

## Review of: "Bioethical Assessment of Research with Humanoid or Humanized Biological Entities with Uncertain Moral Status"

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Potential competing interests: No potential competing interests to declare.

Humanoid or humanized biological entities have uncertain moral status. That is why bioethical assessment of research on these entities is particularly difficult as stated by the authors. The moral status of humans conducted to clear ethical constraints in research, even for intellectually disabled humans. Some elements of the moral status have been considered regarding animals used in research with the following rules: Refine, Reduce, and possibly Replace. I think that the question of humanoid and humanized biological entities rises from a speciesist view: humans discriminate nonhuman animals in research. Hence the necessity to state how humans are these humanoid or humanized entities. This is striking in the human-animal chimera. This is one point that could be present in the introduction.

I do not have much to say about the methods for producing such entities. The CRISPR technique (mentioned once in the text for knockout pigs) is a powerful modifying tool available in organisms, but also in cells, tissue, organs and thus could have been developed more. The description of entities, the possible progresses are well described. I will concentrate on the ethical questions which correspond to the title. This title could be modified because the description of entities represents a major part of the paper. The entities now are cells, tissues, or possibly a part of organ. They are not organisms. It is then difficult to establish a moral status for the produced entities. The main ethical questions are: 1) do the cells, etc. or entities produced to understand mechanisms and remain as entities?, 2) or are these entities an intermediary step for producing organs or organisms? The production of organs could be compared to husbandry it is run nowadays and may be subjected to the same ethical questions. The production of organisms (and humans only in a speciesist angle) should then be confronted to enormous ethical constraints. We are not ready for an Aldous Huxley 1984.

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