Rescuing Human Embryonic Stem Cell Research: The Blastocyst Transfer Method

Forthcoming in *The American Journal of Bioethics*

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April 26, 2005

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Despite the therapeutic potential of human embryonic stem (HES) cells, many people believe that HES cell research should be banned. The reason is that the present method of extracting HES cells involves the destruction of the embryo, which for many is the beginning of a person. This paper examines a number of compromise solutions such as parthenogenesis, the use of defective embryos, genetically creating a "pseudo embryo" that can never form a placenta, and determining embryo death, and argues that none of these proposals are likely to satisfy embryoists, that is, those who regard the embryo as a person. This paper then proposes a method of extracting HES cells, what might be called the Blastocyst Transfer Method, that meets the ethical requirements of embryoists, and it considers some possible concerns regarding this method. It concludes by encouraging future HES cell research to investigate this method.

Key words: embryonic stem cell research, ethics, persons, blastocyst transfer, PGD

The 'embryoist' objection

Human embryonic stem (HES) cell research is under attack in some places. Members of the European Parliament have voted against permitting scientists to carry out research on stem cells taken from embryos.[1] The governments of many countries have also passed legislations against many forms of this kind of research. For example, Germany (Law on Embryo Protection 13 December 1990), Austria (Law No. 275 of 1992), Norway (Law No. 56 of 5 August 1994), Switzerland (Constitution 1999, Article 119, 2x), Brazil (Law No. 8974/95 of 1995), Peru (Law No. 26.842), Costa Rica (Law No. 7739 of 1998) and Ecuador (Article 49, par. 1, of the Constitution 1998) consider as an offence the fertilization of an ovum for purposes other than its reimplantation in the donor. This effectively rules out creating embryos for the sake of HES cell research. Or, Ireland (Constitution, Article 40, par. 3), Hungary (Law No. LXXIX of 1992) and Poland (Law of 7 January 1993 as amended

on 30 August 1996) implicitly prohibit research on the embryo by stating the right to life of the "unborn child" must be respected and protected. In the U.S., the Federal financing of such activities is prohibited, but the authorization of research on the embryo is left to the discretion of each State.[2] To this date, nine States have prohibited such research.[3]

It might be asked, Why such a reaction against HES cell research? After all, because their pluripotency, that is, because of their ability to give rise to most types of cells that constitute human tissues, HES cells could be used to treat debilitating or fatal conditions that would not otherwise be treatable.[4] For example, HES cells could potentially be used to grow nerve cells to repair spinal injuries and restore function to paralyzed limbs; to grow heart muscle cells to replace useless scar tissue after a heart attack; to make brain cells that would secrete dopamine for the treatment and control of Parkinson's disease; to grow cells that make insulin, creating a lifelong treatment for diabetes; to grow bone marrow to replace blood-forming organs damaged by disease or radiation; to make blood cells genetically altered to resist specific disease such as HIV; and to replace diseased blood cells. To be sure, adult stem cells might be able to achieve some of the feats that HES cells potentially could. However, because adult stem cells are multipotent, that is, because they are already specialized, their potential to regenerate damaged tissue is claimed to be limited.[5]

A major reason against HES cell research is that at present, the process of extracting HES cells involves destroying the embryo. HES cells are harvested presently in the following way:[6] After fertilization, and until around the 5 day stage, each cell in the embryo remains totipotent, that is, each cell until then is able to become a new human being if separated and implanted. At around the 5 day stage, the embryo becomes a blastocyst consisting of the trophoblast, which is an outer,

hollow sphere of cells that could go on to implant in the uterus and develop into the extraembryonic membranes such as the placenta, the umbilical cord and the amnion; and the inner cell mass, which could develop into the baby. The cells of the inner cell mass at this point become pluripotent and are the major source of HES cells. HES cells are harvested by removing the trophoblast cells, which are not needed; separating the cells of the inner cell mass, which are the HES cells; and culturing them on a plate of "feeder" cells, that is, cells that will help maintain the stem cells; and isolating the single cells and growing them. The cells that are grown successfully will have high levels of the enzyme telomerase, which maintains normal chromosome length and is characteristic only of cells with unlimited potential to divide.

