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EMBRYONIC STEM CELL-BASED THERAPEUTICS: BALANCING SCIENTIFIC PROGRESS AND BIOETHICS

Ronald Chester[†] and Robert Sackstein^{††}

“I leave this rule for others when I’m dead,
Be always sure you’re right – THEN GO AHEAD!”
Colonel David Crockett

A NARRATIVE OF THE LIFE OF DAVID CROCKETT, OF THE
STATE OF TENNESSEE (1834).

ABSTRACT

The breakneck speed of scientific developments in embryonic stem (ES) cell technologies is, commensurately, ushering forth new bioethical debate(s) regarding these cells. A framework of bioethical principles is presented here to guide biomedical scientists and others engaged in improving human welfare through the application of ES cell-based therapies.

INTRODUCTION: STEM CELL THERAPY

Stem cell-based regenerative therapy offers the prospect of restoring functional integrity to damaged tissues and organs. There is great

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hope in the medical community that regenerative medicine will become established clinical practice and will offer cures rather than therapy for a multitude of debilitating and life-threatening conditions. However, despite its profound potential to alleviate human suffering, the use of embryonic stem (ES) cells for regenerative therapy has raised considerable moral and ethical debate. At the forefront of the concerns raised in this debate has been the notion that pluripotent¹ ES cells can only be obtained from blastocysts, requiring the destruction of viable embryos. Moreover, the possibility that reproductive cloning could result from the creation of autologous² embryonic stem cells in vitro using somatic cell nuclear transfer (SCNT)³ has markedly affected support among scientists and others for this approach. Notably, within the past few years, great strides have been made in developing techniques to create pluripotent ES-like cells without either blastocyst production or disruption of embryos, thereby offering the opportunity to circumvent these primary ethical and moral objections. Still, any manipulation of a human cell to create ES-like cells is expected to raise controversy, especially since these cells may possess the potential for developing into a human being.

Thus, though innovations in the creation of ES-like cells may nullify present ethical concerns about creating embryos in order to destroy them, these techniques and their product(s) may still generate contentious debate. To most appropriately support the clinical use of such advances, biomedical scientists must understand the various ethical and moral perspectives that can dominate discussions for and against any current and emerging stem cell technology. In this article, we briefly review the most recent progress in ES cell technologies, and frame a set of bioethical principles to guide deliberations on the impact of these developments on human welfare. This bioethical framework is certainly not the only one available, but we present it as a practical, straightforward guide to determining what procedures should be utilized in the stem cell field. To this end, we have tried to

¹ Capable of differentiating into one of many cell types.

² From the same organism.

³ In the SCNT process a nucleus from an adult differentiated somatic cell (such as a skin cell) is removed and then fused with an enucleated egg to create a single entity called a clone. The resulting clone carries the genetic material (DNA) of the donor of the somatic cell, and a tiny portion of the mitochondrial DNA from the donor of the egg cell. The clone is identical in essence to its somatic cell donor. See Ronald Chester, *Cloning Embryos from Adult Human Beings: The Merits of Reproductive Research and Therapeutic Uses*, 39 NEW ENG. L. REV. 583, 584 n.6 (2005) (citing Ronald Chester, *Cloning for Human Reproduction: One American Perspective*, 23 SYDNEY L. REV. 319, 321-22 (2001)).

focus on the fundamentals of what otherwise might become overly complex and esoteric bioethical arguments.

I. RECENT PROGRESS IN DEVELOPMENT AND USE OF ESC OR ES-LIKE CELLS

For the purpose of the ensuing bioethical discussion, it is important to briefly review recent advances that enhance the efficiency and safety of deriving pluripotent ESC or ES-like cells for regenerative therapeutics. Presently, pluripotent cells (i.e. cells with the capacity to develop into every cell of an adult animal) can be obtained in several ways:

A. Retrieval of Cells from the Inner Cell Mass of Embryonic Blastocysts

During the earliest development of the embryo, within a few days of conception, dividing cells develop into a hollow cavity (the blastocyst). Thereafter, cells inside the blastocyst continue to divide and form a clump (the inner cell mass). Cells isolated from the inner cell mass, are authentic “embryonic stem cells.”

