"Altered Nuclear Transfer"

Probing the Nature of Being Human

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Over three years ago, William Hurlbut, M.D., a Stanford University physician and ethicist and member of the President's Council on Bioethics, proposed a unique and imaginative alternative to the impasse generated by the embryonic stem cell debate.[1] Deeply committed to the principle that respect for human life in all its stages of development is the cornerstone of law and morality for our civilization, and that under no circumstance is the intentional destruction of the life of an innocent individual deemed morally acceptable, Hurlbut proposed an alternative source of "embryonic" stem cells that would honor these strongly held convictions. The proposal, known as altered nuclear transfer (ANT), is a process by which an intentional alteration of the somatic cell nuclear components, or the cytoplasm of the oocyte into which they are transferred, could create an "artifact (a human creation for human ends) that is biologically and morally more akin to tissue or cell culture."[2] The proposed entity created would be capable of yielding stem cells while lacking the capacity for the "self-directed, integrated organic functioning that is essential for embryogenesis."[3] In other words, ANT would produce a growing cellular structure with human genetic components capable of providing "embryonic" stem cells, but

[1]The President's Council on Bioethics, *Human Cloning and Human Dignity: The Report of the President's Council on Bioethics* (New York: Public Affairs, 2002), 307–320; see also William B. Hurlbut, "Altered Nuclear Transfer as a Morally Acceptable Means for the Procurement of Human Embryonic Stem Cells," http://www.bioethics.gov/background/hurlbut.html.

[2]Ibid., 318.

[3]Ibid.

would not, by definition, be a "human embryo." Hurlbut's proposal has generated no small controversy, and has exposed some of the deeper and more perplexing metaphysical questions surrounding the whole field of genetic engineering as it moves beyond genomics and into proteomics.

The central problem behind the embryonic stem cell debate, and whether it is morally justifiable to use preimplantation-stage human embryos to further understand human biology and cure serious diseases, is the moral status of the preimplantation-stage embryo. This problem has traditionally been formulated by asking questions like, "When does human life, and by implication a human being of moral worth, begin?" But this question then forces one to ask a much more difficult and profound question, if arbitrary and utilitarian conclusions are to be avoided: "What is the essential nature of human life?" Hurlbut's ANT proposal draws on several philosophical and metaphysical concepts, such as "systems biology" and "active developmental trajectories," to help define the essential nature of human life at its earliest stages. The controversy that has resulted from his proposal, as well as the reluctance of many conservative Christian ethicists to embrace these proposals, may in part be due to the way these concepts challenge and stretch the normal "substance" ontologies that are so ingrained in our normal way of thinking about "being" and what it means to be human. The standard metaphysical categories are like old wineskins that will not hold the new wine of proposed technologies. Confusion over primary questions about the nature of being human will necessarily result in erroneous conclusions regarding many cutting-edge technologies being proposed and that may soon become reality.

Discussions on the nature of human life and what it means to be a human person have generally gravitated toward two poles of thought, substantialism and developmentalism. Substantialism advances the idea that the existence of the "substance" of a human being, i.e. a living organism possessing a human genome, defines the existence of a human person. Human beings and human persons are equivalent and are defined simply by virtue of what they *are*, independent of any potential further phases of development or developmental relationships. "The criterion for humanity, thus, was simple and all embracing: if you are conceived by human parents, you are human,"[4] is an elementary way to state the nature of human life from a substantialist perspective. This view, also called a "genetic" or "speciesist" view, has much appeal to many conservative thinkers and emphasizes an important biological aspect of humanness. It also underscores the important truth that the moral worth of all human persons is conferred by their nature as human beings. However, despite its many merits, this view suffers by seeming to reduce the concept of human being to a minimum of biological (molecular) attributes, a perspective which is both static and passive in nature, and ignores the dynamic and relational aspects of being human. While the concept of "substance" does underscore the "some-

[4]John T. Noonan, Jr., "An Almost Absolute Value in History," in *The Morality of Abortion: Legal Historical Perspectives*, ed. John T. Noonan, Jr. (Cambridge: Harvard University Press, 1970), 51.

thing" that endures over time, it must be expanded to take into consideration the dynamic and relational aspects of all entities.

