an animal to be cloned. The egg is then forced to behave as though it were fertilized and proceed to develop as an embryo. This process is called somatic cell nuclear transfer. In the strictest sense, this does not produce an identical clone. Some genetic information is contained outside of the nucleus in organelles known as mitochondria. In somatic cell nuclear transfer, the egg cell that has been enucleated still contains its own mitochondria.

Cloning techniques have a very low success rate. Only 1-2% of embryos survive to become live offspring. In addition, a large proportion of these do not survive to adulthood. Despite the odds, scientists are optimistic about the potential for cloning in terms of medical research and the pharmaceutical industry. Animals can be created with specific genetic mutations mimicking human diseases to further medical research. Animals containing the desired mutation can then be cloned to avoid re-engineering the alteration. The ethical questions raised by such an approach are apparent. The pharmaceutical industry sees a similar use for these genetic techniques. Animals, such as goats and cattle, can be genetically altered and then cloned; these would contain genes coding for a desired protein. The protein can be made to be expressed in the animals' milk and then simply extracted.

No such arguments can be made for human cloning. Apart from ego, the only argument offered for the cloning of humans is for a supply of spare organs.