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Developing Human-Nonhuman Chimeras in Human Stem Cell Research: Ethical Issues and Boundaries

ABSTRACT. The transplantation of adult human neural stem cells into prenatal non-humans offers an avenue for studying human neural cell development without direct use of human embryos. However, such experiments raise significant ethical concerns about mixing human and nonhuman materials in ways that could result in the development of human-nonhuman chimeras. This paper examines four arguments against such research, the moral taboo, species integrity, "unnaturalness," and human dignity arguments, and finds the last plausible. It argues that the transfer of human brain or retinal stem cells to nonhuman embryos would not result in the development of human-nonhuman chimeras that denigrate human dignity, provided such stem cells are dissociated. The article provides guidelines that set ethical boundaries for conducting such research that are consonant with the requirements of human dignity.

But still 'tmust not be thought that in all ways
All things can be conjoined; for then wouldest view
Portents begot about thee every side;
Hulks of mankind half brute astarting up, . . .

And Nature along the all-producing earth
Feeding those dire Chimaeras breathing flame
From hideous jaws—Of which 'tis simple fact
That none have been begot. Titus Lucretius Carus, 50 B.C.E.

The chimera, a mythological creature that was part lion, part snake, and part goat and breathed forth blazing fire, was a figure of both fascination and repulsion to the ancient Greeks (Bazopoulou-Kyrkanidou 2001; Graves 1960, pp. 252–56). It was portrayed at best as

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an inhuman, capricious creature to be avoided and at worst as a brutish, evil monster to be slain. Its form was symbolic of its nature: a monstrous unnatural body signified a monstrous unnatural disposition. The chimera and several other creatures of mixed categories—e.g., the Minotaur, Gorgons, and Sirens—were seen as signs that some terrible disorder permeates the universe, threatening humanity. Some Western historical and cultural sources have continued to maintain that to merge living beings from sharply distinguished categories is to invite evil and chaos.

Medical researchers are assembling new sorts of chimeras today. Some have fused goat and sheep embryos, developing a creature known as the "Geep" that displays some of the characteristics of a goat in a sheep's body, or vice versa (Polzin et al. 1987). In another experiment, researchers have transplanted regions of the quail brain into chicks, producing a creature with features of both (Balaban, Teillet, and Le Douarin 1988). These experiments are intriguing just because they obscure the boundaries between two different animals. Yet they have not resurrected cosmological fears associated with ancient chimeras among research ethics boards or the public, perhaps, in part, because these studies did not involve human components.

Investigators also have inserted nonhuman materials into humans and human bodily materials into nonhumans. They have, for instance, transplanted pig heart valves into human beings in order to treat serious heart disease. Apparently, inserting small amounts of animal tissue into human beings has not been taken to impinge on the humanness of the recipients, and these therapies have not been rejected as unethical. The transfer of human material, such as embryonic stomachs, intestine, tracheas, and lungs, into the bodies of mice has failed to create an ethical stir (Angioi et al. 2002). Researchers also have inserted human blood and skin stem cells into postnatal mice (Kamel-Reid and Dick 1988; Kauffman et al. 1993; Dick et al. 2001; Raychaudhuri et al. 2001) and fetal sheep (Zanjani, Mackintosh, and Harrison 1991) without significant ethical resistance. The transfer of these sorts of stem cells, perhaps because they are not identified with what is essential to being human, does not appear to raise the specter of converting mice and sheep into human beings (Vince 2004).

It is when investigators have proposed transplanting certain adult human stem cells derived from the brain or eye—an outgrowth of the brain—into animal embryos to learn how these cells, whose tissues develop largely in the prenatal period, differentiate, proliferate and regenerate (DeWitt 2002; Krieger 2002) that ethical concerns have been raised. Stem cells as-

sociated with the brain seem to have a close association with what it is to be human. Such trans-species forays are disquieting because they would introduce human central nervous system stem cells into animals during their formative development when their future biological characteristics are beginning to emerge and before their body plans have been completed. Would the human neural stem cells overwhelm the host animals? If embryonic mice with human neural stem cells were subsequently brought to term, would they possess human brains and think like humans or would they remain mice? The creation of human-nonhuman chimeras, some maintain, would be an outcome "too horrible to contemplate" (Wade 2002). The ancient fear of creating a monstrous interspecies chimera still hovers over contemporary Western society.

At least four ethical arguments could be given against the development of such human-nonhuman chimeras: doing so would (1) be morally taboo, (2) be contrary to nature, (3) violate the integrity of the species involved, or (4) denigrate human dignity. These arguments are not wholly separate conceptually and could be combined into one massive and powerful argument against the development of these chimeras. This, however, would obscure the various ethical, logical, and social nuances of each argument. We therefore consider each argument in turn and conclude that only one, the human dignity argument, has sufficient ethical force to warrant prohibiting the creation of human-nonhuman chimeras.

We then query whether the insertion of human neural (retinal or brain) stem cells into prenatal nonhuman embryos and fetuses would, in fact, result in the creation of human-nonhuman chimeras, using an illustration drawn from a proposed retinal stem cell experiment, and explain why this would be of ethical concern. We argue that the proposed experiment would not result in the development of human-nonhuman chimeras of a sort that contravene human dignity but that the transfer of undissociated stem cells would run that danger. Finally, we detail limits beyond which research involving the transfer of human central nervous system stem cells into animal embryos and fetuses should not go.

ARGUMENTS AGAINST THE DEVELOPMENT OF HUMAN-NONHUMAN CHIMERAS

The term "chimera" has been used somewhat loosely in different branches of the biological sciences to describe inter- and intra-species combinations at many levels, from molecules, to cells, to whole organs. For instance, in molecular biology, the term "chimera" sometimes is used

to describe the combination of DNA sequences taken from two separate individuals into a single sequence. In genetics, the term "interspecies hybrid" refers to the result of mating two genetically dissimilar, and normally nonreproductive, individuals, such as the horse and the donkey. In cell biology, the terms "inter- and intra-species nucleo-cytoplasmic hybrids" are used to denote the use of nuclear transfers (cloning). In embryology, "chimeras" are both inter- and intra-species prenatal combinations of cells that originally were derived from two separate zygotes. Finally in transplantation research, "chimeras" sometimes describes the result of xenografting cells, tissues, or whole organs from human beings into animals. The techniques for creating such chimeras are very different, but in principle they all involve the combination of material from two different sources into one. Our present use of the term "human-nonhuman chimeras" refers to entities that might result from transplants of human stem cells into prenatal nonhuman hosts.

THE MORAL TABOO ARGUMENT

Some react to the very thought of creating human-nonhuman chimeras with repugnance. To bring such creatures into the world seems to them an abomination akin to incest or cannibalism. It is an act that they claim is prohibited by taboos found in many cultures that have served to promote human well-being and important social values. To violate them would have serious negative repercussions on those involved and their societies. We term this argument "the moral taboo argument."