B. Somatic Cell Nuclear Transfer (SCNT)

This process is described in footnote 3, *supra*; it raises special considerations because of the inherent capacity for reproductive cloning if ES cells are derived from the cells that divide first (the blastomere stage). Moreover, use of this technique is markedly limited – practically and bioethically – by the need to obtain ova in metaphase II from a healthy donor.⁴

C. Artificial Parthenogenesis by Blockage of the Second Meiotic Division of the Oocyte

A primitive egg (a “germ cell”) undergoes divisions to reduce the number of genes to half the normal amount (a “haploid” cell), so that donor sperm can contribute the other half of the genetic material to make a whole genetic complement (a “diploid cell”). If the reduction division is interrupted, the egg can be triggered into acting as if it is

⁴ See Andrew J. French et al., *Development of Human Cloned Blastocysts Following Somatic Cell Nuclear Transfer with Adult Fibroblasts*, 26 *STEM CELLS* 485, 485 (2008).

fertilized. Notably, this technology cannot yield an embryo capable of fetal development without additional genetic manipulation.⁵

D. Induced Pluripotent Stem (iPS) Cell by Ectopic Expression of Defined Transcription Factors that Will Cause De-differentiation (“Reprogramming”) of a Somatic Cell or an Adult Stem Cell⁶

All genes are regulated by small proteins called “transcription factors.” Some of the key transcription factors that turn on the genes responsible for maintaining cells in the undifferentiated (stem) state have been identified. If these transcription factors are introduced into a mature adult (somatic) cell, they cause the cell to de-differentiate to a more primitive state.

In general, all ESC and ES-like cells suffer from the potential to grow without proper differentiation (dysregulated growth), manifesting most commonly in complex tumor formation, but this problem may be circumvented by driving differentiation of the cells into the intended target cell type coupled with meticulous cell selection to avoid genetic markers associated with pluripotency.⁷ With iPS cells, the potential for cancer transformation is compounded with the introduction of cancer-producing transcription factors, usually proteins (e.g., c-Myc), for reprogramming of the target cell, especially when transcription factors are delivered using viruses (e.g., retroviral vectors). Original reports for generating iPS cells used four transcription factors for a somatic cell.⁸ Recent reports have shown that iPS cells can be created with avoidance of c-Myc⁹ and with fewer transcription

⁵ See Tomohiro Kono et al., *Birth of Parthenogenetic Mice that Can Develop to Adulthood*, 428 NATURE 860, 860 (2004).

⁶ Jeong Beom Kim et al., *Oct4-induced Pluripotency in Adult Neural Stem Cells*, 136 CELL 411, 412 (2009). There is another possible technique whose importance has yet to be shown and thus will not be discussed in this article. Zouh et al. reprogrammed a somatic cell that natively expressed complementing factors into another cell type. This approach has been reported for pancreatic cells wherein exocrine aciner cells were created in vivo to endocrine Beta-cells. It apparently does not require dedifferentiation, but involves “reprogramming” by introduction of three genes whose expressions are typically restricted to embryonic cells.

⁷ Marius Wernig et al., *Neurons Derived from Reprogrammed Fibroblasts Functionally Integrate into the Fetal Brain and Improve Symptoms of Rats with Parkinson’s Disease*, 105 PROC. NAT’L ACAD. SCI. U.S. 5856, 5859-60 (2008).

⁸ Kazutoshi Takahashi et al., *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 CELL 861 (2007).

⁹ Masato Nakagawa et al., *Generation of Induced Pluripotent Stem Cells without Myc from Mouse and Human Fibroblasts*, 26 NATURE BIOTECHNOLOGY 101, 105 (2008).

factors, particularly if the starting cell is favorable to reprogramming, such as an adult stem cell.¹⁰ Moreover, viral vectors¹¹ that do not integrate into the genome, and other strategies that avoid viruses altogether¹² can be used to deliver relevant transcription factors, and chemical agents may be capable of inducing changes in gene expression leading to reprogramming without need for c-Myc or other transcription factors.¹³

For use of blastocyst-derived ES cells, immune rejection of transplanted cells would be likely because disparities would exist between donor and recipient tissue type. However, embryonic stem cells possess some inherent immune privilege¹⁴ and immune rejection would not be expected using cells from the same organism (e.g., ESC from SCNT, ES-like cells from parthenogenesis or IPS cells).

