

# The science and ethics of making part-human animals in stem cell biology

Jason Scott Robert<sup>1</sup>

School of Life Sciences, Arizona State University, Tempe, Arizona, USA

**ABSTRACT** The National Academy of Sciences recently issued voluntary guidelines to govern human embryonic stem cell research. Among other restrictions, these guidelines prohibit certain kinds of combinations of human and nonhuman animal cells, and call for ethics review and oversight of any protocol involving the transfer of human embryonic stem cells into nonhuman animals. In this essay, I discuss the history of and scientific rationales for combining human cells with cells of nonhuman animals, and critically assess the most recent attempts to limit such research on moral grounds—and find them lacking. Nonetheless, as I show, this research remains scientifically and morally contested. I then explore whether and how the NAS's recommended Embryonic Stem Cell Research and Oversight committees will allow for scientifically well-informed moral assessment of this controversial, but possibly important, research.—Robert, J. S. The science and ethics of making part-human animals in stem cell biology. *FASEB J.* 20, 838–845 (2006)

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IN MAY 2005, the National Academy of Sciences (NAS) issued guidelines to govern human embryonic stem cell research (1); though the guidelines are voluntary, they have been adopted by many organizations (2). The guidelines include very few prohibitions, but two of the prohibited activities involve the combination of cells from humans and nonhuman animals. Noting that crossing species boundaries in biology is not ethically problematic as such (1; see also ref 3), the NAS guidelines nonetheless prohibit the transfer of human embryonic stem cells (hES cells) into nonhuman primate blastocysts and the transfer of any embryonic stem cells (including hES cells) into human blastocysts. Also prohibited is the breeding of any animals into which hESCs have been transferred at any time. Additionally, the NAS guidelines recommend ethical review, through Embryonic Stem Cell Research Oversight (ESCR) committees, of all research involving the transfer of hES cells into nonhuman animals at any stage of development (1). But why?

Despite recent articles, news stories, and commentaries exploring the combination of cells from humans and nonhuman animals, what precisely is supposed to be morally problematic with this research is unclear

(3–9). Unfortunately, beyond brief allusions to “concerns that need to be considered” regarding the contribution of hES cells to brains and gametes in the host, the NAS does not cite any specific reasons for their proposed restrictions (1). And while several other commentators have proposed restrictions on this research (6, 7, 9), their reasons are not compelling.

For instance, Karpowicz et al. recommend a moral limit on stem cell research involving the combination of human and animal materials, based on concerns about how the resultant animals might threaten “human dignity” (6, 7). They worry that such an entity created at the embryonic stage would—if implanted and brought to term—possess the emergent neurological and psychological functions characteristic of humans; they thus claim that it would have moral value, and this would somehow denigrate the inherent dignity of human beings. Moreover, in a very recent “Policy Forum” in *Science*, Greene et al. endorse almost exactly the same position, but rather than referring to human dignity as such, they dress up their concerns in the language of human-like cognitive capacities associated with moral status (9). In any event, they do not satisfactorily explain why it would be morally unacceptable to create these part-human animals.

Concerns about human dignity (by any name) are amorphous, unstable, and politically fraught (e.g., refs 10–14). The phrase “human dignity” is often used as a proxy for other moral principles such as autonomy, or respect for persons, and Ruth Macklin has argued that “dignity is a useless concept in medical ethics and can be eliminated without any loss of content” (12). It is certainly true that it is used in many different ways by many different authors. For instance, David Resnik means by human dignity that humans are intrinsically valuable and so should not be subject to complete commodification (10, 11); Francis Fukuyama defines human dignity as “the idea that there is something unique about the human race that entitles every member of the species to a higher moral status than the rest of the natural world” (15); and Timothy Caulfield and Audrey Chapman observe that in some instances human dignity is “not used as a source of moral rights” but

<sup>1</sup>Correspondence: School of Life Sciences, Arizona State University, Tempe, Arizona, PO Box 874501, Tempe AZ 85287-4501, USA. E-mail: jason.robert@asu.edu  
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rather as reflecting “public morality or the common good” (14). Accordingly, to limit or compel scientific research on the grounds of human dignity—without further elaboration of this essentially contested concept—is inappropriate. Nonetheless, many authors (e.g., see refs 6, 7, 9) and indeed the NAS propose human dignity-based moral limits on research to create part-human animals in stem cell research.