This modern substantialist view can be traced back to René Descartes' misconstruction of substance as "that which exists by itself, that which needs nothing else but itself to exist."[5] Substance "in itself" is that unchanging substratum and primary ground of all attributes which makes "relations" ontologically secondary to, and subordinate to, substance. Aristotle, however, had an original concept of substance which allowed for a certain degree of dynamism and relation in that individual substances possessed within themselves the inherent principle governing all the changes and motions that are natural to them. Yet, ultimately, for Aristotle there is still an inward-looking orientation whereby a thing is defined by virtue of its inner structure and mechanism.[6] In the *Summa theologiae* I, Q. 29.4, St. Thomas Aquinas discusses the claim that "in God the individual—i.e., distinct and incommunicable substance—includes the idea of relation."[7] Drawing on Aquinas's teaching, the Catholic philosopher W. Norris Clarke, S.J., retrieves this pre-Cartesian notion of substance as a dynamic center of self-communication and relations, involving both acting and being acted upon. For Clarke, "to be real is to be a dyadic synthesis of substance and relation; it is to be substance-in-relation."[8] The Protestant philosopher C. Stephen Evans similarly states that human persons are substances which must be thought of and treated in dynamic fashion.[9]

At the opposite pole is the developmentalist perspective, which does not view human beings and human persons as equivalent. While an organism may belong to the species *Homo sapiens* by possession of appropriate genomic material, it does not become a human person until it possesses certain developmental and relational characteristics which, in consequence, also confer moral status such as the right to life. Human persons, in contrast to the substantialist perspective, are not what they *are*, but what they *become*. This view seems equally reductionistic as the substantialist view, as it treats the human being as merely a set of potentialities. What is lost is the substantial entity, the "something," that endures over time that cannot become anything else. It overlooks the significance of human biological embodiment, and shows a dualistic understanding of human life. Under various and somewhat arbitrary definitions of what constitutes "personhood," developmentalists divorce the biological component (human life) from the human "person" (human being).

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[5]René Descartes, quoted in W. Norris Clarke, "To Be Is To Be Substance-in-Relation," in *Metaphysics as Foundation: Essays in Honor of Ivor Leclerq*, ed. Paul A. Boggaard and Gordon Treash (Albany, NY: State University of New York Press, 1993), 171.

[6]See Carver T. Yu, *Being and Relation: A Theological Critique of Western Dualism and Individualism* (Edinburgh: Scottish Academic Press, 1987), chap. 4.

[7]Thomas Aquinas, *Summa theologiae*, I, Q. 29.4, reply 3. The translation is from Aquinas, *Summa Theologica*, trans. Fathers of the English Dominican Province (Westminster: Christian Classics, 1981).

[8]W. Norris Clarke, "To Be Is To Be Substance-in-Relation," 166.

[9]C. Stephan Evans, "Human Persons as Substantial Achievers," *Philosophia Reformata* 58.1(1993): 108.

While both the substantialist and developmentalist perspectives contain grains of truth and insight into the nature of human life, both suffer from reductionistic tendencies that ignore important aspects of what it means to be human. Unfortunately, arguments surrounding the nature of human life and its beginning have usually been couched in terms of one of these two polarities. But is there an alternative that can do justice to the insights of both perspectives? This may require a reexamination of the metaphysical nature of reality from the ground up, one that provides an alternative to many of the enlightenment presuppositions we have unconsciously inherited. One such alternative is that proposed by the American philosophical theologian, Puritan, and New England pastor Jonathan Edwards (1703–1758). Sang Hyun Lee has called Jonathan Edward's philosophical theology a "thoroughgoing metaphysical reconstruction, a reconception of the nature of reality itself."[10] This reconstruction is a move from a view of reality as "substance and form"[11] to a "dynamic network of dispositional forces and habits."[12]

For Jonathan Edwards, habits and laws are the abiding principles of being. In his *Miscellanies No. 241*, Edwards states that a soul's essence "consists in powers and habits,"[13] and elsewhere that "it is laws that constitute all permanent being in created things, both corporeal and spiritual."[14] In other words, "things" (all created entities, corporeal and spiritual, sentient and non-sentient) do not *have* habits, but *are* habits and laws (habits are but dispositions of sentient beings).[15] While using a number of different terms for "habit" (*habitus*) throughout his writings, including disposition, tendency, propensity, principle, temper, frame of mind, acquired tendency, or innate disposition, his most concise definition occurs in *Miscellanies No. 241* where he states that "All habits [are] a law that God has fixed, that such actions upon such occasions should be exerted."[16] Edwards goes on to give "habit" a realistic (as opposed to nominalistic) and relational definition. This definition is realistic in that it is not mere custom or regularity of events, but is an ontologically

[10]Sang Hyun Lee, *The Philosophical Theology of Jonathan Edwards* (Princeton: Princeton University Press, 1988), 3.

