ALTERED NUCLEAR TRANSFER: A CRITIQUE OF A CRITIQUE

• **Nicanor Pier Giorgio Austriaco, O.P.** •

"With ANT, the enucleated egg—because of genetic manipulations done either to the egg or to the donor cell or to both simultaneously—is prevented from reprogramming the transferred genome to an embryo-like epigenetic state. . . . no embryo—no organism—is generated."

In his philosophical critique of Altered Nuclear Transfer (ANT) recently published in *Communio*, Adrian J. Walker concludes that ANT is technically and morally indistinguishable from human cloning.[1] In his words, ANT "so long as it deploys the same basic technical strategy for the same basic purpose, always turns out to be a form of human cloning with a twist."[2] Walker's argument is fundamentally flawed. In this critique of his critique, I will argue that Walker's erroneous conclusion stems from a misunderstanding of developmental biology that leads him to mistakenly believe that the physical coming-to-be of a reasonably complete human genome in an enucleated human egg is the essential event that constitutes a new human organism.

[1]Adrian J. Walker, "Altered Nuclear Transfer: A Philosophical Critique," *Communio* 31 (2005): 649-684. For a description of Altered Nuclear Transfer, see William Hurlbut, "Altered nuclear transfer as a morally acceptable means for the procurement of human embryonic stem cells," *National Catholic Bioethics Quarterly* 5 (2005): 145–151.

[2]Walker, "Altered Nuclear Transfer," 662.

Communio 32 (Spring 2005).

In brief, Walker's argument is as follows: He begins by assuming that the event that constitutes a new human genomic identity is also the event that constitutes a new human organism.[3] Thus, somatic cell nuclear transfer (SCNT), also known as cloning, if done with human cells and eggs, would generate a new human organism since it involves the transfer of a reasonably complete human genome into an enucleated human egg. However, as Walker correctly notes, the general strategy of ANT, in order to obtain pluripotent stem cells that are functional and human, must also necessarily involve the transfer of a reasonably complete—albeit genetically engineered—human genome into an enucleated human egg. Thus, in Walker's eyes, SCNT and ANT are technically indistinguishable—both involve transferring a reasonably complete genome into an enucleated egg. Moreover, given his definition of an organism-constituting event cited above, Walker concludes that ANT, like SCNT, if done with human cells, necessarily generates a human organism since it necessarily generates a cellular entity, derived from a human egg, that contains a reasonably complete human genome. He writes: "If ANT thus turns out to be a form of human cloning 'with a twist,' as one newspaper account put it, then the twist—the genetic engineering ANT would undertake—cannot be sufficient to revoke the organismic status of the new entity the procedure would produce. It can only superficially mask organismic identity, not suppress or eliminate it altogether."[4]

In response, I point out that with few exceptions all human cells—one-cell human embryos, human liver cells, and human skin cells, just to name a few of the approximately 260 human cell types—contain a reasonably complete human genome. Thus, the possession of a reasonably complete human genome is a necessary but not sufficient condition for defining a human embryo. Rather, the nature of each human cell depends on what biologists call its epigenetic state, i.e., which subset of the approximately thirty

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[3]Ibid., 664: "It goes without saying that the force of my critique of ANT depends on the truth of my assumption that the event that constitutes a new human genomic identity is also the event that constitutes a new human organism . . . . The constitution of the genome is the basic necessary condition for establishing organismic status whereas the other factors are only necessary conditions for maintaining it once established."

[4]Ibid., 657.

thousand human genes is switched on or off, and, if on, at what level.[5] To put it another way, the human liver cell is a liver cell because it is a cell in which a unique subset of human genes characteristic of liver cells are turned on.[6] In contrast, the human skin cell is a skin cell because it is a cell in which another unique subset of human genes, this time characteristic of skin cells are turned on. Therefore, the nature of a cell is determined not by the presence of a complete human genome in that cell but by the particular subset of human genes of that genome that is turned on in the cell. In other words, the nature of a particular cell is determined not by the genetic state of the cell *per se* but by its epigenetic state.[7]

The primacy of epigenetics over genetics in determining cellular identity within a particular species is a crucial biological fact that invalidates Walker's assumption that every event that constitutes a new human genomic identity—understood by him to be the physical coming-to-be of a reasonably complete human genome in an enucleated human egg—is also an event that constitutes a new human organism. Transferring a reasonably complete human genome into an enucleated human egg is only a necessary but not sufficient criterion for generating a new human organism. The enucleated egg must also be able to *reprogram* the transferred human genome, transforming it from a genome where only those genes associated with the donor cell type, say a human liver cell, are turned on, to a genome where only those genes associated with a single-cell human embryo are turned on. It is this second event—the reprogramming of a human genome into the epigenetic state associated with embryos—that is the essential event that constitutes a new human

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[5]For a comprehensive overview of the field of epigenetics, the study of the epigenetic states of different cells in different organisms, see Bruce Stillman and David Stewart, eds., *Epigenetics,* Cold Spring Harbor Symposia on Quantitative Biology, vol. 69 (Cold Spring Harbor, N.Y.: Cold Spring Harbor Press, 2005).

