Ethics & Medics

A Commentary of The National Catholic Bioethics Center on Health Care and the Life Sciences

A Comprehensive Primer on Stem Cells

A stem cell is any cell that exists in a relatively immature state, and is able to divide to produce one cell that replaces itself and one that will go on to become a more specialized cell type. Because stem cells replace themselves every time they divide, they are considered self-renewing, or "immortal."

There are three broad classes of stem cells: embryonic, adult, and reprogrammed. Human embryonic stem cells are obtained by the destruction of human embryos that are between three and six days old. At this early stage, cells of the embryo are still very primitive and are pluripotent; i.e., they are able to produce all of the cell types found in the mature human body.

In contrast, any stem cell that is found in a specific type of tissue (whether in an older embryo, a fetus, or a more mature individual) is considered an adult stem cell. Adult stem cells are thought to be more limited, making only the types of cells appropriate to the tissue in which they reside. Thus, they are seen as merely "multipotent."

Finally, recent studies have shown that adult body, or "somatic," cells can be reprogrammed to a state very similar to a human embryonic stem cell. These induced pluripotent stem cells, or iPSCs,[1] are not identical to embryonic stem cells,[2] but they are *functional* equivalents; i.e., when transferred to early embryos, both cell types are able to produce all of the cells of the mature body.

How Useful Are They?

Stem cells offer hope for treating medical conditions that are caused by a loss of cells, either due to injury or disease. To realize this hope, several important hurdles must be overcome. First, scientists must determine how to make stem cells mature into stable tissue that survives and functions normally. Second, stem cell derivatives must be safe for transplantation. Finally, scientists must find ways of effectively using stem cells to treat or cure medical conditions.

Independent of the type of stem cell used for therapies, the pathology of many diseases is not sufficiently understood for stem cell treatments to be realistic; transplanted cells would simply fall victim to the same fatal influences that produced the disease initially. Thus, diabetes, Parkinson's disease, Alzheimer's, multiple sclerosis, and many other devastating conditions await a more thorough understanding of what *causes* cells to die before we can effectively treat patients with *any* type of stem cells.

In contrast, injuries such as those caused by heart attack or stroke present a more straightforward opportunity for stem cell therapies. In these cases, the approach to effective treatment (how to coax replacement cells into repairing damaged tissue) is likely to be similar, regardless of what kind of stem cell generates the replacement tissue. Therefore, to determine which stem cell type is likely to be the most useful, we need to ask, How do the three classes of stem cells compare in terms of the ability to produce stably differentiated cells that are safe for use in patients?

What Hope Do They Give?

The serious safety issues raised by human embryonic stem cells have been discussed in detail.[3] Embryonic stem cells produce fatal tumors—indeed, such tumors are the gold-standard test for pluripotency. Embryonic stem cells can also convert to cancer cells.[4] In theory, both of these problems could be addressed by maturing embryonic stem cells into more stable cell types, yet this has proved to be very difficult, with even "differentiated" cells still producing tumors.[5] Despite more than a quarter century of research, the challenge of coaxing embryonic stem cells to form clinically safe cells has not been routinely overcome. Because cells derived from embryonic stem cells would be rejected by the immune system, human cloning has been proposed as a way to make patient-specific embryonic stem cells. However, cloned embryonic stem cells are known to be genetically abnormal, and this is not a simple problem to fix.[6] Thus, embryonic stem cells face serious and long-standing scientific hurdles before they can be safely used in patients.

In contrast to embryonic stem cells, adult stem cells have been used in clinics for decades. Stem cells from *mature* tissue (i.e., present at birth or later) do not cause

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tumors or convert to cancer.[7] Most (but not all [8]) adult stem cells divide more slowly than embryonic stem cells and have more restricted potency. However, some kinds of adult stem cells can differentiate into multiple cell types.[9] Importantly, because adult stem cells can be obtained from the patient, or "immune matched" from birth-related tissues like the umbilical cord and placenta, they will not be rejected.[10] These combined advantages have led to significant medical advances; adult stem cells have provided benefit for over seventy medical conditions in either animal or human studies,[11] and there are currently more than twenty-four hundred U.S.-funded clinical trials using adult stem cells.[12]

Reprogrammed iPS cells have some of the advantages of adult stem cells, and some of the disadvantages of embryonic stem cells. Like embryonic stem cells, iPS cells are pluripotent and therefore produce tumors. The early techniques used to generate iPS cells carried an increased risk of tumor formation, yet the iPS technique has been significantly improved. Current approaches have eliminated any added risk, and *iPSCs are now no more likely to produce tumors or cause cancer than are embryonic stem cells*. Just as for embryonic stem cells, it will undoubtedly be difficult to mature iPS cells into stable, functional cell types. However, initial studies suggest that this hurdle may not be as high for iPS cells as it is for embryonic stem cells.[13] Finally, iPS cells share with adult cells the advantage of being patient-specific. In the last year, scientists have produced a number of iPS cell lines from patients, to study specific diseases in the laboratory.[14] Thus, iPS cells are pluripotent (making them attractive for research), yet have the significant clinical advantage of being patient-specific.

