

# The Science of Stem Cells: Some Implications for Law and Policy

*Abdallah S. Daar and Lorraine Sheremeta*

## **Introduction**

There are few areas of modern biomedical research that have aroused as much controversy as stem cells. Scientists, physicians, patients and patient advocacy groups tend to emphasize the potential therapeutic benefits. Others argue that the potential benefits of stem cells have been exaggerated. Entrepreneurs, and research scientists — who are sometimes one and the same — envision vast medical and financial profits from stem cell therapy. Religious leaders pronounce judgments based strictly on faith and their understanding of when life begins. Those in positions of political power are eager to remain in power and seek a position wherein the fewest number of people are offended by a given policy choice.

At first sight, the development of stem cells does not seem to be very different from other scientific developments, except that in the case of stem cells, an understanding of the scientific facts of stem cell technology *per se*, the embryology and the associated terminology is critically important to making ethically sound policy judgments. The facts, definitions and terminology are confusing and are liable to misuse by those who seek to further a particular position.

It is our position that a coherent discourse needs to be initiated so that regulation in this area, if undertaken, is rational, consistent and informed by a clear understanding of the science and the terminology. In this paper we provide a concise overview of the important scientific facts related to embryology and embryonic stem cells and highlight some recent scientific developments that are salient for the purpose of regulatory development in this field.

## **Why such Enthusiasm over Stem Cells?**

Stem cells are exciting to physicians, scientists and patients because of their potential to develop into many different cell types, tissues and perhaps even organs that can possibly be used to treat large numbers of patients with a variety of diseases.<sup>1</sup> To scientists, stem cells offer a new way of exploring fundamental questions of biology, especially those pertaining to embryonic development.<sup>2</sup> In the living body, stem cells are believed to exist in small numbers in most organs including the liver, blood and brain.

Stem cells have two crucial capabilities: (1) they divide repeatedly into stem cells of their own type; and (2) with appropriate stimuli they can develop or differentiate either into one particular tissue, into a small number of tissues or, as in the case of pluripotent embryonic stem cells, into potentially all types of tissue.<sup>3</sup>

## **Embryonic Stem Cells**

For years, pluripotent embryonic stem cells have been viewed as the holy grail for many scientists, particularly developmental biologists. Murine embryonic stem cells were discovered about 20 years ago, but despite intense research, human embryonic stem cells have eluded scientists until recently. In 1998, almost simultaneously, two research groups in the United States<sup>4</sup> discovered how to purify embryonic stem cells and maintain them in culture in the laboratory. Thomson and his colleagues purified cells from spare embryos from IVF clinics.<sup>5</sup> Gearheart and his

*For years, pluripotent embryonic stem cells have been viewed as the holy grail for many scientists, particularly developmental biologists.*

colleagues purified cells, functionally the same as Thomson's cells, from the gonadal ridges of early abortuses.<sup>6</sup> The type of cells described by Gearheart and his colleagues have been confusingly called "embryo germ cells."

Embryonic stem cells (ESCs), as they feature in much of the current debate, are those cells derived from embryos at the blastocyst stage, which is approximately five to seven days after fertilization.<sup>7</sup> At this stage, within the blastocyst, there is a small fluid collection (cyst) in the embryo and at one pole of the cyst a specialized clump of cells known as the inner cell mass. It is from this inner cell mass that ESCs can be obtained.<sup>8</sup>

Several research teams have now been able to establish cell lines in the laboratory that continue to divide into succeeding generations of daughter cells that are identical to the original ESCs. It is also well established that ESCs can, with appropriate signals, differentiate into many different cell types.<sup>9</sup> This capacity of ESCs to differentiate to other cell types is known as "plasticity."

## **Adult Stem Cells<sup>10</sup>**

Until quite recently it was thought that stem cells found in adult tissues and organs<sup>11</sup> could differentiate only into the particular type of cells that make up the organ where the stem cell resides. Thus it was thought that "neuronal" stem cells could only make neurons, "hematopoietic" stem cells could only make blood cells and so on. In other words, it was thought that the cells were not "plastic" and could not "transdifferentiate" into other cell types. However, over the past few years it has been repeatedly demonstrated that stem cells originating from one organ or tissue can develop into cell types of another tissue.<sup>12</sup> This has been shown in both animals<sup>13</sup> and humans.<sup>14</sup>

It is this plasticity of adult stem cells that has raised hopes that they would be just as good for therapeutic purposes as ESCs. It seems obvious that if adult stem cells were ultimately proven to be as versatile as ESCs then many scientists would opt to work with adult stem cells to avoid the ethical problems associated with ESCs, whether they agree with the critics or not. At present this issue is still in dispute and the evidence is contradictory. Two recent papers have indicated that certain types of adult stem cells in animals<sup>15</sup> and humans<sup>16</sup> are quite plastic. Studies in mice

have shown that cells that have transdifferentiated from another type of adult stem cell can and do function according to the new phenotype.<sup>17</sup> However, soon after publication of these two promising papers, reports began to appear in the literature that cast doubt on the notion that adult stem cells are as versatile as ESCs.<sup>18</sup>

## **Cloning**

There is a lot of confusion surrounding use of the term "cloning," which essentially means "copying," and in this context, "making an identical (or near identical) genetic copy." Both research and service laboratories have been

cloning cells for a long time without controversy. For example, human cell lines such as the HeLa cell line have been used extensively for decades. Cell lines are essentially generations of cloned cells that are maintained *in-vitro*. The subject of cloning became a matter of public debate and

concern after the announcement of the cloning of Dolly the sheep in 1997. The public was concerned that human beings would be cloned for inappropriate purposes. In the context of the current debate we specifically need to distinguish between that which has come to be known as "reproductive cloning" and that termed "therapeutic cloning."