As one can see, this method requires the destruction of the embryo. For many, an embryo is the beginning of a person. In ethics, 'persons' are shorthand for those beings to which we owe the weightiest moral obligations and are typically referred to as rightholders (Kant, 1964, p. 96). Persons typically have a right to life, which means that they have at least some immunity against attack by others. They also have a right to autonomy, which means that they should be the authors of their own lives, and that they should be free to pursue what they regard as a good life, as long as they do not interfere with other persons' pursuits. Persons may also have a right to aid in certain circumstances. For example, if a person is drowning and it would cost me little effort to save her, then I typically have an obligation to save her. If embryos are persons, destroying an embryo to get its stem cells is akin to killing an innocent person to get her organs. Since most people do not believe that one should kill an innocent person only to benefit some other people, at least under ordinary circumstances, many therefore believe that HES cell research should be prohibited

even if it could benefit many people. Let us call this the embryoist objection and let us call those who hold this view, embryoists.[7]

The worry that HES cell research destroys persons is valid of course only if embryos are persons. Many people do not believe this.[8] It is not my purpose in this paper to discuss the moral status of the embryo or to defend the embryoist position. In light of the reactions by many people and nations against present ways of harvesting HES cells, a number of people, including members of the U.S. President's Council on Bioethics, have looked into alternative ways of obtaining HES cells that might circumvent the embryoist objection.[9] One such proposal is parthenogenesis. In parthenogenesis, a developing oocyte, which still has two full sets of chromosomes (oocytes do not become haploid until close to full maturity), is stimulated to begin to develop as if it had been fertilized. In nature, a number of insects and reptiles can reproduce in this manner. Scientifically, it has been shown that through an electric or chemical stimulus, the eggs of mammals such as mice, monkeys and humans can also be induced to begin developing in this manner. Indeed, David Wininger at Stemron of Maryland has grown parthenogenetic human embryos to the blastocyst stage, at which stem cells can be obtained (Lin et al, 2003).[10] This method is believed to be able to circumvent the embryoist objection because it is argued that parthenogenetic embryos are not normal human embryos, since they are neither able to complete gestation nor be born as live offspring. The resulting embryos usually die after a few days.

Another proposal being investigated is using defective embryos to obtain their HES cells or to combine defective embryos to create healthy embryos in order to obtain HES cells. Dr. John Gurdon and colleagues from the Wellcome Cancer Research Institute at Cambridge University (UK) discovered that defective or abnormal cloned frog embryos produced normal stem cells, which can be manipulated

to form any kind of cell in the body (Byrne et al, 2002). Since defective embryos are typically discarded, it might be thought that they could be used to extract HES cells.

A related proposal by a member of the U.S. President's Council on Bioethics, Dr. William Hurlbut, is genetically creating an entity like an embryo, but one that could not form a placenta or could not gastrulate.[11] To create such a "pseudo embryo," Dr. Hurlbut proposes that one can follow the recipe of cloning, where scientists would implant DNA from a donor's cell into a human egg cell that has had its nucleus removed, and then induce the egg to begin dividing. However, before implanting the DNA, the scientists would first turn off certain genes, for example, gene cdx2, which is the gene that directs the formation of the placenta, so that the resultant entity would not be an embryo. If the resultant entity is indeed not an embryo, the embryoist objection would then not be applicable.

Finally, another proposal is to take stem cells from embryos after "embryo death," that is, at a point that is analogous to the stage at which we take organs from people at the end of life. Drs. Donald Landry and Howard Zucker of Columbia University suggest that this point occurs when there is "irreversible arrest of cell division" in the embryo, which might be measured by the amount of time lapsed after cells stop dividing or by the absence of Oct4, which are determinants of growth and differentiation (Landry and Zucker, 2004).[12] Once one determines that an embryo is dead, the embryoist objection, which is premised on the idea that the embryos are alive, would seem not to apply.