So far, the public debate over part-human combinations in stem cell biology has been seriously hampered by deep misunderstandings of the science and of the ethics (16, 17). As the NAS’s proposed Embryonic Stem Cell Research Oversight committees should serve as the future site for resolving competing views of the scientific and moral value of this research, I hope that ESCRO committee discussions will be much better informed. To this end, in this essay I explore interrelated concerns about scientific justifications of experiments involving the aggregation of human and nonhuman cells, and moral justifications of restrictions on such experiments.

I take as a starting point the truism that good studies should be both morally and scientifically well justified. A scientifically well-justified study is not, by virtue of that fact, morally justified. But a morally well-justified study must also be scientifically well-justified—among other faults, it would be a waste of resources to proceed with a study that will not advance knowledge. Accordingly, scientific justification is a necessary but not a sufficient condition for the moral acceptability of proposed research. In what follows, I focus on an important dilemma in the context of stem cell research involving the combination of human and nonhuman cells: it seems that some studies that are scientifically not well justified are viewed as morally acceptable, while some studies that are well justified from a scientific point of view are ruled out *a priori* on moral grounds. I attempt to provide resources for responsibly resolving this dilemma, beginning with a brief history of interspecies cell-transplant research.

## WHAT’S AT STAKE?

Most of the ethical and scientific discussion to date has used the language of *chimeras*. “Chimera” connotes the ancient Greek mythological creature comprising the head of a lion, midsection of a goat, and tail of a snake; but it generally denotes a creature containing discrete cell populations from at least two distinct organisms. Chimeras are supposed to be different from transgenics (created by the interspecies transfer of DNA) and hybrids (created by breeding animals or plants of different species or varieties). Chimeras, created through the transfer of cells from at least one animal to another, need not be interspecies beings; a mouse with cells from another mouse of the same species is no less a chimera than one with cells from a mouse of another species, or from a rat or other animal. Moreover, chimeras can be created at any developmental stage from the early blastocyst through the senescing adult.

As explored by Robert and Baylis (3), chimeras are apparently most controversial when they involve combining human and nonhuman cells. In stem cell biology, the controversy surrounds transferring *human* stem cells into *nonhuman prenatal* hosts (though, presumably, transferring nonhuman stem cells into human prenatal hosts would also be controversial).

The definition of “chimera” as an organism containing discrete cell populations from at least two organisms may sometimes be adequate. But the definition is not universally accepted, it does not always capture the entities that are putatively morally controversial (e.g., embryos created by transferring human nuclear DNA into enucleated rabbit or cow oocytes), and it may capture entities that are by now virtually altogether uncontroversial (e.g., adult organ transplant recipients). Moreover, even what counts as an organism is under debate by biologists, philosophers, and historians (18, 19), so strict definitions of chimeras may end up obfuscating as much as they clarify.

Accordingly, I will generally avoid the term “chimera” except where citing scientific research described specifically as chimera research. Instead, and given that my emphasis is on what can and should be done with human cells in stem cell biology, I will refer instead to part-human entities or animals generated through the combination of human and nonhuman cells, tissues, or organs at any stage. Far more than definitions, what is at issue are the sorts of entities that can be made, the sorts of reasons for making them, and the sorts of ethical issues raised by making such entities.

In 1998 Stuart Newman applied for a patent on the application of particular techniques to create human-nonhuman primate chimeras (20, 21). His aim was to restrict the application of these techniques until an adequate public debate had resolved the moral controversy. This patent application was finally unsuccessful in 2005, after multiple resubmissions (12). In the meantime, *inter alia*, Brustle et al. grafted human neural cells into the brains of embryonic rats (23), Ourednik et al. transferred human neural stem cells into the developing fetal brain of Old World monkeys (24), Goldstein et al. transplanted hES cells into chicken embryos (25), and Almeida-Porada et al. transferred human neural and hematopoietic stem cells into fetal sheep (26).

