An Overview of Chimeras and Hybrids

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The Science of Chimeras and Hybrids: Combining Humans and Nonhumans

What Are Chimeras and Hybrids?

The ancient Greeks used the term *chimera* to refer to a mythical creature with a lion's head, a goat's body, and a serpent's tail.[1] Other chimeras included the faun (part man, part goat) and the minotaur (part man, part bull). Many chimeras inspired fear; for example, the minotaur lived in a labyrinth of caves and ate the flesh of men. Today, the word *chimera* evokes different fears, involving the ethical ramifications of experiments mixing humans and other species. There are two types of interspecies mixes: hybrids and chimeras.

A *hybrid* is the product of breeding two different species (via normal copulation or in vitro fertilization). Each cell in the hybrid's body has a mixture of nuclear genes from both of the parents. When interspecies hybrids are produced, many of them have serious genetic anomalies, are born sterile, or do not survive to birth. Mules, a cross between a female horse and a male donkey, are sterile.[2] The fact that

[1] W. H. D. Rouse, *Gods, Heroes, and Men of Ancient Greece* (New York: New American Library, 2001), 159.

[2] Other hybrid examples are male horse x female donkey (hinny); female horse x zebra male (zebrorse); female donkey x zebra male (zebronkey); all are sterile. S. M. Hopkins and G. C. Althouse, "Reproductive Patterns of Horses," in *McDonald's Veterinary Endocrinology and Reproduction*, 5th ed., ed. M. H. Pineda (Ames: Iowa State Press, 2003), 428.

horses and donkeys can procreate despite the species difference is probably because of their genetic similarity, and because the number of chromosomes that they have is fairly close (sixty-four for a horse and sixty-two for a donkey[3]).

In fertilization between members of the same species, when a cell in the embryo divides, each new cell ends up having the same number of chromosomes as any somatic cell in the body of either of the parents. However, problems occur when two different species (with two different chromosome numbers) breed. During mitosis (cell division), when the embryonic somatic cells divide, each daughter cell ends up having a different number of chromosomes than the original somatic cells of each of the parents. Such breedings often result in embryonic abnormalities, placental incompatibilities, or abnormal feto-maternal interactions, and usually end in miscarriage.[4] If the offspring survives to term, it will probably have a different appearance from the parents and will probably be sterile. In nature, the chemical composition of the zona pellucida (a coating around the oocyte) generally prevents the union of oocyte and sperm from two different species, so many such interspecies crosses do not occur. With in vitro fertilization, however, the zona can be digested by enzymes, allowing for laboratory interspecies fertilizations.[5]

A *chimera* also consists of a combination between two different species. However, the genes of the two species do not combine within the organism as with a hybrid. Rather, the cells in the body of a chimera are a mosaic of cells of different species.[6] One way of producing an interspecies chimera is through in vitro manipulation of an embryo: during the first stages of cell division of the embryo, an embryonic cell from one species is inserted into the blastocyst of the other species. The introduced cell becomes part of the blastocyst without fusing its genetic material with the other cells. The blastocyst cells (including the introduced cell) continue to divide, and a complete organism is formed, with the different species' cells in a variegated pattern throughout the body. Sheep-goat chimeras (known as geeps) have been created this way by combining embryonic cells from sheep and goats at the blastocyst stage.[7]

Morally Legitimate Chimeras

Chimeras of different types of mice are produced routinely in research laboratories as part of the process of creating transgenic mice (mice designed to have a specific

[3] M. H. Pineda, "The Biology of Sex," in *McDonald's*, 203.

[4] Ibid., 229; Hopkins and Althouse, "Reproductive Patterns of Horses," 429; M.H. Pineda, "Reproductive Patterns of Sheep and Goats," in *McDonald's*, 446.

[5] Pineda, "Biology of Sex," 226–229.

[6] Chimeras can also be formed (both artificially and naturally) between male cells and female cells of the same species (commonly known as hermaphrodites), or by the fusion of two zygotes. See Patricia Tippett, "Human Chimeras," in *Chimeras in Developmental Biology*, eds. Nicole Le Douarin and Anne McLaren (Orlando, FL: Academic Press, 1984).