Leon Kass (1997), for instance, claims that repugnance provides the basis for strictures in many societies against such practices as incest, bestiality, and cannibalism. He maintains that we have some rarely articulated and "perhaps not altogether articulable" sense that putting human stem cells and their derivatives into animals would evoke a similar response (President's Council on Bioethics 2003). "[R]epugnance may be the only voice left that speaks up to defend the central core of humanity" (Kass 1997, p. 20). That certain practices elicit repugnance is sufficient to indicate that they are wrong, on this view. Attempts can be made to support such emotional responses with argument, Kass acknowledges, but he asks, "Would anybody's failure to give full rational justification for his or her revulsion at these practices make that revulsion ethically suspect?" (Kass 2001, p. 6; 1997, p. 79). Sheer repugnance is epistemologically foundational to this approach and is said to lead inexorably to the intuition that these sorts of practices are ethically unacceptable.

The force that emotions and intuitions should be given in ethical decision making is a contested philosophical issue. Surely it is ethically sound to feel outrage at the wrongful killing of an innocent person or the rape of a child. What makes such outrage justifiable, however, is not the emotion in itself, but the reasons why one responds with this emotion. We would be reluctant to accept ethical judgments based solely on emotions such as anger, outrage, or revenge without further explanation, for these can occur by chance and may be misplaced. Moreover, at times emotions can obscure, rather than clarify, ethical reasoning. Even those who give emotions considerable weight in making ethical assessments maintain that one must find reasons for such assessments that are based on coherent and supportable ethical standards of judgment (Midgely 2000).

Intuitions, as distinct from emotions, traditionally have been viewed as a response to an authoritative inner voice (Kekes 1986). They are said to have direct epistemological force and to require no further justification. Thus, one straightforwardly intuits that it is right to assist an innocent person who is about to be killed or a child about to be raped. Although intuitions undoubtedly play a role in ethical thinking, it is problematic to view them as providing the foundation for ethical reasoning, for they are fallible and sometimes conflict. What one person, or even a society, regards as an intuitively known truth may be shown to be wrong or rejected as dubious by others. This works against the belief that we have an inborn moral sense through which we derive infallible moral intuitions. For such reasons, W. D. Ross (1930) maintained that intuitions are presumptive. That is, they establish a *prima facie* case for acting in certain ways but can be overruled if there is good reason to dismiss them. As a way of knowing, intuitions need to have the support of some form of reasoning that is intersubjectively available and can be followed by others. In short, the main advantage of intuitions over emotions is that they are less vulnerable to chance changes. Their chief disadvantages are that they can vary from person to person and may prove to be erroneous.

Even so, it is important to acknowledge that taboos based on repugnance and intuition play a significant role in preserving core social values within most societies. They serve to bring order out of cosmological and social chaos in that they establish lines of authority that perpetuate traditions and ways of thinking (Levi-Strauss 1978; Douglas 1966). The taboo against incest, for example, forces societies to expand, bringing in new members who can help them to survive and flourish. However, the same taboos are not held universally across all cultures and, within a culture, can outlive their social role and be displaced.

Are the moral taboos that Kass lists universally accepted? It seems not. A paradigm moral taboo that he maintains is universal, that against cannibalism, is not found in all cultures. Indeed, cannibalism still exists today in some societies as a socially sanctioned practice. Taboos against crossing humans and nonhumans, in particular, have not been held universally. The ancient Egyptians, for instance, depicted some of their revered gods with nonhuman animal heads or bodies, and Native Americans have made use of sacred figures that combine human and nonhuman features.

Moreover, some of the moral taboos that have been entertained in the past within Western culture now are considered wrong or are under ethical siege. Blood transfusions, organ donations, interracial marriage, and homosexuality all have been viewed as morally taboo. Yet society's attitude towards blood transfusions, for example, has undergone complete reversal; what was once morally abhorrent has now become a moral and civic responsibility. Similarly, ancient taboos that once prohibited mixing the human and nonhuman seem to be dissolving today, as is exhibited by the general acceptance of the insertion of pig heart valves into human beings. This variability in inter-categorical taboos indicates that moral taboos alone cannot provide a reliable basis for making ethical assessments about whether to create human-nonhuman chimeras.

Jeffrey Stout (1988, pp. 145–62), in presenting a theory about social taboos, distinguishes the repulsive from the repugnant, or what he terms the "abominable." That which is repulsive mixes categories that we keep sharply separate, but does so in ways that are not socially or cosmologically significant. The repugnant or abominable, in contrast, not only displays great anomalies, but does so in ways that create a major disturbance in the social or cosmological system of a culture. Stout probably would agree that the human ear, although uniquely identified with human beings, does not have major societal or global import and that its transfer to the back of a mouse (Cao et al. 1997) would be repulsive, but not repugnant. However, in cultures that sharply distinguish humans from animals, he might well find that such an experiment would be viewed as abominable just because it obscured that distinction. Violations of moral taboos pose a threat to the established conceptual order on which the social order depends, and members therefore respond to them with repugnance, labeling them as morally taboo.

Repugnance, on Stout's view, which strikes us as well-founded, is not a primitive emotion at the foundation of moral judgments about the creation of such beings as human-nonhuman chimeras. Instead, it arises

from an antecedent commitment to social and cosmological categories relative to which human-nonhuman beings seem anomalous. Thus, it is not the creation of such chimeras that needs defense but the system of social and cosmological categories that informs repugnance toward them and that grounds moral taboos against combining the human and the nonhuman.

Taboos are social conventions that emerge from diverse historical and cultural contexts. They are subject to alteration as the context in which they arise alters. Such change is occurring today as the context in which mixing human materials with those of animals moves away from fearsome chimeric creations of fantasy to human-nonhuman combinations initiated to study the development of human cells and, ultimately, to treat those with diseased tissue (Karpowicz, Cohen, and Van der Kooy 2004). Indeed, it is arguable that there is an ethical imperative today to resist taboos about human-nonhuman chimeras derived from an earlier historical era, since they do not take into account the reasons why such chimeras might rightly be pursued within the contemporary context (Franklin 2003). We conclude that the simple assertion that human-nonhuman chimeras are morally taboo, unvarnished by a rationale or justification, does not provide an adequate basis for rejecting studies using human-nonhuman chimeras or other experiments in which human and nonhuman bodily materials are merged.

THE "UNNATURALNESS" ARGUMENT

The "unnaturalness" argument does not appeal to an inarticulable sense of repugnance or abomination, but it can be seen as a way of explaining the connection between such repugnance and the structure of the universe. The argument objects to the creation of human-nonhuman chimeras on grounds that doing so would be contrary to the orderly way in which the natural world functions (President's Council on Bioethics 2003; Midgely 2000).

This argument maintains that the operations of nature are to be understood and valued in terms of their purposes (Kass 1985). It is indebted to Aristotelian thought, which asserts that every living thing has an inner tendency to reach its appropriate end or goal (*telos*) by exercising certain characteristic biological functions. According to traditional natural law theorists, the very fact that a living entity pursues a particular kind of life through certain biological processes is its own justification (Crowe 1977, pp. 192–245; d'Entreves 1970, *passim*). Moreover, a life that unfolds in accordance with its intrinsic principles of operation displays a kind of

goodness. Accordingly, for natural law theorists, it is a moral good for each kind of being to be aligned with its appropriate end and a moral wrong to alter its natural functioning in ways that distort or violate this end. For these thinkers, the naturalness of a practice provides *prima facie* justification for engaging in it.