[11]Ibid., 4.

[12]Ibid., 77. Edwards is neither the first nor the last to develop an ontology of "disposition," but he does hold a unique position in the history of ideas as a profound and decidedly Christian philosophical theologian engaging with the origins of enlightenment thought in this country.

[13]Jonathan Edwards, *The Works of Jonathan Edwards,* vol. 20, *The Miscellanies (A–500),* ed. Thomas A. Schafer (New Haven, CT: Yale University Press, 1994), 358.

[14]Jonathan Edwards, "Subjects to be Handled in the Treatise on the Mind, No. 36," in Jonathan Edwards, *The Works of Jonathan Edwards,* vol. 6, *Scientific and Philosophical Writings*, ed. Wallace Anderson (New Haven, CT: Yale University Press, 1980), 391.

[15]For Edwards even the very being of God is to be exclusively understood in terms of law-like dispositions and nexuses of dispositions. See Wallace Anderson, "Editor's Introduction," in Edwards, *Works* 6: 8–9, 13–17, 57–58.

[16]Edwards, *Works* 20: 358.

abiding power that possesses a mode of reality even when it is not exercised. The actual existence of a thing is the result of the continuing and immediate exercise of God's own power exercised "according to certain fixed and exact established methods and laws" which are "constant and regular" and ontologically real apart from their manifestation in actual events or actions.[17]

Edwards develops this dispositional ontology while refuting materialism early in his philosophical and scientific writings. In his essay "Of Atoms,"[18] Edwards begins by defining an "atom" (i.e., the fundamental nature of matter, not our modern notion of an atom) as a body that cannot be made less, or whose parts cannot by finite power whatsoever be separated from one another. "Solidity" thereby comes to mean impenetrability or indivisibility which is the *activity of resisting* annihilation, or of persevering to be. Since being and persevering to be are the same things, solidity or resistance is the very being of an atom (solidity is not just a quality but the very being, and solidity is an *activity*). Since annihilation is resisted by all finite forces, this resistance must be infinite power. This can only be the infinite power of God. Indeed, Edwards goes on to maintain that resistance or existence must be the very activity of God:

> All body is nothing but what immediately results from the exercise of divine power in such a particular manner … The certain unknown substance, which philosophers used to think subsisted by itself, and stood underneath and kept up solidity and all other properties, which they used to say it was impossible for a man to have an idea of, is nothing at all distinct from solidity itself; or, if they must needs apply that word to something else that does really and properly subsist by itself and supports all properties, they must apply it to the divine Being or power itself … So the substance of bodies at last becomes either nothing, or nothing but the Deity acting in that particular manner in those parts of space where he thinks fit.[19]

Matter does not even exist as independent substance: "No matter is, in the most proper sense, matter."[20] Bodies are God's actions, which are executed according to the divinely established rules (or habits).[21] Wallace Anderson, commenting on this view of Edwards, notes that "Edwards's predecessors thought of substance as the

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[17]Jonathan Edwards, "The Mind," in Edwards, *Works* 6: 344. Wallace Anderson has remarked that "Nothing is more apparent in [Edwards'] theory of supposed existence than that Edwards conceives general laws of nature to be ontologically prior to the objects and events of the world." ("Editor's Introduction," 109.) For Edwards, habit is also the disposition of the perceiving mind. It functions for Edwards as the principle of knowing; i.e., the propensive power of the imagination's synthesizing activity through which the mind's apprehension of the relational structure of reality becomes possible.

[18]Edwards, *Works* 6: 208–218.

[19]Ibid, 215.

[20]Jonathan Edwards, "Things to be Considered and Written Fully About, No. 26," in Edwards, *Works* 6: 235.

[21]Modern physics may have unwittingly rediscovered, in a certain sense, a fundamental truth of Edwards's dispositional view. If you ask a physicist to describe a hydrogen atom,

owner of properties, while Edwards thought of substance as the doer of deeds."[22] Dispositions (habits and laws) are not merely secondary qualities of "being," but form the very structure of "being" itself.