[6]This subset of liver-specific genes would constitute a *molecular signature* for liver cells. Each human cell type would have a characteristic molecular signature that could be used to distinguish one cell type from another.

[7]Clearly, however, the nature of the cell is also determined by genetics—if a cell lacks a particular gene, then that gene cannot be turned on or off. Thus, epigenetics is dependent upon genetics. However, the argument being made here is that when cells possess identical sets of genes, like most cells that belong to a particular individual or to a particular species, it is epigenetics that distinguishes one cell type from another.

organism.[8] This is the event that gives the single cell—now properly called an embryo—the intrinsic capacity to follow a self-driven, robust developmental pathway that manifests its species-specific organization.[9] In other words, this is the event that properly corresponds to the organism-constituting event that Walker rightly describes as "the absolute starting-point of the process of self-unfolding that only an already existing organism can perform."[10]

Given these biological facts, the difference between SCNT and ANT should be clear: With SCNT, the enucleated egg is allowed to reprogram the transferred genome so that an embryo is generated. In contrast, with ANT, the enucleated egg—because of genetic manipulations done either to the egg or to the donor cell or to both simultaneously—is prevented from reprogramming the transferred genome to an embryo-like epigenetic state. Thus, with ANT, the embryo-specific genes in the transferred genome are not turned on, and so, no embryo—no organism—is generated. Instead, from the very beginning, a cellular artifact, with a subset of genes turned on that differs from the unique subset of genes turned on in a *bona fide* embryo, is created. Ideally, of course, this cellular artifact would be a source for pluripotent stem cells that, if necessary, could be licitly destroyed in the laboratory. In sum, contrary to Walker's flawed proposal, ANT is technically, and therefore, morally distinguishable from cloning.

There is one more objection to ANT related to Walker's argument that is often raised. It goes as follows: a cellular artifact

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[8]In fact, SCNT or cloning is only possible because an enucleated egg is uniquely able to reprogram a transferred genome in this way. Transferring a reasonably complete human genome into a skin cell would never generate an organism because an enucleated skin cell lacks the capacity to reprogram the transferred genome to the epigenetic state associated with embryos.

[9]I suggest the following scientific definition of an organism: A discrete unit of living matter that follows a self-driven, robust developmental pathway that manifests its species-specific self-organization. For this definition, I am indebted to insights from the following authors: B. Goodwin, "Development as a robust natural process," in *Thinking about Biology: An Invitation to Current Theoretical Biology*, ed. W. Stein and F. J. Varela (Reading, Mass.: Addison-Wesley Publishing Co., 1993), 123–148; and Juan de Dios Vial Correa and Monica Dabike, "The Embryo as an Organism," in *The Identity and Status of the Human Embryo*, ed. Juan de Dios Vial Correa and Elio Sgreccia (Vatican City: Libreria Editrice Vaticana, 1999), 317–331.

[10]Walker, "Altered Nuclear Transfer," 664.

generated by ANT containing a reversible genetic defect is not essentially different from an embryo. Both have the potential to develop to maturity since reversing the defect would allow the artifact to develop normally.

In response, I note that there is an important distinction between *active* and *passive* potentials. Active potentials are actualized from within. They tell us about the nature of a thing. In contrast, passive potentials are actualized from without. They do not tell us about the nature of a thing. The distinction is best illustrated with the following example: an acorn can grow into an oak tree. Thus, it has an active potential to become an oak tree. An acorn can also become a crucifix. This, however, requires the intervention of a skilled carpenter. Thus, an acorn only has a passive potential to become a crucifix.

Given this distinction, the difference between an embryo and a cellular artifact should be clear: an embryo has an active potential to become a mature organism. It has the epigenetic state that gives it the intrinsic capacity to develop to maturity. Thus, it is essentially that organism. In contrast, a cellular artifact with a reversible genetic defect only has a passive potential for mature development, a passive potential that can only be realized if a scientist alters its epigenetic state from without. Thus, it is essentially not an organism. It is unlike the embryo. □

NICANOR PIER GIORGIO AUSTRIACO, O.P., *is a priest and assistant professor of biology and adjunct professor of theology at Providence College in Providence, Rhode Island.*