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American Society for Gene &
Cell Therapy Policy Summit

BROAD SOCIETAL CONSENSUS: PUBLIC EDUCATION, ENGAGEMENT AND EMPOWERMENT

OVERVIEW

CRISPR genome editing: terminology

Recent history (2015- present)

Broad societal consensus

Translational pathway forward

Adopt a moratorium

CRISPR Genome Editing: Terminology

Germline Genome Editing

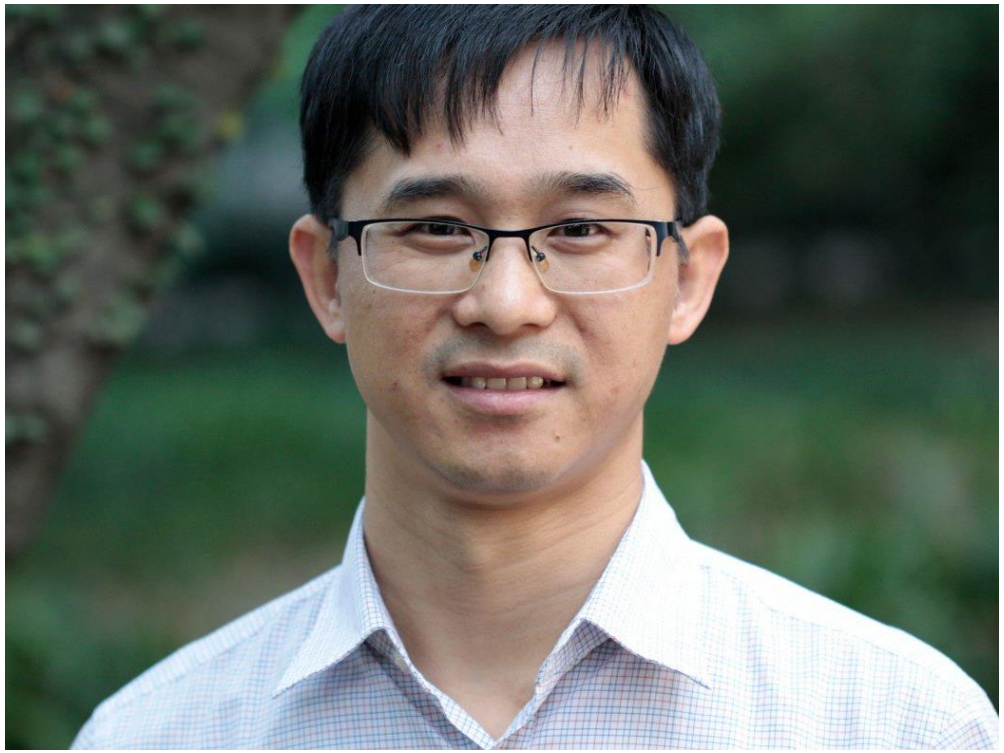
- Involves making genetic changes to reproductive cells (eggs and sperm, as well as the cells that give rise to eggs and sperm) or early stage (one-cell) embryos.

- ~~Clinical use of germline genome editing~~

Heritable Genome Editing

- Involves making genetic changes to reproductive cells (eggs and sperm, as well as the cells that give rise to eggs and sperm) or early stage (one-cell) embryos
- AND transferring these genetically modified cells to a woman's uterus in the hope of initiating a pregnancy that would result in a child with a modified genome. The goal would be a permanent change in the offspring and future generations.

Recent history (2015 – present)




INTERNATIONAL SUMMIT ON
HUMAN GENE EDITING
A GLOBAL DISCUSSION
December 1-3, 2015 Washington, D.C.

It would be irresponsible to proceed with any clinical use of germline editing unless and until

(i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and

(ii) there is broad societal consensus about the appropriateness of the proposed application.

