In It Together: Why Writing Our Genetic Future Should Not Be Left to the Scientists Alone

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ABSTRACT

The public should debate the ethical and social challenges arising from heritable human genome editing (HHGE). The notorious case involving He Jiankui may have led to the disfavor of gene editing and a precautionary approach. While the de facto global moratorium on HHGE is clearly justified considering our current inability to implement it safely and effectively, the difficult ethical considerations should be addressed prior to the ability to initiate widespread HHGE. This piece argues that prospective patients and other members of society beyond the scientific community must be included in the conversation. It emphasizes the potential role of those not directly participating in HHGE science, calling the broader academic community not simply to wait for scientists' results and only afterward react. Pointing to key historical examples, I contend that scientific progress is intrinsically linked with the surrounding societal discussion and that it is not only scientists who can influence where the HHGE story ends.

Keywords: Heritable Human Genome Editing (HHGE), Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9, Patient Well-Being, Reproductive Autonomy, Debate

INTRODUCTION

I. Rogue Scientists

Chinese biophysicist He Jiankui announced the world's first genetically modified babies in 2018. Naturally, the treatment aroused the attention of the world's media, which focused on He's reckless actions. Indeed, in setting up and carrying out the procedure in question, he flouted norms of good scientific practice on a range of levels—errors paid with time in prison.

Since the He controversy, few scientists have aggressively approached heritable human genome editing (HHGE) and challenged the current research norms. The most outspoken exception is the Russian molecular

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biologist Denis Rebrikov of the Pirogov Russian National Research Medical University. He publicly declared his intention to apply clustered regularly interspaced short palindromic repeats (CRISPR) to embryos to help couples avoid passing serious medical conditions to their children. However, Rebrikov met fierce opposition both inside and beyond Russia and, with leading CRISPR scientists and bioethicists abroad describing him as a "cowboy" who had "weak data" and was trying to "grab some attention."[1] So far, Rebrikov's plans have failed to come to fruition. Although there are 126 entries listed in a registry of HHGE research recently created by the World Health Organization (WHO),[2,3] it seems that clinical HHGE has been paused for the time being.

II. Steering the Conversation

A section of the scientific community has been trying to steer the ethical debate on HHGE away from the actions of rogue scientists and back to an issue that is central to the matter—the interests of patients. The majority would agree that the most compelling potential application of germline genome editing is for the prevention of devastating genetic conditions, for example, when both parents carry Huntington's disease, for which "genome editing offers the only prospect of bearing a healthy, genetically related child."[4]

Despite such justification for scientists to continue pursuing research in the area, there has been a notable reticence in the wider academic community regarding making the ethical case for HHGE and clarifying in which medical situations such a technique might be reasonably applied. Even among those who recognize that the HHGE cases' controversies should not be a reason for panic over designer babies, some believe that starting the ethical debate is premature. A key part of the argument is that the current technological and scientific knowledge available is far from ready to deliver on treatments.

A similar stance preventing debate in the wider society is that "difficult questions" about cost, accessibility, and social justice remain.[5] Whether intended or not, the implication is that the position of wider society in the HHGE story should be a reactive one, namely waiting to see what the scientists throw at them and then dealing with it.

I argue that there is not only an immediate need for broader academic and societal input on the ethical and social aspects of the HHGE debate but that there is a deep symbiosis between scientific progress and its surroundings, whereby science both shapes and is shaped by the societal environment in which it takes place. The WHO published a position paper, recommendations, and a framework for governance. The framework for governance describes global standards for the governance and oversight of HHGE.[6] The position paper emphasized the importance of global and inclusive dialogue,[7] and many other boards have also called for broad public engagement.[8] It is imperative that WHO's governance framework meets everyone's needs. After all, as with any medical treatment, it is not the scientist who developed the treatment or the doctor who delivers it that is most important– that honor falls to the patient. In the case of HHGE, the beneficiaries include those members of society who hope to reproduce. Yet HHGE has the potential to impact society. We all should have an opportunity to be a part of world-changing decisions that lead to the creation are made and feel a responsibility to participate.

