

PERSPECTIVE

## Heritable Genome Editing and the Downsides of a Global Moratorium

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### Abstract

In 2018, Dr. He Jiankui reported that he had edited human embryos and transferred them to a woman, causing her to give birth to twin girls with modified genomes. An international group of scientists and ethicists responded by proposing a global moratorium on heritable genome editing (HGE). In this article, I oppose this proposal on several grounds. A global moratorium might encourage participating nations to ban HGE or postpone access to it indefinitely. It might also deter or delay basic research that could lead to safe and effective HGE. Lastly, a global moratorium might induce participating nations to adopt or maintain laws and regulations that stigmatize children born with modified genomes. As an alternative, I argue that nations should regulate HGE for safety and efficacy only and without distinguishing between therapeutic and enhancing modifications.

### Introduction

Heritable genome editing (HGE) of the human germline has potential as a niche assisted reproductive technology. If it can be perfected, men and women who carry genetic mutations may eventually be able to edit their gametes or embryos and have healthy offspring. Unfortunately, a reckless scientist – Dr. He Jiankui – has already used this as yet unperfected technology to bring about the births of children with modified genomes. In response, some experts have demanded a global moratorium with international oversight.

In this Perspective, I should begin by stating I deplore premature and dangerous uses of HGE. However, I would argue that a moratorium is undesirable for three reasons: it may encourage participating nations to ban HGE or postpone access to it indefinitely; it may deter or delay basic research that could lead to safe and effective HGE; and it may induce participating nations to adopt or maintain laws and regulations that stigmatize children born with genomic modifications. As an alternative, I recommend that nations regulate HGE for safety and efficacy only and without distinguishing between therapeutic and enhancing modifications.

### Mulling Over a Moratorium

In 2015, Chinese scientists reported that they had edited the genomes of human embryos. They worked with non-viable embryos and did not try to produce babies.<sup>1</sup> Still,

their experiment split the scientific community. Some condemned it and demanded a voluntary moratorium on all such research.<sup>2</sup> Others found the experiment acceptable, in part because the embryos were nonviable.<sup>3</sup>

Meanwhile, a group of prominent scientists and bioethicists called for examination of the benefits and risks of HGE.<sup>4</sup> Heeding this call, various organizations studied HGE and expressed cautious interest. For example, the Organizing Committee for the first International Summit on Human Genome Editing opined that clinical uses should not proceed until safety and efficacy issues were resolved, societal consensus was reached, and regulatory oversight was imposed.<sup>5</sup> In the United States, the National Academies of Sciences, Engineering and Medicine (NASEM) issued a report stating that clinical trials could be appropriate under the right conditions, including the need to avert a serious disease or condition, lack of reasonable alternatives, and strict oversight.<sup>6</sup> Similarly, in the United Kingdom, the Nuffield Council on Bioethics concluded that HGE should be permitted if certain conditions were met, including safety and reliability, public debate, and strict regulation by a national authority.<sup>7</sup>

In contrast to these thoughtful deliberations, one scientist decided to proceed at once with a dangerous experiment. In November 2018, the media reported that Dr. He Jiankui had transferred human embryos with modified genomes to women in an effort to produce children

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immune to infection with the human immunodeficiency virus (HIV). One woman had already given birth to twin girls.<sup>8</sup> Dr. He released several YouTube videos explaining how he had modified “Lulu” and “Nana” and his reasons for doing so.

Critics writing in *The CRISPR Journal* and elsewhere immediately noted that the twins might not be immune: neither girl received the naturally occurring *CCR5* 32-basepair ( $\Delta 32$ ) deletion that is known to confer some protection against infection with the most common form of HIV.<sup>9</sup> Moreover, even *CCR5* $\Delta 32$  could not protect against infection with less common forms of the virus.<sup>10</sup> Critics also pointed out that people without standard *CCR5* genes were more susceptible to infection with influenza, West Nile, and other viruses. Furthermore, the experiment was medically unnecessary because other ways to prevent and treat HIV infection are available.<sup>8</sup>