There is a pervasive sense of the continuity between humans and nonhumans in much natural law thought (Porter 1999). Yet curiously natural law theorists also maintain that the proper end of human beings differs radically from that of, say, mice or monkeys (Kass 1985, p. 272). The very nature of each sort of living being sets moral limits on human action. To transfer human cells, tissues, and organs into nonhumans in ways that change their function, their progression toward their end or goal, would violate the natural teleology of these beings and therefore would be unnatural and wrong. Aspects of this natural law rationale have been held by some leading scholastic thinkers such as Aquinas (1968, 2a2ae, p. 154) and more recently by some moral theorists (Flanagan 1991; Kass 1985; Midgely 1978). Similar "unnaturalness" arguments have been given against emerging biotechnologies such as the use of xenotransplants, genetic engineering, and cloning.

The "unnaturalness" argument accepts an assumption that remains questionable, namely, that an organism's usual state of flourishing should be valued. However, having a certain mode of reproducing, for instance, is not, in itself, ethically significant (Savulescu 2003). Nature does not come with some sort of built-in ethical import that can be read from it, such that living beings' typical ways of functioning always must be kept intact. It is what one makes of natural functions and structures that is ethically significant. To what ends are they put? Although the realities of nature constrain ethical judgments about the ways in which one ought to treat the natural world, these realities must be subject to interpretive framing in light of philosophical, social, biological, and other understandings.

The teleological guidance of the "unnaturalness" argument requires one to speculate endlessly about the natural purposes of virtually all living entities and their biological components. For instance, it is not clear whether it would be ethically acceptable, on a teleological view, for one human being to donate a kidney to another or to make use of *in vitro* fertilization. By their very "unnaturalness," these practices would seem to violate the natural functions of the human beings involved. Yet these same interventions would help humans achieve their broader "natural" ends of being alive and reproducing.

The basic difficulty with the "unnaturalness" argument is that it does not explain when an intervention into nature is ethically acceptable and when it is not, why certain natural features always bear a certain moral import and therefore should not be changed. That organisms normally function in certain ways in the natural world does not indicate that it is wrong to intervene into these functions or to keep them from reaching their usual biological ends. No bright line is provided by the "unnaturalness" argument to help one distinguish between appropriate and inappropriate interventions. The context in and reasons for which the interventions are carried out have considerable import for assessing whether they are right or wrong.

Moreover, we now know that the natural world is in constant flux. Organisms do not remain static but evolve and change. Although one may appreciate and value the ways in which many aspects of the natural world unfold, there is no reason to think that there are moral requirements built into nature that all things must remain in an unaltered natural state and that humans should not influence the ways that human or nonhuman organisms function. The "unnaturalness" argument makes assumptions about the interpretation of biological phenomena and the elucidation of ethical values that does not, and could not, follow from what we have learned of the evolution and development of humans and nonhumans.

Consequently, we set aside the "unnaturalness" objection to the creation of human-nonhuman chimeras on grounds that it equates, and thereby confuses, biological description with the justification of ethical norms. It therefore provides insufficient warrant for judging the creation of human-nonhuman chimeras to be wrong.

THE SPECIES INTEGRITY ARGUMENT

An objection to the creation of human-nonhuman chimeras often implicit in the moral taboo and the "unnaturalness" arguments is that experiments employing such chimeras would cross species boundaries, which would be ethically unacceptable. No one view of why crossing species boundaries would be wrong has been proposed by those who offer the "species integrity" argument. Indeed, there is no commonly accepted view of just what is meant by species and how to distinguish one species from.

According to the classical conception of species, as depicted by Aristotle, similar biological organisms are members of a "natural kind," a species with an essential and unchanging nature. Members of species share an

essence or property that is common to all of them and that is responsible for each member being the kind that it is (Griffiths 1999). For this reason, species have explanatory priority over concrete individuals in the sense that the resemblances between individuals in a species are explicable in terms of the underlying "natural state" of each individual (Boyd 1999; Griffiths 1999; Hull 1999; Wilson 1999). They are internally homogenous and discontinuous with one another; their boundaries are real and objective. Thus, the original development of species categories was based on the presumption that to define a species involves making an objective determination about what is given straightforwardly in nature.

However, as biologists subsequently attempted to draw boundaries around groups of organisms that they observed in nature, they developed diverse views of what is meant by a species. The delineation of biological species seems to have been developed by ascribing significance to the visible appearances, functions, or behaviors of organisms. Boundaries were then drawn between groupings of living beings on this basis (de Sousa 1984). Thus, Karl Linnaeus, the father of biological taxonomy, grouped species by their visible appearance. However, biologists found that this reliance on outward appearance to capture the meaning of species did little to further scientific hypotheses and predictions, so they chose other characteristics of organisms to define species. They seemed to base their alternate species categorizations largely on biologically interesting or subjectively relevant criteria that furthered their particular scientific interests and approaches (de Sousa 1984).

Ernst Mayr (1988), for instance, focused on the mode of propagation as the most important criterion for defining species, maintaining that species are groups of interbreeding natural populations that are reproductively isolated from other such groups. One of the problems raised by his view, however, is that asexually reproducing organisms, such as bacteria, or the 5 percent of interbreeding birds that are taken to be of different species do not fit into such a classification system. In order to accommodate such exceptions, Mayr stretched his characterization of species by introducing the idea of morphological similarity. An asexual species, he maintained, contains individuals that are as structurally similar to one another as members of a sexual species. This, however, seemed to revert to the unsatisfactory Linnean characterization of species. Some biologists therefore have sought alternative criteria for defining species.

Even if another criterion for distinguishing species, say, genetic similarity, were adopted, this would not wholly resolve the difficulties encountered in

defining species. Categorizing species would become a question of setting acceptable boundaries around ever-fluctuating genetic similarities. Setting genetic species boundaries around humans and chimpanzees, for instance, seems straightforward until it becomes necessary to select a relevant threshold of genetic similarity. What threshold would produce the most accurate phylogeny between these organisms? If one were to restrict the relevant genetic grouping to a subset of the eukaryotic genome, one might not only distinguish between humans and chimpanzees, but also establish separate species categories among humans. Many would reject this result, however, because it would ignore other significant criteria that biologists have adopted for viewing all humans as members of the same species.

Because biologists have chosen differing criteria to identify species based on what has seemed important and scientifically interesting in their own research, we have a tremendous variety of ways of categorizing species. Currently, there is no general agreement, and indeed there may never be, about which categorization is correct. This lack of agreement makes it doubtful that species categorization could bear the moral weight necessary to evaluate the morality of transferring human cells into nonhuman animals. The biological categorization of species is empirical and pragmatic, a constantly developing effort that has little to do with moral judgments. Thus, even if one were to identify an unchallengeable view of what is meant by species, it would remain unclear why the possibility of transferring bodily material from one species to another, as would occur in human-nonhuman chimera studies, would be wrong.

