

ALTERED NUCLEAR TRANSFER AS AN ALTERNATIVE WAY TO HUMAN EMBRYONIC STEM CELLS: BIOLOGICAL AND MORAL NOTES

• Roberto Colombo •

“The product of ANT is not a biological entity devoid of a complete human genome, but a developing organism with its full human genome, i.e., a human organism, a human being.”



1. So-called “Altered Nuclear Transfer” (ANT) is a cytological-embryological procedure aimed at producing human embryonic stem cells by transfer into an enucleated oocyte (ooplast) of a somatic cell nucleus (caryoplast) that has been genetically silenced for one or more genes that are essential for normal early embryonic development. In one version of the proposal currently on the table—a version that typifies the conceptual approach underlying the proposal as such—after nuclear transfer (NT), activation of the recipient oocyte would start cell division (segmentation) as in conventional NT cloning. However, segregation of the trophectoderm cell line from the inner cell mass at the beginning of blastocyst formation (three to four days) would be prevented by the lack of expression of the silenced genes. Therefore, a “true human blastocyst” would not be observed under the microscope.

Instead, only a cell mass—resembling teratomas or the so-called “embryoid bodies”—is expected to develop from the cell division process. From these pluripotent cells endowed with the nuclear genome of the nucleus donor, human embryonic stem cell lines could be obtained and cultured as from blastocysts.

2. According to the proponents of ANT, this laboratory procedure does not intentionally produce a human embryo for the sole purpose of destroying it at the blastocyst stage of development to obtain human embryonic stem cells. The argument for this statement is as follows. As with any human being at any stage of development, the presence of a human embryo requires the presence of a human organism. A human organism is a biological entity that is either a developed human being or is capable of developing into a mature human being. The very early stages of human development (following fertilization or NT) are considered to be those of a human organism, i.e., a human being, only if they will develop into a blastocyst, an implanted embryo, a fetus, and a newborn baby. ANT is devised to intentionally prevent an ooplast from becoming a blastocyst even after NT and activation, but not from the cell division and compaction processes that are the normal prelude to blastocyst formation. Following this meta-biological premise, the proponents of ANT declare that this procedure should be morally admissible since it neither intentionally produces a human embryo by NT nor destroys it at the blastocyst stage to harvest human embryonic stem cells.

3. Arguments opposing the claim that ANT is morally admissible can be summarized as follows.

(a) The concept of organism underlying the argument in favor of ANT is questionable. From a biological (systematic and integrative biology) and philosophical (philosophy of biology) point of view, a living organism—i.e., a living being—is characterized by its intrinsic morpho-functional unity (integration and coordination of the biological parts, such as cells, tissues, organs, etc.), not by its capacity to progress to an advanced stage of development or to a more mature status. A human embryo is a human organism not because it will become a fetus or a newborn baby, but as a result of the intrinsic unity (*indivisum in se*) of its cells, which act as a whole and not as the sum of its parts. Even before the cavitation and the blastocyst expansion processes, early cleaving embryos (pre-morula and morula stages) are not just a “heap of cells,” but an ordered, integrated, and coordinated number of blastomeres that grow

according to a precise developmental plan. Therefore, early cleaving embryos are living organisms.

(b) The argument that refers to the percentage of embryos whose development arrests before or at the blastocyst stage (either *in vivo* or during *in vitro* development) is not a new one to deny the status of a human being to pre-implantation human embryos. However, in the case of ANT it should be emphasized that the failure to develop to the blastocyst stage is not the result of an unwanted defect of the embryo itself (e.g., a genetic or a cytological defect), but the consequence of an intentional act of the biologist. Such an act is against the integrity and the life of the human embryo that will be generated by NT and, as such, is illicit.

(c) The product of ANT is not a biological entity devoid of a complete human genome, but a developing organism with its full human genome, i.e., a human organism, a human being. The procedure by which one or more genes are silenced (called “RNA interference”) is commonly used in laboratory experiments on cultured cells to switch off some genes temporarily in order to investigate the function of the encoded proteins. The targeted gene (DNA sequence) is neither removed nor altered, and its normal expression in the cell culture is restored after the end of silencing. The abnormal embryo development and the lack of formation of a “true human blastocyst” are not the consequences of a defective genome, but an intentionally induced temporary block of the biosynthesis of one or more of the genes that are required for the formation of the trophoctoderm (or for whatever other normal developmental event ANT would suppress).

(d) Gene silencing by RNA interference—as any other biotechnological procedure—must be set up and tested before a reliable protocol can be established. This means that a relevant number of experiments of human ANT will be required to obtain a complete gene silencing and blastocyst formation prevention. Even those who argue in favor of the non-organismic status of the product of ANT should remember that the attempt to avoid blastocyst formation will involve a number of failures, i.e., many human embryos will be destroyed while reaching the blastocyst stage. Such experiments should be considered ethically wrong.

(e) Last but not least, what is at stake—i.e., the life of a human being—is so important that, from the standpoint of moral obligation, the mere probability that a human embryo is involved

in the ANT procedure would suffice to justify an absolutely clear prohibition of such a possible biotechnique (see John Paul II, *Evangelium vitae*, 60). □

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