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Regenerative Medicine and Stem Cell Research

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Topic and Context of the Third IACB Colloquium

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The Third Colloquium of the IACB was held from July 1 to 5, 2007, at St. Mary's University College, Twickenham, London, U.K., to explore the theme "Stem Cells and Regenerative Medicine: How Far Should We Go?" Participants in the colloquium discussed the goals of the emerging field of regenerative medicine and reflected on the means by which cell-based interventions in regenerative medicine are being investigated.

Several methods of obtaining pluripotent stem cells for regenerative medicine have been proposed or investigated after the Pontifical Academy for Life's "Declaration on the Production and Scientific and Therapeutic Use of Embryonic Human Stem Cells" in August 2000.¹ Professor Neil Scolding, a clinical neuroscientist at Bristol University in England, prepared a background paper for this colloquium that reviewed some of the developments requiring ethical reflection, including embryonic biopsy, parthenogenesis, altered nuclear transfer (ANT) and a variation of this procedure called oocyte-assisted reprogramming (OAR), the creation of human-animal "cybrids," and induced pluripotent stem (iPS) cells.

IN THIS ISSUE

A Statement on Regenerative Medicine and Stem Cell Research by the International Association of Catholic Bioethicists is followed by a review of *Incapacity and Care*, a recently-published set of essays on the ethical challenges associated with the care of the cognitively-impaired: the essays make informative reading not only for carers but also for the rest of us who have a personal stake in the subject.

Another topic that the organizers of the IACB Colloquium thought fundamental to address was how far research and clinical applications in regenerative medicine, which is feeding the search for sources of pluripotent stem cells, ought to go. Dame Julia Polak, a renowned pioneer in regenerative medicine, prepared a background paper for the colloquium on evolving goals and latest applications in this field, which include the growing convergence of knowledge in biomaterials engineering, gene therapy, and pharmacotherapy with that of stem cell research. Although there is potential for good in some of these developments, the field is in need of ethical guidance as it ventures into uncharted territory. Participants in the IACB Colloquium formulated some such guidelines in this statement.

The colloquium also enabled Catholic bioethicists from around the world to exchange ideas that they had reflected upon, refined, and expressed in response to recent debates on public policy in their respective countries. For instance, at the time of the colloquium, the federal government and some states of Australia had just legalized the creation of human embryos for research purposes. In New Zealand, the Committee on Assisted Reproductive Technology (ACART) was discussing similar measures. Legislators in Germany were reconsidering a law in 2002 that had banned such research. In the host country for the colloquium, the United Kingdom, where creating embryos for stem cell research including, under certain circumstances, those formed through cloning techniques, has been legal, there was a lively public debate over proposed revisions to the Human Fertilisation and Embryology Act that would allow the creation of "human admixed embryos" for research by combining human and animal gametes.

Sponsorship and Participants

The Third IACB Colloquium was sponsored by the British Association of the Order of Malta. There were seventy-nine participants from twenty countries and six continents. Fifty-three of these participants were able to attend most or all of the colloquium and to participate in the process of forming this consensus statement. Not all of them were associated with the IACB or the Order of Malta. Their areas of expertise included biology, biochemistry, medicine, and various allied health care professions, clinical ethics, law, philosophy, and theology.

Process for Forming a Consensus

Participants in the colloquium read background papers on scientific and ethical topics that had been written for the colloquium by experts in their respective fields.² Guidelines for these papers followed the method that had been explored and tried at previous IACB colloquia. Both the scientific and ethical papers tried to distill succinctly for participants in the colloquium the latest research and thinking on various assigned topics, as well as the historical development of various controversial questions and positions taken on those questions. In addition, the papers in ethics proposed some foundational notions and principles for addressing the dialectically opposed positions that were identified.

Writers of the background papers were encouraged to be in contact with one another during the development of their papers. During the colloquium, participants discussed aspects of these papers in small groups and in the whole assembly. The background papers, reports of the group discussions, and points raised at the colloquium's plenary sessions are the basis of this consensus statement. Participants who were present on the final two days of the colloquium edited an initial draft of this statement and, after the colloquium, each

registered participant was given an opportunity to propose amendments to a revised draft. Their comments were reviewed by an editorial group, which prepared the final version.³ Participants were then given the option of adding their names to indicate their support of the consensus statement.

Highlights of the Consensus Statement

This consensus statement is addressed to Catholics and to Catholic health care and educational institutions as an aid in their reflections and decisions. Participants in this colloquium also hope that this statement will be read broadly in society to foster and contribute to discussions of some perplexing but important ethical issues emerging from regenerative medicine and stem cell research.

The statement begins by bringing together, and in some instances interpreting, elements from philosophy and the Catholic theological tradition that might serve as foundations for reflecting on the goals of regenerative medicine and stem cell research. Part I of the consensus statement presents guidelines for policies, planning, and implementation of appropriate prevention and therapy in regenerative medicine. Part II does the same for various methods of obtaining pluripotent stem cells for research and clinical applications.