II. BACKGROUND TO THE DEBATE: IS AN EMBRYO A PERSON?

Other than possible carcinogenic effects and immune system rejection, the two biggest issues with regard to the four described techniques seem to be: (1) destroying 4-6 day old human embryos to obtain stem cells (Technique A); and even more controversial, (2) whether SCNT should be used to create a cloned human embryo for medical and other purposes (Technique B).¹⁵ Artificial parthenogenesis (Technique C) and the creation of iPS cells (Technique D) are too new to have generated much debate, but assumedly would be less controversial because they avoid destroying an embryo that might develop into a human being.

¹⁰ See Kim et al., *supra* note 6, at 414.

¹¹ Matthias Stadtfeld et al., *Induced Pluripotent Stem Cells Generated Without Viral Integration*, 322 SCIENCE 945 (2008).

¹² See Keisuke Okita et al., *Generation of Mouse Induced Pluripotent Stem Cells Without Viral Vectors*, 322 SCIENCE 949, 950-52 (2008); Knut Woltjen et al., *PiggyBac Transposition Reprograms Fibroblasts to Induced Pluripotent Stem Cells*, 458 NATURE 766 (2009) (demonstrating "successful and efficient reprogramming of murine and human embryonic fibroblasts"); Keisuke Kaji et al., *Virus-free Induction of Pluripotency and Subsequent Excision of Reprogramming Factors*, 458 NATURE 771, 771 (2009).

¹³ Danwei Huangfu et al., *Induction of Pluripotent Stem Cells from Primary Human Fibroblasts with Only Oct4 and Sox2*, 26 NATURE BIOTECHNOLOGY 1269, 1269 (2008).

¹⁴ Nathan J. Robertson et al., *Embryonic Stem Cell-derived Tissues are Immunogenic but Their Inherent Immune Privilege Promotes the Induction of Tolerance*, 104 PROC. NAT'L ACAD. SCI. U.S. 20920, 20920 (2007).

¹⁵ CHRISTOPHER THOMAS SCOTT, STEM CELL NOW 124 (2006).

The threshold question, therefore, is whether an embryo or fetus is a human being. If so, at what point in development does the embryo/fetus achieve this status? Religion has often served as a foundation to address this question. Nevertheless, even amongst specific religious sects, the consensus has shifted over time.

Strict Catholics and other conservatives often recognize human potentiality at an early stage. However, the Catholic position on this matter has changed over time.¹⁶ Saint Thomas Aquinas (1225-1275 A.D.) believed that the human soul was not present at conception, but that it appeared between forty and ninety days later. Yet, by 1987, the Catholic Church had shifted its position by declaring that the embryo was a person from the moment of conception.¹⁷ The Catholic Church is not alone in its concern for the human potentiality of the embryo at its early stages. In fact, many conservative scholars who do not purport to base their views on religion such as Leon Kass, Daniel Callahan, and Francis Fukuyama have expressed similar concerns.¹⁸

Other perspectives do not recognize human potentiality so early in the developmental process. A growing number of moderate Catholic theologians do not consider the embryo an individual human entity until the appearance of the primitive streak (nascent spinal cord) at two weeks.¹⁹ The Jewish tradition asserts that embryos have no moral status until they are implanted and survive forty days.²⁰ Scientific perspectives may focus on viability. Michael Gazzaniga points out that the human brain cannot support vital functions until gestation has reached six months – about the time at which a fetus could survive premature birth in a hospital's neonatal unit.²¹ Interestingly, this is the point at which the Supreme Court in *Roe v. Wade*²² begins to give the fetus rights superior to those of the expectant mother.