## **Reproductive Cloning**

Reproductive cloning by nuclear transfer from a differentiated somatic cell, although conceptualized and developed in other species over decades of research,<sup>19</sup> became a reality in mammals only in 1997. Somatic cell nuclear transplant (SCNT) involves the fusion of somatic cell with an enucleated egg, or the transfer of a nucleus of a somatic cell into an enucleated egg. The somatic cell and egg may be from different individuals or from the same individual.<sup>20</sup>

The report announcing the cloning by SCNT and the birth of Dolly<sup>21</sup> made an enormous impact on the scientific community and the public because it was unexpected and because of the potential implications for human reproductive cloning.<sup>22</sup> While there are some who find it acceptable to clone human beings,<sup>23</sup> the vast majority of commentators consider human reproductive cloning to be unethical.<sup>24</sup> At the international level, the United Nations has recently taken steps to draft an international treaty that would ban human reproductive cloning.<sup>25</sup>

*The facts, definitions and terminology are confusing and are liable to misuse by those who seek to further a particular position.*

## Therapeutic Cloning

Where SCNT is initiated without the intention of implanting the blastocyst in a uterus, it has been termed “therapeutic cloning.”<sup>26</sup> Although SCNT is the common starting point for both reproductive cloning and therapeutic cloning, the important distinction lies with the fact that with “therapeutic cloning” there is no intention of implanting the resultant blastocyst into a uterus of an animal or a human to create a live being.<sup>27</sup> Therapeutic cloning is simply used to create a blastocyst that provides a source from which ESCs can be extracted and cell lines created for research. One possible application of ESCs is to use them to make cells, tissues and/or organs that can be transplanted back into the same person who donated the somatic cell nucleus. This technology is important because it may provide a solution to the significant problem of shortage of organs for transplantation and of the rejection of transplanted organs and tissues by the recipient’s immune system.<sup>28</sup>

## Issues Relevant to Stem Cell Law and Policy

### Frequently used terms require substantial clarification: “Embryo,” “Fertilization” and “Conception”

Traditionally, an embryo is the result of the fusion of a sperm and an egg.<sup>29</sup> The single-celled entity that results from the fusion of a sperm and an egg is a “zygote.” The policy implications of this are that: (1) If legislation refers to an “embryo” as the locus of legal restrictions, then this would not apply to the single celled zygote before it divides; and (2) if an embryo is defined as the entity resulting from union of a sperm and the egg, then the entity resulting from SCNT is not an embryo.<sup>30</sup>

The term “embryo” is highly emotive, particularly when juxtaposed to “destroying” in the process of deriving human ESCs. Those who favour using ESCs for research would prefer that a different term be used here. As a result, the terms “ovasome” and “activated egg” are beginning to appear in the literature. Those who are against using ESCs insist that the term embryo is appropriate and should be used in association with the product of SCNT.<sup>31</sup>

To add yet another layer of complexity to the definition of the term “embryo,” during the rare process called

“parthenogenesis” an egg in the body of a normal animal or human begins to divide on its own and forms recognizable differentiated tissues.<sup>32</sup> Theoretically it would be possible to derive “embryonic” stem cells from such entities.<sup>33</sup> In mammals, an unfertilized egg can be induced in the laboratory to undergo some initial development.<sup>34</sup> At present, parthenogenesis in humans cannot result in a fetus

capable of development into a child even if the parthenogenetic “embryo” were implanted into the uterus. However, recent experiments in primates have

suggested that one day it could be possible to create children from eggs in a parthenogenetic pregnancy – completely eliminating the need for a male partner in procreation. One must question, however, whether the product of parthenogenesis is properly termed an “embryo.”

### Life and “potential”—is there a singularity?

We have noted that it is now no longer necessary that a sperm initiate the division of an egg to become an entity (blastocyst) from which human ESCs can be derived. Any somatic cell can substitute for sperm for this purpose. Ergo, any cell has the “potential” to initiate life. What, then, morally distinguishes a somatic cell from a zygote? The latter is indeed “totipotent,” but its totipotency arises from a non-totipotent cell.

If the moral value of a zygote/embryo is in its potential to go on to form a human child, why not extend this moral consideration to every cell capable of inducing an enucleated egg into becoming a zygote/embryo? If destroying a blastocyst/embryo<sup>35</sup> to obtain ESCs is unethical because of its potential to go on to become a child, why is it not similarly unethical to destroy human somatic cells?<sup>36</sup> There is no doubt that somatic cells have “life” and that since they are human, they have “human life.” If somatic cells have human life, and have the “potential” to go on to form a human infant, why is it that they are not accorded the same moral consideration as zygotes or embryos or blastocysts?

