Complicity in stem cell research: the case of induced pluripotent stem cells

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ABSTRACT: Many who object to human embryonic stem cell (hESC) research because they believe it involves complicity in embryo destruction have welcomed induced pluripotent stem cell (iPSC) research as an ethical alternative. This opinion article aims to show that complicity arguments against hESC research are prima facie inconsistent with accepting iPSC research as it is currently done. Those who oppose hESC research on grounds of complicity should either (i) oppose iPSC research as well, (ii) advocate a radical change in the way iPSC research is done, (iii) demonstrate that complicity arguments against iPSC research are weaker than those against hESC research or (iv) reject complicity arguments against both hESC and iPSC research, either by adopting a more limited conception of complicity that allows acceptance of some hESC research, or by accepting that destroying embryos for important scientific research is not wrong.

Key words: embryonic stem cells / induced pluripotent stem cells / complicity / moral status / embryo research

Complicity in embryonic stem cell research

Debate on the ethics of human embryonic stem cell (hESC) research has long focused primarily on the moral status of human embryos. However, even if one thinks the embryo has significant value and should never be killed for the purpose of research, one need not necessarily condemn all hESC research. After all, hESC researchers need not themselves destroy embryos. They can obtain hESCs elsewhere, for example, from an international stem cell bank. Nevertheless, it has been argued that, in using hESC lines derived through embryo destruction, hESC researchers and those who support their work are always complicit in the destruction of embryos, and that this makes hESC research unethical.

In this article, I will briefly outline the complicity arguments against hESC research. I will then apply these arguments to induced pluripotent stem cell (iPSC) research. Many who object to hESC research for reasons of complicity have welcomed iPSC research as an ethical alternative. I will, however, show that complicity arguments against hESC research are prima facie inconsistent with accepting iPSC research as it is currently done. Those who oppose hESC research on grounds of complicity should either (i) oppose iPSC research as well, (ii) advocate a radical change in the way iPSC research is done, (iii) demonstrate that complicity arguments against iPSC research are weaker than those against hESC research or (iv) reject complicity arguments against both hESC and iPSC research. I will not argue that there are conclusive complicity arguments for or against either hESC research or iPSC research. Instead, I will demonstrate how complicity arguments have been applied selectively in existing debate and outline the options for smoothing out the inconsistencies. First, however, I will briefly outline the concept of complicity.

Complicity

Complicity is a crucial concept in jurisprudence and also lies at the core of many ethical debates, including that surrounding stem cell research. It captures the idea that one can do wrong by being associated, in a certain way, with others’ wrongdoing. What kinds of association actually make one complicit in others’ wrongdoing is controversial, but most accept that one can be complicit in others’ wrongdoing by causally contributing to it in a certain way (Gardner, 2007). When I induce or encourage you, or provide you with the means to commit a murder, and as a result you commit it, I am complicit in that murder.

Many would also accept that one can be complicit in wrongdoing by increasing the likelihood of that wrongdoing (or future instances of it) in certain ways, even if one does not in fact cause it (Kutz, 2007). One way of increasing the likelihood of a wrong is by contributing to a demand. For example, even though the chicken that I order in the restaurant tonight would have died if I had been a vegetarian for all of my life, the fact that I order the chicken instead of the vegetarian option, slightly increases the likelihood that the restaurant will continue ordering chickens and slightly increases the expected number of chickens killed in the future, even if in fact it turns out that no additional chickens are killed. Other ways of increasing the likelihood of a wrong (or future instances of the wrong) include condoning a wrong or fostering more permissive social attitudes towards it. I will refer to complicity through increasing
the likelihood of wrongdoing as complicity through promoting wrongdoing. As with causal contribution, promoting wrongdoing may not be sufficient for wrongdoing: whether it gives rise to complicity may depend on the knowledge or intentions of the supposed accomplice.

Finally, and more controversially, some believe that one can be complicit in a wrong even if one has no effect on the likelihood of the wrong, or future instances of it. According to this view, one could be complicit in wrongdoing by tolerating, cooperating in or benefitting from a wrong in a way that implicitly condones it or shows disrespect for its victims, regardless of the effects on the likelihood of the wrong. For example, some have objected to the beneficial use of data from Nazi ‘medical’ experiments on the grounds that this would amount to a ‘symbolic re-enactment of the original crime and immorality of the experiments’ (Rosenbaum, 1989, p. 65). Going to a party that has been financed by the yield of a bank robbery or the sale of nude photos of a woman taken without her consent is a clear case where one benefits from a wrong in a way that disrespects its victims (Robertson, 2004).

