The American Journal of Bioethics, 7(8): 45–53, 2007

ISSN: 1526-5161 print / 1536-0075 online
DOI: 10.1080/15265160701465361

Open Peer Commentaries

The Global HLA Banking of Embryonic Stem Cells Requires Further Scientific Justification

Zubin Master, Carleton University
Bryn Williams-Jones, Université de Montréal

There is a widely acknowledged shortage of and an increasing demand for transplantable human organs and tissues (e.g., kidney, heart, lung, liver, cornea) in developed and developing countries around the world. In response to this need, Lott and Savulescu (2007) propose the creation of a human embryonic stem (hESC) bank to facilitate the equitable and efficient dissemination of human leukocyte antigen (HLA) matched tissues and organs to patients in need of replacement. Although not an unreasonable proposal, the authors go on to make a much stronger claim. They argue that hESCs are such important tools for addressing the massive unmet global need for organs that it is ethically justified to require mandatory banking of spare embryos, and they argue for the use of financial (or other) inducements to procure embryos for the derivation of hESCs. To justify such a fundamental alteration of the basic ethical norms of human subjects research and tissue donation (i.e., informed choice, voluntary participation, and freedom from coercion), not to mention the allocation of significant public funds required to create a global hESC bank, there must first be clear scientific evidence demonstrating the feasibility of and likelihood that the proposed benefits (i.e., immune tailored transplantable tissues and organs) will ensue; only then can the broader ethical and political issues be debated with any clarity. It is our contention that Lott and Savulescu's (2007) proposal fails on two counts: 1) they have not proven that the problem of immune rejection of transplanted hESCs can be overcome through a global HLA-typed hESC bank; and more generally, 2) they have not substantiated the claim that hESCs will enable the production of whole organs and tissues for transplantation.

To begin with, the notion that transplanted hESCs will be rejected after transplantation has yet to be scientifically substantiated. In fact, research suggests that hESCs may share immune privileges with other embryonic tissue and that direct transplantation may not necessarily generate an immune response. For example, the immune systems of pregnant women can tolerate fetuses that express major histocompatability antigens from the father (Fändrich et al. 2002a). In the laboratory, it has been shown that the injection of either undifferentiated or differentiated hESCs into immunocompetent mice fails to elicit a T cell-mediated immune response (Li et al. 2004). Although levels of major histocompatability complex (MHC) class I expression on hESCs are sufficient for immune recognition, the immunostimulatory properties of hESCs and their differentiated cell types is low compared with that of adult cells, suggesting that allograft rejection of hESCs may be significantly reduced (Drukker et al. 2006). One experiment showed that rat ES-like cells injected into immunocompetent MHC-mismatched rats engraft well without supplementary host conditioning, allowing for long-term acceptance of a second set of transplanted cardiac allografts (Fändrich et al. 2002b). Thus efforts to bank hESCs based on broad HLA types, as proposed by Lott and Savulescu (2007) may not be necessary because hESCs themselves may be immune privileged.

Yet if issues of immunocompatibility of hESCs do arise, other novel scientific methods may, in the not too distant future, be used to derive histocompatible hESCs. For example, it has been shown that parthenogenetic activation of mouse oocytes can be used as a source of embryonic stem cells that contain the full complement of MHC antigens of the ovum donor (Kim et al. 2007). Parthenogenetic activation of human oocytes can occur, and so it is likely that human eggs may also serve as a source for hESCs. Although hESCs derived from parthenogenetic oocytes will only be immune compatible with the female egg donor, such

Acknowledgments: The views expressed here are strictly those of the authors and do not reflect the positions of the Government of Canada or of academic institutions.
Address correspondence to Zubin Master, Centre on Values and Ethics, Carelton University, 3A37 Patterson Hall, Carleton University, Ottawa, ON K1S 5B6, Canada. E-mail: zubin@zubsplace.com

a method may be feasible for some women who require hESCs for regenerative transplantation. Another method to derive immunocompatible hES-like cells, proposed by Cowan et al. (2005), could be to fuse somatic cells from a host with established hESC lines. In their experiment, Cowan et al. (2005) demonstrated that, after fusion, the nucleus of somatic cells can be reprogrammed to confer greater potentiality. Although the expression of MHC antigens on these chimeric cells was not examined, such cells may be less immunoreactive and could serve as a novel means of creating immunocompatible pluripotent cells. Although these two methods require further research to evaluate their feasibility for cell and tissue regeneration, so too does the creation of an HLA bank of hESCs, especially in terms of the ability of hESCs to bypass immune recognition or elicit an immune response.

