

Altered Nuclear Transfer and the Status of the Human Person

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ABSTRACT

Altered Nuclear Transfer (ANT) is a method to create blastocysts that can be used to derive embryonic stem cells. Opponents of ANT contend that the entity brought into being by this cloning method is a severely disabled embryo. The proponents of ANT believe that the entity brought into being through ANT is not an embryo but rather a “biological artifact” that lacks the coordinated organization to maintain a developmental trajectory essential to embryogenesis. In this paper I have summarized and simplified the discussion in order to show where this proposal is philosophically and morally flawed.

ALTERED NUCLEAR TRANSFER (ANT) is a method to create blastocysts¹ that can be used to derive embryonic stem cells.² The proponents of ANT believe that the entity brought into being through ANT is not an embryo but rather a “biological artifact” that lacks the coordinated organization to maintain a developmental trajectory essential to embryogenesis. Although well meaning in their mission to find ethical alternatives to embryo-destroying research, the proponents of ANT have inadvertently put forth their own version of cloning and killing embryos in an effort to resolve the impasse between biotechnology and the protection of nascent human life. It appears that ANT and its variant Oocyte-Assisted Reprogramming (ANT-OAR) are philosophically and

¹ A blastocyst is an embryo in approximately the fifth day of development. In the blastocyst stage embryonic stem cells are first evident.

² Nicanor Austriaco, O.P., “Are Teratomas Embryos or Non-Embryos? A Criterion for Oocyte-Assisted Reprogramming,” *National Catholic Bioethics Quarterly* 5 (2005): 697-706.

morally flawed methods. The problem with these methods is that they rely on epigenetics, systems biology, and empiricism³ rather than on metaphysics to determine the ontological status of the human person from the moment of his coming into being. The empirical/ experimental method of natural science is ill equipped to understand “being *qua* being” because its formal object is too limited. Great philosophical, theological, and scientific minds have weighed in on this issue, some in favor of ANT and some in opposition to it. In this paper I am not going to follow the detailed line of arguments that have already been made but rather I plan to summarize and simplify the discussion in order to show where this proposal is philosophically and morally flawed.

Part One of this paper presents the arguments in favor of ANT/ANT-OAR. Any commentary on these arguments has been avoided until the second section of the paper. Any inaccuracies in the first part of the paper are wholly accidental and in no way meant to dilute the arguments in favor of ANT/ANT-OAR. In Part Two, I will make the case against ANT/ANT-OAR.

PART ONE: THE CASE FOR ANT/ANT-OAR

The *objective* of ANT/ANT-OAR is to produce human pluripotent stem cells (embryonic stem cells) from a biological entity lacking the organization necessary to have the moral status of a human embryo.⁴ The *method* of ANT/ANT-OAR creates a non-embryo biological entity whose coming into being is identical to the process used in cloning an embryo, except for a genetic modification to one or both operators prior to nuclear fusion. The *premises* employed in the argument are as follows:

1. ANT/ANT-OAR does not bring into being a human organism because *ab initio* the biological entity does not have the human organismal

³ By empiricism I mean sole reliance on the scientific method to determine organismal identity.

⁴ W. Hurlbut, “Altered Nuclear Transfer as a Morally Acceptable Means to Procure Human Pluripotent Stem Cells,” <http://www.alterednucleartransfer.com/?page=4a&view=1>.

- infrastructure, that is, no inherent principle of unity.⁵
2. “The physical coming-to-be of a reasonably complete human genome in an enucleated egg is [not] the essential event that constitutes a new human organism.”⁶ Rather it is the epigenetic state in which genes are turned on that determines the cellular identity of a cell/organism.
 3. Genetic engineering prior to nuclear fusion will ensure that the new entity comes into being with an innate insufficiency present *ab initio* to be a human organism.⁷ The effect of this genetic engineering is to change the epigenetic state to be inconsistent with a human organism but not with a human cell.
 4. Because this biological entity does not have the active potential to complete its developmental trajectory, its nature and telos are not those of a human organism but rather of a cellular artifact.⁸
 5. Teratomas are concrete examples of biological entities that exhibit embryonic development at least to the blastocyst stage but are generally not considered to be embryos. Their existence indicates a high probability that ANT/ANT-OAR is ethically sound because their developmental trajectory is similar to the ANT/ANT-OAR-generated cells. *Agere sequitur esse*, act follows being.⁹

The proponents of this view hold that animal studies will determine whether ANT/ANT-OAR-generated cells are embryos or non-embryos.

WHAT ARE ANT AND ANT-OAR?

Both ANT and ANT-OAR, according to their proponents, can create embryo-like/non-embryo organisms or “biological artifacts” that will be a source of human pluripotent stem cells. Both techniques depend on the

⁵ Ibid.

⁶ Nicanor Austriaco, O.P., “Altered Nuclear Transfer: A Critique of a Critique,” *Communio* 32 (2005): 172-76.

⁷ W. Hurlbut, “Altered Nuclear Transfer as a Morally Acceptable Means for Procuring Human Embryonic Stem Cells,” *National Catholic Bioethics Quarterly* 5 (2005): 145-51.

⁸ Austriaco, “Altered Nuclear Transfer,” p. 176.

⁹ Austriaco, “Are Teratomas Embryos...,” p. 706.

procedure called somatic cell nuclear transfer (SCNT), with one distinction. SCNT, the process used to clone Dolly the sheep, uses the nucleus of a cell containing DNA, the genetic code that acts roughly as its blueprint. In somatic cell nuclear transfer, a ripened ovum is taken from an organism, and its nucleus is removed or destroyed. A somatic cell (a cell other than a sperm or egg cell) from the organism to be cloned is then removed. Its nucleus with its DNA is fused with the emptied egg. In this manner, a genetic twin is brought into being.