Jason Scott Robert and Françoise Baylis (2003) attempt to answer this question. They maintain that there are no objectively given species boundaries. However, the belief that there are fixed species boundaries that exist independently has become a fixed part of conventional moral thinking. Because of this, they declare, to endow a mouse or a monkey with human cells in significant numbers or kinds would introduce moral confusion into conventional thinking and diminish the high moral status that human beings are assigned. This possibility, they argue, is so threatening to our social fabric that we need to keep tightly guarded conventional species boundaries between humans and nonhumans. Their argument is, in effect, a version of the "moral taboo" argument, for it maintains that we should not go contrary to deep, long-held societal conventions.

It is a version that requires some evidential support. Critics have argued that the claims that society fears crossing conventional species boundaries and that to cross them would create social and moral chaos need

confirmation (Rollin 2003; Charland 2003; Streiffer 2003). An alternate possibility is that society would take the creation of human-nonhuman chimeras in stride, much as it has when certain animal materials have been transferred to humans, and that it would continue to move along an orderly moral path.

We conclude that the species integrity argument provides no reliable criteria for ascertaining when the lines between species have been crossed, and, were it to do so, no clear argument about when and why crossing them would be ethically unacceptable. It offers no reasons why society should not accommodate new ways of classifying living organisms. Proponents of the species integrity argument believe that the familiarity of species categories in current use is sufficient to justify valuing and retaining them. However, that one is used to thinking about things a certain way is not a strong reason to argue against the development of new ways of thinking about the human-nonhuman chimera (Karpowicz 2003).

THE HUMAN DIGNITY ARGUMENT

In the novel, *The Island of Doctor Moreau* (Wells 1896), a visitor arrives on a remote island and discovers that a mad scientist, Moreau, is conducting experiments designed to turn animals into human beings. The resulting part-animal, part-human creatures, in Wells's fantastic scenario, struggle and ultimately fail to sustain human lives. To the visitor, this experimental manipulation raises strong concerns. "I asked him why he had taken the human form as a model. There seemed to me then, and there still seems to me now, a strange wickedness in that choice." What strikes the visitor as wrongful in Dr. Moreau's experiments is that they diminish and degrade human beings.

Similarly, the core concern that arises in deciding whether it would be ethical to create human-nonhuman chimeras in stem cell research is whether humans and nonhumans would be merged in ways that would denigrate or even eliminate the distinctive value of each, with particular emphasis on the effect on humans. The moral taboo, "unnaturalness," and species integrity arguments presume that there is something about human beings that ought to be honored and protected. It is this element that the human dignity argument addresses.

The notion of human dignity has been evoked in debates about such issues as euthanasia and reproductive cloning. Unfortunately, those who have presented the notion have tended not to elaborate on what they mean by human dignity. For instance, in a recent book, Kass (2002)

expresses concern about the threat to human dignity presented by such recent bioetchnological interventions as reproductive cloning. However, after rejecting the Greek notion of heroic dignity and what he terms a contemporary version of Kantian thought that defines dignity as "choosing for yourself, what ever you choose," he presents only a hint of what he means by the notion. Human dignity, he indicates, has to do with "the worthiness of embodied human life, and the worth of our natural desires and passions, our natural origins and attachments, our sentiments and aversions, our loves and longings" (Kass 2002, p. 18). He does not explain what it is that gives embodied human life this worthiness, thereby leaving one with a vague notion of human dignity that is open to use also by those who take an opposing view of the rightness of reproductive cloning.

Some others who use the notion of human dignity are equally mysterious about its significance. John Robertson (1994), for instance, maintains that it is a violation of human dignity to deny individuals the right to have the kind of children that they want through use of the new reproductive technologies. However, he does not attempt to explain what he means by human dignity and is therefore open to rebuttal by those who claim that it is a violation of human dignity to utilize these technologies. Because of such lack of clarity about the meaning of human dignity, some commentators, such as Ruth Macklin (2003), maintain that it is a useless notion. She asserts, for example, that it means no more than respect for autonomy. Although the violation of human dignity surely includes the loss of control over one's own choices, it means more than this in most contexts in which the notion figures. The person who voluntarily sells himself into slavery denigrates human dignity, even though he has made an autonomous choice. John Harris (1998) also finds the notion unclear and reduces it to "not using individuals as a means to the purposes of others." This, however, is a stricture that follows from the recognition of human dignity, rather than an explanation of what it means.

It was Immanuel Kant (1964; 1956) who brought the concept of human dignity to the fore of Western thought (Hill 1992; Cohen 1999). His view of human dignity is independent of his metaphysical ideas and his special understanding of the moral law (Hill 1992, p. 176). He maintains that humans have an unconditioned and incomparable worth (*Würde*) or dignity because they are moral agents whose actions can be imputed to them (Kant 1964, p. 94). Their dignity is manifested in their capacities to set ends for themselves and to act to achieve them in the practical sphere. Because they have a rational nature and the ability to act on principles,

Kant holds, humans possess a distinctive dignity that cannot be assigned a market price. Alan Gewirth (1992), a contemporary thinker influenced by Kant, maintains that the primary ground on which human agents logically must be said to have dignity is that they have purposes that they can act to fulfill. This generic purposiveness underlies the ascription of dignity to all human agents, he argues.

Although Kant's and Gewirth's views capture an important aspect of human dignity, they omit other significant factors that enter into the common understanding of this concept. Human dignity is a widely shared notion that signifies that humans typically display certain sorts of functional and emergent capacities that render them uniquely valuable and worthy of respect (Karpowicz, Cohen, and Van der Kooy 2004). It is not only the capacities for reasoning, choosing freely, and acting for moral reasons, as Kant argues, or for entertaining and acting on the basis of self-chosen purposes, as Gewirth holds, that are at the core of what is meant by human dignity. The notion also encompasses such capacities as those for engaging in sophisticated forms of communication and language, participating in interweaving social relations, developing a secular or religious world-view, and displaying sympathy and empathy in emotionally complex ways. That is, human dignity is a multi-faceted notion that is characterized by a family of unique and valuable capacities generally found in human beings. No one of these capacities is definitive of human dignity, but taken together, they set out a paradigm case of what it is to have human dignity (Cohen 2003). Further, dignity, as Kant declares, is not associated solely with those who have rank and authority. It is attributable equally to all human beings, regardless of their virtues and vices, their station in life, their disabilities, or their price on the market.

Having human dignity is conceptually distinct from behaving and bearing oneself in a dignified manner. Dignified comportment is a contingent feature displayed by some humans who respond to untoward circumstances in a noble and uplifting manner. Such individuals display what has been termed "personal dignity" (Pullman 2004) or what Aristotle termed "*arete*". Having human dignity, in contrast, is, as Gewirth (1982, pp. 27–28) states, "a characteristic that belongs permanently and inherently to every human as such." A person can behave in ways that are boorish and selfish and thereby diminish her "personal dignity" and yet retain human dignity.