Among the foundational issues discussed at the colloquium was how to express the Church's teaching on the dignity of every human person in a way that would facilitate communication and dialogue with non-Catholic philosophers, scientists, and the public. One approach adopted in this statement is to shift attention to considerations of the "kind" of beings humans are and to apply statistical and historical thinking to this understanding. Thus, a range of characteristics and trajectories of development can be identified as *typical* for human beings without requiring

that every individual possess those characteristics at any given moment in his or her development. This heuristic helped participants to formulate guidelines for evaluating the biological and moral status of entities produced using human genes or embryos in various novel forms of stem cell research as well as for reflecting on the controversial issue of what constitutes legitimate improvement of human beings in regenerative medicine. Another key foundational notion in this statement is that of solidarity, which is the basis for understanding the human species as a "family" and for holding the resources of this world, including the human genome, in trust for the well-being of future generations.

In this consensus statement, points on which there was substantial agreement among the participants in the colloquium are presented in the text, while some differing views or questions that were identified as requiring further investigation and discussion are referred to in the footnotes.

Participants in the colloquium were unanimous in agreeing that developments in stem cell research and regenerative medicine that can contribute to the common good of humankind and are guided by respect for the intrinsic dignity of all human beings as well as the finitude of the human condition should be supported and promoted. For Christians such research and its applications are compatible with gratitude for God's gifts and sharing in God's creative activity through human work.

Not surprisingly, disagreements emerged in the ethical analysis of oocyte-assisted reprogramming (OAR). Some scientists and bioethicists, primarily from the United States, had advocated supporting research on OAR.⁴ A majority of participants in the colloquium agreed that research on OAR is worth pursuing further in animal models to determine whether this technique meets criteria for producing human stem cells that are able to maintain their pluripotency

without the genesis of an embryo, and also whether effective, safe and affordable therapies for human beings can thereby be developed. What those criteria are is a matter for further empirical and philosophical inquiry. A minority among participants in the colloquium questioned the wisdom of even animal models in OAR in light of concerns over what they thought would be an unacceptable use of human reproductive material in the development of future therapies. These concerns merit further reflection and discussion.

Another topic generating some debate in the colloquium was human-animal transgenesis. Although the majority of participants agreed that "transferring human genes with a relatively discrete and well-understood function into a nonhuman organism, under controlled conditions and specifically for a major therapeutic benefit to human beings, such as to produce human insulin, may be ethically warranted," a few participants wondered about possible global changes that even minor genomic changes might have on the entities produced by such research and its clinical applications. This is a question for further reflection as scientific inquiry continues to change our current understanding of human genetics and epigenetics. Besides this empirical dispute, however, the statement also notes the concerns of some colloquium participants that, as unprecedented ways of manipulating genes and producing embryos become available, the modes through which human life is passed on and the relationships that are engendered should be recognized as integral to human identity.

There was vigorous debate among participants in the colloquium on what would constitute legitimate improvement of human beings in regenerative medicine. In the statement, a distinction was made between "non-preventive optimization" and enhancement," and some commonly agreed-upon guidelines were formulated. There was some thought-provoking discussion also

regarding whether gene therapies that affect or may affect the germ line or the reproductive cells of individuals diagnosed with a fatal genetic condition in utero could ever be justified. Because of the limitations of current knowledge and technology, this question is only academic but, in the future, could be an emerging topic of discussion.

The recent developments in direct reprogramming of adult somatic cells to form what are known as induced pluripotent stem (iPS) cells has dramatically changed the context of the debate on using human embryonic stem cells. Human iPS cells can potentially be a practical and ethical source of pluripotent stem cells for research and therapy. Although this technique was not addressed extensively during the colloquium because news regarding it was just becoming available, the same framework for ethical analysis of emerging stem cell technology that was proposed in the consensus statement was applied to it.

Conclusion

The topics covered by the Third IACB Colloquium were challenging for clinicians and bioethicists because of the unprecedented nature of the ethical questions raised by several emerging trends in regenerative medicine and stem cell research. The liveliness and depth of these discussions attested to the degree of preparation and the spirit of open and friendly dialogue of the participants in the colloquium. Also, an international undertaking of this sort would have been impossible without the encouragement, support, and organizational talents of various members of the British Association of the Order of Malta and of the local planning committee headed by Neil Weir. The Fourth IACB Colloquium will be held in Cologne, Germany, from July 12 to 16, 2009. Details regarding membership in the IACB, the Cologne colloquium, and publication of the

background papers and presentations of the Third IACB Colloquium may be obtained from the IACB Web site at <http://www.iacbweb.org>.

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End Notes

¹Other relevant documents from the Pontifical Academy for Life that informed deliberations at the colloquium included "Prospects for Xenotransplantation: Scientific Aspects and Ethical Considerations" (September 26, 2001) and the "Final Statement of the 12th General Assembly and of the International Congress on 'The Human Embryo Before Implantation: Scientific Update and Bioethical Considerations'" (February 27–28, 2006). These documents are available online at http://www.vatican.va/roman_curia/pontifical_academies/acdlife/index.htm.