The Ethics of Stem Cell Research

Although production of human embryonic stem cells requires the destruction of nascent human life, some claim that the potential benefit to patients justifies this research. Yet, if embryos are human beings, arguing that it is permissible to destroy someone who is small and immature in the hope of benefiting someone of larger size or greater maturity is clearly an unethical line of reasoning. The critical question is whether human embryos are mere collections of human cells or *developing human beings*. And this question has been thoroughly addressed by the scientific evidence: [15] Embryos are developing human beings, not tumors or mere collections of human cells. They are small and immature, as all human beings once were, but they are human individuals. As Dr. Leon Kass, former chairman of the President's Council on Bioethics said,

> The moral issue does not disappear just because the embryos are very small or because they are no longer wanted for reproductive purposes: Because they are living human embryos, destroying them is not a morally neutral act. Just as no society can afford to be callous to the needs of suffering humanity, none can afford to be cavalier about how it treats nascent human life.[16]

Ethical objections to embryo-destructive research are based on religiously neutral reasoning that takes into consideration both the scientific evidence and current U.S. law regarding the protection of those who participate in experiments.[17] Protecting human research subjects is an important ethical consideration. The Nazi experiments on Jews, the Tuskegee syphilis experiments on black men, and the Japanese hypothermia experiments on prisoners of war were unethical and were not justified simply because they led to new and exciting discoveries that benefited patients. Science, like all human endeavors, must operate within an ethical framework. This is not a religious objection, it is just common sense.

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1 K. Takahashi and S. Yamanaka, "Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors," *Cell* 126.4 (August 25, 2006): 663–676; and J. Yu et al., Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells," *Science* 318.5858 (December 21, 2007): 1917–1920.

2 Yamanaka's study indicates that 4 percent of the 32,000+ genes examined are expressed differently between iPSCs and embryonic stem cells.

3 Maureen L. Condic, "The Basics about Stem Cells," *First Things* 119 (January 2002): 30–34; and Maureen L. Condic, "What We Know about Embryonic Stem Cells," *First Things* 169 (2007): 25–29.

4 Claudia Spits et al., "Recurrent Chromosomal Abnormalities in Human Embryonic Stem Cells," *Nature Biotechnology* 26.12 (December 2008): 1361–1363; and Nathalie Lefort et al., "Human Embryonic Stem Cells Reveal Recurrent Genomic Instability at 20q11.21," *Nature Biotechnology* 26.12 (December 2008): 1364–1366.

5 See Anke Brederlau et al., "Transplantation of Human Embryonic Stem Cell-Derived Cells to a Rat Model of Parkinson's Disease: Effect of In Vitro Differentiation on Graft Survival and Teratoma Formation," *Stem Cells* 24.6 (2006):1433–1440.

6 David Humpherys et al., "Epigenetic Instability in ES Cells and Cloned Mice," *Science* 293.5527 (July 6, 2001): 95–97; Alex Bortvin et al., "Incomplete Reactivation of Oct4-Related Genes in Mouse Embryos Cloned from Somatic Nuclei," *Development* 130.8 (April 15, 2003): 1673–1680; David Humpherys et al., "Abnormal Gene Expression in Cloned Mice Derived from Embryonic Stem Cell and Cumulus Cell Nuclei," *Proceedings of the National Academy of Sciences of the United States of America* 99.20 (October 1, 2002): 12889–12894; G.Q. Tong et al., "Aberrant Profile of Gene Expression in Cloned Mouse Embryos Derived from Donor Cumulus Nuclei," *Cell and Tissue Research* 325.2 (2006): 231–243; Rita Vassena et al., "Deficiency in Recapitulation of Stage-Specific Embryonic Gene Transcription in Two-Cell Stage Cloned Mouse Embryos," *Molecular Reproductive Development* 74.12 (December 2007): 1548–1556.

7 The exception appears to be stem cells from human fetal tissue, which have produced tumors in at least four patients following transplant. See, for example, N. Amariglio et al., "Donor-Derived Brain Tumor following Neural Stem Cell Transplantation in an Ataxia Telangiectasia Patient," *PLoS Medicine* 6.2 (February 2009): 17.