Of course, many forms of association with wrongdoing do not make one complicit in that wrong. An oft-cited example is the ‘murder victim case’ to which I will return:

**Murder Victim Case:** A teen has been murdered in gang violence. After having received consent of the teen’s parents, a surgeon uses the murder victim’s organ for transplantation to a patient in need of a donor organ.

There is wide agreement that, by transplanting the organ, the surgeon does not become complicit in the murder. It is extremely unlikely that using the organ will cause or promote more gang murders. Moreover, the surgeon’s intentions are unrelated and in some ways diametrically opposed to those of the gang (she tries to save lives), she does not collaborate with the murderers, and presumably rejects the wrongful act she is benefiting from. Thus, the surgeon’s actions do not seem to implicitly condone the murder or show disrespect for the murder victim.

### Complicity arguments against hESC research

Most stem cell researchers working with hESCs do not actually derive these cells—the process in which embryos are destroyed. The majority only use hESCs derived by other researchers, often in other countries. However, many have argued that if embryo destruction is itself wrong, then hESC research always involves complicity in this wrong. For those according no or little value to the embryo, this need not be ethically problematic, since destroying embryos is itself ethically justified: there is therefore no wrong to be complicit in (Guenin, 2004; Devolder and Harris, 2005; Takala and Häyry, 2007; Pennings and Mertes, 2009). But for those who think the embryo should never be sacrificed for scientific research, such complicity may make hESC research unethical (Doerflinger, 1999; Pontifical Academy for Life, 2000; Moraczewski, 2002).

### Promoting wrongdoing through increasing demand for embryonic stem cell lines

Several arguments have been offered for the view that hESC research involves complicity in embryo destruction, or would, if embryo destruction were wrong. A first argument is that researchers who use hESCs create a demand for hESCs and thereby promote further embryo destruction (Doerflinger, 1999; Devolder and Harris, 2005; Mertes and Pennings, 2009). The additional demand for hESCs created by an individual researcher may not actually cause any new hESC lines to be produced. But it does increase the likelihood by some (perhaps small) degree. The effect is clearer at the collective level. Collectively, hESC researchers create a significant demand for hESC cells, and this increases the likelihood that others will produce such cells.

To prevent hESC researchers, and those who support them, from creating such a demand, some jurisdictions, including Germany, have installed a cut-off date to restrict hESC research to already existing hESC lines. However, many authors think that separating the use of hESCs from their derivation by instituting a cut-off date does not altogether avoid complicity in embryo destruction. First, a cut-off date is unlikely to stay in place. Once one accepts that a restricted number of cell lines can be used for research because of the great public health benefits, it becomes hard to justify not increasing this number when existing lines turn out to be insufficient. This has already shown to be the case in Germany where the cut-off date was moved from 1 January 2002 to 1 May 2007. (In the USA, the cut-off date was removed altogether after Obama became president.) It has been argued, then, that if it is known or anticipated that the government will periodically advance the cut-off date, the use of hESCs will continuously induce creation of cell lines in the expectation of the next advance. This is what Guenin has called a ‘failed non-complicity scheme’ (Guenin, 2004).

Furthermore, by using hESCs produced before a cut-off date, one may still influence and stimulate other hESC researchers in less restrictive countries where hESC derivation is allowed and thereby still, indirectly, promote the destruction of embryos (Mertes and Pennings, 2009). This concern was also the reason for considerable opposition to the stem cell policy of the Bush presidency (Doerflinger, 1999).

Some, however, deny that any use of hESCs will increase the likelihood or frequency of embryo destruction as embryos will continue to be discarded on a large scale in the context of IVF treatment regardless of whether hESC research continues (virtually, all hESC lines are derived from discarded IVF embryos). It has been argued that, therefore, hESC research is like the ‘murder victim case’ discussed above (Green, 2002). If using hESCs is similar to using organs from murder victims for transplantation purposes, then, by analogy, even those who believe that stem cell derivation from embryos is murder can accept the use of hESCs, since as a society, we condemn murder but do not object to using organs from murder victims.

