

Genome Editing for Human Benefit: Ethics, Engagement and Governance

Singapore, 12 – 13 November 2019



Case study: Silence and complicity in the case of the first gene-edited babies

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Brief description of the research project

In 2018, the first babies whose DNA had been deliberately altered as embryos were born in China, as part of research led by biophysicist Dr He Jiankui. The experiment was roundly condemned as unethical, but it was later revealed that several researchers outside China previously knew some details about what He was doing, but failed to voice any concerns publicly. This case study will examine the extent to which such third parties have a moral or professional responsibility to report such incidents of unethical research.

Background

While genetic engineering has long been a matter of scientific investigation and ethical reflection, it was only in 2013 that CRISPR-Cas9 was developed as a more precise, cheap and efficient tool for gene editing. Whereas somatic applications continue apace and are relatively uncontroversial, germline applications have met with substantial scientific, medical, and ethical resistance.

At present, the technique is generally viewed as too underdeveloped for human germline applications. There are risks of off-target effects – altering different DNA than one intended – and mosaicism, where the DNA is altered only in some cells. Both could cause substantial complications and deleterious side-effects in resultant children. In addition, our limited understanding of the multiple roles that some genes play caution against such applications. Further to this, some view germline alterations as inherently problematic, with objections that such alterations interfere too much with our fundamental nature; involve ‘engineering’ humans, treating them as mechanistic objects rather than as ends in themselves; or that they put us on a road towards eugenic enhancement.

Nevertheless, Chinese scientist He Jiankui decided to set aside the international concern, and proceed with a clinical trial where the CCR5 genes in embryos were altered to insert a certain mutation. This mutation is believed to confer immunity to HIV; He has stated he was motivated by the desire to prevent the transmission of a disease that he views as devastating. This resulted in the live birth of two girls in 2018, Lulu and Nana. International outcry was swift and near-universal, and He is now under criminal investigation by the Chinese government for numerous transgressions, including not gaining regulatory approvals and appropriate oversight for his experiment.

Before he conducted the experiment, however, He Jiankui was in contact with a number of international colleagues.¹ Some were aware of his plans in early 2016, and had given periodic updates of He’s progress. By one count, around sixty individuals were aware of He’s plans before the story broke.² They generally advised him not to proceed, but at least one urged IRB approval and proper informed consent if he did.³ While the information was circulated to a very small number of individuals, no one alerted the broader scientific community before the babies were born in October 2018.

Ethical issues

We are not in a position to evaluate specific accusations of wrongdoing on the part of international colleagues. Some international colleagues have already been cleared by their institutions of directly assisting in He's experiment; others are still under investigation. However, we can ask more generally: Should those who knew about He's research have informed someone? If so, whom?

To assess this, it is important to be clear on what would be accomplished by alerting relevant parties. One possible result is that, if the local and international outcry had occurred soon enough, He would have been prevented from conducting the experiment in the first place. Even if the news had broken after the first pregnancy had begun, outcry may have prevented further pregnancies; at least one more viable pregnancy was achieved, apparently some time after the first. If we agree with the international scientific community that what He did was unethical, unscientific, premature and overly risky, this would have been a desirable outcome.

In general, researchers' institutions or, failing that, relevant public authorities would be natural bodies to whom apparent wrongdoing should be reported. However, as the international colleagues had no affiliation with institutions where He conducted his work, and little knowledge of local systems, this may not have been feasible in this case. Indeed, colleagues may have reasonably believed those institutions and/or authorities knew what He was doing (those institutions now deny this), based on He's correspondence. Nevertheless, even if local bodies were aware and supportive, the international scientific community holds considerable reservations. Hence, the international community could have been alerted through bodies such as the organizing committee of the first International Summit on Human Genome Editing, which had in 2015 stated that germline applications were impermissible at present. Even though difficult, they could also have informed relevant news services, such as the MIT Technology Review, which was the first to break the story. While such bodies have no legal or regulatory authority, international pressure could have a substantial effect, as evidenced by the effective shutting down of He's research after the news broke.

A more thoroughgoing approach may be to create a formal international notification channel. This could, for example, be connected to the work of the WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing.⁴ Further systems for verification and dissemination of findings of an investigation would have to be developed, though, to prevent abuse, false accusations and undeserved reputational loss.

But do such colleagues have a duty to alert relevant parties? Such a duty could be justified based on two factors: professional and moral. Researchers have a responsibility to uphold the integrity of their profession. He's experiment clearly undermined that on multiple fronts and public trust may be (justifiably) lost when unethical science is allowed to continue. Morally, it would appear the colleagues are in a position of 'easy rescue': by simply tipping off relevant entities, they could prevent what is generally considered to be a substantially unethical experiment, or at least end it early before more harm can be done.

However, countervailing considerations are relevant: when interpersonal and professional relationships are established, there may be a presumption of confidence and loyalty. In the He case, this has been described as a 'circle of trust'². And individual researchers may not be well-placed to confirm the activities of colleagues at other institutions. It must also be acknowledged that incentives and pressures (institutional, professional, financial or otherwise) may not always be aligned with upholding professional responsibilities in cases like this. Navigating these complexities requires considered judgment, care, and perhaps some degree of moral courage.

Conclusions

Given the possibility of preventing serious further wrongdoing, the scientific community should seriously reflect on researchers' duties in relation to internationally unacceptable gene editing conduct. This would encompass what should be done if another clinical application of germline editing occurred, as well as what institutions should be set up to better manage

notifications/reporting of this kind in the future. The case of He Jiankui highlights that relying on researchers and local institutions/authorities to prevent unethical conduct may be inadequate in the area of germline modification.

Recommendations

1. If scientists become aware of another case of reproductive germline gene editing, they have an obligation to report it to a relevant professional body that has articulated appropriate conduct in this area.
2. In the absence of formal reporting mechanisms, the scientific community should consider establishing an international reporting channel for documenting further attempts at conducting germline editing, and other related activities that violate international norms. Mechanisms and resources would have to be made available to monitor and take action (including publicly releasing the information and putting pressure on institutions to curtail the conduct) where concerns were raised.

References

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