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Wishful Thinking Will Not Obviate Embryo Use

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Abstract

Upon hearing of purported nonembryo sources of human pluripotent stem cells, we need to ask not only whether the proposed sources yield such cells, but whether it is true as claimed that it would be morally better to shift to the purported alternatives. I argue that it would not be morally better. When we consider the morality of each proposal in turn, we find as to several that what defends them also defends the use of surplus embryos and clones in general. That leaves no reason to abandon the general case for the special case of compromised life forms. Another of the proposals is morally indefensible. Still other proposed techniques would themselves use or risk using embryos, not to mention that they may fail to produce pluripotent cells of sufficient quality. We shall not achieve a moral gain by adopting any of these proposals in lieu of using donated embryos barred from the womb by donor instructions.

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We have heard it urged that society should forego embryonic stem cell research in the belief that regenerative medicine can succeed without use of embryos. In the first instance, this recommendation has issued from wishful thinking that the scattered multipotent stem cells of the developed human will serve as functional equivalents of the pluripotent embryonic. Other recent proposals foster wishful thinking in another vein. It has been said or assumed that the use of various hypothesized alternatives to embryos would constitute a morally superior way of obtaining pluripotent stem cells (PSC). As proponents of the hypothesized alternatives have trained their sights on the technical challenges of producing such cells, they have been less attentive to establishing their premise of moral superiority. In the following, I consider that premise as to each alternative in turn. Before any of us, especially policymakers, accept an invitation to bet the welfare of sick patients on purported alternatives rather than on expanding embryonic stem cell research, we should know whether that premise of moral superiority is true.

Mutant Clones That Are Not Embryos?

In the first alternative on offer, William B. Hurlbut imagines products of nuclear transfer that are not embryos yet issue in PSC *(1)*. Though he speaks of performing "altered nuclear transfer," he does not suggest any new method of nuclear transfer. Rather he proposes mutating source DNA before transferring it. He speaks of inactivating the *CDX2* gene (thereby precluding formation of a placenta and thwarting implantation), inactivating alleles implicated in "intercellular signalling" and an "integrated pattern of development," and effecting mutations that result in a "level of disorganization."

Suppose that there comes to exist a product of nuclear transfer that for Hurlbut is not an embryo but that yields PSC. I shall refer to such a product as a "hurlclone." It is proposed that we use hurlclones in regenerative medicine and that we forgo, as morally impermissible, the use of surplus embryos and clones other than hurlclones. Without intending to criticize Hurlbut, whose effort

has been well-intentioned, the following refers to his remarks insofar as the hurlclone proposal gains its fullest expression there.

To make plausible that a given hurlclone fails to be an embryo, Hurlbut adduces three considerations. The first is the hypothesis that a hurlclone will "mimic" in defectiveness those products of fertilization that perish in vivo. The assumed premise seems to be that defective products of fertilization are not embryos. That premise collides with common understanding. While it may sometimes occur that fertilization begins and abruptly ends before producing a zygote, we classify as embryos all oocytes activated by fertilization, as well as their prefetal developmental successors. That the successor of an activated oocyte dies without implanting may evidence defects; it does not disqualify it as an embryo.

Secondly, it is suggested that a hurlclone may fail to be an embryo by dint of being so disorganized as not to constitute an organism. But what support is there for the belief that a PSC source could be so disorganized as not to constitute an organism? Hurlbut replies that hurlclones would also "mimic" teratomas and hydatidiform moles, forms in which PSC are found. The suggestion is that if a given one of these degenerate growths is not an organism, neither is a hurlclone. No such conclusion follows. A given teratoma or hydatidiform mole either undergoes embryogenesis or it does not. If it does not undergo embryogenesis, then in that important attribute, it differs from a product of nuclear transfer. If it does undergo embryogenesis, the process is degenerate. The abnormal genetics of the resident PSC are cancerous. An immature oocyte from which such a growth originates may not even develop a zona pellucida. So in either case, the analogy to these growths neglects an important difference between them and the activated oocytes produced by nuclear transfer. That a given PSC source is not an organism does not suggest that a rather different PSC source is not an organism.