ANT proposes to use exactly the same technique as SCNT, with one distinction. A gene in the somatic cell will be “silenced” prior to nuclear fusion in order to prevent the resulting “biological artifact” from developing beyond the blastocyst stage of embryonic development. The blastocyst stage is the point of embryonic development in which the pluripotent stem cells are first evident. It is also the stage where the embryo is capable of implantation. The effect of this genetic engineering is that the trophoblast, which is essential for implantation, does not develop.¹⁰

ANT-OAR is a form of ANT that also relies on SCNT. Where ANT silences a gene, ANT-OAR causes a gene to be over-expressed. Nanog is one of the gene candidates theorized to be a critical factor in the development of pluripotent stem cells. By over-expressing this gene in the somatic cell prior to nuclear fusion, proponents of OAR propose that the resulting “biological artifact” of nuclear transfer would respond to this over-expression of Nanog by immediately producing pluripotent stem cells rather than a developing human embryo. In effect, the over-expression of the Nanog gene would somehow cause the embryonic stage to be bypassed.¹¹

How is it possible to have an embryo-like but non-embryo biological entity? The premises outlined above, answer the question, at least to the satisfaction of the proponents of ANT/ANT-OAR, of how it is possible to

¹⁰ The trophoblast is responsible for many aspects of embryogenesis, for it gives rise to all of the extra embryonic systems (placenta, etc.) and implantation is essential to the continued existence of the embryo.

¹¹ These definitions were distilled from “A Clarification and Defense of Altered Nuclear Transfer” by William Hurlbut, Robert P. George, and Markus Grompe, available at: www.altered nucleartransfer.com.

have an embryo-like biological entity that is nevertheless not an embryo. They use epigenetics to determine whether a biological entity is an embryo or simply a disorganized clump of cells, and they use systems biology to support that determination.

Systems biology is an approach to the human organism that seeks to understand the living whole as a dynamic network of integrated parts. The systems perspective goes beyond the process of cataloging and quantifying all of the parts of a living organism and seeks to understand how each of these parts interacts to bring about the operation of the entire organism. For example, a nerve fires an electrical impulse and stimulates a muscle cell to move. The systems biology approach would require not only that the physical structure of the nerve cell and the type of neurotransmitter be known, but also that the volume of neurotransmitter released be quantified and the exact voltage of the neural impulse be measured. To be sure, this is a simplistic example, but one must realize that the systems view of life can penetrate an organism not only in its parts and functions but in the complex and dynamic network of interacting molecules. The knowledge gained from this in-depth understanding of the functioning of the human organism promises to direct scientists to useful processes that can be manipulated through external controls.¹²

William Hurlbut explains how the systems biology perspective supports the non-organismal status of the ANT/ANT-OAR generated cell. Noting that the living organism, as a unified whole, is composed of partial subsystems, he argues thus:

If severed from the whole, these partial subsystems may temporarily proceed forward in development, but without the larger environment of their organismal system they will become merely disorganized cellular growth. ANT proposes that small (but precisely selected) alterations will allow us to harness these subsystems of partial development, apart from their full organismal context in order to produce ES cells.¹³

¹² Hiroaki Kitano, "Systems Biology: A Brief Overview," *Science* 295, no.5560 (March 1, 2002): 1662-64.

¹³ W. Hurlbut, "Altered Nuclear Transfer," p. 149.

This means that ANT produces not a human embryo but only a subsystem of a human embryo that is capable of partial development akin to embryonic development, but nonetheless incomplete. It is this inability to complete the developmental trajectory typical of a human embryo that keeps this “subsystem” from achieving the moral status of a human embryo:

This technologically-created limited cellular subsystem, from which the ES cells could be obtained, would fail to establish even the most basic features of human organismal infrastructure. A deficiency at the first differentiation of cell types—the distinct formation of the trophoblast and the inner cell mass—means the absence of the most fundamental order. According to Dr. Maureen Condic, a developmental biologist at the University of Utah, “When [the] trophoblast does not form, subsequent development follows a chaotic pattern, suggesting that organismal development has not been ‘disrupted’ in the absence of [the] trophoblast but rather that an organism never existed in the first place.”

The resulting cell system would have no inherent principle of unity, no coherent drive in the direction of the mature human form, and no claim on the moral status due to a developing life. Rather such a partial, disorganized organic potential would more rightly be designated a biological “artifact”—a human creation for human ends. The fact that some part of such a constructed entity will carry a certain momentum of development is morally analogous to the fact that we can grow skin in a tissue culture and may one day grow whole organs or limbs in isolation. Lacking crucial elements in its fundamental constitution, such an entity could never rise to the level of a living being.¹⁴

Coupled with the biological systems perspective, the proponents of ANT/ANT-OAR also look to epigenetics to determine the nature of a given organism: “The physical coming-to-be of a reasonably complete human genome in an enucleated egg is [not] the essential event that constitutes a new human organism.”¹⁵ Rather it is the epigenetic state in which certain genes are turned on that determines the cellular identity of a cell/organism.

What is epigenetics? Almost every type of cell in the body, which has some 260 cell types, possesses a reasonably complete human genome—including one-cell human embryos, human liver cells, and human

¹⁴ W. Hurlbut, “Altered Nuclear Transfer,” pp. 149-50.