However, there are reasons to be skeptical that these proposals will truly satisfy embryoists. In the case of parthenogenesis, there is first an issue that genomic imprinting, a process in which genes remain dormant, could make parthenogenetic embryos unsuitable as a source for HES cells.[13] It is understood that in normal cases,

a human being has two copies of genes: one from each parent; and that at any one time, only one of the copies of some of the genes is active – the other copy of some of the genes is 'imprinted' to be inactive in the offspring early in the process of development that produces eggs and sperm. In a cell derived from parthenogenesis, a gene may have been inactivated before it became an egg. This could cause a problem if, for example, the gene for cardiomyocyte cell development were inactivated by imprinting, and one wished to use the ES cells derived from this parthenogenetic embryo to repair a damaged heart.

But even supposing that this problem could be overcome, an embryoist could regard parthenogenetic embryos to be defective persons. In other words, an embryoist could maintain that the fact that parthenogenetic embryos are not created through fertilization does not mean that they are not persons. Indeed, it seems likely that it is only a matter of time before normal-developing human beings can be created via parthenogenesis. Perhaps our present technique is causing these embryos not to be able to develop into full-term human beings. If so, the fact that parthenogenetic embryos cannot at the moment grow into fully developed human beings does not mean that they are not persons.

Similarly, embryoists would object to using defective embryos in this manner, since they would regard defective embryos still as persons. They would point out that there are many defective human beings in existence, but it does not follow that we can take their organs just because they are defective. Likewise, genetically creating a "pseudo embryo" so that it can never form a placenta is also unlikely to satisfy embryoists for very similar reasons. First, it is doubtful that the difference of one gene could make one embryo a person and another embryo not a person. Secondly, one should in any case distinguish between genetic defects of the genes that make up

V and genetic defects that undermine the development of V (Liao, manuscript). In other words, there is a difference between an embryo's lacking the genes for personhood and an embryo's lacking certain genes such that it could not develop into a person. It is doubtful that by removing the gene for the development of, for example, the placenta, one is in effect removing the gene for personhood. Lastly, if it is possible to turn the gene back on in the stem cells so that the stem cells would not be flawed, as Hurlbut suggests that this is possible, then it should be possible to turn the gene back on in the "pseudo embryo." If so, this would seem to imply that that the "pseudo embryo" was in fact a person all along and just needed gene therapy like other defective embryos. If so, then the embryoist objection would still apply.

Finally, embryoists should also not find the proposal to harvest stem cells from "dead" embryos fully satisfactory. For one thing, there might be ways to jump start embryos that have arrested cell division, much like a defibrillator can be used to jump start an individual with a cardiac arrest. If so, an arrest in cell division does not necessarily mean that an embryo is dead. More importantly, Landry's and Zucker's proposal is premised on the idea that our status quo approach to the practice of IVF would be retained so that there would be an ample supply of "dead" embryos. However, embryoists would object to the current way IVF is practiced, in particular the fact that large numbers of excess embryos are created. Indeed, on Dec. 11, 2003, the senate of Italy passed a bill that limits a woman's chance of pregnancy through artificial fertilization to three embryos, each of which must be implanted in the womb. Given this, relying on using "dead" embryos from IVF would at best be a temporary and limited solution for the embryoists. [14]

In this paper, I would like to propose another compromise solution that could meet the embryoist objection, what might be called the Blastocyst Transfer Method. I

shall discuss how this solution can be technically achieved, and I shall also address some possible concerns that may arise from this method.

Obtaining HES cells without harming the embryo: the Blastocyst Transfer Method

The method I have in mind can be stated quite simply: Extract HES cells without destroying the embryo and, specifically, without harming the embryo's chance of developing into a healthy functioning individual. The embryo would then be implanted and brought to term. One might be able to achieve this in the following way: Instead of destroying the embryo/blastocyst, perhaps one can extract just enough pluripotent HES cells from the inner cell mass to create a stem cell line, but without harming the embryo's chance of developing into a healthy functioning individual. More specifically, at present, we have the ability to extract embryonic cells at the 1-4 day stage using the technique of PGD. This method works as follows: The embryo is held in place on a micromanipulator with a holding pipette. A zona drilling pipette is used to drill a hole through the shell of the embryo using acid Tyrode. The embryo biopsy pipette is then introduced through this opening, and gentle suction is applied to dislodge a single cell from the embryo.

