

A RESPONSE TO THE JOINT STATEMENT, “PRODUCTION OF PLURIPOTENT STEM CELLS BY OOCYTE ASSISTED REPROGRAMMING”

• David L. Schindler •

“The assertion that OAR enables us to create pluripotent stem cells without creating an embryo is certainly true only if the mechanistic philosophy mediating this claim is certainly true, which it is not.”



A group of some 35 pro-life scholars has issued a statement endorsing a proposal claiming to produce pluripotent stem cells without creating and destroying embryos and without producing an entity that undergoes or mimics embryonic development. The method by which this is to be accomplished is a form of altered nuclear transfer (ANT) called oocyte assisted reprogramming (OAR).

The Joint Statement means to present nothing more than a straightforward technical solution to a moral dilemma. It maintains this appearance of innocence, however, by begging a series of questions, and so by importing a number of assumptions, regarding the origin and nature of human life and, at least implicitly, also regarding the meaning of nature, of creation, and of Christian faith itself, and of the implications of these for (scientific) reason. The

Statement proceeds as though these (implied) assumptions are unproblematic, that they do not or should not present ethical problems for persons who share the signatories' pro-life intentions.

The purpose of the present response is to show, on the contrary, that the assumptions carried in the Joint Statement conflict on their face with several significant ethical—and philosophical and indeed theological—principles. Unaware of, or setting aside, these *prima facie* problems, the signatories of the Statement have publicized their assumptions in haste and without the deliberation and sustained argument demanded by and proportionate to the importance of what is at stake. The present response intends to show the gravity of this omission in terms of our ability to mount a truly consistent, reasonable, and persuasive defense of human life.¹

The four clusters of issues considered below do not all bear the same weight. However, they are all necessarily evoked in coming to terms with an integrated vision of life. The Joint Statement implies definite answers with respect to each of the questions raised. Although the present response assumes different, and opposing, answers, the response itself makes no claim of an exhaustive or conclusive argument on behalf of these different answers. Its limited purpose, rather, is to establish the significant *prima facie* conflict asserted above, between the answers presumed by the OAR proponents and some main (philosophical, ethical, and theological) principles of the Christian tradition, as enunciated most immediately in *Evangelium vitae* (and *Veritatis splendor*). The purpose, in short, is to show that the OAR proponents cannot claim to have avoided the

¹For a discussion of the issues evoked in connection with the ANT and OAR proposals, see the articles by Roberto Colombo, Adrian Walker, and myself in *Communio* 31, no. 4 (Winter 2004) and 32, no. 1 (Spring 2005). They are available online at <http://www.communio-icr.com/ant.htm>.

The present statement, for the contents of which I alone take final responsibility, has been written in dialogue with, and is much indebted to, the following persons: Adrian Walker, Ph.D. (*Communio*; philosophical anthropology/biology); Dr. Sara Deola, MD, Ph.D. (National Institutes for Health; medical oncology and histology, genetics); Dr. David Prentice, Ph.D. (Family Research Council and Georgetown University Medical Center; life sciences, medical and molecular genetics); Rev. José Granados, Ph.D. (Pontifical John Paul II Institute for Studies on Marriage and Family; theology, philosophy of the body); David Crawford, J.D., S.T.D. (Pontifical John Paul II Institute; moral theology); Rev. Antonio López, Ph.D. (Pontifical John Paul II Institute; theology); Margaret McCarthy, S.T.D. (Pontifical John Paul II Institute; theological anthropology).

strictures entailed by these principles until they come to terms with the questions formulated below.

1. *Discerning the origin of life:
OAR's proposed criterion for judgment*

(1) (a) The criterion assumed in the OAR proposal for determining the (ontological) identity of the product of the procedure—whether it is a stem cell or a one-celled human embryo made to resemble a stem cell—is flawed.

Instead of inhibiting the expression of a gene, as in the earlier ANT proposal, OAR proposes rather to encourage the premature expression of a gene (the Joint Statement mentions *nanog* as one of several candidates) in order to give the new cell “the distinctive molecular characteristics and developmental behavior of a pluripotent cell.” Like the earlier ANT proposal, however, OAR presupposes an actual fusion of an enucleated oocyte and a somatic cell nucleus, and thus mimics conception. This is true even if the genesis of the new entity and its pluripotent stem-cell-like manifestation occur simultaneously, or with no apparent time interval at all. What OAR proponents call the “epigenetic reprogramming” of the somatic cell nucleus by the oocyte might be more accurately called the pre-planned developmental modification of a human conceptus (brought about by artificial means). The logic of OAR therefore remains the same as in the earlier ANT proposal.