[7] Pineda, "Reproductive Patterns of Sheep and Goats," 446; and Dashka Slater, "Humouse," *Legal Affairs* 1.4 (November-December 2002): 20–28.

gene of interest either expressed or knocked out). A mouse embryonic stem (ES) cell is first genetically modified (sometimes to contain a human gene of interest) and grown in vitro. One or more of these ES cells are introduced into a blastocyst-stage embryo of another mouse (usually one that possesses a different coat color). The new ES cell is integrated into the blastocyst, and the blastocyst is placed into a female mouse's uterus to grow. The offspring is a chimeric mouse (chimeric between the two mouse species) with variegated cell composition and coat color, showing that the ES cell has integrated successfully. In some of the offspring, the transgenic ES cells will have integrated into the germ-cell line (oocytes and sperm) of the mouse, meaning the transgenic properties can then be transmitted to new offspring through normal breeding (which is the final goal of the process).[8] This seems a morally legitimate type of chimera creation, as it generally involves only a single human gene of interest (which does not significantly affect the animal's identity as an animal), and is utilized primarily as a research tool for studying human diseases (or animal diseases which are similar to those of humans).

This type of morally legitimate technique is used to produce animal "bioreactors" as well. This has also been called "molecular pharming." Essentially, ES cells of farm animals (sheep, cattle, pigs, goats, and rabbits) are genetically modified to produce a particular desired (sometimes human) protein in their milk. The modified transgenic ES cells are integrated into another blastocyst, and chimeras are produced as described above. Once the transgenic ES cells have been integrated into the germ-cell line successfully, the offspring can produce the desired protein in their milk, and the milk can be purified to extract the protein of interest. Some instances in which this technique has worked successfully include the creation of sheep that express human clotting factor IX (used in treating human hemophilia); rabbits and goats that produce tissue plasminogen activator (used in treating heart attacks and stroke); goats that produce antithrombin III (used in treating congenital antithrombin III deficiency); sheep that produce human alpha-1-antitrypsin (used in treating alpha-1-antitrypsin deficiency, which can lead to emphysema) and clotting factor IX; and pigs that produce protein C (used in treating congenital protein C deficiency, which causes abnormal blood clotting).[9]

The term *chimera* can also be used to describe an organism that has received a genetically different organ or cell transplant and thus has cells of differing origins in its body.[10] Transplanting animal organs or cells into a human being can be considered a morally legitimate use of chimera technology if the transplant does not change the person's identity in any way. Specifically, the transplant should not significantly change the human being's brain or gametes. The practice of transplanting human cells or organs into an animal, especially in order to study and improve the growth of

[8] Richard M. Twyman and Bruce Whitelaw, "Genetic Engineering: Animal Cell Technology," in *Encyclopedia of Cell Technology*, vol. 2, ed. Raymond E. Spier (New York: John Wiley and Sons, 2000): 803–805.

[9] Ibid., 808–809; R. A. Bowen, "Embryo Transfer in Domestic Animals," in *McDonald's*, 567–569.

[10] Biagio John Melloni, ed., *Melloni's Illustrated Medical Dictionary*, 2nd ed. (Baltimore: Williams and Wilkins, 1985).

the transplants for the purpose of later treating human wounds or disease, can also be morally legitimate. However, this can extend into morally illicit territory if the human cells and organs affect the animal brain in a way that brings about some form of human consciousness. The transplantation of human gametes into animals for the purpose of experimenting with bi-species fertilization would also be morally illicit. The reasoning behind these conclusions is discussed later in this essay.

Genetic Similarities among Primates

If the gametes of a human and those of a species with a very different number of chromosomes were mixed in vitro, it is highly unlikely that fertilization would occur or that an embryo would even develop to the fetal stage. However, the combination of gametes from humans and *nonhuman primates* to make a hybrid would be of greater concern. Nonhuman primates, especially chimpanzees and gorillas, are the type of organism most genetically similar to humans. Also, their chromosome number is close, so theoretically there could be fewer problems with chromosome allocation during mitosis: humans have forty-six chromosomes, while chimpanzees and gorillas have forty-eight. The creation of a human-animal (especially primate) chimera at the embryonic or fetal stage would also be ethically problematic, especially if the chimerism involved transplantation of brain or gonadal cells.

There are, nonetheless, significant differences between nonhuman primates and humans. Although it has been estimated that the genomes of humans and chimpanzees are approximately 98 to 99 percent genetically similar,[11] this claim is misleading for several reasons. When DNA or protein sequences are compared, percentages are commonly used to denote the differences. Scientists find percentages useful because they are a precise, numerical way of denoting difference. However, their use does not necessarily always denote accuracy or reflect reality fully. A percentage is a "scalar, one-dimensional" measure; a body part produced by genes is a "three-dimensional entity."[12] A quantitative percentage in difference between interspecies stretches of DNA or protein does not reveal the qualitative differences in physiology, behavior, and intelligence which are produced by the DNA (all of which are significantly different between man and chimp).