Shortly after the media broke this news, Dr. He described his experiment to a stunned audience at the Second International Summit of Human Genome Editing in Hong Kong (Fig. 1). The Organizing Committee condemned the experiment on various grounds, including insufficient medical justification, failure to protect human subjects, and inadequate transparency.<sup>11</sup> But although the Committee acknowledged that germline editing was not ready for clinical trials, it did not demand a ban. Instead, it called for the development of a transitional pathway for clinical trials that conformed to accepted standards for clinical research.<sup>11</sup>

In March 2019, an international group of scientists and ethicists (the proponents) led by Eric Lander, Françoise Baylis and 16 co-authors published a commentary in *Nature* demanding a stronger response: a temporary

global moratorium on HGE.<sup>12</sup> They offered the following illustration of how a moratorium might work. Each nation that joined the moratorium would declare that it would not allow HGE for five years. If enough nations joined, the five-year period would create a pause during which the world could discuss the technology. When that period expired, each nation could choose to extend the moratorium further or ban HGE outright. But if a nation wished to allow a specific use of the technology, it would first give notice to the world and participate in an international discussion of pros and cons. It would also evaluate the technical, scientific, medical, societal, ethical, and moral aspects of that use to ensure it was justified. Lastly, the nation would determine whether there was a general consensus within its society in favor of proceeding with HGE in general and the specific use in particular. An international body would establish a committee to guide and support this process.<sup>12</sup>

Like the original experiment on nonviable human embryos, the call for a global moratorium has split the scientific community. In the United States, the National Institutes of Health (NIH) embraced the idea of a moratorium.<sup>13</sup> Sixty-two scientists, ethicists, and biotechnology leaders sent a letter supporting a moratorium to the Secretary of the Department of Health and Human Services (DHHS).<sup>14</sup> However, other scientists and medical experts have disagreed.<sup>15,16</sup> Reasoning that responsible uses of HGE could emerge in the future, they argued that a moratorium would interfere with such uses and be hard to eliminate once in place.<sup>16</sup> In a perspective in *Nature Medicine*, Shoukhrat Mitalipov and colleagues suggested the true imperative was not a global moratorium but rather enforcement of existing regulations.<sup>17</sup>



**FIG. 1.** He Jiankui defends his CRISPR babies experiment at the Second International Summit of Human Genome Editing in Hong Kong, November 2018. (Reuters).

### International Analysis

The proposal for a global moratorium seems to assume that a nation can stop HGE through a voluntary declaration. However, an empty pledge will not get the job done. A moratorium must be implemented through legislation or regulation that carries sanctions for violation.

China offers an illustration. In 2003, the Ministry of Science and Technology and the Ministry of Health promulgated Ethical Guidelines for Human Embryonic Stem Cell Research. The Guidelines provide in section 6(1) that blastocysts derived by specified means, including genetic modification, must not be cultured *in vitro* for more than fourteen days.<sup>18</sup> Per section 6(2), once such blastocysts have been used for research, they cannot be implanted into the reproductive tract of humans or other species.<sup>18</sup> Chinese authorities have stated that Dr. He engaged in “officially banned” conduct by editing embryos and using

them for reproductive purposes.<sup>19</sup> However, these Guidelines impose no penalties for violation and did not clearly dissuade Dr. He from engaging in his experiment.<sup>20</sup>

Since then, China's National Health Commission (NHC) has moved swiftly to draft new regulations for clinical research involving new biomedical technologies. Pursuant to the draft regulations, the NHC must approve the use of high-risk technologies in humans, including HGE. Medical institutions that violate the regulations face fines, loss of research funds, and loss of medical licenses.<sup>21</sup> Moreover, China has also proposed revisions to its civil code that will hold scientists liable when experiments on genes in adults or embryos harm human health or violate ethical principles.<sup>22</sup> These steps fall short of an explicit moratorium but should enable China to control HGE by imposing serious consequences on those who make unauthorized or unethical use of it.