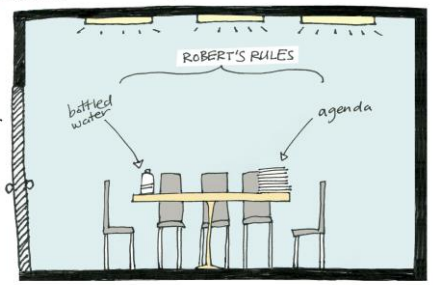
Broad societal consensus

~~Broad scientific consensus~~

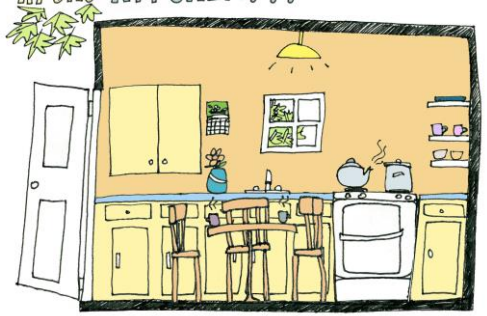
~~Broad societal debate~~

in the LAB?

in the BOARD ROOM?



in the KITCHEN???



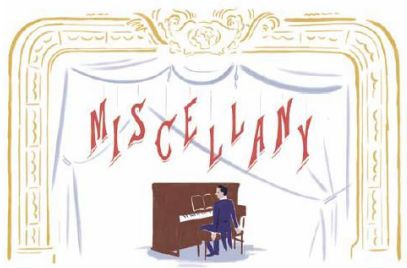
Responsibility: Participants are responsible for voicing their opinions, participating in the discussion, and actively implementing the agreement.

Self-discipline: Blocking consensus should only be done for principled objections. Object clearly, to the point, and without putdowns or speeches. Participate in finding an alternative solution.

Respect: Respect others and trust them to make responsible input.

Cooperation: Look for areas of agreement and common ground and build on them. Avoid competitive, right/wrong, win/lose thinking.

Struggle: Use clear means of disagreement – no putdowns. Use disagreements and arguments to learn, grow and change. Work hard to build unity in the group, but not at the expense of the individual who are its members.



THE BRIEF

This CRISPR Moment

Editing human DNA the way we edit text — are we ready?

FRANÇOISE BAYLIS AND JANET ROSSANT
ILLUSTRATIONS BY KATTY MAUREY

It reads like an all-caps typo from the technical manual that comes taped to the side of a new refrigerator. But CRISPR is going to change your world. It may even—quite literally—change the face of humanity.

Since its discovery four years ago, the gene-editing system known as "clustered regularly interspaced short palindromic repeats" has been used by scientists to make precise alterations in the DNA sequence of living cells. It offers the prospect of treating (and perhaps even eradicating) debilitating genetic conditions, improving fertility treatments, fighting cancer, and allowing the safe transplantation of tissues and organs between species.

Hemophilia, sickle-cell anemia, and muscular dystrophy are just three of the diseases that could eventually become treatable thanks to therapies developed through CRISPR. In late 2015, for instance, three groups of scientists reported that they could infect muscle cells in living Duchenne muscular dystrophic mice with a virus carrying the CRISPR/Cas9 editing cassette. (The latter alphanumeric term refers to a CRISPR system that employs the Cas9 protein.) The researchers then edited the defective dystrophin gene in enough cells to improve muscle function.

On the other hand, CRISPR also raises the spectre of a *Gattaca*-style bioethical dystopia. The technology, some warn, might open the door to large-scale bioterrorism or monstrous, genetically altered human variants. Using CRISPR/Cas9, scientists can make precise genetic alterations to early-stage embryos that are precursors of all the cells contained in a human body. Crucially, this includes the eggs and sperm. Alterations to these "germ cells" are heritable, meaning they will carry over into succeeding generations. This is commonly referred to as "germ-line gene editing." So far, lines of genetically altered plants, flies, fish, mice, and even monkeys have been produced using such gene-editing techniques.

The "clustered regularly interspaced palindromic repeats" employed by CRISPR are genetic sequences that were first discovered in bacteria some twenty years ago. A clever series of experiments and DNA detective work in the early part of this century led to the discovery that CRISPRs carry bits of viral DNA—and use copies of this sequence to recognize and target any invading virus with an enzyme (typically Cas9, as described above) that cuts up and destroys viral invaders.

CRISPR

'Broad societal consensus' on human germline editing

By: Françoise Baylis, Ph.D.