Fantastical as it may seem to many nonscientists, this research involving the combination of human and nonhuman cells prenatally must be understood in its appropriate historical context. Chimeras or cellular mosaics have an important heritage in developmental biology. Cell transplant studies were a staple of experimental embryology in the late nineteenth and early twentieth centuries (27), leading to a wide range of experimental efforts throughout the twentieth century. For instance, in 1969 LeDouarin created embryonic quail-chick chimeras to study neural development (28). Live interspecies embryonic chimeras were first created in mammals in 1980 by Rossant and Frels (29) who, building on prior work in birds and amphibians as well as in mice and other mammals (28, 30–32), successfully

injected inner cell masses from cells of one species of mouse into the blastocysts of another closely related species, and brought them to term. Attempts to combine more distantly related species were unsuccessful until 1984, when Meinecke-Tillmann and Meinecke removed the reproductive barrier between sheep and goats (33), and Fehilly and colleagues reported the first sheep-goat chimera—the “geep” (34).

### WHY CREATE PART-HUMAN ANIMALS?

In contemporary stem cell research, the central rationale (though not the only rationale) for combining human and nonhuman cells is that the resultant animals may be useful assay systems for assessing cell behavior upon transplantation, especially migration, division, and determination (4, 6, 23–25, 35, 36). Foreign cells may be marked and, on transfer to hosts, their behavior and fate may be observed. Indeed, quail-chick chimeras were initially devised as assay systems, to assess cell fate prior to the use of current technologies to mark cells. LeDouarin’s research, mentioned above, represented an important innovation within developmental biology. She was studying chromatin (the complex of nucleic acids and proteins that comprise chromosomes) in quails. She observed that quail chromatin is very condensed, a rarity in the animal kingdom; by contrast, the chromatin of chicks is diffuse and distributed. LeDouarin recognized the experimental opportunity before her: she could transplant chick cells into quail (or *vice versa*) and, as chromatin stains well, stain the sample and readily observe the fate of the exogenous cells. Accordingly, she transplanted cells from one region of the quail embryo to the same region of an age-matched chicken embryo *in ovo*, and thereby established an immensely productive model system for the study of neural crest cell migration, among other basic neurodevelopmental phenomena (28, 37; cf. 4).

With the development of molecular markers, biologists no longer need to create this type of chimeric marking system to be able to observe cell fate in normal development. But these creatures may still be useful for

assessing the behavior of marked cells upon transplantation, and may facilitate the genetic analysis of development (38). Within stem cell biology, where the emphasis is as often on developing therapeutics as on understanding development as such, biologists transplant human cells (embryonic or differentiated) into hosts in order to observe cell potential and so to predict the success of cell-based therapies in humans. Such work was important in the development of bone marrow transplants and in early hematopoietic stem cell research, where mice with human blood systems were a laboratory staple (39–41). These considerations are crucial to the project of scientifically justifying further combinations of human and nonhuman cells.

As assay systems, various part-human combinations are possible, depending (as depicted in **Table 1**) on developmental stage of the host, type of host, and cell source (embryo, fetus, “adult”). Choice of host will be based on a variety of criteria (5). Choice of cell source is important for the project of developing therapeutics; not only will different cells be useful for different purposes, but also, because tumorigenicity is a defining feature of embryonic stem cells, it may be important to culture hES cells prior to transplantation, or to use cells derived from adult organs or tissues.

Beyond the realm of assay systems, there are other potential reasons to combine human and nonhuman cells in stem cell biology. For instance, nonhuman animal fetuses containing human stem cells may be useful as sources of cells, tissues, and organs for xenotransplantation. The process would involve transferring human stem cells into the permissive developmental environment of a nonhuman fetus and then eventually harvesting the resultant organ from the mature animal for transplant into a human (42). Additionally, enucleated nonhuman oocytes transplanted with human DNA may be useful as stem cell sources (43, 44). The latter has been proposed in response to the scarcity of human embryos as a source of stem cells. A “humanesque” embryo may instead be created via transfer of the nucleus from a human somatic cell into an enucleated nonhuman oocyte; the inner cell mass may then be harvested from the chimeric embryo (see **Table 2**).

