

# A Review of Pressing Ethical Issues Relevant to Stem Cell Translational Research

*Ubaka Ogbogu*

## **Introduction**

In recent months, a number of national and international events have led to renewed interest in the ethical issues relevant to stem cell research (SCR). Some of the notable events include: the Korean egg donation and fabricated stem cell experiments/publication scandal,<sup>1</sup> the controversy over the use for research of donated fresh embryos created for reproductive purposes by Canadian stem cell researcher, Andras Nagy,<sup>2</sup> a recently published study on gaps in informed consent procedures in Canadian *in vitro* fertilization (IVF) clinics,<sup>3</sup> and the current debate in the UK over altruistic egg donation for research purposes.<sup>4</sup> Most, if not all of these events, played out in the media and public eye, thereby generating more public debate and controversy in a field arguably considered the most socially controversial and divisive in biomedical research. More importantly, the relatively close proximity between these events has made it difficult for policymakers and researchers to keep pace with the issues. As Canadian researchers edge closer to the first stem cell clinical trials,<sup>5</sup> many would agree it is imperative to identify and examine the most salient and pressing ethical issues relevant to stem cell research.

This investigation is important for two reasons. First, identification and scholarly analysis of these issues will inform the direction of policy-making. Health Canada, the primary science policymaker and regulator, is currently reviewing regulations on a range of matters relating to controlled activities under the *Assisted Human Reproduction Act* (the Act).<sup>6</sup>

It seems axiomatic therefore that by focussing scholarly analysis on the most pressing and relevant ethical issues, ethics researchers are likely to play a significant role in the development of sustainable science policy.

Second, by focussing research on the most important issues, individuals that research ethical, legal and social issues in biomedical research (ELSI researchers) can provide ethical guidance to stem cell researchers. Such guidance is pivotal to the ethical conduct of translational research and maintenance of public trust in stem cell research.

In the following sections of this brief review piece, I identify and outline pressing ethical issues relevant to stem cell research as it moves towards clinical trials and applications. These issues are compiled from consultations with Canadian research ethics experts, stem cell researchers, ethics review board (REB) members, and policymakers, including those within Health Canada, the Department of Justice and the Stem Cell Oversight Committee.<sup>7</sup>

The methods of this study are as follows. Participants were sent email messages soliciting their ideas on what constitutes the most pressing research ethics issues relevant to stem cell translational research. Responses were collated and categorized under broad topic areas. The topics were then reviewed by a panel of experts through teleconference discussions.

Note that no attempt is made to analyze or examine these issues in any exhaustive detail as this is outside the possible



scope of a single paper. However, in some cases, I have provided relevant background information garnered from the panel discussion.

### 1. Consent issues

There was overwhelming consensus among our participants on the need to identify and address issues around informed consent principles and processes within the stem cell clinical research context. This agreement is reflective of the current interest of researchers and policymakers in existing consent processes for human subjects research in Canadian research institutions. Specifically, in September 2005, Health Canada released proposed regulations governing informed consent procedures under the Act for public comment.<sup>8</sup> The regulations will give effect to Section 8 of the Act, which prohibits the use of human reproductive material to create embryos, and the use of *in vitro* embryos for any purpose, without the donor's written consent. Matters addressed by the regulations include conditions for obtaining consent, validity of consent, and conditions for the withdrawal of consent. The regulations will take effect when they are published in the Canada Gazette, Part II, expected in Spring 2006.<sup>9</sup>

Another issue of interest to our participants was a recent empirical study of consent processes in Canadian IVF clinics, which concluded that only one clinic had legally adequate consent procedures for the future donation of cryopreserved embryos for SCR.<sup>10</sup> However, the study did not clearly indicate whether the defaulting clinics were typically involved in providing cryopreserved embryos for SCR. It could therefore be argued that clinics not involved in embryo donation for research have no reason to include the research donation option in their consent forms. In the event that that option becomes available at those clinics, one might expect they would revise their consent forms and guidelines accordingly (perhaps in response to recommendations from REBs). All agreed a follow-up study of consent practices in IVF clinics involved in egg donation for SCR was necessary to determine the extent of compliance with existing consent regulations.

The specific topics identified under this heading are as follows.

- a. Empirical study of consent practices in IVF clinics involved in stem cell research;
- b. compliance with and practicality of consent regulations;

- c. issues around blanket and specific consent, validity of blanket consent, and procedures for obtaining additional consent;
- d. timing of consent, and the right to withdraw consent;
- e. informed consent mechanisms (e.g. providing adequate background information to donors versus merely requiring their signatures on a form);
- f. the role of independent advocates in the consent process; and
- g. international perspectives and approaches to consent regulation and practices.