¹⁵ Austriaco, “Altered Nuclear Transfer,” p. 172.

skin cells. The exceptions are germ cells and red blood cells. (For a clarification of the types of cells in the human body, see Table I in Appendix.) The possession of a complete human genome is a necessary but not sufficient condition for defining a human embryo, but its epigenetic state is what defines a human embryo. Epigenetics is posited by biologists as a way of determining the identity/function of a cell based on which genes are turned on and turned off in that particular cell. For example, the genes turned on in a liver cell differ from the genes turned on in a heart cell even though both possess a complete human genome. This difference in epigenetics is responsible for the function and identity of the particular cell.¹⁶ The epigenetic state of a cell (including a single-cell embryo) is the primary determinant of the cell's identity. How the epigenetic state can result in this level of certainty is explained as follows:

I propose that properly understood, the epigenetic state of a living system reflects its organization and its behavior and thus is a manifestation of its soul. Thus, when it undergoes change, it manifests an underlying change in the ontological nature of the cell. More specifically, I have suggested that genetic manipulations that alter a cell's epigenetic state and its identity, like the overexpression of MyoD, eyeless, Nanog or CDx2, do so by changing the disposition of its material principle to a new form. Again this is an argument grounded in the Aristotelian-Thomistic axiom, *agere sequitur esse*, act flows from being: We know that an isolated skin cell transformed into a muscle cell by MyoD in culture has been transformed ontologically because its organization and its behavior are different. Therefore, properly speaking, the epigenetic state of a cell does not determine its ontological status but manifests it. It is a manifestation of the soul.¹⁷

Therefore, due to the genetic alteration specific to ANT/ANT-OAR, which alters gene expression substantially, the epigenetic state of the ANT/ANT-OAR-generated cell prevents it from becoming a human organism and instead causes it to become a human cell. For example, the gene Nanog is detected in the blastocyst stage when pluripotent stem cells

¹⁶ Austriaco, "Altered Nuclear Transfer," pp. 173-74.

¹⁷ Nicanor Austriaco, O.P., "The Moral Case for ANT-Derived Pluripotent Stem Cell Lines," *National Catholic Bioethics Quarterly* 6 (2006): 517-37.

first appear. However, Nanog is not expressed in the zygote stage. Therefore, relying upon epigenetics to determine cell identity, if Nanog can be teased into early expression *ab initio*, then the epigenetic state of the biological entity will be consistent with pluripotent stem cells instead with those typical of a human embryo.

In other words, according to this criterion, the epigenetic state of the ANT/ANT-OAR biological entity is sufficiently (essentially) different from the epigenetic state of a human embryo and is therefore not a human embryo. These substantially different epigenetic states of the ANT/ANT-OAR entities disable the inherent principle of unity, as well as the developmental and organizational abilities of the growing entity *ab initio*. Using the systems approach, the lack of organismal traits particular to an embryo, viz., the principle of unity that makes an embryo an embryo prevents this biological entity from being a human organism. The strength of this position for the advocates of ANT/ANT-OAR is that the changes to the genetic state of the operators happens prior to nuclear fusion and that this essential order of events prevents the coming into being of a human organism.

The proponents of ANT/ANT-OAR argue that the order of events, prior to nuclear fusion, as well as the epigenetic state distinguishes the active potential from the passive potential of this biological entity and in doing so determines its nature. The product of ANT/ANT-OAR can have the passive potential to become a human embryo but lacks the active potential due to its epigenetic state. For 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.¹⁸

In the case of ANT the genetic defect is a silencing of the CDx2 gene. In the case of ANT-OAR the genetic defect is an over expression of Nanog.¹⁹ Both of these genetic alterations (defects) occur prior to nuclear fusion. The distinction between active (intrinsic) and passive (extrinsic) potentials outlined in the above passage would be useful for ANT in this way. A genetic engineer (an external efficient cause) might be able to turn on the CDx2 gene before the blastocyst stage and thereby change its epigenetic state. The biological entity would then be able to develop along the same trajectory as a normal human embryo. In this manner, the biological entity would have the passive potential to become a human embryo because it would require an external efficient cause (the genetic engineer) to effect the change in substantial form. But it would lack the active potential (the epigenetic state proper to an embryo) to become a human embryo. That is, its nature is ordered not toward becoming an embryo but toward becoming a teratoma. The ANT/ANT-OAR-generated cells and a human embryo are different ontologically because they are organized and tend to behave differently. This is an argument grounded in the Aristotelian-Thomistic axiom, *agere sequitur esse* (act follows from being).²⁰

It is precisely the naturally occurring instances of failed fertilizations (teratomas) that convince the proponents of ANT/ANT-OAR that it is possible to engineer a biological entity that can be embryo-like without being an embryo. Teratomas come in many variations; some are arguably zygotes whose development has gone awry while the identity of others is less certain. (Table 2 in the Appendix outlines the embryogenesis of teratomas, embryos, cloned embryos and ANT/ANT-OAR entities.)

In order to prove the non-embryonic nature of the cell generated by

¹⁸ Austriaco, "The Moral Case..." p. 176.

¹⁹ It is possible that there are other gene candidates that can achieve the same genetic defects as CDx2 and Nanog, but for the sake of simplicity and consistency with current literature on the methods, I will limit the gene candidates to CDx2 and Nanog.

²⁰ Austriaco, "Are Teratomas Embryos..." p. 706.

ANT/ANT-OAR, its advocates propose animal testing that would use the follows methodology:

The method would be to implant the cell into the uterus of a competent female. If the ANT/ANT-OAR generated cell develops into a fetus or a mature organism, then clearly this proposal generates embryos. If however, this cell becomes a tumor, then OAR does not produce embryos since embryos considered as a whole entity do not have the active potential to become tumors.²¹

PART TWO: THE CASE AGAINST ANT/ANT-OAR

ANT/ANT-OAR fails as a morally acceptable means of deriving embryonic stem cells because it brings into being a human embryo with a genetically engineered self-destruct mechanism. The remainder of this paper will outline the arguments against the ANT/ANT-OAR proposal. They are:

1. ANT/ANT-OAR is indistinguishable, technically and procedurally, from the human cloning method of SCNT.
2. ANT/ANT-OAR is not a case of the Thomistic axiom *agere sequitur esse* but rather *esse sequitur agere* (being follows act) that the proponents of these methods apply in determining the nature of the being brought into existence via ANT/ANT-OAR.²²
3. The active potential of a human embryo, which in this case is evidenced by the ability to follow a developmental trajectory, is a sufficient condition but not a necessary condition for determining organismal identity.
4. Epigenetics and systems biology lack sufficient means to determine the ontological status of the human embryo.
5. The comparison of teratomas to the ANT/ANT-OAR-generated cells is a flawed analogy.
6. Animal experimentation will not be able to determine the ontological status of an entity, but only the technological feasibility of the process.

