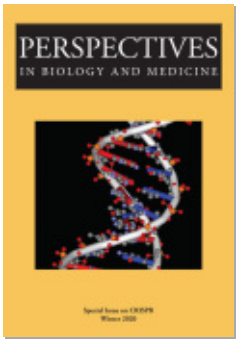
CRISPR's Twisted Tales: Clarifying Misconceptions about Heritable Genome Editing



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Marcy Darnovsky and Katie Hasson

ABSTRACT The raging controversy about whether heritable genome editing should be permitted is shaped and structured by the prevailing and countervailing narratives in circulation. In recent years, considerable shortcomings have come to characterize this discourse; it is now time to identify and correct a number of serious misunderstandings and distortions that have taken hold. This essay begins by briefly evaluating reactions to the November 2018 announcement that gene-edited babies had been born; it asserts that widespread agreement about the researcher's recklessness and dire ethical violations concealed deep fault lines among participants in the heritable genome editing debate. It goes on to consider several key omissions and misrepresentations that distort public understanding and undermine genuine debate. It suggests that the conversation must be refocused away from technical, medical, and scientific considerations toward matters of societal meanings, values, context, and consequences. It concludes with criteria for a broadly inclusive and meaningful decision-making process about whether heritable genome editing has any place in the shared and just future to which we aspire.

In the year since He Jiankui announced the birth of twin girls whose genes were edited as embryos, reactions and revelations have continued, including the recent announcement that He and two colleagues have been sentenced to

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jail time and hefty fines. But what of Nana and Lulu, now infants, whose lives and futures are often missing in discussions of He's ethical violations? Their status remains a mystery. Other than learning that they were born prematurely by emergency C-section, we know nothing about their well-being (Belluck 2019; Rana 2019). We know even less about a third gene-edited child said to have been born last summer.

Meanwhile, the controversy over He's reckless actions—and the debate about reproductive uses of heritable genome modification—have escaped scientific circles and spilled into the media, public, and policy mainstreams. It's become unavoidably clear that the scientific, biotech, and bioethics communities are divided: while some are pushing heritable genome editing toward clinical trials and fertility clinics, others are speaking out in multi-authored articles and statements in support of a strong moratorium and the need for a "broad societal consensus" before any decision is reached. In fact, this divide has been present at least since 2015, when the current chapter of the decades-long debate about heritable genome editing began in earnest (Baltimore et al. 2015a, 2015b; Lanphier et al. 2015).

The speculation that has emerged in the absence of information about Lulu and Nana's status and the swirling public debate about potential uses of a powerful new technology are intimately tied. He Jiankui made his own proactive attempt to control the narrative by preparing a slick public relations campaign for announcing the birth, including a series of YouTube videos replete with emotional appeals on behalf of the parents and an invitation to write to the twins at their own email address (Estreich 2019). And that was just the beginning.

In the absence of reliable information about the "CRISPR babies," some rumors have taken a dubious and sensational turn. One line of speculation has focused on whether the edits made to Lulu and Nana's genomes might have affected their brains. This emerged when a paper was published showing that CCR5 (the gene disabled by He) "not only makes mice smarter but also improves human brain recovery after stroke, and could be linked to greater success in school" (Regalado 2019a). The characterizations quickly escalated—headlines jumped to calling the twins "enhanced" or "superhumans" (Gabbatiss 2019; Hoare 2019). These claims have little basis, but they neatly illustrate our culture's strong appetite for stories about super-smart gene-edited children.

According to another less sensational but equally dubious narrative, the gene-edited twins are probably just fine. One headline asked (and answered), "Will gene-edited babies be healthy? Probably, but nobody knows." The article went on to assert, without evidence: "Many scientists agree that the girls will probably be healthy" (Porotskz 2019). A few days later in the *Guardian*, a biologist said that "both girls will probably be fine," in what seemed to be a throwaway line embedded in a lament about He's experiments having set back the project of "building societal acceptance" for gene editing (Davis 2019).

These stories and others like them become part of the "sociotechnical imaginary" that shapes our thinking about gene editing tools and the ways they should and should not be used (Jasanoff and Kim 2009). In many ways, they echo narratives that have been circulating around human genetic engineering for decades. In this essay, we examine the current state of the controversy about heritable genome editing, with an eye toward the prevailing and countervailing narratives in circulation.

We make our own views clear: there is no good medical argument for altering the genes of future generations; doing so would risk a future of greater inequality and discrimination; and deliberations about whether to proceed should be reoriented toward social consequences and significantly broadened in terms of scope, participants, and process. Our goal here is to make the case that in order to have the societal debate about human germline editing that almost everyone agrees is essential, we need to identify the shortcomings of public discourse thus far and correct a number of misunderstandings and distortions that have taken hold. Doing so would remove one set of barriers to fair and genuine deliberations.

We begin by briefly evaluating reactions to the November 2018 announcement of the gene-edited babies. Although denunciations of He's recklessness and ethical violations were widespread, the responses revealed deep fault lines in the germline controversy. We go on to consider several of the key omissions and misrepresentations that distort public understanding and undermine genuine debate, and to suggest that the conversation be refocused away from technical, medical, and scientific considerations toward matters of societal meanings, values, and consequences. We conclude with criteria for a broadly inclusive and meaningful decision-making process about whether heritable genome editing has any place in the shared and just future to which we aspire.

Nana and Lulu: Understanding the Aftermath

The Second International Summit on Human Genome Editing convened in Hong Kong just days after He Jiankui's bombshell announcement. Reports characterized the swift criticism from the gathered scientists as "near-universal condemnation" but missed the important divergences within that response. Most notable was the Summit Organizing Committee's move: its official concluding statement pivoted directly from denouncing He to proclaiming support for proceeding with heritable genome editing: "It is time to define a rigorous, responsible translational pathway toward [clinical] trials" (Baltimore et al. 2018).

From this perspective, the He incident seemed to be concerning mostly because it might weaken public acceptance of heritable genome editing, and of scientists' jurisdiction over it. Committee member Robin Lovell-Badge's comment to *Nature* was emblematic: "I'm worried about a knee-jerk reaction that might cause countries still working on regulations to make it unnecessarily hard to do

this research" (Cyranoski and Ledford 2018). In a similar vein, three prominent scientists penned an opinion piece titled "Wake-Up Call from Hong Kong" that supported heritable genome editing as soon as "criteria and standards are in place," and abandoned the 2015 National Academies' standard of "broad *societal* consensus" (Baltimore et al. 2015b) in favor of "broad *scientific* consensus" (Dzau, McNutt, and Bai 2018, emphasis added).

Other voices took a different tack. They assessed He's escapade in the context of ongoing efforts by particular scientists and bioethicists to assert their authority over decisions about whether, when, and how heritable genome editing should be used. Despite gestures toward public discussion, they pointed out, proponents are in fact trying to limit its scope and influence (Baylis and Darnovsky 2019; Hasson and Darnovsky 2018; Hurlbut 2018; Hurlbut, Jasanoff, and Saha 2018). Writing a few months after the Hong Kong summit, two observers noted, "Scientists articulated more concern about maintaining their authority to unilaterally transform human biology than a willingness to have a public debate about the ethics of whether—and under what conditions—such transformation should take place" (Frahm and Doezema 2019).