While Edwards never wrote on or envisioned the implications of his dispositional ontology for questions surrounding the beginnings of human life, his thoughts may provide a means to overcome the polarities of substantialist and developmentalist perspectives. A dispositional ontology would collapse the categories of substance and relational/developmental qualities into a single category.[23] What an organism *is* and what it *becomes* are never two separate, completely distinguishable categories. If the essence of an entity is an active disposition to a type of action (e.g., a specific developmental trajectory) and relation, then that entity would be fully actual when its dispositional essence, as determined by its genetic identity, is exerted in actual actions (a developmental trajectory) and relations of a certain kind. According to a dispositional ontology, both human genetic identity *and* active potential and capacity (an inherent disposition for a given trajectory of development) would define the *single* essential nature of a unique human being.[24]

The language and philosophical perspective derived from this form of dispositional ontology is very similar to and supportive of the language of "potential" and "process" that Hurlbut has proposed in defense of the concept of ANT, and may provide a powerful metaphysical justification for the ANT proposal. The language is also complementary to many of the aspects of systems biology (which views the living organism as a whole, a dynamic and relational network of interdependent and integrated parts).[25]

One of the difficulties in evaluating a proposal like ANT is that it stretches the limits of our categories and definitions of human life. If one takes the view that a

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he or she is unlikely to draw a picture showing a proton nucleus and an electron orbit or electron cloud. He or she will rather, at least since Erwin Schrödinger, describe it according to an equation of the form $\Psi_{1s} = \Pi^{-0.5} \{Z/a_0\}^{1.5} e^{-\sigma}$ (for the electron only, in the ground state). But an equation is nothing more than a relational law that describes a disposition "that such actions upon such occasions should be exerted." (Edwards, *Works* 20: 358.)

[22]Anderson, "Editor's Introduction," 67.

[23]For Edwards, this single category becomes essentially "beauty," which he defines as nothing else but proportion in relation. Lee sees also a collapsing of the Thomistic-Aristotelian categories of substance and accident in Edwards's thought. Lee expands on this idea in his *Philosophical Theology of Jonathan Edwards*, 77–82.

[24]While somatic cells have genetic identity to human beings (they have a latent potency and capacity such as exists in all raw materials), they do not possess an inherent active biological disposition (active potency and capacity) for further development into a unique human being. Somatic cell nuclear transfer (cloning) artificially confers such an active potency and capacity on a somatic cell, resulting in a unique human being.

[25]The term "organism as a whole" is a biological concept that refers not to the whole organism (i.e., the sum of its parts), but to that set of vital functions of integration, control, and behavior that is greater than the sum of the parts of the organism. Implicit in this concept is the primacy of the functional unity of the organism. For overviews of systems biology, see Hiroaki Kitano, "Systems Biology: A Brief Overview," *Science* 295.5560 (March 1, 2002): 1662–

disposition to a certain trajectory of development is a "secondary" or "accidental" quality, then it would be difficult to envision how the modifications proposed by ANT would result in anything other than a "damaged" or "terminal" human being. This is one of the major criticisms of many conservative Christian ethicists regarding the ANT proposal, and should be taken very seriously. But if a disposition to a human developmental trajectory is taken to be of the "essence" of the nature of being human, then the ANT proposal may, in certain manifestations, be viewed as morally licit by those who view all human life, from its inception onward, to be sacred and inviolable, since the product of ANT would not be, nor would it ever have been or ever become, a human being.

This brings up two important qualifications. First, most of the discussion in the literature regarding ANT has focused on one particular example, the Cdx2 modification.[26] The Cdx2 gene is crucial for the differentiation of the trophectoderm which, while necessary for embryogenesis, is claimed to be a source of extraembryonic membranes, not embryo tissue.[27] While technically feasible, this may have been an unfortunate (and ethically controversial) example put forward to demonstrate the scientific possibilities of ANT. But the Cdx2 gene modification, as a specific example and thought experiment, is not the crux of the proposal or the central issue. What is important is the overall concept and approach to the problem as a starting

1664. For excellent discussions of the concept as applied to beginning of life issues, see Nicanor P. G. Austriaco, "On Static Eggs and Dynamic Embryos: A Systems Perspective," *National Catholic Bioethics Quarterly* 2.4 (Winter 2002): 659–683; Nicanor P. G. Austriaco, "Immediate Hominization from the Systems Perspective," *National Catholic Bioethics Quarterly* 4.4 (Winter 2004): 719–738.

[26]For example, see Douglas A. Melton, George Q. Daley, and Charles G. Jennings, "Altered Nuclear Transfer in Stem Cell Research—A Flawed Proposal," *New England Journal of Medicine* 351.27 (December 30, 2004):2791–2792.

