

DOES A PATIENT HAVE A CONSTITUTIONAL RIGHT TO THE FREEDOM OF MEDICAL RESEARCH? REGENERATIVE MEDICINE AND THERAPEUTIC CLONING RESEARCH IN CANADA

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Constitutional arguments regarding the freedom of scientific research often focus on the freedom of speech of researchers, with much less attention to the potential constitutional claims that could be made on behalf of patients who may one day benefit from the fruits of that research. This article explores whether patients have a claim to unimpeded medical research under the Canadian *Charter of Rights and Freedoms*, using as a case study the Canadian federal prohibition on human cloning—including “therapeutic cloning” (or the derivation of stem cells that are immunologically compatible with the recipient patient for use in regenerative medicine). The conclusion drawn in this case study is that a constitutional claim can be made in this context and ought to be available as an argument more broadly, although the speculativeness of the eventual benefits of therapeutic cloning research is a significant weakness. The concern over harm to women due to the demand for human oocytes for research and eventual therapy is a credible and compelling one that would justify some restrictions on the research under section 1 of the *Charter*. Nonetheless, the prohibition of all ther-

Les arguments constitutionnels portant sur la liberté de recherche scientifique mettent la plupart du temps l’emphase sur la liberté d’expression des chercheurs, mais beaucoup moins sur les revendications potentielles au nom des patients qui pourraient un jour bénéficier des fruits de ces recherches. Cet article se questionne à savoir si des patients pourraient déposer un recours pour garantir la libre recherche scientifique en vertu de la Charte canadienne des droits et libertés, en utilisant comme exemple l’interdiction fédérale sur le clonage humain, qui inclut le clonage thérapeutique (l’utilisation de cellules souches compatibles immunologiquement avec le receveur pour un usage en médecine régénérative). La conclusion tirée de ce cas de figure est qu’une revendication constitutionnelle est possible et devrait être utilisée de façon plus large, malgré que l’incertitude sur les bénéfices éventuels du clonage thérapeutique constitue une faiblesse importante de l’argument. Les inquiétudes concernant les femmes, compte tenu de la demande pour des ovocytes humains à des fins de recherche et éventuellement à des fins de traite-

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Citation: Jennifer A Chandler, “Does a Patient have a Constitutional Right to the Freedom of Medical Research? Regenerative Medicine and Therapeutic Cloning Research in Canada” (2012) 6:2 MJLH 1.

Référence : Jennifer A Chandler, « Does a Patient have a Constitutional Right to the Freedom of Medical Research? Regenerative Medicine and Therapeutic Cloning Research in Canada » (2012) 6:2 RDSM 1.

apeutic cloning research is vulnerable to the argument that it is overbroad in that it forecloses lines of therapeutic cloning research that do not endanger women.

ment, sont crédibles et convaincantes et pourraient justifier des restrictions sur la recherche en vertu de l'article 1 de la Charte. Par contre, l'interdiction de tout clonage thérapeutique pourrait être perçue comme ratissant trop large, empêchant la recherche sur des types de clonages thérapeutiques ne présentant pas de risques pour les femmes.

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Introduction

Constitutional scrutiny of state restrictions on scientific research usually focuses on the liberty interests of scientists to research, teach and publish as they see fit and the countervailing limits that society is entitled to place on this research where harm to the public interest is feared. Another approach to the constitutionality of state restrictions on scientific research is to consider the interests of the patients who might one day benefit medically from the treatments that medical research makes possible.

This paper explores the question of whether patients have a constitutionally protected interest in unrestricted medical research based on their constitutional right to life, liberty, and security of the person under section 7 of the *Charter of Rights and Freedoms*.¹ Of course, if there is such a right, it will be subject to reasonable limits under section 1 of the *Charter*. Indeed, some forms of restriction on research are now commonplace and easily justified, such as ethical requirements for research involving human subjects. Far less common are government prohibitions on particular research questions or fields of research.

While the focus of this article is the structure and viability of the suggested section 7 claim to medical research unimpeded by government restrictions, it is undeniable that medical research raises questions of broader social and political significance. The choice of research questions, the availability of funds, the likelihood of commercialization of ensuing discoveries, and the eventual access to treatments have socio-political and economic dimensions that are of fundamental importance to patients in need of therapeutic assistance. As a result, an exploration of the proposed section 7 claim against government restrictions on particular lines of medical research can provide only a partial contribution to the more complex problem of balancing liberty, distributive justice, and the public good in the field of medical research. However, the question of whether such a claim can be advanced and what its strong and weak points might be is an important one. It offers a different vantage point upon the way that individual human rights protections might intersect with medical research (beyond a focus on the liberty of researchers). There is also a partial precedent for this type of claim in the American case of *Abigail Alliance*,² where a patient unsuccessfully advanced

¹ *Canadian Charter of Rights and Freedoms*, Part I of the *Constitution Act, 1982*, being Schedule B to the *Canada Act 1982* (UK), 1982, c 11, s 7 [*Charter*].

² *Abigail Alliance for Better Access to Developmental Drugs v Von Eschenbach*, 495 F (3d) 695 (DC Cir 2007), rev'g 445 F (3d) 470 (DC Cir 2006) [*Abigail Alliance*].

a constitutional claim to unimpeded access to an experimental drug that had not yet received government approval. A focus on the extent of a patient's section 7 interests at other points throughout the medical research process thus fits within contemporary thinking about constitutional rights related to health care.

There are also good policy reasons to recognize that patients have a potential constitutional right to unimpeded medical research, even if restrictions may ultimately be justified in particular cases. Without such a right, governments might be able to use "upstream" research restrictions to prevent access to treatments that they might find difficult as a constitutional matter to withhold from patients once the treatments come into existence. For example, a government opposed to abortion could decide to prohibit the clinical testing of an experimental abortifacient drug that looks very likely to be an improvement over existing methods in terms of safety and cost-effectiveness.³ If potential beneficiaries of that research were unable to establish a claim, then governments could try to restrict abortion by preventing the upstream research that might improve access to safe abortion.

I have selected as a case study with which to explore this potential section 7 claim, the Canadian criminalization of therapeutic cloning research⁴

³ Canada is one of the few developed countries that has not approved mifepristone (also known as RU-486) for induced abortion. Erdman et al note that no application has been made to approve the drug in Canada, speculating that this is because of inadequate financial incentives for the pharmaceutical company as well as political bias. Joanna N Erdman, Amy Grenon & Leigh Harrison-Wilson, "Medication Abortion in Canada: A Right-to-Health Perspective" (2008) 98:10 Am J Pub Health 1764 at 1764.

⁴ The terminology in this controversial and cutting-edge area of science is contested. The term "therapeutic" is commonly used to distinguish cloning research aimed at generating stem cells from attempts to generate a cloned living organism ("reproductive cloning"). Some question the use of the word "therapeutic," on the ground that it misleadingly suggests that the research is close to supplying therapies (see e.g. Diane Beeson & Abby Lippman, "Egg Harvesting for Stem Cell Research: Medical Risks and Ethical Problems" (2006) 13:4 *Reprod Biomed Online* 573 at 576; Alexander Morgan Capron, "Placing a Moratorium on Research Cloning to Ensure Effective Control over Reproductive Cloning" (2002) 53 *Hastings LJ* 1057; Jocelyn Downie, Jennifer Llewellyn & Françoise Baylis, "A Constitutional Defence of the Federal Ban on Human Cloning for Research Purposes" (2005) 31 *Queen's LJ* 353 at 355). Others object to the term "cloning" to describe therapeutic cloning since it is said to evoke fears of reproductive cloning (see e.g. Robert P Lanza et al, "The Ethical Validity of Using Nuclear Transfer in Human Transplan-

under the *Assisted Human Reproduction Act*.⁵ Therapeutic cloning research, unlike reproductive cloning, is not intended to produce live cloned human offspring. Instead, the hope is that it may offer a way to generate immunologically compatible stem cells for use in regenerative medicine.

This case study offers an excellent context in which to consider this potential claim for several reasons. First, the science of stem cell research is rapidly changing so that the benefits and harms associated with this research are unstable, potentially making it difficult to establish a harmful deprivation if the research is prohibited or to show that such research produces a harm requiring a prohibition on the research. Other contexts might be simpler, but this case study is a good way to explore the complexities on both sides of the argument, and it is typical of the uncertainty in cutting-edge and controversial scientific fields.

Second, there are several types of arguments in favour of the prohibition on therapeutic cloning research. For example, as is discussed later in the article, one of the central reasons for the prohibition appears to be to protect women from exploitation and the health risks associated with hormonal stimulation and surgical removal of the many egg cells (oocytes) likely to be needed for cloning research. In addition to this compelling harm-based concern, other justifications based on moral judgments about the status of the embryo or the instrumental use of reproductive materials are also invoked. As a result, we may consider the effects on a right to unrestricted medical research of both clearly harm-based justifications for the prohibition as well as justifications where the harm involved is much less clear or is contested.

Although the Supreme Court of Canada frequently rejects claims in which patients seek to have the state provide particular medical treatments, it has also found that the state may violate a patient's section 7 *Charter* rights where it impedes that patient's ability to obtain necessary medical treatment.⁶ The argument explored in this paper also takes the form of a negative right-based argument—that is, the claim is based on a prohibition of research rather

tation" (2000) 284:24 JAMA 3175 at 3175; Jonathan D Moreno, "The Name of the Embryo" (2006) 36:5 Hastings Center Report 3 at 3). I will use the term "therapeutic cloning research," even though "biomedical cloning research" is preferred by some, because this is the terminology that is most widely used and recognized.

⁵ SC 2004, c 2, s 5 [AHRA].

⁶ See *Chaoulli v Quebec (AG)*, 2005 SCC 35, [2005] 1 SCR 791 [*Chaoulli*].

than a demand that research be conducted. However, the claim being explored here does not clearly fit within these precedents because it considers state restrictions on upstream research that might produce new medical treatments rather than state interference with access to medical treatments that have already been established.

Several complexities must be addressed in constructing a section 7 claim to unimpeded medical research in the context of the prohibition on therapeutic cloning research. First, it is unclear whether therapeutic cloning research would generate useful therapies if it were permitted (although many argue that it either will do so or it will at least contribute to the discovery of other useful therapies). As a result, a patient's claim is based on the loss of a speculative benefit. The speculativeness is compounded where the anticipated benefit could potentially be achieved through alternative albeit similarly speculative lines of research that are permitted. As discussed below, there are problems with constitutional rights claims based on speculative harms, although they may not always be insurmountable.

Second, the patient is claiming a violation of a constitutional interest flowing from the restriction of the freedom of a third-party researcher (setting aside the case of a patient who is him or herself a stem cell researcher). Although this seems odd on first glance, a constitutional interest in the freedom of others is typical of claims in the area of access to medical treatment given that patients are usually unable to treat themselves and must rely upon third party assistance.

Third, I anticipate the objection that there can be no right to unimpeded medical research because there is no constitutional right of access to experimental medications, at least under American law.⁷ There is a similarity between these two claimed rights as both involve claims to potential medical benefits and both involve state intervention at points along the path of development of a new therapy. However, as discussed in more detail below, the two contexts are different in that one asserts an interest in research while the other is a demand of access to an existing (albeit experimental) therapy, and the two raise quite different policy concerns. An approach that accepts a right to unrestricted medical research but allows for limitations on that right under section 1 of the *Charter* can accommodate the different reasons for limiting the right in the two contexts of upstream research: prior to the discovery of a therapy and during clinical trials of the therapy once it is discovered.

⁷ *Abigail Alliance*, *supra* note 2.

In addition to these three questions specific to the proposed *Charter* right of patients to freedom of medical research, the constitutional analysis must address two further matters. A violation of section 7 is not established unless the deprivation of the right to life, liberty, or security of the person fails to accord with the “principles of fundamental justice.” If this is the case, a rights violation is established and the analysis turns to the question of whether the violation is justified under section 1 of the *Charter*. These two questions will be the last two issues explored in the constitutional analysis later in this article.

The conclusion drawn in this case study is that a section 7 claim against state restrictions on medical research is available in this context and ought to be available as an argument more broadly, although the speculativeness of the eventual benefit is a significant weakness in this particular context. However, in the context of therapeutic cloning, the concern regarding harm to women is a credible and compelling one that would justify some restrictions on the research under section 1 of the *Charter*. Nonetheless, the prohibition of all therapeutic cloning research is arguably overbroad in that it forecloses lines of therapeutic cloning research that do not endanger women. A preferable approach would be to prohibit cloning research involving oocytes taken from women and girls (apart perhaps from oocytes sourced from ovarian tissue removed for therapeutic reasons).

The outline of the paper is as follows. Part 1 contains an overview of the relevant science. It is important to provide a reasonably detailed overview of the science before moving to the constitutional analysis because these details, such as the level of certainty about whether therapeutic cloning research will produce useful therapies or whether there are alternative routes to similar therapies, are central to the question of whether a future patient is harmed by restrictions on the research. In addition, the overview must provide the factual foundation for assessing the justifications for the governmental restriction on therapeutic cloning research. This scientific review will demonstrate that there is considerable uncertainty over which, if any, of the alternative routes to stem cell therapy will be successful, and that there are various methods in development that would allow researchers to conduct therapeutic cloning research in ways that pose a reduced risk of harm (particularly the exploitation of women for oocytes). Part 2 presents the Canadian prohibition on human cloning, and explores the structure and viability of a section 7 claim against that prohibition brought by patients who might benefit from therapies developed through therapeutic cloning research.

I. The Benefits and Harms of Human Therapeutic Cloning Research and its Alternatives

Many serious human diseases or traumatic injuries involving the loss of cell function may, it is hoped, be cured or their symptoms alleviated using cell replacement strategies in regenerative medicine.⁸ Hematopoietic stem cells derived from bone marrow have been used clinically for decades.⁹ However, researchers hope to find a way to remedy a greater range of conditions with a broader range of cell types. The excitement surrounding stem cells has to do with their capacities both for proliferation and differentiation into multiple cell types.¹⁰ However, not all stem cell types have these capacities to the same degree.¹¹

Pluripotent stem cells are capable of forming every cell type in the adult body. Multipotent stem cells may form a limited set of cell types, while unipotent stem cells can give rise only to one cell type. While all may be useful in particular cases, there is great interest in pluripotent stem cells because of their ability to form any type of replacement cell. Pluripotency is lost as cells differentiate during embryonic development, becoming committed to particular lineages and cell types. Pluripotent cells are found in the inner cell mass of the blastocyst (early embryo). There is some evidence that a small population of pluripotent stem cells may also persist through embryonic development, and thus be available in perinatal tissues, such as cord blood, or even adult tissues. Another source of pluripotent stem cells are the so-called “bioengineered” stem cells, formed by “reprogramming” adult cells. Reprogramming causes the adult cells to regress from their differentiated state back to the pluripotent state, and can now be achieved using several methods, including cloning. Among the key challenges in using pluripotent stem cells therapeutically is that only a pure sample of cells differentiated into the desired cell type should be transplanted, as residual undifferentiated cells may

⁸ K Appasani & RK Appasani, “Introduction to Stem Cells and Regenerative Medicine” in K Appasani & RK Appasani, eds, *Stem Cells & Regenerative Medicine*, (Totowa NJ: Humana Press, 2010) 3.