¹⁶ See Elizabeth Spahn & Barbara Andrade, *Mis-Conceptions: The Moment of Conception in Religion, Science, and Law*, 32 U.S.F. L. REV. 261, 269-73 (1998).

¹⁷ SCOTT, *supra* note 15, at 130.

¹⁸ See *id.* at 137-39. Of these secular theorists who have addressed the topic, we find, for example, Professor Jed Rudenfeld more convincing. He sees “where life begins” as a political choice rather than an ethical decision. See Jed Rudenfeld, *On the Legal Status of the Proposition that “Life Begins at Conception,”* 43 STAN. L. REV. 599 (1990).

¹⁹ SCOTT, *supra* note 15, at 131.

²⁰ See *id.* at 133 (adding that Islam permits interventions in nature that will further the greater good).

²¹ See MICHAEL S. GAZZANIGA, *THE ETHICAL BRAIN* 7 (2005).

²² 410 U.S. 113, 164-65 (1973) (holding that “[f]or the stage subsequent to viability, the State in promoting its interest in the potentiality of human life may, if it chooses, regulate, and even proscribe, abortion except where it is necessary . . . for the preservation of the life or health of the mother.”).

Meanwhile, others do not pinpoint a particular time in development but focus instead on a weighing of benefits and costs. Some Catholic theologians embrace an ethical concept termed “proportionate reason,” which is akin to Utilitarianism. This approach tolerates a lesser evil (killing the embryo now) in order to bring about a greater good for society in the future (stem cell therapies).²³ However, proponents of “proportionate reason” seek to avoid embryo destruction whenever possible;²⁴ therefore, they would likely embrace Technique D if it was proven to be as effective a therapy as is destroying an existing embryo for its stem cells.

Even if an embryo does have some sort of elevated status, perhaps the crux of the matter is whether society allows the use of embryonic stem cells to benefit future scientific discoveries, at the expense of the embryo that must be destroyed. Ted Peters and Gaymon Bennett argue that while we cannot be certain when an embryo becomes human, we can be certain about human suffering and that those who suffer could benefit from discoveries made with embryonic stem cells.²⁵

Several scholars articulate a similar principle regarding sacrifice for the greater good. For example, Laurie Zoloth, a professor of medical ethics at Northwestern University notes that in the Jewish tradition “[i]f one can save a life, one must save a life; if one can heal, one must heal.”²⁶ Thus, according to Zoloth, if healing is mandatory and human embryonic stem cells can heal, they *must* be used. In a like vein, James C. Peterson, a professor of ethics and theology, asks how we can let people die to protect embryos that even if implanted may or may not someday become persons.²⁷ On this score, a number of scholars have pointed out that up to half of normally fertilized eggs never implant, or if implanted, fail to develop.²⁸

As to creating an embryo by SCNT cloning (Technique B) and then extracting its stem cells, there is an abundance of literature, much of it cautionary due to the possible use of the resulting embryo in hu-

²³ See Michael M. Mendiola, *Human Embryonic Stem Cells: Possible Approaches from a Catholic Perspective*, in HUMAN EMBRYONIC STEM CELL DEBATE: SCIENCE, ETHICS, & PUBLIC POLICY 119, 123-24 (Suzanne Holland et al. eds., 2001).

²⁴ See *id.* at 124.

²⁵ Ted Peters & Gaymon Bennett, Jr., *Stem Cell Research and the Claim of the Other in the Human Subject*, 43 DIALOG: J. THEOLOGY 184, 201-02 (2004).

²⁶ See SCOTT, *supra* note 15, at 132 (quoting Interview with Laurie Zoloth, Professor of Medical Ethics, Northwestern University).

²⁷ James C. Peterson, *Is a Human Embryo a Human Being?*, in GOD & EMBRYO: RELIGIOUS VOICES ON STEM CELLS & CLONING 77, 85 (Brent Waters & Ronald Cole-Turner eds., 2003).