8 Rahul Sarugaser et al., "Human Umbilical Cord Perivascular (HUCPV) Cells: A Source of Mesenchymal Progenitors," *Stem Cells* 23.2 (2005): 220–229; and B. M. Deasy et al., "Long-Term Self-Renewal of Postnatal Muscle-Derived Stem Cells" *Molecular Biology of the Cell* 16.7 (July 2005): 3323–3333.

9 Reviewed in Donald G. Phinney and Darwin J. Prockop, "Concise Review: Mesenchymal Stem/Multipotent Stromal Cells: The State of Transdifferentiation and Modes of Tissue Repair—Current Views," *Stem Cells* 25.11 (November 2007): 2896–2902.

10 With over four million births annually in the United States, birth-associated tissues could provide an excellent immune match to most patients.

11 List available at www.stemcellresearch.org/facts/treatments.htm.

[12] A March 2009 search of the federal database at www.clinicaltrials.gov, revealed 2,461 currently funded clinical trials using adult stem cells.

[13] iPS cells have been use to treat Parkinson's disease and sickle cell anemia in animal models. In an interview in *Science* magazine, an author of the sickle cell study indicated that efforts to conduct the study using cloning failed because cloning was too inefficient. Gretchen Vogel, "Reprogrammed Skin Cells Strut Their Stuff," *ScienceNOW* (December 6, 2007). For the original studies see Marius Wernig et al., "Neurons Derived from Reprogrammed Fibroblasts Functionally Integrate into the Fetal Brain and Improve Symptoms of Rats with Parkinson's Disease," *Proceedings of the National Academy of Sciences of the United States of America* 105.15 (April 15, 2008): 5856–5861; and Jacob Hanna et al., "Treatment of Sickle Cell Anemia Mouse Model with iPS Cells Generated from Autologous Skin," *Science* 318.5858 (December 1, 2007): 1920–1923.

[14] F. Soldner et al., "Parkinson's Disease Patient-Derived Induced Pluripotent Stem Cells Free of Viral Reprogramming Factors," *Cell* 136.5 (March 6, 2009):964–977.

[15] Maureen L. Condic,"When Does Human Life Begin? A Scientific Perspective," *Westchester Institute White Paper Series* 1.1 (October 2008): 1–18, reprinted in *National Catholic Bioethics Quarterly* 9.1 (Spring 2009): 129–149.

[16] Leon R. Kass, "Playing Politics with the Sick," *Washington Post*, October 8, 2004, www.washingtonpost.com/wp-dyn/articles/A16510-2004Oct7.html.

[17] Protection of Human Subjects, Research Involving Pregnant Women or Fetuses, 45 *CFR* 46.204 (rev. June 23, 2005).

Faith in Science, Reason in Religion

We live in an age when science and religion are set before us as opposites. Popular thought says that science is grounded in reason, and religion is based in faith. If we want to possess knowledge, we must choose the path of science, even if we arrive at a view of nature that shows us that it lacks any purpose and has been abandoned by God. Some say that science disproves God's existence entirely. If we want to take solace in the feeling that there is some larger purpose in life, then we are free to choose the path of religion, and so embrace the idea that there is a divinity, but this is merely an illusion.

Science is committed to objective facts that are given in nature, while religion is grounded in personal convictions that are private. In science, one begins by reasoning about data discovered through empirical inquiry; in religion one begins with beliefs that lack any solid evidence, but are the expression of our deepest hopes and longings. The hard-headed thinker will follow the path of science and set superstition aside. The soft-headed idealist will overlook the lack of support for his beliefs and make an irrational leap of faith. He will do what Tertullian purportedly advised: choose to believe because it is absurd.

These popular descriptions of science and religion are wrong. If by "faith" we mean the willingness to accept what has not been shown to be true by reason, then science is grounded in faith. Religion, using this same definition, is grounded in reason.

Reason Precedes Faith

The standard view of religion is that it begins with a leap of faith. Here "faith" means to affirm something as true without reason. Thus, one accepts on faith that Jesus Christ rose from the dead because the Bible says so, and Christians accept the inerrant word of the Sacred Scripture on the testimony of its authors. But the Catholic faith has never taken this simplistic approach. Our faith holds that certain truths about God—for example, that God exists—can be known by reason prior to any act of faith.[1] These truths are the basis for our further and additional commitment to the supernatural events recounted in the Bible. Because we already know that there is a God, we accept the authority of the Scriptures as the Word of God.[2]

Proofs for the existence of God have been offered throughout history, often by non-Christians.[3] Most everyone who has not been prejudiced by atheism arrives at the conclusion that the world has a divine origin. There is just too much order and purpose in nature for it to have come about at random. Saint Thomas Aquinas offers various philosophical proofs for the existence of God, for example, through the argument to a First Cause, and then proceeds to describe the attributes that must belong to the Divinity. If the mind can know that God is omniscient, omnipotent, and supremely good, then it makes sense to say that God would reveal his will for us through the inspiration of the scriptural authors.