²¹ Austriaco, "Are Teratomas Embryos...", p. 704.

²² I owe this point to my professor, Fr. Anselm Ramelow, O.P., Dominican School of Philosophy and Theology (Berkeley CA).

7. ANT/ANT-OAR like SCNT would require the use of women's eggs.

ANT/ANT-OAR is based on SCNT with one slight variation and as such is technically and procedurally indistinguishable from SCNT. Table 2 compares these two techniques and outlines how the only difference between the two procedures is a genetic manipulation prior to nuclear fusion. But the place where these two techniques differ measurably is in the developmental capabilities of the biological entities that they produce. In other words, the biological entities differ in their future potential not in their coming-into-being. The ontological status of a human person rests not in what he can do, but how he came into being. Adrian Walker comments on this when he writes:

German Philosopher Robert Spaemann gives us an important clue to finding such criterion when he argues in his book *Personen* that the severely retarded still count as "persons," even though they cannot *de facto* perform "intentional acts," and that they do so simply because they are members of the human species. Spaemann is aware of the danger of "speciesism," of course, and he does not intend to reduce personal being to human being. His point, however, is not that every person is a human being, but that every human being is a person, because "[a] person is any animal the physical make-up of whose species constitutes the species' typical members as thinking intelligent beings, with reason and reflection, and typically enables them to consider themselves the same thinking things in different times and places." Let us call this "Spaemann's Principle."

Spaemann's Principle relies on the manifestation of an important organismal trait—the possession of a certain typical structure – as an index of organismal being. Nevertheless, Spaemann's Principle focuses not on the actual possession of that structure, but on the event by which a human organism normally acquires it: the event of anthropogenesis. By underscoring that a person's appropriate physical structure is owed him on account of his coming into being as a member of the human species, Spaemann's Principle is able to avoid the suggestion that, if he should fail to have appropriate physical structure with 100 percent normality, he is not a human organism. Or to be more precise, Spaemann's Principle implies that even if X is a conceptus that comes into being with massive structural defects that destine him to die within a few seconds, we can still say that it was in X's natural teleology to be a human organism—so long

as X in fact comes into being as a member of the human species.²³

Spaemann's Principle can be used to determine if there is a sufficient distinction between ANT/ANT-OAR and human cloning. If a human clone comes into existence via SCNT as a member of the human species and if ANT/ANT-OAR uses the technique of SCNT to bring its result into being, then the ANT/ANT-OAR entity also comes into being as a member of the human species.

One of the central premises of the ANT proposal concerns the order of events.²⁴ Proponents attach much significance to the claim that the genetic engineering of the somatic cell or the egg cytoplasm occurs *prior* to fusion. Fr. Austriaco asserts that this order of events substantially determines the ontological status of the organism because genetic engineering prior to fusion changes the epigenetic state of the cell and demotes the developmental potential of the organism from active to passive. He cites the Aristotelian/Thomistic axiom, *agere sequitur esse*, act follows being.

There are at least three problems with this line of reasoning. First, the act that Fr. Austriaco uses to establish what kind of being is present is a demonstrated ability to continue a developmental trajectory of embryonic growth. In the case of ANT, this demonstration is provided by the act of implantation in the mother's uterus. Fr. Austriaco argues that it is the active potential (as evidenced by either the *act* of the developmental trajectory of the organism or the *act* of implantation) that allows us to figure out the nature of the organism. The presence of the active potential is *sufficient* for establishing the organismal identity; however, that same presence is not *necessary* for establishing organismal identity. In other words, although the ability of the human embryo to implant in the uterus is a *sufficient* condition for figuring out that a human organism is present, it is not a *necessary* condition: an embryo that is unable to implant is no less of a human organism.

Second, Fr. Austriaco contends that the epigenetic state of an

²³ Adrian J. Walker, "Altered Nuclear Transfer: A Philosophical Critique," *Communio* 31 (2005): 649-84.

²⁴ Hurlbut, "Altered Nuclear Transfer as a Moral...", p. 149.

organism is a manifestation of its soul.²⁵ But he also says that the nature of a cell is determined by the epigenetic state.²⁶ Putting aside the problem with this conflation of terms, and considering the former, even if the epigenetic state of an organism *is* the manifestation of its soul, it still remains an action, an operation, a secondary act. Put simply, action is a manifestation of being, but who says every being must manifest itself?²⁷

Third, Fr. Austriaco's use of the axiom *agere sequitur esse* to justify the claim that a human embryo must *act* in a certain way in order *to be* a human being results in an imperative. That is, his use of this axiom asserts that act *must* follow being, rather than asserting that if this act exists, its proper order is to follow being. The implication of the imperative is that the two terms (*esse* and *agere*) are convertible, because—as used by Fr. Austriaco—they are equally necessary in his premise. This seemingly inadvertent convertibility of terms creates an illegitimate conversion—if act follows being, *agere sequitur esse*, then being follows act, *esse sequitur agere*.²⁸ It does not seem that Fr. Austriaco wants to make this assertion, but his line of reasoning results in it nonetheless.

