

The IVG ‘relatedness paradox’: researchers should mind speculation

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Abstract

Companies and academic labs are pursuing the production of gametes from stem cells. Researchers should be active participators in discussions about speculative scenarios, to avoid that this endeavor to accommodate genetic parenthood undermines the value it is meant to serve – either because of unrealistic or insufficient ethical reflection.

Key words: Research ethics ; IVG ; stem cell-derived gametes ; genetic parenthood

The moral debate about stem cell-derived gametes

After a short breather, discussions about *in vitro* gametogenesis (IVG) are back in the public forum with regulatory questions about corporate ambitions to bring the technique to the fertility clinic [1]. Recent reports that somatic cells of a male mouse were reprogrammed to obtain oocytes (which, after fertilization and gestation, led to seemingly healthy offspring) also flared up attention [2]. While it has been asserted that roughly up until 2019 the ethics debate has managed to keep pace with the science, skepticism about technical feasibility set in among researchers who have spent years trying to produce SCD-gametes, causing some to give upⁱ. Yet, despite technical doubts, and with no successful reproductive applications of person-specific SCD-gametes in humans reported to this day, biotech companies have jumped on the bandwagon, professing future ability to generate gametes from people’s blood cells.

The ethical debate about the production of gametes from stem cells started in the early 00s, and showed a peak during the previous decade [3,4,5]. Most of the attention has gone to the development of functional stem cell-derived (SCD) gametes suitable for reproduction, catering to the preference of those who wish to parent genetically related offspring, and for whom existing assisted reproductive technology (ART) does not yield this outcome. In response, various so-called controversial applications of IVG have raised issues, alongside more pragmatic deliberations in terms of safety and justice concerns [4]. As is often the case for emerging technologies, expected timescales are speculative. In 2008, a subcommittee of the UK's Human Fertilisation and Embryology Authority reported that the timescale for treatment with SCD-gametes was between five to ten yearsⁱⁱ. In 2016, Henry Greely estimated safe and effective reproductive applications of IVG to exist sometime in the next twenty to forty years [6]. Given the range of technical obstacles, the International Society for Stem Cell Research presently categorizes human reproductive use of IVG as “a currently prohibited research activity until safety and ethical issues are resolved”, with “potential for use in human reproduction once safety and efficacy is proven” [7].

In response to this, and in view of IVG's supposed transformative potential, but also because of its intertwining with societal values, it is important that researchers and scientists are active participators in this ethical debate, even – or perhaps especially – where it becomes speculative. This notion of ‘speculation’ is controversial, not only because of its pejorative connotation, but also because of possible downsides of speculation (Table 1). However, if one defines ‘speculation’ as part of anticipatory ethics in an attempt to look out for potential outcomes of theoretical scenarios based on incomplete evidence (as I do for the purpose of this article), such efforts need not be denounced [8]. While this does not answer just when a hypothesis becomes too speculative to be ethically valuable, methodological steps have been suggested to facilitate ‘grounded speculation’, adding some constraints to theorizing based on scientific knowledge [9].

For IVG, I believe that evidence-based insight into realities in the lab can contribute to this, which is a reason to encourage participation of researchers in the ethical debate. I argue that through a

speculative lens, IVG might become a technology that undermines the very societal value for which it is presently being developed, i.e. the value that is attached to genetic relatedness. One may call this the ‘paradox of genetic relatedness’ and I will briefly expand on that in the next section. This matters for researchers and scientists for (at least) two reasons. First, in terms of research ethics, scientists have an obligation to reflect on the ends of scientific work in serving the collective good. Second, and relatedly, there is the responsibility to keep future scenarios in check to avoid that the assumed benefits for which IVG is presently being researched are drowned out – because of either unrealistic or insufficient ethical reflection (thus: either too much or too little speculation).