Third, it is imagined that a hurlclone embodies a "genetic alteration sufficient to prevent embryogenesis" *(2)*. Of course we can readily imagine a doomed clone. Even clones that survive to birth are, in Rudolf Jaenisch's phrase, only "the least abnormal" *(3)*. The question is whether a mutant will yield PSC. In the mouse, Meissner and Jaenisch have demonstrated that one can produce mutant clones that develop to the blastocyst stage and yield PSC, but lack the ability to implant. Their experiment precluded implantability by inserting in the donor genome a gene encoding an RNAi that inhibits *CDX2 (4)*. But as any such maneuver averts the Scylla of utterly defeating a product's ability to issue in PSC, it is drawn to the Charybdis of embryogenesis. In nuclear transfer, activation of the enucleated oocyte initiates embryogenesis. The activated oocyte divides. Its successors replicate their chromosomes and divide. So far as we now know, only after oocyte activation and cleavage does there eventuate the window of opportunity—the pluripotency interlude around day 5 between totipotency and specialization—for an investigator to derive PSC.

We have good reason for scepticism concerning the notion of a PSC-yielding mutant clone that is not an embryo. In the case of a *CDX2* mutant, "an alternative interpretation would be that embryos lacking *CDX2* develop normally until *CDX2* function is required, at which point they die" *(5)*. "The *CDX2*-deficient embryo," say its recent creators, "is not obviously abnormal before the onset of *CDX2* expression" *(4)*.

A Gesture at Morality

But to take the hurlclone proposal in its strongest form, let us assume that there exist hurlclones that are not embryos. Hurlbut seems to think that given the classification of a hurlclone as a nonembryo, it is evident that it is morally permissible to use the hurlclone in research. On the contrary, to justify experiment on any human life form, a moral argument is needed. That need is surely no less when the form is concededly embryo-like.

Hurlbut does not state a moral argument for the use of hurlclones. He does stake a claim that a hurlclone "does not have the principle of life in it," and again that hurlclones "have no inherent principle of unity, no coherent drive in the direction of the mature human form" *(1,6)*. These notions of a physical object possessing a principle or drive are implausible metaphysical posits. If being an object of moral concern depends upon possessing these attributes lying beyond observation, there may be doubt about you and me. A discussant who claims to discern the posssession or lack of such imagined attributes by various living beings will get no farther in the present moral reckoning than will an Hegelian telling an audience of empiricists that the Absolute enters into progress. Even for attributes that are observable and accurately discerned, it remains to argue how they bear on what we should do.

Eventually Hurlbut comes round to gesturing at morality when he projects that source DNA mutations will effect in hurlclones "the level of disorganization deemed essential to fulfill the moral criteria of this project" *(7)*. Here he seems to suggest that some extent of organization is a necessary condition of embryohood for moral purposes. But to gesture at morality is not to state a moral argument. The notion that some extent of organization is a condition of embryohood, or of ineligibility for use solely as a means, is not only nebulous. For Hurlbut as an opponent of embryo use, the notion backfires. As he contrasts "cellular growth lacking integrated form" and "a living organism" *(8)*, he imagines a false dichotomy. Lack of integration is an attribute of every embryo during the several days between the zygotic and blastocyst stages. During that interval, it has been said, the embryo is a mere clump of cells "stuck together" and not interacting, hence not an integrated functional unit *(9)*. It has been argued that by virtue of this circumstance alone, it is morally permissible to use any embryo donated to research. Suggesting that disorganization is a "moral criterion" broaches a defense not only of hurlclone use, but of that which Hurlbut opposes, embryo use in general. Disorganization fails to ground a compelling defense of either practice: during the interval between zygote and blastocyst, the embryo *contains* functional units in the form of totipotent blastomeres. And a functional unit is not the only kind of biological unit. Another kind is a genomic unit, and an embryo is at all times a genomic unit. Just as the status of genomic unit results in moral concern attaching to an embryo notwithstanding nonintegration, the status of genomic unit suffices for moral concern to attach to a hurlclone notwithstanding nonintegration. We have not been given a moral reason why it would be permissible to use a hurlclone as a means. The gesture at morality has failed by dint of the naturalistic fallacy

espied by G. E. Moore *(10)*. It has incorrectly been supposed that a moral conclusion follows solely from a biological classification, namely, from "nonembryo."