My proposal is that we can use a method like this one to extract HES cells at the blastocyst stage, what might be called the Blastocyst Transfer Method (BTM).[15] This method faces some technical challenges. First, the cells of the inner cell mass of the embryo at the 5 day stage become quite tight and our present technique is not sophisticated enough to extract these cells without destroying the embryo.[16] Secondly, to create a stable stem cell line, that is, a line that will continue to grow indefinitely, a large number of HES cells is required. At present, it is estimated that around 200

HES cells are required. It is necessary to consider how one can extract enough HES cells to create a stable stem cell without harming the embryo.

Both of these challenges can, I believe, be overcome. Regarding the first, we should be able to develop techniques that can extract cells from the inner cell mass without harming the embryo. After all, the technique of PGD was itself a recent invention. A few decades ago, it would have been technically impossible to extract one or two cells from the embryo without harming the embryo. It should be possible to use microscopic laser or some microscopic pipette to take part of the inner cell mass for HES cell derivation leaving the rest of the embryo intact and thereby not destroying the embryo. The remaining ICM cells are expected to regenerate, since they are stem cells. [17] No doubt this procedure would impose some added risks to the embryo's ability to implant and to develop normally. But procedures such as PGD and IVF also impose such added risks, but they are typically not objected to on the ground of risk to the embryo.[18] The goal here would be to perform this procedure at a level of risk that is comparable to PGD's and IVF's.

In fact, there is already some evidence suggesting that BTM could work. In particular, embryos of various animals such as cattle, sheep, swine, horses, monkeys, rabbits and mice have been bisected at the blastocyst stage to produce twin offspring (and in a few cases, they have been trisected or quartered) (Williams et al., 1984; Kippax et al., 1991).[19] The bisection is a highly invasive procedure as it involves cutting the blastocyst in half with a microscalpel (Williams, 1998) or pulling apart the embryo with two glass needles (Willadsen, 1984). The pregnancy rates achieved with bisected bovine embryos (50 to 60%) were similar to the intact embryos (55 to 61%), although the latter is higher (Lopes et al, 2001).[20] This technique is now commonly used by the cattle embryo transfer industry nearly to double the number of embryos

available for transfer. Thus far there has been no evidence for increased incidence of birth defects or abnormal offspring from this procedure (Lewis, 1994). In light of this, some have even proposed that this technique could be used to help infertile couples who at present have 10–28% success rates for single in-vitro fertilization (IVF) procedures (Wood and Trounson, 2000).

For our purpose, if there is at present a 50 to 60% chance of successfully producing calves from bisecting bovine blastocysts, then it seems that taking much less than half of the inner cell mass of a human embryo could increase the survival rate of the embryo. In any case, that 50 to 60% survive indicates that it is possible to take cells from the inner cell mass without destroying an embryo. In other words, it shows that BTM is possible. The scientific question then becomes how much stem cells we can take so that the survival rate of the embryo is comparable to that of PGD while at the same time we would have taken enough cells to propagate a stem cell line.

Lest it leads to confusion, let me just note that while BTM seeks to use a technique like PGD, it is not PGD. First, while the latter is now technically possible, the former is not. Secondly, it is true that in PGD, because the cells removed at the 1-4 day stage are totipotent, there is a chance that these cells could form viable embryos.[21] But BTM removes cells at the 5-7 day stage where the cells have become pluripotent. Pluripotent cells cannot form viable embryos. So, this concern does not arise.

Regarding the second technical challenge, we should investigate the lower bounds of the number of HES cells needed to create a stable stem cell line. For example, it might be possible to maintain a cell line with 100 HES cells or less. Indeed, scientists have been investigating new and more efficient ways of maintaining stem cells. For example, some scientists have discovered that HES cells can be grown

with the help of special cells from bone marrow (Cheng et al, 2003). HES cells are usually grown in the lab on a "feeder layer" of mouse cells. Feeder cells send as yet unknown signals to the primitive human HES cells, preventing them from turning into more "grown-up" cell types, such as bone, fat, or brain cells. It has been found that human marrow stromal cells can also act as feeder cells for human HES cells, letting them divide without differentiating. If we can improve ways of maintaining HES cells, we would require less HES cells to maintain a stable stem cell line.