Human dignity is degraded and demeaned when the family of valuable capacities at its core are deliberately and wrongfully diminished or

eliminated. This occurs when human beings are subjected to such acts as murder, torture, enslavement, rape, or maiming. These sorts of acts and practices are wrong not only because they injure humans physically and psychologically, but also because they deny them the exercise of their dignity-associated capacities, treating them instrumentally as mere things with no special value. Proponents of an argument from human dignity would maintain that to create a human-nonhuman chimera would either diminish or wholly eliminate the possibility that humans could exercise the cluster of capacities and characteristics that are associated with human dignity, treating them solely as a means to others' ends. By giving nonhumans some of the physical components necessary for development of the capacities associated with human dignity, and encasing these components in a nonhuman body where they would either not be able to function at all or function only to a highly diminished degree, those who would create human-nonhuman chimeras would denigrate human dignity. The torturer or the enslaver of human beings denies them the option of exercising the capacities associated with human dignity. The creator of the human-nonhuman chimera would do even worse—he or she knowingly would diminish or eliminate the very capacities associated with human dignity.

The argument from human dignity against the development of human-nonhuman chimeras might be criticized as a form of the species integrity argument. Helga Kuhse (2000, pp. 69–70) makes the point that "it would not be enough to say that human life has dignity because it takes the form of a featherless biped or because humans have opposing thumbs." Surely she is correct. The characteristics that are taken to define humans as a biological species have no particular ethical importance in most contexts. However, humans are not considered to have dignity because they are *homo sapiens*, but because they possess a cluster of capacities that matter ethically and that members of that species generally exhibit (Savulescu 2003).

A reverse criticism of the argument from human dignity might be raised: because human dignity is not identified with humanness but with the possession of certain capacities, only those humans with such capacities can be said to have dignity (Beyleveld and Brownsword 2001, p. 23). However, those who are human and yet display a limited subset of these capacities, say, the newborn infant or the person with severe disabilities, still have human dignity its proponents declare. We tend to ascribe it to all humans, no matter how seriously impaired or ill they may be, because there is no clear agreement about just how many dignity-associated capacities a person

must possess to be said to have human dignity. To avoid the possibility of mistakenly failing to treat those with severe disabilities as ends in themselves, human dignity proponents ascribe dignity to all humans.

Is the argument from human dignity a form of the "unnaturalness" argument? Does it presume that humans share a certain essence of humanness that must not be changed? The argument from human dignity does not maintain that there is some actual essence that corresponds to what it is to be human. Instead, it presumes an ordinary notion of humans as a group of beings who generally share certain kinds of capacities among which are some of the distinctive capacities associated with human dignity.

Another possible criticism of the argument from human dignity is that it wrongly denigrates the value of nonhuman animals. Although some who present the argument from human dignity maintain that animals have less worth than humans or even no worth, such views are not essential to the argument from human dignity. Nonhuman animals can be taken to have various characteristics and capacities of their own that give them a unique sort of worth that differs from that of humans; this need not detract from human dignity. Frans de Waal (1996, p. 210), for instance, maintains that nonhuman animals exhibit attachment and empathy; internalization of prescriptive social rules; concepts of giving, trading, and revenge; and tendencies toward peacemaking and social maintenance. However, they do not exhibit the capacities to make ethical judgments about available alternatives, to reject some alternatives on ethical grounds, to act on the basis of their judgments about those that are ethical, or to engage in speech, complex communication, or certain other dignity-associated capacities to the same degree and in the same kind as humans. The family of capacities associated with human dignity seems to belong uniquely to human beings. This is not to deny that humans have certain ethical obligations to nonhuman animals but to point out that animals, including those with capacities that resemble those of humans in several respects, have a different sort of worth from that of humans.

Although the human dignity argument needs further delineation and refinement, it does not fall into many of the difficulties to which the other arguments against the creation of human-nonhuman chimeras are prone. It maintains that it would be wrong to create human-nonhuman chimeras, but it has not yet explained in terms of the specifics of stem cell research just how doing so would violate human dignity. We therefore turn to consider what would transpire if certain human stem cells that are among the biological components especially associated with the cluster of

capacities that characterize human dignity were transferred to nonhuman animal embryos.

WHETHER DEVELOPMENT OF HUMAN-NONHUMAN CHIMERAS IN NEURAL STEM CELL RESEARCH WOULD VIOLATE HUMAN DIGNITY

At the core of the concerns related to human dignity raised by the possibility of developing human-nonhuman chimeras is that certain human components closely connected to the cluster of abilities associated with human dignity would be transferred to nonhumans. Capacities such as those for carrying out discursive and moral reasoning, engaging in complex communication, and forming multifacted social relations especially are associated with the human brain, whether one views the relationship between thought and the brain as one of materialistic identity, dualistic correlativity, or in some other way. Thus, human-nonhuman chimeric research challenges human dignity and becomes ethically problematic when it involves the introduction of substantial numbers of human brain or retinal (an outgrowth of the brain) cells into a nonhuman. Just how might such research violate human dignity?

Although it is fantastical, we at least can envision that some investigators might attempt to transplant a whole adult human brain into a nonhuman animal in order to study certain important neurological questions, resulting in a human-nonhuman chimera. To create such a chimera would violate human dignity because the resulting being could not fully exercise the dignity-related capacities associated with the human brain, due to its role as a research subject specifically produced to serve as a human proxy in experiments that it would be unethical to undertake on human beings themselves. The development of such a chimera arbitrarily would limit the ways in which certain human characteristics and capacities associated with human dignity could be exercised in a nonhuman setting and therefore would contravene human dignity. Consequently, the decision to manufacture a nonhuman research subject with a human brain and, at most, diminished capacities for various forms of human-like cognition and action would violate human dignity.

It is clear that the transfer of a whole human brain into a nonhuman animal would result in a human-nonhuman chimera that could exhibit many of the capabilities associated with human dignity. Would the transfer of human brain or retinal stem cells into nonhuman research subjects similarly result in a human-nonhuman chimera of a sort that contravenes human dignity? If human retinal stem cells, when transplanted into the

prenatal mouse or monkey, were to proliferate and develop into a whole human-like brain and if human-like capacities associated with human dignity were to emerge in such animals to some degree, the creation of this research subject would contravene human dignity. However, if the human retinal stem cells, following such a transplant, did not form a functioning human brain and were not integrated with the host's basic neurological functions, but were simply present in the nonhuman brain, the resulting being would not exhibit the cluster of distinctive capacities associated with human dignity. Such a transfer, therefore, would not violate human dignity.

Prenatal chimeras involving transplants of adult and embryonic neural human stem cells into nonhumans have been carried out, and to date none has demonstrated any evidence that such transplants result in the emergence of altered human-like features or functions in the nonhuman (Goldstein et al. 2002; Ourednik et al. 2001). It is important to understand why this is the case and to consider whether the opposite might occur in the future. In order to do this, one first needs to examine what neurobiology has to say about mammalian nervous system development.

Even if human retinal stem cells were to integrate with the mouse's or the monkey's basic neurological functions and were to replace the photoreceptors of the nonhuman, they would not control the way that the nonhuman brain functioned. Although the human retinal stem cells would become functional light-sensing cellular devices connected in a chain of similar devices that communicate messages within the animal eye or brain, the overall architecture of the animal's brain would not be affected by the presence of these cells. They simply would transmit light stimulus information to the brain of the chimera itself. The neurological functions of the nonhuman brain would remain unaltered because their organization would be governed by the animal host. The human cells would change with their environment to mimic the nonhuman host's native morphology and function and their genetic dissimilarity relative to the host would make no difference in the way in which the host brain functioned. They would become the practical equivalent of mouse or monkey cells. Thus, the human retinal cell component would not cause the unaltered mouse or monkey to develop human psychological, cognitive, or other capacities associated with human dignity.