²Neil Scolding, "The Use of Human Stem Cells from Embryonic and Other Sources in Medical Research and Potential Therapies"; Patrick H. Byrne and J. Michael Stebbins, "Ethics and Human Development: Embryonic Stem Cell Research and Altered Nuclear Transfer (ANT)"; Julia M. Polak, "Regenerative Medicine"; and Daniel Sulmasy, "Dignity, Disease, and the Canons of Therapeutic Responsiveness: Notes towards an Analysis of Regenerative Medicine." These papers will be published by the IACB, together with invited addresses by Albrecht von Boeselager, Norman Ford, David Albert Jones, Bishop Elio Sgreccia, Margaret Somerville, William Sullivan, and Helen Watt, in a forthcoming volume of proceedings.

³The initial draft was prepared by John Heng based on colloquium papers and addresses by the authors listed in note 2 as well as on reports of group discussions by Patrick Byrne, Gerald Gleeson, Christine Jamieson, Hazel Markwell, John Ozolins, John Sherrington, Noël Simard, and Michael Stebbins. The revised draft was prepared by John Heng and William Sullivan based on the comments of various participants at the colloquium, and on the written feedback submitted after the colloquium by Patrick Byrne, Paul Chummar, Richard Egan, Norman Ford, Hans Geisler, Nigel Griffin, John Hui, John Kleinsman, Jaro Kotalik, Kevin O'Rourke, John Ozolins, Noël Simard, Margaret Somerville, Michael Stebbins, Paulina Taboada, Joseph Tham, and Patricio Ventura-Juncá. The final version was reviewed by John Heng, David Albert Jones, William Sullivan, and Neil Weir.

⁴"Production of Pluripotent Stem Cells by Oocyte-Assisted Reprogramming: Joint Statement with Signatories, June 20, 2005," *National Catholic Bioethics Quarterly* 5.3 (Autumn 2005): 579–583.



STATEMENT ON REGENERATIVE MEDICINE AND STEM CELL RESEARCH

International Association of Catholic Bioethicists

Introduction

1. Regenerative medicine is a rapidly expanding field that has evolved to include three strategies: *replacement* of damaged tissues and organs in the body by means of tissue engineering and implantation, *repair* of damage at the genetic, molecular, and cellular levels, and *regeneration* by mobilizing the body's own capacity for replacement and repair, for example, through the use of drugs.¹ Regenerative medicine has raised unprecedented philosophical, legal, ethical, and theological questions. These include questions about the status of the entities used or made for such research, human identity and what is essential to human well-being, the goals of health care, and the relationships of human beings to the rest of the natural world, to one another, and to God. Some foundational principles are required to address adequately the particular ethical issues that are emerging. We affirm the following principles.

Foundational Principles

2. Human beings belong to what might be called a "natural kind" whose members manifest characteristic coordinated patterns of development and share a distinctive range of abilities and traits at each developmental stage.² For instance, humans are the kind of beings that can experience emotions, wonder, question, understand, reflect, deliberate, choose freely, love, laugh, be creative, be drawn to what is transcendent and worship. The exercise of these capacities varies from individual to individual and over an individual's lifetime, but he or she always maintains the identity of a human being. All human beings, including those who have

severe physical or mental disabilities, are members of the human family.

3. A human being is a unity and a totality of biological, psychological, intellectual, social, and spiritual aspects. Therefore, no human being should be regarded or treated as reducible to only a part of his or her whole being, such as to his or her genetic makeup. Nor should human beings be regarded or treated as having bodily and spiritual components that operate fully independently of each other. Disease, disability, and death are limitations of being embodied that are experienced by all human beings, but so is the spiritual capacity to yearn for, and respond to, what transcends the material world.

4. For Christians, the ultimate purpose of a human life is friendship with God through living, dying, and rising—body and spirit—with Christ. Christians understand genuine progress in a human being as realizing more fully the image of God in oneself through being united to Christ and imitating him.³

5. Human beings have a shared origin and are social beings. The bonds of interdependence among human beings are the basis of solidarity in the human family.

6. All human beings have intrinsic value and dignity. Christians understand this dignity to rest, above all, on God's invitation of friendship to each human being.⁴

7. A society is just when it recognizes and respects the principle of equal intrinsic dignity of all human beings. This entails enabling all human beings to share in the common good, that is, the good of the

community considered as a whole, especially taking care of vulnerable people and others who have been excluded or are at risk of being excluded from participating in society.

8. Showing human solidarity and promoting the common good include exercising responsible stewardship over the resources of this world and holding them in trust for the well-being of human beings in future generations.⁵

9. Human beings naturally strive for knowledge and to improve their living conditions. For Christians, every human being is called to be grateful for God's gifts while also having the privilege of sharing in God's creative activity through his or her work.⁶

10. Scientific and technological progress should always be guided by respect for the intrinsic dignity of all human beings, the intention to contribute to the common good, and acknowledgment of the finite human condition.

11. As long as there is uncertainty in particular lines of research or their applications concerning ethical issues like the possibility of significant harm to human beings, society should adopt a precautionary approach.