CRISPR ('Clustered Regularly Interspaced Short Palindromic Repeats') is a new gene editing technique that can be used to change the genome of living cells by deleting, repairing or replacing genes.[1] This technology can be used to change somatic cells (i.e., body cells whose genomes are not transmitted to subsequent generations) or germ cells (i.e., sperm and eggs whose genomes are transmitted to subsequent generations). To date, no CRISPR-edited human cells have been transferred to humans. In the near future, the hope is to move to clinical trials using CRISPR-edited human somatic cells. In the distant future, there is the prospect of using CRISPR-edited human gametes or early human embryos for reproduction. The genetic modification of gametes or early embryos would result in germline editing, as the genetic changes would be passed on to offspring and subsequent generations.

At the time of writing, there is common knowledge of two basic science projects involving gene editing of early human embryos in a research setting. In April 2015, the journal *Protein & Cell* published work by a research group in China at Sun Yat-sen University in Guangzhou (led by Canquan Zhou and Junjiu Huang) that involved making genetic alterations to nonviable human embryos.[2] The research aimed to repair a genetic defect that causes beta thalassemia (a potentially fatal blood disorder). No genetically modified human embryos were transferred to initiate a pregnancy. More recently in February 2016, the United Kingdom's Human Fertilisation and Embryology Authority (HFEA) approved a research license renewal application submitted by Kathy Niakan from the Francis Crick Institute. The license application was for human embryo research that would include knocking out the *OCT4* gene in healthy embryos to better understand embryonic development with the hope of eventually contributing to advances in pregnancy and fertility treatment.[3] The HFEA approval was subject to ethics approval "from an appropriately constituted research ethics committee".[4] At the time of approval, the HFEA underscored the fact that "as with all embryos used in research, it is illegal to transfer them to a woman for treatment."[5]

The first of these two human embryo projects spurred considerable ethical debate and angst, as the research demonstrated both the potential to modify the human genome across generations, and the inherent risks in doing so. In the months preceding the publication of the research (and according to some 'in anticipation of the publication of the research'),[6] there were calls for a voluntary moratorium on modifying the human germline[7,8] to allow for careful deliberation on the risks and benefits of the technology and "the attendant ethical, social, and legal implications of genome modification".[9] In the ensuing debate, many agreed that the research, though not intended for use in pregnancy, nevertheless crossed an ethical rubicon and would lead to the creation of 'designer babies' and the introduction of a new eugenics.

"At the time of writing, there is common knowledge of two basic science projects involving gene editing of early human embryos in a research setting."

In response to this burgeoning debate, in December 2015, the U.S. National Academies of Science, the U.S. National Academy of Medicine, the Royal Society, and the Chinese Academy of Science hosted an International Summit on Human Gene Editing. At the close of the International Summit, the Organizing Committee of ten

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comment

Human germline genome editing and broad societal consensus

Françoise Baylis

Should human genome editing be limited to somatic cells, or should germline genome editing also be permitted? Should (apparently) permissible human genome editing be limited to therapeutic purposes, or should enhancement purposes also be permitted? Who decides, and on what basis?

Everyone who has heard of CRISPR–Cas9 gene editing probably has an opinion about whether (and if so, how) this technology should be used in humans. "If you have the skills and the knowledge to fix these diseases, then frickin' do it", said one patient advocate[1]. Others, including scientists, are more cautious. For example, Eric Lander, head of the Broad Institute, writes, "It has been only about a decade since we first read the human genome. We should exercise great caution before we begin to rewrite it … authorizing scientists to make permanent changes to the DNA of our species is a decision that should require broad societal understanding and consent."[2]

No one discounts the scientific and therapeutic promise of human gene editing[2]. The technology could be used to treat sickle cell anaemia, metabolic liver disease, human immunodeficiency virus (HIV) infection, progressive blindness, heart disease, cancer, Alzheimer's disease, Huntington's disease, and so on. Many, however, including myself, worry about the hubris and the potential negative consequences of the discrete goal of trying to take over the evolutionary story. Those who share this worry about the introduction of heritable genetic modifications typically draw a clear demarcation between somatic cell gene editing to hopefully cure individual patients, and germline gene editing to hopefully create genetically healthy individuals capable of having genetically healthy offspring[3]. Another worry concerns the use of human gene editing not merely to treat or eliminate hereditary illnesses, but also to enhance non-medical physical and mental characteristics (for example, to improve athletic abilities).