Hence, I think it should be possible to achieve these aims. In any case, these aims are not more difficult to achieve than alternative compromise solutions such as genetically creating "pseudo embryos." Certainly, we should attempt them if only to extend our knowledge in this area. Again, no one has attempted to see if one can take parts of the inner cell mass without harming an embryo. Nor does anyone know the lower bounds of the number of HES cells needed to create a stable stem cell line.

If we could extract HES cells without destroying the embryo and, specifically, without harming the embryo's chance of developing into a healthy functioning individual, and if we would then implant the embryo and bring the embryo to term,[22] it seems that the embryoist objection would be met.

A violation of the embryo's autonomy?

Embryoists might however be skeptical of this proposal. In particular, they might worry that BTM would violate the embryo's autonomy as a person (Liao, 2005a). Typically, to perform operations that might have some chance of harming a person's welfare, that person's consent is necessary. Not doing so is deemed as a violation of that person's autonomy. Hence, for example, before taking a person's blood, consent

from the blood donor is typically sought. Given that the consent of the embryo cannot be obtained, embryoists might argue that the procedure I described is ethically flawed.

It is true that consent is typically required when one performs an action on a person that might affect that person's well-being. However, there can be exceptions to this requirement. For instance, consent from a person is typically not necessary if the intended action is to benefit the person and the benefit is deemed to outweigh the harm. Hence, suppose an unconscious person needs a life-saving operation. Although the person has not consented to the operation, since the operation is intended to benefit this person and let us suppose that the benefit of the operation outweighs the potential harm, it is typically permissible to perform it.

In addition, in certain circumstances, consent may not be necessary if an action would bring very little or no harm to an individual but would greatly benefit others. For example, consider the Magic Blood Case.

> Suppose a person has a special kind of blood such that a very small amount of this blood would be able to save the lives of millions of people. The special effects of this blood would disappear though if the person had any knowledge that someone would be taking his blood. However, it is quite easy to take some of his blood without his knowledge. Doing so would have very little effect on this person, since the blood would replenish itself the next day and the person would not even know that some blood has been taken from him because the amount required is very little and does not harm the person at all.

Would it be ethical to take this person's blood without his knowledge? It seems that if this person would not be harmed in any way and the benefit would be great, even though this does not observe the requirement of consent, such action would be permissible given what is at stake. Indeed, consider a closer to life example: Suppose a person, X, requires immediately a certain type of blood for blood transfusion and the only source for this type of blood is in another patient, Y, who is presently comatose. Taking a small amount of blood from Y would not harm Y at all; but because Y is comatose, one is unable to obtain Y's consent. Would it be permissible to take the

blood from Y to save X? Again, it seems that if Y would not be harmed at all, then such action should also be permissible given the benefit to X. Certainly, consequentialists, who would allow imposing even 'large' harm on people as long as overall benefits outweigh overall losses, should not object to these actions since little harm would be imposed while the benefit would be great (Savulescu, 2002). And, unless one is a strict deontologist who believes that moral rules are absolute and admit of no exceptions – for example, a strict deontologist would accept that one should not lie to a Nazi even if doing so would save lives – a reasonable deontologist should also accept these actions, since neither the sleeping person nor the comatose person would be harmed physically.

If this is correct, then there could be two ways in which extracting stem cells from an embryo is permissible, even if one could not obtain the consent of the embryo, namely, if doing so would benefit the embryo and the benefit outweighs the harm, or if doing so would not harm the embryo but the benefit to others is great.

A violation of the embryo's dignity?

Embryoists should generally have no problem with extracting stem cells from an embryo that would directly benefit the embryo and the benefit on the whole outweighs the harm. However, some embryoists may be uneasy about the second proposal, despite my disclaimer that there must be little or no harm to the embryo and the benefit to others must be great. In particular, they may be concerned that in this circumstance, the embryo's dignity would be violated, because if embryos are persons, then they should be treated as ends and not as mere means.[23] Creating these embryos and taking stem cells from them for the benefit of others seem though to be treating them as means rather than as ends.

