E. Christian Brugger devotes a considerable portion of his essay “ANT-OAR: A Morally Acceptable Means for Deriving Pluripotent Stem Cells. A Reply to Criticisms” to responding to David Schindler’s critique of the OAR proposal in the pages of Communio. Brugger singles out for particular rebuttal Schindler’s claim that supporters of OAR have not yet given us sufficient assurance that the procedure would not produce human embryos. As Brugger reads him, Schindler is demanding more evidence on this score than he can reasonably ask for. His interrogation of OAR, lacking any sound...
scientific or philosophical foundation, rests instead on an irrational, ultimately dualistic unwillingness to let the physical evidence garnered in laboratory experiments decide whether OAR produces embryos or not:

It is absurd to claim that an entity is a human organism when it expresses itself neither materially nor temporally in ways characteristic of human organisms. As I said, this is dualist; it denies discernibly human material characteristics to something human; the entity looks, expresses itself, and behaves like a pluripotent stem cell; it does not express itself in a way characteristic of a human organism, nor does it have any peculiarly human organismic behavioral characteristics; but it just might be informed by a human soul. This is like claiming that a human soul might be trapped inside a stone. If we can distinguish between any cell and a zygote, we should be able to distinguish between an ANT-OAR cell and a zygote.

Brugger boils Schindler’s position down to this: there are serious grounds for thinking that OAR produces embryos even if the OAR product “looks, expresses itself, and behaves like a pluripotent stem cell.” Unfortunately, Brugger is setting up a straw man here, for Schindler’s actual contention is precisely that the OAR product does not and cannot look and act like a pluripotent stem cell in at least one decisive respect: its coming into being. For if we compare OAR with SCNT, Schindler insists, we find that OAR uses exactly the same event—exactly the same fusion of an enucleated egg and a somatic cell nucleus—that SCNT uses to clone a human embryo. What Schindler is really asserting, then, is that, even if the OAR product looks and acts more or less like a pluripotent stem cell in other respects, its coming into being looks and acts sufficiently like the coming into being of a human embryo to raise serious questions about OAR. Far from asserting that physical tokens in general are irrelevant to distinguishing embryos from stem cells, Schindler is simply insisting that there is one physical token that trumps all the others in the particular case of OAR: has the new entity come into being in a sufficiently human species-specific way? In the following essay, I would like to restate and defend Schindler’s reasons for thinking that OAR supporters have not yet ruled out a Yes answer.

2.

As just noted, Schindler’s critique of OAR in the first part of his essay rests on the claim that OAR involves the same fusion of an enucleated oocyte and a somatic cell nucleus as cloning does. One element of Brugger’s response is based either on a misquotation of Schindler’s text or on Brugger’s reliance on a draft version of the article. His citation from Schindler refers in one place to a “fusion of an oocyte,” without the adjective “enucleated,” which is duly present in the published text. Brugger tries to make the case that Schindler’s insistence on the notion of “fusion” betrays an ignorance of the basic scientific structure of OAR: “[i]t is not the ‘fusion’ of a somatic cell nucleus and an oocyte,” Brugger reminds us. This is correct, of course, but it does not affect Schindler’s point in the least, which is that the fusion in question is the fusion of an enucleated egg cell and a somatic cell nucleus, as in SCNT. In Schindler’s view, this fusion is prima facie a “mimicked conception,” not because its mechanics are the same as in natural conception, where “a sperm penetrates an egg, [and] the nuclei fuse, giving rise to a diploid zygote with a totipotent epigenetic state,” but because its result is the same—as the (admittedly rare) successes of SCNT show can be the case. Obviously, OAR is not in vitro fertilization. Schindler’s question is simply whether, given its dependence on the same fusion of cellular materials as SCNT depends on, OAR might not be cloning. One may think that Schindler’s answer to this question is wrong, but one has to refute his arguments, rather than ruling them out of court as resting on flawed science. What, then, are these arguments?