The differences between mouse and primate brain complexity can be explained partially by differences in the number of cell cycles that occur during each species's neurogenesis (Kornack et al. 1988). *In vivo* brain

development studies have shown that primate cells divide more slowly than those of mice. Discrepancies between the brain size of primates and mice arise because primate progenitors have a longer developmental window and, although they divide slowly, they nevertheless go through many more divisions than those of developing mice. Such discrepancies reveal biological phenomena that differentiate human from nonhuman brains. Human neural progenitors or stem cells transplanted into mice or primates would produce human-like neural tissues in these nonhumans only if the cells somehow anticipated how much time was left during development and, in response, sped up their cell divisions to achieve the human-like end result—and this within the limits imposed by the experimental nonhuman host skull. However, human cells have little ability to predict anything about their nonhuman environment, or to discern when they should divide more or less rapidly to produce a human eye or brain. During development much, if not most, of a cell's behavior is not intrinsic, but rather is governed by forces arising from outside the cell itself.

What is more plausible and highly likely is that human stem cell proliferation in the mouse or monkey would be modulated by the mouse or monkey because the host's cells greatly outnumber the donor's cells. An example of such host-mediated recruitment is provided by human-mouse blood stem cell transplants in which human blood stem cells have not over-proliferated and overwhelmed the nonhuman host's blood system (Kamel-Reid and Dick 1988). Human blood stem cells do not continue to divide until human blood levels are achieved because the cells are recruited by the host, according to the host's needs. In short, the nonhuman host governs the way that these human blood stem cells function after their transfer.

Brain size is similarly regulated during development. Xenografted human stem cells would not be able to achieve human brain size and the human brain organization needed to give rise to human neural functions and behaviors when transplanted to nonhuman hosts. Both the mouse and the monkey chimeras would have to possess heads swollen many times their ordinary size to be able to accommodate a human brain. This scenario is unlikely. It is far more likely that human tissue would develop into the host's native form and would have no effect on the mouse or monkey's neural capacities. Even a monkey chimera whose thalamus and cortex were largely human-derived would not possess human capacities if the human neurons were to lie in different, nonhuman, functional networks. The same is true of even the closest relatives of the human, such as the chimpanzee, whose brain does not possess the same architecture

and organization as the human brain. The reasons why human networks differ from those of nonhuman primates are not known. It appears to have little to do with brain size itself, but instead with the time span of overall neuronal development and increases in the frequency of cell division of the neuronal progenitors that contribute to specific regions of the cortex during development (Finlay et al. 1995). It is very doubtful that a human brain could be developed outside a human body.

Given this evidence, the transplantation of human retinal stem cells into nonhuman mouse or monkey eyes or brains, as in our example, should result in the development of the same tissues and the same tissue organization that are endogenous to the mouse or monkey. This reveals that the human stem cell chimeras are not so much a test of characteristic human neural development, as a proof that human cells can contribute to a comparable, nonhuman animal's development.

One important caveat remains about the human retinal or brain stem cell chimera. This has to do with the state of the human stem cell transplant. *For the reorganization and host-driven control of transplanted human stem cells to occur, these cells must be separated or dissociated from one another when they are transplanted*. It is likely that this dissociation weakens the organization already present in a mass of cells prior to their transplantation and forces the human cells to reorganize themselves in response to the host environment. Whole organs or masses of undissociated cells should not be transferred from humans to nonhumans because doing so would risk the development of characteristic human pattern development and formation in the nonhuman animal host.

Two studies speak to this issue. First, the study noted previously that involved transplantation of undissociated goat cell masses into sheep blastocysts has shown that, during early development, the targeted replacement of the whole inner cell mass—a small clump of cells that will become the entire embryo—can bias the chimera to assume donor-only characteristics (Polzin et al. 1987). This means that the host animal develops characteristics of the animal from whom the inner cell mass was derived. In this instance, the replacement of the entire sheep inner cell mass with that of the goat resulted in the loss of any host sheep cells that could direct transplanted cell organization. The sheep was effectively replaced by the goat because only the goat cells remained to instruct the embryo's development.

Quail-chick chimeras, also mentioned previously, provide a second, striking example of interspecies-derived behavioral alterations (Balaban et

al. 1988). These chimeras were developed by transplanting whole regions of the quail brain into chicks. The resulting tissue into which those quail brain regions developed was quail-like, yet it was present in the chick body. The methodology used in this second experiment, like that of the sheep-goat experiment described above, did not use dissociated cell transplants. Instead, it involved the excision of a whole third of the chick brain region and its subsequent replacement with the corresponding region of the quail. In the resulting transplanted region, the host cells outnumbered those of the donor and thus directed its development.

Both of these studies bear little similarity to the stem cell experiments under discussion here because these studies involve the transfer of undissociated cells. The first involved the transfer of cell masses and the second of whole regions of the brain. In addition, both of these experiments used animals whose developmental stages were more closely related to each other than are either humans and monkeys or humans and mice, animals that would be used in some proposed retinal stem cell studies. It is unlikely, but theoretically conceivable, that an embryonic human cortex xenograft into chimpanzees, which are closely related to humans, could develop into a human-type neocortex and that the host chimpanzees would exhibit to some degree some human capacities relevant to human dignity. Similarly, if an experiment were conducted in which an entire chimpanzee inner cell mass were replaced with a human embryonic stem cell mass, one could theorize that this might result in a human embryo developing within a pregnant chimpanzee and would raise human dignity issues. In contrast, all available evidence indicates that the use of dissociated stem cells does not produce functional alterations in the host recipient. This is why the use of dissociated cells has been accepted in human brain cell grafts into human patients (Boer 1993).

The retinal stem cell chimeras presented in the example above would involve the dissociation of cultured human cells prior to transplantation. These cells would then interact with the developing monkey cells as they were reorganized by the host. The chimeras produced in these retinal stem cell experiments would remain functionally ordinary mice and monkeys with some human cells. The human cells would contribute to basic functions of these animals but would not cause them to exhibit the sorts of distinctive human functions and capacities that are pertinent to human dignity.

However, if we were to accept the moral taboo, "unnaturalness," or species integrity arguments discussed above, we likely would be obliged to

conclude that we should put an end to all interspecies combinations. To be consistent, both prenatal and postnatal stem cell transplant experiments, all transgenic modifications, and all xenotransplantation would have to be condemned as unethical and brought to a halt. Yet, as we have seen, the moral taboo, "unnaturalness," and species integrity arguments do not clearly demonstrate that all human-nonhuman combinations are wrong in principle. Consequently, they leave us with few compelling reasons to argue against a systematic and careful foray into the study of stem cell chimeras involving the transplantation of human brain or retinal stem cells into nonhumans. We suggest that it is appropriate to pursue such studies given certain restrictions on their design related to the argument from human dignity.