Furthermore, the assertion that an organism must be able to *act* in order to *be* is a flattening of the first and second act of being. Properly understood, the first act of being (*esse*) is the actuality of existence, the determination of being. The second act of being (*agere*) flows from the first act; it is a manifestation of being. That is, the second act is an *operation* of the first act, not its *determination*. Dr. Steven Long elucidates this point²⁹ when he uses the related axiom, *operatio sequitur esse* to draw attention to the idea that substances can suffer privations which impede their operation without causing them to lose specific nature:

²⁵ Austriaco, "The Moral Case for ANT," p. 534.

²⁶ Austriaco, "Altered Nuclear Transfer..." p. 174.

²⁷ I owe this point to Fr. Anselm Ramelow, O.P.

²⁸ *Ibid.*, through personal communication.

²⁹ For this point, I am indebted to Dr. Steven Long, Professor of Theology, Ave Maria University (Naples, FL).

If every deprivation of operation were held necessarily to bring about a new species, then it would seem to follow that only perfect members of species exist. Now, it is quite true that from a defect in operation one may be able to find some reason for that failure in the being, whether temporary or more permanent, but (importantly) the failure in being is not necessarily equivalent to a failure to be a member of the species. This is an important distinction.³⁰

For example, the privation of a higher brain in the case of an anencephalic human fetus³¹ does not negate his membership in the human species; it only results in a failure in his ability to live outside of the womb. Similarly, ANT/ANT-OAR entities may well have the same nature as any other human conceptus, but different capabilities for growth, as do all human persons; that is, their privation (in the case of ANT, the inability to implant in the uterus), does not negate their ontological status as members of the human species.

The first part of this paper quotes Fr. Austriaco's use of the analogy of an acorn to clarify the difference between active potential and passive potential as it relates to ANT. He explains that it is the switching on and switching off of genes—a change in the epigenetic state—that determines which potential is actualized and therefore what type of being is present in the “biological entity.” In the case of ANT, the first genetic intervention switches off the CDx2 gene; the second intervention turns it back on. The first intervention affects a radical change in the organism and causes it to be a “cellular artifact” rather than a human embryo; the second intervention affects an even more radical change in that it causes the “cellular artifact” to switch back to being an embryo and to continue along its interrupted gestational path. Is it actually possible to change a “cellular artifact” (the ANT-generated cell) into an embryo by simply switching on a gene that had been previously switched off? Can a tumor really become a human person? Does a tumor have the passive potential to become a human person? Is this a realization of an entity's passive potential, or is this a way of curing a genetic defect, i.e., of setting free an active potential? If the

³⁰ Ibid., through personal communication.

³¹ See <http://medical-dictionary.thefreedictionary.com/Anencephalic+Fetus>.

latter is true, it prompts the question: How can something that does not exist be cured?³²

Determining the order of events is central to ascertaining the acceptability of ANT/ANT-OAR. In the use of ANT-OAR genetic engineering is performed on one or both of the operators (egg/donor somatic cell) prior to fusion. The egg and donor somatic cell are then fused. Because of the genetic alteration in step one, the donor cell is immediately de-differentiated to a pluripotent state. The genetic engineering on the operators prior to fusion of the enucleated egg and the somatic cell is thus thought to be so radical that it causes the fused egg/donor genome entity to bypass the effects of nuclear fusion typical of a procedure that otherwise brings into being a new human organism. In other words, the genetic engineering performed on the egg and/or donor somatic cell somehow changes their nature so radically that although nuclear fusion (virtually identical to what occurs in SCNT) takes place, the effect of this fusion is wholly different from the normal effect of nuclear fusion.

The claim made by the proponents of ANT/ANT-OAR is that the epigenetic state of these operators has been changed sufficiently to change their nature when fused. A single-cell cloned embryo is not really an embryo when certain genes are expressed/silenced *ab initio* but, instead, is a disorganized clump of cells able to produce pluripotent stem cells. This claim ignores the logic of the order of events that brought the entity into being in the first place, as Adam Walker points out:

Much depends, then on whether or not ANT truly does circumvent anthropogenesis as Austriaco claims. Now, as he describes in his article, it seems to do just that by preventing the egg cell from reprogramming the donor genome into an embryo-like epigenetic state. Unfortunately, this description leaves out a detail that may seem small but actually calls into question the description's accuracy. It is this: the egg cell cannot reprogram the donor nucleus until the two have fused. Having fused, however, they are now one new entity, which means that, if anything can be said to reprogram the donor cell genome, it is no longer the (unfused) egg *per se*—which strictly speaking no longer exists—but precisely the new entity itself. What this suggests, and what Austriaco does not

³² Again, I owe this point to Fr. Anselm Ramelow, O.P.

seem to see, is that ANT, like cloning, cannot help but leave its product at least some of the innate spontaneity that is characteristic of the ordinary human conceptus. I say, “cannot but help,” because unless the enucleated egg and the donor cell fuse—and so become the new entity endowed with inner spontaneity I just alluded to—they cannot initiate the process that will lead to pluripotent stem cells.³³

Fr. Austriaco’s explanation of ANT-OAR is that the somatic cell nucleus is deprogrammed back to its pluripotent state bypassing embryogenesis. A consequence of this line of reasoning is that it causes us to ignore the fusion of egg and donor cell that otherwise signals a new conceptus and to focus our attention instead on the epigenetic state of the new entity, which resembles the epigenetic state of pluripotent stem cells rather than the epigenetic state of a whole organism.³⁴ Another element being ignored is the egg. In SCNT, the cytoplasm of the egg is essential to reprogram the donor cell genome and to initiate embryogenesis. Are we meant to believe that the egg does not function in this way because of the over-expression of *Nanog*? Rather, in the case of ANT-OAR, does the egg function as a time machine that transports the somatic cell back to its pluripotent state? Then why use an egg at all if the egg is simply functioning as another somatic cell? Why not digress adult stem cells back to a state of pluripotency (without the use of eggs) and avoid the ethical debate altogether?³⁵ The answer is obvious: the egg exercising its particular telos of co-participation in the creation of

³³ Adrian Walker, “The Primacy of the Organism. A Response to Nicanor Austriaco,” *Communio* 32 (2005): 177-87.