²⁸ SCOTT, *supra* note 15, at 135.

man reproduction.²⁹ Nevertheless, harvested stem cells from cloned patients have the enormous advantage of not causing rejection by that patient's immune system. However, many worry that the embryo clone could be used for reproductive purposes, rather than for therapy.³⁰ Assuming proper regulation of embryonic cloning, we do not believe that this concern overcomes the advantages of using cloned embryos for therapy.³¹

III. A FRAMEWORK FOR BIOETHICAL ANALYSIS

Against this scientific and ethical backdrop, what considerations should dictate the use of particular ES-type cells? While science continues to make discoveries that may be of use to us, in each case, *should* these discoveries be utilized? These questions can be addressed by framing the analysis based on three fundamental bioethical approaches: (1) Utilitarian (weighing costs/harm versus benefits); (2) Autonomistic (preserving/protecting individual liberty in decision-making); and (3) Moralistic (deciding "rightness" or "wrongness" based on moral imperatives).

A. Utilitarian Analysis

Under the Utilitarian approach, the one most generally adopted by biomedical scientists, one first weighs the costs against the benefits of a procedure and then decides on the basis of this calculus whether or not it should be pursued. A ready example that relies on this approach is the system of triage employed by medical professionals when their resources are limited and they must decide how best to apply them. (E.g., treating terminal injuries last.)

²⁹ See, e.g., Leon R. Kass, *The Wisdom of Repugnance: Why We Should Ban the Cloning of Humans*, 32 VAL. U. L. REV. 679 (1998); June Mary Zekan Makdisi, *The Slide from Human Embryonic Stem Cell Research to Reproductive Cloning: Ethical Decision-Making and the Ban on Federal Funding*, 34 RUTGERS L.J. 463 (2003); The President's Council on Bioethics, *The Moral Case Against Cloning for Biomedical Research*, 18 ISSUES L. & MED. 261, 272 (2003). In a more positive vein, see, e.g., Ronald Chester, *To Be, Be, Be . . . Not Just to Be: Legal and Social Implications of Cloning for Human Reproduction*, 49 FLA. L. REV. 303 (1997); see generally John A. Robertson, *Why Human Reproductive Cloning Should Not in All Cases Be Prohibited*, 4 N.Y.U. J. LEGIS. & PUB. POL'Y 35 (2000) (arguing that society should permit human reproductive cloning as an alternative or supplement to services that help families overcome infertility); see generally John A. Robertson, *Liberty, Entity and Human Cloning*, 76 TEX. L. REV. 1371 (1998) (evaluating the public policy issues surrounding the practice of human cloning).

³⁰ See, e.g., Makdisi, *supra* note 29.

³¹ See, e.g., Chester, *Cloning Embryos*, *supra* note 3; Chester, *Cloning for Human Reproduction*, *supra*, note 3.

Utilitarian thinking is consequentialist thinking: one does not determine whether the procedure should be pursued until one has determined the results of the cost/benefit calculus. Any Utilitarian analysis must consider various factors. For example, when weighing costs against benefits is each side weighed in the short-term, mid-term or long-term? Would a large gain over the long-term outweigh a short-term cost? Likewise, whose utility would we be measuring? One might begin by weighing total social costs versus total social benefits, but what if different segments of society bear the costs than those who enjoy the benefits? These and similar questions bedevil even the most Utilitarian of decision-makers. However, when measured rigorously (often statistically) and weighed against one another, the costs and benefits of a given procedure typically provide the most scientifically sound decisions.

B. Human Dignity

Two other perspectives from which the question of “ought” can be viewed, Autonomistic and Moralistic, each involve the concept of human dignity and are deontological in nature: they attempt to tell us what is ethical before we know the results of any Utilitarian calculus. Deryck Beyleveld and Roger Brownsword view agency (the capability of acting) as the basis of human dignity and thus note that human beings ostensibly “only acquire rights at some time after birth.”³² Nonetheless, “precautionary reasoning requires [the rest of us] to recognize duties to the unborn in proportion to the degree to which the unborn display characteristics associated with the ability to display agency.”³³ To strike the proper balance, let us briefly consider the two basic views of human dignity.³⁴

1. Autonomistic Viewpoint

The first approach is that of human rights as autonomy, which emphasizes human choice and liberties. This Autonomistic viewpoint stresses the inalienable rights of each individual. It applies directly

³² DERYCK BEYLEVELD & ROGER BROWNSWORD, HUMAN DIGNITY IN BIOETHICS AND BIOLAW 157 (2001).