---

6Ibid.
7As Brugger insists, the egg used in nuclear transfer is an enucleated one, with only its cytoplasm left. But that is just the point: the egg is enucleated so that the somatic cell nucleus—which has been detached from its cytoplasm—can receive a new cytoplasm so as to form a single cell. If no such fusion of the enucleated egg and the somatic cell nucleus into a new cell took place, then OAR proponents would be in the difficult position of maintaining the—frankly absurd—claim that OAR has the (magical?) power to turn this nucleus, which is itself not a cell, but a part of one, into a whole cell complete with a new cytoplasm.
3.

Schindler’s claim that OAR involves “mimicked conception” is not a description of the stated intent of the OAR proposal, but rather the conclusion of an argument that goes like this. If SCNT fuses an enucleated oocyte and a somatic cell nucleus to produce an embryo—to “mimic conception” as to result, though not as to method—and if OAR can succeed only under the same conditions under which SCNT succeeds, then OAR prima facie involves a “mimicked conception,” too. The force of this argument rests on Schindler’s demonstration that epigenetic modification of the cellular materials, pre-transfer or no, is not sufficient to guarantee, beyond a reasonable doubt, that the procedure does not involve the creation and/or destruction of embryos. In his rebuttal, Brugger offers two arguments against this demonstration, one scientific and one philosophical. Both, I will suggest, do not suffice to vitiate the prima facie appearance that OAR is a form of cloning. In explaining why this is so, I will also be restating what I take to be the core of Schindler’s argument that “epigenetics is not enough.”

(1) Brugger’s scientific counter-argument is that the zygotic epigenetic state, while not a sufficient condition for the existence of a new human individual, is certainly a necessary condition of it. The zygotic epigenetic state is, or is co-essential with, the materia apta, the requisite material platform for the actualization of a new human individual (more on the materia apta below). By the same token, he would argue, if, prior to transfer, we can prevent the epigenetic reprogramming action of the enucleated oocyte from yielding a zygotic epigenetic state, then we can effectively remove this platform and, in so doing, prevent any human individual from ever coming into existence in the first place. Conversely, if we can ensure that the enucleated egg’s reprogramming action results in a pluripotent stem-cell-like epigenetic state, then we can create an entity that, ab initio, was never a human embryo, but always a human pluripotent stem cell:

A one-celled embryo is by definition totipotent. The entity created by ANT-OAR is ab initio pluripotent. It therefore cannot be an embryo. But might it not pass, ever so instantaneously, through a state of totipotency during reprogramming? In principle, no. If Nanog expression (or expression of some other transcription factor, or combination of transcription factors and
precise gene modifications, etc.) is definitional of the state of pluripotency; and forced Nanog expression (or forced expression of . . .) characterizes ab initio the “biological artifact” that ANT-OAR brings into existence, being intentionally made to do so before nuclear transfer, then the entity never was totipotent. 9

The main problem with Brugger’s argument here is that it overlooks the fact that there is an interval of time between (1) the fusion of the enucleated oocyte and the somatic cell nucleus and (2) the completion of the reprogramming process. 10 One implication of the existence of this interval is that the enucleated oocyte cannot carry out its epigenetic reprogramming without first fusing with the somatic cell nucleus into a new cell. Brugger notwithstanding, OAR is not literally a form of direct cellular dedifferentiation, but the creation of a new cell that is the suppositum, the “ontological subject,” both of the reprogramming process and of whatever epigenetic states that process eventually results in. 11 The fusion of the


10 I am indebted for this valuable insight, as well as for much that I will say in the present paragraph, to José Granados, “ANT-OAR: Is Its Underlying Philosophy of Biology Sound?” in the present issue of Communio. It should be pointed out that, even if the time of the interval mentioned here is reduced to a seeming zero, the doubt that OAR produces an embryo remains as alive as before. Why? Because the time interval reflects a deeper logical sequence of defining events that come in the following order: fusion of the relevant cellular materials, initiation of the reprogramming process, formation of the “zygotic” epigenetic state. OAR has to work with this logical sequence, no matter how much it shortens the time between the stages: it needs the fusion of the cellular materials to have the reprogramming process, and it needs the reprogramming process to end up with (it hopes) pluripotent stem cells. According to Schindler, this shared sequence indicates enough identity with cloning to raise serious doubts whether OAR does not produce embryos, after all.