It is important to note that the Kantian dictum that one should treat persons as ends and not as mere means does not forbid one to treat persons sometimes as means (Kant, 1964, pp. 95-96). When you purchase something at a store and pay the shopkeeper, you are treating the shopkeeper as a means. But this is permissible because you are not treating the shopkeeper as a *mere* means. In our case, as long as the embryos are not harmed, are brought to term, loved and cared for, like other children, these embryos would still be treated as ends, even if they might have been created with the intention of saving someone else. Indeed, most people believe that it is permissible for someone to have a child, X, in order to obtain his cord blood so that another child, Y, can be saved using the cord blood (Spriggs and Savulescu, 2002). As long as X is loved and cared for like any other child, while this treats X as a means, it does not treat X as a mere means.[24]

Other embryoists might respond that in practice, to develop BTM without harming embryos, it seems that one would have to harm some embryos initially, since the only way to know whether the procedure is safe is by bringing tampered embryos to term. But if this is the case, it seems that this would be treating these embryos as mere means, since they would be harmed and sacrificed for the benefit of others. If so, even granting that the end result would be acceptable to embryoists, how could the development of this procedure satisfy the embryoists?

This is an important concern. To address it, let me outline a research process that would ensure that embryos are not treated as mere means. In particular, initially, we should attempt this technique only on animals until we have solid evidence that this procedure does not cause developmental problems in tampered animal embryos and the resulting offsprings. When we proceed to the human trial stage, we should meet the same standards the Institutional Review Board (IRB) uses to protect born

human subjects, and we should at the start apply this technique only to embryos that have serious diseases and that could directly benefit from stem cell therapy.[25] There is evidence from umbilical cord blood (UCB) stem cell research that even though an individual's own UCB stem cells might contain some genetic defects, using one's own cord blood is still significantly better than nothing and not much worse than using someone else's stem cells, which would have the additional problem of human leukocyte antigen (HLA) matching (Kurtzberg et al, 1996; Conrad et al, 1998). Presumably, embryoists would believe that these embryos ought to be brought to term, and presumably, they would also accept that the relatively small probability that these embryos would be harmed by this procedure would be outweighed by the gains of stem cell therapy. Since the benefit is intended for these embryos, arguably, they are not being treated as mere means.

Later, we might offer this procedure to parents who wish to keep a stem cell bank for their children in case their children develop certain degenerative diseases later on in life. Again, since the tampered embryos are still the beneficiaries, this should also be acceptable to embryoists. An analogy here may be parents' allowing their children to receive polio shots, which involve certain amount of risk to the child, including possible death, but which also benefits the child. Once we begin privately banking stem cells, we could then encourage those parents who have banked their children's stem cells to allow these stem cells to be propagated so that we can use them for further research or to create a public stem cell bank for everyone. Again, since the intended beneficiaries of the initial banking of the stem cells are still the embryos, the embryos would not have been treated as mere means.

I would argue further that once BTM is deemed to be safe after longitudinal studies, that is, once we have determined that the risks to the tampered embryos are

indeed minimal and the benefits to others are great and safe, we could then allow the creation of embryos in order to save, for example, siblings. As I have explained, while this treats the embryos as means, it does not treat them as mere means, now that the procedure is safe. This added proposal is bound to be controversial, for reasons already stated. But even without it, the previous steps would have already allowed us to have stem cell banks without treating embryos as mere means. Hence, there is a way to research and implement this procedure while meeting the embryoists' concern about the embryo's dignity and not treating the embryo as a mere means.