As the controversy about heritable genome editing continues to unfold, we can trace many of these divergent views back to earlier iterations of this conversation. Clarifying some key points will hopefully make it easier to see what's at stake.

A Closer Look at the Current Debate

Most discussions of heritable genome editing skew strongly toward questions about medical trade-offs: whether the procedures can be made safe and effective enough to justify the inevitably remaining risks for any resulting children and their future progeny. But heritable genome editing is not, by definition, a medical matter. Strictly speaking, it would not save any lives, cure any disease, treat any patient, or prevent anyone from getting sick, because it could affect only human beings who do not yet exist.

In contrast, somatic gene editing has justifiably revived hopes for medical innovations for existing patients. After several decades of gene therapy disappointments and tragedies, researchers are beginning to see successes. As with any new medical approach, safety and efficacy must be tested; with current price tags reaching to the low millions of dollars, the affordability of gene therapy is also a critically important matter. But somatic gene editing is well within the bounds of medicine, and no one is proposing to stop it. In other words, somatic and germline applications of human gene editing are quite different: the former treats patients, the latter alters embryos.

Yet many discussions of human genome editing fail to make this distinction. One recent commentary warns that the recently proposed moratorium on heritable genome editing would risk "forestalling life-saving treatments" (Metzl 2019).

This sort of claim is frequently heard but difficult to understand. Is the author arguing that a moratorium on efforts to create "CRISPR babies" would somehow undercut gene therapies that might help existing people? Is he suggesting that editing the genes of a human embryo should be counted as a "life-saving treatment"? Or does he mean something else entirely?

Another recent commentary with a title referencing germline modification proclaims that "Gene-editing technologies have great potential to treat and possibly cure thousands of genetic diseases and viruses that plague humankind" (Loike 2019). Is this a statement about somatic gene therapies or about heritable genome editing? There's no way to be sure. If the former, let's hope it's right (hyperbole notwithstanding). If the latter, it's deeply misleading.

A Medical Need?

Of course, parents care deeply about their future children's health. But those who risk passing on genetic disease don't need to manipulate embryonic genes: every one of them could ensure an unaffected child by using third-party eggs or sperm. Those who object that this would not provide full genetic kinship could use the embryo screening technique pre-implantation genetic diagnosis (PGD). Selecting embryos—deciding what kind of people we should welcome in to the world—is ethically fraught, but germline modification would only amplify that concern.

The availability of these options makes the medical argument for heritable genome editing tenuous at best. But the broader public considering the question is likely to know little about them. Awareness of PGD is particularly low, in part because so many media accounts downplay or ignore it. In the summer of 2016, some 15 months after the first use of CRISPR to alter the genes of human embryos in a lab, we examined the 40 news articles and commentaries about human gene editing that had appeared in the *New York Times*, the *Washington Post*, and the *Guardian*. Fully 85% didn't even mention PGD (Djoulakian 2016), perhaps because doing so would disrupt the all-too-common but deeply misleading salvation narrative about revolutionary techno-scientific breakthroughs.

Proponents of heritable genome editing have advanced several rationales for its advantage over PGD. They note correctly that in rare cases, prospective parents would not be able to produce unaffected embryos, and so could not use PGD. Homozygosity for Huntington's disease is a frequent example. But only a tiny number of people homozygous for Huntington's have been identified in the entire medical and scientific literature, and sadly many of them did not live to reproductive age (Lander 2015). Another rationale—that some prospective parents have moral objections to PGD and would prefer to "rescue mutant embryos" (Ma et al. 2017)—falls flat since PGD would be needed to deselect improperly edited embryos (Ranisch 2019). Other proponents point out correctly that multiple IVF cycles would sometimes be required to produce sufficient embryos. Of course, this is true in general for fertility treatment (Lander et al. 2019).

The debate about heritable genome editing thus turns not on preventing the births of children with inheritable disease, but on providing genetically related children to those few people for whom PGD wouldn't work. While we can sympathize with parents who place high value on full genetic kinship, we can also recognize this as a desire, not a medical need, and weigh this social benefit for a few against the societal risks that heritable genome editing would visit on us all (Baylis 2019a; Mills 2019).

Thinking Clearly About Sick Babies

Another confusion that distorts the debate about heritable genome editing concerns the kind of disorders it could even theoretically target. Consider an incident at the first International Summit on Human Gene Editing in 2015. During an open mike period, a woman named Sarah Gray spoke through tears about having watched her baby die shortly after birth. She pleaded passionately for scientists to do whatever it takes to save children like hers—to disregard the risks of heritable genome editing and "frickin' do it."

Gray's comment was quoted in numerous media reports by top science journalists as a dramatic argument in support of heritable genome editing (Begley 2015; Stein 2015; Travis 2015; Yong 2015). None of the journalists noted that heritable genome editing could not have helped Gray's baby. His condition, anencephaly, has no clear genetic basis; in this case, the baby had a healthy identical twin and doctors said they found "epigenetic differences in [the babies'] cord blood" (Vitez 2015). Gray would have had no way to know before getting pregnant that her baby was at risk. Nor would she have reason to consider germline editing if she were contemplating a subsequent pregnancy.

How many people, hearing or reading about this bereaved mother's heart-rending plea, were left with a distorted understanding? That reporters repeated and continue to repeat this story (and similar pleas from parents and patients) is but one instance of the hyperbole, exaggerated claims, and misunderstandings that are far too prevalent in the current public conversation about heritable genome editing (Begley 2019).

Could We Open the Door Just a Crack?

A number of recent influential statements envision moving forward with heritable genome editing, but in a controlled manner. The US National Academies of Sciences, Engineering, and Medicine (NAS) took this approach in its 2017 report *Human Genome Editing: Science, Ethics, and Governance*. It includes a list of prerequisite criteria described as so rigorous that they might "have the effect of preventing all clinical trials involving germline genome editing." Yet the report's bottom-line recommendation—that such clinical trials be permitted—was widely understood as a green light into territory that dozens of nations and a

binding international treaty have concluded should remain off-limits (Lowthorp and Darnovsky 2017).

The NAS report also downplays the somatic-germline distinction, suggesting that what matters is the condition targeted in the embryo. It endorses embryo editing for what it considers medical conditions, while deeming inadvisable (for now) those that would alter a future child's behavioral or cosmetic traits. Conceding that this line is inherently blurry, it recommends creating "reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition." But it says nothing about the feasibility of this task, let alone how the reliability of these mechanisms might be determined or ensured, especially in the face of the commercial and marketing pressure that would surely ensue. In fact, because the US Food and Drug Administration allows physicians to prescribe "off-label" uses of drugs or devices, there is no ready way to control what US doctors do once a medical treatment has been approved (Charo 2019). If heritable genome editing were permitted in the US for a limited set of indications, fertility doctors could legally use it for any purpose.