³⁴ This point actually concedes for the sake of argument that the conceptus does degrade into pluripotent stem cells. It is not known whether this change is even possible.

³⁵ In December 2007, Japanese scientist Shinya Yamanaka published the results of his study, which successfully reprogrammed skin cells back to a pluripotent state *without* the use of eggs. This process is essentially distinct from the ANT-OAR process described above in that it does not rely on embryogenesis. It is a pure reprogramming of a somatic cell. These pluripotent stem cells were found to be indistinguishable from embryonic stem cells and for all practical purposes should render the ANT/ANT-OAR debate obsolete. Accessible at: <http://www.nytimes.com/2007/12/11/science/11prof.html>.

a new organism is essential to the ANT-OAR process because it is a reproductive process that brings into being a new human person; in other words, it relies on a conception event. Schindler stresses the critical point of conception to the all-at-once wholeness of the human person:

As *an unum per se*, an organism's coming-into-being bears an all-at-once character. An organism thus bears a wholeness of actuality that is complete "before" any development can occur.³⁶

The reliance on epigenetics rather than metaphysics to determine the organismal identity of the cell generated by ANT/ANT-OAR makes it possible to ignore the conception event that begins the entire process and that makes any development possible. Conception, i.e., the species-typical coming-into-being of this kind of organism, is an observable indicator that is more likely than any other active potential or behavior (e.g., ANT-implantation) because the *esse* can always be deprived of its *agere*.³⁷

Epigenetics and systems biology can only look at the active potential of a being, that which can be observed and measured. Epigenetics is concerned with appearance, not with being. The *esse* comes from a substantial form and cannot be either observed or measured. Therefore these two approaches cannot determine the nature of the being. More specifically, it cannot resolve the mystery that surrounds the fusion of egg and sperm or of the enucleated egg and donor cell genome, for they do not take into account the metaphysical realities that transcend the physicality of the human body—essence and form.³⁸ Simply put, these two empirical methods cannot tell us if the matter of the conceptus has received the substantial form of the soul, as Fr. Austriaco is quoted as asserting in the first part of this paper. This is the point when life begins, but it cannot be determined by the epigenetic state of the organism:

³⁶ D.L. Schindler, "Veritas Splendor and the Foundations of Bioethics: Notes towards an Assessment of Altered Nuclear Transfer and Embryonic (Pluripotent) Stem Cell Research," *Communio* 32 (2005): 195-201.

³⁷ I owe this point again to Fr. Anselm Ramelow, O.P.

³⁸ Walker, "Primacy of the Organism," p. 187.

Epigenetics cannot determine cellular identity (understood as nature) unless by cellular identity we mean a certain phenotype characteristic of the earliest stages of human life. Epigenetics may be a (co)determinant of a one-celled human embryo's phenotypic profile, but it is not the primary determinant of its ontological status tout court—or even, for that matter, of the phenotype—only the one-celled embryo is.³⁹

It is Spaemann's Principle, not epigenetics, that is critical in determining cellular and organismal identity. The relevant question, therefore, is this: Did this organism come into being in the species-specific manner typical of a cloned human embryo? Systems biology takes the entire operation and organization of the organism into account in order to determine organismal identity. In practical terms, for the proponents of ANT/ANT-OAR, the developmental trajectory is the benchmark of organismal rather than cellular identity. This logic is backwards. A being can develop because it exists, but its ability to develop does not determine its existence:

In a word, the nature of the organism is not determined in the first instance by its capacity to progress to a more mature stage of development: being an organism is not synonymous with (progressively) manifesting organismal traits.⁴⁰

As stated above, any approach to determining organismal identity that relies on organismal traits—systems biology and epigenetics in this case—is empirical in nature and is incapable of establishing the ontological status of a human embryo, which is fundamentally a metaphysical question.

Another weak element of the ANT/ANT-OAR proposal is its use of the teratoma analogy. Table 2 in the appendix outlines the different types of teratomas.⁴¹ If teratomas are failed fertilizations that can sometimes

³⁹ Walker, "Primacy of the Organism," p. 184.

⁴⁰ Schindler, "*Veritas Splendor...*," p. 196.

⁴¹ As noted in the table, some forms of teratomas are grossly defective human organisms, while others are more akin to tumors and probably lack the ontological status of a human embryo. The discussion, however, is far from over. The teratomas that are used by the proponents of ANT as a test case for ANT are the non-embryo variants. To be consistent for the purposes of this argument, I

develop to the point of producing pluripotent stem cells and subsequently develop into tumors, and if tumors do not have the moral (and ontological) status of human embryos, then cells generated by ANT/ANT-OAR that are capable of developing to a point of producing pluripotent stem cells and then developing into tumors must also lack the moral (and ontological) status of a human embryo. The unstated premise is that teratomas and cells generated by ANT/ANT-OAR are the same type of entities. This premise is incorrect. It not only fails to meet the metaphysical test of sameness based on how the two entities came-into-being, but also fails to meet even a materialistic test of sameness.

From a materialistic point of view, teratomas—parthenotes or whole hydatidiform moles—are products of asexual reproduction (see Table 2). Cells generated by ANT/ANT-OAR are products of sexual reproduction, however many generations removed. Parthenotes are a result of an unfertilized egg spontaneously dividing; there are no paternally derived chromosomes. Whole hydatidiform moles occur when two sperm penetrate an egg with no nucleus. The resulting entity has no maternally derived chromosomes. ANT/ANT-OAR entities, on the other hand, rely on SCNT, which in turn relies on the sexual reproduction (from a prior generation) of the organism that provides the donor somatic cell genome. This somatic cell, which provides the total genome for the ANT/ANT-OAR entity, has 23 pairs of chromosomes—23 inherited from the donor’s mother and another 23 from the father. The difference between this ANT/ANT-OAR entity and a cloned embryo is that the ANT/ANT-OAR entity has one or more genes silenced or over-expressed. For the teratoma- ANT analogy to be accurate, it would be necessary to modify the proposed ANT/ANT-OAR process to reflect an asexual genetic configuration. For example,

Step 1: the nuclei of two sperm could be extracted from a donor organism.