We suggest that the beginnings of an appropriate distinction between somatic cells and zygotes (or embryos or blastocysts) lie in the act of sexual union of the sperm and egg.<sup>37</sup> Perhaps it is the sexual conjugation of these two gametes, with the resultant admixture of DNA and the crucial event of genetic recombination, with its unpredictability in terms of the resultant new phenotype, that imparts the specific moral boundary – a kind of cosmic biological “singularity” – that is afforded to the zygote and

*Ergo, any cell has the “potential” to initiate life.*

its subsequent developmental forms. This, and the further issues of whether full “human life,” and indeed “personhood,” with all their moral considerations and interests, begin at the moment of fertilization, whether the “singularity” comes at a later stage, or whether moral considerations, interests and personhood accrue gradually with embryonic/fetal development,<sup>38</sup> are thorny issues that are at the crux of this debate.

### ***Cloning may be unsafe***

Recent evidence indicates that animals born through reproductive cloning using SCNT have genetic abnormalities.<sup>39</sup> Ian Wilmut, the researcher who led the team that cloned Dolly the sheep, has recently reported that Dolly has developed premature arthritis and that this is likely due to the cloning process.<sup>40</sup> This raises the likelihood that stem cells, and by implication, cells, tissues and organs derived from them, may be in some way defective and that the defects may not be apparent until quite late in the life of the transplanted cells, tissues or organs. However, the science is at a very early stage and this possibility is one further argument for continuing research in this area.

### ***Application of the so-called “14 Day Rule”***

The UK *Human Fertilisation and Embryology Act*<sup>41</sup> permits experimentation on human embryos up to the 14-days post-fertilization stage. The justification for this 14-day rule<sup>42</sup> is that it is immediately after this stage (i.e. on day 15) that the “primitive streak” is formed. Up until that point the embryo is simply a symmetrical cluster of cells. The primitive streak gives the embryo a body axis such that head, tail, left and right can be defined and physically orientated in relation to each other. Additional reasons proffered for the 14-day cut-off point are that up to that point: (1) implantation into the womb has not yet been completed;<sup>43</sup> and (2) the embryo still has the potential to split to form identical twins.<sup>44</sup>

### ***Why can't we expand and use existing ESC cell lines?***

Some argue that therapeutic cloning and the development of new cell lines should not be permitted because there are already in existence numerous existing embryonic stem cell lines that can be used in research or for developing therapeutic products. This argument seems reasonable in light of the fact that one of the characteristics of ESCs is their indefinite capacity to divide into succeeding generations of stem cells. However it must be remembered that scientific knowledge concerning the biology of human ESCs is still in the very early stages and much more

research needs to be done. The reality may be that existing cell lines will be insufficient.

Reasons for this include the following:

- It remains difficult physically to grow human ESCs reliably and in sufficiently large numbers;
- Despite the fact that some 64 existing ESC lines were believed to exist worldwide in August 2002 (when President Bush made his announcement regarding the federal funding of stem cell research)<sup>45</sup> these cell lines do not provide sufficient diversity for research;
- Successive generations of stem cells may be susceptible to accumulated genetic mutations, some of which may affect the functional characteristics of the cells;
- Logistical issues with respect to the distribution of the cell lines as well as intellectual property considerations may be hindering the distribution of the existing cell lines;<sup>46</sup>
- Jurisdictions are putting restrictions on the sharing of ESC cell lines,<sup>47</sup> in the same way that countries have attempted to control the movement of plant, animal and human genetic material;<sup>48</sup> and
- The existing lines cannot provide “personalized” stem cells for auto-transplantation – one of the main objectives for proceeding with stem cell research and development of therapeutic cloning.

### ***When used in patients, human ESCs are, in fact, xenotransplants***

- The current definition of xenotransplantation includes not only cells, tissues and organs from another species,<sup>49</sup> but also human cells that, while outside the body, come into contact with cells or fluids from another species. For technical reasons, all of the 64 cell lines approved in the United States have been grown in the presence of mouse cells (that provide crucial growth factors). Since these human ESCs have been exposed to murine cells, for regulatory reasons the FDA would consider them to be the equivalent of xenotransplants if they, or their progeny, were to be transplanted into humans. To avoid this regulatory hurdle it will be necessary to develop human ESCs without exposure to cells, fluids or tissues of other species.<sup>50</sup>

With respect to this point, it is important to note that a scientist in Singapore has recently developed a technique that does not require the exposure of ESCs to mouse cells *in vitro*.<sup>51</sup>

## Conclusion

The science of stem cells, while at a very early stage, is developing rapidly and creating enormous challenges for ethicists and policy-makers. Canadian legislators are preparing to debate Bill C-13,<sup>52</sup> a bill that will, if passed, regulate the development and use of embryonic stem cells. Legislators must do this in an unsettled and evolving global regulatory environment concerning embryonic stem cell research that varies from the permissive (in the United Kingdom), to the very restrictive (in Germany), to the apparently conservative (in the United States). They face a challenging task, for it is difficult for non-specialists to easily comprehend all of the complexities, not only of the science and technology, but also of the relevant embryologic facts that are so crucial to this discourse. The formulation of sound policy and legislation requires a thorough understanding of the science because the moral considerations involved are intimately linked to them. A further challenge is that the common terms used in this discourse have strong emotional associations linked to the debate about the beginning of life and are confusing, partly because of different usage (or abuse) over time. Indeed a case has been made for developing new terminology<sup>53</sup> to remove the ambiguity and to clarify the issues.