11 See Brugger, 756; 763. Brugger’s vagueness about the subject of epigenetic reprogramming is very telling. “[a]fter nuclear transfer into an enucleated oocyte,” he writes on pages 755–756, “the epigenetic state is reprogrammed from its formerly highly specialized state back to a state of totipotency. It goes through a process of epigenetic dedifferentiation. If it reaches its terminus, the reprogrammed cell is a zygote, a one-celled embryo, with the genotype of the donor of the somatic cell.” In the first sentence, and at the beginning of the second, the subject of the reprogramming is the epigenetic state of the somatic cell nucleus. In the middle of the second sentence, though, the subject suddenly shifts to the “reprogrammed cell.” This shift of subjects gives the impression that the cell
cellular materials results, in other words, in an entity that *puts itself* in the zygote epigenetic state through self-directed action. In other words, the simplest interpretation of the facts is that a new human being has come into existence and is running itself through the epigenetic reprogramming process. But the OAR proposal aims to modify only the *outcome* of this process. For the same reason, it leaves completely open the possibility that the procedure has created a human embryo with a defective developmental path. The fact that OAR programs—in modifications in its product’s epigenetic state before nuclear transfer does not affect this situation in the least. Since these modifications would actually take effect only at the end of the logical sequence of fusion—new cell—initiation of reprogramming process, programming them in before nuclear transfer does not guarantee that there was no embryo at the beginning of that sequence. Brugger’s insistence that OAR modifies prior to nuclear transfer turns out to be something of a red herring.

12If we do not follow this interpretation, then we have to deal with at least two problematic implications. First, we commit ourselves to saying that the process of fertilization is not the beginning of human life, but is itself an intermediate stage prior to the completion of the zygotic epigenetic state. Second, we have the difficulty of explaining what is the ontological subject of the obviously teleological, directed process of forming the zygotic epigenetic state. If this subject is not already a human being, then how can it direct itself into the epigenetic state of a human being?

13It is also worth pointing out that Brugger is vague on just how the transcription factors like Nanog involved in OAR are “characteristic of the pluripotent state” (Brugger, 756). Sometimes he seems to suggest that they are definitive of what a pluripotent stem cell is. But then he also acknowledges that they are just necessary conditions for the appearance of pluripotency. Which is it? It seems to me that the latter alternative must be the correct one, since, as Brugger says, the factors in question “appear to be essential for establishing and maintaining the state of pluripotency” (ibid.)—which means that they are (so far as we know based on the current state of the research) effective/instrumental causes of pluripotency, not the sum and substance of it. But if the mere presence of Nanog (or whatever) is not what defines a stem cell as such, but only what helps it establish and maintain its stem-cellness, then the premature forcing of its expression is perfectly compatible with the
(2) Brugger bases his philosophical argument against Schindler on the Aristotelian-Thomistic notion of *materia apta*, the material organization required as a platform to sustain a given substantial form. According to Brugger, *materia apta* provides this platform because it is the seat of what he calls the “active potencies” that enable the substantial form to display its characteristic operations in the given matter. On Brugger’s account, however, the zygotic epigenetic state is definitive of the *materia apta* for humanness and so determines the “active potencies” for the behavior characteristic of human organisms.\(^{14}\) By the same logic, suppressing the OAR product’s zygotic epigenetic state deprives it of the platform for the active potencies of humanness—and so deprives it of its human status. If this suppression can be made to coincide with the new entity’s coming into being through pre-transfer biochemical modification of what will be its initial epigenetic state, then, by the same logic, it will never have been a human organism at all. Since *agere sequitur esse*, Brugger reasons, the prevention of the *materia apta* for the active expression of a human being’s characteristic operations is necessarily the prevention of the genesis of any human being in the first place.