The United States provides another example. The U.S. Food and Drug Administration (FDA) claims it has jurisdiction over clinical trials of HGE.<sup>6</sup> After human embryos were first edited in 2015, the U.S. Congress added a rider to the Consolidated Appropriations Act, 2016, providing that the FDA could not acknowledge receipt of applications to conduct such clinical trials.<sup>23</sup> Since then, Congress has repeatedly attached this rider to annual appropriations legislation, thereby establishing a *de facto* moratorium on HGE.<sup>24</sup> Those who conduct unauthorized clinical trials of reproductive technologies can be charged with federal crimes and punished with prison and fines.<sup>25</sup>

### Three Objections to a Global Moratorium

#### 1. A global moratorium may encourage participating nations to ban HGE or postpone access to it indefinitely

Once one realizes that a global moratorium requires implementation, its downsides become clearer. Proponents may view it as a temporary measure that can be easily rescinded. However, that is not correct. As social scientists know, human beings have a *status quo* bias, that is, an inclination to oppose change.<sup>26</sup> Once a nation adopts legislation or regulation to stop HGE, even temporarily, it will have decided against use of that technology. Political leaders and their constituents may resist efforts to lift the moratorium because doing so will change the *status quo*. They may find it more comfortable psychologically to renew the moratorium or replace it with a permanent ban.

To illustrate, consider the *de facto* moratorium that presently prevails in the United States. In theory, Congress could end this moratorium at any time by omitting the rider that prevents the FDA from acknowledging

receipt of applications for clinical trials of HGE. The FDA could then receive and review applications to ensure clinical trials were reasonably safe for participants.<sup>27</sup> In practice, however, Congress may find it difficult to omit the rider, for legislators are human and must overcome their natural inclination to oppose change.

Indeed, recent events suggest that the rider has already developed staying power. In 2019, Democrats on an appropriations subcommittee in the House of Representatives decided to leave it out of a draft appropriations bill for 2020. In their view, the rider was a covert means of limiting key scientific research and a public debate was preferable. However, Republicans objected and the full Committee on Appropriations later restored the rider to the bill.<sup>28</sup>

Critics of the global moratorium have also raised the specter of the Dickey-Wicker Amendment, another rider attached to appropriations legislation.<sup>29</sup> Generally, it bars the DHHS from funding experiments in which human embryos are created for research, or destroyed, discarded, or exposed to risk of serious harm or death.<sup>30</sup> The Amendment has endured for over twenty years and continues to impede embryonic stem-cell research.<sup>31</sup> It serves as a reminder that “temporary” measures can persist indefinitely.<sup>29</sup>

#### 2. A global moratorium may deter or delay basic research that could lead to safe and effective HGE

Moratorium supporters argue that couples who carry dangerous genetic mutations have options, including prenatal screening, donor gametes, adoption, and preimplantation genetic testing (PGT),<sup>12</sup> a process whereby couples screen in vitro embryos for mutations prior to transfer.<sup>32</sup> In their view, routine preconception genetic screening could help more couples identify their risk in time to use these options.<sup>12</sup> Other observers believe that editing of somatic cells is the solution.<sup>2</sup>

Although routine preconception genetic screening can help identify genetic risks, some couples may find existing options inadequate. Donor gametes and adoption eliminate the genetic link between parent and child. Prenatal screening can identify a child at risk, but somatic therapies may come too late to cure disorders affecting motor neurons or the brain.<sup>15</sup> And useful though it may be, PGT cannot help everyone. Some couples generate so few transferable embryos that their odds of achieving pregnancy and birth are low, even after multiple cycles.<sup>15</sup> Moreover, if one member of a couple carries two copies of a mutated dominant allele, or both members carry two copies of a mutated recessive allele, all embryos will be affected and no transfer is possible.<sup>15</sup>

Thus, even the proponents concede that HGE may have legitimate uses. As an example, they cite genetic

correction: that is, conversion of a mutation that causes a serious single-gene disorder into the standard allele.<sup>12</sup> Therefore, let us assume that scientists should be encouraged to invest their time and energy in perfecting molecular editing tools and testing them on non-human animals and human gametes and embryos. This basic research can determine if genetic correction has therapeutic potential. Over time, it may generate enough data to convince regulators that clinical trials are reasonably safe for human subjects. Such trials may, in turn, lead regulators to approve genetic correction.