A non-embryoist concern

At this point, many would agree that BTM would satisfy the embryoists, but they may doubt that it would satisfy the non-embryoist proponents of HES cell research. In particular, it might be argued that to get from the research stage to the clinical stage of being able to use HES cells for therapeutic purposes would, under this proposal, be unacceptably long, since it would require that this technique be possible, which may not be forthcoming for quite some time. It is true that there are more hurdles to go through under this proposal. However, because of the general ethical acceptability of the proposal, it could also be the case that more scientists, individuals, governments and organizations would be interested in supporting this kind of approach to HES cell research, with the net effect that we are able to get to the clinical stage faster. Indeed, many nations that now ban HES cell research or that do not publicly fund this research may revise their positions in light of the possibility of the method proposed. So, it is an open question as to whether research into BTM would slow down or speed up the possibility of HES cell therapy.

Conclusion

HES cell research is under attack and in some countries, including in the United States, it runs the risk of being banned, because present ways of extracting HES cells involve destroying the embryo, which for many is equivalent to killing a person. Compromise solutions such as parthenogenesis, the use of defective embryos, genetically creating a "pseudo embryo" that cannot form a placenta, and determining embryo death have been proposed, but I have argued that they are unlikely to satisfy the embryoists. In this paper, I proposed that the Blastocyst Transfer Method could meet the embryoist objection. Non-embryoist proponents of HES cell research would of course prefer that HES cell research be permitted now, so that we can reap its therapeutic benefits soon. But as I have argued, pursuing BTM may enable us to reap the therapeutic benefits of HES cells even sooner because more people may be interested in investing in this particular technique given its general ethical acceptability. In any case, if we are serious about having any sort of compromise solution as many people seem to seek, then something along the lines I have suggested may be the most pragmatic way to proceed.

Acknowledgements

I would like to thank Ariff Bongso, Alfonso Gomez-Lobo, Julian Savulescu, Ruth Faden, Hilary Bok, Andy Siegel, Glenn McGee, Peter Singer, Wibke Gruetjen, Tristram Engelhardt, Tod Chambers, Dena Davis, participants of the Hong Kong Baptist University Conference on the Ethics of Regenerative Medicine, and the two anonymous reviewers at AJOB for their comments on early drafts of this paper. The Oxford University Uehiro Centre for Practical Ethics and the Center for Human

Values at Princeton University provided generous support and stimulating work environment during which the paper was written.

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[1] http://www.europarl.eu.int/activities/default_en.htm, April 10, 2003.

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[3] Fla. Stat. Ann. § 390.0111(6); La. Rev. Stat. Ann. § 9:121 et. seq.; Me. Rev. Stat. Tit. 22 § 1593; Mass. Ann. Laws. Ch. 112 § 12J; Mich. Comp. Laws. §§ 333.2685 to 2692; Minn. Stat. Ann. § 145.421 (applies only until 265 days after fertilization); N.D. Cent. Code §§ 14-02.2-01 to –02; 18 Pa. Cons. Stat. Ann. § 3216; R.I. Gen. Laws. § 11-54-1.

[4] There are three levels of potency in stem cells. They may be totipotent in that they are able to develop into all the different types of cells needed for a complete and functioning organism; or, pluripotent in that they are able to give rise to most types of tissue but not capable of bringing a functioning organism into existence; or multipotent in that they are able to give rise to a limited number of tissue types. While totipotent and pluripotent stem cells are found primarily in early embryo cells, multipotent cells are found in adult human body (e.g. bone marrow cells or neural stem cells).

[5] There is evidence that adult-derived stem cells may have more potential to be coaxed to develop into different tissue types than previously believed, though some have disputed this. For a good overview of this debate, see Wagers and Weissman, 2004.

[6] A research team led by James Thomson of the University of Wisconsin reported in the 6 November 1998 issue of *Science* that they were able to use this technique to grow HES cells in culture. See also Shamblott et al, 1998.

[7] Some might think that the term ‘embryoist’ is derogatory, comparable to racist or sexist. This is not so. No one would think that humanist is a derogatory term.

[8] It might be worth mentioning that some people could have some reservations about embryonic stem cell research even though they do not believe that embryos are persons. These individuals hold the view that while embryos are not persons, they are still biological human beings having certain moral standing and deserving of a certain amount of respect. See, e.g. Steinbock, 2000; Dworkin, 1993.