III. Shutting Down the Academic Debate

At the 30th Annual Conference of the Japanese Association for Bioethics, which took place in late 2018 after He's experiment, the discussion about HHGE was shut down quickly. Notwithstanding the understandable issues raised with He's case, one participant after another stood up to voice support for an outright and complete ban on the use of CRISPR.[9] The ban was based on the grounds that editing the human genome

would result in a cascade of unforeseen and irreversible consequences for future generations. One participant forcefully argued that "the deoxyribose nucleic acid (DNA) rubicon should never be crossed for above all, it was deeply immoral to do so when there was no way of obtaining the consent of those who would actually stand affected—our descendants."[10] Another saw it as putting humanity on a slippery slope toward enhancements, and some feared the catastrophic mistakes that might result from their use.[11]

While the above event provides just one snapshot of the debate that was taking place around the world at the time, it captures the strong reservations in the scientific community. It is a common view, not only in Japan, that the human genome is something sacred, a relic handed down from generations, that we ought to treasure and preserve. In support of such a view, religious and other more pragmatic reasons are offered. For example, some may fear the disasters that might befall us if we choose to intervene in the process through which we pass our genetic code from one generation to another.

Such arguments are certainly still at the heart of the ethical debate, but the foundations upon which they are built are by no means universally accepted. Stanford University bioethicist Henry Greely writes, "the human germline genome" does not exist; instead, each of us has a unique genome.[12] Greely argues that HHGE is no different from the changes our genomes have undergone through numerous medical interventions. For example, synthetic insulin has increased the number of people with DNA variations that lead to diabetes. Those with this condition would have died as a child in the past. However, now they live long enough to be able to reproduce. Similarly, the transition from hunting to farming centuries ago resulted in a greater number of copies in our gene pool of starch-digesting genes.

Yet Greely suggested that, practically, HHGE is "not very useful in the near- to midterm" (by which he means "the next several decades")[13] "mainly because other technologies can attain almost all the important hoped-for benefits of [HHGE], often with lower risk," citing embryo selection and somatic gene editing as two alternative options. Greely argued that applying HHGE for enhancement beyond disease prevention and is currently not a realistic option because we lack the necessary knowledge. In Greely's opinion, "how worried should we be [about HHGE]…? A bit, but not very and not about much."[14] Greely's assertions that other scientific debates should take precedence and that the concerns are not ripe for debate yet are concerning.

IV. Why Shutting Down the Debate Might Not be a Good Idea

First, the timeframe described by Greely seems somewhat out of line with that described by leading scientists. As far back as 2018, at the same Summit where He made his revelations, George Q. Daley stressed that HHGE is scientifically feasible here and that the ethical considerations can no longer be put off:

> "…a number of groups have applied gene editing now to human embryos in the context of in vitro fertilization and attempting to determine variations of a protocol that would enhance the fidelity and reduce mosaicism. I think there has been an emerging consensus that the off-target problem is manageable, and in some cases even infinitesimal. There are some interesting proofs of principles, like diseases such as beta-thalassemia that could potentially be approached with this strategy."[15]

It would also be possible to challenge Greely on various other aspects. One of which would be the number of cases to which HHGE would be relevant and the kinds of moral allowances that might be made, and each case concludes that more urgency is required in the ethical debate. Greely suggests that most people can

use preimplantation genetic testing (PGD), which is the embryo selection process, and that perhaps HHGE could apply to couples where both have the same autosomal recessive gene.[16] Greely rules out considering HHGE in cases where PGD is applicable. Greely concedes PGD does not already represent the answer on this topic, as it often fails to provide couples with enough healthy embryos to transfer. As a resolution to this issue, he points to the creation of eggs using induced pluripotent stem cell (iPSC) techniques, whereby eggs can potentially be created from other cells.[17] However, given the extremely limited success of iPSCs in the clinical arena to date, in vitro gametogenesis is a highly speculative solution. Certainly, the progress of iPSC research is not such a safe bet that placing all our hopes on it at the expense of HHGE techniques is currently justified. (Also, it should be noted that making eggs using the iPSC technique is hardly an ethical problem-free area itself.) In summary, the cases of couples looking to conceive that Greely rules out by pointing to PGD should be kept on the HHGE table, as various other scholars have suggested.[18]

Many of us debating HHGE are not scientists, so the best we can do is draw from the information we glean from those more technically capable. As a society, we are not just passive observers of science; we should have influence over decisions that impact society. Indeed, even if the available science is not yet at a place where we should be worried about large-scale ethical and social concerns, the story will continue to unfold in the future. While Greely is happy to see the human race "muddle through" the ethical challenges of scientific breakthroughs, such a position fails to recognize that society at large is far from powerless.