Despite the interspecies DNA differences, chimps and gorillas are still the most genetically similar organisms to humans. If the gametes of a human and a chimp were mixed, genetic fusion seems more likely than if the gametes of a pig and a human were mixed. Already, "cybrid" (cell hybrid) cell lines have been made between somatic cells of humans and chimpanzees and between somatic cells of humans and gorillas.[13]

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[11] M.-C. King and A. C. Wilson, "Evolution at Two Levels in Humans and Chimpanzees," *Science* 188.4184 (April 11, 1975): 107–116.

[12] Jonathan Marks, *What It Means To Be 98% Chimpanzee: Apes, People, and Their Genes* (Berkeley: University of California Press, 2002), 24.

[13] Antoni Barrientos, Lesley Kenyon, and Carlos T. Moraes, "Human Xenomitochondrial Cybrids: Cellular Models of Mitochondrial Complex I Deficiency," *Journal of Biological Chemistry* 273.23 (June 5, 1998): 14210–14217.

There have been recent experiments creating a number of human-animal chimeras, as well as experiments involving cloning techniques that use the gametes of humans and animals.[14] One of the latter studies was celebrated in the mainstream media by some scientists as "a big advance";[15] however, ethical examinations of this and the other experiments were rarely made in the mainstream press.

An Ethical Analysis of Human-Animal Chimeras and Hybrids

Dignity of Chimeras and Hybrids

The combination of humans with animals at an intimate level has been discussed as a concern at least since the writing of the Old Testament.[16] It has been of particular concern in recent years because of advances in genetic manipulation, in vitro fertilization, and cloning techniques, which make human-animal combinations easier to create in the laboratory.

Many animal research models containing human genes have been created by scientists over the last couple of decades. Most of these are considered morally licit. For example, the "OncoMouse," a transgenic mouse exhibiting a human cancer gene, was patented in 1988 by Harvard researchers and is used for cancer research.[17]

One would presume that at some point, human-nonhuman transgenic organisms with enough humanness would be considered human enough to be accorded a certain level of human dignity. Organisms which possess a particularly human phenotype or exhibit certain human behaviors would seem to be worthy of increased respect. One would not know for certain if a human soul had been infused at any point into the chimeric entity, but if the chimera showed evidence of humanness, it seems that one should assume that perhaps a human soul has been infused, and treat it accordingly.

Some, however, would deem human-animal organisms to be a lower order of being, not worthy of full respect or dignified treatment. Joseph Fletcher, an educator and theologian, wrote with enthusiasm about creating human-nonhuman chimeras to perform societal drudge-work:

[14] Ying Chen et al., "Embryonic Stem Cells Generated by Nuclear Transfer of Human Somatic Nuclei into Rabbit Oocytes," *Cell Research* 13.4 (August 2003): 251–263.

[15] Rick Weiss, "Cloning Yields Human-Rabbit Hybrid Embryo," *Washington Post*, August 14, 2003, A4.

[16] See Exod. 22:18, Deut. 27:21, Lev. 20:15–16, and Lev. 18:23 ("You shall not have carnal relations with an animal, defiling yourself with it"). All scriptural quotations are from the *New American Bible*, St. Joseph Edition (New York: Catholic Book Publishing, 1992).

[17] Slater, "Humouse"; and Mark Dowie, "Gods and Monsters," *Mother Jones* (January–February 2004), http://www.motherjones.com/news/feature/2004/01/12_401.html.

> Chimeras or parahumans might legitimately be fashioned to do dangerous or demeaning jobs. As it is now, low-grade work is shoved off on moronic ... individuals, the victims of uncontrolled reproduction. Should we not "program" such workers thoughtfully instead of accidentally, by means of hybridization?[18]

Some activists have tried to take it into their own hands to prevent the creation of human-animal chimeras. In 1997, biologist Stuart Newman and economist and biotechnology critic Jeremy Rifkin submitted a patent application for certain laboratory-created human-animal chimeras.[19] Their aim was not to actually create the chimeras; rather, they wanted to hold the twenty-year patent on such research in order to keep others from attempting to create and patent such creations.[20] The patent office rejected their application numerous times; each time, Newman's lawyers were able to argue it back to life.[21] One continuing objection by the patent office was that the chimera would be too "human." The Thirteenth Amendment against slavery means that no human being can be owned (and thus, no human being can be patented). Newman's case was rejected for the final time in August 2004, and Newman and Rifkin allowed the six-month appeal period to lapse in February 2005.[22]