Part I: Regenerative Medicine

12. For the points that follow, we will consider *therapy*, *prevention*, *non-preventive optimization*, and *enhancement* as distinct goals in regenerative medicine:⁷

a. Illness, disability, or injury disturb human beings in ways that detrimentally affect their overall functioning, sense of well-being, and relationships. *Therapy* is directed toward helping to overcome these challenges. An example is regenerating insulin-producing

cells in the pancreas in order to treat diabetes mellitus.

b. *Prevention* aims to decrease the risk of developing or progressing in an illness or disability, or of being injured. An example is enhancing regeneration of muscle tissue after injury to prevent fibrosis that would interfere with muscle function.

c. *Non-preventive optimization* seeks some excellence within the range of possible human variations in development, traits, and abilities in the absence of symptoms or signs of an illness, disability, or injury. An example is implanting engineered tissues into healthy athletes to optimize performance.

d. *Enhancement* is intending to make human beings radically different by enabling human beings to go significantly beyond the range of developmental patterns, traits, and abilities that is currently present in human beings. This is the goal, for example, of the so-called transhumanists who seek to use technology to eliminate the aging process in human beings and to extend human lives indefinitely.

13. Precaution is warranted for applications of research in regenerative medicine that are directed toward non-preventive optimization in the sense defined in no. 12c if

a. going beyond the goals of therapy and the prevention of illness or injury, optimizing a particular human trait or ability adversely affects the overall well-being or development of individuals by harming them physically, psychologically, or socially; or

b. such efforts would undermine the principle of justice outlined in no. 7; or

c. genetic or other means are employed that make the identity and worth of some human beings conditional on the wishes or ambitions of other human beings.

14. From a Christian theological perspective, enhancement in the sense defined in no. 12d goes beyond what human beings are responsible for in participating in God's creative activity. Accepting the finite limits of the human condition, while cooperating with God to improve the conditions for human functioning and well-being within those limits, are human responses that emanate from gratitude for the gift of creation and a trust that human beings are "fearfully and wonderfully made."⁸

Guidelines for Appropriate Prevention and Therapy in Regenerative Medicine

15. As regenerative medicine develops, we propose the following guidelines for evaluating what is appropriate to research and to applying such research.⁹

a. Sustaining or Restoring Overall Well-Being and Functioning

The goal of regenerative medicine, as a healing art, should be to sustain or to restore the overall well-being and functioning of persons receiving care. This may involve one or more strategies including

i. preventing the cause or symptoms of a disease or further decline associated with the progression of a disease;

ii. eliminating the cause of a disease, or treating or managing its symptoms;

iii. mitigating the limiting effects of a disease, disability or injury, and their disruption of the activities and relationships of the person receiving care, even if that person is not restored to full physical health.¹⁰

b. Respecting Limits

Regenerative medicine should observe the following limits:

i. As finite beings, human beings develop disease or risk being injured some time in

their lives, depend on other human beings to a degree, age, and die. The goal of regenerative medicine should be to help individuals in the ways outlined in no. 15a and not to overcome the finite human condition as such.

ii. Since human beings are a unity and a totality of biological, psychological, social, and spiritual aspects, genetic, biochemical, or biological approaches in regenerative medicine should be complemented by other approaches to prevention and therapy as well as by support from disciplines such as nursing, psychology, social work, and pastoral care as needed.

c. Proportionality

In regenerative medicine, a line of research should not be pursued as long as there is lack of moral certainty¹¹ on ethical issues such as a significant risk of severe harm to human beings. Any expected risks of harm or other burdens involved in prevention or therapy should be proportionate to the benefits or potential benefits for persons receiving care and their loved ones. In assessing what is proportionate in this context, health care providers and persons receiving care should be informed by the virtue of *prudencia* (practical wisdom) so as to be guided by an understanding of the human being as a unity and a totality of biological, psychological, social, and spiritual aspects.

d. Parsimony

Prevention or therapy in regenerative medicine should be sufficient but not more than is required to address a person's need.

Further Ethical Considerations

16. The contemporary tendency to market youthfulness and to deny that aging and dying are a part of human life should be resisted in setting research priorities in medicine and its allied health care professions. People who are aging suffer from symptoms of various degenerative

disorders and other illnesses that can and should be appropriately prevented or treated, according to the guidelines proposed in no. 15. Aging itself, however, should not be regarded as an illness, except if it is premature relative to other aspects of an individual's life and development, such as in progeria. We encourage discussion about whether current directions and investment in research best serve the interests of people who are aging, whose basic health care is often inadequate in both more-developed and less-developed countries. We support ethical developments in regenerative medicine and in other areas in health care that are intended to enable people to age well and to die well rather than to extend life indefinitely.

17. The use of gene therapies in regenerative medicine should be guided by an adequate understanding of the human being (see nos. 2 to 6 above) and a respect for the human genome as one important element of what constitutes the identity of human beings and also what is special to each human being.

a. The value and dignity of a human being is not conditional on his or her being free of a genetic disorder.

b. If it were possible through gene therapy to eliminate or mitigate the harmful effects of a genetic disorder on the survival or development of a human embryo in order to improve his or her well-being and functioning, this would be consistent with respecting his or her intrinsic human dignity. The means to do this, however, would have to be ethical.

c. Gene therapies that affect or may affect the germ line or the reproductive cells of human beings, and have an impact on future generations, should not be pursued.¹²

18. The benefits of therapies that are developed in regenerative medicine should be shared as equitably as possible, both within a country and globally. Every effort should be made to ensure that there should

not be an unjust gap between those who have access to appropriate therapies and those who do not. In decisions about developing and applying new therapies in regenerative medicine, affordability in light of social justice should be an important consideration, and priority in the allocation of health resources should be given to the needs of the most vulnerable human beings.