TABLE 1. *Part-human adults, fetuses, and embryos as assay systems in stem cell biology*<sup>a</sup>

	Reason for creation	Typical life trajectory
Adult	Assay system for assessing cell fate and tumorigenicity of transplanted stem cells; produced <i>in vivo</i>	Observed for any sign of pathology or behavioral manifestation of graft; may be euthanized, followed by preparation for histological, genetic, and other biological analysis
Fetal	Prenatal (and postnatal) assay system for assessing cell fate and tumorigenicity of transplanted stem cells; produced <i>in vivo</i>	May be destroyed prenatally or brought to term; organs prepared for histological, genetic, and other biological analysis
Embryonic	Very early prenatal assay system for assessing cell fate and potential tumorigenicity of transplanted stem cells; produced <i>in vitro</i>	Generally destroyed early in development, may be implanted in host uterus for further development prior to termination or birth; upon destruction, prepared for histological, genetic, and other biological analysis

<sup>a</sup>These combinations are subject to further distinctions based on the type of host and the type of cell transferred.

**TABLE 2.** *Part-human fetuses and embryos as sources of cells, tissues, and organs*<sup>a</sup>

	Reason for creation	Typical life trajectory
Fetus	Source of humanized cells or organs for potential xenotransplant	Generally brought to term and, where necessary, euthanized prior to organ harvest
Embryo	Source of humanesque stem cells for research purposes	Destroyed at the blastocyst stage upon isolation of the inner cell mass

<sup>a</sup>These combinations are subject to further distinctions based on the type of host.

Advanced Cell Technology has patented the technique for generating embryos by fusing human nuclei with cow oocytes (45), while Chen et al. have fused human nuclei with rabbit oocytes to generate embryos as a source of stem cells (43).

### WHY NOT?

Different scientific and ethical issues attach to the different kinds of entity described in Tables 1 and 2. Embryos created as stem cell sources result from the fusion of a human nucleus and a nonhuman enucleated oocyte. Some of the relevant concerns are those that attend all cloning protocols (primarily safety, welfare, and “human dignity” considerations), compounded by the additional scientific and moral concerns that attend many transgenic and interspecies protocols, such as worries about zoonotic infection. Worries about zoonotic infection also attend the creation of fetuses as sources of cells, tissues, and organs for xenotransplantation, even though such part-human fetuses, when brought to term and allowed to develop, may help to avoid the problem of immune rejection.

Similar moral and safety concerns may apply in the case of part-human animals created for use as assay systems. Additionally, prenatal animals may or may not be implanted in a uterus, gestated, or birthed; also, they may be aborted during gestation or euthanized postnatally; these different eventualities may generate further ethical concerns.

As safety considerations permeate all of biology and biotechnology research, I will assume for the sake of argument that while the safety risks of combining human and nonhuman cells are unknown, they fall within the range of present-day tolerability.

Moral concerns about cross-species research as such have to date remained amorphous and poorly articulated (as explored in ref 3). The most recent attempts to morally justify restrictions on combining human and nonhuman cells in stem cell biology are no exception. Karpowicz et al., for instance, begin by arguing in favor of transplanting human cells into nonhuman embryos on the grounds that we can learn something important from such humanized models, and that the potential good consequences for humans compel us to promote such research through biological humanization (6). But they also stipulate that the resultant creatures must not be too human; that is, they must not possess human functions “that are necessarily associated with moral worth” (46), or else they would somehow violate human

dignity—the putatively bad consequence of moral humanization (6,7). Accordingly, they assert the ethical impermissibility of transplanting moderate to large numbers of human stem cells into some kinds of nonhuman embryos, and require strict monitoring of the consequences of transferring even small numbers of human stem cells (6).