An attempt has been made to clarify the science and the terminology in the hope that this will assist Canadian legislators as they face the daunting challenge of debating *Bill C-13*.

---

*Abdallah S. Daar, Professor of Public Health Sciences, Professor of Surgery, Director, Program in Applied Ethics and Biotechnology, University of Toronto Joint Centre for Bioethics, Toronto.*

*Lorraine Sheremeta, Research Associate, Health Law Institute, Faculty of Law, University of Alberta.*

*Professor Daar's grant support was provided by the Program in Applied Ethics and Biotechnology (supported by the Ontario Research and Development Challenge Fund, GlaxoSmithKline, Merck and Co., Sun Life Financial, the University of Toronto, the Hospital for Sick Children, Sunnybrook and Women's College Health Sciences Centre and the University Health Network) and the Canadian Program on Genomics and Global Health (supported by Genome Canada).*

1. See National Academies Committee, *Biological and Biomedical Application of Stem Cell Research, Stem Cells and the Future of Regenerative Medicine* (Washington: National Academies Press, 2002) at 8, online: The National Academic Press <<http://books.nap.edu/books/0309076307/html/8.html>> (date accessed: 16 October 2002).

<i>Condition</i>	<i>Number of Patients Affected in the US</i>
Cardiovascular disease	58 million
Autoimmune diseases	30 million
Diabetes	16 million
Osteoporosis	10 million
Cancers	8.2 million
Alzheimer's disease	5.5 million
Parkinson's disease	5.5 million
Burns (severe)	0.3 million
Spinal cord injuries	0.25 million
Birth defects	0.15 million/yr

2. *Ibid.* at 1, wherein it states that “. . . [s]tem cell research offers unprecedented opportunities for developing new medical therapies for debilitating diseases and a new way to explore fundamental questions of biology.”
3. The zygote and the very earliest cells of the embryo are capable of differentiating into all tissues, including the extra-embryonic membranes and parts of the placenta that are required for the development of a complete organism. For this reason, these cells are termed “totipotent.” Embryonic stem cells [ESCs] theoretically can form all of the different cell types and tissue that make up the organism, but they cannot make the extra-embryonic membranes/placenta. They are termed “pluripotent.” ESCs cannot, by themselves, form a complete organism.
4. There are some reports indicating that Ariff Bongso, a researcher in Singapore, was the first person to discover embryonic stem cells, but failed to patent them. See D. Gay, “Asia's Stem Cell Savant” (24 August 2001), online: AsiaWeek.com <<http://www.asiaweek.com/asiaweek/magazine/Enterprise/0%2C8782%2C171449%2C00.html>> (date accessed: 11 November 2002).
5. J.A. Thomson *et al.*, “Embryonic Stem Cell Lines Derived from Human Blastocysts” (1998) 282 *Science* 1145.
6. M.J. Shambloot *et al.*, “Derivation of Pluripotent Stem Cells from Cultured Primordial Germ Cells” (1998) 95 *Proc. Nat'l. Acad. Sci.* 13726. The difference in the source of the cells described by Thomson and those described by Gearheart does not now feature much in the debate, but the ethical and legal implications are obviously quite different.
7. Traditionally “fertilization” describes the essential process of *sexual* reproduction wherein two specialized haploid cells – the male and female gametes (in humans these are, respectively, the sperm and the ovum (egg)) – join to form a diploid zygote that may go on to develop into a new organism. The sperm and egg are “haploid” in that they only contain half of the genetic material (23 chromosomes) needed to create a normal new individual. The zygote contains the full complement of genetic material (46 chromosomes in total; 23 from each parent). “Conception” to some has the connotation not only of fertilization, but also of the subsequent implantation of the embryo into the mother's uterus. However, common usage has fertilization and conception as interchangeable terms. The defining act of all sexual reproduction is the fusion of sperm and egg cells and their nuclei, which give rise to an opportunity for genetic recombination. The artificial laboratory process of inserting a nucleus of a diploid adult cell (a somatic cell) into an egg whose own nucleus has been removed (enucleated) is *not a sexual* process because there is no fusion of nuclear genetic material from two individuals.

Accordingly, we still must ask whether the laboratory process of nuclear transfer is tantamount to “fertilization” and whether it is at all appropriate to use the term “conception” when describing this process. After implantation into the uterus a human embryo continues to be termed an “embryo” until about 10 weeks when it is termed a “fetus.”