19. New therapies in regenerative medicine should be developed using ethical sources of cells and materials. There should not be unjust exploitation or infliction of significant risk of serious harm on human beings to obtain cells and materials. In Part II we present some ethical reflections on sources of stem cells for regenerative medicine.

Part II: Sources of Stem Cells

Introduction

20. Stem cells are primitive cells in the body that are able, to varying degrees, to multiply continuously in the right conditions and to develop into different types of specialized cells.¹³ Interest in stem cells has arisen mainly because of their usefulness as a source of cells for regenerative medicine.

Embryonic Stem Cells

21. An adequate understanding of the status of the human embryo cannot be based only on descriptions of the embryo's appearance or manifest abilities at any stage of development. The whole sequence of an embryo's development, much of which occurs on the biochemical level, is coordinated and functionally interrelated.¹⁴

22. Science affirms that, from the one-cell stage, the human embryo is always executing a single, unified process of developing.¹⁵ At

every stage of development, the individual human embryo is preparing for subsequent stages so that, in the right circumstances, he or she is able progressively to replace primitive patterns of functioning with ever more differentiated patterns and to integrate them into complex systems that are interdependent. This unified development occurs in ways and directions that are distinctive of human beings.¹⁶ Like all of us, the human embryo, at every stage of development, is a human being with potential and not just a "potential human being."

23. Christian theology complements the insights of science. For Christians, every human being is made "in the image and likeness of God."¹⁷ God's involvement and care are present throughout each individual human being's existence from his or her beginning. In the Christian tradition, "the ambiguity in the appearance of the embryo has never been thought of as taking the embryo out of the realm of the human, the God-made and the holy."¹⁸

24. In stem cell research and therapy, human embryos should be treated with the respect proper to all human beings and should be protected. It is ethically unacceptable to

a. deliberately destroy human embryos at any stage of development;

b. expose a developing human embryo to significant risk of serious harm for research purposes;¹⁹ or

c. intentionally use reproductive technology to produce a human embryo, by fertilization or other means such as cloning, for the sole purpose of growing tissues or organs, or to obtain stem cells.

25. Catholic institutions should use only stem cell lines that do not require illicit cooperation with destroying or harming human embryos, or promoting such destruction or harm.²⁰

26. Embryonic stem cell research, by contrast with research involving adult stem cells, has thus far yielded no successful therapies for human beings. Society should examine carefully the practical difficulties and affordability of such research and their applications in regenerative medicine, as well as the risks of harm and other ethical difficulties.

Adult Somatic Stem Cells, Including Cord Blood Stem Cells

27. As stated by Pope Benedict XVI in his address to participants in the symposium on "Stem Cells: What Future for Therapy?" held in Rome in September 2006, adult somatic stem cell research "deserves approval and encouragement when it felicitously combines scientific knowledge, the most advanced technology in the biological field, and ethics that postulate respect for the human being at every stage of his or her existence."²¹ We strongly endorse pursuing research using adult somatic stem cells, including cord blood stem cells, to determine whether effective, safe, and affordable therapies can be developed.

28. Informed and voluntary consent of cell and tissue donors is required for both research and therapy using adult stem cells,²² and due consideration needs to be given to the cultural and religious beliefs of individuals and their families.²³

Stem Cells from Human-Animal Combinations

29. Stem cell research involving human-animal combinations must respect the integrity of human and nonhuman life. Combining human and nonhuman genes, gametes, or embryos, by fertilization or other means, is an affront to human dignity if it undermines or compromises the identity and status of the entities that are thereby produced.

30. It is always ethically unacceptable to make

a. a hybrid embryo by joining together human and animal gametes;

b. a chimera or mosaic embryo by combining cells of a human embryo with cells of a nonhuman embryo; or

c. a “cybrid” or “cytoplasmic hybrid” embryo by causing a human somatic cell or its nucleus or the combination of a human egg and a human sperm to fuse with the enucleated egg of another species.

31. Transferring human genes with a relatively discrete and well-understood function into a nonhuman organism, under controlled conditions and specifically for a major therapeutic benefit to human beings, such as to produce human insulin, may be ethically warranted.²⁴

32. Transferring nonhuman genetic material into a human organism raises additional serious concerns about unpredictable risks of harm to human beings and of the compromising or contaminating of the human genome which could affect future generations. To consider such a project would require extensive prior experimentation solely in nonhuman species and a compelling ethical justification.

Stem Cells from Parthenotes and Entities Produced by Oocyte-Assisted Reprogramming (OAR), a Variant of Altered Nuclear Transfer (ANT)

33. A requirement for producing pluripotent stem cells for research to be ethical is that it does not involve producing, harming or destroying human embryos. All human embryos, including those that are severely damaged and short-lived, show evidence of typical human self-organization and self-directed development in the manner explained in no. 22 above. Examples of

entities that do not manifest development of this kind from their beginning are teratomas and complete hydatidiform moles. A thorough series of animal experiments is a necessary condition for attaining the required moral certainty²⁵ as to whether or not the entities produced in a particular research program show evidence of typical human embryological development.