### 2. Egg and gamete donation / Use of fresh embryos

An examination of gamete donation issues is very timely given the recent Korean egg donation scandals and the proposed UK regulations on altruistic egg donation. In Canada, there is already some debate on the extent of legislative protection of women's reproductive rights as they relate to gamete donation. One point of controversy is the use for research, of fresh embryos originally produced for reproductive purposes. Although the Act prohibits the creation of embryos specifically for research purposes, there is no prohibition in the Act against donating fresh embryos created for reproductive purposes to research. Some have called for a moratorium on the practice because it is "morally problematic" under the ethical code that regulates the medical profession, and increases the risk of harm to patient undergoing fertility treatments.<sup>11</sup> Also, there are recent concerns about the growing trend of women advertising their ova for sale on the Internet.<sup>12</sup> These concerns are closely linked to fears about the potential for commodification of human genetic material. Given the centrality of gamete donation to stem cell research, it is important to examine the merits of existing donation options, especially in the light of ethical concerns. Research is also needed on borderline issues such as gamete donation and the protection of donor interests through informed consent, and the avoidance of conflicts of interest in procuring research material.

Specific research topics identified by participants include:

- a. donor-researcher relationships broadly considered;
- b. donor anonymity, linkeability, traceability; and
- c. the use of fresh embryos produced for reproductive purposes for research.



### 3. Conflicts of Interest

Conflicts of interest involving researchers, academic institutions, funding agencies, ethics review boards and industry have emerged as a key research ethics issue in biomedical research.<sup>13</sup> Several factors account for this, the most significant of which is, arguably, the interest in commercializing resulting therapies. In Canada for example, most research funders are mandated to commercialize research outcomes and have taken significant steps to incorporate this mandate into funding decisions and the management of their research portfolios. Conflicts of interest pose an ethical dilemma because they compromise research integrity and the safety of human participants. In Canada, the well-known Olivieri and Healy incidents are the best examples of the problems conflicts of interest pose in the biomedical research environment.<sup>14</sup>

Identified topics include:

- a. pressure drivers other than commercialization, e.g., individual and institutional reputation;
- b. oversight and regulatory mechanisms (including professional and institutional as well as more formalized oversight systems);
- c. the role of research funding institutions in the management of conflicts of interest (is it appropriate for funding institutions to regulate behavior or should this be left to regulatory agencies?); and
- d. international approaches to oversight of conflicts of interest.

### 4. Governance Issues

The discussion on governance is overarching as it contemplates on all of the other areas identified in this paper. Given the important connection between governance and science policy, our participants were of the view that research was needed on strategies that adopt a holistic approach to governance beyond that of traditional ethics review.<sup>15</sup> To facilitate this broad study, it was deemed important to isolate the governance issues and treat them as a single topic. Specific issues identified include:

- a. management of consent, specifically, administrative mechanisms;
- b. the scope and effect of provincial and federal health information regulations;
- c. current approaches to health assessment technology — are they adequate for assessing stem cell therapies?;
- d. designing governance systems, specifically, the relevance of donors and recipients' experiences versus the concerns of researchers and regulators; and

- e. adaptability of oversight/governance mechanisms to new circumstances (are there adequate learning loops in the form of quality assurance and quality improvement?).<sup>16</sup>

### 5. Public Trust and Education

Maintaining public trust in stem cell research is, arguably, the most important social issue influencing the ethical and legal direction of SCR. A number of claims exist in the literature about the connection between scientific research and public trust, the most significant of which are that public perceptions influence science policymaking,<sup>17</sup> that media hype and sensationalism of scientific issues influences public perception of science, especially controversial technologies like SCR,<sup>18</sup> and that the “aura of secrecy and mystique that surrounds science, and the sense that work is being conducted ‘behind closed doors’ breeds public distrust.”<sup>19</sup> The corollary of these claims is that it is imperative to explore unique strategies for properly informing public opinion on SCR. In order to facilitate this goal, our participants identified the following topics for study.

- a. The impact of public perception on researchers' perspectives (e.g. do researchers abandon research for fear of controversy? Do public perceptions affect the direction or conduct of research?);
- b. beliefs and attitudes of human research subjects towards the conduct of research; and
- c. role and impact of patient advocacy and advocate groups in shaping public perceptions.