Unfortunately, a global moratorium may discourage basic research in two ways. First, by joining the moratorium, a nation sends the message that performing HGE is wrong. Even if the moratorium is intended as a temporary measure to buy time for a broader debate, some scientists may instinctively shun a field that has drawn such a strong negative response from authorities. Others may be reluctant to gamble their careers and reputations on basic research that may never lead to clinical trials or approvals if their nation extends the moratorium indefinitely or enacts a permanent ban.

Second, some fear that a global moratorium will discourage funding of basic research.<sup>33</sup> Again the United States offers an example. The NIH has already stated that it will not fund genome editing in human embryos.<sup>34</sup> State governments and private entities remain free to fund such experiments. However, some may hope to earn a return on their investments in the form of clinical trials leading to marketable treatments. At present, they already face considerable risk because Congress has prevented the FDA from acknowledging receipt of applications for clinical trials. But if the United States decides to join a global moratorium, their risk will increase.

To illustrate, suppose Congress decides that its appropriations rider is an inadequate response to HGE. It enacts a new law that imposes a five-year moratorium. This law also commits the United States to participate in a global discussion of pros and cons, evaluate technical, scientific, medical, societal, ethical and moral issues, and discern societal consensus before proceeding with genetic correction or any other specific use of the technology. Investors may be reluctant to fund basic research under such circumstances. The hypothetical law not only delays clinical trials, but conditions them on a global discussion with an unpredictable outcome, evaluation of multiple factors, some of which are subjective, and a societal consensus that may be impossible to achieve or document. Of course, Congress can later amend a law that proves burdensome or unworkable, but investors cannot count on it doing so.

### 3. A global moratorium may induce participating nations to adopt or maintain laws and regulations that stigmatize children born with genomic modifications

Proponents of a moratorium raise concerns about the social impacts that HGE could have, including stigmatization of and discrimination against persons born with genetic disabilities, pressure on parents to enhance children, psychological harm to children with modified genomes, religious and moral opposition, unequal access leading to increased inequality, division of the human species into subspecies, and pollution of the gene pool.<sup>12</sup> These concerns are not universally shared and have been vigorously critiqued.<sup>26,35</sup> However, let us put them aside for the moment, and focus instead on a point often overlooked: regulation is never entirely benign. It may provide benefits, but it also imposes costs, some of which arise when people circumvent it.

The global moratorium is intended to stop the birth of children with modifications. However, HGE has some appealing uses, such as genetic correction. Given that fact, some nations may reject the moratorium, allow clinical trials, and eventually authorize safe and effective treatments. Other nations may join the moratorium initially but eventually lift it so they can proceed with genetic correction. Still others may ignore the moratorium altogether and offer whatever modifications the market will bear, including enhancing ones.

Today, parents travel abroad to obtain assisted reproductive technologies that are not legal in their own countries.<sup>36</sup> Tomorrow, parents faced with prohibitory laws or regulations may travel to nations where HGE is available legally or on the black market. As a result, it seems likely that children will be born with modifications even if a moratorium is in place.

Proponents may retort that regulation need not be perfectly enforceable in order to be worthwhile. Certainly a global moratorium will prevent many children from being born with genomic modifications. However, it may harm those who are born, as this section explains.

**Social stigma.** Social stigma arises when a condition such as race, religion, nationality, or disability marks a person as undesirable or unworthy. Stigma can evolve from derogatory stereotypes that undermine members of an unpopular group.<sup>35</sup> At present, very few children with genomic modifications exist, and pseudonyms have shielded their identities, making it difficult to know how they are viewed. However, public opinion polls on gene editing provide a starting point for discussion.