Meanwhile, Greene et al. (9) limit their focus to grafts of human neural cells into nonhuman primate hosts, and propose restrictions on such research based on six considerations: the ratio of foreign to endogenous cells at transplant; the stage of brain development; the species of nonhuman primate host; the brain size of the host species; the site of the cell transplant; and the condition of the brain prior to transplant. The authors conclude that some experiments are likelier than others to raise ethical concerns about moral status, especially experiments that may result in the transfer of characteristically human cognitive capacities into nonhuman hosts. Accordingly, they assert that while it may be permissible to transplant a small number of human neural stem cells into the healthy brain of a distantly related adult monkey, it would be unacceptable to graft the cells into closely related species at an early developmental stage so as potentially to comprise a large proportion of the host’s brain.

In their short article, and possibly because it is a short article, Greene et al. (9) do not address the complex relationship between cognitive capacity and moral status. Rather, they seem to take for granted that the biological humanization of a nonhuman primate brain might lead to the moral humanization of the resultant animal (or, perhaps, the moral dehumanization of *Homo sapiens*), and that this would be bad. Then they suggest restrictions on biological humanization to avoid this putatively bad result. But the very point of conducting these sorts of studies using part-human creatures as assay systems is to learn about human cells in a human-like setting—that is, to learn something important to the development of therapies for humans from experiments involving biologically humanized models. The “less controversial” experiments that Greene et al. would permit (see above) are also among the less scientifically defensible studies.

And there is the rub. An important tension between moral and biological humanization remains unaddressed in the literature. At least for part-human animals as assay systems, it remains unclear in particular cases whether we can learn enough from biologically humanized but morally nonhumanized animals to jus-

tify conducting the research at all. The putative scientific value of these part-human animals rests in their biological humanness; to restrict their biological humanness, for whatever reason, is to restrict their scientific value. If the part-human animals are not biologically human enough to be scientifically informative as biological assays, then they should not be created regardless of vague concerns about human dignity.

## JUSTIFYING THE CREATION OF PART-HUMAN ANIMALS

The scientific rationales for creating part-human embryos and fetuses as cell and tissue sources (Table 2) are different from the scientific rationales for part-human animals as assay systems (Table 1). For the former, the relationship between moral and biological humanization is not especially complex. Nonetheless, whether biologically humanized humanesque embryos and sheep with human livers will be publicly deemed morally nonhumanized remains to be seen. And once the humanesque cells and humanized livers are retrieved from these part-human animals, scientists may wish to transplant these cells and livers into nonhuman hosts, thereby creating new part-human animals as assay systems.

It is with part-human animals as assay systems that the greater difficulty rests. These animals, like many transgenic animals in widespread use in biology laboratories, are supposed to model the human context so as to facilitate inferences from animals to humans (4). Recently, a group of stem cell biologists debated the validity of such assays for studying human embryonic stem cells, and recommended transplanting human embryonic stem cells into nonhuman blastocysts as one way to test the potential for global incorporation into host tissue *in vivo* (35). (Alternative tests would involve transplanting cells into defined tissue environments in nonhuman fetuses or adults, or into humans.) On this view, the part-human animal would permit observation of how human stem cells behave on transplantation, and thereby lessen the gaps between nonhuman animal and human, and between lab and clinic. But while prenatal interspecies research of this sort may indeed generate exciting data, what these *data* are *evidence of* is not always clear.

The scientific value of part-human animals in assessing the potential of human stem cells remains contested in part on the grounds of what has been dubbed “*Xenopus*’ paradox” (4). The ancient Greek Zeno of Elea proposed a number of paradoxes of motion, including this one: in order for an object to move a certain distance, it must first move half that distance; but before it moves half that distance, it must move one-quarter of that distance; but before it moves one-quarter of that distance, it must move one-eighth of that distance; and so on, *ad infinitum*. Accordingly, the object will never move the originally intended distance. The analogy with part-human animals in stem cell research is as follows: there is an inferential gap be-

tween nonhuman animal models (such as mice, rats, or nonhuman primates) and humans; while part-human animals may be thought to bridge the gap, we may end up learning more about the part-human animal itself than about either source or host, such that instead of bridging the gap, the part-human animal generates two new inferential gaps (one between the source and the part-human animal, and the other between the part-human animal and the host). Any further attempts to bridge the gap will be subject to the same considerations, such that the inferential gap can never be successfully bridged.