There are two main problems with Brugger’s argument here. (i) First, Brugger’s invocation of the Aristotelian-Thomistic doctrine of *materia apta* misses the point. Schindler is not denying this doctrine, but claiming that the fusion of the enucleated oocyte and the somatic cell nucleus itself already provides a sufficient *materia apta* for the existence of a human being. Brugger fails to address the crucial question, which is not whether or not OAR can modify the outcome of epigenetic reprogramming, but whether or not such modification is by itself sufficient to rule out the creation of a new human embryo. (ii) This brings me to the second problem with Brugger’s philosophical argument, which is that it comes perilously close to overturning the Aristotelian-Thomistic priority of act over potency, especially when Brugger faults Schindler for failing to understand that “it is precisely the character of the organic material, which includes *inter alia* the material’s genetic imprinting, that possibility that we have created an embryo with a developmental defect, rather than a pluripotent stem cell.

determines the possibilities for humanness.” As far as I can tell—and it is difficult to tell because his argument is vague and tangled here—Brugger seems to be confusing the active potencies, as nature-rooted powers, with the material basis of their expression, and then taking the latter as quasi-constitutive for human identity. But if active potencies flow from actualized natures, and not vice versa, then the absence/modification of the zygotic epigenetic state is not by itself sufficient to dispose of the question Schindler has raised. It leaves completely open the possibility that OAR creates embryos with developmental defects set to go off already in the zygotic stage of their existence. And so we find ourselves back at square one.

4.

The scientific and philosophical battering rams that Brugger deploys to knock down Schindler’s doubts against OAR leave them not only unbowed, but also unbloodied. Let me briefly explain why I do not think that any possible arguments would be enough to dispel them.

Normal conception follows a certain logical-temporal sequence: first, the process of fertilization and the concomitant coming-into-being of a new human individual, and then the initiation of the epigenetic reprogramming process. SCNT also follows this process, except that it substitutes the fusion of an enucleated egg and a somatic cell nucleus for fertilization—which is why Schindler speaks of a “mock fertilization” in this context.

---

15 Ibid.
16 See Granados, “ANT-OAR: Is Its Underlying Philosophy of Biology Sound?”
17 One of the connotations of the term “mock” or “mimicked conception/fertilization” is that even SCNT, which alters the natural event of conception, still has to rely on it in some sense. Whatever else it does, SCNT relies on the same logical-temporal sequence as nature does: fusion of the relevant cellular materials—coming into being of a new individual—epigenetic reprogramming. The fact that the relevant cellular materials are no longer sperm and egg, but somatic cell nucleus and enucleated oocyte, does not change this fact, for if the fusion of the enucleated oocyte and the somatic cell nucleus did not have by nature at least some of the powers that the fusion of the egg and the sperm does, then SCNT would never produce embryos. The fact that, in spite of this, most trials of SCNT fail to produce viable embryos is no argument against this consideration.
Cloning failures are better explained by the unnatural conditions to which it subjects the cellular materials than by the assumption that they retain nothing of the natural teleology inherent in the sperm-egg fusion. SCNT does not replace nature, but mutilates it—while keeping just enough of it to lend it whatever (limited) efficacy it has.

Of course, Brugger might retort that there are certain characteristic attributes that, like the “inseparable accidents” of Scholastic philosophy, cannot be lacking to a human organism, so that their non-appearance always and necessarily signifies that no human organism is present, either. Now, this retort is partly correct, in that there are such “inseparable accidents” that, while being accidents, are nonetheless necessarily entailed by the essence of the species homo.
Nevertheless, this retort overlooks the fact that an entity can have the specific essence of man, and so be “owed” the attributes that follow inseparably from that essence, while failing to have the actual physical wherewithal to instantiate those attributes. For example, a child born with a neck disease that made it physically impossible for him to laugh would still be a human being who, by virtue of his sharing in the specific essence “man,” ought to be able to laugh. Put more simply, the child is naturally a “laughing animal,” even if he cannot laugh because of a grave physical impediment. I recognize, of course, that a typical physical equipment goes with the essence of the human being; my point is simply that the equipment can be defective in individual cases without this meaning that there is no human being present who, by virtue of his human status, ought to have that equipment. In either case, the principle gets turned on its head, and agere sequitur esse comes to mean esse sequitur agere.