⁹ Christian Leeb et al, “New Perspectives in Stem Cell Research: Beyond Embryonic Cells” (2011) 44:1 *Cell Proliferation* 9 at 11 [Leeb et al, 2010a].

¹⁰ Appasani & Appasani, *supra* note 8 at 3; Rouven Muller & Claudia Lengkerke, “Patient-Specific Pluripotent Stem Cells: Promises and Challenges” (2009) 5 *Nature Reviews Endocrinology* 195 at 195; Christian Leeb et al, “Promising New Sources for Pluripotent Stem Cells” (2010) 6 *Stem Cell Reviews and Reports* 15 [Leeb et al, 2010b].

¹¹ Leeb et al, 2010a, *supra* note 9.

continue to proliferate following transplantation, giving rise to tumours.¹² Continuing research on cell development is producing strategies to address these risks.¹³ Recently, researchers have also reported having achieved transdifferentiation, or the conversion of one adult cell type to another adult cell type, apparently without having to return to the pluripotent state.¹⁴

Another consideration that arises with cell replacement therapies is the question of immunological incompatibility. This is addressed with immunosuppressive drugs in the context of organ transplantation. These drugs have harmful effects on patients, including increased exposure to infection and cancer due to the suppression of the immune system.¹⁵ For a time, there was hope that the problem of immune rejection may be less acute for some forms of stem cells. For example, there are signs that embryonic stem cells express lower levels of the proteins leading to immune rejection, although they appear to lose this immunoprivileged status once they are fully differentiated.¹⁶ Some adult stem cells, such as mesenchymal stem cells, were also thought to be tolerated by the immune system, but they also appear to lose this after differentiation.¹⁷ As a result, another hope for future stem cell therapies is that we may find ways to produce immunologically compatible replacement cells, perhaps by sourcing stem cells from the patient's own body or by reprogramming a patient's own adult cells. Other proposed solutions to this prob-

¹² Timothy J Nelson et al, "Stem Cell Platforms for Regenerative Medicine" (2009) 2:3 *Clinical & Translational Science J* 222 at 223; Leeb et al, 2010b, *supra* note 10 at 19-20.

¹³ Nelson et al, *ibid* at 223.

¹⁴ Manuel Masip et al, "Reprogramming with Defined Factors: From Induced Pluripotency to Induced Transdifferentiation" (2010) 16:11 *Molecular Human Reproduction* 856.

¹⁵ Karen English & Kathryn J Wood, "Immunogenicity of Embryonic Stem-Cell-Derived Progenitors After Transplantation" (2010) 16 *Current Opinion in Organ Transplantation* 90 at 90; Suzanne Kadereit & Alan Trounson, "In Vitro Immunogenicity of Undifferentiated Pluripotent Stem Cells (PSC) and Derived Lineages" (2011) 33 *Seminars in Immunopathology* 551 at 553-54.

¹⁶ Junfeng Ji, Bonan Zhong & Mickie Bhatia, "Genetic Approaches in Human Embryonic Stem Cells and Their Derivatives: Prospects for Regenerative Medicine" in Anthony Atala et al, *Principles of Regenerative Medicine*, 2d ed (London: Elsevier, 2011) 179 at 192; English & Wood, *supra* note 15 at 91.

¹⁷ Xi-Ping Huang et al, "Differentiation of Allogeneic Mesenchymal Stem Cells Induces Immunogenicity and Limits Their Long-Term Benefits for Myocardial Repair" (2010) 122:23 *Circulation* 2419.

lem are to attempt to minimize the problem of immune rejection by creating a stem cell bank sufficiently diverse to ensure a reasonable match with most patients, or to find ways other than the use of immunosuppressive drugs to address the problem of immune rejection.¹⁸

Some of the potential sources of stem cells have given rise to ethical concerns. The chief debates or concerns have to do with sources involving the destruction of the embryo, the instrumental use of the embryo and human reproductive materials for non-reproductive purposes, and the risk to women of supplying oocytes for use in stem cell derivation.¹⁹

We can categorize the main sources of stem cells for therapeutic applications as follows: endogenous stem cells (derived from the patient), exogenous stem cells (not derived from the patient), and bioengineered stem cells (including methods of reprogramming the patient's own cells, such as cloning). The following review will discuss these stem cell sources and their characteristics. The precise characteristics and comparative therapeutic utility of these various types of cells are not fully established.²⁰

1. Endogenous stem cells

The key advantages of endogenous stem cells are their immunological compatibility, and their avoidance of the ethical concerns associated with embryonic stem cells or certain bioengineered stem cells. Endogenous stem cells may be obtained perinatally (e.g. from umbilical cord blood, the placenta or amniotic fluid), although this is unlikely to have been done for every potential patient. They may also be obtained from certain adult tissues.

With respect to differentiation potential, cord blood contains a mixture of adult-like stem cells, as well as embryonic-like stem cells that seem both pluripotent and capable of long-term proliferation.²¹ Stem cells have also been located in various adult tissues. Despite having been thought to be only multipotent or unipotent, rather than pluripotent, and having displayed lim-

¹⁸English & Wood, *supra* note 15 at 93.

¹⁹Additional concerns may also arise in relation to particular techniques, as is discussed below. For example, the creation of inter-species clones involves the insertion of a human nucleus into an animal oocyte which, for some, involves an unethical blurring of species boundaries.

²⁰Nelson et al, *supra* note 12.

²¹*Ibid* at 224; Leeb et al, 2010b, *supra* note 10 at 20.

ited expansion capacity for lineage-committed adult stem cells,²² researchers have recently discovered rare adult cell populations in various tissues that show greater differentiation potential than was thought possible of adult stem cells.²³ These cells can be expanded *in vitro* (at least in animal studies) and seem to offer a promising source of self-compatible cells for therapy. The number and quality of these highly plastic cells seems to decline with age.²⁴

2. Exogenous stem cells

Exogenous stem cells are derived from non-self sources, and create a risk of immune rejection. These non-self stem cells include human embryonic stem cells (“hES cells”), stem cells obtained from perinatal sources (e.g. cord blood), and adult stem cells.

hES cell lines are pluripotent and have now been successfully differentiated into various types of cells.²⁵ These cells are considered particularly promising due to their capacity for indefinite proliferation in cell culture, differentiation potential, and other characteristics suggesting good cell longevity (e.g. long telomere length).²⁶

However, ethical or moral debates continue to surround hES cell research. In particular, the derivation of an hES cell line usually involves the destruction of the embryo. Attempts to address this concern involve one of two strategies. One strategy is to use blastomere biopsy, which involves the removal of a single cell (as in pre-implantation genetic diagnosis conducted during *in vitro* fertilization (“IVF”)), and does not destroy the embryo. The second proposed strategy is to use embryos considered to be non-viable. This strategy might include the use of irreversibly arrested IVF embryos or the deliberate creation of non-viable embryos, such as through parthenogenetic ac-

²² Nelson et al, *supra* note 12 at 225; Jennifer Hipp & Anthony Atala, “Sources of Stem Cells for Regenerative Medicine” (2008) 4 Stem Cell Reviews 3 at 4; Leeb et al, 2010a, *supra* note 9 at 10.

²³ See Donald O Rodgerson & Alan G Harris, “A Comparison of Stem Cells for Therapeutic Use” (2011) 7:4 Stem Cell Rev 782 at 783.

²⁴ *Ibid* at 784, 790; Muller & Lengkerke, *supra* note 10 at 195.

²⁵ Nelson et al, *supra* note 12 at 222.

²⁶ *Ibid*.

tivation of unfertilized oocytes.²⁷ It is not clear, however, that these techniques fully answer ethical objections about the treatment of the embryo.²⁸

3. *Bioengineered stem cells*

In addition to the above-mentioned sources of embryonic, perinatal or adult stem cells, researchers have found methods to bioengineer stem cells with useful properties. In particular, it is possible to “reprogram” adult somatic cells (e.g. skin cells), returning them to a state of pluripotency and proliferative potential similar to hES cells. Whether or not they have the same characteristics and therapeutic potential as hES cells is not yet established.²⁹

²⁷ Muller & Lengkerke, *supra* note 10 at 199; Tiziana AL Brevini et al, “Parthenogenesis as an Approach to Pluripotency: Advantages and Limitations Involved” (2008) 4:3 Stem Cell Rev 127 at 128-30; Ronald M Green, “Can We Develop Ethically Universal Embryonic Stem-Cell Lines?” (2007) 8:6 Nat Rev Genet 480 at 482 [Green, “Ethically Universal Lines?”]; Sayaka Wakayama, Eiji Mizutani & Teruhiko Wakayama, “Nuclear Transfer Embryonic Stem Cells as a New Tool for Basic Biology” in Appasani & Appasani, *supra* note 8, 351 at 358.

²⁸ Brevini et al, *supra* note 27 at 128; Hipp & Atala, *supra* note 22 at 6; Green, “Ethically Universal Lines?”, *supra* note 27; Immaculada de Melo-Martin, Zev Rosenwaks & Joseph J Fins, “New Methods for Deriving Embryonic Stem Cell Lines: Are the Ethical Problems Solved?” (2006) 86:5 Fertil Steril 1330; Svetlana Gavrilov, Virginia E Papaioannou & Donald W Landry, “Alternative Sources of Human Embryonic Stem Cells” in Atala et al, *supra* note 16, 215 at 217.

²⁹ Sayaka Wakayama, James M Cummins & Teruhiko Wakayama, “Nuclear Reprogramming to Produce Cloned Mice and Embryonic Stem Cells from Somatic Cells” (2008) 16:4 Reprod Biomed Online 545 at 547-48; Wakayama, Mizutani & Wakayama, *supra* note 27 at 355-56; Fanyi Zeng & Qi Zhou, “Induced Pluripotent Stem Cells: On the Road Toward Clinical Applications” in Appasani & Appasani, *supra* note 8, 427 at 429-30; Masip et al, *supra* note 14; Muller & Lengkerke, *supra* note 10; Stéphanie Boué et al, “Analysis of Human and Mouse Reprogramming of Somatic Cells to Induced Pluripotent Cells: What is in the Plate?”, online: (2010) 5:9 PLoS One e12664 <www.plosone.org/home.action>; Mark H Chin et al, “Molecular Analyses of Human Induced Pluripotent Stem Cells and Embryonic Stem Cells” (2010) 7:2 Cell Stem Cell 263; Zhumur Ghosh et al, “Persistent Donor Cell Gene Expression Among Human Induced Pluripotent Stem Cells Contributes to Differences With Human Embryonic Stem Cells” (2010) 5:2 PLoS ONE e8975; Elie Dolgin, “Flaw in Induced-Stem-Cell Model. Adult Cells do not Fully Convert to Embryonic-Like State” (2011) 470:7332 Nature 13; Gretchen Vogel, “Reprogrammed Cells Come Up Short For Now” (2010) 327 Science 1191; Rodgerson & Harris, *supra* note 23 at 791; AI Marques-Mari et al, “Differentiation of Germ Cells and Gametes From Stem Cells” (2009) 15:3 Hum

Nonetheless, the techniques are promising in that they should theoretically produce immunologically compatible cell lines. However, caution is warranted given that the extensive manipulation of these cells could create abnormalities that might trigger an immune reaction, albeit one that is predicted to be less severe than to non-genetically identical cells.³⁰

Among the bioengineering techniques available to reprogram adult somatic cells are “somatic cell nuclear transfer” (also known as cloning) and variants on that approach, induced pluripotency leading to what are called induced pluripotent stem cells (“iPS cells”), and transdifferentiation. Another approach that does not involve reprogramming adult somatic cells but is intended to provide immunologically tolerated pluripotent cells for therapeutic use is the creation of a “universal stem cell line.”

In “somatic cell nuclear transfer” or cloning, the nucleus of an adult differentiated cell is transferred into an oocyte from which the nucleus has been removed. The oocyte appears to contain chemical factors that reprogram the genetic material contained in the inserted nucleus. The cell, once stimulated, develops as an embryo that could, if permitted, lead to a live birth as has been demonstrated in many types of mammals.³¹ If the process aims at or culminates in a live birth, it is referred to as reproductive cloning. This need not be the case, as the embryo may also be used to derive a line of embryonic stem cells in the same way as hES cells are derived from non-cloned embryos. The process of creating cloned embryonic stem cells is commonly referred to as therapeutic cloning. These cloned stem cells are nearly genetically identical to the nucleus donor, with the exception of the mitochondrial DNA, which comes from the oocyte cytoplasm.³² The non-self mitochondrial

Reprod Update 379 at 387 (“their global gene expression and DNA methylation patterns are similar but not identical to that of [embryonic stem cells]”); Chang-Qing Xie et al, “A Comparison of Murine Smooth Muscle Cells Generated From Embryonic Versus Induced Pluripotent Stem Cells” (2009) 18:5 Stem Cells and Dev 741 (embryonic stem cells and induced pluripotent stem cells exhibit different gene expression profiles for unknown reasons).

³⁰ C Tang and M Drukker, “Potential Barriers to Therapeutics Utilizing Pluripotent Stem Cell Derivatives: Intrinsic Immunogenicity of In Vitro Maintained and Matured Populations” (2011) 33:6 Semin Immunopathol 563; Kadereit & Trounson, *supra* note 15 at 553-54.

³¹ Wakayama, Mizutani & Wakayama, *supra* note 27 at 353 (reporting that reproductive cloning has been achieved in sixteen mammalian species).

³² Kadereit & Trounson, *supra* note 15 at 554.

DNA could theoretically cause an immune response.³³ Researchers have demonstrated that cloned stem cell transplants are not rejected in cattle and mice.³⁴ Indeed, several researchers have demonstrated the successful therapeutic use of cloned stem cells to treat mice with immune deficiency and a form of induced Parkinson's disease.³⁵

As for the use of cloning in humans, the 2004 report by the Korean researcher Hwang Woo-Suk of the successful derivation of a human cloned stem cell line was later retracted over falsified results and breaches of research ethics.³⁶ Since then, researchers have succeeded in creating cloned human blastocysts,³⁷ although the successful derivation of human cloned stem cell lines has not yet been reported.³⁸ Nonetheless, cloned stem cells have been derived in non-human primates.³⁹

Cloning is currently very inefficient although researchers are at work on techniques to improve efficiency.⁴⁰ The derivation, reported in 2007, of two rhesus macaque cloned stem cell lines required 304 macaque oocytes,⁴¹ although another attempt, reported in 2009, demonstrated that cloning was much more efficient with some somatic cell donors than with others. This led

³³ M Drukker, "Recent Advancements Towards the Derivation of Immune-Compatible Patient-Specific Human Embryonic Stem Cell Lines" (2008) 20:2 *Semin Immunol* 123 at 127; Kadereit & Trounson, *supra* note 15 at 554.