Heritable genetic modifications

With CRISPR–Cas9 gene editing, the ethics of creating 'designer babies' has taken on a certain urgency as the prospect of creating generations of genetically modified humans now seems within reach. In the past couple of years, three studies involving genome editing of human embryos have been published. In addition, the goal of editing the genomes of the sperm and egg (and the progenitors of those cells) prior to *in vitro* fertilization has been identified.

The prospect of creating generations of genetically modified humans now seems within reach.

In very general terms, there are urgent research ethics concerns about the safety of the technology (resulting from incomplete editing, inaccurate editing, off-target mutations, on-target mutations with unintended consequences, and mosaicism), the unlikely prospect of a favourable harm/benefit ratio (where potential medical benefit outweighs research risks), and the inability to obtain consent from those who would be born following genetic modification. There are also more complex ethical concerns about opportunity costs and the proper balance between increasing reproductive options and promoting social justice, the commodification of children, the exacerbation of existing inequalities, the rebirth of eugenics, and the introduction of new forms of discrimination and stigmatization resulting from the medicalizing and pathologizing of difference.

Public attention was drawn to these issues in 2015 when researchers at Sun Yat-sen University in Guangzhou, China, published a paper reporting the genetic manipulation of non-viable human embryos using CRISPR–Cas9[4]. This publication prompted the US National Academy of Sciences — in coordination with the US National Academy of Medicine, the Chinese Academy of Sciences, and the UK's Royal Society — to co-host an International Summit on Human Gene Editing. The overarching goal of the summit was to "explore the many questions surrounding the use of gene editing tools in humans"[5]. To quote the opening remarks of David Baltimore, Chair of the Organizing Committee, "Today, we sense that we are close to being able to alter human heredity. Now we must face the questions that arise. How, if at all, do we as a society want to use this capability?"[5].

I was a member of the 12-person Organizing Committee of the International Summit on Human Gene Editing. In that role, I was a signatory to the *On Human Gene Editing: International Summit Statement* issued in December 2015 at the close of the summit[6]. The statement included four conclusions, one of which outlined an apparently simple, yet exquisitely complex, two-part ethical framework for evaluating human germline gene editing. That conclusion stipulated that "it would be irresponsible to proceed with any clinical use of germline editing unless and until: (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and (ii) there is broad societal consensus about the appropriateness of the proposed application". Another conclusion stressed the need for ongoing international conversation to continue to explore contentious issues surrounding human gene editing. In response to the statement, the presidents of the four co-hosting organizations agreed that they would work with other academies around the world to continue the conversation[5].

The conclusions on germline gene editing and on the need for ongoing discussion

world view

Credit: Danny Abriel/ Dalhousie Photography

Questioning the proposed translational pathway for germline genome editing

Despite opprobrium from the scientific community, the creation of the first CRISPR babies by germline genome editing has led to a debate more about execution than intent. We need public education, engagement and empowerment to reach 'broad societal consensus' on whether, not how, to pursue heritable genome editing, argues Françoise Baylis.

In late November 2018 the future came crashing into the present when Jiankui He, a researcher in Shenzhen, China, self-reported that he had created the world's first CRISPR babies. While many thought it was only a matter of time before this happened, few thought it would be this soon: only three-and-a-half years after researchers in Guangzhou, China, first reported the use of CRISPR technology to edit human embryos in the laboratory.

The global response to the unexpected news that supposedly healthy twin girls had been born from embryos genetically modified to confer resistance to HIV was swift and almost uniformly critical. In condemning He, a number of scientists were quick to distance themselves from this 'rogue' scientist and to reassure the general public that responsible scientists could, and would, do 'well' what He had done 'poorly'.

