

## Problems of "Therapeutic Cloning"

Until now, talk of a possible source of human replacement tissue has centered on embryonic stem cells, the production of which has been extremely controversial. They are a typical product of "consuming embryonic research," so called, because in obtaining them from a human embryo produced by artificial fertilization in vitro, the embryo is destroyed.

The most important research technique for which such embryos are obtained is "therapeutic cloning." In principle, a human egg cell is denucleated, that is, the DNA is removed, and in its place is put the nucleus of a somatic (body) cell. The egg cell is stimulated with a short electrical pulse, and it then develops into the blastocyst, from which stem cells can be removed. These are identical with those of the donor of the somatic cell nucleus.

Normally it goes unmentioned, that it is only a small step from this so-called "therapeutic cloning" (because, it is claimed, in this way a therapy for diseases can be developed) to what is called "reproductive cloning." The only difference is that the development of the embryo is not interrupted in the early blastocyst stage; instead the embryo is implanted in a uterus and a complete organism develops-an exact genetic copy of the donor. "Dolly," the first cloned sheep, was produced by this method, and here is the basis for the widespread fear that the same method that is used for "therapeutic cloning" can also be used for the selective breeding of humans.

In addition to the obvious moral consideration, there are still other serious disadvantages that make this path to the development of human "replacement parts" appear to be untenable.

The danger of tumors. So far there has been no solution to the problem of developing in the laboratory an unmistakable identifier for stem cells that can distinguish them unequivocally from cancer cells. For this reason, it is also not possible to produce sufficiently pure cell cultures from stem cells. So far, with embryonic mouse stem cells, a purity of only 80 percent has been achieved. That is in no way sufficient for cell transplantation as a human therapy. In a cell culture for therapeutic purposes, there must not be a single undifferentiated cell, since it can lead to unregulated growth, in this case to the formation of teratomas, a cancerous tumor derived from the germ layers. This problem would not be expected with adult stem cells, because of their greater differentiation.

Genetic instability. Only recently a further problem has emerged. Fundamental doubt of the suitability of embryonic stem cells for transplantation has come to the surface because of the genetic instability of cloned cells.

Cloned animals like Dolly give the outward appearance of full health, but the probability of their having numerous genetic defects is very high. Moreover, the entire cloning procedure is extremely ineffective. Most cloned animals die before birth, and of those born alive, not even half survive for three weeks. In the best case, there is a success rate of 3 to 4 percent.

One of the reasons for this high failure rate has now been discovered by the German scientist Rudolf Jaenisch at the Institute for Biomedical Research at the Massachusetts Institute of Technology, and his colleague, Ryuzo Yanagimachi. Their conception is that in cloning-that is, when the nucleus of a somatic cell is inserted into a denucleated egg cell-the reprogramming of the genes does not proceed properly, so that not all of the genes that are necessary to the early phase of embryonic development, are activated. Even when cloned animals survive at all, probably every clone would have subtle genetic abnormalities that would frequently become noticeable only later in life.

Jaenisch performed his experiments with mice that had been cloned using embryonic stem cells in place of the

somatic cells, which produces better results. But to his surprise, the reprogramming of the inserted genetic material by the embryonic cells proceeded in a very unregulated way. There were no two clones in which the same pattern of gene activation was found, and Jaenisch is convinced that the use of embryonic stem cells was clearly responsible.

What consequences follow from this for the therapeutic use of human embryonic stem cells-consequences that will in fact be multiplied through cloning-are not yet foreseeable.

From *The Case for Adult Stem Cell Research*  
Courtesy of Wolfgang Lillge, M.D.