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Fostering a Prevention Mindset for Responsible Gene Editing

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Abstract

In this special issue, we solicited three commentators to discuss issues specific to the responsible conduct of research as it relates to the birth of gene-edited children. We explore the ethics of prevention and its ties to the responsible conduct of gene editing research to introduce three commentaries addressing: (1) the relevance of cultural and regulatory context in China, (2) how to actualize calls for greater public engagement, and (3) where we might improve graduate education of genomic researchers.

Keywords

ethics; prevention; gene editing; CRISPR twins

Introduction

In late 2018, Dr. He Jiankui announced the birth of twin girls that had undergone germline gene editing, leading to global research ethics and governance controversy. Several issues surrounding the integrity of the research have been raised including transparency, appropriate oversight, and the adequacy of ethics training of the investigator (Krimsky 2019). This incident has resulted in several scholars calling for an international moratorium on germline gene editing (Lander et al. 2019) requiring greater scientific and ethical consensus before proceeding forward (Jasanoff and Hurlbut 2018; Baylis and Darnovsky, 2019).

Germline editing has often been considered a moral bright line because such modifications in heredity bear implications for all future generations (Hurlbut 2019). Yet arguments reaching back decades defend prevention via somatic and germline gene editing in light of health professionals' core commitment to using best available forms of intervention (Wivel and Walters, 1993; Zimmerman 1991). In this special issue, we solicited three commentators to discuss issues specific to the responsible conduct of research. We explore the ethics of

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prevention and its ties to responsible conduct of research in gene editing, introduce three commentaries addressing: (1) the relevance of cultural and regulatory context in China, (2) how to actualize calls for greater public engagement, and (3) where we might improve graduate education of genomic researchers.

Seeking Cultural and Regulatory Context for Genetic Prevention

First, as Kleiderman and Ogbogu (2019) note, better understanding and improvement of the Chinese regulatory context is crucial to responsible research, if not more important, than developing an international consensus. Local and national efforts should seek to counter faulty assumptions about the Chinese context and its difference from other regulatory or ethical systems of evaluation (Nie and Pickering 2018). An ethics of prevention, too, would emphasize the role of engaging with affected communities in furthering the authors' vision of developing local research ethics frameworks. These efforts would have questioned He's informal polling efforts which detected support for HIV gene editing, but which have received less attention for distinct methodological and ethical flaws (Regalado 2018; Salloch et al. 2014).

In addition, public perceptions of germline gene editing, especially for "enhancement" purposes beyond human health, will continue to be especially controversial (Scheufele et al. 2017; Gaskell et al. 2017, McCaughey et al. 2016). While CCR5 gene editing trials are likely to continue in humans through somatic gene editing in adults living with HIV (Allen et al. 2018), its uses to enhance HIV resistance and prevent the disease remains ethically dubious. HIV cure or remission research is also fraught with ethical issues that merit attention independent of gene editing (Dubé et al. 2017). As bench science bridges to clinical trials, crucial lessons from HIV prevention research reflect the importance of engaging with communities, especially those in low-resource settings (Lo et al. 2015). Through decades of HIV prevention research public health research communities have developed interdisciplinary ties to social and behavioral research (Gaist and Stirratt 2017). As gene editing accelerates, early career scholars need training to recognize not only *what* social ramifications their research could have, but *who* brings that contextual expertise to the team.

Getting Specific about Inclusive Public Discourse around Responsible Scientific Governance

Second, Matthews and Iltis (2019) join the call for greater social discourse about the ethical issues raised by gene editing. The authors' emphasis on greater social engagement comes at a time when the language around developing international consensus has also subtly but significantly shifted from a call for societal consensus to scientific consensus (Baylis and Darnovsky, 2019). While calls for greater transparency sometimes speak to a movement toward more inclusive science policy, we need greater clarity about what role the public or stakeholders play in scientific governance (Juengst 2017). For example, Jasanoff (2003) highlights the potential for civic voices in scientific governance to temper the kind of scientific hubris exhibited long before the actions of He Jiankui.

The inclusion of stakeholders in scientific governance can also help to address possibilities for sustaining and exacerbating stigmatization. As this scandal illustrates (Subbaraman 2018), prevention efforts often unintentionally send those living with the condition the message that some lives are not worth living, perpetuating stigmatization (Hoffman 2017). As precision prevention proceeds either through germline or somatic gene editing, an ethics of prevention can attend to how social attitudes toward disease and disability frame individual and community acceptance or rejection of interventions (Shakespeare 2005). Social understandings of genetics also influence social attitudes, which can alter how diseases are stigmatized both due to genetic essentialism but also tendencies to associate historically oppressed groups with predisposition to disease (Fisher and Harrington 2013).

Lessons from Public Health in Education for Future Genomic Researchers

Third, Yarborough (2019) highlights the need for improvements in science education, one that better questions the “naïve confidence” students seem to have about the power of science to change the world. Here again, an ethics of prevention is instructive. One need look no further than the tangled history of disease prevention of even successful eradication of smallpox to understand both the allure and the myth of medical breakthroughs (Gross and Sepkowitz, 1998). Such historical analyses set the stage for a more nuanced understanding for tempering the hype surrounding precision genetics (Caulfield 2018).

Attendance to both individual and population prevention will matter for precision medicine because these efforts reflect underlying moral commitments of population health, including the direction of attention to scalability and access. He Jiankui’s efforts to recruit among HIV serodiscordant couples also struggling with infertility took place in a broader ongoing regional (Vergano and Cho 2018) and global struggle to make ART more accessible (Inhorn and Patrizio 2015). For comparison, somatic gene replacement therapy to treat and prevent Leber’s congenital amaurosis (LCA) is often cited as a genetic prevention success story, offering a safe and effective intervention for vision impairment previously considered medically untreatable (Dias et al. 2018). In contrast to He’s research, LCA human gene editing trials underwent thorough regulatory oversight and were preceded by extensive animal studies, including in sheepdogs discovered to have the same genetic condition (Acland et al 2001). Yet the success case of LCA reveals the financial barriers to emerging genetic technologies targeting rare diseases. Pharmaceutical research and development is estimated to cost billions of dollars; for a sole patient seeking gene editing, the price tag of Spark Therapeutic’s LCA somatic gene therapy, Luxterna, is \$850,000 for both eyes (Lee et al. 2019).

Conclusion

“Precision prevention” has developed as a term that captures behavioral, socioeconomic, epidemiological and biological strategies to reduce the morbidity and mortality of a specific disease within a population (Rebbeck 2014). As precision prevention continues, this issue’s commentaries move research ethics toward a companion conversation around the ethics of prevention.

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