



Commentary

Chimeras intended for human gamete production: an ethical alternative?

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ABSTRACT

Human eggs for basic, fertility and stem-cell research are in short supply. Many experiments that require their use cannot be carried out at present, and, therefore, the benefits that could emerge from these are either delayed or never materialise. This state of affairs is problematic for scientists and patients worldwide, and it is a matter that needs our attention. Recent advances in chimera research have opened the possibility of creating human/non-human animal chimeras intended for human gamete production (chimeras-IHGP). In this paper, I examine four arguments against the creation of such chimeras and prove that all of them are found wanting. I conclude by showing that there is a strong moral reason for scientists to pursue this research avenue.

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Introduction

Different strategies have been proposed for increasing the supply of human eggs for research purposes: compensating women for egg donation, obtaining human eggs from aborted fetuses, posthumous egg donation, and in-vitro gametogenesis. Serious research efforts are dedicated to in-vitro gametogenesis at the moment (Hendriks et al., 2015). Each of these options, however, is faced with different ethical dilemmas and regulatory constraints (Baylis, 2009; Ellison and Meliker, 2011; Greely, 2016).

One possible avenue for solving the egg shortage problem is to create human/non-human animal chimeras intended for human gamete production (chimeras-IHGP). One way in which this can be achieved is through interspecies blastocyst complementation. In this technique, a non-human animal blastocyst is obtained from a mutant strain in which 'a gene critical for the development of a particular lineage is disabled' (Wu et al., 2016, 2017). Afterwards, this blastocyst is complemented with human stem cells, which will compensate for the existing niche.

Despite ongoing research and scientific and ethical discussions about the development of chimeras capable of producing solid organs, such as kidneys and hearts for transplantation purposes, no wide discussion

of the possibility of creating chimeras-IHGP has taken place. Scientists have only discussed how to avoid creating chimeras capable of producing human gametes (Rashid et al., 2014). A possible explanation for this is that many scientists consider that developing such chimeras is so 'ethically and politically problematic', that it is not even worth discussing this option. For example, Rashid et al. (2014), while discussing interspecies complementation for organ generation, have stated that:

[We are] sensitive to the fact that research with the potential to present the following hypothetical scenarios warrants particularly thorough consideration prior to commencement. (. . .) (2) Situations wherein functional human gametes (eggs or sperm) might develop from precursor cell types in an animal, and where fertilization between either human (or human-derived) gametes and animal gametes might then occur. (Rashid et al., 2014, p. 408)

In order to avoid the above, scientists are developing methods of target-organ generation that would preclude the accidental generation of human gametes within human/non-human animal chimeras (Kobayashi et al., 2015; Rashid et al., 2014). Owing to space constraints in this paper, I only discuss creating chimeras-IHGP for obtaining human gametes for research purposes. The ethical issues concerning use of chimera-generated human gametes for reproductive purposes,

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just as with in-vitro generated gametes for reproductive purposes, are important and need further exploration. For an up-to-date review of the scientific state of in-vitro gametogenesis, see [Hendriks et al. \(2015\)](#); for an up-to-date review of the ethics debate on in-vitro gametogenesis, see [Smajdor and Cutas \(2015\)](#) and [Segers et al. \(2017\)](#).

At this point, we must ask: why might developing chimeras-IHGP be so morally problematic that it should not be attempted? Four arguments against the creation of chimeras IHGP seem promising: human dignity would be violated by their creation; the value of human gametes would be debased by being generated within chimeras; generating such creatures is problematic because a human, or hybrid, pregnancy could ensue; and the research benefits of using such gametes do not outweigh the harms (death or pain) that the chimera would suffer. In what follows, I assess these arguments and show that they are found wanting, and then present an argument in favour of creating such type of chimera.

Human dignity

Appeals to human dignity when objecting to new biomedical research are common. It, therefore, seems natural that some may claim that the creation of chimeras-IHGP would constitute a violation of human dignity, and consequently that such creatures should not be created. The problem with this position is that it is not at all clear how human dignity could be violated by the mere creation of such creatures, as the claim that the creation of any human/non-human animal chimera (of which chimeras-IHGP are a subset) inherently violates human dignity is just false. We do not consider that the existence of a NOG mouse with engrafted human cells violates human dignity, even when it is a human/mouse chimera. Neither, do we consider that human dignity is violated when someone receives a pig heart valve, which effectively turns them into a chimera.