³⁴ Heiner Niemann et al, "Somatic Cloning and Epigenetic Reprogramming in Mammals" (2011) in Atala et al, *supra* note 16 129 at 147; Hipp & Atala, *supra* note 22.

³⁵ Wakayama, Mizutani & Wakayama, *supra* note 27 at 361-62.

³⁶ Donald Kennedy, "Editorial Retraction" (2006) 311 *Science* 335.

³⁷ Andrew J French et al, "Development of Human Cloned Blastocysts Following Somatic Cell Nuclear Transfer (SCNT) with Adult Fibroblasts" (2008) 26:2 *Stem Cells* 485; Miodrag Stojkovic et al, "Derivation of a Human Blastocyst after Heterologous Nuclear Transfer to Donated Oocytes" (2005) 11:2 *Reprod Biomed Online* 226.

³⁸ Nelson et al, *supra* note 12 at 226.

³⁹ JA Byrne et al, "Producing Primate Embryonic Stem Cells by Somatic Cell Nuclear Transfer" (2007) 450:7169 *Nature* 497.

⁴⁰ Muller & Lengerke, *supra* note 10 at 198; Satoshi Kishigami et al, "Significant Improvement of Mouse Cloning Technique by Treatment with Trichostatin A after Somatic Nuclear Transfer" (2006) 340 *Biochem Biophys Res Commun* 183; Wakayama, Mizutani & Wakayama, *supra* note 27 at 353.

⁴¹ Byrne et al, *supra* note 39.

the authors to suggest that “[b]ased on our current SCNT blastocyst formation rate of 43% and [embryonic stem] cell isolation efficiency of 29%, as few as 10 or less primate oocytes could be sufficient to derive one cell line. Thus, the continued systematic optimization of SCNT approaches will likely succeed in the efficient generation of patient-specific [embryonic stem] cells for therapeutic applications.”⁴² In cattle and pigs, species for which there is a larger data set than for other mammals, it is possible to see that cloning efficiency has steadily increased as technical skill and knowledge have accumulated.⁴³ Despite these hopeful signs, the fact remains that many oocytes are likely to be required in human cloning research, and, if that research is successful, for the derivation of cloned stem cell lines to treat patients. This leads to one of the central concerns with therapeutic cloning research—the medical risk to women of supplying oocytes for the research.

Recognizing the risk of harm to women, various alternative methods of cloning that do not endanger women have arisen although they are also experimental and they may raise other ethical concerns. These strategies include cell fusion, “stembrids,” inter-species somatic cell nuclear transfer (“iSCNT” or inter-species cloning), the use of failed IVF oocytes, the use of immature oocytes, or the use of oocytes created from pluripotent stem cells.

Cell fusion involves the fusion of a donor cell with an hES cell, which creates a cell that has double the normal number of chromosomes, and that is both unstable and genetically incompatible with the donor.⁴⁴ It is possible to remove the hES cell chromosomes selectively from the hybrid cell to generate a genetically compatible cell.⁴⁵

Stembrids are cells formed when a donor somatic nucleus is inserted into an enucleated hES cell.⁴⁶ A similar approach involves the transfer of the nu-

⁴² Michelle Sparman et al, “Epigenetic Reprogramming by Somatic Cell Nuclear Transfer in Primates” (2009) 27:6 *Stem Cells* 1255.

⁴³ Niemann et al, *supra* note 34 at 135.

⁴⁴ Muller & Lengerke, *supra* note 10 at 199.

⁴⁵ Leeb et al, 2010b, *supra* note 10 at 17. They note that the continued pluripotency of these cells must still be verified.

⁴⁶ Yury Verlinsky et al, “Cytoplasmic Cell Fusion: Stembrid Technology for Reprogramming Pluripotentiality” (2006) 2:4 *Stem Cell Rev* 297; Nick Strelchenko et al, “Reprogramming of Human Somatic Cells by Embryonic Stem Cell Cytoplasm” (2006) 12 *Reprod BioMed Online* 107.

cleus into an enucleated zygote.⁴⁷ Supernumerary embryos formed in IVF could be used in this way, although they are also scarce and this technique would still run into the objections related to embryo destruction.

Animal oocytes may also be used for cloning with a human nucleus, producing an inter-species cytoplasmic hybrid.⁴⁸ One report exists of the successful derivation of stem cells using a cybrid formed from the insertion of a human nucleus into a rabbit oocyte, although this has not so far been replicated.⁴⁹ Researchers in the UK have been granted several licenses to pursue iSCNT research.⁵⁰ The utility of iSCNT-derived stem cells for clinical purposes is currently quite uncertain.⁵¹

Oocytes that fail to fertilize during IVF procedures could also be used for cloning without posing additional risk to women, who are already exposed to the risks of oocyte retrieval as a result of fertility treatments.⁵² However, the quality and utility of these oocytes is in question.

⁴⁷ International Society for Stem Cell Research, "Ethics Report on Interspecies Somatic Cell Nuclear Transfer Research" (2009) 5 Cell Stem Cell 27 at 28 [ISSCR, "Ethics Report"].

⁴⁸ Josef Fulka Jr et al, "Cybrid Human Embryos: Warranting Opportunities to Augment Embryonic Stem Cell Research" (2008) 26:9 Trends in Biotech 469.

⁴⁹ *Ibid*; Young Chen et al, "Embryonic Stem Cells Generated by Nuclear Transfer of Human Somatic Nuclei into Rabbit Oocytes" (2003) 13 Cell Res 251; Young Chung et al, "Reprogramming of Human Somatic Cells using Human and Animal Oocytes" (2009) 11 Cloning and Stem Cells 213.

⁵⁰ United Kingdom Human Fertilisation and Embryology Authority, "HFEA Statement on Licensing of Applications to Carry out Research using Human-Animal Cytoplasmic Hybrid Embryos", online: HFEA <www.hfea.gov.uk/418.html>. Françoise Baylis, "Animal Eggs for Stem Cell Research: A Path Not Working" (2008) 8(12) Am J Bioethics 18.

⁵¹ Niemann et al, *supra* note 34 at 147; Fulka et al, *supra* note 48; Zeki Beyhan, Amy E Iager & Jose B Cibelli, "Interspecies Nuclear Transfer: Implications for Embryonic Stem Cell Biology" (2007) 1:5 Cell Stem Cell 502; Chung et al, *supra* note 49.

⁵² Sharon F Sneddon et al, "Gene Expression Analysis of a New Source of Human Oocytes and Embryos for Research and Human Embryonic Stem Cell Derivation" (2011) 95:4 Fertil Steril 1410.

Immature oocytes can be matured *in vitro* for use in cloning, although they appear to be inferior to mature oocytes for this purpose.⁵³ The immature oocytes might come from ovarian tissue removed for therapeutic reasons.⁵⁴ The maturation of immature oocytes from fetal tissues for use in SCNT is also possible, although it may provoke renewed ethical disputes over research using fetal tissues.⁵⁵

Finally, it may one day be possible to cause pluripotent stem cells (such as hES cells or iPS cells) to differentiate into oocytes, providing a source of “artificial” oocytes for use in cloning. Multiple researchers have reported the derivation of primordial germ cells from pluripotent human cells (both hES cells and human iPS cells).⁵⁶ The possibility of producing functional sperm in this way was demonstrated when one researcher reported the birth of live mouse pups conceived using sperm derived from mouse embryonic stem cells.⁵⁷ These results are still some distance from producing functional oocytes *in vitro*, but the research does demonstrate continued progress in this direction.⁵⁸

⁵³ Andrew J French, Samuel H Wood & Alan O Trounson, “Human Therapeutic Cloning (NTSC): Applying Research From Mammalian Reproductive Cloning” (2006) 2 Stem Cell Rev 265 at 271.

⁵⁴ *Ibid.*

⁵⁵ *Ibid.*; Mary Carrington Coutts, “Fetal Tissue Research” (1993) 3:1 Kennedy Inst Ethics J 81; Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (Ottawa: Government of Canada, December 2010), ch 12, s E.

⁵⁶ Sofia Gkoutela, Anne Lindgren & Amander T Clark, “Pluripotent Stem Cells in Reproductive Medicine: Formation of the Human Germ Line In Vitro” in Appasani & Appasani, *supra* note 8; Marques-Mari et al, *supra* note 29; Zsolt Peter Nagy & Ching-Chien Chang, “Artificial Gametes” (2007) 67:1 Theriogenology 99.

⁵⁷ Karim Nayernia et al, “In Vitro-Differentiated Embryonic Stem Cells Give Rise to Male Gametes that Can Generate Offspring Mice” (2006) 11 Dev Cell 125; H Moore & B Aflatoonian, “From Stem Cells to Spermatozoa and Back” (2007) 65 Soc Reprod Fertil Suppl 19; Jinlian Hua & Kuldip Sidhu, “Recent Advances in the Derivation of Germ Cells From Embryonic Stem Cells” (2008) 17:3 Stem Cells Dev 399.

⁵⁸ See generally Guang-Bin Zhou, Qing-Gang Meng & Ning Li, “In Vitro Derivation of Germ Cells From Embryonic Stem Cells in Mammals” (2010) 77:7 Mol Reprod

The risk to women is not the only objection to human therapeutic cloning research. The technique involves the creation and subsequent destruction of the cloned embryo. Some have argued that the product of cloning is not, strictly speaking, an embryo, at least for questions of moral status, although this is unlikely to persuade opponents.⁵⁹ Here too, researchers have suggested an alternative technique to avoid concerns about the destruction of the embryo, namely “altered nuclear transfer.” This technique involves the genetic modification of the donor nucleus prior to its insertion into an enucleated oocyte, so that it can develop pluripotent cells but is incapable of implanting in a uterus and so is developmentally non-viable. This approach is still vulnerable to the charge that it involves the creation and destruction of an embryo—albeit a “severely disabled embryo.”⁶⁰

The second method of reprogramming adult somatic cells to create self-compatible pluripotent stem cells emerged in 2006 with the creation, by Takahashi and Yamanaka, of induced pluripotent stem cells (iPS cells).⁶¹ Their method involved inserting genes that code for a set of proteins (known as transcription factors) into the genome of an adult skin cell. The technique raised great hope as it seems to offer a way to generate self-compatible stem cells from a plentiful and easily accessible source of adult cells without re-

Dev 586; Emanuele Pelosi, Antonino Forabosco & David Schlessinger, “Germ Cell Formation from Embryonic Stem Cells and the Use of Somatic Cell Nuclei in Oocytes” (2011) 1221 *Ann N Y Acad Sci* 18; Sarita Panula et al, “Human Germ Cell Differentiation from Fetal- and Adult-Derived Induced Pluripotent Stem Cells” (2011) 20:4 *Hum Mol Genet* 752; Debra JH Mathews et al, “Pluripotent Stem Cell-Derived Gametes: Truth and (Potential) Consequences” (2009) 5 *Cell Stem Cell* 11.

⁵⁹ See e.g. JES Hansen, “Embryonic Stem Cell Production through Therapeutic Cloning has Fewer Ethical Problems Than Stem Cell Harvest from Surplus IVF Embryos” (2002) 28 *J Med Ethics* 86; Insoo Hyun & Kyu Won Jung, “Human Research Cloning, Embryos, and Embryo-Like Artifacts” (2006) 36:5 *Hastings Center Report* 34; Moreno, *supra* note 4 at 3.

⁶⁰ Green, “Ethically Universal Lines?”, *supra* note 27 at 482; Brevini et al, *supra* note 27 at 129; Hipp & Atala, *supra* note 22 at 6. For discussions of the technique of altered nuclear transfer see William B Hurlbut, “Ethics and Embryonic Stem Cell Research: Altered Nuclear Transfer As a Way Forward” (2007) 21:2 *Biodrugs* 79; Zachary J Kastenber & Jon S Odorico, “Alternative Sources of Pluripotency: Science, Technics and Stem Cells” (2008) 22 *Transplant Rev (Orlando)* 215 at 217.

⁶¹ Kazutoshi Takahashi & Shinya Yamanaka, “Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors” (2006) 126 *Cell* 663.

quiring the use of an embryo. However, it also raises some concerns for eventual therapeutic application. The technique poses a risk of cancer, because one of the inserted genes is associated with cancer, and also because the process of inserting genes causes potentially dangerous disruption of the genome.⁶² Researchers have sought ways around this problem, including methods of inducing pluripotency that use other types of molecules, non-integrating methods of gene delivery, or involve only the temporary insertion of the genes.⁶³ The therapeutic use of iPS cells has been demonstrated in a rat model of Parkinson disease, a mouse model for acute myocardial infarction, and mouse models of genetic diseases.⁶⁴ A recent note of caution has been sounded over the potential immunogenicity of iPS cells, and signs that the immune response to them varies according to the method by which iPS cells are produced suggests that there is much more to learn about what happens to these cells during reprogramming.⁶⁵ Nonetheless, these cells might avoid some of the ethical concerns associated with hES cells and cloned stem cells. It is not necessary to use oocytes to create iPS cells, and it is widely thought that iPS cells do not raise concerns about the destruction of the embryo or the instrumentalization of the embryo. However, some have suggested that there may nonetheless be objections to iPS cells similar to those raised against the destruction of the embryo because iPS cells, too, have the potential to form live offspring.⁶⁶

⁶² Nelson et al, *supra* note 12 at 226; Masip et al, *supra* note 14 at 861.

⁶³ See Maureen L Condic & Mahendra Rao, "Alternative Sources of Pluripotent Stem Cells: Ethical and Scientific Issues Revisited" (2010) 19:8 *Stem Cells Dev* 1121; Masip et al, *supra* note 14 at 861; Reiesha D Robbins et al, "Inducible Pluripotent Stem Cells: Not Quite Ready for Prime Time?" (2010) 15 *Curr Opin Organ Transplant* 61; Kuldip S Sidhu, "New Approaches for the Generation of Induced Pluripotent Stem Cells" (2011) 11:5 *Expert Opin Biol Ther* 569.

⁶⁴ Zeng & Zhou, *supra* note 29 at 429, 437 n 21, referring *inter alia* to Jacob Hanna et al, "Treatment of Sickle Cell Anemia Mouse Model with iPS Cells Generated from Autologous Skin" (2007) 318 *Science* 1920.

⁶⁵ Tongbiao Zhao et al, "Immunogenicity of Induced Pluripotent Stem Cells" (2011) 474:7350 *Nature* 212; Effie Apostolou & Konrad Hochedlinger, "iPS Cells Under Attack" (2011) 474:7350 *Nature* 165.