The situation in the United Kingdom is different. There, the Human Fertilisation and Embryology Authority (HFEA) has broad power over fertility treatment and human embryo research. It decides, for example, which uses of PGD are permitted, and could presumably draw up a similar list for heritable genome editing (HFEA 2019). The recommendations of a recent influential British report, from the Nuffield Council on Bioethics, would relieve HFEA from having to make such determinations (Nuffield Council 2018). In contrast to the NAS report, the Nuffield Council recognizes that heritable genome editing is best understood as a matter of parental preference rather than seen through a medical lens. Extending this logic, it allows that all kinds of trait alteration could be permitted, including "enhancing senses or abilities." In other words, the Nuffield Council implicitly endorses heritable genome editing "for whatever purposes biotechnology companies could choose to commercialize or fertility clinics [could choose] to market" (Dickenson and Darnovsky 2019).

To be clear, both the NAS's report (at 329 pages) and the Nuffield Council's (205 pages) acknowledge the existence of social and ethical risks. Both raise concerns about stigmatizing people with disabilities, exacerbating existing inequalities, and introducing new eugenic abuses. But for the most part, they treat these topics lightly and briefly, and make no apparent connection between them and their recommendation to move ahead.

Social Contexts and Consequences

What social and policy matters are most relevant to a realistic conversation about heritable genome editing? What would it look like to center these?

This section identifies a few key aspects of the social and historical context into which the introduction of inheritable genome editing is being contemplated. These and related topics urgently need robust investigation and consideration.

Commercial Dynamics

In the United States, assisted reproduction takes place largely in the private sector. Against the background of a tattered and fragmented health-care system, the fertility industry boasts hundreds of clinics, pulls in annual revenues estimated at $2.1 billion (IBISWorld 2018), and operates with minimal regulation. Fertility procedures are marketed like any other commoditized service; extra "add-ons" (many of them untested) are used as enticements even in countries such as the UK, whose national health system offers limited coverage for fertility treatment (Weaver 2018).

In these and other jurisdictions, the full weight of the fertility industry's marketing machinery would be expected to kick in if heritable genome editing were permitted. A foretaste is provided by the way cell-free DNA prenatal tests have been introduced and marketed. These tests spread extremely swiftly into routine prenatal care, despite recommendations for caution by medical professionals' organizations. And the companies selling them have marshaled slick promotional campaigns and websites, despite the ways in which the persuasion inherent to advertising obliterates previous commitments in the field to non-directive genetic counseling about prenatal tests (Estreich 2019).

Fertility doctors are already making (spurious) claims to control nonmedical traits in order to drum up business. A decade ago, Jeffrey Steinberg of the Fertility Institutes in Los Angeles announced a program offering embryo selection for hair, eye, and skin color (Center for Genetics and Society 2009). He shelved it after intense criticism, but now, as an add-on to PGD for "gender selection," his clinic is "once again accepting parents wishing to participate in this exciting enhancement of reproductive possibilities" (Fertility Institutes 2019).

Another fertility doctor, John Zhang, is open about wanting to develop techniques so that "parents can select hair or eye color, or maybe improve their children's IQ." Says Zhang, who gained notoriety when he flouted US law by going to Mexico to produce a baby using nuclear genome transfer, "Everything we do is a step toward designer babies" (Mullin 2017).

Thinking Clearly About "Designer Babies"

Zhang's designer-baby enthusiasm is unusual in its bluntness, though as we've noted, authors of sober reports also appear to embrace a future of human genetic enhancements. At the same time, it's increasingly common to hear that we need not worry about designer babies because it will always be too technically difficult to actually produce meaningful enhancements (Harris 2019; Janssens 2018; Regalado 2019b).

It's important to resist overblown claims about the extent to which genes influence traits, especially behavioral and cognitive ones. Yet it's also significant that enhancement enthusiasts are drawing up lists of "protective gene variants" that could give a future child an edge. George Church's list includes genes that confer extra-strong bones, lean muscles, insensitivity to pain, and low odor production (Knoepfler 2015). A new approach to genetic fortune-telling is the "polygenic score," a single number calculated from variations at many genetic loci that is supposedly correlated with traits including "educational attainment" (Lee et al. 2018).

Genetic prediction or control of educational attainment is highly dubious. But the biological reality of this and other proposed genetic alterations may be far less meaningful than the claims that would be made about such "improvements" and the beliefs (and dollars) that would be invested in them. Consider the hypothetical wealthy families that would spend hefty sums of money for genetic upgrades offered by fertility clinics. Whether or not their resulting children's enhancements translated into actual abilities, the kids would be treated as special by their families, nannies, tutors, and teachers. The belief that they were superior would shape their self-understandings, their relationships, their lots in life.

In a recent study demonstrating that perceptions about genes are indeed powerful, researchers found that informing—or misinforming—people about their genetic status resulted in measurable changes in "physiology, behaviour and subjective experience" (Turnwald et al. 2019, 48). Having randomly assigned individuals to receive either a "high-risk" or "protected" genetic test result for obesity, they found that "merely receiving" this information changed the subjects' "cardiorespiratory physiology, perceived exertion and running endurance during exercise" (48). In a test that involved giving the subjects a meal, it altered "satiety physiology and perceived fullness" (48).

Further, the boost that children of wealthy families already benefit from would be interpreted as biological and attributed to their genetic upgrades. Would the mere perception that some children were biologically better than others exacerbate social stratification, discrimination, and inequality? Should we risk creating a world of genetic "haves" and "have-nots"?

Risking a Future of Genetic Inequality

An earlier wave of controversy about altering the genes of future generations swelled at the turn of the millennium, in the aftermath of Dolly the sheep and the run-up to the human genome "map." At that time, both enthusiasts and skeptics were far more likely than participants in today's debates to flag the potential for heritable genetic modification to promote vastly increased inequality. The Princeton molecular geneticist Lee Silver (1997), for example, eagerly anticipated the emergence of a "GenRich" 10% (and dubbed the 90% hoi polloi the "Naturals"). On a global level, Silver (2000) wrote, "the already wide gap between wealthy

and poor nations could widen further and further with each generation until all common heritage is gone." The 1997 film *Gattaca,* which remains a touchstone in conversations about genome editing, portrayed a dystopian future of rigid genetic stratification and surveillance.

In the decades since, the United States has experienced dramatically widening gaps in wealth and income; persistent disparities in access to basic health care, not to mention expensive fertility treatments; and ratcheted-up pressures on and by parents for their children to "get ahead." If heritable genome editing were rolled out in fertility clinics, access to it would almost certainly be stratified, and that disparity would almost certainly be tolerated.

Add to these basic socioeconomic observations the history and legacy of 20th-century eugenic abuses, the ongoing salience of eugenic temptations, the revival of discredited ideas about "race" as a biological rather than social and political category, and the new twist on biological determinism in the form of polygenic scores. Absent transformative changes, heritable genome editing would be introduced into a society marked by resurgences of racism and xenophobia that are justified at least in part by biological determinism. In this context, it would be imprudent to dismiss the potential for a new market-driven eugenics.

