Using Morally Controversial Human Cell Lines after Dignitas personae

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Abstract. Human cell lines are well-characterized laboratory cultures of human cells derived from a single source. In recent years, much moral controversy has surrounded human cell lines and biological materials obtained from aborted fetuses and destructive human embryo research. *Dignitas personae* instructs scientists of good conscience to avoid using biological materials of illicit origin, to distance themselves from evil, and to avoid scandal. The author suggests that the Instruction allows a scientist to delay discontinuing the use of a morally controversial cell line for a reasonable amount of time and allows a citizen of conscience to financially support—in a limited and restricted manner governed by prudence—philanthropic organizations that fund controversial biomedical research programs. *National Catholic Bioethics Quarterly* 10.2 (Summer 2010): 265–272.

Human cell lines are well-characterized laboratory cultures of human cells derived from a single source.[1] Human cell lines are essential tools in contemporary molecular and cellular biology. They are used in a diverse range of biomedical research programs to uncover the root causes of disease, to discover and to test drugs, and to develop

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[1] For a history of the development of human cell lines, see Rene Leiva, "A Brief History of Human Diploid Cell Strains," *National Catholic Bioethics Quarterly* 6.3 (Autumn 2006): 443–451.

therapeutic regimens. Not surprisingly, their use also leads to the invention of biological reagents and techniques that become commonplace in the laboratory.

In recent years, there has been much moral controversy surrounding two categories of human cell lines and biological materials obtained from and with them: cell lines derived from aborted human fetuses and cell lines derived from cultured human embryos who are killed in the process.[2] For the sake of illustration, I will refer to two morally controversial cell lines in this essay, HEK 293, a human embryonic kidney cell line derived from fetal material obtained from an elective abortion,[3] and H1, an embryonic stem cell line derived from the destruction of a human IVF embryo.[4] With the recent publication of the revised National Institutes of Health Guidelines for Human Stem Cell Research requested by the Obama administration, the number of morally controversial human cell lines will only increase, because the NIH has now agreed to fund research with human embryonic stem cell lines derived from the destruction of human IVF embryos donated by couples for research purposes.[5]

In this essay, I would like to explore the moral questions raised by the use of morally controversial cell lines by beginning with a summary of the teaching in *Dignitas personae*, the recent Instruction on bioethics published by the Congregation for the Doctrine of the Faith.[6] I will then address three moral questions raised by the use of morally controversial cell lines in light of the teaching put forward in *Dignitas personae*. First, may a scientist of good conscience continue use of a morally controversial cell line that he discovers he is already using in his laboratory?

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[2]For discussion, see Alexander R. Pruss, "Cooperation with Past Evil and Use of Cell-Lines Derived from Aborted Fetuses," *Linacre Quarterly* 71.4 (November 2004): 335–350; and Neil Scolding, "Cooperation Problems in Science: Use of Embryonic/Fetal Material," in *Cooperation, Complicity and Conscience*, ed. Helen Watt (London: Linacre Center, 2005), 105–117.

[3]For a description and a history of the HEK 293 cell line, see Frank L. Graham et al., "Characteristics of a Human Cell Line Transformed by DNA from Human Adenovirus Type 5," *Journal of General Virology* 36.1 (July 1977): 59–72; and Frank L. Graham, "Cell Line Transformation," *Current Contents* 8 (February 24, 1992): 8, http://www.garfield.library.upenn.edu/classics1992/A1992HC31200001.pdf. For a moral analysis of the use of HEK 293, see Alvin Wong, "The Ethics of HEK 293," *National Catholic Bioethics Quarterly* 6.3 (Autumn 2006): 473–495.

[4]For a description of how cell line H1 was derived, see the seminal paper by James A. Thomson et al., "Embryonic Stem Cell Lines Derived from Human Blastocysts," *Science* 282.5391 (November 6, 1998): 1145–1147. A recent survey revealed that H1 is the second most commonly used human embryonic stem cell line: 61 percent of 534 peer-reviewed human embryonic cell studies published from 1999 to 2008 used H1. For details and discussion, see Christopher Thomas Scott, Jennifer B. McCormick, and Jason Owen-Smith, "And Then There Were Two: Use of hESC lines," *Nature Biotechnology* 27.8 (August 2009): 696–697.

[5]National Institutes of Health, "National Institutes of Health Guidelines on Human Stem Cell Research," at *Stem Cell Information* Web site (Bethesda, MD: NIH, 2009), http://stemcells.nih.gov/policy/2009guidelines.htm.

[6]Congregation for the Doctrine of the Faith, *Dignitas personae* (September 8, 2008).

Next, may he take advantage of reagents and techniques derived from these cell lines? Finally, may a citizen of good conscience contribute financially to private philanthropic foundations that may fund biomedical research involving these controversial cell lines?