A more charitable reading of this kind of argument would rest upon the claim that creating a chimera-IHGP would create a being with human dignity. Therefore, it may be claimed that given this, and the belief that creatures in possession of a dignity ought not be used merely as a means to an end, chimeras IHGP should not be created. If this is what it is meant, then what would actually follow is that how we treat such creatures determines whether their dignity is violated, or not ([Palacios-González, 2015a](#)). From this position, it would also follow that we have the same moral obligations towards such chimeras as we have towards other human persons. If human dignity is tied to the possession of certain higher mental capacities, then as long as the chimeras-IHGP lack them, there would be no danger of violating their human dignity, as they would not possess it in the first place. Precluding the generation of human brain cells through genetic engineering, a strategy examined by [Rashid et al. \(2014\)](#), when creating chimeras-IHGP would highly reduce the possibility of accidentally creating a chimera with human brain cells. Therefore, as long as the chimeras-IHGP that we create do not possess higher mental capacities, it is simply not true that creatures with human dignity would be created, and even less that human dignity would be violated.

The value of human gametes

It may also be argued that chimeras-IHGP ought not be created because to do so would debase the value of human gametes. In order

to answer this question, we first need to specify the kind of value that human gametes possess. Human gametes could possess two different types of value: inherent value or instrumental value. This means that they could be valuable in themselves or that they could be valuable as a means to achieve others' ends ([Palacios-González, 2015b](#)).

To defend the proposition that human gametes have intrinsic value is to assert that they have interests, that we have obligations towards them, and that the obligations we have towards them are based, at least partly, on their interests ([DeGrazia, 2008](#)). This position is implausible. What interests could a gamete have? To create an embryo? And if this were so, are we morally required to help gametes create embryos so they can fulfil their interests?

If it is held that human gametes do not have intrinsic value, they may still possess instrumental value. This means that they can have value as tools that we could use to achieve other ends. For example, most people resorting to IVF value their gametes not for themselves but as means to create a child. If it is true that human gametes only possess instrumental value then we have to ask if the value of chimera generated human gametes should be considered inferior to that of human-generated human gametes. The answer to this question, however, does not seem likely to be positive. Given that instrumental value is task-dependent, we have to assert that the instrumental value of chimera-generated human gametes should be assessed by examining how they perform as tools for achieving a certain goal. It is in relation to their capacity to achieve certain ends that we should judge them as valuable or not. For example, the instrumental value of chimera-generated human gametes for human embryonic stem-cell research should be assessed by establishing if they achieve the purpose intended by the researchers.

Given that (a) human gametes do not possess intrinsic value (that could be debased) and that (b) they can only possess instrumental value (which is task-dependent), we must conclude that the debase-ment of value argument is found wanting and thus fails to provide moral reasons for not creating chimeras-IHGP.

Chimera human pregnancy

A third argument against the creation of chimeras-IHGP is that generating them is morally problematic because a human, or hybrid, pregnancy could ensue. Even if we accept, for the sake of argument, that we should not attempt, or allow, for chimeras to become pregnant with a human conceptus, it does not follow from this that we should not create chimeras-IHGP. This argument depends on the *likelihood* of a human or hybrid pregnancy ensuing, and this is a *practical* issue that can be easily dealt with. Henry T. [Greely \(2013\)](#) has proposed five courses of action to avoid these scenarios: creating chimeras of only one sex; using chimeras that are reproductively immature and euthanizing them before they reach reproductive maturity; sterilizing them; euthanizing them if they become pregnant; physically segregating them by sex.

If our intention is to create chimeras-IHGP for their human eggs, then the first course of action seems the most appropriate in order to avoid 'human pregnancies': we should only create female chimeras. This would be the most sensible thing to do given that there is no shortage of human sperm for research purposes. In a scenario in which it is desirable to create chimeras capable of producing both female

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