Particularly Vulnerable Groups

Well short of a full-blown *Gattaca*-style future, heritable genome editing could all too easily stoke harmful eugenic outcomes and pernicious ideas about the biological bases of socially disfavored traits. Any human feature considered less than optimal could be grounds for embryonic editing, from short stature to dark skin, from a low polygenic score for educational attainment to a high one for obesity risk (Khera et al. 2019; Lee et al. 2018).

In the 20th century, people with disabilities were targets of eugenic discrimination, sterilization, and murder. Since then, disability and social justice advocates have warned about eugenic impulses in prenatal selection practices, as well as in efforts to "fix" or "improve" via genetic modification. Influential statements about heritable genome editing, including the reports issued by the NAS and the Nuffield Council, address these concerns and critiques but are not persuaded against recommending that heritable genome editing be developed.

If consequences for people with disabilities are at least considered, heritable genome editing's impacts on women are largely ignored (Baylis 2019a). As an assessment of the Nuffield report coauthored by one of us points out, "Gene editing of course requires in vitro fertilization (IVF), with its attendant burdens, comparatively low success rates, and possible risks" (Dickenson and Darnovsky 2019). Many women tolerate these adversities in their quests to become mothers (or to sell their eggs or gestational capacities), but that does not mean they should be missing from considerations of whether to entertain the normalization of heritable genome editing.

Possible outcomes for gene-edited children—beyond safety risks—must also be explored, and to date seldom have been. The experiences of adoptees and the donor-conceived demonstrate that children are often intensely interested in their biological origins. Would some designed children feel they were created as products, and resent it? Would some parents develop over-inflated expectations based on the costly outlays they had made? If genetic upgrades became upscale standards, would entirely new familial relationships and predicaments ensue? Bill McKibben broaches these possibilities in his recently released *Falter: Has the Human Game Begun to Play Itself Out?* (2019b):

> The minute you turn a person into a product, that product faces the inevitable fate of all products—obsolescence. You've been in the clinic with your first kid, put down your money, made your selections. OK. You come back five years later for kid number two. Technology has marched on. You're able to get better upgrades for this one. (McKibben 2019a)

Expertise on these kinds of concerns and questions seldom lies with scientific researchers; deliberations will require contributions from a range of methodologies and varieties of expertise. All these matters—social, political, and historical contexts; likely and possible outcomes—must be addressed through inclusive, genuine, substantive public engagement about heritable genome editing.

Opening Up the Conversation

How can we foster these kinds of conversations—and make sure that they feed into decision-making in meaningful ways? Most existing models for public "education" or "consultation" won't get us there.

The essential first steps toward achieving public empowerment in decision-making about heritable genome editing involve a much-broadened perspective on who should have a say, and a clearer, more expansive view of what's at stake. Beyond that, designing forums and other mechanisms for meaningful deliberation by empowered publics, and building a political and scientific culture that takes it seriously, will require considerable creativity, time, effort, and resources.

Public Engagement That Falls Short

Across the spectrum of stances toward heritable genome editing, there is a perhaps surprising amount of agreement on the need for public participation and debate. It is widely acknowledged that the issues raised go well beyond scientific laboratories and fertility clinics, and that some sort of democratic deliberation and governance is appropriate. This recognition was behind the call for "broad societal consensus" that was included in the final statement of the organizers of the 2015 International Summit on Human Gene Editing (Baltimore et al. 2015b).

But, as discussed above, what is meant by public participation can vary greatly, and the commitment to "broad societal consensus" has seemingly waned in the intervening few years. Many of the models for public engagement that have been employed or proposed fall short by limiting, devaluing, or undermining genuine participation of diverse publics.

So far, the leaders of scientific organizations have initiated and shaped what passes for public and policy debate about heritable genome editing (Dzau, McNutt, and Bai 2018; National Academies 2019). They have staked a claim for scientific self-regulation of this powerful new technology and scientific control of public education about it. As Sheila Jasanoff (2019) and Ben Hurlbut (2017) have detailed, these moves are in keeping with a pattern established at the 1975 Asilomar Conference on Recombinant DNA. Scientists claim for themselves the prerogative to determine which scientific facts and social issues are eligible for discussion.

One way scientists assert control over public and policy discussions is by insisting that discussions be limited to (their own assessments of) what is technologically possible at present or in the near future. This produces a self-fulfilling prophecy of inevitability, in which law and ethics forever "lag" behind the rapid pace of technological developments (Jasanoff 2019). It can also have the effect of narrowing the framing and content of the debate to scientific, technical, and medical risks, reinforcing the assumption that scientists are the most appropriate authorities on what should be considered a legitimate concern. This model tends to assume that any opposition stems from a lack of knowledge, and that once the knowledge deficit is corrected, everyone will agree with going forward. When public objections don't fit into this frame, they are often rejected as ignorant or emotional. Based on these assumptions, public involvement takes the top-down form of education efforts that allow limited, if any, space for public deliberation to influence decision-making (Baylis 2019a).

The 2017 National Academies report illustrates some of the ways in which a model of public involvement that prioritizes scientific self-regulation can fall short of genuine engagement. The NAS study group laid out a set of conditions that would permit potential future uses of heritable genome editing only to prevent serious diseases and when there are no other alternatives. It also advocated for broad public debate, but with a sleight-of-hand shift: it stated that public discussion could determine which (if any) enhancement uses of heritable genome editing might be acceptable. In this turn away from earlier calls for "broad societal consensus" before proceeding with any use of heritable genome editing, the NAS treated the question of *whether* to proceed as settled, and they reduced public deliberation to a limited set of questions about how and when it would be used.

Opinion polls are another problematic model for public participation in decision-making about heritable genome editing. They tightly constrain, in advance, the scope of the issue and the range of potential viewpoints, reducing the complexities surrounding human genome editing to a series of yes/no or

multiple-choice questions. Further, the results of opinion polls are highly influenced by the framing and wording of questions, and the background information that is provided (or not). Typically, survey instruments about heritable genome editing have not included essential facts such as the availability of established alternatives to heritable genome editing. A recent AP-NORC poll, for example, asked respondents whether they favor or oppose editing the genes of embryos for "Preventing an incurable or fatal disease that the child would inherit, such as cystic fibrosis or Huntington's"—with no mention of options such as third-party gametes or PGD (Neergaard 2018). At best, polls provide a snapshot, but there is no opportunity for conversation to develop.

Public engagement processes that are more interactive can also be problematic if they rely on pre-packaged panels in which small groups of laypeople are convened to learn about and discuss controversial topics. These events, which are usually time-constrained, often begin by asking participants to learn "the science" from predesigned materials that, unless carefully prepared, can easily skew understanding and discussion. Discussion topics and endpoints are often determined in advance. And in any case, there are seldom meaningful mechanisms that would allow the results of these discussions to influence policy-making decisions (Baylis 2019a).