The paradox of genetic relatedness

One could consider IVG’s undermining potential a product of unchecked theoretical speculation about how sperm and eggs could one day be produced from ‘stray’ non-reproductive cells, so that a factual genetic link (and a respective genetic parenthood status) could be inflicted on people, as an effect of shedding dead skin or blood. If somatic cells can be turned into stem cells, and stem cells into gametes, it might become possible to reproduce unwittingly after someone else collects discarded cells and uses them for reproductive purposes. This is one of the controversial (potential) applications of IVG that was first contemplated ten years ago and described as ‘unwitting parenthood’[10]. How – if at all – would this affect the dominant appreciation of genetic relatedness? We may no longer value genetic parenthood in the same way if it becomes routine to be ascribed a parenthood status without one’s knowledge or consent, and future ethical reflection would be welcome to consider this further. Is this theoretical scenario a reason to anticipate that developing IVG – to accommodate the value of genetic relatedness – might one day topple into undermining the value it is meant to serve?

Much will depend on one’s moral views on whether one is wronged (and why) when one becomes a genetic parent unwittingly, and beliefs about the relationship between genetic relatedness and parental responsibilities. Such open-ended ethical deliberations, and however speculative this as yet unrealistic scenario may be, leads into questions about whether such applications of IVG might be the

point at which the societal value of genetic relatedness turns against itself. One may consider it a ‘49/51 idea’: as long as we are on the ‘49’ side, facilitating the value of genetic relatedness seems beneficial, but beyond the tipping point the presupposed benefit might topple into its opposite.

Research ethics

Why should researchers care about such theorizing? The short answer is: research ethics. A thin description of research ethics pertains that, as science is not value-neutral but rather reproduces societal values and through that influences our behavior and aspirations, researchers should minimally be thoughtful of this. As science is permeated by normative assumptions, scientists have a responsibility to reflect on the ends of the research they are performing [11]. Responsibility, as an element of research ethics, is generally considered a commitment to maximize expected benefits and minimize potential harm. Those notions stand in want of specification, and because (rather than despite) of that, scientists have a deontological duty to actively participate in the moral debates about topics in their field that may serve or imperil the good of society.

As regards IVG, this moral debate is largely about the ethical significance of helping people satisfy a desire to have genetically related offspring. How far should we go to accommodate this? To be sure, the *de facto* societal importance attributed to genetic relatedness in parent-child relationships has been a constant throughout the history of ART. IVG is only one recent addition to a long list of technologies envisioning this aim. Ethical principles like respect for reproductive autonomy at least give some valence to the belief that such reproductive aspirations should be taken seriously. However, the fact *that* many people have such a reproductive desire for genetic parenthood does not conclude the ethical debate about how important we *should* find that goal. That is precisely the topic of ethical debate.

In addition to their role as citizens, scientists have a special role in this debate as experts in the topics in question [11]. Their privileged technical insights allow them to assess how risky, (un)feasible and (un)realistic certain prospects are. Importantly, descriptions of risks (for instance) are not vetoes,

but they are morally relevant aspects in ethical deliberations. Similarly, and in defense of speculation, evaluations of feasibility should not be clouded by a narrow short-term focus on technical possibilities.

Public trust and societal value

With the exotic hypotheticals in place about IVG, unwitting parenthood and the paradox of genetic relatedness, one may wonder how much scientists should weigh in on the bioethical debate about whether the endorsement of IVG – in the name of genetic relatedness – might eventually lead to the dissipation of the value that it is meant to serve. The outlines of speculative bioethical considerations are preferably sharpened in response to pragmatic and practical-ethical assessments of relevant factors in the present and immediate future. Reality in the research lab is one of those factors, and given their respective expertise and responsibilities, scientists have an obligation to introduce that to the ethical conversation in and outside the lab. Communication about such realities and future scenarios is about protecting public trust in science and about protecting values that society underpins. Given science's relationship with society's values, and provided that the value of genetic relatedness in parent-child relationships is rightfully allocated socio-moral importance, researchers cannot shake off the future-oriented imaginations about IVG.