8. At the early (blastocyst) stage in the development of mammalian embryos, the embryo is a spherical body comprising of an inner cell mass that will become the fetus and an outer ring of cells that will become part of the placenta. The process of obtaining ESCs from the inner cell mass is such that the embryo is destroyed. “Destroy” is an emotive word, hence the use by some of the term “disaggregate.” Were it possible to take just a tiny piece of the inner cell mass, to derive ESCs, and to allow the blastocyst to continue development as a healthy embryo, much of the current controversy would dissipate. This is not currently possible. However, at a certain stage it is possible to “biopsy” an embryo to perform genetic testing. This procedure is known as “pre-implantation genetic diagnosis” (PGD) and has been allowed in some jurisdictions.
9. M. Li *et al.*, “Generation of Purified Neural Precursors from Embryonic Stem Cells by Lineage Selection” (1998) 8 *Curr. Biol.* 971; N. Lumelsky *et al.*, “Differentiation of Embryonic Stem Cells to Insulin-Secreting Structures Similar to Pancreatic Islets” (2001) 292 *Science* 1389.
10. Adult in this context simply means “from tissues or organs that already exist as such, and in which each cell has the full, diploid, complement of genetic material.” Examples would be the skin, liver, kidneys and bone marrow. The term adult is applicable even if the skin, liver, kidney or bone marrow cell are obtained from an infant.
11. Cells make up tissues (such as skin and bone) and organs (such as the liver and kidneys). Many tissues and organs are made up of several cell types, each serving a different function. In the pancreas, for example, there are cells that make digestive enzymes and others that make insulin. Some tissues, such as the skin, are also often referred to as organs.
12. E. Legasse *et al.*, “Purified Hematopoietic Stem Cells Can Differentiate into Hepatocytes In Vivo” (2000) 6 *Nat. Med.* 1229; K.A. Jackson *et al.*, “Regeneration of Ischemic Cardiac Muscle and Vascular Endothelium by Adult Stem Cells” (2001) 107 *J. Clin. Invest.* 1395.
13. J.H. Kim *et al.*, “Dopamine Neurons Derived from Embryonic Stem Cells Function in an Animal Model of Parkinson’s Disease” (2002) 418 *Nature* 50.
14. Y. Jiang *et al.*, “Pluripotency of Mesenchymal Stem Cells Derived from Adult Marrow” (2002) 418 *Nature* 41.
15. *Supra* note 13.
16. *Supra* note 14.
17. “Genotype” refers to the specific individual genetic constitution of an organism. “Phenotype” refers to the detectable outward manifestations (appearance) of an organism. An organism’s genotype, in concert with the environment, determines the organism’s phenotype. Although all cells in an organism have the same genotype, in differentiated cells only some of the genes are expressed. This explains why cells normally look, behave and function differently in different tissues.
18. See A.J. Wagers *et al.*, “Little Evidence for Developmental Plasticity of Adult Hematopoietic Stem Cells” (2002) 297 *Science* 2256; R.F. Castro *et al.*, “Failure of Bone Marrow Cells to Transdifferentiate into Neural Cells In Vivo” (2002) 297 *Science* 1299.
19. See timeline in A. Daar & J-F. Mattei, “Medical Genetics and Biotechnology: Implications for Public Health”, World Health Organization Document No. WHO/EIP/GPE/00.1; available from the World Health Organization through Dr. Tikki Pang (pangt@who.int) or Dr. Abdallah Daar (a.daar@utoronto.ca). It may also be accessed online after registration at <<http://discuss.who.int:8080/upload/daarmattei.DOC>> (date accessed: 20 November 2002).
20. If the donor and the enucleated egg are not from the same person, the resultant entity will likely have a mixture of DNA from the two individuals. This is because, during the enucleation process some mitochondrial DNA (which is in the cytoplasm, not in the nucleus) in the egg will remain behind. Normally, mitochondrial DNA plays only a small role in determining the phenotype of the resultant organism. It is involved primarily in the coding for energy related proteins. Mitochondrial DNA under normal circumstances is inherited only through the maternal line; however, very recent evidence indicates that in some instances there can be paternal inheritance of mitochondrial DNA, see M. Schwartz & J. Vissing, “Paternal Inheritance of Mitochondrial DNA” (2002) 347 *N.E.J.M.* 576.
21. I. Wilmut *et al.*, “Viable Offspring Derived from Fetal and Adult Mammalian Cells” (1997) 385 *Nature* 810; A.E. Schnieke *et al.*, “Human Factor IX Transgenic Sheep Produced by Transfer of Nuclei from Transfected Fetal Fibroblasts” (1997) 278 *Science* 2130. Other mammalian species have been cloned. These include mice, cattle, cats and monkeys. See for e.g. T. Shin *et al.*, “A Cat Cloned by Nuclear Transplantation” (2002) 415 *Nature* 859. It has not yet been possible to clone some species, including the dog and the human.
22. Korean scientists and scientists at Advanced Cell Technologies have claimed to have cloned human embryos, but their work has been met with much skepticism amongst scientists. See R. Weiss “Cloned Human Embryo Created, South Korean Researchers Say” *Washington Post* (17 December 1998) A3; see also BBC News, “Details of Hybrid Clone Revealed” (18 June 1999), online: BBC News <<http://news.bbc.co.uk/1/hi/sci/tech/371378.stm>> (date accessed: 11 November 2002).
23. See D.C. Wertz, “Twenty-One Arguments Against Human Cloning, and Their Responses” (1 August 1998) online: The Gene Letter <<http://geneletter.com/archives/twentyonearguments.html>> (date accessed: 2 October 2002). This article rebuts common arguments against the reproductive cloning of humans. It points out, however, that the unpredictability of psychological impacts on cloned children remains the strongest argument against cloning. See also S-K. Templeton “Cloning – one step closer” *The Sunday Herald* (28 July 2002). In this article it is reported that leading philosopher Dame Mary Warnock (of the Warnock Commission that led to the UK *Human Fertilisation and Embryology Act*, *infra* note 30) has called for the blanket ban on human cloning to be lifted and has stated that she