34. Parthenotes are formed from human eggs that are stimulated to behave as though they have been fertilized. These seem to develop in a direction that is characteristically human during embryogenesis for at least some period of time. Research on such parthenotes, therefore, does not fulfill the criterion for ethical research outlined in no. 33.

35. Oocyte-assisted reprogramming (OAR) is one variant in a range of techniques involving cloning known as altered nuclear transfer (ANT), which changes the expression of certain genes in the DNA of the nucleus taken from a somatic cell as well as the cytoplasm of the enucleated egg into which it is inserted. In OAR *Cdx2* genes are inactivated and the expression of the genes for *Nanog* and *Oct3/4* are increased. *Nanog* is found in stem cells but not in single-cell embryos. It is hypothesized that OAR produces stem cells that are able to maintain their pluripotency without the genesis of an embryo. Research on OAR is worth pursuing further in animal models to determine whether this is true and, if so, whether effective, safe, and affordable therapies for human beings can be developed.²⁶

Induced Pluripotent Stem (iPS) Cells

36. A research program designed to dedifferentiate or to reprogram adult somatic cells into pluripotent embryonic stem cells is worth pursuing further to determine whether such research can generate effective, safe, and affordable therapies.²⁷

Signatories

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End Notes

¹ For a current review, see Julia Polak, "Regenerative Medicine," 1. Paper prepared for the 3rd IACB International Colloquium, Twickenham, U.K., July 3, 2007.

² "Natural kind" here is a technical philosophical term for a collection of entities that are identified as instances of a particular kind of thing, differentiated from other kinds of things, because their characteristics and activities manifest certain distinctive law-like principles. For the human natural kind, these principles are drawn from various areas of knowledge that inform our understanding of what it is to be human. A particular individual need not individually express *all* of these law-like principles in order to be classified correctly as a member of the human natural kind. See Daniel Sulmasy, "Dignity, Disease, and the Canons of Therapeutic Responsiveness: Notes towards an Analysis of Regenerative Medicine," 2–3. Paper prepared for the 3rd IACB International Colloquium, Twickenham, U.K., July 3, 2007.

³ International Theological Commission, "Communion and Stewardship: Human Persons Created in the Image of God" (July 23, 2004), n. 91, www.vatican.va/roman_curia/congregations/cfaith/cti_documents/rc_con_cfaith_doc_20040723_communio-stewardship_en.html.

⁴ See Vatican II, "Pastoral Constitution on the Church in the Modern World" (*Gaudium et Spes*), n. 12, http://www.vatican.va/archive/hist_councils/ii_vatican_council/documents/vat-ii_cons_19651207_gaudium-et-spes_en.html; and *Catechism of the Catholic Church*, n. 27, <http://www.vatican.va/archive/catechism/p1s1c1.htm#l>.

⁵ In some cultures, such as some African ones, the notion of human life presupposes a connection between past, present, and future generations.

⁶ Vatican Council II, "Pastoral Constitution on the Church in the Modern World" (*Gaudium et spes*), n. 34: "Thus, far from thinking that works produced by man's own talent and energy are in opposition to God's power, and that the rational creature exists as a kind of rival to the Creator, Christians are convinced that the triumphs of the human race are a sign of God's greatness and the flowering of his own mysterious design. For the greater man's power becomes, the farther his individual and community responsibility extends. . . . People are

not deterred by the Christian message from building up the world, or impelled to neglect the welfare of their fellows. They are, rather, more stringently bound to do these very things." See also "On Human Labor" (*Laborem Exercens*), n. 25.

⁷ These distinctions are adapted from those proposed by Daniel Sulmasy in "Dignity, Disease, and the Canons of Therapeutic Responsiveness," the background paper that he wrote for the colloquium. A crucial distinction in the discussions at the Third IACB Colloquium was between intentionally seeking to optimize or enhance human beings as an end in itself and as a foreseen but not intended outcome of some other end within medicine.

⁸ Psalm 139: 14.

⁹ These guidelines are adapted from those proposed by Daniel Sulmasy in "Dignity, Disease, and the Canons of Therapeutic Responsiveness," 8–10.

¹⁰ For an elaboration, see Daniel P. Sulmasy, "A Biopsychosocial-Spiritual Model for the Care of Patients at the End of Life," *Gerontologist* 42, special issue 3 (2002): 24–33.

¹¹ "Moral certainty" is not as stringent a requirement as absolute certainty. A judgment may be deemed morally certain if it is the most reasonable account of all relevant data that are available and if as much care as possible has been taken to raise and to consider pertinent questions.

¹² There was some speculative discussion of whether an exception could be made if it were technically feasible to correct lethal genetic disorders like trisomy 13 or trisomy 18, or diseases with life-shortening or other devastating effects such as cystic fibrosis, in a developing human embryo or fetus, at a stage when his or her sex cells or gametes would be affected genetically.