⁶⁶ This requires a technique called tetraploid complementation, which involves the injection of iPS cells into a blastocyst with twice the normal number of chromosomes (tetraploid). The tetraploid cells can form the supporting extra-embryonic tissue, but cannot contribute to the developing embryo. See Hans-Werner Denker, "Induced Pluripotent Stem Cells: How to Deal with the Development Potential" (2009) 19:S1 *Reprod Biomed Online* 34; Katrien

“Transdifferentiation” or “lineage reprogramming” is also under investigation, and involves the conversion of differentiated cells from one cell type to another without passing through a pluripotent intermediate.⁶⁷ For example, a 2008 study in mice demonstrated the alleviation of diabetes by direct in vivo conversion of pancreatic cells to insulin-secreting cells by infecting the mouse pancreas with a virus bearing genes for specific transcription factors associated with insulin-secreting pancreatic cells.⁶⁸

Finally, another form of “bioengineering” not involving reprogramming of adult cells would be to create a “universal donor” stem cell line. The idea here is that a line of hES cells could be genetically modified to eliminate or suppress the factors that give rise to immune rejection. In theory, this would produce a stem cell line with the pluripotency and proliferative capacities of hES cells without the immunological risks to patients of transplants from exogenous sources.⁶⁹ Increased understanding of the behaviour of the types of stem cells, such as the way that hES cells lose their seemingly immunoprivileged status during differentiation, may also lead to other strategies to modify their immunogenicity.⁷⁰

4. Conclusion

A review of the current state of stem cell science reveals a rapidly-moving field, in which many promising lines of research exist but where there is still very much to learn. We do not yet know which approach will be the best for cell replacement therapies, or for creating cellular models of dis-

Devolder, “To Be or not to Be? Are Induced Pluripotent Stem Cells Potential Babies and Does it Matter?” (2009) 10:12 EMBO Reports 1285; Ronald M Green, “Ethical Considerations” in Atala et al, *supra* note 16, 1117 at 1118.

⁶⁷ Xioajing Huang, James Oh & Sean M Wu, “Regenerative Strategies for Cardiac Disease” in Appasani, *supra* note 8, 579 at 584-85; Masip et al, *supra* note 14; Chris Jopling, Stephanie Boue & Juan Carlos Izpisua Belmonte, “Dedifferentiation, Transdifferentiation and Reprogramming: Three Routes to Regeneration” (2011) 12 Nat Rev Molec Cell Biol 79.

⁶⁸ Qiao Zhou et al, “In Vivo Reprogramming of Adult Pancreatic Exocrine Cells to β -Cells” (2008) 455:7213 Nature 627.

⁶⁹ Nelson et al, *supra* note 12 at 222-223. Zaruhi Karabekian, Nikki Gillum Posnack & Narine Sarvazyan, “Immunological Barriers to Stem-Cell Based Cardiac Repair” (2011) 7:2 Stem Cell Rev 315 at 322.

⁷⁰ English & Wood, *supra* note 15 at 91.

ease and injury in which to study these conditions and to test treatments.⁷¹ Both of these uses are potentially beneficial for sick and injured patients, even though the latter does not involve cellular transplants and so raises fewer patient safety issues.

One important observation from the review is that one of the objections to therapeutic cloning—risk to oocyte donors—may be avoidable through the use of other sources of oocytes or other cloning techniques. This would appear to weaken the claim that all cloning should be banned. On the other hand, other techniques to obtain self-compatible pluripotent cells (such as induced pluripotency) weaken the claim that patients will be harmed if we prohibit therapeutic cloning research. However, we do not know for certain that therapeutic cloning techniques that avoid risk to women will ultimately be satisfactory, nor do we know for certain that alternative forms of stem cells will be adequate. We are not even certain whether we need pluripotent stem cells for cell replacement therapies at all if transdifferentiation works to supply those cell types that are unavailable from multipotent adult stem cells. Should other ways of dealing with the immune rejection problem succeed, we may not need to pursue personalized stem cell lines for clinical applications, although there may still be a need for a method such as cloning or induced pluripotency to create cellular models for studying diseases and their treatment.

In conditions of uncertainty about which lines of biomedical research are likely to generate the best results, a society needs to choose where to invest its scarce resources. We currently do this in a way that depends on multiple constituencies, each facing a slightly different set of incentives. This diversity within our system of channeling research resources leaves open the possibility for work to proceed on unfashionable or seemingly less promising paths while still encouraging most of the time and resources to be invested in the most promising lines of research. In essence, we usually leave it up to scientists (motivated by curiosity, professional recognition, and the pursuit of research funding), public research funders (motivated to demonstrate results valued by taxpayers), and enterprises (motivated to pick commercial winners) to decide where to invest resources.

⁷¹ Masip et al, *supra* note 14 at 862. Certain types of diseased cells cannot easily be obtained from patients for testing treatments or studying disease processes *in vitro*. For example, blood cells can be obtained much more easily than nerve cells. However, some of these relatively inaccessible cell types could potentially be derived through cloning or induced pluripotency techniques.

We do not generally step in to prohibit lines of research considered to be a waste of resources unless there are compelling ethical or harm-based reasons to do so. Indeed, it seems a very risky approach to pick the best lines of research and to ban the others particularly where much is unknown and our predictive abilities are poor. The risks of foreclosing one line of research are not just limited to the loss of the potential therapies that the research might directly have produced. It may also lead to losses more indirectly, given that one line of research might generate insights useful in another area. For example, research on hES cells provided the background knowledge necessary for the discovery of the technique to create iPS cells.⁷² Scientists working with iPS cells argue that we need to continue working with hES cells because they are needed in order to understand the basic mechanisms of pluripotency and self-renewal, and to offer the point of reference against which the characteristics of iPS cells can be judged and understood.⁷³ A recent large review of the scientific literature supports the position that iPS and hES cell research are complementary and interdependent.⁷⁴ Similar arguments are made about the need to continue with therapeutic cloning research—particularly interspecies cloning which does not consume human oocytes—notwithstanding the development of iPS cells.⁷⁵

Of course, where there are compelling reasons to prohibit or restrict lines of research, we may and sometimes should do so notwithstanding that otherwise valuable knowledge may be lost. The widespread consensus on ethical restrictions on human subject research demonstrates the legitimacy of some limitations on unfettered scientific research.

⁷² Insoo Hyun et al, “New Advances in iPS Cell Research Do Not Obviate the Need for Human Embryonic Stem Cells” (2007) 1:4 *Cell Stem Cell* 367; Kristina Hug & Göran Hermerén, “Do We Still Need Human Embryonic Stem Cells for Stem Cell-Based Therapies? Epistemic and Ethical Aspects” (2011) 7:4 *Stem Cell Rev and Rep* 761; Han Lee et al, “Induced Pluripotent Stem Cells in Regenerative Medicine: an Argument for Continued Research on Human Embryonic Stem Cells” (2009) 4:5 *Regenerative Medicine* 759, suggests that research on embryonic cells was essential to identifying culture conditions for maintaining and differentiating stem cells, as well as to identifying the transcription factors needed for reprogramming cells to create iPS cells.

⁷³ Juan Carlos Izpisua-Belmonte et al, “Induced Pluripotent Stem Cells and Reprogramming: Seeing the Science Through the Hype” (2009) 10:12 *Nat Rev Genetics* 878.

⁷⁴ Christopher Thomas Scott et al, “Democracy Derived? New Trajectories in Pluripotent Stem Cell Research” (2011) 145:6 *Cell* 820.

⁷⁵ ISSCR, “Ethics Report”, *supra* note 47.

In the case of therapeutic cloning research, various benefits are envisaged, ranging from an improved basic understanding of cell development, to more applied benefits in the form of a means of creating cellular models of human disease or in the form of self-compatible stem cells for regenerative medicine. Whether we will achieve these benefits and whether these benefits could be achieved in other ways are both unknown at present. As argued above, even if therapeutic cloning research does not appear promising it seems unwise as a matter of policy to ban the research unless there are compelling ethical or harm-based reasons to do so. The reasons put forward against therapeutic cloning research (setting aside opportunity cost arguments for the reasons mentioned above) are that the research

1. destroys embryos, which have moral status;
2. involves the instrumentalization of the nascent human life;
3. puts women at risk by creating a large demand for oocytes; and
4. raises the risk of reproductive cloning by perfecting a technique that may then be used illegally.

Some of these concerns likely motivated the prohibition on all forms of cloning in the Canadian *Assisted Human Reproduction Act*.⁷⁶ Yet, there is considerable variation in the response to therapeutic cloning research even amongst countries with similar cultures and political systems, suggesting a lack of consensus on whether these concerns justify a prohibition on the research. Caulfield et al observe that the UK permits both therapeutic cloning research and inter-species cloning, while Australia permits therapeutic cloning research but prohibits inter-species cloning, and Canada prohibits therapeutic cloning research but may permit inter-species cloning.⁷⁷ The purpose of Part II of this article is to consider the constitutionality of the Canadian prohibition on therapeutic cloning research. In particular, could patients who

⁷⁶ *AHRA*, *supra* note 5.

⁷⁷ Timothy Caulfield et al, "The Stem Cell Research Environment: A Patchwork of Patchworks" (2009) 5:2 *Stem Cell Rev and Rep* 82. Ogbogu & Rugg-Gunn suggest that iSCNT is permitted under the *AHRA*, *supra* note 5, because the process creates a "hybrid" not an "embryo," although they note there is some ambiguity in the *Act*, and it is possible that the hybrid could be considered a cloned embryo, in which case the prohibition on the creation of embryos for research would apply as would the ban on cloning (Ubaka Ogbogu & Peter Rugg-Gunn, "The Legal Status of Novel Stem Cell Technologies in Canada" (2008) 9:5 *J Intl Biotech Law* 186).

might potentially benefit medically from this research claim that their section 7 rights to life and security of the person have been infringed contrary to the principles of fundamental justice and, if so, are those infringements nonetheless justified under section 1 of the *Charter*?

II. Does a Patient have a Right to Unrestricted Medical Research Under Section 7 of the *Charter*? The Case of Therapeutic Cloning Research

1. *The Prohibition on Human Cloning in the Assisted Human Reproduction Act*

The federal *Assisted Human Reproduction Act* (“*AHRA*”) was enacted after a lengthy period of study and debate, and some parts of it have recently been adjudged to be an unconstitutional invasion of the provincial legislative jurisdiction.⁷⁸ However, the criminal prohibitions in section 5, including the provision prohibiting human cloning, survived constitutional challenge.

Several of the provisions of the *AHRA* are relevant to this discussion. Section 5(1)(a) explicitly prohibits human cloning by “any technique.”⁷⁹ A “human clone” is defined as an embryo that “contains a diploid set of chromosomes obtained from a single...human being, foetus or embryo.”⁸⁰ Section 5(1)(b) prohibits the creation of an *in vitro* embryo for non-reproductive purposes.⁸¹ These two provisions independently make therapeutic cloning by somatic cell nuclear transfer illegal, given that the process arguably creates an embryo. Arguments similar to those advanced here against the ban on therapeutic cloning could also be advanced against the ban on the creation of embryos for research purposes.

Some of the alternative techniques described above may actually avoid the cloning prohibition under section 5(1)(a) of the *AHRA*. At the same time, other suggested alternatives may actually be prohibited by different parts of section 5 of the *AHRA*. The objective in raising this point is to show how the constitutional analysis of cutting-edge fields of science may involve both legal uncertainty and scientific uncertainty.

⁷⁸ *Reference re Assisted Human Reproduction Act*, 2010 SCC 61, [2010] 3 SCR 457.

⁷⁹ *AHRA*, *supra* note 5.

⁸⁰ *Ibid* s 3.

⁸¹ *Ibid*.

For example, there is some discussion of whether interspecies cloning is prohibited by the *AHRA*. Section 5(1)(j) prohibits the creation of a hybrid for the purpose of reproduction and also prohibits the transplantation of a hybrid into a human or non-human life form (presumably “transplantation” refers to implantation for gestational purposes, rather than transplantation of stem cells derived from the hybrid).⁸² Several scholars have argued that an interspecies clone is classified as a “hybrid”⁸³ rather than as a “clone” or an “embryo” and so may legally be created and transplanted for non-reproductive purposes.⁸⁴

In another example, section 5(1)(f) prohibits the alteration of the genome of a human cell or *in vitro* embryo “such that the alteration is capable of being transmitted to descendants.”⁸⁵ Since iPS cells are sometimes created through genetic alteration, and iPS cells have been shown to be capable of forming fertile offspring in mice, it would seem that these genetic alterations are capable of being transmitted to descendants.⁸⁶ Ogbogu and Rugg-Gunn argue that iPS cells are not caught by section 5(1)(f) because the genetic alterations become capable of being transmitted to descendants only if the cells are differentiated into germ cells, a process they suggest may therefore be banned by the *AHRA*. However, it is not clear why a genetic alteration becomes “capable of transmission” only at the stage at which an iPS cell is differentiated into a germ cell. Another interpretation is that the alteration becomes “capable of transmission” at an earlier stage or at some later stage of manipulation (such as the creation of an embryo, or the implantation of an embryo in a woman). The point here is not to settle the interpretation of the *AHRA*, but to point out the uncertainty surrounding the legal viability of some of the potential alternatives to therapeutic cloning research.

Note also that if Ogbogu and Rugg-Gunn are correct that the differentiation of germ cells from genetically-modified iPS cells is caught by section

⁸² *Ibid.*

⁸³ A “hybrid” is defined to include the “ovum of a non-human life form into which the nucleus of a human cell has been introduced” (*ibid* s 3(e)).

⁸⁴ Ogbogu & Rugg-Gunn, *supra* note 77 at 187; Roxanne Mykitiuk et al, “The Canadian Assisted Human Reproduction Act; Protecting Women’s Health While Potentially Allowing Human Somatic Cell Nuclear Transfer Into Non-Human Oocytes” (2007) 7:2 *Am J Bioethics* 71.

⁸⁵ *AHRA*, *supra* note 5.

⁸⁶ Xiao-yang Zhao et al, “Viable Fertile Mice Generated From Fully Pluripotent iPS Cells Derived From Adult Somatic Cells” (2010) 6:3 *Stem Cell Rev and Rep* 390.

5(1)(f), this would presumably make it impossible to use artificial oocytes derived from this kind of iPS cell for cloning, even though the enucleation of the artificial oocyte (during the process of somatic cell nuclear transfer) would make it impossible for the modification to be transmitted to offspring. Of course, methods of creating iPS cells that do not involve genetic modification would avoid this problem, as Ogbogu and Rugg-Gunn point out.

2. Does a Patient Have a Right to Unrestricted Medical Research Under Section 7 of the Charter?

a) Introduction

The freedom of scientific research,⁸⁷ and the public interest in and right to the fruits of that research are internationally recognized values.⁸⁸ Of course, the need for and legitimacy of limits on some methods and areas of scientific research are also widely-accepted, particularly to avoid harm to health and safety and to protect fundamental human rights. More controversial though are limits to research where the anticipated harm consists of the erosion of conventional morality or socio-political structures.