The Defense Justifies the General Case

If a moral defense for using a hurlclone has not been offered, what defense could a proponent construct? The proponent may begin from the understanding that a hurlclone has been formed from cells donated to medicine for the purpose of hurlclone formation. Hence a hurlclone itself may be considered donated.

But that does not suffice. A compelling defense requires this premise: *intrauterine transfer of the donated being has been forbidden through a permissible exercise of donor discretion*. I shall call this "the no-transfer premise." The no-transfer premise is needed to establish that no wrong will occur to any woman transferee or offspring. While Hurlbut takes pains to point out that his mutations will be effected in source DNA prior to transfer, hence prior to existence of a hurlclone, this serves only to defend nuclear transfer per se. There remains a plausibly asserted duty that places demands upon us concerning what happens in respect of an embryo-like form after creation *(11,12)*. That is a duty not to cause a woman to bear, or to bring forth, any seriously defective offspring. To establish that hurlclone research will not violate that duty, the defense needs the no-transfer premise. The defense also needs the no-transfer premise to meet the following concern. An investigator, motivated by the incentive to render a hurlclone sufficiently embryo-like as to yield PSC, may not be able to establish to a moral certainty that no possible person corresponds to a hurlclone. Despite Hurlbut's optimism that knowledge yielded by future experiments will allow one to predict nonimplantability, the only decisive assay for nonimplantability is intrauterine transfer. That is not a morally permissible experiment. The defense must rely on the no-transfer premise. It needs that premise so that it may hold that to a hurlclone there does not correspond any possible person harmed by experiment, and for whose welfare there obtains a duty to rescue.

The defense of hurlclone use also needs a moral premise. Otherwise it will fall into the naturalistic fallacy. By parity of reasoning with the invocation of informed consent to justify tissue use, but without begging the question against the view that an embryo-like hurlclone is a distinct being to which moral concern attaches, the defense of hurlclone use may invoke this premise: *it is permissible to use solely as a means to a humanitarian end an embryo-like being if the donor's instructions have forbidden intrauterine transfer.*

From the no-transfer premise and the foregoing moral premise, one may deduce that it is permissible to use a hurlclone donated to medicine. If we have reasonable grounds to believe that use of hurlclones in research could contribute to the relief of suffering and disability, it would be virtuous to pursue such research.

The foregoing analysis reveals the following. For an embryo-like being, one does not lay a moral ground for experiment solely by interposing distinctions concerning biological characteristics. Such distinctions may appear contrived, self-serving, or morally arbitrary. The most secure moral ground consists in the decisions of people—the morally permissible decisions of those privileged to decide what happens to their cells.

Notice the following about the no-transfer premise. The premise is not peculiar to hurlclones. It may also be satisfied for any embryo outside the womb. For as I have elsewhere argued *(13,14)*, no woman lies under a duty to undergo the transfer into her of an embryo lying outside her. Nor are progenitors obliged to give up for adoption an embryo created from their cells. When the no-transfer premise is satisfied either for an embryo donated as such (e.g., a surplus embryo) or formed from donated cells (e.g., a clone), the second moral premise also comes to bear. That a donee may permissibly use embryo-like beings permissibly barred from the womb remains tenable for a donated embryo because a prohibition of intrauterine transfer so bounds the developmental potential of an embryo that the embryo cannot develop beyond about day 10. We could not gain anything for an embryo already barred from the womb, or for any other being in the universe, by classifying it as a person for purposes of the duty not to kill and declining to use it in research. Nor does a possible person correspond to an embryo barred from the womb. As we have reasonable grounds to believe that we could contribute to the relief of suffering and disability by using donated embryos in stem cell research, it is virtuous to pursue that research. What is more, all leading moral views assert some version of the duty of mutual aid. This duty commands us to come to the aid of those in peril when we have reasonable grounds to believe that we can assist them without unreasonable cost. Since we can perform human embryonic stem cell (hESC) research at no cost in potential lives, and since we cannot gain anything by classifying embryos barred from the womb as persons, and since we have reasonable grounds to believe that hESC research will succeed, the duty of mutual aid beckons us to such research as a collective duty.