Step 2: the CDx2 gene of both sperm nuclei would be silenced.

Step 3: the two sperm nuclei would then be fused with the enucleated egg.

This process would accurately mimic the process that brings a whole

will mean by teratoma the non-embryo type.

hydatidiform mole into being by adding the genetic alteration necessary to ANT. The problem is that any resulting embryonic stem cells would be useless because they would lack a complete genome of maternal and paternal chromosomes. ANT/ANT-OAR does not bring into being an organism akin to a teratoma. The analogy is inaccurate and misleading. The genome of the teratoma (whether a parthenote or a whole hydatidiform mole) is derived from either maternal chromosomes or paternal chromosomes, respectively. The genome of the ANT/ANT-OAR entity is derived from both maternally and paternally inherited chromosomes. Therefore, ANT/ANT-OAR entities are not teratomas.

Finally, ANT/ANT-OAR is going to be tested first in animals. The testing procedure and what it hopes to demonstrate have been outlined in the first part of this paper. These studies will yield one of three results:

1. The ANT entity will successfully gestate—this would prove its humanity but disallow the use of ANT on ethical grounds.
2. The ANT entity will not be able to reach the blastocyst stage and will be unable to produce embryonic stem cells. In this case ANT will be proved to be technically unfeasible.
3. The ANT entity will be able to reach the blastocyst stage, produce embryonic stem cells and then die with a physical structure resembling a tumor. In this case the technical feasibility of ANT has been proved.

The problem with all three of these results is that they fail to answer the crucial question of what the organism produced in scenarios (2) and (3) were before they perished. This sort of testing would only be able to determine if the hypothesis, that a genetically modified human entity can produce embryonic stem cells without continuing along a developmental pathway, is correct. A mother who miscarries because her child suffers from a privation (a genetic defect), does not grieve her “cellular artifact”; she grieves her unborn child regardless of the point in the “developmental trajectory” where that child dies. Animal experimentation cannot give us knowledge about the metaphysical or ethical concerns of ANT/ANT-OAR only about the technical feasibility of the process. David Schindler speaks to the inherent limits of empirical knowledge to unfold the ontological mystery of the nature of an organism:

Mystery is woven into the fabric of organic reality, into the very nature of an organism. Mystery expresses the non-deterministic (not exhaustively mechanical) being and causal agency proper to an organism. Mystery does not signify an unknown laying somehow simply behind or beyond the organism in its proper structure (cf. vitalism). Mystery and knowledge with respect to the being and behavior of an organism are not inversely related: mystery does not first begin where knowledge leaves off, nor does knowledge come to an end where mystery first begins.

On the one hand, then: empirical observation is necessary for understanding the nature of organic life and determining when it actually occurs. And experimentation is necessary to determine how parts of an organism behave such that they can be coordinated appropriately in relation to the organism as a whole. Thus, in the present case involving ANT and the generation of pluripotent (or embryonic) stem cells, empirical observation and experimentation (for example, on animals) could rightly said to be necessary to determine whether an entity produced by ANT is an organism (embryo) or not, as well as, further, to determine how to organize or manipulate the behavior of ESCs (embryonic stem cells) or PSCs (pluripotent stem cells) such that they will be coordinated (for example) into well-functioning liver cells or brain cells.

At the same time, however, empirical observation and experimentation are, for all of that, not sufficient for determining the nature of organic life and when it actually occurs, or for knowing exactly how (or whether!) these ESCs (PSCs) can be coordinated into well-functioning liver cells or brain cells. The limit to the knowledge characteristic of empirical observation and experimentation, in other words, is intrinsic. "Intrinsic" does not mean that the knowledge resulting from empirical observation and experimentation is exact and exhaustive as far as it goes but that eventually it reaches (what is always a progressively moving) limit beyond which it becomes inexact and incomplete. "Intrinsic" means rather, and more basically, that there is a limit operative within the empirical-experimental knowledge in its original and abiding constitution as such....

...Empirical-experimental knowledge in a word, is intrinsically limited insofar as the causal agency constitutive of an organism, as a whole and in its parts, is not exhaustively mechanistic.⁴²

Herein lays the fundamental problem with ANT/ANT-OAR; it relies solely on empirical data, on that which can be observed and measured. As David Schindler writes above, mechanical knowledge is useful but limited, and when we are investigating an issue as fragile as the criteria for when life

⁴² Schindler, "*Veritas Splendor...*," pp. 197-98.

begins, relying solely on empirical methods is unacceptable.

There is another important issue that needs to be brought up by the ANT proposal. Where are the eggs going to come from? For the sake of argument, let us say that no human life is formed in the ANT/ANT-OAR process. Let us also assume that ANT/ANT-OAR successfully produces human pluripotent cells that are not deformed in any way despite all of the genetic tampering, and that they treat/cure every disease known to mankind. What has happened? What has happened is that a near insatiable demand for women's eggs has been created. It is nearly impossible to control the supply of a commodity once the demand has been established. We have only to look at the underground trafficking of human organs to prove that point.

Is it morally acceptable to use a woman's eggs to produce "biological artifacts," even if such a thing could be done? Is not the purpose of human eggs already a given that is not to be redefined to suit some purpose of modern science? But even if this teleological challenge could be overcome, we are still left with the question of whether or not eggs can be removed from women without harming their bodily integrity. Even if this could be done, we are left with still another question. Can the dignity of women be respected while their very bodies are seen as a source for a commodity?

