Draft Ethical Principles for Therapeutic Assisted Reproductive Technologies

He Jiankui,1,4 Ryan Ferrell,1 Chen Yuanlin,1 Qin Jinzhou,1,2 and Chen Yangran1

Abstract
The germline gene-editing field has several detailed preclinical research guidelines but lacks concise and plain-language ethics statements on ultimate clinical uses. The general public deserves a clear vision of the future to gauge the field’s ultimate intentions and have meaningful input and discussion about its progress. We propose the identification of a core set of fundamental human values to frame, guide, and restrict clinical applications that communities around the world can share and localize based on religious beliefs, culture, and public-health challenges.

Introduction
More than seven million children are born every year with lethal or debilitating diseases of genetic or partially genetic origin.1 Gene surgeries, including CRISPR* gene editing and mitochondrial donation techniques, promise new therapeutic strategies during in vitro fertilization (IVF) to cure or prevent these diseases before a child can suffer.

The potential utility and, for some, the controversy of gene editing to treat unborn children, including the availability and effectiveness of preimplantation genetic diagnosis for many genetic diseases, has prompted scientific societies and other worldwide organizations to publish a raft of guidelines about permissible preclinical research.2 Guidelines for ultimate clinical practices, however, remain less defined. What should be our proposed ethics and actual red lines?

A clear vision of the future, succinctly stated in plain language, is needed for the public to gauge the field’s eventual intentions and have meaningful conversations about how gene surgery may or may not affect their family, friends, and neighbors.

Surveys conducted in 2018 of >2,500 Americans3 and 4,000 Chinese4 show the general public of both countries are generally receptive to gene surgery in human embryos—if the sole purpose is to treat serious diseases. Respondents rejected enhancements, with the notable example of increasing intelligence being opposed by about 80% of Americans and 70% of Chinese respondents. Despite contrasting regulatory frameworks—the United States passed a law in 2015 explicitly to prohibit the U.S. Food and Drug Administration from reviewing of any applications,5 whereas China maintains a ministerial guideline6 drafted in response to cloning concerns7 some 15 years prior to the emergence of CRISPR—a cross-cultural ethical divide did not emerge in the American and Chinese surveys. Support for therapeutic uses of gene surgery in embryos was high, even among a majority of highly religious Americans.

On the other hand, many survey respondents also reported they were relatively uninformed about the gene-editing field. So, current public views on gene surgery may be forming based on widely shared personal ethics toward medicine and mercy. This is an open invitation for the scientific community to support the public in making informed decisions about gene surgery’s clinical utility, limitations, risks, regulatory needs, and future role in society.

Open Dialogue
Open dialogue has helped shape regulations and advance cultural attitudes in the field of IVF and other assisted reproductive technologies (ART) for >40 years. As a result, initial worries and warnings around eugenic applications

*Clustered Regularly Interspaced Short Palindromic Repeats.

1Department of Biology, Southern University of Science and Technology, Shenzhen, P.R. China; 2Department of Human Reproductive Medicine Center, Third Affiliated Hospital of Shenzhen University, Shenzhen, China.

*Address correspondence to: He Jiankui, Department of Biology, Southern University of Science and Technology, 1088 Xueyuan Boulevard, Shenzhen, Guangdong 518055, P.R. China, E-mail: hejk@sustc.edu.cn

© He Jiankui et al., 2018; Published by Mary Ann Liebert, Inc. This Open Access article is distributed under the terms of the Creative Commons License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
have not transpired. Clinicians have proven responsible stewards of medical procedures that have helped fertility-challenged couples raise more than eight million healthy children.  

We believe the gene-editing research community therefore has a duty to speak more openly and plainly to the public and lawmakers, despite this being an unfamiliar role for many scientists (including ourselves). Our community should also address ethics more inclusively, as others including Montoliu et al.9 and Jasanoff and Hurlbut have argued,10 by discussing and developing guidelines in more cosmopolitan and inclusive venues that include affected families and public stakeholders. Proactively educating journalists is crucial too. Likewise, science journalists and editors share a duty to translate research responsibly for the general public. Sensationalism has been an unfortunate part of media coverage since the emergence of IVF in the 1970s,11 with the prophesy of Huxley’s Brave New World,12,13 rapid cultural extinction,14,15 and barcoded or discombobulated babies serving as fallback tropes16–20 that many patient groups would prefer not share equal footing with balanced reporting.21 Another fallback is the overused term “designer baby”: this is an epithet aimed at invoking disgust, which is a common mechanism behind hate.22,23 Parents hope to protect their newborn’s life from a known debilitating, familial disease. Call them “gene surgery babies” if one must or better yet ordinary people who have had surgery to save their life or prevent a disease.