[27]One of the major ethical critiques of this particular proposal is suggested by experiments in mice with multiple tissue blastocyst reconstitution. (See, for example, R. L. Gardner, S. C. Barton, and M. A. H. Surani, "Use of Triple Tissue Blastocyst Reconstitution to Study the Development of Diploid Parthenogenetic Primitive Ectoderm in Combination with Fertilization-Derived Trophectoderm and Primitive Endoderm," *Genetical Research* 56.2–3 [October–December 1990]: 209–222. This study showed that parthenogenetic mouse fetuses could live longer when placed into trophectoderm tissue which contained some normal trophectoderm cells.) Such studies suggest that a developing embryo with a defective trophectoderm can be "rescued." With ANT, the supposition is that the inner cell mass of a blastocyst produced by Cdx2-alteration would be able to be placed into a normal trophectoderm and thereby live. After implantation, the resulting reconstituted blastocyst (normal trophectoderm + ANT-derived inner cell mass) could develop normally, eventually to birth and beyond, therefore strongly suggesting that the ANT-derived blastocyst should be considered a true embryo. But one can also question whether conceptualizing the inner cell mass as "embryonic," and the trophectoderm as "extra-embryonic" (and not an intrauterine developmental organ of the embryo itself) is merely semantic. By reconceptualizing the the trophoblast and inner cell mass as constituting the organism as a whole, the above argument involving the "rescue" of an "embryo" by blastocyst reconstitution does not hold.

point for discussion. Specific examples will have to be justified individually, with respect to both their scientific and their ethical merits.

Second, the morally licit nature of the ANT proposal rests on the assumption that fully potent human embryos are not subsequently altered or damaged in such a way as to change their specific developmental trajectory, even if it did not result in the death of the organism. For instance, one may envision a process whereby a normal, developing embryo was altered genetically or environmentally, resulting in aborted development but continuing with limited cellular growth and reproduction, akin to an immortal cell line. In this case the inherent disposition of the organism is altered artificially, and this would be equivalent to the death of the organism itself. The ANT proposal has always maintained that alterations to nuclear material would occur before transfer into an oocyte, such that entities produced are from their *inception* (ab initio), from their very beginning, lacking the substantial and dispositional nature of human beings. Human embryos are not produced and altered in such a procedure; they are not produced at all.

Both the technology of ANT and the metaphysics of dispositional ontology represent new and speculative ways to think about the nature of being human, and present new perspectives for evaluating the ethical ramifications of modern genetic technologies. Both the science and technology of ANT and the metaphysics of dispositional ontology also raise many questions that must be answered in tandem before coming to firm conclusions regarding the scientific and moral worth of these proposals. For instance, what are feasible limits and possibilities of ANT to generate the necessary and coveted stem cell lines? Can these proposals be tested accurately in animal models and transferred safely to human cell lines without jeopardizing human embryos? What are the minimal degrees of cellular alteration necessary to permanently alter the inherent active disposition for organized growth and development? And finally, given that even partial hydatidiform moles can have partial, albeit limited, initial developmental trajectories, what defines the outer limit for a truly human developmental trajectory?[28] These questions will admittedly be both difficult and expensive to answer. But a door has been opened by the passage of Proposition 71 by California voters allowing the bypass of federal restrictions on funding for embryonic stem cell research, and by the legislative activity that is now occurring in other states to follow suit with similar proposals. These events make the pragmatic need for creative, imaginative, and morally unproblematic alternatives to the destruction of human embryos for utilitarian purposes an extremely high priority for Christian scientists, legislators, theologians, and ethicists. Neither local or federal funding restrictions, nor diversion of funds toward adult stem cell programs (despite the very real and clinically relevant promises of this avenue of research) will stem the tide of public support for and willingness to fund embryonic stem cell research.

[28]J. Huarte and A. Suarez suggest that spontaneous fetal motility would define the minimal developmental potentiality of a human embryo ("On the Status of Parthenotes: Defining the Developmental Potentiality of a Human Embryo," *National Catholic Bioethics Quarterly* 4.4 [Winter 2004]: 755–770).

Whatever the merits or faults of the ANT proposal, Hurlbut has provided us with a unique model of ethical reasoning. Instead of responding to current technological advances with retrospective ethical evaluations and judgments, with the usual attempt to find moral patterns of thought to justify foregone conclusions, Hurlbut is providing a constructive scientific proposal that begins with specific moral constraints, that life begins at conception and needs to be protected. The ultimate importance of the ANT proposal is not so much in the specifics of the science or technology, but in the constructive dialogue it will engender over the nature and beginning of human life, with a commitment to the belief that legitimate scientific goals can be achieved within the constraint of the utmost sanctity of all human life. The care one gives to these questions, and the priority one gives to the protection of all human life, will have immediate and far-reaching consequences for our society and culture that will transcend the mere material and utilitarian promises of stem cell research itself.