In the UK, large-scale public consultations about new human genetic technologies have become routine. Though on their face they appear impressive, some seem to be carefully managed to produce a predetermined outcome. One such exercise was undertaken in 2013 by the HFEA to gauge public opinions about nuclear genome transfer (so-called "mitochondrial replacement"), a form of cellular engineering that, like heritable gene editing, would be passed down through the generations. The HFEA claimed to have found "broad public support" for the procedures in question; their conclusion was echoed in numerous major news outlets. In recent years, the 2013 consultation has been put forward as a model to follow for heritable genome editing. But a closer look calls that recommendation into serious question. According to the HFEA's own report on the 2013 findings, the part of the consultation in which the largest number of participants by far was involved—an open online questionnaire—actually found majority *opposition*. While sentiment was more favorable in several workshops and focus groups and in a public opinion survey, it was still mixed and varied considerably; in addition, the HFEA report noted that "for some participants their trust in the safety of these techniques is relatively fragile, and easily disrupted by new information" (Cussins and Shanks 2013; Cussins and Lowthorp 2018).

None of these efforts to involve the public in discussions about heritable genome editing have emphasized the element of shared decision-making that Françoise Baylis (2019a) has argued is the key to public empowerment. Efforts to develop robust forms of public engagement that are up to this task should begin by expanding our understanding of who should be at the table and what the stakes of the conversation are.

What's at Stake, and Who Is at the Table?

Hyperbolic claims that heritable genome editing can deliver "life-saving treatments" produce false hopes for parents and patients; so do slightly more subtle suggestions that it will offer the best or only way to "prevent incurable and fatal diseases." With the spotlight thus trained on safety and efficacy, and the conversation dominated by scientists, doctors, and medical ethicists, it's unsurprising that the debate is skewed and that fundamental questions about what's at stake are obscured. While societal risks may be mentioned, they tend to get little limelight. With all the attention on heritable genome editing in recent years, there has not been sustained and careful consideration of social and historical contexts, commercial dynamics and pressures, or systemic inequalities and discrimination. The reports discussed above assume that heritable genome editing will soon be proven safe and effective, and proceed from there to introduce guidelines as to how it should be put into practice. Sorting out the question of whether it should be used at all is beyond their expertise and their sphere of attention.

Recognizing the social and political implications of human germline editing opens up a much wider range of topics for consideration, and therefore requires a broader range of voices and perspectives. On issues of social context and consequences, biomedical expertise is not best suited. On the other hand, women's health advocates, disabled people and communities, and those working to reduce economic and racial inequities, for example, are uniquely situated to address these key issues. Broad and inclusive public debate should invite and involve these diverse voices and forms of expertise, particularly those coming from organized civil society. Meaningful discussion of the potential social consequences of heritable genome editing must move beyond narrow groups of experts to include and value the contributions of people who are already attuned to and working to dismantle the social inequities that would influence the use of germline modification and that could be exacerbated by it (Piracés 2019).

But genuine inclusivity in these deliberations will require challenging the technical and medical framings that favor the perspectives and expertise of doctors and scientists, constrain the questions that are asked, and delimit the risks and benefits that are seen as relevant. Simply broadening participation in the authorship of such reports or in more public conversations about heritable genome editing is insufficient if the parameters of the considerations are determined in advance. Empowered public deliberation can only take place if we keep the scope open-ended, so that both the question of whether to use heritable human genome editing at all and the range of matters to be closely examined are open to discussion.

While the societal concerns raised in this essay ought to be central, part of the goal of genuine public deliberation should be to allow as-yet-unforeseen questions and issues to bubble up. This can happen only if scope, framing, and con-

tent remain open. This, rather than a series of yes or no questions, is what could potentially foster "broad societal consensus" (Andorno et al. 2020; Baylis 2019a).

Toward Public Empowerment

Some who object to the call for "broad societal consensus" dismiss it as "simply impossible" (Charo 2019, 977). Meanwhile, others are already mobilizing the creativity, effort, and resources that will be required to engage the public toward this goal. One influential group has suggested a "global observatory" and laid out key questions for determining how to define and facilitate "broad societal consensus" while identifying institutional challenges for pursuing this project (Hurlbut et al. 2018; Jasanoff and Hurlbut 2018; Saha et al. 2018). Our organization has proposed a "Social Summit on Heritable Genome Editing," with majority participation by scholars from the humanities and social sciences, and by civil society advocates for social justice and the public interest. Such a convening would model broad and inclusive participation, focus on how to promote nontechnical expertise and perspectives in the broader controversy, and foreground the implications of heritable genome editing for a fair, inclusive, and sustainable future.

Baylis has proposed "public empowerment" in place of the existing models of public education or engagement. Her model is built on a process-based understanding in which "broad societal consensus" is defined not as unanimity or majority rule, but rather as unity (Baylis 2019a). She elaborates: "Decision-making by consensus is about engaged, respectful dialogue and deliberation, where all participants recognize at the outset that knowledge is value laden; that we can and should learn from each other; and that no one should impose his or her will on others" (Baylis 2019b). These and other proposals offer potential paths forward. Widespread support for a moratorium on heritable genome editing, including from influential groups of scientists, bioethicists, and biotechnology executives, has reinforced both the calls for broad and inclusive public engagement and the need for adequate time and resources to facilitate it (Lander et al. 2019).

While attention to heritable genome editing from mainstream political figures in the United States has been nearly nonexistent in the most recent round of controversies, a recent bipartisan resolution introduced in the Senate gives the sense that this may be changing (S.R. 275 2019). The resolution's condemnation of He Jiankui's reckless and unethical experiments, and especially its emphasis on the necessity of international cooperation and "broad public debate," are promising signs that lawmakers are taking this seriously as a social and political issue, not just a scientific one. The resolution could go much further, by proposing concrete steps toward fostering public engagement and by calling for the worldwide moratorium on heritable genome editing necessary to provide time for these conversations to take place. But passing the resolution would represent an important step by US elected officials toward promoting democratic deliberation and claiming a role for the public in decisions about heritable genome editing.

Conclusion

As we work to open and enrich these deliberations, a first step is recognizing how the existing discourse shapes the kinds of public engagement and empowerment that are possible. Despite decades of science fiction about genetically modified humans, and despite recent headlines about "CRISPR babies," heritable genome editing has so far not found a prominent place on the mainstream political or policy agenda, especially in the US. But there are signs that this may be changing, including a spate of recent and forthcoming CRISPR books, television series, independent films, and documentaries aimed at a general audience. Civil society is also beginning to activate around this issue, particularly in response to He Jiankui's reckless actions (Center for Genetics and Society 2018). The recently proposed US Senate resolution indicates that more elected officials are also starting to pay attention. Perhaps in a few years' time we'll be seeing the meetings in church basements, the webinars, and the letter-writing campaigns that have been characteristic of other social movements taking on issues in which scientific and technical matters are key (such as climate change, nuclear power, and pesticide use).

Now is the time to closely examine the stories we tell about Lulu and Nana and about heritable genome editing more broadly. In particular, it will be essential to interrogate the assumptions these stories carry about the public's role in deciding how such powerful technologies should and should not be used. A recent outrage surrounding public education and engagement efforts by the NAS illustrates why this continues to be so important.