Dr. Leon Kass, former chairman of the President's Council on Bioethics, has written of the "wisdom of repugnance" in analyzing human cloning: "Revulsion is not an argument ... In crucial cases, however, repugnance is the emotional expression of deep wisdom, beyond reason's power fully to articulate it.... Shallow are the souls that have forgotten how to shudder."[23] Perhaps such is also the case with instinctual repugnance at human-animal combinations. In 2004, the council published *Reproduction and Responsibility*, in which it advises prohibiting "the production of a hybrid human-animal embryo by fertilization of human egg by animal sperm or of animal egg by human sperm" and the transfer of a "human embryo into the

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[18] Joseph Fletcher, *The Ethics of Genetic Control: Ending Reproductive Roulette* (New York: Anchor Press/Doubleday, 1974), 173.

[19] Slater, "Humouse"; and Dowie, "Gods and Monsters."

[20] Newman "has grave concerns about genetically manipulating human embryos," because he believes it could lead to designer babies (which he dubs "yuppie eugenics") and the creation of human clones. Interestingly, he claims, "I'm pro-choice.... I don't want to valorize the embryo in any way. But I think it's damaging to the human community to get into a mindset where you can produce human embryos for any purpose." Slater, "Humouse."

[21] For example, "when the agency objected to using human embryonic cells to help create a chimera, ... Newman's lawyers pointed out [that] it is legal to abort 100-percent-human embryos, and would make no sense to grant part-human embryos greater protection." Dowie, "Gods and Monsters."

[22] Rick Weiss, "U.S. Denies Patent for a Too-Human Hybrid," *Washington Post*, February 13, 2005, A3.

[23] Leon R. Kass, "The Wisdom of Repugnance," in Leon R. Kass and James Q. Wilson, *The Ethics of Human Cloning* (Washington, DC: AEI Press, 1998), 17–19.

body of any member of a nonhuman species."[24] The report states emphatically that "an ex vivo human embryo ... belongs *only* in a *human* uterus."[25]

The National Academies Press published their *Guidelines for Human Embryonic Stem Cell Research* in 2005, in which they gave recommendations for various types of human embryonic stem cell research. The (secular) authors favor human embryonic stem cell research (which destroys human embryos) in many cases. However, they state that

> research in which hES [human embryonic stem] cells are introduced into nonhuman primate blastocysts, or in which animal … ES cells are introduced into human blastocysts, should … not be conducted at this time. These kinds of studies could produce creatures in which the lines between human and nonhuman primates are blurred, a development that could threaten to undermine human dignity. Finally, … hES cells introduced into nonhuman hosts might be able to generate gametes, so any such human/nonhuman chimeras should not be allowed to breed.[26]

The authors recognize that the creation of certain human-animal chimeras is fraught with ethical danger.

Identity Change

The Pontifical Academy for Life, in *Prospects for Xenotransplantation* (which can be used for guidance regarding human-animal chimeras and hybrids, since it considers the related issue of interspecies organ and tissue transplantation), considers any change in "personal identity" to be a major criterion in analyzing the morality of interspecies transplants: "in general, the implantation of a foreign organ into a human body finds an ethical limit in the degree of change that it may entail in the identity of the person who receives it."[27] For example, xenotransplantation of monkey hearts and kidneys into human bodies has been done numerous times since 1963[28] and is considered morally legitimate, because it is generally acknowledged that it does not

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[24] President's Council on Bioethics, *Reproduction and Responsibility: The Regulation of New Biotechnologies* (Washington, DC: President's Council on Bioethics, 2004), 221. Available online at http://www.bioethics.gov/reports/reproductionandresponsibility/_pcbe_final_reproduction_and_responsibility.pdf.

[25] Ibid., 220 (original emphasis).

[26] National Academies, *Guidelines for Human Embryonic Stem Cell Research* (Washington, DC: National Academies Press, 2005), 55.

[27] Pontifical Academy for Life, *Prospects for Xenotransplantation: Scientific Aspects and Ethical Considerations* (September 26, 2001), n. 10; reprinted in *The National Catholic Bioethics Quarterly* 2.3 (Autumn 2002): 481–505. The Pontifical Academy for Life considers "personal identity" to be "the relation of an individual's *unrepeatability* and *essential core* to his *being* a person (ontological level) and *feeling* that he is a person (psychological level)" (n. 10, original emphases).

