



The Use of Human Embryos in Stem Cell Research

By Lori P. Knowles

Human embryonic stem cells (hES) are derived from the inner cell mass of human blastocysts. Five days after an egg is fertilized by sperm, the resulting cell, smaller than the dot on this “i,” is known as a blastocyst. The outer shell of the blastocyst, if it matures and survives implantation, would become placental tissue, and the inner cell mass would become the tissues of the human body. It is in this inner cell mass that hES are found and can be extracted. The extraction of hES qualifies as research on human embryos. Ethical issues of hES research, therefore, overlap with those of embryo research.

Moral Status of the Embryo

The primary ethical issue at the heart of debates over hES research revolves around the moral status of the embryo. There are a number of legitimate but incompatible views on the moral and legal status of the human embryo. At one end of the spectrum of beliefs, some view the human embryo as just a collection of cells no different from skin cells or other cells in the body. According to this belief, there is no need to treat these cells differently than other cells and research on them is permissible, provided the donors of the cells give proper consent. At the other end of the spectrum, some believe the human embryo is a person with the same moral status as a baby, child or adult – and consequently, with all the rights those people possess. According to this belief it is not possible to condone experimenting on embryos, just as we do not experiment on living persons without their consent.

Between these two extremes is a middle position which holds that it is possible to believe both that life begins at conception and that embryo research is permissible. Many

people, cultures and religions believe that while human life begins at conception embryos are not people – the blastocyst and embryo are cellular structures with the potential to become people, *if they are implanted and survive pregnancy and birth*. In this view however, embryos do not have the same moral value as living people, and do not possess the same rights. This intermediate view regards embryos as special in a way that demands respect such that they are not wasted or used frivolously and have limits and restrictions on their use.

Which Embryos Should Be Used in Research?

A decision to use any embryos in research is a compromise between the moral cost of using embryos which many believe have a connection to the human community and the moral cost of foregoing research that may help ameliorate the lives of existing children and adults. Once the decision to permit embryo research is made there still remain many open questions about what research to permit and under what circumstances. One of the issues of controversy in embryo research and hES research concerns *which* embryos can and should be used for research. There is disagreement over whether it is appropriate to create embryos solely for research purposes, and what techniques should be used to create those embryos.

Many people and governments feel that an appropriate restriction on embryo research, including hES research, is to limit the use of embryos in research to those embryos that are surplus to infertility treatments – those embryos that created by IVF in an attempt help a woman get

pregnant. Very often more embryos are created than are needed to achieve pregnancy, or a couple decides that they no longer need all the embryos created for any number of reasons. Those embryos that are surplus will be frozen (cryopreserved) and can be stored, destroyed, donated to another couple or donated for research.

Embryo Disposition

If a woman has had all the children she wants or a couple no longer wants their embryos, they are faced with several options. They may discard the embryos, which normally involves thawing the embryos and allowing them to perish; they may keep the embryos frozen for an indefinite period of time; they may donate the embryos for research, including stem cell research; or, they may donate the embryos to other infertile couples who would implant the embryos and hope to have a child. This last option is called embryo donation, but is also sometimes referred to as embryo “adoption.”

In some countries, such as Italy and Germany, embryo adoption is forbidden. By contrast, there are a few jurisdictions that mandate that all embryos created either be “adopted” or that they be made wards of the state. For instance, in Louisiana no viable embryos created by IVF for implantation can be discarded and the clinician who creates them is a temporary guardian until they are “adopted.” This differs from embryo donation in that the gamete donors lose control over the ultimate disposition of their embryos. In Canada, embryo adoption is not directly regulated. The *Assisted Human Reproduction Act* forbids the sale of reproductive material including eggs, sperm and embryos, but there is no law that forbids a couple from donating an embryo to another infertile couple, provided no payment is involved.

Recent research suggests that most women and couples prefer not to donate frozen surplus embryos to third parties. Gamete donors can experience significant emotional attachment and concern for their embryos and will go to great effort to ensure that they do not become children outside of their care. For this reason, embryo donation is relatively rare. In the largest survey of fertility patients on the issue, Duke University found that of over 1000 couples with frozen embryos about half said they would use the frozen embryos in future attempts to get pregnant (reproductive projects), while around 21 percent said they would donate them to science, including use in

stem cell research. Less than 7 percent said they would choose embryo donation.¹

Where couples do not wish to give their embryos to another couple, they are faced with the choice of storing the embryo indefinitely, having it destroyed or donating it for research. A number of clinics will not store embryos indefinitely due to space and cost constraints and ultimately the embryos are allowed to thaw and are discarded. Additionally, storing embryos usually incurs yearly fees which can influence couples to discontinue storage and thaw their embryos for discard. Since many frozen embryos will ultimately be discarded, couples often feel that donating the embryo for research allows some good to come from its creation in the first place. This includes donation for hES research. The primary issues surrounding the use of these embryos relate to obtaining informed consent without undue inducement and not by those with a conflict of interest.