The constitutionality of restrictions on scientific research is often addressed as a matter of the freedom of expression of researchers, a freedom that is explicitly recognized in constitutional human rights documents in some jurisdictions.⁸⁹ In Canada, there is no explicit mention of such a freedom in the *Charter of Rights and Freedoms*, although several legal scholars have considered the Canadian ban on human cloning from the perspective of a researcher's constitutional rights.⁹⁰

⁸⁷ See *International Covenant on Economic, Social and Cultural Rights*, 16 December 1966, 993 UNTS 3, arts 15, 16 (entered into force 3 January 1976).

⁸⁸ *Universal Declaration of Human Rights*, GA Res 217(III), UN GAOR, 3d Sess, Supp No 13, UN Doc A/810, (1948) art 27, online: <www.un.org/en/documents/udhr>; *Universal Declaration on Bioethics and Human Rights*, UNESCO Gen Conference Res 33/36 (19 October 2005) art 15, online: <unesdoc.unesco.org/images/0014/001461/146180e.pdf>.

⁸⁹ Amedeo Santosuosso, Valentina Sellaroli & Elisabetta Fabio, "What Constitutional Protection For Freedom of Scientific Research?" (2007) 33:6 J Med Ethics 342.

⁹⁰ See e.g. Barbara Billingsley & Timothy Caulfield, "The Regulation of Science and the *Charter of Rights*: Would a Ban on Non-Reproductive Human Cloning

However, researchers are not the only ones with a fundamental interest in scientific research. The question thus arises as to whether those with a particularly deep personal interest in the scientific research, namely those whose lives or health may be improved by that research, have a constitutionally-protected interest in the freedom of the research as well. American legal scholars have explored this question in the context of therapeutic cloning research or embryonic stem cell research, reaching varying conclusions about whether the argument is likely to succeed under existing US precedents.⁹¹

The constitutional analysis in Canada is likely to differ from that in the US for various reasons, including the different analytical methods used in the two jurisdictions to determine the scope of constitutionally protected rights and to identify qualifications on those rights.⁹² We must thus embark on a Canadian-focused analysis under the *Charter*, using the prohibition on human cloning as the focus for the exploration.

The specific question to be explored is whether the prohibition on all human cloning in section 5 of the *AHRA* violates the section 7 rights of patients who may one day benefit from treatments or medical knowledge de-

Unjustifiably Violate Freedom of Expression?" (2004) 29:2 Queen's LJ 647; Downie, Llewellyn & Baylis, *supra* note 4. In the US context, see Lori B Andrews, "Is There a Right To Clone? Constitutional Challenges to Bans on Human Cloning" (1998) 11:3 Harv JL & Tech 643.

⁹¹ See e.g. Russell Korobkin, "Stem Cell Research and the Cloning Wars" (2007) 18 Stan L & Pol'y Rev 161; Cass R Sunstein, "Is There A Constitutional Right to Clone?" (2002) 53 Hastings LJ 987; John A Robertson, "Embryo Culture and the 'Culture of Life': Constitutional Issues In the Embryonic Stem Cell Debate" (2006) U Chicago Legal F 1; Joshua W Sussman, "Freedom, Fate, and the Fear Of Frankenstein: Due Process Protection For Embryonic Stem Cell Research" (2009) 11:4 U Pa J Const L 1077; Kristin M Hicks, "Embryonic Stem Cell Research and the Theory Of Medical Self-Defense" (2008) 21:2 Harv JL & Tech 547. See also the overview of potential constitutional issues provided from a Canadian perspective by SA Muscati, "Therapeutic Cloning and the Constitution: A Canadian Perspective" (2001) 22:1 Health Law Can 7.

⁹² See e.g. Peter W Hogg, *Constitutional Law of Canada*, 5th ed (Markham: Carswell, 2007) at 789: "[T]he American Bill of Rights contains no limitation clause, and many of the guaranteed rights are expressed in unqualified terms...American courts have had to imply qualifications on the rights in order to accommodate legitimate restraints...In Canada, the courts can point to s. 1 as authorizing the development of limits on the guaranteed rights."

rived through therapeutic cloning and, if so, is the infringement nonetheless justified under section 1 of the *Charter*?

The constitutional analysis will proceed in three main steps. First we must consider whether there is a deprivation of the right to life, liberty, or security of the person. Here, we need to address several complexities in the analysis. Can the loss of a chance at a therapy deprive a patient of his or her section 7 rights? I will argue that the loss of an uncertain medical benefit can and should be understood as a deprivation of section 7 rights, although in the case of the prohibition on human cloning the claim may be weak. Another question is whether a restriction on the actions of a third party researcher constitute a deprivation of the patient's section 7 rights? I will argue that it is well-established on the precedents that it can be.

Second, we must consider whether the deprivation is in accordance with the principles of fundamental justice or not. This is a challenging step in section 7 jurisprudence, as it is not always clear what the principles of fundamental justice are, or how they relate to the later analysis under section 1. One principle that has been recognized in the jurisprudence as a principle of fundamental justice is that laws should not unnecessarily infringe *Charter* rights, and so laws that are overbroad will not accord with the principles of fundamental justice. The primary (and, in my view, most clearly legitimate) objective of the ban on therapeutic cloning research is to protect women from the demand for oocytes for research. I will argue that the law is overbroad because it needlessly forecloses lines of human cloning research that do not endanger women. An alternative approach would be to ban the use of oocytes sourced from women and girls (except for immature oocytes from tissue removed for therapeutic purposes) in cloning research. Some may think that there are even less restrictive approaches to protecting women (such as banning compensation for oocytes), but a government can reasonably (and, thus, constitutionally) take the position that this would be insufficient.

Third, having established a violation of section 7, we must determine whether the infringement is justified under section 1 of the *Charter*. I will address the various objectives that might underlie the ban on therapeutic cloning research, concluding that the most clearly valid objective is to protect women. The overbreadth of the legislation, discussed also in the context of the principles of fundamental justice, is relevant here. A law that is overbroad cannot be said to impair a *Charter* right as little as reasonably possible, a requirement to establish justification under section 1.

- b) Does the Ban on Therapeutic Cloning Research Constitute a Deprivation of a Patient's Section 7 Interests in Life or Security of the Person?

Section 7 of the *Charter* states that “[e]veryone has the right to life, liberty and security of the person and the right not to be deprived thereof except in accordance with the principles of fundamental justice.”⁹³ It is clear from the existing case law that a right to access existing medical treatments is included in one or more of the rights to life, liberty, and security of the person protected by section 7 of the *Charter*.⁹⁴ The underlying subject matter—an interest in one’s health, and medical treatment to preserve it—is thus covered by section 7, and is at issue in the case of prohibitions on medical research. However, there are a number of key differences between the existing precedents and the argument being advanced here. The analysis will be organized around three key points. First, it is unclear whether therapeutic cloning research will produce useful therapies and so the patient’s claim is based on the loss of a speculative benefit. The effect of this speculativeness on the viability of the constitutional claim must therefore be considered.

Second, the analysis addresses the question of whether a patient can advance a claim based on a restriction of the freedom of a third-party researcher. This is ultimately not particularly different from the existing precedents dealing with section 7 rights in the medical context, which often involve challenges to laws prohibiting third parties from providing those treatments.

Third, American courts have rejected a constitutional claim of access to experimental drugs for terminal patients, and it may seem that the lack of a constitutional right to an experimental drug ought to entail the lack of a constitutionally protected interest in other steps of the research and development process for novel therapies. As argued below, this does not follow, particularly under a Canadian constitutional analytical approach, which allows for the articulation of a fairly general concept of a right, with the necessary limitations to be dealt with under the separate limiting provision of section 1 on a case by case basis. Since one can imagine cases in which a government might try to foreclose medical research for illegitimate reasons (as with the

⁹³ *Charter*, supra note 1 s 7.

⁹⁴ *R v Parker* (2000), 146 CCC (3d) 193, 188 DLR (4th) 385 (ONCA) [*Parker* cited to DLR] (medical marijuana use); *Rodriguez v British Columbia (AG)*, [1993] 3 SCR 519, 107 DLR (4th) 342 [*Rodriguez* cited to SCR] (physician assisted suicide); *R v Morgentaler*, [1988] 1 SCR 30, 63 OR (2d) 281 [*Morgentaler*] (abortion); *Chaoulli*, supra note 6 (private health insurance).

hypothetical case of a ban on testing an improved new abortifacient drug, discussed below), it seems unwise to declare out of hand that there can never be a constitutional challenge to a restriction on medical research.

The effect of speculativeness

In the context of bans on medical research, we are dealing with potential medical treatments rather than existing medical treatments. The underlying subject matter—medical treatment—is of deep importance to patients and to their interests in life and security of the person. This is particularly the case for patients who lack effective treatments or cures for their conditions. However, does the ban on “upstream” research engage their section 7 interests? The problem here lies in the uncertainty about whether the research would have succeeded in producing a useful treatment as well as in whether other lines of permissible research might lead to the same or maybe superior treatments. From the perspective of the patient, what is being lost is a chance at a beneficial therapy—albeit a chance whose precise value is difficult to establish.

Medical research exists along a spectrum of increasing likelihood that it will benefit patients medically. At one end we can put scientific inquiry in which knowledge is pursued for its own sake, and at the other we can put advanced clinical testing of a specific therapeutic application. As we move from the first to the last point on this spectrum, the possible therapeutic benefits become more concrete and eventually are demonstrated convincingly enough to receive regulatory approval or to enter standard medical practice. Between these poles lie many potential types of scientific inquiry, increasingly targeted at specific therapeutic applications. The following is a list of possible classes of scientific research, in order of increasing likelihood of generating a beneficial therapeutic application:

1. pursuit of knowledge for its own sake in the area of human biology and disease;
2. exploration of aspects of human biology and disease with a particular therapeutic application in mind;
3. generation of evidence of the potential effectiveness of a particular therapeutic application (e.g. testing in experimental models); and
4. generation of evidence of the safety and effectiveness of a particular therapeutic application in humans (e.g. clinical trials in humans).

At some point, the speculativeness of the benefit should be sufficiently reduced to allow a patient to claim that a government ban on the research encroaches on their section 7 interests. Furthermore, it seems to be good policy to recognize the availability of such a claim. It would otherwise be possible for a government to stave off the development of a treatment that it could not constitutionally withhold from patients later. The following hypothetical illustrates this point. Imagine that a government, seeking to prevent an increase in abortion, decided to prohibit the clinical testing of a new abortifacient drug that looked very likely to be a considerable improvement over existing methods in terms of safety and cost-effectiveness. There is some (albeit little) speculativeness in this hypothetical about whether the clinical testing will culminate in a safer form of abortion. If potential patients were unable to establish a claim because of the speculativeness of the benefit, then governments could try to restrict abortion by preventing the upstream research that might improve access to abortion.

If this intuition is correct, it demonstrates that one may have a section 7 interest in a potential medical treatment and the unimpeded medical research that may bring it to fruition, at least where the chance of success is reasonably high. The issue then is not whether the claim has to do with an established treatment or research aimed at developing a treatment, but instead how likely it is that the research will give rise to a treatment.

It is worth noting that the constitutional law contemplates the protection of other “upstream” actions that, individually, seem to be of only speculative worth—and sometimes seem likely to be worthless. One such context is the right to freedom of expression, which is justified not just as of inherent value to the individual, but also for its beneficial social consequences. Courts often refer to consequentialist justifications for freedom of speech, including the pursuit of the “truth” through the “marketplace of ideas.”⁹⁵ The marketplace of ideas theory expressly contemplates that some speech may seem clearly useless or offensive, yet it is still often protected on the theory that the competition of clashing views is the best route to the “truth.”⁹⁶ In other words, we do not know which expression is valuable, therefore we protect all of it because of the possibility that even the most offensive and seemingly useless speech may be valuable. A parallel contention can be made with respect to medical research. We do not know which lines of research will turn out to be useful, and it may be that the cross-fertilization of different lines of research

⁹⁵ See *Grant v Torstar Corp*, 2009 SCC 61 at paras 47-50, [2009] 3 SCR 640.

⁹⁶ *R v Sharpe*, 2001 SCC 2 at para 21, [2001] 1 SCR 45.

will, like a marketplace of ideas, produce the best outcomes. Of course, as with expression, there may be good harm-based reasons to infringe a constitutional interest in medical research, but that is a separate question from whether the speculativeness of the benefit bars the recognition of a constitutional interest in the first place.

Notwithstanding these arguments, one Canadian precedent that seems to run against the idea that one can claim a section 7 right to a speculative benefit is *Operation Dismantle v Canada*.⁹⁷ In that case, the plaintiffs argued that the Canadian government's decision to permit US cruise missile testing in Canada violated their section 7 rights because it heightened the risk of nuclear war. Their claim was struck out as disclosing no reasonable cause of action. The Supreme Court rejected the appeal, declaring that the claim that the government's decision would increase the risk of nuclear war was too hypothetical and speculative to ever be capable of proof at trial, even with the assistance of expert opinion. In essence, it depended upon the reactions of other countries to Canada's decision, and this was "not capable of prediction, on the basis of evidence, to any degree of certainty approaching probability."⁹⁸ The Supreme Court explained that remedial action to forestall future harm may be appropriate and available in some cases, but not "where the link between the action and the future harm alleged is not capable of proof."⁹⁹

This case stands as a fairly clear statement that where benefits or harms of a law are so speculative as to amount to guesswork, it will be impossible for a court to find that a deprivation of a section 7 interest is likely to follow from the impugned law. It does not stand for the proposition that speculativeness will always bar a section 7 claim. Indeed, the reference to "certainty approaching probability" suggests that something less than full certainty is needed.

Turning to the prohibition of human cloning research, there is considerable uncertainty over whether therapeutic cloning research will generate a useful cell replacement therapy. There is perhaps more confidence that knowledge gained during the research might contribute more indirectly to the development of stem cell therapies—for example, by shedding light on the processes of nuclear reprogramming that lead to refinements of induced

⁹⁷ *Operation Dismantle v The Queen*, [1985] 1 SCR 44, 18 DLR (4th) 481 [*Operation Dismantle* cited to SCR].

⁹⁸ *Ibid* at para 18.

⁹⁹ *Ibid* at para 30.

pluripotency techniques. If experts in stem cell science are able to show that the ban on therapeutic cloning research is more likely than not to delay or prevent the discovery of safe and effective stem cell therapies, this may offer enough evidence of harm to meet the “probability” threshold identified in *Operation Dismantle*.