The claim by its proponents that OAR avoids bringing an embryo into existence does not derive from the empirical evidence *per se*. On the contrary, it is essentially mediated by a criterion for interpreting the empirical evidence, and this criterion is a philosophical one. The Joint Statement says that “the nature of each cell depends on its epigenetic state.” This claim, undefended in the statement, is what legitimates the proposal in the signatories’ eyes. How? If the identity of a cell depends on its epigenetic state, and the totipotent zygote is a uni-cellular entity, then, so OAR’s proponents reason, timely and strategic epigenetic modifications should suffice to prevent such a zygote from coming into existence in the first place.

This line of reasoning is questionable. Epigenetics can determine only the phenotypical manifestation of the cell whose identity is at issue, not its (ontological) identity as such. Thus, the mere act of modifying the epigenetic profile of the OAR product

cannot be sufficient to prevent that product from being, or having been, an incipient human organism. Once again, OAR, like ANT, is really a means of artificially replicating conception.

An organism is characterized as such by virtue of its intrinsic unity as an *unum per se* and thus bears an all-at-once wholeness that is nontemporal, while simultaneously and intrinsically including temporal development. The organism in its all-at-once wholeness transcends and comprehends even as it presupposes organic parts in the totality of their developing coordination. The point is that, given this understanding of organism, epigenetics can never be the first cause, but only an expression of an already existing organismic being—one whose origin has to be sought in that all-at-once instantaneous production called conception.

Of course, proponents of OAR/ANT intend to bypass conception altogether. But the only reason they think they can do so is their over-burdening of epigenetics with a constitutive significance for the organism as such that it does not and cannot have. Only on the assumption of this causal overburdening does it become at all plausible to think that the modification of an epigenetic profile is sufficient to remake the act by which human beings originate into some other kind of act, viz., an act that produces a pluripotent stem cell (or something that closely resembles one).

OAR/ANT is above all a theoretical or conceptual proposal, and, as such, its theory is mediated from top to bottom by mechanistic premises. For what else can we call the confusion of phenotype (based on epigenetics) with substantial identity upon which the argument for OAR hinges? If, in fact, substantial identity is essentially a matter of epigenetics, then the organismic whole is no more than the sum of its parts, and the absence or presence of an organism is simply a matter of reshuffling the epigenetic pieces—a classic mechanistic maneuver.

In a word, the assertion that OAR enables us to create pluripotent stem cells without creating an embryo is certainly true only if the mechanistic philosophy mediating this claim is certainly true, which it is not.

(b) For this reason, OAR's cautionary note that researchers will experiment with nonhuman animals before proceeding with humans begs the question of whether the criterion for interpreting the empirical data is sound, and indeed creates seriously misleading expectations. Such experimentation can affirm the technical feasibility of the procedure; but this in itself cannot yield an answer

to the crucial question: namely, whether the entity produced by OAR is a non-embryo or on the contrary an embryo that is gravely defective. Experimentation on nonhuman animals will only confirm what the proponents already think they know—but in fact what is just in dispute. That this is so is made clear in a statement by one of the signatories and main authors of the OAR proposal:

Let us put an OAR-generated mouse cell into a mouse and see if it grows up. If it becomes a mouse then OAR makes embryos. However, if the OAR-generated cell becomes a tumor, then OAR does not produce embryos, since organisms never become tumors.²

Let us analyze this passage. Given OAR's mechanistic premise—namely, that the nature of the unicellular zygote as such depends on its epigenetic state—the experimentation recommended here will beg, and cannot but beg, a principled answer to the crucial question: namely, whether the entity produced by OAR fails to grow into a mouse because it is a mouse embryo that is gravely defective or because on the contrary it is not a mouse embryo at all. On the other hand: insofar as the recommended experimentation yields its expected results—that is, yields entities that develop into “tumors”—, the experimentation will in fact have certainly confirmed only its original mechanistic premise regarding the nature of an embryo, even though researchers, on the basis of their faulty philosophical assumptions, will claim to have demonstrated that OAR produces a non-embryo rather than a gravely defective embryo.

In short, experimentation on animals as a matter of principle (*insofar as it remains within the ambit of the OAR proponents' mechanistic premise*) will not and cannot prove what it sets out to prove, even as such experimentation will create, and cannot but create, the (dangerous) illusion of having delivered just that proof. Its success will be that of a self-fulfilling prophecy.