³³ *Id.*

³⁴ See generally Roger Brownsword, *Stem Cells and Cloning: Where the Regulatory Consensus Fails*, 39 NEW ENG. L. REV. 535 (2005) (explaining these two views and Utilitarianism in relation to the issues involved in human cloning); Roger Brownsword, *Bioethics Today, Bioethics Tomorrow: Stem Cell Research and the Dignitarian Alliance*, 17 NOTRE DAME J.L. ETHICS & PUB. POL’Y 18 (2003) (examining two accounts of human dignity in relation to the recent debate in the United Kingdom over human embryonic stem cell research).

only to those humans who have the capacity for autonomy (i.e. possess “agency”). Thus understood, it generally allows competent decision-makers such as patients, doctors and researchers to make their own choices. The intersection of these choices would be what lawyers understand as contract.

For example, a legally competent patient could make whatever “deal” he or she wishes with a doctor as long as this bargain does not harm others and such a bargain would be viewed as ethical.³⁵ The beauty of this approach, as contrasted with that of the Moralists, is that we do not have to prejudge whether a particular bargain fits into our own personal view of what is right and what is wrong. It is presumptively ethical. No external authority constrains such bargains. The basic issue this approach presents for stem cell research is whether one should consider the unborn as “others” who must not be harmed by the bargain, even though these unborn do not display agency.

2. Moralist Viewpoint

Moralist positions also derive conceptually from human rights, yet they generally limit the application of stem cell techniques rather than enabling them. Such views are generally dominated by firm convictions regarding “human dignity” which their adherents are willing to impose on the analysis, regardless of what freely contracting individuals might desire, or that which is dictated by strict cost/benefit analysis.³⁶

Although it can be called a human rights approach, the Moralistic view is really about others telling us what our human rights are, rather than about competent individuals making their own decisions about this (so long as they do not harm others). The Moralistic view has largely determined the distribution of US federal monies for stem cell research for nearly a decade.

³⁵ Beyleveld and Brownsword argue that there must be a good reason for restricting (or failing to support) choices made by contractors. “If we practise what we preach, contractors will enjoy freedom in two spheres – the relation to their choice of contractual projects, purposes, and particular terms (term freedom) and in relation to their co-contractors (partner freedom).” BEYLEVELD & BROWNSWORD, *supra* note 32, at 212. Still, Beyleveld and Brownsword argue that contractors’ freedom must be restricted to some extent by the rights of third parties and their human dignity. *Id.*

³⁶ See, e.g., Kass, *supra* note 29, at 689 (“[T]he ethical judgment on cloning can no longer be reduced to a matter of motives and intentions, rights and freedoms, benefits and harms, or even means and ends. It must be regarded primarily as a matter of meaning: Is cloning a fulfillment of human begetting and belonging?” Kass thinks not.).

IV. HOW THE THREE BIOETHICAL APPROACHES MIGHT BE APPLIED TO STEM CELL PROCEDURES

These three bioethical approaches might apply to the stem cell techniques outlined above in the following ways:

A. Utilitarian Cost/Benefit Analysis

The potential benefits of stem cell research in treating disease are apparent to most biomedical scientists. On the cost or “harm” side of the equation, some thinkers might include procedures that undermine human rights. However, if factors such as destruction of the embryo are not included or at least are not weighted heavily as a cost, the main consideration under cost/benefit analysis is that of the safety of a given procedure. For example, the use of iPS cells (Technique D) in therapy, while it would seem to eliminate many concerns of the Moralists regarding destruction of an embryo, could be questioned under the Utilitarian calculus because of the threat of inducing cancer in the patient. Though avoidance of viral integration and of known carcinogenic transcription factors (e.g., c-Myc) certainly improve the safety profile of this technique, the epigenetic and transcriptional reprogramming that promotes the iPS state could alone predispose the cell to malignant transformation.