As the research proceeds in the stem cell field, more information is likely to be gained on the potential utility of therapeutic cloning research (e.g. by extrapolation from developments in therapeutic cloning research in non-human animals, or by observing the results of research from countries where therapeutic cloning research is permitted) as well as on the adequacy or inadequacy of alternatives to therapeutic cloning research. This may reduce the uncertainty about whether the prohibition on therapeutic cloning research can be said to endanger a patient’s life or health, depriving the patient of his or her section 7 interests.

A review of the literature suggests that, at present, few researchers would be willing to guess at whether or not therapeutic cloning is likely to become a therapeutically viable treatment. More might accept that the ban on therapeutic cloning research (and perhaps any ban on research in the stem cell field) is more likely than not to delay or hinder the discovery of the optimal form of stem cell therapy.

The problem of indirect interests in the freedom of others

A patient who complains that restrictions on research have violated his constitutional rights is really complaining about restrictions on the freedom of third parties (researchers). There may be a few exceptions where researchers are pursuing a treatment or cure for their personal use. However, most cases will likely involve a claim that one’s rights are infringed by restrictions imposed on another person.

Human interdependency is such that this is not an unusual or necessarily problematic obstacle. Many people are unable by themselves to take a whole range of actions on their own behalf, and they often rely on the assistance of others. This is nearly always the case in the medical context. Courts recognize this and have accepted without much comment that a patient has a potential constitutional claim where it is the freedom of a willing third party to provide medical treatment that is being curtailed. This makes sense. If a state could constitutionally prohibit others from assisting someone unable to vindicate their own constitutionally-protected interests, this would be a way to achieve indirectly what would be constitutionally invalid if done directly. In-

deed, this interdependency, giving rise to constitutional interests in the freedom of others, is implicitly recognized in a range of non-medical contexts as well.¹⁰⁰

A couple of examples will illustrate that a prohibition on providing assistance to a person may violate that person's constitutional rights notwithstanding that it is the liberty of a third party that is directly curtailed. In *Rodriguez v British Columbia (AG)*,¹⁰¹ the Supreme Court of Canada considered the constitutionality of the *Criminal Code* provision prohibiting third parties from assisting someone to commit suicide.¹⁰² The plaintiff's challenge was ultimately unsuccessful, but not because she was challenging a restriction on the freedom of third parties. The challenge failed because the Supreme Court found that the deprivation of her section 7 interests was not contrary to a principle of fundamental justice. The fact that her section 7 interest in security of the person was engaged by the restriction of third party assistance was recognized and accepted.¹⁰³

In *R v Morgentaler*,¹⁰⁴ the Supreme Court of Canada considered the constitutionality of the *Criminal Code* provisions dealing with abortion. In that case, three physicians challenged the legislative scheme that criminalized the actions of both the physician and the woman undergoing an abortion. The scheme contemplated an exemption where abortion was needed to protect a pregnant woman's life or health, but the Supreme Court found it unworkable. The provisions were struck down, on the basis that they all violated a preg-

¹⁰⁰ The Supreme Court has repeatedly interpreted the right to freedom of expression as including a listener's right to receive information (see e.g. *Little Sisters Book & Art Emporium v Canada*, 2000 SCC 69 at para 41, [2000] 2 SCR 1120). The US Supreme Court similarly finds a right to receive information, and has allowed potential recipients standing to challenge restrictions on other speakers (see e.g. *Virginia State Board of Pharmacy v Virginia Citizen's Consumer Council*, 425 US 748 (1976)). In *Benner v Canada*, [1997] 1 SCR 358, 143 DLR (4th) 577, the Supreme Court allowed the male applicant for citizenship to claim that his rights were violated by a law that discriminated against women by applying different citizenship rules to those born of Canadian fathers versus Canadian mothers. The necessary relationship to his mother meant that the son was affected by discrimination against her.

¹⁰¹ *Supra* note 94.

¹⁰² *Criminal Code*, RSC 1985, c C-46, s 241(b).

¹⁰³ *Rodriguez*, *supra* note 94 at para 137.

¹⁰⁴ *Morgentaler*, *supra* note 94.

nant woman's section 7 interest in security of the person. The constitutional right invoked here was clearly that of the patient, not the physician, and it was used to strike down a criminal prohibition applicable to the physician (as well as a criminal prohibition applicable to the patient).

In *Hitzig v Canada*, dealing with access to medical marijuana, the Ontario Court of Appeal stated,

“...a criminal sanction applied to another who would assist an individual in a fundamental choice affecting his or her personal autonomy can constitute an interference with that individual's security of the person.”¹⁰⁵

The parallel between these cases and the prohibition on medical research is that patients will generally rely on third parties to conduct the research that is of interest to them. As is the case with medical treatment, the fact that the interests of patients are inextricably bound up in the freedom of willing third parties to conduct research provides the foundation for the potentially constitutionally-protected interest in that freedom.

In sum, a potential patient is not foreclosed from challenging a prohibition on medical research under section 7 by reason only that the prohibition applies directly to a third party, and only indirectly affects their interests.

If there is a right to medical research, is there a right of access to the resulting treatment?

A right to unimpeded medical research does not necessarily mean that there will be a right of access to an experimental drug prior to government approval. Nor does it necessarily mean there will be a right of unimpeded access to the resulting treatment. Differing governmental objectives may come into play once there is an actual treatment available, such as the protection of vulnerable patients from exploitation or dangerous treatments.

In the American case, *Abigail Alliance*, the plaintiff claimed a right of access to an experimental drug prior to the completion of its clinical testing and government approval.¹⁰⁶ The claim was framed as a right of access by terminally ill patients to experimental drugs that had passed limited safety (Phase I) trials but had not yet been proven safe and effective in subsequent

¹⁰⁵ *Hitzig v Canada* (2003), 231 DLR (4th) 104 at para 95, 177 CCC (3d) 449.

¹⁰⁶ *Abigail Alliance*, *supra* note 2.

broader testing. The Court of Appeals rejected the claim, saying there is no such constitutional right, although it expressly refrained from commenting on the “broader question of whether access to medicine might ever implicate fundamental rights.” The Court of Appeals emphasized the fact that the drug in this case had not been shown to be safe or effective, and that it might in fact be harmful.

This case might seem to suggest that there is no right to only potentially beneficial treatments. By extension, this might seem to suggest that there can be no right to unimpeded upstream research, the benefits of which are even more speculative. However, this is a false analogy. The plaintiff in *Abigail Alliance* was seeking to consume an experimental drug that might potentially be beneficial or harmful, she was not seeking to overturn a ban on clinical testing of the experimental drug. Different policy justifications exist for prohibiting access to an experimental drug and prohibiting research that may generate a new drug. Research will not harm the potential patient, although consuming a drug may do so. Concerns about the exploitation of desperate patients or the integrity of the clinical trials system¹⁰⁷ do not arise until there is an experimental treatment that can be tested in humans. The type of claim being explored in this article (an interest in the continuation of research that may generate a medical therapy) may have other problems but they are different from those raised in *Abigail Alliance*.

Evidently, this case is not binding authority in Canada. However, even if a similar case were brought in Canada, it would be unwise to decide it in a manner that forecloses the possibility of a patient’s constitutional challenge to restrictions on potential medical benefits, whether this consists of a challenge to a research ban or a ban on access to an experimental treatment. As I have argued earlier, there are good reasons to leave open this possibility, and to address the appropriate limitations on that right under section 1 in the varying circumstances of each case.

The principles of fundamental justice

¹⁰⁷ One of the reasons put forward to justify restricting patient access to drugs that have not yet gone through full testing is that if many patients were able to insist on getting the untested but promising drug they would likely do so rather than take part in a drug trial where they run the risk of falling into a placebo group. This would make the process of clinical drug trials more difficult. See Eugene Volokh, “Medical Self-Defense” (2007) 120:7 Harv L Rev 1813 at 1830.

According to the judicial interpretation of section 7 of the *Charter*, a deprivation of the right to life, liberty, or security of the person will be unconstitutional only if it fails to accord with the “principles of fundamental justice.” The content of the principles of fundamental justice is a source of some uncertainty in *Charter* jurisprudence, and the considerations at this stage sometimes overlap with analysis under section 1 of the *Charter*.

In essence, the Supreme Court has said that the principles of fundamental justice are legal principles that are “to be found in the basic tenets of our legal system.”¹⁰⁸ In addition, they must be generally accepted as “vital or fundamental to our societal notion of justice,”¹⁰⁹ and “capable of being identified with some precision and applied to situations in a manner that yields an understandable result.”¹¹⁰

One candidate for a relevant principle of fundamental justice in the context of restrictions on potentially life-saving or health improving medical research is a putative fundamental right of self-defense or self-preservation. Volokh advances this argument in the US context invoking the long legal tradition of recognizing a right to protect one’s life from attack, the constitutional right to bear arms, and the judicial recognition of a constitutional right to abortion after the point at which a fetus is viable when a woman’s life is in danger (“medical self-defense”).¹¹¹ This line of reasoning ultimately failed to help the plaintiff in *Abigail Alliance* where the Court of Appeals said that access to experimental drugs was not the same as access to life-saving medical treatment because the experimental drugs are only potentially helpful and in fact may be harmful. This ruling does not directly settle the point for a claim to unimpeded medical research for reasons discussed above.

Whether a similar argument about self-defense as a principle of fundamental justice could be made in Canada is uncertain. Certainly, the appeal to self-defense based on a right to bear arms is unlikely to succeed. Canadian courts have rejected arguments that restrictions on the possession or owner-

¹⁰⁸ *Reference re s 94(2) of the Motor Vehicle Act (British Columbia)*, [1985] 2 SCR 486 at paras 31, 24 DLR (4th) 536.

¹⁰⁹ *Rodriguez*, *supra* note 94 at para 141.

¹¹⁰ *Ibid.*

¹¹¹ Volokh, *supra* note 107. See also Mary Briody Mahowald, “Self-Preservation: An Argument for Therapeutic Cloning, and a Strategy for Fostering Respect for Moral Integrity” (2004) 4:2 Am J Bioethics 56.

ship of firearms violate section 7.¹¹² On the other hand, the Supreme Court has implicitly recognized a fundamental interest in self-preservation in the context of the criminal defense of duress. In *R v Ruzic*, the Supreme Court determined that it was a principle of fundamental justice that morally involuntary conduct (including actions taken under threat of death or serious bodily harm) should not be criminalized. As the Court put it, “[d]epriving a person of liberty and branding her with the stigma of criminal liability would infringe the principles of fundamental justice if the accused did not have any realistic choice.”¹¹³

It seems unlikely that unimpeded access to necessary medical treatment itself constitutes a principle of fundamental justice given the Supreme Court’s failure to mention it in its various rulings on section 7 impediments to medical treatment. In its ruling on access to medical marijuana in *R v Parker*, the Ontario Court of Appeal made various statements suggesting that unimpeded access to drugs needed to protect life and health is a requirement of fundamental justice,¹¹⁴ it ultimately relied on other principles of fundamental justice that had already been established in other cases—including the requirement that legislation not be arbitrary and that defences not be illusory. As a result, this case does not provide a particularly solid foundation for unimpeded access to necessary medical treatment as principle of fundamental justice.

The courts have tended to be very cautious in recognizing new principles of fundamental justice, instead often invoking one of a set of well-established principles that focus on defects in the legislative scheme such as arbitrariness, vagueness, or overbreadth. In the present case study, the prohibition on therapeutic cloning in the *AHRA*, the “overbreadth” principle may prove applicable. Overbreadth refers to a situation in which the state uses means which are broader than is needed to achieve a legitimate objective, thereby needlessly infringing a protected *Charter* right.¹¹⁵

¹¹² *R v Montague*, 2010 ONCA 141, 206 CRR (2d) 146; *Hudson v Canada (AG)*, 2007 SKQB 455, [2008] 6 WWR 572 (Sask CA).

¹¹³ *R v Ruzic*, 2001 SCC 24 at para 47, [2001] 1 SCR 687.

¹¹⁴ *R v Parker*, *supra* note 94 at paras 136-137, 139.

¹¹⁵ See *R v Heywood*, [1994] 3 SCR 761 at 792-93, 120 DLR (4th) 348; RJ Sharpe & K Roach, *The Charter of Rights and Freedoms* (Toronto: Irwin Law, 2009) at 237-38.

For reasons that will be discussed in more detail within the next section (dealing with section 1), the only justification for the prohibition that is clearly valid from the legal perspective is the protection of women from harm. If this is correct, then the prohibition on cloning is likely overbroad because of the various potential avenues of therapeutic cloning research that could be pursued without risking the health of oocyte donors. Alternatives to the use of oocytes procured at risk to women donors include: cell fusion, “stembrids,” inter-species cloning, the use of failed IVF oocytes, the use of immature oocytes, or the use of oocytes created from pluripotent stem cells. Rather than prohibiting cloning outright, the law could instead prohibit therapeutic cloning research using oocytes taken from women and girls (with the possible exception of oocytes from ovarian tissue excised solely for therapeutic reasons). Such an approach would provide equivalent protection for women from the health risks of supplying oocytes for research while leaving open the possibility of therapeutic cloning research.

c) Is the Ban on Therapeutic Cloning Research Justified Under Section 1 of the Charter?

If the foregoing discussion has been correct, and patients may make a claim that the Canadian ban on therapeutic cloning research violates their section 7 interests in a manner contrary to the principles of fundamental justice, the next question is whether the violation is nonetheless justified under section 1 of the Canadian Charter of Rights and Freedoms.

Section 1 states that the guaranteed rights and freedoms are subject to “such reasonable limits prescribed by law as can be demonstrably justifiable in a free and democratic society.”¹¹⁶ Whether or not the limit is so justified is determined using the Oakes test,¹¹⁷ which involves two main steps. First, the objective of the law must be sufficiently important to warrant overriding a constitutionally protected right or freedom. Second, the means chosen must be a proportionate response given the objective of the legislation. This proportionality is assessed by considering whether the law is rationally connected to the objective, whether it impairs the Charter right as little as is reasonably possible, and whether the harmful effects on the rights holder are proportionate to the benefits sought by the law.

¹¹⁶ *Charter*, *supra* note 1 at s 1.

¹¹⁷ *R v Oakes*, [1986] 1 SCR 103, 26 DLR (4th) 200.

The objective of the law

It is not always easy to identify the Parliamentary objectives in enacting legislation. In the case of the *Assisted Human Reproduction Act*, the *Act* itself contains a declaration of principles that sheds some light on its underlying objectives.¹¹⁸ Those that are relevant to cloning demonstrate a legislative concern with the health of children born through assisted reproduction, the health of women, the need to protect human individuality and diversity and the integrity of the genome, and the need to secure the benefits of assisted human reproductive technologies and associated research by taking “appropriate measures for the protection and promotion of human health, safety, dignity and rights in the use of these technologies and in related research.”