Just shy of a year after He Jiankui's announcement, the NAS debuted a new suite of online public education and engagement materials on a range of issues called "The Science Behind It." For human gene editing they prepared an FAQ page, a quiz, and a short video that combined explanations of how CRISPR works with clips from a staged focus group. They chose to introduce these materials to social media with this message from the official NAS Twitter account on September 30:

> Dream of being stronger? [emoji of muscled bicep] Or smarter? [emoji of human brain] Do you dream of having a top student or star athlete? Or a child free of inheritable #diseases? [emojis of a young boy in a tie in front of a chalkboard and a young girl playing basketball] Can human #GeneEditing eventually make this and more possible? #TheScienceBehindIt Take the quiz! (@theNASciences, Sept. 30, 2019)

The video was promoted with this description: "He's got his father's eyes, his mother's nose, and neither of their inheritable diseases, all thanks to human gene editing! Sound like the stuff of science fiction or science future? Watch the video to find out what traits these 5 strangers would and wouldn't change!" In it, actors impersonating focus group participants stand in front of a cartoon image

of a human figure, choosing whether they would or wouldn't use gene editing for a range of suggested improvements: to enhance vision, prevent baldness, get a higher IQ, or "create 'the perfect' human being."

Reaction on social media and elsewhere was harshly negative. Critics drew attention to the glib and condescending tone throughout the materials, the casual normalization of human enhancement and "designer babies," and the conflict arising from an apparent endorsement of germline enhancement by the very body that has taken it upon itself to develop a framework for clinical applications of germline editing ("if society concludes that heritable human genome editing applications are acceptable") (Shanks 2019b). Even those known to support heritable genome editing panned the production's focus on enhancing intelligence and athletic ability. Alta Charo, a member of several NAS committees on human gene editing, told the Associated Press she was "disappointed." Another NAS regular, Dean of Harvard Medical School George Q. Daley, called it "the definition of hubris," though he clarified his basic position by adding, "We are not there yet" (Marchionne 2019). In response, NAS deleted the tweet and eventually all the germline materials that were part of "The Science Behind It." Via Twitter, they further stated, "Our 2017 report recommends that we should not proceed with human genome editing for purposes other than treatment or prevention of disease and disability" (@theNASciences, Oct. 1, 2019).

This episode handily illustrates many of the misconceptions identified in this essay. The NAS's slippage among the goals of heritable genome editing—as a "therapy," as a way to fulfill parental desires, as a means to enhance one's children—is evident. The conflation of "disease and disability" is repeated. Societal effects of heritable genome editing and its potential for exacerbating inequality go unexamined.

Beyond these unfortunate confirmations of the routine distortions in CRISPR discourse, the incident also reveals troubling assumptions in how scientist-dominated bodies view the public's role. While most of the critiques focused on the completely inappropriate promotion of heritable genome editing for human enhancement, none noted that the enactment of public engagement was in fact completely in line with the NAS's own recommendations. Its 2017 report recommends "broad ongoing participation and input by the public" that would "help regulatory bodies define the definitions of and boundaries between such terms as 'therapy' and 'enhancement,'" and that would inform them "about the individual and societal values to be placed on the benefits and risks before clinical trials for such enhancement interventions could be authorized" (NAS 2017, 176–77).

In other words, the NAS's own study committee carved out the topics of enhancement and "designer babies" as the only ones appropriate for public participation. Yet in response to a sloppy public relations campaign, several people closely affiliated with the NAS seemed to imply that public fixation on these

topics could only arise from uneducated and emotional lay reactions. In this self-contradictory view, nonscientists cannot join the decision-making process about heritable genome editing until they receive careful instruction in "the science behind it," and then they must remain confined to areas of debate that can be easily dismissed.

The coming decision about heritable genome modification is likely to have consequential repercussions for all of us. Without a clear view of what's at issue and at stake, we can't have transparent and informed conversations, let alone the broadly inclusive and meaningful deliberations we desperately need to make decisions about whether heritable genome editing has any place in the shared and just future to which we aspire.

References

Andorno, R., et al. 2020. "Geneva Statement on Heritable Human Genome Editing: The Need for Course Correction." *Trends Biotechnol.* DOI: 10.1016/j.tibtech.2019.12.022..

Baltimore, D., et al. 2015a. "A Prudent Path Forward for Genomic Engineering and Germline Gene Modification." *Science* 348: 36–38. DOI: 10.1126/science.aab1028.

Baltimore, D., et al. 2015b. "On Human Gene Editing: Statement by the Organizing Committee of the First International Summit on Human Gene Editing." Dec. 3. Washington, DC: National Academies. http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a.

Baltimore, D., et al. 2018. "On Human Genome Editing II: Statement by the Organizing Committee of the Second International Summit on Human Genome Editing." Washington, DC: National Academies. http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11282018b.

Baylis, F. 2019a. *Altered Inheritance: CRISPR and the Ethics of Human Genome Editing.* Cambridge: Harvard University Press.

Baylis, F. 2019b. "Before Heritable Genome Editing, We Need Slow Science and Dialogue 'Within and Across Nations.'" *STAT*, Sept. 23. https://www.statnews.com/2019/09/23/genome-editing-slow-science-dialogue/.

Baylis, F., and M. Darnovsky. 2019. "Scientists Disagree About the Ethics and Governance of Human Germline Editing." *Hastings Cent Bioethics Forum*. https://www.thehastingscenter.org/scientists-disagree-ethics-governance-human-germline-genome-editing/.

Begley, S. 2015. "Dare We Edit the Human Race? Star Geneticists Wrestle with their Power." *STAT*, Dec. 2. https://www.statnews.com/2015/12/02/gene-editing-summit-embryos/.

Begley, S. 2019. "As Calls Mount to Ban Embryo Editing with CRISPR, Families Hit by Inherited Diseases Say, Not So Fast." *STAT*, April 17. https://www.statnews.com/2019/04/17/crispr-embryo-editing-ban-opposed-by-families-carrying-inherited-diseases/.

Belluck, P. 2019. "Gene-Edited Babies: What a Chinese Scientist Told an American Mentor." *NY Times*, April 14. https://www.nytimes.com/2019/04/14/health/gene-editing-babies.html.

Center for Genetics and Society. 2009. "Embryo Screening for 'Complexion' Advertised by Controversial Fertility Clinic." Press Statement, Feb. 12. https://www.geneticsandsociety.org/press-statement/embryo-screening-complexion-advertised-controversial-fertility-clinic?id=4521.

Center for Genetics and Society. 2018. "Civil Society Statement to the Organizers of the Second International Summit on Human Genome Editing." https://www.geneticsandsociety.org/internal-content/civil-society-statement-organizers-second-international-summit-human-genome.

Charo, R. A. 2019. "Rogues and Regulation of Germline Editing." *N Engl J Med* 380: 976–80. DOI: 10.1056/NEJMms1817528.

Cussins, J., and L. Lowthorp. 2018. "Germline Modification and Policymaking: The Relationship Between Mitochondrial Replacement and Gene Editing." *New Bioethics* 24 (1): 74–94. DOI: 10.1080/20502877.2018.1443409.