Consider first public opinion in the United States. According to a 2018 poll performed shortly after Dr. He announced the birth of Lulu and Nana, 71% of respondents favored editing embryos to prevent a baby from inheriting an incurable or fatal disease, while 67% approved such editing to lower the risk of cancer or other diseases that appear later in life. However, 69% of respondents opposed editing embryos to alter traits like athletic ability or intelligence.<sup>37</sup> Another poll conducted before Dr. He's announcement produced similar results: 72% of respondents deemed it appropriate to alter an unborn baby's genes to treat a serious congenital disease or condition, while 60% said gene editing was appropriate to decrease the lifetime risk of developing a serious disease or condition. However, 80% of respondents opposed gene editing to make babies smarter.<sup>38</sup>

Next, consider public opinion in China. In early 2018, Chinese academics surveyed attitudes toward gene editing in adults and children.<sup>39</sup> Their poll did not address HGE specifically but the results are instructive nevertheless. Eighty-one percent of respondents accepted gene editing to treat hereditary heart disease, while >70% accepted correction of mutations that cause cancer.<sup>40</sup> Interestingly, >70% accepted gene editing to prevent HIV infection, hinting at cultural attitudes that may have encouraged Dr. He to proceed.<sup>40</sup> However, only 24% and 22% of respondents accepted gene editing to increase intelligence or athletic ability, respectively.<sup>40</sup>

A public that accepts HGE to prevent hereditary disease and cancer is likely to accept children with modifications intended to achieve those goals. In particular, children who receive wild-type alleles in place of mutated ones may face little social stigma since genetic correction standardizes their genomes. Regrettably, Dr. He's reckless experiment could itself become a source of stigma if the public gets the impression that all HGE, including genetic correction, is inherently dangerous and bad.

Lulu and Nana present a more complicated case. The alterations made to their *CCR5* genes could have detrimental as well as beneficial effects. On the one hand, according to a recent study of UK biobank data on >400,000 individuals aged 41 to 76, those who possessed two copies of *CCR5Δ32* were 20% less likely to reach age 76 than those who had one or no copy.<sup>41</sup> One possibility is increased susceptibility to influenza may be to blame.<sup>42</sup> This research has led to some speculation that Lulu and Nana could die earlier than their peers.<sup>43</sup> On the other hand, the media have also suggested that Lulu and Nana may have superior recuperative ability<sup>44</sup> because stroke victims

who possess the *CCR5Δ32* variant have stronger cognitive function and recover better from neurological impairments than those without it.<sup>45</sup> Others have noted that mice with decreased *CCR5* function exhibit improved cognition.<sup>46</sup>

These speculations, based on very preliminary data, suggest that certain stereotypes may attach to Lulu, Nana, and any others with modified *CCR5* genes. On the negative side, these individuals may be expected to die young. On the positive side, they may be perceived as recuperation superstars who learn better than others. Oddly, the positive stereotypes may carry more social stigma because they suggest enhancement, which the public generally opposes.

Next, consider children with modifications intended as enhancements. Many objections to enhancement promote stereotypes.<sup>35</sup> I will address one objection that reflects current public attitudes. A 2018 public opinion poll asked respondents if gene editing would be available only to the wealthy and thus increase inequality. Fifty-eight% said that outcome was very likely and another 29% said it was fairly likely.<sup>38</sup> The proponents of the moratorium also note that unequal access to HGE could increase inequality.<sup>12</sup>

This inequality claim implicitly assumes that children with such modifications have superior traits that give them an advantage over others.<sup>35</sup> Otherwise, unequal access would not increase inequality. However, intelligence and other desirable traits are very difficult to engineer because they depend on many genes working together with the environment.<sup>6,15</sup> Further, even exceptional traits do not guarantee success. A person born with an innate talent must invest time and effort to develop it and obtain a competitive advantage.<sup>35</sup>

Here, however, the effects of the inequality claim matter more than its accuracy. The claim assumes that children with enhancing modifications are superior and advantaged. Thus, it not only provides the public with an appealing explanation for its instinctive opposition to enhancement, but also teaches that these stereotypes are true. Moreover, by linking the children to inequality, the claim insinuates that they are unjust.<sup>35</sup> In this way, the claim stigmatizes the children.