[28] "A History of Xenotransplantation Experiments," *Frontline,* PBS, online program materials for "Organ Farm"(aired March 27, 2001), http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/etc/cron.html.

change individual identity. However, some organs in the human body, "such as the encephalon [brain] and the gonads [ovaries or testes], are indissolubly linked with the personal identity of the subject because of their specific function."[29] Thus, *Prospects* states that human-animal interspecies transplants of brains or gonads (for the purposes of procreational transmission of identity) cannot be morally licit.[30]

There are also some genes which could be inserted between species that would change an organism's identity, and others that would not. Likewise, there is a difference between performing interspecies transplantation when the recipient is an adult and inserting cells into a recipient at an embryonic or fetal stage. With the latter comes the real possibility of alteration of the individual's identity. Animal experiments have shown that, because cells at these stages of life are highly plastic in nature and because the architecture of the body (including the brain) is still in development, an introduced cell and its progeny can be incorporated into the embryo in a seemingly random fashion.[31] One cannot say with certainty if the identity of a chimeric individual who received transplanted cells at an early stage has been significantly changed, but the likelihood is that it *has*, because of the highly formative time frame of introduction of the cells.

A July 2005 article in *Science* by a large group of researchers evaluated the moral issues involved in the grafting of human neural stem cells into nonhuman primates. They stated that "the issue … is the extent to which human/NHP [nonhuman primate] neural grafting might change capacities in a way that changes moral status."[32] They stated specific concerns regarding time of engraftment:

> We … expect that the potential for [human] engrafted cells [into nonhuman primates] to have significant functional influence will be markedly greater for engraftment at very early stages of development than for engraftment into the established architecture of adult brains. Although neural progenitor cells engrafted into the neonatal primate brain disseminate widely and integrate throughout the brain, the mature primate brain tends to resist incorporation of engrafted cells.[33]

Thus, the time of engraftment is acknowledged to be an important factor in the evaluation of ethicality of certain chimeric experiments.[34]

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[29] Pontifical Academy for Life, *Prospects*, n. 11.

[30] Ibid., note 61. An exception is given only for gonad transplants performed to "restore a sufficient hormonal function," and only if the "integrity of the subject's personal identity has been ensured" and a "disassociation [of the procedure] with procreation has been established."

[31] See Twyman and Whitelaw, "Genetic Engineering" 804–805; Pineda, "Reproductive Patterns of Sheep and Goats," 446; and Graça Almeida-Porada and Esmail D. Zanjani, "A Large Animal Noninjury Model for Study of Human Stem Cell Plasticity," *Blood Cells, Molecules, and Diseases* 32.1 (January–February 2004): 80.

[32] Mark Greene et al., "Moral Issues of Human–Non-Human Primate Neural Grafting," *Science* 309.5733 (July 15, 2005): 385.

[33] Ibid., 386.

[34] The biggest concern of Greene et al. was experiments in which human neural stem cells are transplanted into animals that are closely related to the human species and which are done at an early developmental stage of the animal. They said that "experiments of great-

Recent Research

Various types of human-animal interspecies experiments have been published in the last few years. Several of these experiments consisted of growing human cells in immature animals, creating chimeric organisms. One group, as reported in a number of published studies, injected human stem cells from adult bone marrow into fetal sheep. They found that the cells were distributed throughout the sheep's body and differentiated into human blood, liver, skin,[35] and heart cells.[36] Another group injected human stem cells from adult bone marrow into fetal pigs and found human cells throughout the pigs' blood. Fused pig-human cell hybrids were also found in the epithelium.[37] Another team discovered that human blood cells from umbilical cords injected into the livers of immunodeficient newborn mice led to the development of human immunological cells and lymph nodes in the mice.[38] None of these studies mentioned whether human cells differentiated into brain cells or human gametes in the animals, either of which could be ethically problematic. However, it could be that the brains and gonads were simply not dissected for this information.

Some experiments had the specific purpose of transplanting human stem cells into the brains of other animals. Researchers in Germany transplanted stem cells from human cord blood into adult rat brains.[39] The human stem cells were found to differentiate into neuron-like cells inside the rat brain, and had disseminated widely throughout the brain. The human cells could be detected in the rat brains up to three months post-transplantation. Another group, led by Eugene Redmond, professor of

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est concern are those in which human neural stem cells are engrafted into the developing brains of great apes and constitute a large proportion of the engrafted brain. On the basis of this concern, and on doubts about scientific merit, some of us believe that engraftment of human neural cells into great apes should not be permitted, particularly early in neural development." Ibid.