¹³ The range of cell types that stem cells are capable of becoming varies. According to terminology that is widely accepted, cells are considered to be "totipotent" if they are able to develop as an organism, "pluripotent" if they can become any type of cell in the body, and "multipotent" if they are able to differentiate into a more limited range of cell types. Some researchers call multipotent adult stem cells "progenitor cells".

¹⁴ Patrick H. Byrne and J. Michael Stebbins, "Ethics and Human Development: Embryonic Stem Cell

Research and Altered Nuclear Transfer (ANT)." Paper prepared for the 3rd IACB International Colloquium, Twickenham, U.K., July 3, 2007, pp. 2–3.

¹⁵ After implantation in the womb, this development continues in a biochemical and physiological relationship with the mother. Also, up to roughly fourteen days after fertilization when gastrulation or the development of the tissue or germ layers occurs, the formation of human twins from a single zygote is possible. For an argument that the possibility of twinning does not entail that the developing human embryo is not an individual, see Alfonso Gómez-Lobo, "Individuality and Human Beginnings: A Reply to David DeGrazia," *Journal of Law, Medicine and Ethics* 35.3 (Fall 2007): 457–462.

¹⁶ Byrne and Stebbins, "Ethics and Human Development," 5–9. See also Congregation for the Doctrine of Faith, *Donum vitae* (February 22, 1987), I, 1: "Certainly no experimental datum can be in itself sufficient to bring us to the recognition of a spiritual soul; nevertheless, the conclusions of science regarding the human embryo provide a valuable indication for discerning by the use of reason a personal presence at the moment of this first appearance of a human life: how could a human individual not be a human person? ... Thus the fruit of human generation, from the first moment of its existence, that is to say from the moment the zygote has formed, demands the unconditional respect that is morally due to the human being in his bodily and spiritual totality." Available online at http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_19870222_respect-for-human-life_en.html.

¹⁷ Genesis 1: 26–27.

¹⁸ David A. Jones et al., "A Theologians' Brief: On the Place of the Human Embryo within the Christian Tradition and the Theological Principles for Evaluating Its Moral Status," *Ethics and Medicine* 17.3 (Fall 2001): 143–153, on p. 150.

¹⁹ In the last few years, some scientists have been working on techniques to derive human embryonic stem cells, purportedly without destroying the "donor" embryo. See, for example, I. Klimanskaya et al., "Human Embryonic Stem Cell Lines Derived from Single Blastomeres," *Nature* 444.7118 (November 23, 2006): 481–485. Participants noted ethical difficulties with such approaches, such as the risk of significant harm to the embryo and the

possibility of wasting embryos that are not used to derive the stem cell lines.

²⁰ For further discussion of the issue of licit and illicit cooperation, see Helen Watt (ed.), *Cooperation, Complicity and Conscience*, London: Linacre Centre, 2006; and Catholic Health Association of the United States, "Report on a Theological Dialogue on the Principle of Cooperation: Executive Summary," *National Catholic Bioethics Quarterly* 7.4 (Winter 2007): 773–776.

²¹ September 16, 2006; http://www.academiavita.org/template.jsp?sez=DocumentoMagistero&pag=papi/disc_staminali/disc_staminali&lang=english.

²² In the case of cord blood stem cells, there was a question about who may give appropriate consent for its use. Some participants mentioned the concept of "anticipated consent," which has been proposed in the bioethics literature, but this was not pursued further.

²³ For example, some cultures have rituals involving the placenta and umbilical cord after birth.

²⁴ See Pontifical Academy for Life, "Prospects for Xenotransplantation: Scientific Aspects and Ethical Considerations" (September 26, 2001), n. 1, http://www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20010926_xenotrapianti_en.html. A few participants, however, thought that all human-nonhuman transgenesis is unacceptable because genomic changes may have global effects on the organism and its development such that even a minor genomic change may not be discrete. Also, the human genome is the means by which human life is transmitted, and thus caution should be exercised in the insertion of even a part of the human genome into a developing nonhuman embryo. For an elaboration, see N. Tonti-Filippini et al., "Ethics and Human-Animal Transgenesis," *National Catholic Bioethics Quarterly* 6.4 (Winter 2006): 689–704.

²⁵ See note 11 for a definition of "moral certainty."

²⁶ See "Production of Pluripotent Stem Cells by Oocyte-Assisted Reprogramming: Joint Statement with Signatories, June 20, 2005," *National Catholic*

Bioethics Quarterly 5.3 (Autumn 2005): 579–583. Other techniques of ANT, and the ethical issues arising from these, were not examined at the colloquium. Some participants expressed the view that human eggs ought never to be used for a reproductive-like purpose, i.e., any purpose directed at generating a new entity, even if there was moral certainty that such an entity is not a human being.

²⁷ In June 2007, at around the time of the IACB Colloquium, an advance electronic version of a report on reprogramming of adult mouse cells was available, which was subsequently published as M. Werner et al., "In Vitro Reprogrammed Fibroblasts Have a Similar Developmental Potential as ES Cells and an ES Cell-like Epigenetic State," *Nature* 448.7151 (July 19, 2007): 318–324. In November 2007, there was an electronic pre-publication of a report of iPS cells being generated from adult human fibroblasts. See T. Takahashi et al., "Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors," *Cell* 131.5 (Nov. 30, 2007): 861–872.