What we have just learned is that a compelling moral justification for using donated hurlclones consists in an argument that justifies using every donated embryo. The argument justifies hurlclone use regardless whether a hurlclone is or is not an embryo. It justifies research using donated embryos in general. The moral analysis of hurlclone use does not lead to a ground for confining research to that special case; it leads to support for research using the entire universe of donated embryos, surplus and clone. Upon taking into account the duty of mutual aid, it even follows that research using donated embryos is collectively obligatory.

As a mathematician would say, when we have established a result for the general case, we need not confine ourselves to the special case. The PSC resident in teratomas and hydatidiform moles, to which Hurlbut likens hurlclones, are not, as Hurlbut claims, the "functional equivalent" of hESC *(15)*. If they were, scientists would be content to study them without need of hESC. These embryonal carcinoma cells are deranged as hESC are not. If hurlclones so mimic degenerate forms as to issue in cells of this cancerous sort, that will be no advance. Embryonal carcinoma cells have been studied to advantage since 1957. We need studies of normal cells. We need studies of numerous cell lines reflecting genetic diversity of healthy and afflicted individuals within a population. *Ex hypothesi*, a hurlclone's genome is so abnormal that it could never begin embryogenesis. *CDX2*, for instance, is an important gene; inactivating it could cause lots of problems—even if not enough to scuttle the prospect of deriving PSC, doubtless enough to affect the scientific usefulness of lines derived. Hurlbut surmises that

after stem cells are derived from hurlclones, the genetic malengineering might be reversed, as Meissner and Jaenisch achieved in their derived cell lines by deleting the gene for the inhibitor RNAi. But in a given case it could happen that the derived cells remain abnormal in some respect.

Cleavage-Arrested Embryos

An organism may be brain dead and yet, for some time after death, some of its cells may remain alive. Two biologists have urged that we regard "irreversibly arrested embryos," recognizable by failure to cleave after some specified time, as "organismically dead" *(16)*. They contend that since it is moral to remove living organs from a brain dead adult, it should be moral to remove cells from a cleavage-arrested embryo. In particular, they envision attempts to derive PSC from such of an irreversibly arrested embryo's blastomeres as are still alive.

What constitutes embryonic death and how we may reliably detect it are open questions. Cessation of growth understood as irreversible cleavage arrest is a plausible criterion. Confirming irreversibility may be difficult if, for instance, some embryos appear to cease growing, go through a resting phase, and then resume dividing. For their part, Landry and Zucker understand cleavage arrest to occur when cellular integration ceases. That understanding is problematic as to embryos prior to the stage at which integration begins. But let us assume that embryonic death is defined as, and reliably detectable as, irreversible cleavage arrest.

Cleavage arrest may occur as early as twenty-four hours after activation. If an arrested embryo is young enough, a removed totipotent blastomere will be capable of developing to maturity. For moral purposes, it will be an embryo. One could avoid this situation by using somewhat older cleavage-arrested embryos, if healthy blastomeres can then be obtained.

The present technique for deriving hESC begins with many cells taken from the inner cell mass of a blastocyst. While Landry and Zucker point out that there will likely exist some cells in a cleavage-arrested embryo that are not abnormal, we can only assume that most cells of a cleavage-arrested embryo are abnormal or dead. It is not known whether a mere handful of healthy blastomeres will issue in hESC. The chances and efficiency of derivation seem much higher when using a healthy embryo than when using a few blastomeres from a cleavage-arrested embryo. Even if someone succeeds in deriving hESC from cleavage-arrested embryos, it seems likely that by virtue of aneuploidy or whatever genetic defects have produced cleavage arrest in each case, the hESC will be abnormal in significant respects. "Scientists," George Daley has said, "will remain suspicious that they are abnormal and might lead to erroneous conclusions in research" *(17)*.