### Promoting wrongdoing through altering attitudes to embryo destruction

However, there is a second way in which using hESCs might promote embryo destruction: by altering our attitudes to it. In discussing whether the use of tissue from aborted fetuses is analogous to the use of organs from murder victims, Gillam (1997) distinguishes three mechanisms by which using the murder victim’s organs might result in more murders: (i) by changing society’s moral beliefs about murder, (ii) by decreasing the state’s efforts to deter it and (iii) by...
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strengthening incentives to commit murder. Because condemnation of murder is so deep-rooted in our moral psyche and is strongly reinforced by law worldwide, she argues that it is very unlikely that any of these effects will occur if we use organs from murder victims; it is therefore safe to allow this. But the circumstances of abortion differ from those of criminal murder: condemnation of abortion is not deeply rooted in almost everyone’s intuitions, abortion legislation differs from country to country and has changed over time, and abortion is generally performed by the medical profession within a regulatory framework. These circumstances make it more likely that lobbying from pro-choice groups and the potential benefits of fetal tissue research will provide an incentive to relax existing abortion regulation or will result in reduced efforts to prevent abortion. In such a climate, it may also be easier for women to justify their decision to abort their fetus. Gillam’s point is that the differences in circumstances between abortion and criminal murder make it more likely that fetal tissue research will result in an increase in the number of abortions performed than that transplantation of organs from murder victims will increase the murder rate.

Gillam’s reasoning also applies to hESC research as the circumstances are very similar to those of fetal tissue research (Takala and Háyry, 2007). Using hESCs derived by others may, through mechanisms similar to those described by Gillam, indirectly promote embryo destruction. For example, the benefits of hESC research may weaken efforts to reduce the number of embryos discarded in IVF. Indeed, because hESC research has the potential to benefit many more people than fetal research and the moral status of early embryos is more controversial than that of older fetuses, restrictions on the use of embryos for research and therapies might be more easily loosened than the abortion regulations that Gillam has in mind. The use of hESCs may also cause those already uncertain about the moral status of the embryo to feel increasingly comfortable about the use of embryos for beneficial research.

Implicitly condoning wrongdoing and disrespecting its victims

Another argument for the view that hESC research involves complicity in embryo destruction focuses not on complicity through promoting wrongdoing, but through implicitly condoning it or showing disrespect to its victims. Unlike the surgeon in the murder victim case, those using hESCs co-operate with, and in some cases share the aims of, those supplying and deriving hESC lines, which, according to some, implies that they cannot distance themselves from the wrong they are benefiting from. It has been argued that, therefore, they implicitly condone the destruction of embryos and express disrespect for them (Doerflinger, 1999; Moraczewski, 2002). According to some views, this makes hESC researchers, and those who support them, complicit in embryo destruction.

Promoting and condoning embryonic stem cell research

Thus, it has been argued that hESC research (i) promotes embryo destruction by creating a demand for hESCs, and by softening social attitudes to it, and (ii) implicitly condones the hESC derivation process and expresses disrespect for the embryo. Some believe that these associations make hESC researchers complicit in wrongdoing, assuming that embryo destruction is itself wrong. And some believe that this complicity makes hESC research wrong as well, thus adding complicity arguments against hESC research. [Some think that not all complicity with wrongdoing is itself wrong. It could, for example be that, only by being complicit in a wrong, one could avoid being complicit in a greater wrong. Complicity may not always be wrong, but it is presumptively wrong: it is wrong unless a justification is present.]

Complicity in iPSC research

For those according great value to the embryo, hESC research raises thorny issues concerning complicity in embryo destruction. Fortunately, scientists have developed the iPSC technique. iPSCs are hESC-like cells created by directly reprogramming somatic cells using genetic manipulation. Just like somatic cell nuclear transfer (SCNT) or cloning, the iPSC technique could allow the generation of disease- and patient-specific pluripotent stem cells. However, unlike SCNT, the iPSC method does not rely on a supply of oocytes, nor does it rely on the creation and destruction of human embryos.

Many have welcomed the iPSC technique as the long sought after ‘ethical’ method to obtain pluripotent stem cells. President Bush’s Council on Bioethics (2005) called iPSCs ‘ethically unproblematic’. The president of the Pontifical Academy for Life, Archbishop Rino Fisichella (Christian Telegraph, 2010) said that with the development of iPSCs, the ethical debate…can now be considered closed’ and Krauthammer (2007), former member of the President’s Council of Bioethics, wrote that ‘the embryonic stem cell debate is over’ now that there is ‘an ethically neutral way to produce stem cells’. Opponents of hESC research are not alone in welcoming iPSC research; those who accept hESC research have also expressed their contentment. Stem cell biologists Rao and Condic (2008, p. 4) wrote that ‘direct reprogramming represents an…ethically uncompromised method for generating patient-specific stem cells…’. Moreover, in countries where hESC research is prohibited or severely restricted, iPSC research is regarded as ethically unproblematic or remains unregulated. The same is true at the institutional level. For example, catholic hospitals that ban hESC research do not seem to have moral reservations towards iPSC research.