Core Principles
To help advance the constructive dialogue over the past 40 years that has ensured the ethical use of ART to help fertility-challenged couples conceive healthy children,

1. Mercy for families in need (悲悯之心)
A broken gene, infertility, or a preventable disease should not extinguish life or undermine a loving couple’s union.
   For a few families, early gene surgery may be the only viable way to heal a heritable disease and save a child from a lifetime of suffering.

2. Only for serious disease, never vanity (有所为更有所不为)
Gene surgery is a serious medical procedure that should never be used for aesthetics, enhancement, or sex selection purposes — or in any way that would compromise a child’s welfare, joy, or free will. No one has a right to determine a child’s genetics except to prevent disease.
   Gene surgery exposes a child to potential safety risks that can be permanent. Performing gene surgery is only permissible when the risks of the procedure are outweighed by a serious medical need.

3. Respect a child’s autonomy (探索你自由)
A life is more than our physical body and its DNA. After gene surgery, a child has equal rights to live life freely, to choose his or her occupation, to citizenship, and to privacy. No obligations exist to his or her parents or any organization, including paying for the procedure.

4. Genes do not define you (生活需要奋斗)
Our DNA does not predetermine our purpose or what we could achieve. We flourish from our own hard work, nutrition, and support from society and our loved ones. Whatever our genes may be, we are equal in dignity and potential.

5. Everyone deserves freedom from genetic disease (促进普惠的健康权)
Wealth should not determine health. Organizations developing genetic cures have a deep moral obligation to serve families of every background.

FIG. 1. Five core principles for gene surgery in human embryos.
we suggest the medical and patient community identify a core set of fundamental human values that clarify for the public the clinical future of early-in-life genetic surgery in plain terms and within a document as brief as possible. Lawmakers in countries wishing to permit clinical trials and eventual regulatory submissions could build on these values to write cohesive rules that can still account for their country’s distinctive mix of religious beliefs, culture, and public-health challenges. (A preface to a final document could also helpfully summarize the known risks, existing options such as preimplantation genetic diagnosis, how gene surgery/genome editing works, its limitations, and example use cases.)

As our laboratory (at South University of Science and Technology in Shenzhen, P.R. China) has studied the feasibility and safety of CRISPR/Cas9-mediated genetic surgery in nonviable and viable human and monkey embryos for several diseases over the past several years, we have thought deeply about ethical foundations for regulation in discussions between researchers, patients and advocates, and ethicists both in China and abroad. These discussions lead us to propose that, at a minimum, five core principles should be addressed in a modernization of Chinese regulations—and indeed any country’s guidelines or laws—permitting gene surgery for ART: (1) a clear social purpose, (2) impermissible uses, (3) rights after treatment, (4) the human spirit’s transcendence of DNA, and (5) a special duty to reduce economic inequality. We therefore propose five plain-language principles as a first draft of an ethical foundation to guide and restrict the use of therapeutic ART (see Fig. 1).

Of note, we hold additional but less universal beliefs that further restrict the use of gene surgery, including the need to prioritize local population health needs and focus only on treating disease via prevalent, natural genetic variants. We expect other groups will also hold additional views beyond the principles outlined here (Fig. 1). That diversity will make the world better.

We hope this call to action will help foster a more frank and plain-language dialogue about the ethics of gene surgery. In particular, we hope this approach may provide an additional way to solicit meaningful collaboration with the millions of valued members of our society who live with disabilities or serious medical conditions and who deserve to have a key role in shaping any guidelines that direct this field’s future, whether that happens at traditionally scientific conferences, in print, or elsewhere.

We also hope that the humanity of this debate is not forgotten amid controversy. Many parents have lost children to genetic diseases. While these families are a minority, real lives and suffering are at stake.

Author Disclosure Statement
No competing financial interests exist.

References

15. Editorial. By 2020 we won’t have sex to have babies—just IVF. Daily Telegraph, May 17, 2010.
19. Park A. A new technique that lets scientists edit DNA is transforming science—and raising difficult questions. TIME, July 4, 2016.