Dignitas personae on Biological Materials of Illicit Origin

In a two-paragraph section subtitled "The Use of Human 'Biological Material' of Illicit Origin," *Dignitas personae* begins by reiterating the truth of the natural moral law that condemns the experimental use of and the killing of human beings: "The use of human embryos or fetuses as an object of experimentation constitutes a crime against their dignity as human beings who have a right to the same respect owed to a child once born, just as to every person" (n. 34).[7] The recent NIH Guidelines for Human Stem Cell Research published by the Obama administration are gravely immoral and unjust precisely because they would encourage the further destruction of human IVF embryos by scientists seeking new embryonic stem cell lines that could then be used in research programs funded by federal monies from the NIH. No scientific or medical discovery, no matter how significant, could ever justify the killing of an innocent human being.

After condemning all acts that attack the life or physical integrity of both fetal and embryonic human beings, the Instruction goes on to address the morality of researchers using biological material of illicit origin "which has been produced apart from their research center or which has been obtained commercially" (n. 35). To put it another way, *Dignitas personae* asks the question, may scientists of good conscience use morally controversial cell lines or materials derived from them if the scientists themselves were not involved in the killing of the fetus or the embryo? In response, the Instruction concludes that scientists of good conscience have a duty "to refuse to use such 'biological material' even when there is no close connection between the researcher and the actions of those who performed the artificial fertilization or the abortion, or when there was no prior agreement with the centers in which the artificial fertilization took place" (n. 35). In other words, according to *Dignitas personae*, scientists of good conscience should avoid using all morally controversial cell lines, including HEK 293 and H1, and other biological materials derived from them.

The Congregation for the Doctrine of the Faith explains that scientists of good conscience should not use biological materials of illicit origin to distance themselves from evil and to avoid scandal: "This duty springs from the necessity to remove oneself, within the area of one's own research, from a gravely unjust legal situation and to affirm with clarity the value of human life" (n. 35). Indeed, I know of a scientist of good conscience who, in using a human embryonic stem cell line he had obtained from another institution, led his colleagues in the laboratory to conclude

[7]CDF, *Dignitas personae*, citing John Paul II, *Evangelium vitae* (March 25, 1995), n. 63.

that the ends—the scientific discoveries that come from human embryonic stem cell research—must be able to justify the means, that is, the killing of the embryonic human being. This scientist has since had a change of heart and has distanced himself from embryonic stem cell work.

Scientists should also refrain from using these morally controversial cell lines because their use may also lead to further acts of grave evil. For instance, it is not unreasonable to predict that the use of the human embryonic stem cell line H1 could lead to scientific discoveries that would prompt other scientists to desire more cell lines of this type and thus destroy more human embryos. In the end, heroic acts are demanded of scientists of good conscience who seek to respect and protect the inviolability and the dignity of human life in a culture that does not hesitate to instrumentalize human beings.

Significantly, in reaching the conclusion that scientists should not use materials of illicit origin, *Dignitas personae* explicitly rules out the criterion of independence that had been proposed by some moralists, who had suggested that a scientist of good conscience could avail himself of morally controversial biological materials as long as he was not involved in the actual destruction of the human being that was necessary for the derivation of that material.[8] In our current political and social climate, the Congregation for the Doctrine of the Faith has discerned that prudence dictates that we strenuously avoid any complicity or even any hint of complicity with evil in science.

Finally, it is important to emphasize that *Dignitas personae* makes two additional points, both of which are critically important in this discussion. First, it acknowledges that a citizen of good conscience may have grave and morally proportionate reasons to justify the use of morally controversial biological materials. For instance, certain vaccines used in the United States and elsewhere were developed using cells obtained from the corpses of aborted fetuses.[9] May families of good conscience vaccinate their children with these morally controversial reagents? In response, the Instruction explains that "danger to the health of children could permit parents to use a vaccine which was developed using cell lines of illicit origin" (n. 35). However, according to *Dignitas personae*, these parents retain the duty to make known their disagreement and to ask that their health care system make other types of vaccines available.

Next, the Instruction makes the distinction between those scientists who make the decision to use morally controversial cell lines and those scientists who have

[8]For one articulation of an argument that embraces the so-called criterion of independence see Ron Hamel and Michael R. Panicola, "Embryonic Stem Cell Research: Off Limits? Two Ethicists Discuss a Technological Breakthrough in the Context of Catholic Health Care," *Health Progress* 87.5 (September–October 2006): 23–29.

[9]For discussion, see Angel Rodríguez Luño, "Ethical Reflections on Vaccines Using Cells from Aborted Fetuses," *National Catholic Bioethics Quarterly* 6.3 (Autumn 2006): 453–459; and Alexander R. Pruss, "Complicity, Fetal Tissue, and Vaccines," *National Catholic Bioethics Quarterly* 6.3 (Autumn 2006): 461–470.

no say in the matter: "Moreover, in organizations where cell lines of illicit origin are being utilized, the responsibility of those who make the decision to use them is not the same as that of those who have no voice in such a decision." (n. 35). Those scientists in the former category—usually called the principal investigators of their laboratories—have a greater responsibility to make sure that their research groups witness to the absolute dignity and the sacredness of human life.