[35] Almeida-Porada and Zanjani, "Large Animal Noninjury Model," 80; and Sylvia Pagán Westphal, "'Humanised' Organs Can be Grown in Animals," *NewScientist.com* (December 17, 2003), http://www.newscientist.com/article.ns?id=dn4492.

[36] Judith A. Airey, "Human Mesenchymal Stem Cells Form Purkinje Fibers in Fetal Sheep Heart," *Circulation* 109.11 (March 23, 2004): 1401–1407.

[37] Gaia Vince, "Pig-Human Chimeras Contain Cell Surprise," *NewScientist.com* (January 13, 2004), http://www.newscientist.com/article.ns?id=dn4558; Brenda M. Ogle et al., "Spontaneous Fusion of Cells between Species Yields Transdifferentiation and Retroviral Transfer in Vivo," *FASEB Journal* 18.3 (March 2004): 548–550. The pig-human cell hybrids exhibited both human and pig surface markers and contained chromosomal DNA coding for both human and pig genes.

[38] Steven Reinberg, "Scientists Create Mice with Human Immune Systems," *HealthDay* (April 1, 2004), http://www.healthday.com/printer.cfm?id=518212; Elisabetta Traggiai et al., "Development of a Human Adaptive Immune System in Cord Blood Cell-Transplanted Mice," *Science* 304.5667 (April 2, 2004): 104–107.

[39] Gesine Kögler et al., "A New Human Somatic Stem Cell from Placental Cord Blood with Intrinsic Pluripotent Differentiation Potential," *The Journal of Experimental Medicine* 200.2 (July 19, 2004): 123–135.

psychiatry and neurosurgery at the Yale University School of Medicine, has been performing experiments (with the intention of studying ways to cure Parkinson's disease) in which human neural stem cells are transplanted into African green monkeys.[40] The experiments by both groups seem questionable in terms of whether the transplanted human cells might cause any significant difference within the rats or monkeys, to the point where they might develop human intellection or other human characteristics. Certainly, with the monkeys there would seem to be more risk, since they are more closely related to humans than are rats, especially regarding brain size and structure. Dr. Redmond believes it extremely unlikely that a "humanized monkey" will be produced by his experiments, because of the very small percentage of human cells that are introduced into the monkey brains.[41]

In an interview in July 2005, Dr. Irving Weissman, a Stanford University professor and cofounder of the biotechnology company StemCells, Inc., discussed his desire to perform experiments in which he would transplant human neural stem cells into the brain of special mice which would lose all their mouse neurons.[42] Thus, the remaining neurons in the mouse brain would be of only human origin. Because he anticipated an ethical backlash if he proceeded with these experiments, Weissman first sought advice and ethical oversight from an ethicist and law professor at Stanford, Hank Greely. The ethicist's advice was to carry out the experiments, but to carefully study the mouse brains for possible appearance of human structures or for "odd misshapen mouse structures," at which point the experiments should be stopped and reevaluated.[43] The reason Weissman gives for performing these and similar experiments is to be able to study the functioning of both normal and diseased human neurons in the context of an in vivo animal model, so as to eventually find ways to treat human neurological diseases. As of this writing in November 2005, there have been no reports that Weissman has carried out these experiments yet.

The experiments proposed by Weissman seem morally questionable, primarily because of the proportion of human neurons versus mouse neurons which would populate the mouse brain. Greely says that he has found in discussions with neurosci-

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[40] Kimberly B. Bjugstad et al., "Neural Stem Cells Implanted into MPTP-Treated Monkeys Increase the Size of Endogenous Tyrosine Hydroxylase-Positive Cells Found in the Striatum: A Return to Control Measures," *Cell Transplantation* 14.4 (2005): 183–192. See also Eugene Redmond, interview by Tom Bearden, *Online NewsHour with Jim Lehrer* transcript, PBS television, July 2005, http://www.pbs.org/newshour/bb/science/july-dec05/chimeras_redmond-ext.html.

[41] Redmond and his coworkers transplant approximately "8 to 10 million [human] cells in a [monkey] brain that maybe has 20 to 40 billion cells" Redmond interview by Beardon, PBS transcript.