Fresh or Frozen Embryos

The Canadian bioethics community has had a debate over the propriety of using fresh – as opposed to frozen – human embryos in hES research. It has been speculated that fresh embryos may be better for the derivation of hES than frozen embryos, although there is currently no conclusive research to support this. Opponents of the use of fresh embryos contend that women ought not to be put in a situation where they are asked to give away embryos for research. The primary objection to requests for fresh embryos is that they would take place in the context of infertility treatments since that is when embryos are created. To donate some of these fresh embryos to research rather than freeze them for future use could necessitate an additional cycle of ovarian hyperstimulation and egg retrieval if a woman needs to try another cycle of IVF. Therefore, all embryos that are created and are viable for transfer should be implanted or preserved for future use.

In addition, some ethicists argue that it is nearly impossible for women to make autonomous, informed choices to donate fresh embryos under these circumstances. This is particularly true they assert, given that the request for research donation is likely made by the physician who

1 Lyerly, AD., “Fertility patients’ views about frozen embryo disposition: results of a multi-institutional U.S. survey.” *Fertility and Sterility* 05 December 2008, DOI: 10.1016/j.fertnstert.2008.10.015

has thus far been the person with the power to “save the woman from a childless life.”² In addition, it has been argued that clinicians are bound by professional ethics and have an obligation to maximize the likelihood of reproductive success on the part of their patients. This obligation constrains them from using any fresh embryos for purposes not related to a patient’s reproduction.³ Issues arising from the relationship between a clinician and patient raise concerns about informed consent and management of conflicts of interest. While the fresh versus frozen debate is particular to Canada, it highlights many of the same points that arise with respect to the issue of donating fresh ova for research.

One other source of embryos that has been proposed for hES research is those fresh embryos that are not viable for reproduction. They might have a genetic defect or simply appear to not be successful candidates for achieving pregnancy. A new technique called “DNA” fingerprinting, announced in Australia, holds potential to identify embryos that have the greatest genetic potential for reproduction.⁴ Embryos not viable for transfer to a woman may be a good source for hES derivation. Using these embryos could help address concerns about conducting research on “potential people” since non-viable embryos lack the potential to become people. In late 2006, the Australian embryo research legislation was amended to permit the derivation of hES lines from embryos deemed genetically unsuitable for implantation. Critics of this approach claim that embryos possessing genetic defects are not a good source for stem cell research, although this issue is not yet settled.

Creating Embryos for Research Purposes

Since it is relatively easy to create embryos using IVF the question has been raised whether or not embryos should be created specifically for research purposes. For scientists wishing to study the fertilization process and to improve IVF techniques this is an important tool. While this issue has been raised in previous discussions about

human embryo research, it takes on particular importance in the context of stem cell research. Two of the principal benefits of stem cell research require the creation of embryos with specific properties. These benefits are autologous transplantation (transplantation using one’s own tissues) and the creation of disease model cell lines.

Autologous transplantation requires the creation of embryos with the genetic profile of the transplant recipient. From those embryos hES are extracted for culture into a cell line and eventual creation of genetically identical tissue and/organs for transplantation. Transplanting genetically identical tissue avoids the phenomenon of rejection or graft versus host disease. Although autologous transplantation using SCNT was initially touted as the primary benefit of hES research another powerful benefit from stem cell research is the creation of disease-specific stem cell lines.

Research in understanding genetic diseases, and testing drugs therapies on those diseases can be greatly aided by studying stem cell lines created to express various genetic disorders. These cell lines can be created either by using an embryo that researchers know to manifest the genetic disorder, or by creating one through SCNT. Autologous transplantation research and creation of disease-specific stem cell lines can be subject to three objections. The first is that both avenues of research require the creation of embryos specifically for research purposes. The second objection is that this research requires a supply of human ova and finally, this research uses SCNT which is a cloning technique and therefore, raises concerns about a slippery slope into reproductive cloning.

Creating embryos, without the intention of ever implanting them, that is to say specifically for a research project, is controversial and has been a major dividing line in embryo research policy around the world. Many countries restrict the use of embryos in research to those embryos that are surplus to a reproductive project. Very often more embryos are created during infertility treatment than are needed to achieve pregnancy. This is because it is unknown how many cycles of IVF will be needed to achieve pregnancy, and whether the embryos created will all be of suitable quality to be implanted.

2 McLeod, C., Baylis, F., Donating Fresh Versus Frozen Embryos to Stem Cell Research: In Whose Interests? *Bioethics* (2007) Nov; 21(9): 465-477.