supports cloning of babies for infertile couples. She believes that in future there should be no major ethical obstacles to human reproductive cloning for medical reasons if it can be proven safe. See also J.A. Robertson, "The question of human cloning" (1994) 24 Hastings Center Report 6; J.A. Robertson, "Human cloning and the challenge of regulation" (1998) 339 N.E.J.M. 119.

24. *Supra* note 19 at ch. 2; F. Baylis & J. Downie "Ban Cloning. Do you copy?" *The Globe and Mail* (3 July 2002) A13, online: Dow Jones Interactive <<http://ptg.djnr.com/ccroot/asp/publib/story.asp>>(date accessed 21 November 2002).
25. R. Willing "UN Plan Would Ban Cloning to Create Human Baby" *USA Today* (23 September 2002) A3; see also Agence France-Presse "UN Fails to Reach Accord Banning Reproductive Cloning" (28 September 2002) online: Dow Jones Interactive <<http://ptg.djnr.com/ccroot/asp/publib/story.asp>> (date accessed: 15 November 2002); J. Preston "U.S., Pushing for Broader Ban, Blocks U.N. Anti-Cloning Move" *The New York Times* (8 November 2002) 8, online: Dow Jones Interactive <<http://ptg.djnr.com/ccroot/asp/publib/story.asp>> (date accessed: 21 November 2002). Human embryos can be cloned also by a much less controversial process known as "embryo-splitting"(blastomere separation). Embryo splitting is a process that occurs in nature fairly frequently and results in the birth of identical twins. This process is used extensively in animal husbandry. In humans, embryo splitting could be used to increase the number of embryos for *in vitro* fertilization but in fact has only been reported experimentally once. In September 1994, a special issue of the Kennedy Institute of Ethics Journal was published on the ethics of embryo splitting or cloning. The volume includes papers originally prepared for a workshop on embryo splitting sponsored by the National Advisory Board on Ethics in Reproduction (NABER) and NABER's report, see National Advisory Board on Ethics in Reproduction, "Report on Human Cloning through Embryo Splitting: An Amber Light" (1994) Kennedy Institute of Ethics Journal 251. The impetus for the project was embryo-splitting research conducted by Drs. Jerry L. Hall, Robert J. Stillman, and others, at George Washington University and presented in October 1993 at a joint meeting of the American Fertility Society and the Canadian Fertility and Andrology Society. See also R. Macklin, "Cloning without prior approval: a response to recent disclosures of noncompliance" (1995) 5 Kennedy Institute of Ethics Journal 57.
26. At present the term "therapeutic cloning" is used in this context although it is still primarily a research procedure. However, one of the aims of this type of research is to study the possibility of therapy. The President's Council on Bioethics, *Human Cloning and Human Dignity* (Washington D.C.: The President's Council on Bioethics, 2002) online: The President's Council on Bioethics <<http://www.bioethics.gov/cloningreport/glossary.html>> (date accessed: 20 September 2002).
27. *Supra* note 7.
28. Other than in identical twins, who have essentially the same genetic constitution, any cell, tissue or organ transplanted between two human individuals (allotransplantation) would be rejected by the recipient's immune system. To avoid

rejection, drugs can be used to suppress the recipient's immune system. If, however, the donor of the somatic cell for SCNT is the ultimate recipient, he or she will not reject the transplanted cells, tissue or organs derived from the stem cells. Essentially a transplant of this type is an "autotransplant."