Zeno’s paradox of motion is only apparent: throw a rock, and it will indeed move as intended. Biologists may be inclined to interpret *Xenopus*’ paradox in a similar way, as a pseudo-problem. But *Xenopus*’ paradox may be less merely apparent and superficial than biologists might initially presume, for there is no equivalent in stem cell biology to just throwing a rock. Of course, just creating a part-human animal might work. But consider these results: mouse stem cells, when transplanted into other mice, generate teratocarcinomas—malignant tumors (47). But when human stem cells are transplanted into mice, they generate only benign tumors (48). At least two incompatible inferences are possible: 1) that human stem cells will behave nonpathogenically when transplanted into no matter what host; or 2) that transplantation of stem cells into closely related species (or within the same species) increases the likelihood of tumor formation.

If we make the first inference, and proceed with cell transplant clinical studies in humans, all will be well; unless the second inference is the correct one, in which case all hell will break loose. Unfortunately, interspecies research alone cannot provide evidence to decide between these alternative inferences. (See also ref 49 for a related cautionary tale.)

In fact, interspecies research of this sort is itself responsible for introducing a number of potentially confounding variables, including differences in cell-cycling, morphogenesis, and life span. Moreover, cell culture conditions are extremely idiosyncratic and methodology varies between cell types and species. This suggests that cell-cell signaling and response to other biochemical signals might be species-specific, and so might confound attempts at interpreting data from part-human animal studies (4, 50).

Now, consider an alternative to creating part-human animals. Let us assume that the best environment for assessing the potential, including potential tumorigenicity, of human stem cells is a permissive, prenatal environment: the fetus—or, better still, the early embryo. If the eventual aim is to move from lab to clinic, one possible trajectory is to proceed from mouse-mouse studies directly to human-human studies without pausing to create part-human embryos or fetuses. Transplanting human stem cells into <14-day-old human embryos, while morally controversial, may be no more controversial (or at least it would be controversial in a different way) than transplanting human stem cells into

embryonic mice or fetal macaques. And *Xenopus*' paradox would thus be avoided. (Coincidentally, creating human-human embryos is substantially less scientifically controversial than creating part-human animals with human stem cells.)

None of this is to say that scientists should not be creating part-human animals—or that they should be transplanting human cells into human embryos or fetuses. All I have shown is that the value of creating part-human animals cannot be taken for granted, and that scientists will face important challenges in generating a valid *prima facie* case for combining human and nonhuman cells.

## EVALUATING RESEARCH PROPOSALS

To restrict creating some kinds of part-human animals on the *a priori* grounds that it might threaten human dignity (as in refs 6, 7) or inappropriately elevate the moral status of part-humans (as in ref 9) may have the net effect of restricting many more kinds of stem cell research involving human and nonhuman cells than the authors intend. All ethical studies must be scientifically well-justified. The most straightforward justification will rest on the value of biological humanization: the more biologically human the assay system, the less likely it is that inferential difficulties will arise. But without a clear rationale (or at least without presenting a clear rationale), these authors worry about moral humanization, and so propose to limit biological humanization, thereby undercutting the possible value of the research.

It is noteworthy that both sets of authors—as well as the authors of the NAS guidelines—include scientists as well as ethicists. It is thus surprising to see them endorse *a priori* limits on acceptable research. I agree with them that, in some cases, proposed research should be deemed unacceptable, but urge that acceptability be negotiated on a case-by-case basis by appeal both to well-articulated scientific justifications and adequately elaborated moral concerns. This is the only way through the dilemma before us: those studies that are least scientifically contestable (such as transplanting human cells into closely related nonhuman primates or humans) are those that are apparently most morally controversial in terms of human dignity, while those studies that are most scientifically problematic (such as transplanting small numbers of human cells into distantly related nonhuman animals) are those that are apparently least morally controversial in terms of human dignity. Here I have identified some of the scientific considerations that should come into play; several of the moral (and legal) issues have been debated in an exchange in *The American Journal of Bioethics* (3). But much more remains to be said as we enter the era of Embryonic Stem Cell Research Oversight (ESCRO) committees.