However, iPSC research might raise concerns about complicity similar to those surrounding hESC research.

Promoting wrongdoing through increasing demand

We saw that hESC research likely creates a demand for embryo destruction. Similarly, iPSC research likely creates a demand for hESC research, and thus for more hESC lines. The most efficient way to further develop and perfect the iPSC technique is to compare it with the hESC technique, which is still considered the gold standard (Baker, 2009; Daley et al., 2009). For example, recent research has highlighted the need for improving the differentiation potency of iPSCs and this requires comparisons with hESCs (Hu et al., 2010). It is not only the case that researchers should compare iPSCs with existing findings on hESCs; to make comparisons it is also important that hESC research continues. For example, to investigate whether iPSCs are functionally equivalent to hESCs, the latter need to be understood in much greater detail. To further
develop the iPSC technique, iPSC scientists will have to rely on comparisons with past and ongoing hESC research. The work on iPSCs may thus create a demand for further hESC research.

There are also various other ways in which iPSC research could more indirectly promote hESC research. iPSCs share many features with ESCs, but they are not identical. Different methods of obtaining pluripotent stem cells may prove more useful for particular purposes. For example, suppose iPSC research is unable to solve a particular problem but shows that hESC research likely would be able to solve it. Imagine a scenario where iPSCs are used in important biomedical research that may benefit patients with heart disease. However, it turns out that the final (but essential) step in the research process cannot be done using iPSCs. There are, however, good scientific reasons to think that hESCs are more promising candidates for doing the last step. This would create a strong incentive to do the relevant hESC research; an incentive that would not have existed had the iPSC research not been done. This may also apply to therapeutic uses of iPSCs and hESCs. Doubts have been raised about the usefulness of iPSCs for therapy. But if iPSC research highlights that hESCs are likely to be promising for certain therapeutic uses, there will be a strong temptation to fund and do this hESC research. Of course, one could say that these arguments could apply to adult stem cells as well. They may also promote hESC research in this way. But there is a difference. Unlike adult stem cells, iPSCs and hESCs are both pluripotent cells and, in the case of hESCs produced through SCNT, patient-matched pluripotent stem cells, and are, therefore, much more regarded as complementary (Henderson, 2010). This has resulted in a closer collaboration between researchers from both fields than between researchers working on hESCs and adult stem cells. The fields of hESC and iPSC research progress in parallel and mutually support one another. Just as the use of already existing hESCs is likely to inspire and stimulate hESC research in less constric- tive countries where hESC derivation is allowed, iPSC research is likely to inspire and stimulate hESC research.

Implicitly condoning wrongdoing

We also saw, in the previous section, that supporting hESC research might be regarded as implicitly condoning embryo destruction because hESC researchers are cooperating with and sharing the aims of those deriving and supplying hESCs, which, implies they are not distancing themselves from embryo destruction. Supporting research using iPSCs may implicitly condone hESC research in a similar way. Research on iPSCs relies heavily on knowledge gained in hESC research. The understanding of cell reprogramming that informed the derivation of iPSCs may implicitly condone hESC research as it is to suggest that hESC researchers implicitly condone embryo destruction. Consequently, those selectively supporting iPSC cell research implicitly condone what they in fact reject: hESC research.

Promoting and condoning embryonic stem cell research

Two of the reasons for thinking that hESC research involves complicity in embryo destruction—promoting wrongdoing by increasing demand, and implicitly condoning wrongdoing—also suggest that iPSC research involves complicity in hESC research. So if hESC research is wrong for reasons of complicity, then there is at least a good prima facie reason for thinking that iPSC research is wrong for similar reasons.

Consider the following analogous hypothetical case:

Surgeons worldwide are working on a new surgical technique (NT) that could save many lives and reduce morbidity considerably. However, the most promising way to develop NT is through research on organs obtained through painful and fatal operations on randomly chosen innocent people; the physiological effects of the torture on the organs provide crucial information for the research. Many people have lost their partners, friends and family members in this way and everyone is constantly worried about who will be selected next. Some think the benefits outweigh the harm, but many think that the operations are evil, and that those using the organs to test NT are complicit in this evil. Fortunately, a group of surgeons has developed a new method for testing NT that does not require the horrific operations; instead, computer simulations are used. Surgeons using the computer simulations closely collaborate with surgeons removing and using the organs, as this method is still considered the most efficient method to further develop NT. Moreover, there is growing consensus that the organ and computer simulation methods are complementary, which gives surgeons even more reason to collaborate and promote one another’s work. Both methods mutually support each other. The government and people who think the operations are evil are happy with the development of the computer-simulated technique for perfecting NT. So happy that they ignore or remain silent on its close association with the ongoing evil operations.