29. *Supra* note 7.
30. See BBC News, "Human Cloning Ban 'To Become Law'" (29 November 2001), online: BBC News <[http://news.bbc.co.uk/1/hi/uk\\_politics/1683647.stm](http://news.bbc.co.uk/1/hi/uk_politics/1683647.stm)> (date accessed: 11 November 2002). In recent British legislative history there has been a great deal of confusion over whether there existed a loophole in the expanded *Human Fertilisation and Embryology Act, 1990*, (U.K.), 1990, c. 37. Section 3(3)(d) of the *Act* expressly prohibits one type of cloning technique, namely the nuclear substitution of any cell whilst it forms part of an embryo. Further, s. 3(1) of the *Act* requires a licence from the Authority for any creation, use or storage of a human embryo outside the body. The technique used to create Dolly involves nuclear substitution into an egg and not into an embryo. Thus it is not specifically covered by s. 3(3)(d). Prolife Alliance and others have argued that, as fertilisation is not involved, s. 3(1) also does not apply. The Prolife Alliance brought a legal suit against government claiming that organisms created by SCNT are not "embryos" according to the legislative definition because they are not created by the fertilisation of an egg by a sperm. The original high court ruling agreed with the position taken by the Prolife Alliance. The Court of Appeal reversed the lower court's decision. The result is that any scientist in the UK that wants to use SCNT requires a license from the licensing authority (Human Fertilisation and Embryology Authority). Stop-gap legislation in the UK was passed to close this perceived loophole.
31. Indeed, one of the earliest tasks undertaken by President Bush's Council on Bioethics was to work its way through this morass of terminology; see The President's Council on Bioethics, *supra* note 26.
32. See for e.g. J.B. Cibelli *et al.*, "Parthenogenetic Stem Cells in Nonhuman Primates" (2001) 295 Science 819.
33. ESCs can also be derived from a type of human tumor called a teratoma. A teratoma is a germ cell tumor comprised of elements of different types of tissue from one or more of the three germ cell layers, which include the endoderm, mesoderm and ectoderm.
34. *Supra* note 32.
35. The term "blastocyst" seems more neutral and less emotive than "embryo." However, a blastocyst technically is simply an early embryo.
36. Every person normally sheds billions of cells from the skin, mouth, intestine etc. Additionally, human cells in blood and leftover tissue are routinely discarded from medical facilities.
37. In the case of *in vitro* fertilization (IVF), fertilization remains "sexual" in that sperm and an egg are combined in a process that mimics the natural process wherein the haploid sperm is fused with the haploid egg to form a normal diploid zygote. Furthermore, in IVF there is a specific intention that the resultant blastocyst will be implanted into the uterus. The purpose of IVF is the intentional creation of a child that is the combined product

of gametes from a “mother” and from a “father.” Conversely, SCNT is a totally *asexual* process both in technique and intent.

38. The positions of the three monotheistic religions are particularly apt to this part of the debate – particularly the “singularity” of ensoulment. For further discussion of this matter, see A.S. Daar & A. Khitamy, “Bioethics for Clinicians: Islamic Bioethics” (2001) 164 C.M.A.J. 60; see also A. Sachedina, “Islamic perspectives on research with human embryonic stem cells” in National Bioethics Advisory Commission, *Ethical Issues in Human Stem Cell Research, Religious Perspectives*, vol. 3 (Rockville, Maryland: US Government Printing Office, 2000) at G1-G6; for Roman Catholic views on research involving human embryonic stem cells see *Ethical Issues in Human stem cell research (ibid.* at G1-G6); for a Jewish contribution to the discourse, see L. Zoloth, “The ethics of the eighth day: Jewish bioethics and genetic medicine” in *Ethical Issues in Human stem cell research (ibid.* at J1-J26); for views of the Presbyterian Church see “Presbyterians vote in favor of fetal, embryonic, and stem cell research”, online: Eurekalert <[http://www.eurekalert.org/pub\\_releases/2001-06/SaRN-Pvif-1406101.php](http://www.eurekalert.org/pub_releases/2001-06/SaRN-Pvif-1406101.php)> (date accessed: 12 November 2002); other positions include the United Methodist Church, “GBCS General Secretary's letter to President Bush to Extend Moratorium on Human Embryo Stem Cell Research”, online: United Methodist Church, General Board of Church and Society <<http://www.umc-gbcs.org/gbpr118a.htm>> (date accessed: 12 November 2002); and the Southern Baptist Convention, “Resolution No. 7 on Human Embryonic and Stem Cell Research”, online: Southern Baptist Convention '99 <<http://www.sbcannualmeeting.org/sbc99/res7.htm>> (date accessed: 12 November 2002).
39. D. Humphries *et al.*, “Abnormal Gene Expression in Cloned Mice Derived from Embryonic Stem Cell and Cumulus Cell Nuclei” (2002) 99 P.N.A.S. 12889; see also K. Eggan *et al.*, “Hybrid Vigor, Fetal Overgrowth, and Viability of Mice Derived by Nuclear Cloning and Tetraploid Embryo Complementation” (2001) 98 P.N.A.S. 6209. We have mentioned above that as a cell differentiates some of its DNA is “switched off” and that this is why, despite originating in just one cell (the zygote), the body is made up of many different kinds of tissue. The miracle of SCNT is that the enucleated egg seems able to reprogram the genes in the donated nucleus, winding the clock back from the adult (somatic, differentiated) state to the most primitive stage whence embryonic development starts afresh. Exactly how it does this is still being worked out; it must be a hugely complex process, explaining the numerous failures. Indeed, the miracle is that it happens at all, and it is therefore not surprising that errors can occur.
40. BBC News, “Cloned Sheep Dolly Has Arthritis” (4 January 2002), online: BBC News <<http://news.bbc.co.uk/2/hi/science/nature/1741559.stm>> (date accessed: 11 November 2002).
41. The UK *Human Fertilisation and Embryology Act, supra* note 30 set up the Human Fertilisation and Embryology Authority (HFEA), an oversight body in the UK in 1991. It ensures that all UK treatment clinics offering *in vitro* fertilisation (IVF) or donor insemination, or storing eggs, sperm or embryos, conform to high medical and professional standards and are inspected regularly. The HFEA is charged with licensing and monitoring all human embryo research, and overseeing research in the field as well as considering the ethical implications of a number of key issues, and following the national debate.
42. The Committee of Inquiry into Human Fertilisation and Embryology, *Report* (London: H.M.S.O., 1984) at 66. The 14-day period has been criticized by some as being purely arbitrary. See also D. N. Irving, “When Do Human Beings Begin?” “Scientific” Myths and Scientific Facts” online: The Protection of Conscience Project <<http://www.consciencelaws.org/Examining-Conscience-Issues/background/GenScience/BackGenScience02.html>> (date accessed: 14 November 2002). Embryos rarely survive for 14 days *in vitro*. However, with increasing scientific knowledge and better tools, it may be possible to maintain embryos to this stage more easily. The implication is that until day 14 the embryo does not have much moral value because it is simply “a loose cluster of undifferentiated cells” and that it is only after 14 days that there is “differentiation, individuality, a nervous system.” This view is obviously not shared by all. See for e.g. Anthony Fisher’s review of Mary Warnock’s 2002 book “Making Babies: is there a right to have children” (28 September 2002), online: The Tablet <<http://www.thetablet.co.uk>>.
43. Historically the term “embryo” was used by many only after implantation into the uterus. Prior to implantation, the entity has been termed a “pre-embryo,” but this term (perhaps originating in botany) is not often used today. “Pre-embryo” is fraught with difficulties, since to some people it indicated less need to worry about the rights of the entity being discussed, since “pre” implies “not yet”. A term that was used for a while and for which some presuppose a derivation of “pre-embryo” is “pre-implantation embryo,” which is a much more neutral term and one that happens to be factually correct.
44. In other words there is still some “totipotentiality” although such totipotent cells have not been found or purified at this stage of embryonic development. This does not appear to be a convincing argument. The logic for this may be that the “personhood” is not yet fixed if there is still some potential for another “person” to come into existence.
45. President George W. Bush, “Remarks by the President on Stem Cell Research”, Remarks (Washington D.C.: Office of the Press Secretary, 2001) online: The Whitehouse <<http://www.whitehouse.gov/news/releases/2002/08/200110809-2.html>> (date accessed: 20 September 2002). Bush’s decision does not apply to state funding of embryonic stem cell research. Indeed in 2002, California passed a law allowing embryonic stem cell research and the use of SCNT for therapeutic cloning; U.S., S.B. 253, *An Act to add article 5 (commencing with Section 125115) to Chapter 1 of Part 5 of Division 106 of the Health and Safety Code, relating to medical research*, 2001-02, Reg. Sess., Cal., 2001 (enacted). For commentary on the bill see California Advisory Committee on Human Cloning, *Final Report*, online: Stanford Law School <<http://www.law.stanford.edu/features/greely/>>. At the time of President Bush’s announcement concerning the use of federal funds for stem cell research, it was claimed that there were 64 such cell