The National Academy of Sciences' proposal to create ESCRO committees in institutions that conduct hES cell research offers a potential partial resolution. An

ESCRO committee would be charged with reviewing any protocol proposing the derivation or research use of hES cells. The ESCRO review would not replace the review of Institutional Review Boards or, where appropriate, that of Institutional Animal Care and Use Committees, but would supplement it. ESCRO committees would also be charged with monitoring ongoing hES cell research, ensuring compliance with the NAS and other guidelines, and a mandate for the ethics education of hES cell researchers. ESCRO committees could function as the appropriate space for negotiating the value of scientifically or morally controversial research involving human stem cells—beyond the rhetoric of “human dignity.”

While the NAS guidelines currently prohibit transferring any embryonic stem cells (including hES cells) into human blastocysts and any hES cells into nonhuman primate blastocysts (which is why the resolution is at best partial), the guidelines leave the approval of other forms of research, including interspecies research involving hES cells, to the discretion of ESCRO committees:

*All research involving the introduction of hES cells into nonhuman animals at any stage of embryonic, fetal, or postnatal development should be reviewed by the ESCRO committee. Particular attention should be paid to the probable pattern and effects of differentiation and integration of the human cells into the nonhuman animal tissues (1).*

Prohibiting certain kinds of research does not count as a permissive invitation to create all other kinds of part-human animals, for all such research will be subject to examination by the review and oversight committee. Accordingly, any protocol for such research must be well-justified, and must withstand scientific, ethical, and political scrutiny. I hope that members of ESCROs will have the freedom—and indeed be encouraged—to articulate, explore, and either endorse or abandon specific scientific and ethical objections to proposed research.

While affording the opportunity for sensible local negotiation of the value of certain kinds of hES cell research, ESCRO committees are not panaceas. Just as local Institutional Review Boards are only partially successful as mediators of the scientific validity and ethical acceptability of research involving human subjects, we are not in a position to expect more from ESCRO committees. The success of an ESCRO committee will depend heavily on many factors, including committee membership, how well staffed the committee is, how well financially supported it is, whether it has any independence from the research mission of the institution in which it is based, and whether the scientists proposing protocols see ESCRO review as an opportunity to justify their research or as a regulatory hurdle to be overcome.

This last point is especially important. Presumably, even though the results of particular experiments cannot be fully anticipated, scientists have good scientific reasons for conducting their experiments. That is,

while scientists cannot predict exactly how experiments will turn out (else there would be no reason to perform the experiment), scientists surely do have reasons for performing one experiment and eschewing another. It is not too much to ask scientists to make these reasons transparent, such that a research program wears its logic on its sleeve, for anyone to see. This is especially important where the stakes are high, as when public trust in science may be significantly undermined by the imperative of discovery.

Judging from the negative public response to proposals to create part-human animals (e.g., 16, 17), stem cell researchers will have a difficult task in disabusing the image of mad scientists run amok. Well-articulated scientific justifications may help to dispel the appearance of hubris and irresponsibility. But to date scientists are partially responsible for generating this image, especially when they turn away from public justification of their research and demand to be left alone, unburdened by nonscientific rules and regulations. The problem with this response is that it fails to recognize the social context in which scientific research is deeply embedded; it fails to take seriously that scientific research, like all scholarly research, is a public enterprise—even where the research funds are not provided directly by the state, the research itself is undertaken in a civic context, bound by rules, regulations, and political mores.

Good will, on all sides, is a condition of the scientific endeavor. It is only in the context of frank attempts to justify research—and, concurrently, frank attempts to explicate the nature of moral concerns—that sound science will move forward. FJ

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