First question: Evangelium vitae (EV), paragraph 60, states that a life is begun “from the time that the ovum is fertilized”—thus from the time an oocyte and a sperm cell, or, in the case of a mimicked conception involving nuclear transfer, an enucleated oocyte and a

²Fr. Nicanor Austriaco, O.P., cited in “Catholic Ethicists Support Emergent Stem-Cell Technique,” *National Catholic Register*, July 10-16, 2005.

somatic cell nucleus, are fused. How, in light of the foregoing comments, does the biotechnique proposed by OAR avoid the stricture enunciated in *EV* that “what is at stake is so important that, from the standpoint of moral obligation, the mere probability that a human person is involved would suffice to justify an absolutely clear prohibition”?

2. *Ontological dependency and its implications
for scientific inquiry*

(2) The proponents of OAR miss the ontological subtleties of the beginning of human life. Recognition of ontological dependence and mystery is necessary for judging rightly the original *fact* and not merely the *value* (or dignity) of the human embryo.

Another one of the signatories and main authors of the OAR statement, for example, says in an interview given coincident with the release of the statement that

there is no mystery about when the life of a new human individual begins. It is not a matter of subjective opinion or private religious belief. One finds the answer not by consulting one’s viscera or searching through the Bible or the Koran; one finds it, rather, in the basic texts of the relevant scientific disciplines. Those texts are clear. . . . Of course, science cannot by itself settle questions of value, dignity, or morality.³

To be sure, this comment was intended merely to affirm that human life begins at conception. However, while appealing to scientific textbooks may seem an easy way of settling the issue (and even appears sufficient in most arguments regarding abortion, in reference to embryonic life that already manifests initial signs of organized cellular development), this statement’s apparent reduction of life’s origins to a merely scientific-empirical question is a concession to positivism that is most dangerous precisely in the context of proposals like ANT-OAR, which mimic the mysterious origin of life mechanically in order to harness its power.

³Robert George, interview by Kathryn Lopez, “Scientific Breakthroughs,” *National Review Online*, 29 June 2005, interview text available online at <http://www.nationalreview.com/interrogatory/george200506290814.asp>.

As the comments in (1) suggest, determination of the presence of life *in its most subtle beginnings* is precisely *not* obvious in the manner of a positivistic fact, but always involves philosophical mediation (even if only unconsciously). Apprehending life in its most subtle beginnings involves a cognitional act that is not only empirical but also (at least implicitly) metaphysical in nature, an act which, rightly exercised, recognizes the mystery *characteristic* of the organism in its very *givenness*.

To insist on a cognitional act that goes beyond the empirical to the metaphysical is not at all to suggest that one can or should stop looking at the physical. On the contrary, it is to look at the physical more comprehensively.⁴

As already indicated, the organism in its actual wholeness is ontologically prior to the organism in the coordinated action of its parts, even as the coordinated action of its parts is simultaneously-subordinately necessary for that actual wholeness. This mutual if asymmetrical dependence of whole and parts, as constitutive, implies that the being and indeed the existing nature of an organism is in the first instance dependent, hence received: given to itself and not self-generated. The organism is not an absolute first cause of itself as a whole or in its parts. Because the being of the organism as such is first *given*, this givenness remains the inner and abiding condition of its acting.

The ontological dependence/givenness of the organism is so key because it is precisely here that we see the (paradoxical) link between God and the creature's *originality*—and just so far *independence*—as a creature. That is, God gives the organism to itself and so creates an originality⁵ that by definition we *cannot* know or control exhaustively, an originality that we *therefore should not* attempt or claim to know or control exhaustively.

But OAR does involve, at least implicitly, a claim to know and control the beginning of human life exhaustively—exhaustively

⁴The OAR proponents, for example, do not look (carefully enough) at the fact of the fusion of the oocyte and the donor cell nucleus because they have already decided that, in principle, on the level of theory, that fusion should not matter . . . because of the mechanistic assumption that epigenetics determines cellular identity and so the identity of the embryonic one-celled organism.

⁵In fact, nature as a principle of motion was already Aristotle's way of thinking about this originality.

enough, that is, to be able to remake the act that originates a new human being into an act that (seemingly) originates only a pluripotent stem cell. OAR's reliance on science (in its conventional understanding) to discern the presence and absence of incipient human life is not neutral or innocent, but rather involves, concretely, an implicit claim to be able to control that life's origins. But this claim could be true only if human beginnings were radically transparent to human ingenuity and technique—only if, in other words, they were bereft of mystery. OAR's constitutive failure to perceive, and to reckon with, the mystery of human beginnings, is already sufficient to raise serious ethical red flags about OAR. To miss the mystery of human origins is to miss the substance of human dignity, and so to participate in the depersonalization of the embryo to which OAR claims to be an alternative.

