



# Emerging Issues in Human Embryonic Stem Cell Research: Chimeras

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# Ethical Issues

- n Bracketing
  - Traditional animal ethics issues
  - Standard issues about research involving, or following downstream from, the destruction of human embryos
  - Public health issues about xenotransplantation
  
- n Consent Issues
- n The Moral Status Framework (Streiffer 2005)



## Consent Issues

- n Ideally, the consent process for somatic cell, gamete, or embryo donors would inform donors that resulting hES cells, cell lines, or their derivatives might be incorporated into a nonhuman animal, especially for animals in early stages of development.
- n Prospectively, under what conditions, if any, should that requirement be waived?
- n Retrospectively, under what conditions, if any, should cell lines be grandfathered in even though the consent process did not inform donors of that possibility?



## The Moral Status Framework

- n Under what circumstances, if any, would the introduction of human material render an animal the moral equivalent of a normal human adult? (“enhance the animal’s moral status”)
- n Under what circumstances, if any, is it morally permissible to enhance an animal’s moral status?



## Which Status Enhancements Are Permissible?

- n A status enhancement is not itself morally problematic, and is in fact a prima facie benefit.
- n But enhancing an animal's status is permissible only if there are reasonable assurances in place that its new moral status will be adequately respected.
  - Even supposing animal regulations were adequate to begin with, it is not enough to follow those regulations with respect to an animal that is now the moral equivalent of a normal human adult.



## The Situation to Be Avoided

- n A situation in which a transplant of human material into a developing animal renders the animal the moral equivalent of a normal adult human ...
- n and the animal continues being treated as animals are usually treated in biomedical research.



## Which Status Enhancements Are Permissible?

- n In most (all?) contexts, adequately respecting the new moral status of an enhanced animal will be incompatible with the research objectives which motivated the use of an animal to begin with.
  - Interventions that are nontherapeutic and more than minimal risk
  - Confinement
  
- n And if the research objectives for a study are compatible with the study's being performed on an individual with our moral status, then using human subjects in that study would be permissible, and would also be scientifically superior if the research objectives are to gain knowledge related to human development or human health.
  
- n Hence, in most (all?) contexts, status-enhancing research is unethical.



## The Practical Difficulties

- n Under what circumstances, if any, would the introduction of human material render an animal the moral equivalent of a normal human adult? (“enhance the animal’s moral status”)
  - Ethical Question: What effects would a transplant need to have to enhance an animal’s moral status?
  - Scientific Question: Which transplants would have those effects?



## The Practical Difficulties: The Ethical Question

- n What effects would a transplant need to have to enhance an animal's moral status?
  
- n Why is it that we have our comparatively high moral status?
  - Cognitive Capacity Views
  - Species Membership Views
  - Potentiality Views
  - ...



## The Practical Difficulties: The Scientific Question

- n What is the chance of different transplants bringing about those kinds of effects?
  - Stage of development at the time of transplant
  - Species of recipient; length of gestational period
  - Proportion of human cells being introduced
  - Aggregation or disaggregation of the cells
  - Plasticity of the cells; possibility of specialized cells dedifferentiating
  - Impact on neural tissue and cognitive capacities
  - Disposition of chimeric research subject



# National Academy of Sciences Guidelines

- n A prohibition on all “research in which hES cells are introduced into nonhuman primate blastocysts.” (1.2(c))
- n A prohibition on the “introduction of hES cells into nonhuman mammalian blastocysts” except where “no other experiment can provide the information needed”. (6.7)
- n Review for “all protocols involving the combination of hES cells with nonhuman embryos, fetuses, or adult animals” to look for “the consequences of the human contributions to the resulting chimeras.” (6.4)
- n Minimal review of introductions into adult animals, except where “the human cells could contribute in a major organized way to the brain of the recipient animal,” in which case “it is desirable” that there should be a strong scientific justification and prior proof of principle using nonhuman cells. (6.5)
- n More extensive review when hES cells, their derivatives, or other pluripotent cells are transplanted into fetal animals that are allowed to develop to adulthood, to look for “major functional contributions to the brain.” (6.6)



## Reflections on the NAS Guidelines

- n The Moral Status Framework offers a way to sharpen those recommendations as to what the ESCRO review should be looking for.
- n From the perspective of the Moral Status Framework, the two prohibitions are unnecessarily restrictive:
  - On almost any view of moral status, some hES cell transplants into mammalian or nonhuman primate blastocysts would not enhance moral status.
  - The NAS's focus on effects on the brain seems to presuppose a cognitive capacity view of moral status, and on such a view, status enhancements could be avoided by an early termination policy.
  - Such a termination policy could require termination either prior to the onset of consciousness or prior to the onset of the particular cognitive capacities held to be responsible for the moral status of normal adult human beings (the latter would be more difficult to implement).