Canadian legal academics are split on the proper characterization of the legislative objections behind the ban on cloning.¹¹⁹ Rather than trying to offer a persuasive interpretation of Parliament’s actual legislative objectives in banning human cloning, I will take a different approach. I will consider the main concerns about therapeutic cloning research that one may find in the literature and will consider the extent to which these concerns furnish constitutionally valid objectives. These concerns have to do with (1) the risk of harm to women from the demand for oocytes, (2) the ascription of moral status to the embryo and resulting concern about the destruction of the embryo, (3) the instrumentalization of nascent human life that might be implicit in the deliberate creation and use of embryos for research, and (4) the risk that if therapeutic cloning is permitted, the risk of reproductive cloning increases (the “slippery slope” argument). It is possible that in enacting the *AHRA*, some of these issues were not among the motivating concerns of the Canadian Parliament. However, it seems likely that the actual objectives of the legislation respond to one or more of these concerns.

Concern #1: Harm to women

The first and, in my view, most compelling concern is that cloning research is likely to consume a large number of oocytes. These oocytes must be obtained at some risk to women due to hormonal manipulation and surgical removal. These risks, which are also faced by women undergoing *in vitro* fertilization treatment, include the possibility of ovarian hyperstimulation syndrome (which can range from mild to severe and life-threatening), as

¹¹⁸ *AHRA*, *supra* note 5 s 2.

¹¹⁹ See Billingsley & Caulfield, *supra* note 90; Downie, Llewellyn & Baylis, *supra* note 4.

well as the risks of infection and injury during the surgical removal of the eggs. In addition, there is uncertainty about whether the hormones pose an elevated long-term risk of some cancers.¹²⁰ The demand for oocytes will only increase if therapeutic cloning turns out to be clinically useful and commercially promising.¹²¹ Most authors agree that this is a risk, and opponents of cloning bans quickly shift to arguments about less restrictive ways of ensuring protection of women such as through research ethics board oversight (i.e. to watch for undue inducement, and to ensure proper disclosure of risks), or through a ban on payment. These arguments will be discussed further in the context of the proportionality analysis of section 1 below. For the moment, we can safely conclude that the protection of women from harm to their health through oocyte donation is a legitimate legislative objective. Whether the means chosen is proportionate will be addressed below.

Concern #2: Moral status of the embryo

The second common justification for prohibiting therapeutic cloning research is based on the conviction that the embryo has a moral status equivalent or similar to a human being, and it is thus unethical deliberately to destroy an embryo or to use it solely as a means to benefit others.¹²² Therapeutic cloning research usually involves the destruction of the cloned embryo in order to derive cloned embryonic stem cells. Alternatives such as blastomere biopsy (which would take one cell) would not destroy the embryo, but may also be viewed as unethical if one attributes moral status to the embryo since it creates a risk of harm without corresponding benefit to the cloned embryo.

The difficulty with the protection of the embryo as a legislative objective is that it rests on a contested moral judgment about the moral status of the very early embryo and reasonable people differ about whether the embryo has a status equivalent to a person, a status equivalent to a collection of somatic cells like skin cells, or something in between.¹²³ It is thus a shaky basis for a law in a pluralistic society. Furthermore, the attribution of moral status

¹²⁰ For a recent discussion of these risks, see B Ellison & J Walker, "Assessing the Risk of Ovarian Hyperstimulation Syndrome in Egg Donation: Implications for Human Embryonic Stem Cell Research" (2011) 11:9 Am J Bioethics 22. See also F Baylis & C McLeod, "The Stem Cell Debate Continues: The Buying and Selling of Eggs for Research" (2007) 33 J Med Ethics 726.

¹²¹ Beeson & Lippman, *supra* note 4.

¹²² The President's Council on Bioethics, *Human Cloning and Human Dignity: An Ethical Inquiry* (Washington, DC: Public Affairs, 2002) at 173-82.

¹²³ *Ibid* at 152-53.

to the embryo is inconsistent with Canadian jurisprudence, which does not attribute personhood to the embryo.¹²⁴ Finally, the fact that the *AHRA* allows supernumerary embryos created during IVF to be used in research establishes that the protection of the embryo due to its moral status is not a likely objective of the Canadian legislature in enacting the ban on therapeutic cloning research.¹²⁵

Concern #3: Instrumentalization of nascent human life

The third common objection to therapeutic cloning research relates to the position that the deliberate creation and use of embryos for research represents the unethical instrumentalization of nascent human life. This is a different objection to the one based on the moral status of the embryo, and one may still object to this instrumentalization even if one does not accept that an embryo has full moral status.

The exact nature of the concern with the instrumentalization of nascent human life is difficult to articulate, but seems to be that (1) it is inherently disrespectful and undignified to treat nascent forms of human life as tools and/or that (2) the instrumental outlook on nascent human life is likely to lead to other harmful social or psychological consequences (such as a tendency to view all human or other life in instrumental terms).

With respect to the first point, there is some debate over whether the use of embryos in medical research is disrespectful or undignified. Some argue that far from undermining human dignity, using early embryos to discover treatments to cure disease and alleviate suffering would promote human dignity. Others accept that the embryo ought to be treated with respect, but that this is achieved by using it only for weighty rather than trivial or contemptuous purposes.¹²⁶

On the second point, Heidegger raised a similar concern in his discussion of technology, suggesting that by taking a relentlessly instrumental perspective, in which everything is to be mastered and bent to our human purposes,

¹²⁴ *Tremblay v Daigle*, [1989] 2 SCR 530, 62 DLR (4th) 634. This case interprets the Quebec Civil Law and the *Charter of human rights and freedoms*, RSQ, c C-12, but it also comments on the Anglo-Canadian tradition.

¹²⁵ *AHRA*, *supra* note 5 s 10(2).

¹²⁶ Bonnie Steinbock, "The Science, Policy and Ethics of Stem Cell Research" (2007) 14:S1 *Reprod BioMed Online* 130; MJ Sandel, "Embryo Ethics: The Moral Logic of Stem-Cell Research" (2004) 351:3 *N Engl J Med* 207.

we are at risk of coming to see ourselves in similar instrumental ways, losing our humanity and missing the real essence and value of the natural world.¹²⁷ In the end, it is not uncommon for people to react to scientific advances with unease, particularly advances that blur settled and comfortable boundaries (e.g. between artificial and natural, animal and human, or man and woman)¹²⁸ or that upset familiar ways of doing things (e.g. assisted reproductive technologies).¹²⁹ With time, many practices originally rejected as unnatural or immoral have come to be widely accepted and welcomed, and others, formerly accepted, have come to be rejected. It is difficult to know therefore when this kind of unease ought to be a constitutionally legitimate basis for prohibiting a particular practice.

The Supreme Court of Canada has struggled with when legislation may be justified by reference to collective moral norms rather than by demonstrated harm. In *R v Malmo-Levine; R v Caine*, the Supreme Court explicitly rejected the idea that the only constitutionally acceptable ground upon which the majority may limit the liberty of the individual is on the basis of harm (i.e., the “harm principle” familiar from John Stuart Mill’s *On Liberty*).¹³⁰ However, despite denying that the harm principle is the touchstone for identifying constitutionally valid criminal law, the Court routinely looks for and invokes forms of harm to justify restrictions on liberties.¹³¹ The challenge, of

¹²⁷ Martin Heidegger, “The Question Concerning Technology” in *The Question Concerning Technology and Other Essays*, translated by William Lovitt (New York: Harper & Row, 1977) 3.

¹²⁸ Martijntje Smits, “Taming Monsters: The Cultural Domestication of New Technology” (2006) 28 *Technol Soc* 489 at 495.

¹²⁹ Korobkin, *supra* note 91 at 173 observes that IVF was criticized as “immoral interference with the natural process of procreation” at the outset, despite now being largely uncontroversial.

¹³⁰ *R v Malmo-Levine; R v Caine*, 2003 SCC 74 at para 129, [2003] 3 SCR 571 [*Malmo-Levine*].

¹³¹ See e.g. *R v Butler*, [1992] 1 SCR 452, 89 DLR (4th) 449 [*Butler*]. The Court, after discussing whether moral disapprobation was an acceptable basis for the obscenity law, concluded that the basis of the law was not moral disapprobation anyway but the avoidance of harm from the reinforcement of the inequality of women (*ibid* at para 82). Similarly, the ruling in *Malmo-Levine* was based on harm, despite the rejection of the harm principle in that case (*supra* note 130 at para 136). *R v Labaye*, 2005 SCC 80, [2005] 3 SCR 728 [*Labaye*] also supports the idea that some form of harm must be shown to justify a criminal prohibition, despite the objections of the dissenting judges, who thought the majority position was inconsistent with the rejection of the harm principle in *Malmo-Levine*.

course, is in determining what counts as harm that legitimizes the use of state coercion.¹³² In cases such as *R v Butler* (dealing with “obscenity”) and *R v Labaye* (dealing with “common bawdy houses”) the Court has stated that criminalization is justified to prevent behaviours that normalize socially harmful attitudes or that induce harmful attitudinal shifts.¹³³ Not every shift in attitude or values will be harmful, however. In order to ensure that the criminal law is not used as an illiberal instrument to enforce majoritarian customs and preferences, the Court accepts only claims about harmful attitudinal shifts that are viewed as harmful on the basis of fundamental moral values, such as those embodied in the *Charter*.¹³⁴

The prohibition on cloning in the *AHRA* may reflect a concern with the instrumentalization of nascent human life. After all, the *Act* prohibits the creation of embryos for purposes other than reproduction and restricts embryo research to the use of supernumerary embryos created for IVF purposes. This might reflect a greater unease with the deliberate creation of embryos for research, while the instrumental use of embryos that were not created for that purpose and that will be discarded is viewed as a “lesser degree” of instrumentalization. Another interpretation is that the legislative prohibition on the creation of embryos for research purposes is really aimed at protecting women from the demand for oocytes, rather than a condemnation of the instrumentalization of very early human life.

Ultimately, I suspect that the objection to cloning based on the undesirability of encouraging an instrumental view of nascent human life is insufficient to offer a constitutionally robust “pressing and substantial objective” for the prohibition of therapeutic cloning research. Even if there were a clear majority moral position on this matter (which, I suspect, there is not),¹³⁵ *But-*

¹³² Bradley W Miller, “Morals Laws in an Age of Rights: Hart and Devlin at the Supreme Court of Canada” (2010) 55 *Am J Juris* 79; *Malmo-Levine*, *supra* note 130 at para 127.

¹³³ *Labaye*, *supra* note 131 at para 46; *Butler*, *supra* note 131.

¹³⁴ *Butler*, *ibid* at paras 80-81.

¹³⁵ As noted earlier, both the UK and Australia (countries with similar cultures and political systems to Canada) permit therapeutic cloning (Caulfield et al, *supra* note 77). Notably, UN members were unable to agree on a treaty to ban therapeutic cloning research despite agreement that reproductive cloning should be prohibited. See Helen Pearson, “UN Ditches Cloning Ban: Delegates Opt for Compromise Statement” *Nature* (22 November 2004) online: <www.nature.com/news/2004/041122/full/news041122-2.html>. The General Assembly adopted

ler makes it clear that majoritarian moral judgments about which attitudinal shifts are harmful cannot constitutionally be imposed unless they are based on fundamental values like those embodied in the *Charter*. It is clear that the instrumental use of human beings would be contrary to fundamental *Charter* values, which include “respect for the inherent dignity of the human person,”¹³⁶ but it is not clear that this extends to very early stage embryos, which are not legally recognized as “human persons.”

Concern #4: Slippery slope to reproductive cloning

A fourth justification for the ban on therapeutic cloning research in humans is that researchers will be able to learn about and perfect the process of human cloning, thereby raising the risk that an unscrupulous person will illegally engage in reproductive cloning.¹³⁷ There is currently strong and widespread consensus that human reproductive cloning should be opposed on safety grounds, although some question the strength of other arguments against the practice.¹³⁸ The concerns expressed in section 2 of the *AHRA* regarding human individuality and diversity, as well as the health and well-being of children born through assisted reproductive technologies, explain the ban on reproductive cloning. It is conceivable that the ban on therapeutic cloning is also intended to promote the same values by reducing the risk that someone might attempt reproductive cloning.

The objectives of protecting human individuality, diversity, and the health and well-being of children are indeed “pressing and substantial objectives.” The ban on therapeutic cloning research is put forward as a second line of defence to buttress the direct criminalization of reproductive cloning. The prohibition against therapeutic cloning in order to protect women is also a second and indirect line of defence added to the direct prohibition against

Declaration 59/280 on March 8, 2005, which was ambiguous as to whether therapeutic cloning research ought to be banned (see *United Nations Declaration on Human Cloning*, GA Res 59/280, UNGAOR, 59th Sess, UN Doc A/Res/59/280 (2005)). The diversity of international views is revealed in the delegates’ statements after the vote (see UNGAOR, 59th Sess, 82d Plen Mtg, UN Doc A/59/PV.82 (2005)).

¹³⁶ See *Oakes*, *supra* note 117 at para 64.

¹³⁷ The President’s Council on Bioethics, *supra* note 122 at 164, 189; Capron, *supra* note 4 at 1061-62.

¹³⁸ S Camporesi & L Bortolotti, “Reproductive Cloning in Humans and Therapeutic Cloning in Primates: Is the Ethical Debate Catching Up With the Recent Scientific Advances?” (2008) 34:9 *J Med Ethics* e15.

paying for gametes. The simultaneous pursuit of multiple strategies to control a proscribed behaviour is a legitimate governmental approach where it is deemed necessary and each strategy is, itself, constitutional.

Nevertheless, the slippery slope justification in this case is weakened by the fact that a ban on therapeutic cloning is unlikely to have much effect, if any, on the risk that someone will illegally attempt reproductive cloning. After all, human therapeutic cloning research is permitted and is proceeding in multiple jurisdictions outside Canada. Non-human reproductive cloning research is permitted in Canada and elsewhere and has succeeded in producing cloned mammals of many species. Cloning techniques are thus being slowly refined despite the *AHRA*. Against this backdrop, the ban on therapeutic cloning research does not seem to add much, if anything, to the criminalization of reproductive cloning as a means to prevent reproductive cloning. Laws that violate *Charter* rights and yet do little or nothing to advance even admittedly important legislative objectives are unlikely to satisfy the last step of the section 1 proportionality analysis, which demands that the beneficial effects of the legislation be proportionate to the harm of infringing *Charter* rights. Recent case law suggests that the Supreme Court will consider the actual benefits or effectiveness of legislation (rather than merely the importance of the objective) in determining whether the infringement of a *Charter* right is justified.¹³⁹

Alternatives, opportunity costs, and the realism of the end goal of personalized medicine.

In the literature, one may also find other arguments against therapeutic cloning research, namely, that (1) there are better alternative lines of research,¹⁴⁰ (2) the dream of widely available personalized cloned stem cell therapies is financially impossible, and (3) the personalized cloned stem cell therapies will only be available to the wealthy.¹⁴¹ These concerns are fundamentally about two things: the waste of resources and the exacerbation of social inequality. For the reasons that follow, they have not been included as possible legislative objectives that motivate the *AHRA*. As a result, they are not considered further in this article in the discussion of the balancing exercise under section 1 of the *Charter*, which weighs the benefits of the law in

¹³⁹ Sharpe & Roach, *supra* note 115 at 76-77.