If one cannot eliminate the possibility that an apparently arrested embryo contains one or more live totipotent blastomeres capable of development to maturity, a consensus moral justification for using removed blastomeres must have recourse to the premise that one may permissibly use an embryo-like being permissibly barred from the womb. As we saw in the case of a hurlclone, that premise supports the use of all donated embryos barred from the womb. Speaking of cleavage-arrested embryos, R. M. Hare writes, "It is hard to see what is lost if such embryos with no potentiality for turning into babies are destroyed, since they will perish anyway." To this he adds, "it is just as hard to see why the same does not apply to other embryos with no hope of survival" *(18)*. If it is permissible to use cells taken from cleavage-arrested embryos on the ground that it would be futile to transfer them to a uterus, it should be permissible to use embryos that are barred from the womb. Given a justification for use of normal surplus embryos and clones, we have no reason to diminish the chances of success in research by using only defective embryos.

Parthenotes

Parthenogenesis consists in the development of an embryo from an oocyte activated without insertion of foreign DNA. Human parthenotes are doomed for inability to develop a functional placenta, and so it has been thought that they might serve as subjects of study and as a source of PSC yet escape classification as objects of moral concern.

The classification of a parthenote as an embryo seems conceded by saying, as in scientific parlance, that a parthenote develops to the blastocyst stage. A parthenote is in any case a developing organism. Moral concern will attach in view of the possibility, which may someday be actual, that one can intervene genetically to overcome abnormalities in imprinting implicated in placental failure. If that were accomplished, placental failure would seem a mere accidental attribute. Because imprinting is an observable chemical change in DNA, it is possible in principle to effect imprinting by external intervention. In mice a technique has been practiced that effectively supplies to a developing organism unimprinted alleles that in sexual reproduction would come from the paternal genome *(19,20)*. The most decisive defense of parthenote use is the circumstance that the donor has prohibited intrauterine transfer, the circumstance that justifies the use of all embryos so barred.

Parthenote genomes carry only maternally imprinted genes, and their epigenetic regulation further distinguishes parthenotes from products of fertilization and cloning. It is not known whether, if human stem cells can be derived from parthenotes, they will be pluripotent, or if they are, whether they "will behave as robustly as embryonic stem cells" *(21)*. Since parthenogenesis activates a female germ cell without introducing foreign DNA, it produces only females. So even if the process were to enable autologous transplantation, it would avail only young fertile female patients. Parthenotes are another special case for which we ought not settle when we can justify the general case.

Use of Embryos Before Transfer to Womb

In preimplantation genetic diagnosis (PGD), a fertility clinician removes a blastomere from an embryo at the eight-cell stage or thereabouts, then performs genetic tests on the blastomere. The justification for risking this procedure relies on the remarkable fortuity that in a high percentage of cases, an embryo will survive the intrusion and the loss of a cell—the cells evidently are not yet codependent—and can mature without apparent harm. The risk of PGD is not zero—some significant percentage of embryos die upon blastomere removal, and we lack evidence to say that in those that survive, there are never long-term detriments—but it is argued that PGD is permissible by virtue of its benefits. It can reveal genetic defects knowledge of which will allow a patient to deselect an embryo in favor of another embryo, or to gain

the peace of mind that an embryo selected for transfer into her is healthy. Some patients elect the procedure, though most do not.

Now it has been proposed to use blastomere removal as a method of obtaining hESC. As a technical matter, this will pose the earlier mentioned problem of how many companions a blastomere needs in order to grow in culture into hESC. In PGD, at most two blastomeres are taken from an eight-cell embryo. In the mouse this difficulty has been overcome by using hESC as companions *(22)*, but in the human that would represent no moral advance, since obtaining hESC consumes embryos. Apart from that, indications are that at best, blastomere removal will be much less efficient than standard techniques for obtaining hESC *(17)*.

In point of morality, consider first the case in which a stem cell investigator removes and uses a blastomere from an embryo whose progenitor has decided against intrauterine transfer. In that case the procedure breaks no new ground. It merely constitutes another technique for exploiting a surplus embryo donated to medicine. Removal of a blastomere will kill the embryo if not performed early enough; if performed early, at the eight-cell stage or thereabouts, there is a good chance that the embryo can survive the removal, but the procedure will leave the embryo to disintegrate shortly thereafter unless frozen indefinitely. At any stage, the procedure uses the embryo. This will evoke the usual responses—condemnation by opponents of embryo use, approval by the view that I have offered.