[42] Irving Weissman, interview by Tom Bearden, *Online NewsHour with Jim Lehrer* transcript, PBS television, July 2005, http://www.pbs.org/newshour/bb/science/july-dec05/chimeras_weissman-ext.html.

[43] Hank Greely, interview by Tom Bearden, *Online NewsHour with Jim Lehrer* transcript, PBS television, July 2005, http://www.pbs.org/newshour/bb/science/july-dec05/chimeras_greely-ext.html.

entists that "it's the architecture that's important in brains, not the building materials [i.e., the neurons themselves] … what's important is the size, shape, structure of the brain, because the mouse skull is much, much smaller than ours."[44] Thus, he thinks that injecting human neurons into a mouse brain would not be morally questionable. However, in his opinion, "doing this kind of an experiment with a chimpanzee would I think raise much more serious questions about conferring some … human cognitive powers on the chimpanzee."[45] I would tend to think, however, that it is a mixture of the two which would have an effect on the moral evaluation of a particular experiment: both the architecture of the skull *and* the type of cell injected are important. If the cell is a human neuron, then there is the possibility of humanlike connections between the neurons, which brings with it the possibility of humanlike cognition of some sort (whether the architecture and size of the skull are humanlike or not).

Another recent interspecies experiment consisted of the creation of human-nonhuman embryos via cloning techniques (i.e., insertion of human somatic cells into enucleated animal oocytes). The biotech company Advanced Cell Technology inserted human somatic cells into enucleated cow oocytes to produce human stem cells.[46] Chinese researchers did the same, using rabbit oocytes.[47] Renegade "researcher" Panayiotis Zavos inserted human granulosa cells into enucleated cow oocytes to "practice" his human cloning techniques.[48] Technically, the products of these types of experiments cannot seem to be considered either true chimeras or true hybrids. The products are not chimeras, because they are not a variegated mix of different species of cells or organs within one individual, and they are not true hybrids, because the nuclear DNA does not combine between the two species (because the oocytes have been enucleated prior to insertion of the somatic nuclear DNA). Nonetheless, perhaps they could be considered "quasi-hybrid" experimental entities, as there are two species of DNA present (nuclear DNA from one species and mitochondrial DNA from the other species' oocytes) in each cell of the resultant embryos, and there could be some slight interaction between the two DNAs. Although mitochondrial DNA generally keeps separate and distinct from nuclear DNA in cells, and does not combine with the nuclear DNA, there is likely to be some cross-talk interaction between the two.[49]

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[44] Ibid.

[45] Ibid.

[46] Advanced Cell Technology, "Advanced Cell Technology Announces Use of Nuclear Transfer Technology for Successful Generation of Human Embryonic Stem Cells," press release, November 12, 1998, http://www.advancedcell.com/press-release/advanced-cell-technology-announces-use-of-nuclear-transfer-technology-for-successful-generation-of-human-embryonic-stem-cells.

[47] Chen et al., "Embryonic Stem Cells," 251–263.

[48] Andy Coghlan, "First Human Clone Embryo Ready for Implantation," *NewScientist.com* (September 15, 2003), http://www.newscientist.com/article.ns?id=dn4168. Granulosa cells are cells that surround the oocytes in ovaries.

[49] Ulrich Mühlenhoff and R. Lill, "Mitochondria: Methods for Preparation," in *Encyclopedia of Life Sciences*, vol. 12, eds. Sarah Robertson et al. (London: Macmillan Publishers Ltd., 2002), 108.

All of these types of quasi-hybrid experiments are ethically problematic, at least partly because of this (morally repugnant) interaction that can occur between the animal mitochondrial DNA and the human nuclear DNA within the embryo. In addition, the embryos in these experiments were created with the intention that they would later be killed, to obtain their stem cells or to preclude further growth, and if there is a chance that these embryos are human at all, it is wrong to kill them.