¹⁴⁰ Katrien Devolder & Julian Savulescu, "The Moral Imperative to Conduct Embryonic Stem Cell and Cloning Research" (2006) 15 Cambridge Q Healthcare Ethics 7; Baylis & McLeod, *supra* note 120 at 727.

¹⁴¹ Devolder & Savulescu, *ibid* at 16.

achieving “pressing and substantial” legislative objectives against the harms of limiting *Charter*-protected rights. However, a short discussion is included below in order to provide a comprehensive view of the objections to therapeutic cloning research that are contained in the literature.

With respect to the first objection—that therapeutic cloning research is a waste of resources—it is extremely difficult to be sure which of the available lines of research is preferable, and it may be that simultaneous research along synergistic lines would ultimately be best. Unless there are independent reasons to prohibit human cloning, the existence of alternatives does not explain why a criminal prohibition is needed. As discussed earlier, we normally rely upon researchers, funders, and the market to channel resources among various alternative lines of medical research rather than to criminalize those expected to be a waste of resources.

It is true that, ultimately, we may decide that personalized stem cells are too expensive and impractical, preferring strategies related to stem cell banks,¹⁴² although there are concerns that such an approach might disadvantage members of minority ethnicities.¹⁴³ A parallel strategy, with personalized stem cells for minority or rare haplotypes and banked cells for everyone else might ultimately be best. It is also important to recall that therapeutic cloning research may contribute to treatments in other ways that do not pose the kinds of impracticalities that personalized stem cell therapies might. For example, therapeutic cloning research and iPS cell research could help researchers to create cellular models of particular diseases in order to understand them or to test treatments.¹⁴⁴ Again, the usual mechanisms for determining whether a particular line of research is likely to be useless ought to apply here unless there are independent reasons to criminalize therapeutic cloning research.

The concerns, based on social justice, that medical research is stacked too much toward the ailments of the wealthy or that the fruits of the research are accessible only to the wealthy are widespread and well-founded con-

¹⁴² See Izpisua-Belmonte, *supra* note 73 at 880.

¹⁴³ See e.g. Hilary Bok, Kathryn E Schill & Ruth R Faden, “Justice, Ethnicity, and Stem-cell Banks” (2004) 364:9429 *Lancet* 118 at 119.

¹⁴⁴ Devolder & Savulescu, *supra* note 140 at 18; The President’s Council on Bioethics, *supra* note 122 at 146; J Savulescu & L Skene, “The Kingdom of Genes: Why Genes from Animals and Plants will Make Better Humans” (2008) 8:12 *Am J Bioethics* 35 at 35.

cerns. A thorough treatment of this topic is beyond the scope of this article, but it is worth noting that the argument applies much more broadly and could equally condemn many other lines of modern biomedical research (as well as other ways that affluent societies spend their resources other than on biomedical research). Again, we do not normally address this problem through the criminalization of medical research likely to generate expensive therapies. Unless there are reasons specific to therapeutic cloning research itself, the fact that it is predicted not to generate the most socially useful results could be addressed with a shift in public funding away from it, and other lines of research deemed unlikely to be socially useful, toward research considered more socially desirable. There is some danger in this approach given that we may be wrong about what turns out to be most useful, although it is a decision that a society could legitimately and perhaps should take given the scarcity of resources. Nonetheless, the ultimate distributive impact of particular medical research and its therapeutic applications is also hard to predict, and depends in part on health care funding models.

In sum, it seems unlikely that these considerations are among the legislative objectives of Parliament in enacting the *AHRA*. In addition, it would be very unusual and would likely be unwise to prohibit a particular line of medical research on these grounds alone.

Summary on the extent to which the potential objectives are “pressing and substantial”

The objective of protecting women from exploitation is sufficiently important to constitute a “pressing and substantial” objective under section 1 of the *Charter*. The moral status of the embryo, or the prevention of the instrumentalization of very early human life seem less likely to meet this requirement.

While the prevention of reproductive cloning does constitute a “pressing and substantial” objective (in order to protect children born from assisted reproductive technologies, and to protect human individuality and diversity), the criminalization of therapeutic cloning research does not seem to add much, if anything, to the objective of preventing reproductive cloning that is not already achieved through the direct criminalization of reproductive cloning. I draw this conclusion based on the fact that the necessary cloning techniques are being developed elsewhere, so a ban designed to prevent the perfection of the techniques in Canada will have little or no effect on the likelihood of an illegal attempt at reproductive cloning. A law that does not achieve its objective with complete success is not for that reason unconstitutional, but a law that infringes a *Charter* right while contributing little or nothing is less likely to be justified. Although I will not pursue the analysis of this objective further, it is possible

that a court might find that even a small contribution to delaying the development of techniques that could be used illegally in reproductive cloning would justify the ban on therapeutic cloning research.

Accordingly, in the following section 1 proportionality analysis, I focus on the most compelling objective underlying the prohibition on therapeutic cloning—that of protecting women from exploitation.

Is the prohibition on therapeutic cloning research a proportionate legislative response to the risk posed by that research to women?

The second stage in the section 1 analysis is to consider whether the state infringement of a *Charter* right is a proportionate response given the legislative objectives. This is assessed by considering whether the law is rationally connected to the objective, whether it impairs the *Charter* right as little as is reasonably possible, and whether the harmful effects on the holder of the right are proportionate to the benefits achieved by the law.

There seems little doubt that the objective of protecting women from the risks associated with a growing demand for oocytes to fuel cloning research is rationally connected to a prohibition on therapeutic cloning research. It is less clear that the prohibition does so in a manner that impairs *Charter* rights as little as reasonably possible.

One response to the concern about the risk that women will be exploited or offered undue inducements to risk their health by donating oocytes is that it is enough to ban compensation for oocytes (as the *AHRA* already does). Others reject even a prohibition on compensation, arguing that research ethics oversight is enough to avoid undue inducement.¹⁴⁵ Some doubt that this is sufficient, pointing to the difficulties of doing so as well as to the fact that this approach places great faith in the oversight abilities of ethics review boards.¹⁴⁶ The topic is a controversial one, even within the International Society for Stem Cell Research, whose task force was sharply divided during attempts to create guidelines for how to treat oocyte donors.¹⁴⁷ The guidelines now list various requirements intended to protect female donors (in-

¹⁴⁵ See R Klitzman & MV Sauer, “Payment of Egg Donors in Stem Cell Research in the USA” (2009) 18:5 *Reprod Biomed Online* 603; SL Crockin, “A Legal Defense for Compensating Research Egg Donors” (2010) 6 *Cell Stem Cell* 99; Insoo Hyun, “Fair Payment or Undue Inducement?” (2006) 442:7103 *Nature* 629-630.

¹⁴⁶ Editorial, “Safeguards for Donors” (2006) 442:7103 *Nature* 601.

¹⁴⁷ Erika Check, “Ethicists and Biologists Ponder the Price of Eggs” (2006) 442:7103 *Nature* 606-07.

cluding guarding against undue inducement and monitoring for the disproportionate recruitment of poorer donors).¹⁴⁸ Ultimately, the practice of paying people to undergo invasive and potentially risky removal of bodily tissue that they would not otherwise undergo for their own therapeutic benefit raises reasonable concerns, and a prohibition on compensation for oocyte donation falls well within the range of measures that a government could reasonably take.

In addition, a government could reasonably decide that it wants to offer more protection to potential donors than it thinks will be provided by a ban on compensation. For example, a government could point to several reasons to question the adequacy of a ban on compensation. First, women remain exposed to non-financial pressures and inducements, as was demonstrated by serious ethical concerns about the sourcing of oocytes from junior members of Woo-Suk Hwang's laboratory.¹⁴⁹ Second, the demand for oocytes might fuel either an illicit market in Canada or contribute to licit or illicit markets abroad. Finally, where it is permissible to take and use tissue donated altruistically, we can expect increased pressure to permit payment for valuable resources that are not donated in sufficient quantities altruistically.¹⁵⁰ Some may question whether these are justifiable reasons to prohibit therapeutic cloning research, suggesting that the practices in the Hwang lab were an aberration or pointing out that in the context of organ transplants we ban organ sales but not transplantation. This may be true, but a government may be more willing to tolerate these risks in the context of organ transplantation (where a relatively small number of patients exists) than in the context of therapeutic cloning research. Many of the concerns associated with fuelling a demand for oocytes and the potential inadequacy of a ban on compensation are borne out in the organ donation context including in relation to non-financial pressures and inducements (e.g. family pressure to donate to a sick

¹⁴⁸ International Society for Stem Cell Research, "Guidelines for the Conduct of Human Embryonic Stem Cell Research", online: ISSCR <www.isscr.org>.

¹⁴⁹ Seoul National University, *supra* note 36. According to this report, Dr. Hwang claimed not to have known that his laboratory members had donated eggs, although he accompanied one graduate student who donated eggs to the hospital for the collection of her eggs. See also Françoise Baylis, "For Love or Money? The Saga of Korean Women Who Provided Eggs for Embryonic Stem Cell Research" (2009) 30:5 *Theor Med Bioeth* 385.

¹⁵⁰ See e.g. Crockin, *supra* note 145, who writes that (in the US context) reproductive egg donors can be compensated, as can other human research subjects, and argues that research egg donors should be treated no differently.

family member), illicit markets, and pressure to legalize compensation. Again it seems to fall within the range of reasonableness for a government to conclude that a ban on compensation would not be adequate in the circumstances.

Another response to concerns about endangering women is that financial incentives be permitted only for women undergoing IVF who already face the risks of oocyte retrieval. This might take the form of reduced fees for IVF in exchange for “egg-sharing.”¹⁵¹ This too raises concerns, particularly as it is likely that women who are less well-off are most likely to participate, it reduces a woman’s own chances to produce frozen embryos for later implantation should initial attempts fail, and it may increase the pressure for aggressive ovarian stimulation to ensure a large number of eggs.¹⁵² The significance of the financial factor in overcoming a fertility patient’s reluctance to share eggs is suggested by the fact that when Belgium began to reimburse the full costs of IVF in 2003, the number of those choosing to share eggs with other IVF patients dropped by about 70%.¹⁵³

As a result, a government could reasonably reject the foregoing options (which are less restrictive on research than a complete ban on therapeutic cloning) as inadequate to meet its objectives. However, there is an alternative approach that would provide equivalent protection to women while not foreclosing therapeutic cloning research in Canada. Methods of cloning that do not use oocytes at all (e.g. cell fusion or stembrids), that use artificial oocytes (created from iPS cells or hES cells), that use non-human oocytes or that use immature oocytes taken from human ovarian tissue removed solely for therapeutic reasons would not threaten women. It is true that these options are experimental, but they may turn out to be effective alternatives. A more narrowly tailored prohibition would thus prohibit therapeutic cloning research using oocytes or precursor cells taken from girls and women but would permit cloning research where it made use of one of the alternatives mentioned above. As a result, the Canadian prohibition on therapeutic cloning research

¹⁵¹ Celia Roberts & Karen Throsby, “Paid to Share: IVF Patients, Eggs and Stem Cell Research” (2008) 66:1 Soc Sci & Med 159.

¹⁵² *Ibid* at 164. But see MY Thum et al, “Does Egg-Sharing Compromise the Chance of Donors or Recipients Achieving a Live Birth?” (2003) 18:11 Hum Reprod 2363, which examines 276 instances of egg-sharing and finds success rates to be the same for egg-sharers and non-egg-sharers.

¹⁵³ See Guido Pennings & Paul Devroey, “Subsidized In-Vitro Fertilization Treatment and the Number of Egg Sharers” (2006) 13:1 Reprod Biomed Online 8 at 8.

arguably fails the second branch of the section 1 proportionality test—it does not infringe the section 7 rights of potential beneficiaries of the research as little as reasonably possible.

Conclusion

Freedom of scientific research, within appropriate and justified limits, is an important value that is recognized in international human rights instruments. While this value is often understood as an interest of researchers, the importance to the broader public of this research (particularly the right to share in the fruits of the research) is also recognized internationally.

So far, constitutional arguments regarding the freedom of scientific research have tended to focus on the freedom of speech of researchers, with much less attention to the potential constitutional arguments that could be made on behalf of potential patients. In my view, this latter argument is available, particularly where the benefits from research are shown to be reasonably probable rather than highly uncertain.

As for prohibitions on earlier stages of research, the argument becomes more challenging because the benefits of the research are often highly speculative. This makes it difficult to demonstrate that any weighty harm has been done to the patient in foreclosing a potentially useful line of research. Nonetheless, in some cases, it may be possible to predict with reasonable certainty (greater than the balance of probabilities, for example) that the research will contribute to the development of another therapy even if it is unclear that the particular therapy envisaged by the research will ultimately be successful. It is possible, for example, that human therapeutic cloning research would produce information regarding human cell reprogramming that would enable more rapid refinement of iPS cells for therapeutic purposes.

The possibility of a patient's *Charter* right to unimpeded medical research has been explored here by focusing on the Canadian ban on therapeutic cloning research in humans. While several potential legislative objectives may underpin the legislation, the one that seems most likely to be constitutionally valid is that of protecting women from the risks associated with donating the oocytes one assumes would be needed for the research and subsequent treatment of actual patients. Assuming it is possible to overcome the hurdle of speculativeness in establishing that this prohibition does infringe the section 7 rights of potential patients, the infringement in this case appears to be overbroad (and thus contrary to the principles of fundamental justice) since methods of cloning research that do not endanger women as oocyte do-

nors are available. A prohibition on cloning research using oocytes sourced from women and girls (with the possible exception of immature oocytes taken from ovarian tissue excised for therapeutic purposes) would provide equivalent protection for women while permitting the research to proceed. In addition, other methods of achieving therapeutic cloning without oocytes (such as cell fusion) are available without putting oocyte donors at risk, and methods of creating artificial oocytes (such as from iPS cells or hES cells) would similarly permit therapeutic cloning using oocytes but without the risk to donors. This overbreadth is also relevant at the stage of the section 1 analysis, and suggests that the law does not infringe the section 7 rights of potential patients as little as is reasonably possible.

Stem cell science is moving extremely rapidly, making it challenging to analyze the constitutionality of specific restrictions on aspects of stem cell research. However, there remains a real risk that restrictions on the research may impede the discovery of useful therapies. Where prohibitions are found to be necessary they should be crafted as narrowly and precisely as possible. Finally, as advances in biomedical science generate further novel therapies, the constitutional resolution of any ensuing clashes in interests and values will be incomplete if it considers only the freedom of researchers. The interests of patients who might potentially benefit from new treatments should also be represented and given due consideration in the balance.