### 6. Novel Therapies

As stem cell research continues its advance towards clinical trials and therapeutic applications, there is growing interest in questions of infrastructure and delivery platforms for clinical testing and cellular therapies. The concerns here range from issues related to clinical trial oversight to the management of delivery systems to ensure equitable access to the benefits of stem cell research. While these issues are not unique to stem cell research, it is important to explore their unique application to stem cell clinical trials and movement of novel therapies. Topics to be examined include:

- a. stem cell banks and clinical trial registries; and
- b. the adequacy of our current system of oversight for both innovative therapies and clinical trials for addressing the unique challenges presented by stem cell research.



## Conclusion

Advances in SCR continue to generate considerable ethical and legal issues as the science moves towards clinical applications. Most of these issues are either unique to or pose unique questions for researchers, policymakers, stakeholders, and the public. Understanding and applying the best ethical practices in the conduct of SCR therefore requires a “process of identification of international ethical standards and practices [that] include concerted efforts to engage people throughout the world in honest conversations about the science and ethics of stem cell research and its converging applications.”<sup>20</sup> This paper addressed this goal by providing a rough guide to ELSI researchers on what issues to focus attention. Although the issues identified here are by no means exhaustive, they are matters of current concern and interest to policymakers, ethics experts and stem cell researchers. Research on these issues is therefore necessary in order to ensure that SCR progresses in ethically acceptable ways.

---

*Ubaka Ogbogu is a Research Associate, Health Law Institute, Faculty of Law, University of Alberta, Edmonton.*

This research is funded by a grant from the Canadian Stem Cell Network, a member of the Network of Centres of Excellence (NCE) program. The author would like to acknowledge and thank the following for their invaluable contribution to the writing of this article: Timothy Caulfield, Rosario Isasi, Michael McDonald, Jane Steblecki and Omolaya Oladipo.

1. See “S Korea cloning pioneer disgraced” *BBC News* (24 November 2005), online: BBC News <<http://news.bbc.co.uk/1/hi/world/asia-pacific/4465552.stm>>; David Cryanoski, “Blow Follows Blow For Stem-Cell Work” (2006) 439 *Nature* 8; Evan Y. Snyder & Jeanne F. Loring, “Beyond Fraud — Stem-Cell Research Continues” (2006) 354 *New England Journal of Medicine* 321.
2. See “Canada’s first embryonic stem cell lines, Mount Sinai Hospital” *Medical News Today* (9 June 2005), online: Medical News Today <<http://www.medicalnewstoday.com/medicalnews.php?newsid=25867>>. See also Jeffrey Niskier & Angela White, “The CMA Code of Ethics and the Donation of Fresh Embryos for Stem Cell Research” (2005) 173 *Canadian Medical Association Journal* 621 [Niskier & White].
3. Francoise Baylis & Natalie Ram, “Eligibility of Cryopreserved Human Embryos for Stem Cell Research in Canada” (2005) *Journal of Obstetrics and Gynaecology Canada* 949.
4. See “Cloning research egg donor plan” *BBC News* (14 February 2006), online: BBC News <<http://news.bbc.co.uk/1/hi/health/4711564.stm>>. The term “altruistic egg donation” refers to the procurement of eggs from donors not undergoing medical procedures. Altruistic donation is already allowed in the UK to help infertile couples conceive. UK’s human embryo research regulator, the Human Fertilisation and Embryology Authority (HFEA), is currently considering a set of recommendations that will allow stem cell scientists to procure eggs from donors who are not undergoing medical treatment. In Canada, altruistic egg donation for the purpose of creating an embryo is a controlled activity under the *Assisted Human Reproduction Act*. This means that it is a licensed activity that can only be carried out in accordance with regulations made under the Act. No regulations or licences have been issued to date.
5. See “Researchers look to stem cells to aid recovery from stroke” *Stem Cell Network News* (15 October 2002), online: Stem Cell Network <<http://www.stemcellnetwork.ca/news/articles.php?id=194>>.
6. S.C. 2004, c. 2.
7. The consultations are part of a study on ethical, legal and social issues (ELSI) relevant to emerging stem cell therapies. The study is funded by the Canadian Stem Cell Network and led by the Health Law Institute of the University of Alberta.
8. Assisted Human Reproduction (Section 8) Regulations, C. Gaz. 2005. I 3165; “Health Canada introduces first proposed regulations under the *Assisted Human Reproduction Act*” *Health Canada News Releases* (19 September 2005), online: Health Canada <[http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/2005/2005\\_100\\_e.html](http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/2005/2005_100_e.html)> [Health Canada News Release].
9. Health Canada News Release, *ibid*.
10. *Supra* note 3.
11. Niskier & White, *supra* note 2 at 622.
12. “Women advertising ova for sale on the Internet” *CTV News* (8 March 2006), online: CTV <[http://www.ctv.ca/servlet/ArticleNews/story/CTVNews/20060308/women\\_eggs\\_060308/20060308?hub=Health](http://www.ctv.ca/servlet/ArticleNews/story/CTVNews/20060308/women_eggs_060308/20060308?hub=Health)>. The sale of sperm or ova, offering to sell sperm or ova, and advertising for the sale



of sperm and ova is not prohibited by the Act. In other words, the man or woman who provides their gametes for sale cannot be charged with an offence. This approach was adopted on the basis that gamete donors, especially women, may often be vulnerable and exploited, and hence it was decided not to create an offence for their sale of their gametes.