Regarding this case, we would be tempted to say that those working on the computer-simulated technique are complicit in the organ research, and that those doing research on the organs are complicit in the evil operations via which they are obtained. But for those who think that destroying embryos is wicked like the operations, hESC research is analogous to the organ research in this case, while iPSC research is analogous to the computer-simulation research.

Consistently applying complicity arguments

The connections between iPSC and hESC research are similar to the connections between hESC research and embryo destruction. Research on hESCs arguably promotes embryo destruction through increasing demand; similarly iPSC research arguably promotes hESC research in the same way. Engaging in hESC research arguably also
implicitly condones embryo destruction, in part because it involves significant interaction with those who destroy embryos. Engaging in iPSC research involves even more significant interaction with hESC researchers and thus, even more plausibly, implicitly condones hESC research.

Given that the connections are similar, it is difficult to see how those who oppose hESC research on the grounds that it involves complicity in wrongful embryo destruction can escape the conclusion that engaging in iPSC research is also wrong, in virtue of its complicity in wrongful hESC research. Consistency requires that considerations of complicity are invoked in both cases.

There seem, then, to be four options.

First, one could reject both hESC research and iPSC research on grounds of complicity. This option is, however, unappealing, given the immense promises of both types of research.

A second option is to advocate a change in the ways iPSC research is done so that it would no longer involve complicity in hESC research. However, this option is equally unappealing. It would not only considerably slow down iPSC research, it would also make it much more unlikely that the goals of iPSC research will actually be achieved.

Third, one could seek some principled basis for thinking that the complicity arguments for rejecting hESC research are stronger than the complicity arguments for rejecting iPSC research. For example, it could be argued that it is complicity through softening our attitudes that is most important or through showing disrespect for the victims of the wrong. This softening of attitudes seems to be a genuine possibility in the case of hESC research, but may be less of a concern in the case of iPSC research. Alternatively, it could perhaps be argued that being complicit in a wrong is typically less problematic than committing the wrong itself. If so, it could be argued that the moral costs of hESC research are smaller than those of actually destroying embryos, while the moral costs of iPSC research are smaller still. Each time one takes a step away from the original wrong, one’s complicity with that wrong becomes less problematic. Thus, the moral costs of iPSC research may be small enough to be outweighed by the great benefits of the research even if the same is not true for hESC research. Such arguments hold out the promise of drawing a morally relevant distinction between hESC and iPSC research. However, there is at the very least an obligation on those who endorse iPSC research but reject hESC research to furnish a persuasive argument of this sort. If no such argument can be provided, support for iPSC research should be withdrawn.

Finally, one could reject complicity arguments against both hESC and iPSC research. One could, for example, adopt a more limited conception of complicity that leaves scope for allowing some hESC research (and thus also iPSC research). For example, many who accord high value to the embryo have argued that those merely using stem cells obtained by others are not complicit in the prior destruction of embryos as long as the hESCs were not created at the researchers’ request, and their participation in hESC research happens ‘after the fact’ (when the embryos are already dead) and was not necessary for the destruction of the embryos to occur (Prieur et al., 2006; Outka, 2009). These criteria are regarded as sufficient to avoid complicity in embryo destruction through causal contribution. Accepting a more limited concept of complicity—one that implies that only when one actually and significantly causally contributes to more embryo deaths—could allow one to consistently accept both iPSC and hESC research. [However, some may question this approach on the ground that it is an intellectually dishonest position.]

Of course, there is another possibility for rejecting complicity arguments against both iPSC and hESC research. One could deny that killing early embryos for important scientific research is wrong. If destroying embryos for important scientific research is ethical, then there is no wrong to be complicit in. Both hESC research and iPSC research would then be ethically acceptable.

Conclusion

Many who object to hESC research for reasons of complicity have welcomed iPSC research as an ethical alternative. I have shown that complicity arguments against hESC research are prima facie inconsistent with accepting iPSC research as it is currently done. Those who oppose hESC research on grounds of complicity should either (i) oppose iPSC research as well, (ii) advocate a radical change in the way iPSC research is done, (iii) demonstrate that complicity arguments against iPSC research are weaker than those against hESC research or (iv) reject complicity arguments against both hESC and iPSC research, either by adopting a more limited conception of complicity that allows acceptance of some hESC research, or by denying that destroying embryos for important scientific research is wrong.

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