Cussins, J., and P. Shanks. 2013 "Broad Public Support for '3-Parent Babies' and Crossing the Human Germline? Not What the Data Say." *Biopolitical Times,* March 21. https://www.geneticsandsociety.org/biopolitical-times/broad-public-support-3-parent-babies-and-crossing-human-germline-not-what-data.

Cyranoski, D., and H. Ledford. 2018 "How the Genome-Edited Babies Revelation Will Affect Research." *Nature,* Nov. 27. https://www.nature.com/articles/d41586-018-07559-8.

Davis, N. 2019. "Nessa Carey: 'The Most Worrying Thing About Gene Editing Is That It's Really Easy.'" *Guardian*, March 2. https://www.theguardian.com/science/2019/mar/02/nessa-carey-interview-china-gene-editing-big-pharma-100000-genomes-project.

Dickenson, D., and M. Darnovsky. 2019. "Did a Permissive Scientific Culture Encourage the 'CRISPR Babies' Experiment?" *Nat Biotechnol* 37: 355–57. https://www.nature.com/articles/s41587-019-0077-3.

Djoulakian, H. 2016. "Editorial Precision? Snapshot of CRISPR Germline in the News." *Biopolitical Times*, Aug. 1. geneticsandsociety.org/biopolitical-times/editorial-precision-snapshot-crispr-germline-news.

Dzau, V. J., M. McNutt, and C. Bai. "Wake-Up Call from Hong Kong." *Science* 362: 1215. DOI: 10.1126/science.aaw3127.

Estreich, G. 2019. *Fables and Futures: Biotechnology, Disability, and the Stories We Tell Ourselves*. Cambridge: MIT Press.

Fertility Institutes. 2019. "Choose Your Baby's Eye Color." http://www.fertility-docs.com/programs-and-services/pgd-screening/choose-your-babys-eye-color.php.

Frahm, N., and T. Doezema. 2019. "Are Scientists' Reactions to 'CRISPR Babies' About Ethics or Self-Governance?" *STAT,* Jan. 28. https://www.statnews.com/2019/01/28/scientists-reactions-crispr-babies-ethics-self-governance/.

Gabbatiss, J. 2019. "Gene-Edited Chinese Babies May Have 'Enhanced Brains' Scientists Say." *Independent,* Feb. 22. https://www.independent.co.uk/news/science/gene-edited-baby-china-brain-intelligence-hiv-he-jiankui-crispr-a8792386.html.

Harris, R. 2019. "Why Making A 'Designer Baby' Would Be Easier Said Than Done." *All Things Considered,* May 2. NPR. https://www.npr.org/sections/health-shots/2019/05/02/719665841/why-making-a-designer-baby-would-be-easier-said-than-done.

Hasson, K., and M. Darnovsky. 2018. "Gene-Edited Babies: No One Has the Moral Warrant to Go It Alone." *Guardian*, Nov. 27.

Hoare, C. 2019. "Genetically-Modified Babies to Become 'SUPERHUMANS with Enhanced Brains', Scientist Warns." *Express*, Feb. 25. https://www.express.co.uk/news/science/1092029/crispr-modified-babies-china-he-jiankui-superhumans-spt.

Human Fertilisation and Embryology Authority (HFEA). 2013. *Medical Frontiers: Debating Mitochondria Replacement, Annex IV: Summary of the 2012 Open Consultation Questionnaire*. London: Wellcome Trust. https://wellcome.ac.uk/sites/default/files/wtp041408.pdf.

Human Fertilisation and Embryology Authority (HFEA). 2019. "Approved PGD and PTT Conditions." https://www.hfea.gov.uk/treatments/embryo-testing-and-treatments-for-disease/approved-pgd-and-ptt-conditions/.

Hurlbut, J. B. 2017. *Experiments in Democracy: Human Embryo Research and the Politics of Bioethics*. New York: Columbia University Press.

Hurlbut, J. B. 2018. "Human Genome Editing: Ask Whether, Not How." *Nature* 565: 135. DOI: 10.1038/d41586-018-07881-1.

Hurlbut, J. B., S. Jasanoff, and K. Saha. 2018. "The Chinese Gene-Editing Experiment Was an Outrage: The Scientific Community Shares Blame." *Washington Post*, Nov. 29.

Hurlbut, J. B., et. al. 2018. "Building Capacity for a Global Genome Editing Observatory: Conceptual Challenges." *Trends Biotechnol* 36: 639–41. DOI: 10.1016/j.tibtech.2018.04.009.

IBISWorld. 2018. "Fertility Clinics Industry in the US: Market Research Report." *IBISWorld,* Jan.. https://www.ibisworld.com/industry-trends/specialized-market-research-reports/life-sciences/blood-organ-banks/fertility-clinics.html.

Janssens, A. C. J. W. 2018. "Those Designer Babies Everyone Is Freaking Out About—It's Not Likely to Happen." *Conversation*, Dec. 10. https://theconversation.com/those-designer-babies-everyone-is-freaking-out-about-its-not-likely-to-happen-103079.

Jasanoff, S. 2019. *Can Science Make Sense of Life?* Cambridge: Polity Press.

Jasanoff, S., and J. B. Hurlbut. 2018. "A Global Observatory for Gene Editing." *Nature* 555: 435–37. DOI: 10.1038/d41586-018-03270-w.

Jasanoff, S., and S. H. Kim. 2009. "Containing the Atom: Sociotechnical Imaginaries and Nuclear Power in the United States and South Korea." *Minerva* 47: 119–146. https://www.jstor.org/stable/41821489?seq=1#page_scan_tab_contents.

Khera, A.V., et al. 2019. "Polygenic Prediction of Weight and Obesity Trajectories from Birth to Adulthood." *Cell* 177: 587–96. DOI:10.1016/j.cell.2019.03.028.

Knoepfler, P. 2015. "A Conversation with George Church on Genomics and Germline Human Genetic Modification." *Niche*, March 9. https://ipscell.com/2015/03/georgechurchinterview/.

Lander, E. S. 2015. "Brave New Genome." *N Engl J Med* 373: 5–8. https://www.nejm.org/doi/full/10.1056/NEJMp1506446#t=article.

Lander, E. S., et al. 2019. "Adopt a Moratorium on Heritable Genome Editing." *Nature* 567: 165–68. DOI: 10.1038/d41586-019-00726-5.

Lanphier, E., et al. 2015. "Don't Edit the Human Germline." *Nature* 519: 410–11. DOI: 10.1038/519410a.

Lee, J. J., et al. 2018. "Gene Discovery and Polygenic Prediction from a Genome-Wide Association Study of Educational Attainment in 1.1 Million Individuals." *Nat Genet* 50: 1112–21. https://www.nature.com/articles/s41588-018-0147-3.

Loike, J. 2019. "Pro/Con: Should a Moratorium Be Imposed on Human Germline Editing? Manipulating Human Genes." *CQ Researcher* 29: 17–18. http://library.cqpress.com/cqresearcher/document.php?id=cqresrre2019042600.