B. Autonomistic Analysis

Under the Autonomistic view, stem cell therapeutics of any type should be pursued if a legally competent person or persons want it and it does not harm others. Let us first consider a bargain between legally competent individuals that affects an embryo. Clearly the embryo itself is not a legally competent individual capable of making its own bargains. Still, at some point in its development, harm to it must be taken account of by the Autonomistic perspective: it becomes an “other” to which respect must be paid. “The autonomous choices of the researcher [for example to create, test, manipulate and store embryos] and of women [to terminate pregnancies] must be measured by their legitimacy”³⁷ with regard to their respect for human dignity.

Take for example the question of abortion under *Roe v. Wade*.³⁸ For the first three months of pregnancy, the rights of the embryo/fetus

³⁷ BEYLEVELD & BROWNSWORD, *supra* note 32, at 32-33.

³⁸ 410 U.S. 113 (1973). It should be noted that the subsequent case of *Planned Parenthood of Southeastern Pennsylvania v. Casey*, 505 U.S. 833 (1992), modified the strict trimester approach by using the more elastic fetal viability approach. Since the principles underlying these approaches are similar, we will use *Roe*

are given no credence; for the second three months, they are balanced against the rights of the mother; and for the final three, coinciding roughly with the period in which a fetus can survive outside the womb, the rights of the fetus become predominant. Thus the contract between doctor and patient is subject to greater and greater limitations as the embryo/fetus develops. Further, these limitations are not simply imposed because of the rights of third parties who may be legally competent.

When assessing “harm to others” as a limitation on free contract, one should note that as development proceeds in the womb, the law as expressed in *Roe*³⁹ increasingly regards “others” as including the fetus, and perhaps shortly after birth, the young “non-agent” child. Even at these later stages of development children are not legally competent to make free choices themselves. However, we all recognize that even a freely-bargained “deal” to kill a two-week old child would be prohibited.

One observation that can be made from considering these matters is that anyone who agrees with the *Roe* analysis should have little problem with destroying an embryo or fetus up to three months old. Neither is such an entity “viable” under *Planned Parenthood*. Since stem cell research is concerned primarily with blastocysts at the 4 or 5 day stage, the rights of the fetus at some later stage should be of no concern to stem cell research.

Still many do not agree with the ideas expressed in *Roe v. Wade*.⁴⁰ Some specific ethical questions of “embryo empowerment” arise with the destruction of an existing embryo (Technique A) and of an embryo created by SCNT.⁴¹ However, an embryo is not a legally competent person capable of entering the bargains that a human rights view, stressing individual autonomy, would allow. The only way the embryo might enter such bargains would be through an agent like a guardian. In the United States, attempts by Moralists to have such agents appointed have been stymied by the lack of settled law defining the embryo as a person. In general, only persons can have legal guardians. Technique C – parthenogenesis – is immune from even these potential problems because it cannot yield an embryo capable of fetal development without further genetic manipulation. Technique D can be freely employed by consenting adults because it involves no embryo.

in the analysis for ease of expression.

³⁹ See generally *Roe*, 410 U.S. 113.

⁴⁰ *Id.*

⁴¹ Chester, *Cloning Embryos*, *supra* note 3.

C. Moralistic Analysis

This approach, which seeks to prevent stem cell research where an embryo is involved, can be quickly understood by examining the French Dwarf-throwing case that went before the Conseil d'Etat in the mid-1990s.⁴² Although the dwarfs in question wanted to be hurled in exhibitions so that they could make a living (human rights as autonomy view), it was ultimately decided that this was an affront to human dignity and the practice was banned. Here the same Moralistic view that would protect a non-viable embryo, trumped the Autonomistic human rights position, even though the dwarfs in question were, unlike the embryos, legally competent agents.