Thus we accept what the Bible teaches about God's plan for salvation through the sending of his Son. This doctrine is not known to reason, but is an article of faith that is based on a prior knowledge of the existence and attributes of God. Similarly, Jesus' resurrection from the dead contravenes the laws of nature. Reason cannot understand how such an event could even be possible, any more than it can understand that God is three Persons. These truths are accepted on faith, but we would not accept them if we did not already know certain truths about God through reason alone. Catholics do not make a leap of faith—at least not those who know their tradition. We first accept the "preambles to the faith," as they have been called by the great doctors of the Church, and on the basis of this solid grounding in reason, we then assent to supernatural doctrine.

Faith Precedes Science

The scientist takes an opposite path. He begins with certain beliefs about nature that he accepts without evidence. Thus, he believes, for example, that nature is a material object, driven by mechanical impulse and devoid of purposes. None of these beliefs are themselves known by science, but all are accepted as necessary premises if the scientific enterprise is to begin.

Consider the claim that life is nothing more than a certain configuration of matter. Under this belief, one holds that life is a material phenomenon and that scientific analysis will eventually show that all of life is reducible to matter. This may indeed be true; we certainly cannot rule it out ahead of time, but when we look at the evidence, we find that there has never been one recorded example of

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life originating out of matter. Life always originates from other living things. The media is constantly telling us that scientists are on the verge of such a discovery, but as of now life remains a fundamental mystery. Even if some are convinced that life is reducible to mater, there is simply no conclusive proof for this at the present time. It remains an object of belief. To accept the view that life is reducible to matter, therefore, is to accept a claim about nature that cannot be known by reason.

The same is true for the belief that all natural motion can be explained in purely mechanical terms. The paradigmatic example of mechanical motion is that of billiard balls on a pool table. Considered in themselves, they have no purpose, at least none outside the intentions of the players. They strike each other and ricochet according to the exact mechanical laws of physics. If all natural motion reduces to this type of motion, then even the most complex and elaborate behavior—such as the spiders spinning of a web to catch his prey—lacks any real purpose. This apparently purposeful behavior is only the random motion of material particles under the direction of mechanical law. The biologist may say that "the spider spins his web in order to catch his prey," but this language is just a place-holder for the longer and more detailed mechanical description that will be given later on. When it is given, science will confirm that there are no purposes in nature.

Here again we have a belief. The hard-headed scientist contends that nature appears to be designed, but is not.[4] We are told that when science is completed, at some distant point in the future, this lack of purpose will become obvious to all. For the present, however, the assertion follows only if one accepts it on faith. The same is true for "scientific naturalism," the belief that science is the sole avenue to truth. Under this belief, no other field of inquiry besides science can give us knowledge in the proper sense of the term. Religious convictions, for example, can tell us nothing that is true, but only what we hope or wish to be true. This is because religion is not grounded in experience, but makes a leap of faith, and so is inherently irrational. But as we have just seen, this is not a proper description of religion, at least, not for Catholics. Catholics lay a foundation for their faith in the work of reason.

If faith means the acceptance of something as true in the absence of a rational proof, then science is based on faith, for it accepts various premises about nature without proof, such as, the belief that all of nature is material. Religion, in contrast, begins with the evidence for God's existence that is given in nature. Through logical inquiry and deductive inference, it arrives at a rational understanding of God and the Divine attributes. To this rational knowledge, religion then adds its articles of faith.

Reversing the Caricature

Thus science and religion, as these are typically caricatured, turn out to be their opposites. Religion begins with certain truths about God that can be known by reason, and to this it adds articles of faith. Science begins with certain beliefs that cannot be known by reason, and to these it adds the discoveries of reason. Science has a dogmatic foundation. Religion does not.

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[1] *Catechism of the Catholic Church*, 2nd ed., trans. U.S. Conference of Catholic Bishops (Vatican City: Libreria Editrice Vaticana, 1997): n. 31. "These are also called proofs for the existence of God, not in the sense of proofs in the natural sciences, but rather in the sense of 'converging and convincing arguments,' which allow us to attain certainty about the truth."

[2] Thomas Aquinas, *Summa theologiea*, I, 1.1.

[3] Aristotle, for example, offers persuasive arguments in his *Physics*, book VIII, and in his *Metaphysics*, book XII.

[4] Richard Dawkins, *The Blind Watchmaker: Why the Evidence of Evolution Reveals a Universe without Design* (New York: W.W. Norton, 1996), 1.

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