CONCLUSION

In conclusion, despite the good intentions of its authors, the ANT/ANT-OAR proposal fails to meet the ethical standards essential to moral scientific research. The concept of an embryo-like non-embryo is an oxymoron. If embryonic stem cells have yet to produce even a pure tissue culture, let alone a therapeutic cure, (and the real and immediate promise for therapeutic cures rests with adult stem cell research), why must we focus our resources on creating a morally acceptable derivation of embryonic stem cells? If we (including the proponents of ANT/ANT-OAR) disagree with the premise of destroying nascent human life, why must we not only "play ball" with those who advocate for life-destroying research but also allow them to set the rules? Given that over 73 diseases are now

being treated with adult stem cell therapies⁴³ and that umbilical cord blood is chock full of pluripotent-like stem cells, why are pro-life scientists, theologians, and ethicists pushing the envelope toward embryonic stem cell therapies? Adrian Walker offers these thoughts:

Thus, by attempting a technological solution to a moral impasse, ANT leaves in place a logic that “if it can be done, it may be done” that gave rise to the impasse in the first place—and not only leaves it in place, but participates in it. Not of course by intentionally undermining the commitment to the protection of embryonic human life, but by unintentionally weakening it nonetheless through the claim to solve our moral impasse by re-writing the very nature of anthropogenesis itself. For if we could do that, then we could lay hold of, and control, the inner principle of the dignity of the human being we claim to be upholding—and so would do away with any intrinsic, given-in-the-nature-of-things standard in the name of which to cry “stop” when biotechnology threatens that dignity.⁴⁴

If human life is sacred, is not the beginning of human life all the more sacrosanct? Should we protect its mystery from the foraging of developmental science? Natural science cannot answer the question of being because the study of being *qua* being supersedes natural science. Natural science can only study that which proceeds from the act of being. The reliance on the experimental method to determine a metaphysical question leads ethicists down the wrong path and gives a false sense of security that ethical due diligence has been conducted and ethical standards met. As stated in the introduction, natural science is the wrong tool for the job.

The ANT/ANT-OAR proposal prompts the question: How far can we manipulate the origins of life before we have manipulated it too far? Maybe we have gone too far when we feel the need to ask the question. In his defense of ANT/ANT-OAR, Dr. Paul J. Hoehner writes:

The controversy that has resulted from this proposal, as well as the reluctance of many conservative Christian ethicists to embrace these proposals, may in part

⁴³ David Prentice, “Adult Stem Cell Treatments: 9 Faces of Success” at <http://www.frc.org/get.cfm?i=BC06I01&f=WA07D01>.

⁴⁴ Walker, “Altered Nuclear Transfer,” p. 683.

be due to a way these concepts challenge and stretch the normal “substance” ontologies that are so ingrained in our normal way of thinking about “being” and what it means to be human. The standard metaphysical categories are like old wineskins that will not hold the new wine of proposed technologies.⁴⁵

This metaphor of the “new wine” is perhaps more poignant than Dr. Hoehner intended. In the New Testament, the “new wine” is the gospel. Are technologies the new gospel? Should we look to technology to determine what it means to be human? I argue that if the new technologies do not fit into the classical metaphysical categories that have remained relevant for more than two millennia, perhaps we should insist that the new technologies need to adhere to nature rather than to manipulate nature in order to serve technology.

It has been suggested that it is anti-science to oppose ANT/ANT-OA-R.⁴⁶ Is it anti-science to oppose the ANT/ANT-OAR proposal? Perhaps the most radical approach that a contemporary scientist can take is to turn his back on reproductive technology that degrades the human person into a sum of integrated parts and to return to a reverence for the nature of the human person, the radical notion that the mystery of life is to be pondered and held in awe, not systematically decoded or technologically abused. Contrary to being an anti-science position, the idea of discovering the natural telos of each creation without changing that nature demonstrates a restraint that only a true lover of nature can exhibit.⁴⁷

⁴⁵ P. Hoehner, M.D., “Altered Nuclear Transfer: Probing the Nature of Being Human,” *National Catholic Bioethics Quarterly* 5(2005): 261-69.

⁴⁶ Edward J. Furton, “A Defense of Oocyte-Assisted Reprogramming,” *National Bioethics Center Quarterly* 5 (2005): 465-68.

⁴⁷ I would like to thank Dr. Peter Colosi and Vivian Dudro for their editorial assistance and comments on earlier versions of this paper.

Table 1 – Human Cell Types

| Cell Type | Description | Genetic Configuration | Examples |
|----------------------------|---|--|--|
| Somatic cell | Every cell in the body except the germ cells | 46 individual chromosomes, organized into 23 pairs of chromosomes. Each pair comprises a chromosome inherited from the father and the mother. Diploid configuration | Skin cell, liver cell, heart cell, nerve cell. |
| Germ cell | The sex cells that give rise to unique organisms when combined via fertilization | At maturity, these cells have 23 chromosomes. These 23 chromosomes are a mixture of maternal and paternal chromosomes, selected during meiosis. ⁴⁸ Haploid configuration. | In males, sperm. In females, eggs (ova). |
| Single-celled human zygote | A unique organism brought into being through <i>in vivo</i> or <i>in vitro</i> fertilization, or cloning (SCNT) | 23 chromosomes inherited from the mother, 23 chromosomes inherited from the father. Combined to give rise to 23 pairs of chromosomes. Diploid configuration. | Steve, Maureen, Adrian, Nicanor. |

⁴⁸ Meiosis is the type of cell division by which germ cells (eggs and sperm) are produced. Meiosis involves a reduction in the amount of genetic material. See <http://www.accessexcellence.org/RC/VL/GG/meiosis.html>.