Finally, a child's genomic modifications will not be obvious to the naked eye. Anonymity may provide a partial refuge against stigma, and a child may find it easy to pass as unmodified.<sup>35</sup> However, imagine a future world in which a wide variety of modifications are available. If a child is exposed as the product of genetic correction or other minor edits, others may suspect she has also been enhanced. Thus, even though the changes made to her genome are minute and confer no superiority or advantage,

the stereotypes and stigma associated with enhancement may still attach to her.

Some may counter that children born through in vitro fertilization (IVF) do not incur social stigma. However, IVF differs in that it does not alter the genomes of gametes or embryos. Critics may still question whether IVF is moral, safe, or affordable, but they do not claim that it produces superior children who pose a competitive threat. Moreover, IVF is legal in the United States. Its progeny do not come into the world bearing a stamp of legislative disapproval.<sup>35</sup> Children born despite laws against HGE will face greater challenges, as I discuss below.

**Legal stigma.** Laws also can stamp a disfavored group as undeserving and unworthy. Laws that relegate racial minorities to separate facilities offer the classic example of legal stigma. The U.S. Supreme Court deems racial segregation unconstitutional because it brands minorities as inferior.<sup>47</sup> However, physical segregation is not the only way that the government can stigmatize those who possess disfavored traits. It can also try to prevent them from coming into existence; and when they are born anyway its efforts mark them as undeserving and unworthy.<sup>25</sup>

To join the global moratorium, a nation must have laws or regulations that prohibit attempts to create children with modified genomes. Whether the laws or regulations are already in place or adopted in response to Dr. He's experiment, they send the message that children with modified genomes should not exist. The rationales provided for the laws or regulations lend further content to this legal stigma.

For example, as noted above, Congress has enacted an appropriations rider that bars the FDA from acknowledging receipt of applications for clinical trials. In 2015, the Committee on Appropriations for the House of Representatives released a report indicating the new rider was necessary for unnamed safety and ethical reasons.<sup>48</sup> This rationale suggests that Congress only wanted to stop dangerous adult conduct. Yet, it could have achieved that goal by allowing the FDA to regulate.

By disabling the FDA instead, Congress sent a stronger message: HGE was so unsafe and unethical that it had to be halted altogether before it inevitably produced defective children.<sup>35</sup> Congress could eliminate this stigma by lifting the rider and permitting the FDA to receive applications for clinical trials. Such action would intimate that healthy births are possible but leave the agency in control of risky adult conduct.

Of course, Congress could go in the opposite direction. Inspired by the call to global action, it may enact a new law that imposes a moratorium for a fixed number of

years or bans HGE altogether. The new law may include findings explaining its purpose. If not, legislative history may illuminate the reasons for its enactment.

Suppose Congress asserts that HGE must be stopped because unequal access to it could increase inequality. As discussed, this inequality claim assumes that children with enhancing modifications are superior, advantaged, and unjust. By relying on the claim, Congress expresses the view that the children should not exist because of these disfavored traits. Then, if Americans travel to obtain HGE from foreign clinics, children with modified genomes may be born and raised in the United States, where they will bear the stigma of having been conceived in circumvention of a law that marks them as superior, advantaged, and unjust.<sup>35</sup> This stigma may extend even to those born via genetic correction if the public suspects that they have also received enhancing modifications.

Some may protest that any legal stigma is purely theoretical because a global moratorium will ensure that no children with modified genomes are born. However, as explained above, that is incorrect. Some nations will make HGE available, legally or illegally.

Others may draw analogies between laws against HGE and laws against rape and incest, which deter improper sexual activity without necessarily blaming or stigmatizing children who may be born. However, this analogy is inapt. Rape is a crime because sex occurs against the will of the victim, and not because the child she may bear has bad traits.<sup>49</sup> Incest is a crime in part because resulting offspring may have genetic defects, but also because it offends religious principles, damages the family unit, often involves child abuse, and is considered immoral.<sup>50</sup> By contrast, if authorities ban HGE to combat inequality, their goal is to prevent the birth of children who are superior, advantaged, and unjust. Such a ban frames children with disfavored traits as the central problem, and that is why it imposes legal stigma on them.