Violation of the Imago Dei*?*

Significantly changing the identity of an organism by combining human and non-human cellular or genetic material (especially at the embryonic or fetal stage) could be construed as a violation of the dignity of the human person. John Paul II, in his "Theology of the Body," uses the term "original solitude" to refer to the human condition of man, including his distinctness from the animals.[50] Genesis 2:19 states that "the Lord God formed out of the ground various wild animals and various birds of the air, and he brought them to the man to see what he would call them." John Paul II describes this as a "test" and a way for man to understand his place in creation better:

> The first meaning of man's original solitude is defined on the basis of a specific test or examination which man undergoes before God (and in a certain way also before himself). By means of this test, man becomes aware of his own superiority, that is, that he cannot be considered on the same footing as any other species of living beings on the earth.[51]

By naming the animals, man sees what he "is not," and he asserts himself as a person, with subjectivity, consciousness, and rationality. Man's body also has significance in this context: Adam's body makes evident to him that he is different from the animals.[52]

Man was also made in the image of God.[53] Interestingly, John Paul II points out that in the biblical description,

> man's creation is essentially distinguished from God's preceding works. Not only is it preceded by a solemn introduction ["Let us make man in our image, after our likeness."], as if it were a case of God deliberating before this important act, but above all, man's exceptional dignity is set out in relief by the "likeness" to God of whom he is the image.[54]

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[50] The term also has another meaning in John Paul II's theology, referring to Adam's lack of female companionship.

[51] John Paul II, General audience of October 10, 1979, *Theology of the Body: Human Love in the Divine Plan* (Boston: Pauline Books and Media, 1997), 36.

[52] "We apply [the term 'original solitude'] to man in his totality. His body, through which he participates in the visible created world, makes him at the same time conscious of being 'alone.'" John Paul II, General audience of October 24, 1979, *Theology of the Body*, 38.

[53] Gen. 1:26–27: "Then God said: 'Let us make man in our image, after our likeness.' ... God created man in his image, in the divine image He created him; male and female He created them." John Paul II points out that "the biblical narrative does not speak of his likeness to the rest of creatures, but only to God." General audience of September 12, 1979, *Theology of the Body*, 28.

[54] John Paul II, General audience, September 12, 1979, *Theology of the Body*, note 1, 90.

The dramatic way in which man is created highlights man's incomparable dignity.

The Old Testament has strong proscriptions against sexual relations with animals.[55] The injunctions were so strong that death was the punishment for transgression. There were also other strong proscriptions, such as those against various forms of incest.[56] Many of the rules followed by the Hebrews seem to have had a number of reasons behind them. It was considered a virtue to follow these rules just for the sake of doing what God wanted; however, these rules often also seemed to provide better physical, spiritual, and emotional health in those who followed them. The incest regulations, besides helping keep societal peace, also probably kept the Israelites genetically healthy, because inbreeding is medically known to lead to increased congenital abnormalities and certain genetically linked diseases in a population. Perhaps in a somewhat analogous way, the antibestiality regulations had a reasoning behind them which was hidden in some sense. Perhaps these regulations served to preserve human health and dignity in some way, and to specifically keep the human (i.e., the *imago Dei*) separate from the nonhuman (the non–*imago Dei*) with regard to procreation and potential genetic crossing. One could venture that God not only abhors the unspeakable act of sexual relations between animals and humans, but also the combining of their genetic constitutions at a certain level.

The Incarnation, the Word made flesh, speaks to us of the dignity of being human and the dignity of the human body.[57] Jesus Christ did not come as an animal, but specifically as a human being, in a human body. This bespeaks the dignity which God accords human beings and their bodies, and how precious the human race is to him.[58] It thus seems to lean toward blasphemy to purposely combine the genetic or bodily materials of a human being and an animal in a way that changes either of their identities. To mix the *imago Dei* with the non–*imago Dei* seems a violation, and evokes a certain repugnance. Perhaps this repugnance is a sign of wisdom.

[55] See Exod. 22:18: "Anyone who lies with an animal shall be put to death"; and Lev. 18:23: "You shall not have carnal relations with an animal, defiling yourself with it; nor shall a woman set herself in front of an animal to mate with it; such things are abhorrent." See also Deut. 27:21 and Lev. 20:15–16.

[56] See Deut. 27:22, Lev. 18:6–14, and Lev. 20:17, 19–21.

[57] See *Gaudium et spes*, n. 22: "In reality it is only in the mystery of the Word made flesh that the mystery of humanity truly becomes clear.… Human nature … has been raised in us also to a dignity beyond compare. For, by his incarnation, he, the Son of God, has in a certain way united himself with each individual." Vatican Council II, "Pastoral Constitution on the Church in the Modern World, *Gaudium et spes*, December 7, 1965," in *Vatican Council II*, vol. 1: *Constitutions, Decrees, Declarations,* ed. Austin Flannery (Northport, NY: Costello Publishing Company, 1996), 185.

[58] Isa. 43:1, 4: "O Israel: Fear not, for I have redeemed you; I have called you by name: you are mine. … you are precious in my eyes."