The Continued Use of Morally Controversial Cell Lines

For scientists of good conscience, *Dignitas personae* rules out undertaking biomedical research that involves morally controversial human cell lines. In light of its moral analysis, I propose that the Instruction also sheds light on another moral question that I have encountered in my own apostolate as a Catholic bioethicist and a working molecular biologist: May a scientist of good conscience who discovers that he is *already* working with a morally controversial cell line continue to use these cells?

In response, I propose that a scientist of good conscience should discontinue using the morally controversial cell line. As *Dignitas personae* points out, for scientists of good conscience, "the duty to avoid cooperation in evil and scandal relates to their ordinary professional activities, which they must pursue in a just manner and by means of which they must give witness to the value of life by their opposition to gravely unjust laws" (n. 35). However, I also suggest that to ensure that he fulfills the demands of justice, a scientist of good conscience who discovers that he is already working with a morally controversial cell line should be able to delay discontinuance for a reasonable amount of time.

At least two different scenarios are possible here. First, there is the case of the principal investigator who discovers that his laboratory uses a morally controversial cell line, say the HEK 293 cell line, to accomplish a particular task for his research team's experiments, for example, to grow an adenovirus. He may need time to find an alternative, noncontroversial cell line for his laboratory's experimental needs or, if one is not available, to switch research programs. This process may take months, or even years, especially if the principal investigator's research program—a set of experiments that were described in a grant proposal and funded as such for a particular period of time by a funding agency—requires the use of a particular morally controversial cell line that has no alternatives. In justice, while he is trying to find alternatives for his work, the personal investigator may need to complete ongoing experiments to justify continued use of the federal monies that were approved for a specific grant.

The process of discontinuing use of a morally controversial cell line may also take time because of the impact of this change of research priorities on the lives and well-being of the other scientists involved: In my view, a principal investigator who intends to shut down a research project or program that uses a morally controversial cell line needs, in justice, to identify alternative projects, or in some situations, alternative employment opportunities, for his research staff before acting on his moral convictions. He has a moral obligation to ensure the livelihood and well-being of his associates who depend on him for their employment. Again, fulfilling

this moral mandate may take time. Nonetheless, during this transition period, the principal investigator of good conscience needs to make all reasonable and prudential effort to make his moral position in defense of the dignity of human life clear and unambiguous.

Next, there is the case of the junior investigator—a postdoctoral fellow, a graduate student, or a laboratory technician—who discovers that he is working on a research project in a particular laboratory that requires the use of a morally controversial human cell line like HEK 293. He too may need time either to find alternative cell lines or to identity an alternative project. However, as *Dignitas personae* makes clear, the responsibility of the junior investigator differs from that of the principal investigator. A junior scientist may not be able to convince his supervisor that he needs to change protocols or projects. In this case, he will need to discern his future actions in prudence. He may discern that he needs to resign from his current laboratory to find employment and training elsewhere. This would be heroic.

It is also possible, however, that the junior investigator may discern that there are grave reasons for his staying to complete his research project—supporting his wife and children during a particularly prolonged recession, for instance—that would justify his continued use of the morally controversial cell lines. This too would be justifiable. Nonetheless, like the parents of good conscience who have immunized their children with vaccines developed using a morally controversial cell line, the junior investigator of good conscience continuing his research with HEK 293 needs to make all reasonable effort to minimize use of the controversial cell lines, to seek other alternatives, and to make his moral position in defense of the dignity of human life clear and unambiguous.

The Use of Biological Reagents and Techniques

As I noted above, the use of controversial moral cell lines has also led to and will continue to lead to the invention of biological reagents and techniques that become commonplace in the laboratory. For example, nearly forty-five years ago, HEK 293 cells were used to discover the calcium phosphate technique that is widely used in laboratories throughout the world to introduce foreign DNA into a mammalian cell.[10] More recently, HEK 293 cells were also used to develop the adenovirus vectors that have been used to reprogram adult somatic cells into induced pluripotent cells without the need of cancer-causing retroviruses.[11] May a scientist of good conscience undertake research with these reagents or techniques derived from or with morally controversial cell lines?

[10]For details. see F. L. Graham and A. J. van der Eb, "A New Technique for the Assay of Infectivity of Human Adenovirus 5 DNA," *Virology* 52.2 (April 1973): 456–467; and S. Bacchetti and F. Graham, "Transfer of the Gene for Thymidine Kinase to Thymidine Kinase-D Human Cells by Purified Herpes Simplex Viral DNA," *Proceedings of the National Academy of Sciences USA* 74.4 (April 1977): 1590–1594.