What I have called OAR’s conceptual flaw is not superficial, for it sits in the very attempt to get stem cells without embryos while using nuclear transfer to do it. Nor can scientific experimentation remedy this inner contradiction in the OAR proposal. The reason for this is not that experimental testing in itself is worthless. It is that the construction of the experiments for testing OAR will necessarily partake of the OAR proposal’s conceptual flaw, and so will either bypass the central issue—when is a human organism actually present?—or yield outcomes that can appear favorable only on the assumption of some form of mechanism. I am not suggesting, of course, that we should move the discussion to a purely theoretical plane, without any reference or deference to the empirical phenomena. I am rather suggesting that OAR—and so the experiments designed to test it—focuses on the wrong set of empirical phenomena and then justifies this wrong focus with untenable arguments. I am suggesting, in other words, that OAR has a built-in, fatal neglect of what may be the one decisive phenomenon in the present context: the fusion of the enucleated egg and the somatic cell nucleus that, very arguably, establishes a human esse whose agere OAR modifies in its expression, but not in
its substantial basis. Even if OAR succeeds in producing a pluripotent epigenetic state, then, there remain serious reasons for doubting whether it has not obtained it on the back of an embryo.\textsuperscript{19}

If I am right, Schindler and Brugger, or, more generally, the editors of \textit{Communio} and the signers of the Joint Statement in favor of OAR, do not disagree because the former foolishly deny the principle of agere sequitur esse, while the latter sensibly defend it. No, both parties agree about the centrality of agere sequitur esse, but differ as to when they think it starts to be relevant: with fertilization or its “mock” equivalent, the fusion of enucleated egg and somatic cell nucleus (the editors of \textit{Communio}), or only on the completion of epigenetic reprogramming (OAR supporters)? Moreover, although the two answers are symmetrical in their intention to privilege the agere sequitur esse principle, they are not at all symmetrical in their respective fidelity to it. Interpreting epigenetic reprogramming as a teleological self-unfolding revelatory of an already-existing human organism, the first answer expresses the Thomistic principle to a tee, whereas the attempt to establish the second answer and vitiate the first ends up with an inversion of this principle that logically requires question-begging and/or mechanism. The tables, in other words, have been completely turned, and it turns out that Schindler, and not Brugger, is the real Aristotelian here. For Schindler is not, as Brugger asserts, dualistically

\textsuperscript{19}Let me record, however, my skepticism about the likelihood of OAR’s really managing to produce pluripotent stem cells. The OAR concept supposes, after all, the theoretical possibility of sufficiently replicating the conditions under which a pluripotent stem cell normally arises—in what is in fact an abnormal environment, whose distinctive commonality with the normal one is the presence of certain pluripotency-related transcription factors, such as, for example, Nanog. This decision to treat the normal environment and process in which stem cells arise as if it were cleanly replaceable or simply irrelevant seems logically to entail the mechanistic assumption that, for all practical purposes, a stem cell is nothing but a nucleus+cytoplasm+active Nanog (and/or other similar factors). Unless we live in a mechanistic universe, however, such a decision is very likely to have visible consequences that will render the claim that OAR has directly created stem cells suspect even from a (sufficiently perceptive) empirical point of view. We just do not, and probably never will, have the sort of control over the nature of human origins which OAR seems to bank on. If we did, then, as I said just now, there would be no need for nuclear transfer, and direct cellular dedifferentiation would be firmly within our grasp.
ignoring the human body, but arguing that proponents of OAR are—and, that, in so doing, they are unwittingly colluding in the erosion of respect for that body in the earliest stages of its existence.

5.