SETTING LIMITS ON STEM CELL RESEARCH INVOLVING THE TRANSFER OF HUMAN NEURAL STEM CELLS TO NONHUMANS

Scientific understanding of the development of human stem cells would be furthered through studies such as the retinal stem cell investigations discussed above. The hope of offering therapeutic benefit to those who suffer from conditions leading to blindness and other serious eye conditions drives most of such research. Yet the pursuit of scientific understanding and medical benefit should be tempered by ethical considerations.

The ethical boundaries that we provide here for research in this field are based on human dignity concerns. We have argued that psychological and cognitive capacities associated with human dignity would not develop in nonhuman hosts in the aforementioned retinal stem cell chimera experiments if methods of proceeding with this research were limited in certain ways (Karpowicz, Cohen, and Van der Kooy 2004). We offer the following guidelines for setting boundaries for experiments involving the transfer of human brain and retinal stem cells into nonhuman prenatal nonhuman animals.[1]

(1) In chimeric experiments involving transfers of human brain or retinal stem cells into early nonhuman embryos, the number of cells transferred should be limited to the smallest number necessary to reach reliable scientific conclusions in order to overcome any possibility that the resulting chimera would be considered able to develop capacities and characteristics associated with human dignity;

(2) The host animal chosen for the development of early blastocyst chimeras should not be overly morphologically or functionally related to humans in order to avoid any risk that the host's unique neurological

networks, which would just be developing, might be susceptible to human incursion; and

(3) Dissociated human stem cells, rather than postanatomical tissue transplants, should be used in the development of both early and later prenatal chimeras in order to guard against any possibility that characteristic human pattern development and formation associated with human dignity might take place in the nonhuman host. These limitations are directed toward avoiding the development in nonhumans of human-like capacities that fall into the cluster having to do with human dignity.

The juxtaposition of bodily materials of different sorts of living beings has become more acceptable since the ancients first developed the notion of the monstrous chimera. However, what is at issue today is not the mixing of materials from members of different species, which is accepted as ethical in several different research contexts, but whether the transfer of certain sorts of human materials, such as brain and retinal stem cells, to nonhuman animals would put human dignity at risk.

Some fear that in a posthuman future, society will use biotechnological manipulations of human materials to create new kinds of beings that resemble but do not fully approximate human beings. They believe that the assembly of such creatures would sacrifice that which is distinctive and significant about human beings and therefore would denigrate human dignity. We maintain that is possible to pursue the sort of neural stem cell research addressed here without violating human dignity if certain precautions are taken along the lines indicated in the above guidelines. The goal of these stem cell chimera studies is to support, rather than to denigrate, both human dignity and human well-being. Their pursuit does not threaten the belief at the core of our social ethic that human beings have a certain distinctive dignity, but instead upholds that central conviction.

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NOTE

1. We recognize that there is a remote possibility that transfers of human neural stem cells to embryonic nonhuman animals might have an effect on the germ cells of those animals. One of us has addressed this topic elsewhere (Cohen 2003), but it deserves fuller discussion in the future.

REFERENCES

Angioi, Karine; Hatier, Renée; Merle, Michel; and Duprez, Adrien. 2002. Xenografted Human Whole Embryonic and Fetal Entoblastic Organs Develop and Become Functional Adult-Like Micro-Organs. *Journal of Surgical Research* 102: 85–94.

Aquinas, Thomas. 1968. *Summa Theologica*, trans. Blackfriars. New York: McGraw Hill.

Balaban, Evan; Teillet, Marie-Aimee; and Le Douarin, Nicole. 1988. Application of the Quail-Chick Chimera System to the Study of Brain Development and Behavior. *Science* 241: 1339–42.

Bazopoulou-Kyrkanidou, Euterpe. 2001. Chimeric Creatures in Greek Mythology and Reflections in Science. *American Journal of Medical Genetics* 100: 66–80.

Beyleveld, Deryck, and Brownsword, Roger. 2001. *Human Dignity in Bioethics and Biolaw*. Oxford: Oxford University Press.

Boer, Gerard J. 1993. Ethical Guidelines for the Use of Human Embryonic or Fetal Tissue for Experimental and Clinical Neurotransplantation and Research. Network of European CNS Transplantation and Restoration (NECTAR). *Journal of Neurology* 242: 1–13.

Boyd, Richard. 1999. Homeostasis, Species and Higher Taxa. In *Species: New Interdisciplinary Essays*, ed. R. A. Wilson, pp. 141–85. Cambridge, MA: MIT Press.

Cao, Yilin; Vacanti, Joseph P.; Paige, Keith T.; et al. 1997. Transplantation of Chondrocytes Utilizing a Polymer-Cell Construct to Produce a Tissue-Engineered Cartilage in the Shape of a Human Ear. *Plastic Reconstructive Surgery* 100: 297–302.

Charland, Louis C. 2003. Are There Answers? *American Journal of Bioethics* 3 (3): W1–2.

Cohen, Cynthia B. 1999. Selling Bits and Pieces of Humans to Make Babies: "The Gift of the Magi" Revisited. *Journal of Medicine and Philosophy* 24: 288–306.

———. 2003. Creating Human-Animal Chimeras: Of Mice and Men. *American Journal of Bioethics* 3 (3): W3–5.

Crowe, Michael. 1977. *The Changing Profile of the Natural Law*. The Hague: Martinus Nijhoff.

d'Entreves, Alexander P. 1970. *Natural Law: An Introduction to Legal Philosophy*, second revised edition. London: Hutchinson.

de Sousa, Ronald. 1984. The Natural Shiftiness of Natural Kinds. *Canadian Journal of Philosophy* XIV: 561–81.

de Waal, Frans. 1996. *Good Natured: The Origins of Right and Wrong in Humans and Other Animals*. Cambridge, MA: Harvard University Press.

DeWitt, Natalie. 2002. Biologists Divided over Proposal to Create Human-Mouse Embryos. *Nature* 420: 255.

Dick, John E.; Guenechea, Guillermo; Gan, Olga I.; and Dorrell, Craig. 2001. Distinct Classes of Human Stem Cells that Differ in Proliferative and Self-Renewal Potential. *Nature Immunology* 1: 75–82.

Douglas, Mary. 1966. *Purity and Danger*. London: Routledge and Kegan Paul.

Finlay, Barbara L., and Darlington, Richard B. 1995. Linked Regularities in the Development and Evolution of Mammalian Brains. *Science* 268: 1578–84.

Flanagan, Owen J, Jr. 1991. *Varieties of Moral Personality: Ethics and Psychological Realism*. Cambridge, MA: Harvard University Press.

Franklin, Sarah. 2003. Drawing the Line at Not-Fully-Human: What We Already Know. *American Journal of Bioethics* 3 (3): W25–27.

Gewirth, Alan. 1982. *Human Rights*. Chicago: University of Chicago Press.

———. 1992. Human Dignity as the Basis of Rights. In *The Constitution of Rights: Human Dignity and American Values*, ed. Michael J. Meyer and William A. Parent, pp. 1–9. Ithaca: Cornell University Press.

Goldstein, Ronald S.; Drukker, Micha; Reubinoff, Benjamin E.; and Benvenisty, Nissim. 2002. Integration and Differentiation of Human Embryonic Stem Cells Transplanted to the Chick Embryo. *Developmental Dynamics* 225: 80–86.