### A Viable Alternative to a Global Moratorium

As an alternative to a global moratorium, I propose that nations adopt and enforce legal regimes that regulate HGE for safety and efficacy. Under such an approach, scientists will remain free to conduct basic research in which human gametes and embryos are edited in the lab. However, regulators will not permit uterine transfers of such gametes or embryos until and unless doing so is safe for mothers and children.

Moratorium proponents contend that this approach is inadequate because it does not address whether it is "wise" to use HGE.<sup>12</sup> Similarly, expert reports have advocated incorporating values other than safety and efficacy into regulatory decisions. The NASEM report

opposed clinical trials for purposes other than treating or preventing disease or disability, at least for now, but it also urged that future decisions be informed by social values developed through public discussions of benefits and risks, including the risk that enhancements would introduce or exacerbate social inequities.<sup>6</sup> The Nuffield report argued that heritable genome edits must promote the welfare of future persons and not worsen social division.<sup>7</sup>

However, a regulatory system that focuses narrowly on safety and efficacy has its own advantages. It does not invite legislators and regulators to block access to a technology that may be lifesaving for some on the basis of speculative theories about psychological damage to children, increased inequality, speciation, pollution of the gene pool, and so on.

This proposal also treats genetic correction and other therapeutic modifications the same as enhancing ones. It does so for two reasons. First, the blurriness of the therapy-enhancement distinction creates an opportunity for manipulation. For example, the proponents of the global moratorium classify substitution of a naturally-occurring genetic variant to reduce the risk of disease as an enhancement, thereby relegating it to the same dubious category as attempts to confer superior memory or infrared vision.<sup>12</sup> Although Dr. He altered *CCR5* without adequately considering the risks, basic research may eventually point to other genetic variants that protect against disease or disability without imposing unreasonable risk. The enhancement label should not be used to deny access to them.

Second, a therapy-enhancement distinction does not accommodate biological complexity. A law or regulation can be drafted to permit genetic corrections that restore wild-type alleles. But if that law or regulation also prohibits enhancement, it may block other modifications that are intended to protect against disease but also improve the body or brain. Occasionally, a sympathetic regulator may stretch the facts or law to approve a therapeutic modification that is modestly enhancing. However, a surer way to keep regulatory options open is to drop the therapy-enhancement distinction.

The public views therapeutic uses more favorably than enhancing ones.<sup>37,38,39,40</sup> However, safety and efficacy regulation will tend naturally to distinguish modifications with a therapeutic or medical purpose from most others.<sup>35</sup> Regulators may first allow clinical trials of genetic correction. They will wait longer to authorize modifications that have a medical purpose—such as substitution of a genetic variant that confers immunity against disease—because such modifications can have good and bad effects.<sup>12</sup> They will be reluctant to permit modifications

intended as enhancements because of the biological complexity involved.

The evolving story of Russian biologist Denis Rebrikov illustrates the potential of national regulation to curtail dangerous experiments. To the dismay of many, he initially proposed disabling *CCR5* in human embryos so that HIV-positive women can gestate offspring without transmitting the virus – but only after seeking prior approval from three Russian government agencies.<sup>51</sup> Rebrikov has also discussed plans to edit the embryos of five deaf couples so that their children can hear. (PGT is not an option because each member of the couples is homozygous for the mutated *GJB2* gene.) Again, he plans to seek prior approval from authorities.<sup>52</sup> Those who review his applications will recall the backlash against Dr. He's experiment. They will also have access to research linking *CCR5*Δ32 to shortened life expectancy and *GJB2* mutations to skin and eye disease and cancer.<sup>53</sup> Thus, it is highly probable that Russian regulators will refuse permission to conduct these experiments.

## Conclusion

In this article, I have argued that a global moratorium is inadvisable for three reasons. The moratorium might encourage participating nations to ban HGE or postpone it indefinitely. It might deter or delay basic research that could lead to safe and effective HGE. Lastly, a moratorium might induce participating nations to adopt laws and regulations that stigmatize the children who are destined to be born with genomic modifications in any event. My alternative proposal is that nations should regulate HGE for safety and efficacy only and without distinguishing between therapeutic and enhancing modifications.

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