13. There is vast literature on the subject. See e.g. Timothy Caulfield, "Commentary: An Independent Voice?: Conflicts of Interest and Research on Ethical, Legal and Social Issues" ((2005) 13:2 & 3 Health Law Review 114; Justin E. Bekelman, Yan Li & Cary P. Gross, "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review (2003) 289 The Journal of the American Medical Association 454; Patricia Baird, "Getting it Right: Industry Sponsorship and Medical Research" (2003) 168 Canadian Medical Association Journal 1267; Michael M.E. Johns, Mark Barnes & Patrik S. Florencio, "Restoring Balance to Industry-Academia Relationships in an Era of Institutional Financial Conflicts of Interest: Promoting Research while Maintaining Trust" (2003) 289 The Journal of the American Medical Association 741; Timothy Caulfield, "The Commercialization of Human Genetics: A Discussion of Issues Relevant to the Canadian Consumer" in Bartha Maria Knoppers & Alan Mathios, eds., *Biotechnology and the Consumer* (Dordrecht, The Netherlands: Kluwer Academic Publishers, 1998) 125.
14. The Olivieri and Healy incidents have a number of common elements. Both were medical researchers at the University of Toronto who experienced negative consequences including the loss of their jobs, for disclosing adverse information about drugs tested in their research. The drug manufacturers were major research funders at and donors to the University of Toronto, a situation that led the university to abandon support for the researchers. For a full account of the Olivieri case, see A.M. Viens & J. Savulescu, "Introduction to the Olivieri Symposium" (2004) 30 Journal of Medical Ethics 1. See also A. Schafer, "Biomedical Conflicts of Interest: A Defence of the Sequestration Thesis — Learning From the Cases of Nancy Olivieri and David Healy" (2004) 30 Journal of Medical Ethics 8; R. Rhodes & J.J. Strain, "Whistleblowing in Academic Medicine" (2004) 30 Journal of Medical Ethics 35.
15. Governance for ethical research involving humans has been an important topic in the Canadian bioethics community. For an overview of past initiatives in this area, see Michael McDonald, "Special Issue: Canadian Governance for Ethical Research Involving Humans" (2005) 13:2 & 3 Health Law Review 5.
16. See generally Michael McDonald, "The Governance of Health Research Involving Human Subjects: Reflections on Ethical Policy for Scientific Research" (2000) 6:11 *Transactions Science and Ethics: Royal Society of Canada Special Issue* 49.
17. See Robin Downey, Rose Geransar & Edna Einsiedel, "Angles of Vision: Stakeholders & Human Embryonic Stem Cell Policy Development" in Edna Einsiedel & Frank Timmermans, eds., *Crossing Over: Genomics in the Public Arena* (Calgary: University of Calgary Press, 2005) 61.
18. See David F. Ransohoff & Richard M. Ransohoff, "Sensationalism in the Media: When Scientists and Journalists May Be Complicit Collaborators" (2001) 4 *Effective Clinical Practice* 185. See also "Media 'sensationalising science'" *BBC News* (3 March 2006) online: BBC <<http://news.bbc.co.uk/2/hi/science/nature/4771154.stm>>. Compare Tania M. Bubela & Timothy A. Caulfield, "Do the Print Media 'Hype' Genetic Research? A Comparison of Newspaper Stories and Peer-Reviewed Research Papers" (2004) 170 *Canadian Medical Association Journal* 1399.
19. Tania M. Bubela & Timothy Caulfield, "Media Representations of Genetic Research" in Edna Einsiedel & Frank Timmermans, eds., *Crossing Over: Genomics in the Public Arena* (Calgary: University of Calgary Press, 2005) 117 at 126.
20. The Hinxton Group: An International Consortium on Stem Cells, Ethics and Law, Consensus Statement (24 February 2006), online: The Phoebe R. Berman Bioethics Institute, John Hopkins University <<http://www.hopkinsmedicine.org/bioethics/finalsc.doc>>.