Graves, Robert. 1960. *The Greek Myths*. Vol. 1. New York: Penguin.

Griffiths, Paul E. 1999. Squaring the Circle: Natural Kinds with Historical Essences. In *Species: New Interdisciplinary Essays*, ed. R. A. Wilson, pp. 210–28. Cambridge, MA: MIT Press.

Harris, John. 1998. Cloning and Human Dignity. *Cambridge Quarterly of Healthcare Ethics* 7: 163–67.

Hill, Thomas E., Jr. 1992. *Dignity and Practical Reason in Kant's Ethical Theory*. Ithaca and London: Cornell University Press .

Hull, David L. 1999. On the Plurality of Species: Questioning the Party Line. In *Species: New Interdisciplinary Essays*, ed. R. A. Wilson, pp. 23–48. Cambridge, MA: MIT Press.

Kamel-Reid, Suzanne, and Dick, John E. 1988. Engraftment of Immune-Deficient Mice with Human Hematopoietic Stem Cells. *Science* 242: 1706–9.

Kant, Immanuel. 1956. *Critique of Practical Reason*, trans. Lewis White Beck. Indianapolis: Bobbs-Merrill.

———. 1964. *Groundwork of the Metaphysics of Morals*, trans. H. J. Paton. New York: Harper and Row.

Karpowicz, Phillip. 2003. In Defense of Stem Cell Chimeras: A Response to "Crossing Species Boundaries." *American Journal of Bioethics* 3 (3): W17–19.

———; Cohen, Cynthia; and Van der Kooy, Derek. 2004. It is Ethical to Transplant Human Stem Cells into Nonhuman Embryos. *Nature Medicine* 10: 331–35.

Kass, Leon F. 1997. The Wisdom of Repugnance. *New Republic* 2: 17–26.

———. 1985. Teleology, Darwinism, and the Place of Man: Beyond Chance and Necessity? In his *Toward a More Natural Science: Biology and Human Affairs*, pp. 249–75. New York: Free Press.

———. 2001. Why We Should Ban Human Cloning Now: Preventing a Brave New World. Available at *http://www.thenewrepublic.com/052101/kass052101_print.html*. Accessed 25 May 2005.

———. 2002. *Life, Liberty, and the Defense of Dignity: The Challenge for Bioethics*. San Francisco: Encounter Books.

Kaufman, R.; Mielke, V.; Reimann, J.; et al. 1993. Cellular and Molecular Composition of Human Skin in Long-Term Xenografts on SCID Mice. *Experimental Dermatology* 2: 209–16.

Kekes, John. 1986. Moral Intuition. *American Philosophical Quarterly* 23: 83–93.

Kornack, David R., and Rakic, Pasko. 1988. Changes in Cell-Cycle Kinetics During the Development and Evolution of Primate Neocortex. *Proceedings of the National Academy of Sciences*. 95: 1242–46.

Krieger, Lisa M. 2002. Treading New Ethical Ground, Scientists Put a Bit of Man into a Mouse. *Mercury News* (8 December). Available at *http://www.sililconvalley.com/mid/silicon valley/business/columnists/gmsv/47001*. Accessed 25 May 2005.

Kuhse, Helga. 2000. Is There a Tension Between Autonomy and Dignity? In *Bioethics and Biolaw, vol. II: Four Ethical Principles*, ed. Peter Kemp, Jacob Rendtorff, and Niels Mattson Johansen, pp. 61–74. Copenhagen: Rhodos International Science and Art Publishers and Centre for Ethics and Law.

Levi-Strauss, Claude. 1978. *Myth and Meaning*. London: Routledge and Kegan Paul.

Macklin, Ruth. 2003. Dignity Is a Useless Concept. *British Medical Journal* 327: 1419–20.

Mayr, Ernst. 1988. *Toward a New Philosophy of Biology: Observations of an Evolutionist*. Cambridge, MA: Harvard University Press.

Midgely, Mary. 1978. *Beast and Man: The Roots of Human Nature*. New York: Meridian.

———. 2000. Biotechnology and Monstrosity: Why We Should Pay Attention to the "Yuk Factor." *Hastings Center Report* 30 (5): 7–15.

Ourednik, Vaclav; Ourednik Jitka; Flax Jonathan D.; et al. 2001. Segregation of Human Neural Stem Cells in the Developing Primate Forebrain. *Science* 293: 1820–24.

Polzin, V. J.; Anderson, D. L.; Anderson, G. B.; et al. 1987. Production of Sheep-Goat Chimeras by Inner Cell Mass Transplantation. *Journal of Animal Science* 65: 325–30.

Porter, Jean. 1999. *Natural and Divine Law: Reclaiming the Tradition for Christian Ethics*. Grand Rapids: William B. Eerdmans.

President's Council on Bioethics. 2003. President's Council on Bioethics Meeting of 16 October. Available at *http://bioethisprint.bioethics.gov/transcripts/oct03/session2.html*. Accessed 25 May 2005.

Pullman, Daryl. 2004. Death, Dignity and Moral Nonsense. *Journal of Palliative Care* 20: 171–78.

Raychaudhuri, S.; Sanyal, M.; Raychaudhuri, S. K.; et al. 2001. Severe Combined Immunodeficiency Mouse-Human Skin Chimeras: A Unique Animal Model for the Study of Psoriasis and Cutaneous Inflammation. *British Journal of Dermatology* 144: 931–39.

Robert, Jason Scott, and Baylis, Francoise. 2003. Crossing Species Boundaries. *American Journal of Bioethics* 3 (3): 1–13.

Rollin, Bernard E. 2003. Ethics and Species Integrity. *American Journal of Bioethics* 3 (3): 15–16.

Robertson, John A. 1994. *Children of Choice: Freedom and the New Reproductive Technologies*. Princeton, NJ: Princeton University Press.

Ross, W. D. 1930. *The Right and the Good*. Oxford: Oxford University Press.

Savulescu, Julian. 2003. Human-Animal Transgenesis and Chimeras Might Be an Expression of Our Humanity. *American Journal of Bioethics* 3 (3): 3–5.

Stout, Jeffrey. 1988. *Ethics After Babel: The Languages of Morals and Their Discontents*. Boston: Beacon Press.

Streiffer, Robert. 2003. In Defense of the Moral Relevance of Species Boundaries. *American Journal of Bioethics* 3 (3): 37–38.

Vince, Gaia. 2004. Pig-Human Chimeras Contain Cell Surprise. *New Scientist* 13: 42.

Wade, Nicholas. 2002. Is the World Ready for a Man-Mouse? *New York Times* (28 November): 15.

Wells, H. G. 1896. *The Island of Dr. Moreau*. Garden City, NY: Garden City Publishing.

Wilson, Robert A. 1999. Realism, Essence, and Kind: Resuscitating Species Essentialism? In his *Species: New Interdisciplinary Essays*, pp. 188–207. Cambridge, MA: MIT Press.

Zanjani, Esmail D.; Mackintosh, F. Roy; and Harrison, Michael R. 1991. Hematopoietic Chimerism in Sheep and Nonhuman Primates by In Utero Transplantation of Fetal Hematopoeitic Stem Cells. *Blood Cells* 17: 349–63; discussion pp. 364–66.