The fact that recognition of the ontological dependence (and corresponding mystery) of the organism indicated here exceeds simple positivistic determination, or empirical verification *per se*—and hence exceeds a science limited to such verification—does not render such recognition merely a “subjective opinion” or indeed “private religious belief.” On the contrary, ontological dependence is a matter of the reality of the organism, and hence is objectively accessible to all reasonable human beings (even if religious belief is necessary for an adequate or complete understanding of this reality).

The considerations introduced here may appear arcane to some, but such an objection misses the point that this is just where the present capacities of biotechnology, and specifically OAR, have brought us: namely, to the question of the meaning of embryonic life in the mysterious subtlety of its *origin* or *original nature*, an origin which, involving as it does *ontological* dependence, remains effective *within* the embryo as a whole and in all of its parts for the duration of its existence.

On their face, then, the interview statements above block us in principle from recognizing ontological dependence and its corresponding mystery as integral to the objective meaning—being and acting—of the embryo, and thus from insisting that science itself, conceived in light of its proper intention of intelligence, needs to remain open to integrated completion in and through philosophical (and indeed, finally, also theological) reflection.

Second question: If ontological dependence is truly *in* the organism, indeed is constitutive *of* the organism, does it not have methodological implications, and in turn ethical implications bearing

on the nature of (scientific) method? What does ontological dependence with its corresponding mystery signal in terms of the *principled* limits, both in our ability to know exactly when embryonic life has begun, and in our ability, consequently-simultaneously, to control that origin with exactness? Do not the mechanistic assumptions of the OAR proposal, reinforced by positivistic implications such as those carried in the above interview statements, force deleterious prejudgments in response to these questions?

3. *Scientific method: working with nature or against it?*

(3) The pluripotent stem cell research advocated in OAR proceeds by manipulating cells in an *in vitro* environment in and from their origins. Adult stem cell (ASC) research, on the other hand, presupposes cells that have matured in their natural-organic environment. ASC research thus *depends* in a more substantial and significant way on nature herself, on the organismic causality proper to nature. ASC research thus follows in more integrated fashion the *order given by nature*, which is to say the *givenness of order* proper to nature in its rightful understanding.

ASC research, then, is carried out in a manner more respectful of the integrated environment proper to organisms, the logic of which is irreducibly different from that of the necessarily fragmented environment provided *in vitro*. Research with embryonic stem cells has reported no significant progress in terms of producing healthy tissues or organs—producing on the contrary only severely defective ones—while adult stem cell research on the contrary is reporting increasingly significant results.⁶

Third question: Might there not be a philosophically principled, and not merely empirically based, reason for the difference in

⁶Cf., for example, the statement contained in the letter by some 55 scientists to Senator John Kerry during the 2004 presidential election campaign: “there is scant evidence that embryonic stem cells will form normal tissues in a culture dish, and the very versatility of these cells is now known to be a disadvantage as well—embryonic stem cells are difficult to develop into a stable cell line, spontaneously accumulate genetic abnormalities in culture, and are prone to uncontrollable growth and tumor formation when placed in animals.” Cf. also C. Allegrucci, C. Denning, H. Priddle, and L. Young, “Stem-Cell Consequences of Embryo Epigenetic Defects,” *Lancet* 364 (2004): 206–208.

research results? Given the irreducible difference between the causality exercised in integrated-organic environments and that exercised in (necessarily) fragmented *in vitro* environments, and given the consequent inability of the latter ever to replicate the former completely and exactly in all its subtlety, should we not expect the cells (tissues, organs) generated in these respectively different environments to be different and to behave differently, even if that difference cannot be readily observed? What are the warrants for assuming that such differences, possibly indiscernible in an empirically discrete manner or in the relatively short run, may not for all that still turn up in the form of defects whose severity will become clear only in the long run?

Perhaps it should be stressed that this is not an argument from ignorance, or an appeal to mystification. It is rather an observation that, so long as the above questions have not been settled, it is at the very least highly imprudent to pursue a research strategy like OAR—imprudent, that is, given the strictures of *Evangelium vitae*.