[9] In this paper, I do not consider the ethical implications of using presently abandoned embryos in IVF freezers around the world. One reason is that some embryoists would argue that just as it would be better to allow comatose persons to die than to use their bodies for therapeutic purposes, so if embryos are persons, then it would be better to allow these embryos to die than to use them for research or for therapeutic purposes. Secondly, embryoists would argue that abandoned embryos should all be implanted or never be created in the first place. If so, using abandoned embryos in IVF freezers would

at best be a temporary solution for the embryoists. The proposals I shall now discuss, on the other hand, could be truly compromise solutions.

[10] Cells taken from one of the embryos survived for a few days.

[11] http://www.bioethics.gov/transcripts/dec04/dec03.doc. The predecessor to this approach is to modify an embryo, for example by inserting trophoblast inhibitor genes into, or knock out genes from, early embryo cells so that these cells can never form a placenta (Trounson and Gillam, 1999). This proposal faces the objection by the embryoists that genetically modifying an embryo so that it can never form a placenta is deliberately damaging a person.

[12] For a similar proposal based on letting embryos die, see Mahowald, 2004.

[13] For a good discussion of this issue, see, e.g. Kent et al, 2003.

[14] The President's Council on Bioethics has a fourth proposal which is to de-differentiate a differentiated cell so that it would become a pluripotent stem cell. As far as I know, scientifically we are still very far from being able to do so.

[15] This paper was shown to various members of the President's Council on Bioethics during 2003-2004. Recently, the Council has briefly mentioned a similar proposal, what it calls the 'single blastomere biopsy.' http://www.bioethics.gov/transcripts/dec04/session6.html; http://www.bioethics.gov/transcripts/march05/session5.html. As far as I know, however, the Council has not developed this proposal in great detail or considered its ethical implications. One objection it faces is that the cell extracted could still retain the potential to form a viable embryo, as it is being extracted between the 1-4 day stage. If so, the embryoist objection would not have been circumvented. See, e.g., Murray, 2005 for this point. As I shall shortly explain, BTM is not vulnerable to this objection.

[16] Personal communications with Prof. Ariff Bongso, founder of HESI, Embryonic Stem Cell International and Research Professor and Scientific Director of the Assisted Reproductive Technology Program at the National University of Singapore. Professor Bongso and his research group were also the first to isolate HES cells from human embryos. They grew HES cells for two passages (subcultures) but did not produce a HES cell line (Bongso, 1994). Later James Thomson produced the first HES cell line in 1998.

[17] Prof. Bongso suggested that this could be a possibility.

[18] The likelihood of accidentally damaging the embryo during the removal of a totipotent cell in PGD is very low, projected to be about 0.6% (Hardy et al, 1990). Furthermore, the European Society for Human Reproduction and Embryology data show that 13689 of 14040 biopsied embryos (98%) survived the biopsy procedure. People typically object to PGD on grounds that it involves the destruction of embryos; that it may lead to eugenics; it may lead to gender bias, it is 'unnatural'; and so on (ESHRE PGD Consortium Steering Committee, 2001).

[19] I thank one of the anonymous reviewers at AJOB for prompting me to think further about this kind of research.

[20] In some studies, the pregnancy rate achieved by the intact embryos is around 70% (Wood and Trounson, 2000).

[21] For this reason, the President Council's proposal of 'single blastomere biopsy' may not circumvent the embryoist objection.

[22] Some might wonder whether implanting embryos at the blastocyst stage would lower the implantation success rate. In fact, the opposite is true. As it is well known in IVF clinics, an embryo that survives to the blastocyst stage has on the whole a better success rate of implantation over a traditional 2-3 day transfer.

[23] I thank Alfonso Gomez-Lobo for prompting me to discuss this objection in greater detail.

[24] This said, creating an embryo with morally dubious motives initially is, as I have elsewhere argued, morally objectionable, even if one later gives up those motives and comes to love the child for the child's sake (Liao, 2005b).

[25] To determine whether an embryo has a serious disease that is treatable using stem cell therapy, one might begin by considering an embryo's family history. If there is a family history, PGD might then be performed to ascertain that in fact the embryo has such a disease.