Much the same issue arises with the situation regarding women wishing to carry another's child in exchange for money. In the United States, the law on such surrogacy is both tangled and inconsistent because of sharply conflicting bioethical positions. Under the Moralistic view, such an exchange would be an affront to the human dignity of the woman offering her womb for a price. The Autonomistic position would, by contrast, stress the right of a legally competent woman to make her own free bargains. This example also exposes a striking paradox within the Moralistic perspective: while such an embryo could not be used for stem cell research because it is deemed "viable," that same embryo is actually denied viability by forbidding its implantation in the womb of a surrogate.

Finally, it should be noted that Moralists appear quite concerned with what is or is not "human." The assumption is that humans are special animals and that their dignity, unlike that of other animals, cannot be compromised. In support of this view it is certainly true that while other animals can become highly adapted to a particular environment, they cannot, unlike humans adapt simultaneously to many different environments. Whether this and other factors argue for a uniqueness in humans that should be especially protected is a topic for another day.

Under the Moralistic perspective, both Techniques A and B would be banned because embryos capable of being implanted and developing into human beings should not, because of their human potential, be destroyed for their stem cells. Parthenogenesis (Technique C) would be viewed as an affront to human dignity because: (1) of the need to procure oocytes from a healthy female (generally for a price); (2) of the belief that the whole process is "inhuman" due to its asexual

⁴² Conseil d'Etat (October 27, 1995) req. nos. 136-727 (Commune de Morsang-sur-Orange) and 143-578 (Ville d'Aix-en-Provence).

nature; and (3) further manipulation of the parthenote might produce an implantable embryo that could become a human being. This leaves open the important question of whether Moralists would support the use of Technique D, which bypasses use of fetal tissue by genetically engineering the requisite cell phenotype.

While it might be assumed that Moralists would not object to Technique D, some in their number may still view such techniques contentiously because the cell manipulation(s) may connote defying nature (or “playing God”). Moreover, though iPS cells lack totipotency,⁴³ the mounting information about the molecules that bind to a protein to regulate the role of that protein in embryogenesis could conceivably lead to the creation of more primitive embryonic phenotypes from iPS cells, which in turn raises the prospect of reproductive cloning.⁴⁴ Of course, Utilitarians could treat this, as well as other potential moral problems in stem cell procurement, not as absolutes leading to prohibition, but rather as costs to be weighed against possible benefits of the procedure.

CONCLUSION

The goals of biomedical scientists, physicians and other biomedical decision-makers are clearly aligned on the purpose of advancing new therapeutics to alleviate human suffering, and this mission critically depends on achieving relevant moral/ethical consensus for any emerging medical therapy. Thus, appropriately, biomedical advances are intermeshed with bioethical debate.

The framework of bioethical principles outlined herein is clearly preliminary. However, we think it sufficiently detailed to prompt communication among biomedical scientists and medical decision-makers evaluating innovations in deriving ES-type cells. The application of these principles will enable constructive and practical discussion, which should ultimately improve judgments made by health care providers regarding ESC-based regenerative therapeutics.

In general, biomedical scientists should take into account, within the Utilitarian cost/benefit analysis, how the knowledge gained from stem cell research impacts concepts of human dignity. Conversely,

⁴³ The capability of developing into a complete organism or differentiating into any of its cells or tissues.

⁴⁴ See generally Chester, *Cloning Embryos*, *supra* note 3 (suggesting that once the cloning of embryos becomes widely accepted, the use of such clones for reproduction is essentially inevitable and that lawmakers should not attempt to ban the use of cloning for reproduction while at the same time permitting its use for therapy and research).

biomedical decision-makers should be cautious about relying too heavily on the Moralistic approach in assessing developments in stem cell therapeutics insofar as this approach constrains the scientific calculation of the risks and benefits of any given technology or procedure and the free choice(s) of the individuals involved. We believe that Moralistic positions are best utilized not in an absolutist way, but by considering them as “costs” in Utilitarian calculations or as “harm to others” when assessed from Autonomistic perspectives. Thus, Moralistic positions would not, alone, prejudge the ethicality of a particular procedure, but would be weighed against other values, in the determination under the Utilitarian and Autonomistic approaches of whether a given procedure ought to be utilized.