4. The “nuptial body” and the finality of the gametes

(4) OAR assumes that manipulation of the oocyte is unproblematic. It assumes that the finality for procreating life proper to the oocyte makes no intrinsic ethical demand upon the experimental researcher. Even if in an immediate way this problem of the finality of the gametes is not as serious or damning as the cloning problem, it still is of major significance when the problematic is looked at from a larger perspective: at the very least, OAR appears to treat the body as “pre-moral,” that is, in an objectifying way as merely a quarry for “parts” (however much intended to be health-enhancing to some human being).

To be sure, the “parts” of a person’s body are rightly made available to another person in cases like organ transplants (assuming certain conditions such as voluntariness and the like). The difference in the case of the gametes, however, is (*inter alia*) that sound philosophical and ethical principles have always recognized the special significance of the finality of the human body’s sexual/reproductive organs, by virtue of their being bound up so directly with the origins of life.

Fourth question: Is this reduction of the oocyte to a mechanism for harvesting parts consistent with the Church's theology of the body, for example, with the finality of the gametes as implied in John Paul II's notion of the "nuptial body"? Has the oocyte not become in OAR rather an instance of the "pre-moral" body rejected in *Veritatis splendor* (see n. 48)? Does not OAR *eo ipso* do violence to the human body at the source and original place of its (mysterious) procreative capacities?

5. *Why the haste?*

As stated at the outset, the Joint Statement on behalf of OAR implies definite positions with respect to the issues outlined above. The positions it implies, however, are left largely unargued. The Statement has been put forward in a question-begging fashion relative to the issues raised, all of which bear significantly on our capacity to defend reasonably—consistently and persuasively—an integrated vision of human life and its dignity.

Why the rush to judgment and the foreclosure of argument through the issuing of a manifesto, in matters of such vital importance?

The proposal has been put forward as a strategy for preempting the movement in the United States Congress to overturn President Bush's ban on federal funding of stem cell research involving the destruction of embryos. More broadly, the proposal was put forward to blunt the criticism of President Bush that he is anti-science—which is why the ANT proposal was suggested to the White House already before the election—and to help pro-life candidates in general for the same reason. Even if one has grave reservations about the potential fruitfulness of such a strategy in purely political terms (as I do), one can and should applaud the pro-life intentions of the signatories that drive the strategy. At the same time, the content of the strategy should cause grave concern among those who share these pro-life intentions. I conclude with a single comment in this connection.

Evangelium vitae affirms that, "when it is not possible to overturn or completely abrogate a pro-abortion law," it may be legitimate nevertheless to support proposals "aimed at limiting the harm done by such a law. . . . This does not in fact represent an illicit cooperation with an unjust law, but rather a legitimate and proper attempt to limit its evil aspects" (n. 73). The conditions of

such support, however, are clear. Those who support such laws must see to it that their absolute personal opposition to procured abortion is well known (n. 73); and they must not cooperate formally in practices which, even if permitted by civil legislation, are evil and contrary to God's law (n. 74).

To be sure, the signatories of the Joint Statement are known for their opposition to procured abortion: they all understand abortion as the unjust taking of a human life and condemn it.

The difficulty in the present case, however, is that, despite their clear opposition to abortion, the signatories have failed to show conclusively that OAR does not present us equally with a species of the evil of homicide: that OAR is not the cloning of defective humans. Having presupposed (however unwittingly) a mechanistic criterion for determining the nature of embryonic life, they in fact advocate the OAR procedure as something *intrinsically ethically good*.

In a word, the signatories have put forward a proposal whose *intention* clearly expresses opposition to the killing of embryos even as its *logic* permits what is quite possibly a more subtle form of just that killing. The proposal for this reason fails to meet the conditions indicated in *Evangelium vitae*.⁷

More generally, the OAR proposal would set in place, as a matter of public policy, a logic of research—a mechanistic logic with respect to nature, to creation, to the nuptial body—that attenuates at its source and in its root meaning the Catholic vision of life. The OAR proposal thus removes from its proponents' intended witness to the dignity of human life the larger and deeper framework of meaning and truth within which alone, finally, that dignity is understandable and sustainable.

The question therefore must be asked whether, in proposing OAR as a political strategy, the signatories have not given away the very heart of what they mean to protect . . . and for what? □

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⁷Given (1) the fusion of the oocyte and the somatic cell nucleus and given (2) the fact that epigenetics does not determine cellular identity, and so does not determine the identity of the embryonic one-celled organism, then at the very least we have to act as if OAR/ANT involves the mimicked conception of a human entity: cf. *EV*, 60.