Lott and Savulescu (2007) discuss somatic cell nuclear transfer (SCNT) as a potential source of immunocompatible hESCs, but dismiss this method as scientifically unfeasible. Yet they repeatedly state that hESCs will lead to the design and production of transplantable tissue and organs, a claim that they also fail to justify scientifically. While we agree that there is a real potential that hESCs will be able to contribute to the regrowth or repair of damaged tissues, it is far from being evident that hESCs will lead anytime soon to the economic and timely production of complex whole organs for transplant. Lott and Savulescu (2007) take for granted that the production of whole organs will soon be realized, and use this supposition as one of the primary justifications for the creation of an international hESC bank. Yet there is simply no evidence presented to support their position that "an hESC bank could relieve pressure on current organ procurement and allocation programs, thereby increasing the relative availability of donated organs and improving organ transplantation-related health outcomes" (Lott and Savulescu 2007, 37).

Given the complete lack of scientific evidence to support their claim, it becomes much harder for Lott and Savulescu (2007) to justify the mandatory banking of hESCs, or even the somewhat less controversial use of opt-out mechanisms (in which couples going through *in vitro* fertilization have not expressed explicit views on the disposition of spare embryos) or financial incentives to help procure embryos. Regardless of whether we accept the utilitarian arguments for hESC banking—which most countries have rejected for blood and organ donation programs—in the absence of robust scientific evidence, it is one thing to claim that spare embryos should be *solicited* for an hESC bank, but quite another to argue that the "needs of transplant patients outweigh the rights of couples, clinics, or disinterested governments to determine the fate of unwanted embryos" (Lott and Savulescu 2007, 37).

The science of cloning, the immunoreactivity of hESCs, the creation of chimeric cells, the derivation of hESCs from parthenogenetically activated oocytes, and the potential of hESCs to treat degenerative or diseased cells and tissue still require significant scientific research. As such, we argue that much progress must first be made in understanding these scientific and clinical issues before sufficient evidence exists to justify the global banking of hESCs for clinical application. But even if such evidence were available, we would still be skeptical of Lott and Savulescu's (2007) claim that hESCs are the best way to alleviate the current organ shortage, or that widely accepted norms in research and medical ethics ought to be changed. Altering research ethics norms based on unsubstantiated or unjustified scientific evidence is simply morally irresponsible. ■

REFERENCES

Cowan, C.A., K. Atienza, D. A. Melton, et al. 2005. Nuclear reprogramming of somatic cells after fusion with human embryonic stem cells. *Science* 309(5739): 1369–1373.

Drukker, M., H. Katchman, G. Katz, et al. 2006. Human embryonic stem cells and their differentiated derivatives are less susceptible to immune rejection than adult cells. *Stem Cells* 24(2): 221–229.

Fändrich, F., B. Dresske, M. Bader, et al. 2002a. Embryonic stem cells share immune-privileged features relevant for tolerance induction. *Journal of Molecular Medicine* 80(6): 343–350.

Fändrich, F., X. Lin, G. X. Chai, et al. 2002b. Preimplantation-stage stem cells induce long-term allogeneic graft acceptance without supplementary host conditioning. *Nature Medicine* 8(2): 171–178.

Kim, K., P. Lerou, A. Yabuuchi, et al. 2007. Histocompatible embryonic stem cells by parthenogenesis. *Science* 315(5811): 482–486.

Li, L., M. L. Baroja, A. Majumdar, et al. 2004. Human embryonic stem cells possess immune-privileged properties. *Stem Cells* 22(4): 448–456.

Lott, J. P., and J. Savulescu. 2007. Towards a global human embryonic stem cell bank. *American Journal of Bioethics* 7(8): 37–44.