[11]For details, see Matthias Stadtfeld et al., "Induced Pluripotent Stem Cells Generated without Viral Integration," *Science* 322.5903 (November 7, 2008): 945–949.

In response, I propose that scientists of good conscience should make all reasonable effort to avoid using the products of research involving morally controversial cell lines for the same reasons outlined in *Dignitas personae*: They should avoid all possible complicity with evil, and they should avoid scandal. This directive will become even more important when reagents are developed using human embryonic stem cell lines derived from the destruction of human embryos lest scientists of good conscience inadvertently lead others to further acts of grave evil or to scandal. Instead, scientists of good conscience should use moral alternatives—there are now alternative techniques for introducing foreign DNA into mammalian cells[12]—or seek to replicate experiments in other cell lines that are not morally controversial. These efforts to recreate reagents will take time, and they may slow research, but these acts constitute heroic acts of virtue that witness to the inviolability and the dignity of human life.

Philanthrophic Funding of Biomedical Research

Finally, as we noted earlier, with the publication of the revised NIH stem cell guidelines, it is likely that the use of morally controversial cell lines will increase. More specifically, it is likely that these cell lines will be used in a diverse range of research projects seeking cures for different diseases, research projects that are often funded by private foundations that rely on the philanthropy of citizens to support biomedical research. The Juvenile Diabetes Research Foundation International, for instance, has been a notorious advocate of human embryonic stem cell research.[13] May a citizen of good conscience donate or continue to donate funds to private foundations that may direct their monies to research involving morally controversial cell lines, especially human embryonic cell lines derived from the destruction of human embryos?

In response, I propose that they can as long as their charitable giving is done prudently. For instance, donors of good conscience should ask the development or grants officer of the foundation who is responsible for procuring donations to direct their financial contributions to research that does not involve controversial cell lines. Requests of this kind would not only distance citizens of good conscience from any complicity with evil but also educate the staff of a foundation on issues of human dignity that they do not often consider. In my experience, philanthropic foundations make every reasonable effort to respect the wishes of their donors. If the option of earmarking donations to morally laudable projects is not available, then citizens of good conscience should refrain from contributing to that organization to avoid cooperating with evil.

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[12] For one survey of transfection protocols, see "Transfection of Cloned DNA" (section 6 of chapter 10), ed. David H. Margulies, in *Current Protocols in Immunology* (Hoboken, NJ: John Wiley, 2001), http://cda.currentprotocols.com/WileyCDA/CPTitle/isbn-0471522767,descCd-tableOfContents.html.

[13] For details, see Juvenile Diabetes Research Foundation, "Stem Cells Are Critical to Scientific Understanding of Diseases, Therapies, and Cures," *Stem Cell Facts*, May 2009, http://advocacy.jdrf.org/files/General_Files/Advocacy/2009/0509_SC_1_therapies.pdf.

Donors of good conscience should also be sensitive to the possibility of public scandal. Certain philanthropic organizations that support biomedical research—the Juvenile Diabetes Research Foundation International and the New York Stem Cell Foundation, for instance—have very publicly advocated policies promoting the use of morally controversial cell lines.[14] Money should not be given to these foundations, even if the funds are explicitly targeted for morally licit projects, lest the donation lead others to unwittingly support the other gravely immoral endeavors involving morally controversial cell lines also promoted by these organizations.

Finally, a critic may ask, what about the question of fungibility? Would donations earmarked for morally acceptable projects not permit a philanthropic foundation to use its other funds to pay for immoral research? Certainly, the possibility for this exists, and donors of good conscience could prudentially refuse to contribute to a private foundation that funds any research involving morally controversial cell lines. However, in prudence, these same donors could also decide—justifiably in my opinion—to contribute specially earmarked funds to private foundations devoted to biomedical research in the hope that their philanthropy would contribute to cure disease. This would be particularly true for those donors who support those specialized, often smaller, philanthropic groups dedicated to those rare diseases neglected by large funding agencies like the NIH, the National Science Foundation, and the Medical Research Council. Nonetheless, like the parents of good conscience who have immunized their children with vaccines developed using morally controversial cell line, these donors need to make their moral position in defense of the dignity of human life clear and unambiguous.

In sum, as *Dignitas personae* reminds scientists and other citizens of good conscience, there is an urgent need to mobilize consciences in favor of life and to remind people in the field of health care that there is an intrinsic and undeniable ethical dimension in the health care profession. Heroic acts that witness to the inviolability and the dignity of human life will be necessary ingredients for these mobilization efforts.

[14]Both organizations have promoted social policies advocating destructive human embryo research to obtain pluripotent embryonic stem cell lines. For details, see their Web sites at http://advocacy.jdrf.org/ and http://www.nyscf.org/get_involved/advocate.html.