lines in existence around the world. In the United States, federal funding is only available to research conducted using cell lines in existence prior to August 9, 2001, the date of Bush's announcement. In fact, the reality seems much more restrictive. Scientists have complained that only a few of these lines are actually available. Moreover, some of the available lines are said to be difficult to cultivate, and in some cases carry hefty price tags or heavy intellectual-property entanglements; see Editorial, "A human stem cell project?" (2002) 418 *Nature* 1.

46. "Growing Pains of Stem Cell Research," Editorial, *The Washington Times* (28 August 2002) A20.
47. K.S. Jayaraman, "India Shuts Door on Embryonic Export Market" (2002) 419 *Nature* 238.
48. D. Dickson, "China Brings in Regulations to Put a Stop to 'Genetic Piracy'" (1998) 395 *Nature* 5.
49. The current working definition of "xenograft" within Health Canada includes the transfer of living cells, tissues and organs from one species to another (animal-to-human transplantation) as well as human body fluids, cells, tissues or organs having *ex vivo* contact with live non-human animal cells, tissues or organs (Personal communication, Amanda Collier, Biologics and Genetic Therapies Directorate, Health Canada, 2 October 2002). The United States Department of Health and Human Services has a similar definition.

50. On the regulation of xenotransplantation in Canada, see Health Canada, "Towards Regulatory Frameworks for Blood and Blood Components Intended for Transfusion and Cells, Tissues and Organs Intended for Transplantation", online: Health Canada <[http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/info\\_kit\\_e.pdf](http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/info_kit_e.pdf)> (date accessed: 2 October 2002).
51. See "First Fully Human Embryonic Stem Cell Line Created in Joint Singapore-Australia Venture" *Transplant News* (12 August 2002). ES Cell International and its collaborative partner, the National University of Singapore, announced the creation of the world's first human embryonic stem cell line grown entirely without exposure to mouse cells or other non-human components.
52. *An Act respecting assisted human reproduction*, 2<sup>nd</sup> Sess., 37<sup>th</sup> Parl., 2002 (1<sup>st</sup> reading 9 October 2002) [*Bill C-13*].
53. See the President's Council on Bioethics, *supra* note 26.

|