V. Society Influencing Scientific Progress

There are some notable examples of society's impact on scientific progress. For example, political policies led to the development of nuclear technology for war and strategic deterrence, despite societal objections seen through demonstrations of people protesting using the slogan "no nukes." Furthermore, the Bush administration drastically limited the use of embryonic stem cells in the 2000s due to a strong religious and cultural influence on policy.[19] Societal debate potentially serves as a powerful factor in guiding science. Where societal acceptance is ambiguous, science tends to operate on its own. But where science would impact life's fundamental issues like war, how embryos should be valued, or the end of life, society should weigh in and influence the role of science. Societal views on the current global moratorium on HHGE could lead to a ban, as has been advocated.[20] On the other hand, societal views that value HHGE as a way to expand reproductive autonomy may justify permitting its use. Opening an ethics debate about it would enable scientists to pursue technologies that society deems justifiable as well as set limits for where they should stop.

Making this process more difficult, the He affair has clearly colored public discourse on HHGE in a way that inhibits debate. In Japan, a sequence of questionnaires in 2016, 2018, and 2019 showed that the widely publicized HHGE scandal led to a significant decline in the acceptance of genome editing technology in general, particularly for human reproduction. Specifically, the surveys revealed a stark rise in disapproval of the technology's use on fertilized human eggs—from 12 percent in 2018 to 29 percent in 2019.[21] The three scientists that conducted these surveys suggested that "the news of the twin babies in China had a substantial influence on the Japanese public," damaging the reputation of HHGE.[22] It seems likely that the public distaste for HHGE was prompted by He's research rather than considerations about the scientific potential of HHGE The change in public opinion may also make politicians and scientists more hesitant when it comes to taking the lead in the HHGE debate. Ultimately, this can restrict the public discussion of the central ethical challenges of the technology and hinder efforts to determine whether there is a responsible path forward other than an outright ban. Stressing the importance of the issue again to potential patients and failing to engage further with the HHGE debate is surely not something society

should allow. While there are many important ongoing debates about genetics, like biohacking and DIY hobbyists, HHGE deserves attention as well. In fact, attention to the ethics of HHGE should help — more awareness of how these tools can be applied and what germline genome editing is will make people more alert to the existing danger and better understand how to mitigate it. Perhaps more importantly, a clear message from society to researchers about what objectives are reasonable to pursue regarding the HHGE technologies will facilitate good science. Having a publicly determined criterion would allow scientists to not live in fear that they might be blacklisted for seeking progress in grey areas and instead confidently chase progress where it is allowed.

VI. What Now?

HHGE is here (or will be soon) and brings many ethical and social challenges. However, the challenges should not be left to individual scientists and couples in desperate situations to manage alone.

Moving toward how these challenges can be met practically, it is helpful to draw a parallel with the issue of implementing human rights. In the early 21st century, political philosopher Michael Freeman of the University of Essex lamented that implementing human rights had been left to lawyers. Although legal experts were clearly essential in putting together the global human rights framework, Freeman's concern was that they were not best placed to understand implementing human rights in various contexts. Setting out a broader, interdisciplinary approach, he called for social scientists to tackle these difficult questions, ultimately moving human rights forward around the world.

Similarly, in medical technology like HHGE, scientists are crucial to the story, but at the same time, they are not trained to deal with all the accompanying challenges. Bioethicists are also important, clarifying the arguments that society needs to resolve. There is a need for even wider input from across the scholarly community. For instance, as with human rights, international and domestic regulation is required, and clearly, the legal community has a role here. Moreover, as described by Freeman, since all law is political in its creation and has impacts across society, political scientists and sociologists can provide impactful input.

CONCLUSION

We are in it together, and we have roles to play in the discussion of HHGE. Societal discourse does not always trail the scientific reality, but rather, it can condition the path that science will follow. Given the importance of what is at stake, not only for the potential patients, but for humanity, we should not leave the HHGE debate only to scientists, and we should not leave it until later.

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[1] Cohen J. "Embattled Russian scientist sharpens plans to create gene-edited babies," *Science*, 21 Oct. 2019. doi:10.1126/science.aaz9337.

[2] World Health Organization. "WHO issues new recommendations on human genome editing for the advancement of public health," News release, 12 July 2021, www.who.int/news/item/12-07-2021-who-issues-new-recommendations-on-human-genome-editing-for-the-advancement-of-public-health.

[3] World Health Organization. "Human Genome Editing Registry," https://www.who.int/groups/expert-advisory-committee-on-developing-global-standards-for-governance-and-oversight-of-human-genome-editing/registry.