3 Nisker, J., White, A., “The CMA Code of Ethics and the donation of fresh embryos for stem cell research.” *CMJA* (2005) Sept; 173(6). doi:10.1503/cmaj.050453.

4 Jones, GM., Cram, DS., Song, B., Kokkali, G., Pantos, K., and Trounson, AO., “Novel strategy with potential to identify developmentally competent IVF blastocysts.” *Human Reproduction* (2008) May; 23(5); 1138-1144.

A primary reason behind this restriction on embryos available for research is related to the protection of women's health. If embryos are donated for research while a woman was actively pursuing her infertility treatment she might need to undergo further ovarian stimulation to produce more embryos for future treatments. There are risks associated with ovarian stimulation that should be avoided if possible. If only those embryos that are surplus to reproductive projects are donated for embryo research this extra risk can be avoided.

The other primary objection to creating embryos specifically for research is based on both the intentions of the person creating the embryo and the corresponding chance the embryo might be implanted. The ethical issue at the heart of this controversy is whether creating embryos for an entirely instrumental purpose – a research purpose – contravenes a moral rule that people must always be treated as an end, and not merely as a means. In other words, treating people in an instrumental fashion is viewed as inherently morally wrong. Even for people who do not believe that embryos are people in the same sense as children and adults, their connection to the human community may require that they also not be treated as a means to an end. According to this opinion, creating embryos without any chance that they will be implanted does not respect their special status as human life (albeit not human persons). To create embryos for possible implantation and then decide to donate them for research does not use them as a mere means, but as ends (with the intention to reproduce and with the possibility for implantation) *and* subsequently as a means (to potentially life-saving research).

A majority of countries in which hES research is possible have adopted this position and prohibited the creation of embryos for research. Many countries, including Canada, Australia and many European countries have agreed not to create embryos for research through the ratification of the Council of Europe *Convention on Human Rights and Biomedicine*. Australia amended its embryo research legislation to permit the creation of embryos for research by SCNT in 2006. Other countries have decided to permit the creation of embryos specifically for research. In great part this is because there are avenues of hES research that appear to hold significant medical benefit and require the creation of embryos.

An Overview of International Policies on Embryo Research

Since the announcements of the isolation of hES in 1998, numerous countries have grappled with whether and to what extent to permit research on embryos. Countries such as France and Germany, with restrictive embryo research policies, have loosened their restrictions to permit hES research to take place. Countries like Britain, Sweden and Israel, with permissive embryo research regimes, have gone farther to permit broad hES research thereby becoming scientific hubs for hES research. Some countries continue to have policies that forbid any interventions with the human embryo that are not in its benefit and, therefore, no embryo research is permitted in these countries. Ireland, Austria, and Italy fall into this category.

A large number of countries, including Canada, have struggled with how to create responsible embryo research policy but permit stem cell research from both adult and embryonic sources. Some countries, including Canada, have chosen an intermediate or middle ground approach between very restrictive and very liberal. Others countries like Australia, have liberalized their policies. Most countries have adopted some legal interpretation of a view that the embryo is something less than a full person, but that it has a special connection with the human community such that it deserves special respect in the form of limits and restrictions on its use in research. Where the use of embryos in research is condoned, limits on the use of those embryos include:

- Embryos and gametes must be donated with free and informed consent.
- Systems for conflicts of interest management must be in place for the procurement of gametes and embryos.
- The science must be valid and high quality (it must not be frivolous).
- No animal models or animal embryos are adequate for the research (human embryos are necessary, no other embryo will do).
- The number of embryos is not excessive (they will not be wasted).
- Research must take place within the first fourteen days after fertilisation (not including any time frozen), after which the embryo must be destroyed. This is to avoid using embryos after the first appearance of

the primitive streak, which is the precursor to brain development. The primitive streak appears sometime around day 21 and not before day 17.

- Review of research protocols, by research ethics boards (REBs in Canada) is required. Embryo research protocols are almost always subject to review, to determine a number of the issues around scientific validity, necessity of human embryos, etc. Such review keeps unnecessary destruction of embryos to an absolute minimum – something that is important not just for ethical reasons, but also to maintain public support of embryo research.

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Despite significant policy and regulatory differences, there are some issues of consensus and contention for all countries trying to create stem cell policy. Issues of relative consensus include the need for informed consent to stem cell research, and appropriate management of conflicts of interest. Issues of contention include the compensation for and commercialization of gametes and embryos, and the creation of human and non-human animal chimeras (see Knowles L., "[Ethics of Research Using Hybrids, Chimeras and Cytoplasmic Hybrids](#)" Stem Cell Network for more information on chimeras).

The international regulations form a patchwork that continues to evolve. For a comprehensive look at global stem cell policies visit the [STEMGEN](#) website.

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