In conclusion, I would like to point out that, even if the argument I have just outlined is shown to be mistaken, and the concept of OAR is not problematic from the point of view of natural philosophy and morality, the fact remains that the procedure will not be 100 percent reliable. Even if I am dead wrong in the foregoing essay, in other words, OAR will still occasionally mistakenly produce embryos. Now, Brugger admits this, but he argues that, so long as the incidence of mistaken embryos is “statistically negligible,” there can be no reasonable doubts about the morality of OAR. Why not? Because the intention not to produce embryos can justify the risk of occasionally mistakenly producing some by the principle of double effect, as Brugger explains in the following passage:

If failure rates are statistically negligible, and testing otherwise consistently establishes that the entity produced from ANT-OAR is not an embryo but a pluripotent cell; and the firm intention is to protect the value of human life by never producing a human organism; then it may be reasonable to proceed with testing in human cells knowing that a very remote possibility exists that an embryo may result; that possibility is accepted as an unwanted and unintended side effect of an otherwise morally justifiable act.

There are two serious problems with this argument, it seems to me. First of all, even if we were to suppose that it is statistically

20 Indeed, it is Brugger who risks dualism when he argues that the zygotic epigenetic state must already be present in “active potency” before humanity can be instantiated, forgetting that the organization of matter required for that state is itself logically dependent on the instantiation of humanity already having happened.

21 I leave aside the fact that the transition from animal to human experimentation will also require a certain number of trials before a reliable experimental protocol for human OAR is established—a time in which similar mistakes are also very likely.

very unlikely that OAR would mistakenly produce an entity that
even Brugger would call an embryo, a supposition that is not at all
clear given the highly speculative nature of the OAR proposal, the
fact of the matter is that no one could be sure that it would not
produce such an entity—until it was too late. Imagine a parallel
situation: a friend gives you a gun with 20,000 chambers and invites
you to play Russian Roulette with the assurance that only two or
three of the chambers are actually loaded. Since any given chamber
might be loaded, you would be foolish to accept the challenge on
the grounds that the odds were seemingly in your favor. After all,
the first pull of the trigger might put one of the 3/20,000 bullets into
your skull. Would it not be just as foolish to pursue human OAR,
since on any given trial you might be making an embryo-producing
mistake? Wouldn’t trying human OAR be tantamount to playing
Russian Roulette with embryos?

My second problem is with Brugger’s invocation of the
principle of double effect. While double effect does legitimate the
knowing risk of side-effects otherwise impossible to be chosen
ethically, it does not do so in just any situation. It confers this legitimacy
only in view of abnormal circumstances that pressingly require or
recommend the action to which the knowing risk of otherwise
unchooseable side-effects is inevitably attached. Since the—let us be
perfectly honest—remote possibility that the scientific community
may one day give up conventional methods of embryonic stem cell
research for something like OAR, or the less remote, but still distant,
potential for medical advances, does not meet this test of urgency,
the principle of double effect has no real relevance to Brugger’s case.
But if double effect does not apply here, then what Brugger’s
argument logically amounts to is this: a possible future good (the
conversion of the scientific community; potential medical advances)
justifies a present evil (the possibility of accidentally making a
“statistically negligible” number of embryos). This sort of argument
logically entails, or expresses, something less like traditional Catholic
moral theology and more like proportionalism. Does Brugger really
want to go this route?

Brugger’s precipitous appeal to double effect bears out, it
seems to me, the pertinence of one of the central questions of
Schindler’s essay that Brugger nowhere addresses: whence the haste to make ANT-OAR work—even at the (supposedly acceptable) risk of possibly sacrificing a few human lives? Is it really so important to assure embryonic stem cell researchers that they can have what they want, after all? Wouldn’t it be better to put the brakes on the ANT-OAR project, at least for a while, and to ponder the implications of what, I hope to have shown, are not at all irrational cavils, but strong and serious reasonable doubts about its conceptual and moral viability? It strikes me that advocates of ANT-OAR have nothing to lose and everything to gain by doing so.

ADRIAN J. WALKER is an associate editor of Communio.