The procedure will constitute a moral innovation in case the embryo is later transferred to a womb. The novelty of this case, it is imagined, is the anticipated happy result that no embryo is sacrificed and instead that an embryo develops into a healthy baby despite removal of a blastomere.

An opponent of embryo use might immediately object that the procedure will sacrifice at least one embryo in the form of a totipotent removed blastomere. While a totipotent blastomere at the two-cell stage possesses the capability of developing as an organism to maturity (as in monozygotic twinning), the situation has become otherwise by the eight-cell stage. By then, blastomeres evidently have lost the ability to organize development—to become embryos.

The moral infirmity of the procedure lies elsewhere. We first observe that the risk to an embryo of blastomere removal, although small, is not zero. The embryo could die or suffer some deficit not immediately detected but manifesting later in life. The procedure will be morally wrong if it uses an embryo in a manner that risks if not inflicts harm—to the embryo and to the possible person corresponding to the embryo—without facilitating the pregnancy or fostering the offspring's health. For a physician to broach removing a blastomere without doing anything to facilitate a pregnancy or the offspring's health would be equivalent to broaching an appendectomy for a child who does not need the operation but whose appendix is sought for research. It has been suggested that blastomere removal could avail the offspring by allowing derivation of an hESC line that could be used to produce specialized cells as and when sickness or disability strikes in the offspring's life. But apart from not knowing what lies ahead in the practice of autologous transplantation and what will be the optimal techniques of regenerative medicine down the road, it seems likely that a cell line originated before birth, if it survives, will be less serviceable in the patient's care than one obtained by nuclear transfer contemporaneously with a later malady. Hence in order for the proposed alternative nowadays to yield a cognizable benefit for an offspring, I assume that it must include PGD. To accomplish both stem cell derivation and PGD will require at least one cell for each operation. Suppose then a patient considering PGD for diagnostic reasons. For the physician who must advise on the risks of PGD, it will be unclear how to discuss the further option to aid research. But it would appear that the clinician would have to propose the following. To allow for an attempt to derive hESC, the clinician will not perform genetic tests immediately after blastomere removal *(23)*. Genetic testing destroys any blastomere on which performed, or otherwise renders it incapable of issuing in hESC. So the physician will culture the removed blastomere(s) so as to issue in multiple cells. At least one cell will then be used for genetic testing. (The clinician must be confident that testing of cells from the culture is a reliable proxy for a test performed earlier on a blastomere.) Other cells will be used for stem cell derivation.

But proceeding in the foregoing way is problematic. In waiting for one or more cell passages before performing genetic testing, the clinician may be interposing a delay in effecting intrauterine embryo transfer as test results are awaited. Whether and to what extent the physician interposes delay will depend on when intrauterine transfer is already scheduled, including whether the plan is to develop the embryo to the blastocyst stage before transfer. Interposed delay might require the clinician to freeze the embryo while awaiting the genetic test results. The clinician advances the interest of maximizing the chances of a healthy offspring by minimizing, lest things go wrong in imprinting or otherwise, the time that the embryo is held awaiting transfer. For the offspring, the shorter the time outside the womb, the better. Granted, the patient has already chosen to take on the risk of PGD alone. But interposing additional delay to serve an interest other than the embryo's would be morally objectionable. It would impermissibly impose a risk in respect of the health of an offspring in order to obtain stem cells.

If any additional delay occurs, the procedure would reduce to another instance of embryo use. By dint of risk to intended offspring, it would be a less defensible use than the use of surplus embryos or clones barred from the womb. It would also not furnish a large supply of hESC lines. Only a relatively small proportion of patients elects PGD. Given the procedure's likely inefficiency, it may require many donations to obtain one cell line.