If scientists assess the unwitting parenthood scenario to be realistically possible in the future, then they have the ethical responsibility to speak up, lest the paradox of genetic relatedness materializes, undermining a central reproductive value. If, to the contrary, a future in which such a scenario is utterly unrealistic, it is equally important that science weighs in to avoid moral bewilderment. If it does not, and imaginations run amok in an unchecked manner, public support for this technology may crumble, equally failing to serve the value it was meant to attend to. It is, in that respect, fathomable that the more futuristic scenarios of IVG are likely to provoke more controversy, which, in turn, might drown out support for and recognition of the benefits for which this technology is presently being researched. Historic experience with the cloning debate is illustrative: had it kept pace with the research, it might have prevented “the global hyperventilation over Dolly”[11].

Concluding remarks

The bottom-line is that researchers in the rapidly developing field of bio-medical sciences, charged with interests and imaginations, should be active participants in ethical conversations – even if, and especially when speculation is a significant dimension. If we appreciate that scientists have an ethical responsibility to commit to societal values, they should use their voice to avoid an unchecked, but also an underdeveloped, ethical debate. As realities and scientific obstacles may change, this duty is constantly renewed in a continuous work in progress.

Declaration of interests

The author declares no competing interests.

Resources

ⁱ<http://blog.practicaethics.ox.ac.uk/2019/01/human-in-vitro-gametogenesis-and-the-same-sex-marriage-debate/> ; <https://www.technologyreview.com/2022/08/23/1056921/lab-made-human-sex-cell/>

ⁱⁱwww.yumpu.com/en/document/read/51229888/annual-report-2008-09-human-fertilisation-embryology-authority

References

1. Cyranoski, D., *et al.* (2023). Intellectual property and assisted reproductive technology. *Nat. Biotechnol.* 41, 14–20
2. Murakami, K., *et al.* (2023). Generation of functional oocytes from male mice in vitro. *Nature* 615, 900-906
3. Testa, G., and Harris, J. (2004). Ethical aspects of ES cell-derived gametes. *Science* 305, 1719

4. Segers, S., *et al.* (2017). Balancing ethical pros and cons of stem cell derived gametes. *Ann. Biomed. Eng.* 45, 1620-1632
5. Notini, L., *et al.* (2020). Drawing the line on in vitro gametogenesis. *Bioethics.* 34,123-134
6. Greely, H.T. (2016). *The End of Sex and the Future of Human Reproduction* (Harvard University Press).
7. Clark, A.T., *et al.* (2021). Human embryo research, stem cell-derived embryo models and in vitro gametogenesis: Considerations leading to the revised ISSCR guidelines. *Stem Cell Rep.* 16, 1416–1424.
8. Racine, E., *et al.* (2014). The value and pitfalls of speculation about science and technology in bioethics: The case of cognitive enhancement. *Med. Health Care Philos.* 17, 325-37.
9. Roache, R. (2008). Ethics, speculation, and values. *NanoEthics* 2, 317-27.
10. Smajdor, A., and Cutas, D. (2014). Artificial gametes and the ethics of unwitting parenthood. *J. Med. Ethics* 40,748-751.
11. Wolpe, P.R. (2006). Reasons scientists avoid thinking about ethics. *Cell.* 125,1023-1025. 10.1016/j.cell.2006.06.001

Table 1:

Common arguments for and against speculation about science and technology in bioethics [8,9]	
<i>Pro</i>	<i>Con</i>
Analyses grounded in speculation are instrumental to anticipate potential ethical problems prior to an emerging technology's dissemination.	Analyses grounded in speculation may amplify expectations about unlikely scenarios, which may hinder the uptake of beneficial developments if these expectations are negative, or induce unrealistic hopes if they are positive.
Speculation and theorizing about (presently) improbable future scenarios can be functional in pursuing morally valuable scientific projects.	Allocating time and energy to bioethical speculation about (presently) improbable future scenarios distracts from more pressing and morally urgent matters.
Speculative activity and anticipation are integral to the bioethical endeavor to assess upcoming ethical pros and cons associated with science and emerging technology.	Misalignment between realistic scientific evidence and anticipatory ethical theorizing may diminish the credibility of bioethics.