The International Association of Catholic Bioethicists (IACB) is a community of scholars and clinicians supported by national associations of the Order of Malta. Its mission is to foster discussion of new and controversial questions in bioethics and to facilitate collaboration in investigating these questions. The IACB was established in 2004 to promote such opportunities in a milieu that emphasizes rigorous scholarship, friendship, and prayer.

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How are we best to care for, to respect and to protect the cognitively-impaired?

A review

Bernadette Tobin

A cognitively-impaired man who had been chronically psychotic for many years suffered religious obsessions. He became increasingly violent during his psychotic episodes, resisting attempts to feed him. He would sometimes say that he wished to starve to death, though he also expressed confidence that God would save him. Two psychiatrists, and an ethics committee, thought that his 'wish' to starve to death should be respected. The Chief Justice of an Australian Supreme Court, though he recognized the distress caused both to the man himself and to the staff caring for him, called this view *'an outrageous approach to ethical standards which require a free and informed consent before a course involving such grave risk as premature death is adopted'*. So, how are we best to care for, and respect and protect, the cognitively-impaired? As the editor of a new collection of essays entitled *Incapacity and Care: Controversies in Healthcare and Research*ⁱⁱ says:

'This is a question for all of us, but especially for health professionals and those with an immediate personal stake in the subject, such as those already caring for loved ones or contemplating their own likely future state of mental impairment.'

This is a most worthwhile collection. For example:

David Albert Jones asks us to rethink our grounds for respecting non-autonomous persons. He argues that the contemporary dogma, that 'human person' is not a synonym for human being but rather a category that draws attention to an extra feature or set of features that some human beings have and others lack, is incorrigibly arbitrary and undermines the idea of human equality. So we need to retrieve the ancient sense of ourselves as substantial beings of a certain kind: rational animals. But this Greek thought, though it discourages us from thinking that there could be human beings who are not persons, is not enough. For, in grounding respect or dignity in the capacity for rational or autonomous acts, it too seems to involve a test of (potential) mental capacity before we acknowledge common humanity. If what is important is autonomous freedom of action, then there is nothing obviously important about people who cannot exercise this freedom. So we need to go back to an earlier view found in the Hebrew Scriptures, that God has no partiality to persons, and thus that we should show no partiality to persons. For the roots of the idea of equal respect and dignity lie not with Greeks but with the Jews and Jesus Christ. Here we see a clear difference of attitude between Greek philosophy and Judeo-Christian teaching to the idea of dependence. For Aristotle, the best man should hate to be dependent, should strive

to be a benefactor to others rather than beholden to others. But Aquinas prays that he will share what he has with those in need and humbly receive from others what he needs himself. This theology, with its associated philosophical anthropology, encourages us to give up the idea of the autonomous agent as the paradigm of a person, for it emphasizes that persons are constituted by relationships to others, and by interdependence. So human equality is rooted not in abilities but in common membership of a community of need and independence. Then we can ground respect for non-autonomous person not in abstract judgment about beings which possess a rational nature but in an immediate recognition of a fellow member of our community or one who could or should be a member *if we show the proper solidarity that is in our nature to show*. So we should not ask: Is this comatose patient a person? But rather, by giving due respect to him or her, we will discover ourselves as persons and our capacity to be in solidarity with our neighbour.

Aaron Kheriaty explains the truth recognized in a psychiatrist's (sympathetic) quip that severely psychiatric patients may be 'crazy but not stupid'.

Anthony McCarthy sets out the issues which are debated in the controversy, amongst the 'new natural lawyers' as well as others, over whether the prevention of harm can justify sterilisation.

Helen Watt, who used to think that non-consensual, non-therapeutic research should be prohibited, explains why she has changed her mind.

Wendy Hiscox analyses the Dutch and Belgian experience of legalizing euthanasia and reveals a serious lack of control over the practice in both places: the so-called strict and precise guidelines are being routinely ignored and gradually relaxed.

John Finnis explains why, though there is nothing in the UK's Mental Capacity Act 2005 which challenges Catholic teaching or invites a Catholic to do wrong (indeed, the spirit of this Act, as of the Mental Health Act 1983, is recognizably the spirit of a culture formed by the Christian doctrine of love of neighbour), nonetheless he would have voted against its enactment. He says:

'For sound legislation must protect individuals and the community against people whose conscience is not sound, or who by reason of conflict of interests, partiality, and other unconscionable motives wish to make unconscientious and wrong choices. Against such forms and sources of injustice the Act provides irresponsibly inadequate protection, and its statutory provisions and arrangements are capable of facilitating and in a sense encouraging both injustice and moral decay.'

Johanna Valiquette sets out the burdens, and the benefits, of providing PEG tube feeding to people with end-stage dementia. As she says, there can be ethically reprehensible reasons for omitting, and for providing, medically assisted nutrition.

As I said, *Incapacity and Care* is well worth an attentive read.

ⁱ *Australian Capital Territory v JT*. [2009], ACTSC 105 (28 August 2009)

ⁱⁱ *Incapacity and Care; Controversies in Healthcare and Research*, Edited by Helen Watt, The Lincare Centre, Oxford, 2009.