[4] Daley GQ, Lovell-Badge R, and Steffann J. "After the Storm–A Responsible Path for Genome Editing," *New England Journal of Medicine* 380, no. 10 (2019): 897-9. doi:10.1056/NEJMp1900504.

[5] Daley GQ, Lovell-Badge R, and Steffann J. "After the Storm–A Responsible Path for Genome Editing," *New England Journal of Medicine* 380, no. 10 (2019): 897-9. doi:10.1056/NEJMp1900504

[6] World Health Organization. "WHO issues new recommendations on human genome editing for the advancement of public health," News Release, July 12, 2021, www.who.int/news/item/12-07-2021-who-issues-new-recommendations-on-human-genome-editing-for-the-advancement-of-public-health.

[7] WHO 2021. Human Genome Editing: Position Paper, WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing.

[8] Daley GQ, Lovell-Badge R, and Steffann J. "After the Storm–A Responsible Path for Genome Editing," *New England Journal of Medicine* 380, no. 10 (2019): 897-9. doi:10.1056/NEJMp1900504.

[9] 30th Annual Conference of the Japanese Association for Bioethics, 8-9 Dec. 2018, Kyoto Prefectural University, Kyoto.

[10] 30th Annual Conference of the Japanese Association for Bioethics, 8-9 Dec. 2018, Kyoto Prefectural University, Kyoto.

[11] 30th Annual Conference of the Japanese Association for Bioethics, 8-9 Dec. 2018, Kyoto Prefectural University, Kyoto.

[12] Greely HT. "Why the Panic Over 'Designer Babies' Is the Wrong Worry," *LeapsMag*, 30 Oct. 2017, leapsmag.com/much-ado-about-nothing-much-crispr-for-human-embryo-editing; Greely HT. "CRISPR'd babies: human germline genome editing in the 'He Jiankui Affair'," *Journal of Law and the Biosciences* 2019; 6(1): 111–83. doi: 10.1093/jlb/lsz010; Greely HT. *CRISPR People: The Science and Ethics of Editing Humans* (Massachusetts: Massachusetts Institute of Technology Press, 2021).

[13] Greely HT. "Why the Panic Over 'Designer Babies' Is the Wrong Worry," *LeapsMag*, 30 Oct. 2017, leapsmag.com/much-ado-about-nothing-much-crispr-for-human-embryo-editing.

[14] Greely HT. "Why the Panic Over 'Designer Babies' Is the Wrong Worry," *LeapsMag*, 30 Oct. 2017, leapsmag.com/much-ado-about-nothing-much-crispr-for-human-embryo-editing.

[15] Daley, G. (n.d.). *Genome-editing-pathways to Translation*. Transcript of the Human-Genome Editing Summit 2018 Hong Kong. Retrieved March 17, 2022, from https://diyhpl.us/wiki/transcripts/human-genome-editing-summit/2018-hong-kong/george-daley-genome-editing-pathways-to-translation/

[16] Greely HT. "CRISPR'd babies: human germline genome editing in the 'He Jiankui affair'," *Journal of Law and the Biosciences* 2019: 6(1): 111–83. doi:10.1093/jlb/lsz010.

[17] Greely HT. *CRISPR People: The Science and Ethics of Editing Humans* (Massachusetts: Massachusetts Institute of Technology Press, 2021).

[18] Rasnich R. "Germline genome editing versus preimplantation genetic diagnosis: Is there a case in favour of germline interventions?." *Bioethics* 2020; 34(1): 60–9.

[19] Murugan, Varnee. "Embryonic stem cell research: a decade of debate from Bush to Obama." *The Yale journal of biology and medicine* vol. 82,3 (2009): 101-3.

[20] Lander E, Baylis F, Zhang F, et al. "Adopt a moratorium on heritable genome editing," *Nature* 2019; 567(7747): 165–8. pmid:30867611.

[21] Watanabe D, Sato Y, Tsuda M, and Ohsawa R. Increased awareness and decreased acceptance of genome-editing technology: The impact of the Chinese twin babies. *PLoS ONE* 2000; 15(1): 1-13. doi:10.1371/journal.pone.0238128.

[22] Watanabe D, Sato Y, Tsuda M, and Ohsawa R. Increased awareness and decreased acceptance of genome-editing technology: The impact of the Chinese twin babies. *PLoS ONE* 2000; 15(1): 1-13. doi:10.1371/journal.pone.0238128.