Oocyte Transformation Without Embryogenesis

The idea has lately been broached of creating a PSC directly from an oocyte. It has been imagined that, in a variation of nuclear transfer, one might fuse an enucleated oocyte and somatic cell after engineering either or both to overexpress genes (e.g., *nanog*) thought to effect pluripotency. It is envisioned that the resultant would possess "characteristics . . . immediately different from, and incompatible with, those of an embryo" *(24)*.

Notwithstanding what may be achieved in mice, at present it is not known whether and with what qualities this procedure

will produce human PSC, or how they might differ from hESC. The case of embryonic germ cells, pluripotent yet different from hESC, exemplifies that pluripotency is not a univalent quality. It does seems likely that to develop the technique will require experiments that will, if only inadvertently, produce and sacrifice embryos, and that the products will not differ morally from hurlclones unless the feat is accomplished of getting an egg to divide without there occurring any process recognizable as activation or embryogenesis. Thus we are back to the justification of embryo use.

Another technique would fuse somatic cells and hESC to produce PSC. But that obviously requires the use of embryos to obtain hESC.

Dedifferentiation

Cells are said to dedifferentiate when they revert from specialization to multipotency or even pluripotency. There has been posed as an alternative to hESC research the feat of inducing cells to dedifferentiate. This urging is a bit like proposing to score a touchdown by dreaming rather than running a play. Inducing dedifferentiation is the holy grail of hESC research. Some progress in understanding dedifferentiation to multipotency has been made, but a substantial part of the work uses hESC (e.g., *25*). Inducing dedifferentiation itself could produce totipotent cells, perhaps even to the extent of the capability to develop as embryos. Perfecting the process requires understanding the reprogramming observable in clones, preferably without introducing more abnormalities, as in hurlclones, than already occur. As it is not known whether cells that are pluripotent in consequence of dedifferentiation will behave in the same way as hESC whose plasticity has never been less than pluripotent, it could result that investigators can more reliably direct the differentiation of hESC than of dedifferentiated cells. Carrying the ball across the goal line seems unlikely to occur without some use of embryos.

Amniotic Epithelial Cells

A recent report describes "the significant plasticity and differentiation potential" of amniotic epithelial cells, cells available from the placenta following birth *(26)*. As it has not been observed that a population of these self-renews, it has not been claimed that they are stem cells. Amniotic epithelial cells have been observed to issue in some cell types of all three germ layers, but it is not clear that they are pluripotent. They differ from hESC in that they do not express telomerase or form tumors, and they have not yet been observed to be capable of issuing in all cell types of the developed human. Even if amniotic epithelial cells are pluripotent, the question arises, as for other pluripotent cells, whether they are functionally equivalent to hESC.

Conclusion

Justifying the first three proposals takes one to an argument that justifies use of all donated embryos barred from the womb. This should not be surprising. Each of those proposals would use something so close to an embryo that it may be splitting hairs to deny that it is one. The fourth proposal cannot be implemented without introducing an awkward overture to a patient by a fertility clinician whose duty is not to research but to the patient and offspring. It would seem that for the envisioned practice to yield anything more than a paucity of cells, the practice would have to impose an additional risk on offspring. Thus none of these four present a morally preferable alternative to embryo use in general. In concept, oocyte transformation without embryogenesis would produce in the end something not even embryo-like, but in practice may inadvertently sacrifice embryos. How long should we wait to see if it yields PSC? We must ask the same question about efforts to achieve dedifferentiation, which themselves benefit from use of embryos, and about studies of amniotic epithelial cells.

If we are to optimize progress in regenerative medicine, we cannot allow wishful thinking to cloud our moral judgments any more than our scientific. To the extent that purported embryo alternatives use or produce embryos or lean on a defense that encompasses the use of embryos, a choice to pursue them and to renounce use of embryos would not be a moral improvement from the point of view that holds embryo use to be wrong. From the point of view that holds humanitarian use of donated embryos virtuous, a choice to prefer the purported alternatives would work a moral detriment. It would renounce an immediately available and justifiable means while gambling that alternatives yield hESC or functional equivalents. In this context, delay and failure are measured in death and suffering. With a justification before us for donated embryo use, we ought not confine research to malengineered clones, defective cells, and inefficient methods. We ought not force the relief of suffering to work with one arm tied behind its back.

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