Lowthorp, L., and M. Darnovsky. 2017. "Reproductive Genome Editing and the U.S. National Academies Report: Knocking on a Closed Door or Throwing It Wide Open?" *Bioethica Forum* 10 (2): 65–67. http://www.bioethica-forum.ch/docs/17_2/06_Lowthorp_BF10_02_2017.pdf.

Ma, H., et al. 2017. "Correction of a Pathogenic Gene Mutation in Human Embryos" *Nature* 548: 413–19. https://www.nature.com/articles/nature23305.

Marchionne, M. 2019. "Group Pulls Video That Stirred Talk of Designer Babies." *AP News*, Oct. 2. https://www.apnews.com/2f7cc05b8b034a4787271cdd875581e9.

McKibben, B. 2019a. "Climate Change Is 'Greatest Challenge Humans Have Ever Faced,' Author Says." Interview by D. Davies. *Fresh Air,* April 16. NPR. https://www.npr.org/2019/04/16/713829853/climate-change-is-greatest-challenge-humans-have-ever-faced-author-says.

McKibben, B. 2019b. *Falter: Has the Human Game Begun to Play Itself Out?* New York: Henry Holt.

Metzl, J. 2019. "Human Gene Editing Is Too Transformative to Be Guided by the Few." *Financial Times*, March 27. https://www.ft.com/content/6ebc7f3e-4ff5-11e9-8f44-fe4a86c48b33.

Mills, P. 2019. "Three Venues for Discussing Human Gene Editing." *Issues Sci Technol* 35 (3). https://issues.org/issue/35-3/.

Mullin, E. 2017. "The Fertility Doctor Trying to Commercialize Three-Parent Babies." *MIT Technol Rev*, June 13. https://www.technologyreview.com/s/608033/the-fertility-doctor-trying-to-commercialize-three-parent-babies/.

National Academies of Sciences, Engineering, and Medicine (NAS). 2017. *Human Genome Editing: Science, Ethics, and Governance*. Washington, DC: The National Academies Press. DOI:10.17226/24623.

National Academies of Sciences, Engineering, and Medicine (NAS). 2019. *Human Genome Editing Initiative*. http://www.nationalacademies.org/gene-editing/index.htm.

Neergaard, L. 2018. "AP-NORC Poll: Edit Baby Genes for Health, Not Smarts." Associated Press, Dec. 28. http://apnorc.org/news-media/Pages/AP-NORC%20Poll-Edit-baby-genes-for-health%2C-not-smarts.aspx

Nuffield Council on Bioethics. 2018. *Genome Editing and Human Reproduction*. London: Nuffield Council. http://nuffieldbioethics.org/project/genome-editing-human-reproduction.

Piracés, E. 2018. "Let's Avoid an Artificial Intelligentsia: Inclusion, Artificial Intelligence, and Human Rights." *Points Blog,* Oct. 12. https://points.datasociety.net/lets-avoid-an-artificial-intelligentsia-inclusion-artificial-intelligence-and-human-rights-3905d708e7ed.

Porotskz, P. 2019. "Will Gene-Edited Babies Be Healthy? Probably, But Nobody Knows." *ScienceLine*, Feb. 28. https://scienceline.org/2019/02/will-gene-edited-babies-be-healthy-probably-but-nobody-knows/.

Rana, P. 2019. "How a Chinese Scientist Broke the Rules to Create the First Gene-Edited Babies." *Wall Street J*, May 10. https://www.wsj.com/articles/how-a-chinese-scientist-broke-the-rules-to-create-the-first-gene-edited-babies-11557506697#comments_sector.

Ranisch, R. 2019. "Germline Genome Editing versus Preimplantation Genetic Diagnosis: Is There a Case in Favour of Germline Interventions?" *Bioethics*. DOI: 10.1111/bioe.12635.

Regalado, A. 2019a. "China's CRISPR Twins Might Have Had Their Brains Inadvertently Enhanced." *MIT Technol Rev*, Feb. 21. https://www.technologyreview.com/s/612997/the-crispr-twins-had-their-brains-altered/.

Regalado, A. 2019b. "We Won't Use CRISPR to Make Super-Smart Babies—But Only Because We Can't." *MIT Technol Rev*, Jan. 18. https://www.technologyreview.com/s/612774/we-wont-use-crispr-to-make-super-smart-babiesbut-only-because-we-cant/.

Saha, K., et al. 2018. "Building Capacity for a Global Genome Editing Observatory: Institutional Design." *Trends Biotechnol* 36: 741–43. DOI: 10.1016/j.tibtech.2018.04.009.

Shanks, P. 2019a. "Moratorium on Germline Gains Momentum." *Biopolitical Times*, May 9. https://www.geneticsandsociety.org/biopolitical-times/moratorium-germline-gains-momentum.

Shanks, P. 2019b. "More Than a Misstep: The NAS Twitter Debacle Represents an Abuse of Authority." *Biopolitical Times*, Oct. 1, 2019. https://www.geneticsandsociety.org/biopolitical-times/more-misstep-nas-twitter-debacle-represents-abuse-authority.

Silver, L. M. 1997. *Remaking Eden: Cloning and Beyond in a Brave New World*. New York: Avon.

Silver, L. M. 2000. "Reprogenetics: How Do a Scientist's Own Ethical Deliberations Enter into the Process?" Paper presented at Humans and Genetic Engineering in the New Millennium: How Are We Going to Get "Genetics" Just in Time? Copenhagen: Danish Council of Ethics. https://repository.library.georgetown.edu/handle/10822/523362.

Stein, R. 2015. "Scientists Debate How Far to Go in Editing Human Genes." *All Things Considered*, Dec. 3. NPR. https://www.npr.org/sections/health-shots/2015/12/03/458212497/scientists-debate-how-far-to-go-in-editing-human-genes.

Turnwald, B. P. 2019. "Learning One's Genetic Risk Changes Physiology Independent of Actual Genetic Risk." *Nat Hum Behav* 3: 48–56. https://www.nature.com/articles/s41562-018-0483-4?fbclid=IwAR3uTtksOn6iyMRf5awv3lG8kbcoX9i-Z0aGylWlITBUxEPtNsr5dobs0lE.

Travis, J. 2015. "Inside the Summit on Human Gene Editing: A Reporter's Notebook." *Science*, Dec. 4. https://www.sciencemag.org/news/2015/12/inside-summit-human-gene-editing-reporter-s-notebook.

Vitez, M. 2015. "Thomas Gray Lived Six Days, But His Life Has Lasting Impact." *Inquirer*, March 29. https://www.philly.com/philly/health/20150329_Thomas_Gray_lived_six_days__but_his_life_has_lasting_impact.html.

Weaver, M. 2018. "Private IVF Clinics Urged to Stop Charging for Expensive Add-Ons." *Guardian*, Nov. 12. https://www.theguardian.com/society/2018/nov/12/private-ivf-clinics-urged-to-stop-charging-for-expensive-add-ons.

Yong, E. 2015. "What Can You Actually Do with Your Fancy Gene-Editing Technology?" *Atlantic*, Dec. 2. https://www.theatlantic.com/science/archive/2015/12/what-can-you-actually-do-with-your-fancy-gene-editing-technology/418377/.