This response is disconcerting insofar as it suggests that the ethical issue with He's research was one of execution, not intent. And yet, the question about intent—is it ethical to proceed with human germline editing?—logically precedes the question about execution—how can we proceed ethically with human germline editing? Until the first question has been fully explored and authoritatively answered in the affirmative, the second question is moot.

Following He's surprise announcement, prominent scientists David Baltimore and Feng Zhang independently condemned He's research. In so doing, they both referenced the concluding Statement from the 2015 International Summit *On Human Gene Editing* (http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a), according to which it would be irresponsible to proceed with any clinical use of germline editing unless and until safety and efficacy is assured and a "broad societal consensus about the appropriateness of the proposed application" has been achieved.

Notwithstanding this clear admonition from Baltimore and Zhang, and the more general hue and cry that He had violated international consensus, the concluding Statement from the Second International Summit *On Human Genome Editing* (held a few days after He's announcement) asserted that it is now "time to define a rigorous, responsible translational pathway toward such trials" (http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11282018b). That the opprobrium directed at He should lend itself to this conclusion is both surprising and troubling.

Among the proposed criteria for acceptable germline genome editing, the 2018 Summit Statement listed "strict independent oversight, a compelling medical need, an absence of reasonable alternatives, a plan for long-term follow-up, and attention to societal effects." What this amounts to in practical terms, however, is most unclear.

What is the appropriate standard for "strict independent oversight" of germline genome editing? Jiankui He maintains that his research was reviewed and approved by the relevant institutional research ethics committee. This system of local (and, sometimes, voluntary) oversight has been common for CRISPR research involving human embryos. One exception to this practice is the research conducted by Kathy Niakan in the United Kingdom, where there is national mandatory oversight by the Human Fertilisation and Embryology Authority. Should national (or international) oversight replace local institutional oversight?

What is a "compelling medical need" for germline genome editing? According to He, HIV infection is a major problem in China, where it can have a devastating impact on quality of life because of stigma. Others, however, maintain that the risk of HIV infection is not an adequate medical indication. Meanwhile the US National Academies of Sciences, Engineering, and Medicine and the Nuffield Council on Bioethics suggest that the desire for healthy genetically related children by prospective parents who are at risk of passing on a serious genetic disease to their children is (might be) a compelling medical need. Who decides?

What is a "reasonable" alternative to germline genome editing? For example, with respect to the risk of HIV infection, is sperm washing before IVF a reasonable alternative means of reproduction for prospective parents? And are safe-sex education and antiviral drugs reasonable alternatives for future offspring? Or, with respect to the risk of transmitting a serious genetic disease to one's children, are adoption, sexual reproduction followed by prenatal testing and abortion, IVF followed by pre-implantation diagnosis and embryo selection, or IVF using healthy donor sperm or eggs reasonable alternatives?

What is a sufficient "plan for long-term follow-up" of children born of germline genome editing? Parents cannot be forced to enrol their children in research for life (or even until the age of majority). And once the children are adults, they cannot be coerced into ongoing research participation. So, what kind of long-term plan would satisfy this requirement?

And finally, what does "attention to societal effects" of germline genome editing require? Public education? Public engagement? Public empowerment? For those of us committed to public empowerment, we can but insist on the importance of public education and public engagement in working toward a "broad societal consensus" on whether to pursue heritable human genome editing.

Until the first question has been fully explored and authoritatively answered in the affirmative, the second question is moot.

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Competing interests
The author declares no competing interests.

Inclusivity, responsibility, self-discipline, respect, co-operation, struggle, benevolence

SECOND INTERNATIONAL SUMMIT ON

HUMAN GENOME EDITING

November 27-29, 2018 The University of Hong Kong

THE ACADEMY OF SCIENCES OF HONG KONG
THE ROYAL SOCIETY
U.S. NATIONAL ACADEMY OF SCIENCES
U.S. NATIONAL ACADEMY OF MEDICINE

- “Germline genome editing could become acceptable in the future if these risks are addressed and if a number of additional criteria are met.
- Progress over the last three years and the discussions at the current summit, however, suggest that it is time to define a rigorous, responsible translational pathway toward such trials.”

Translational pathway forward

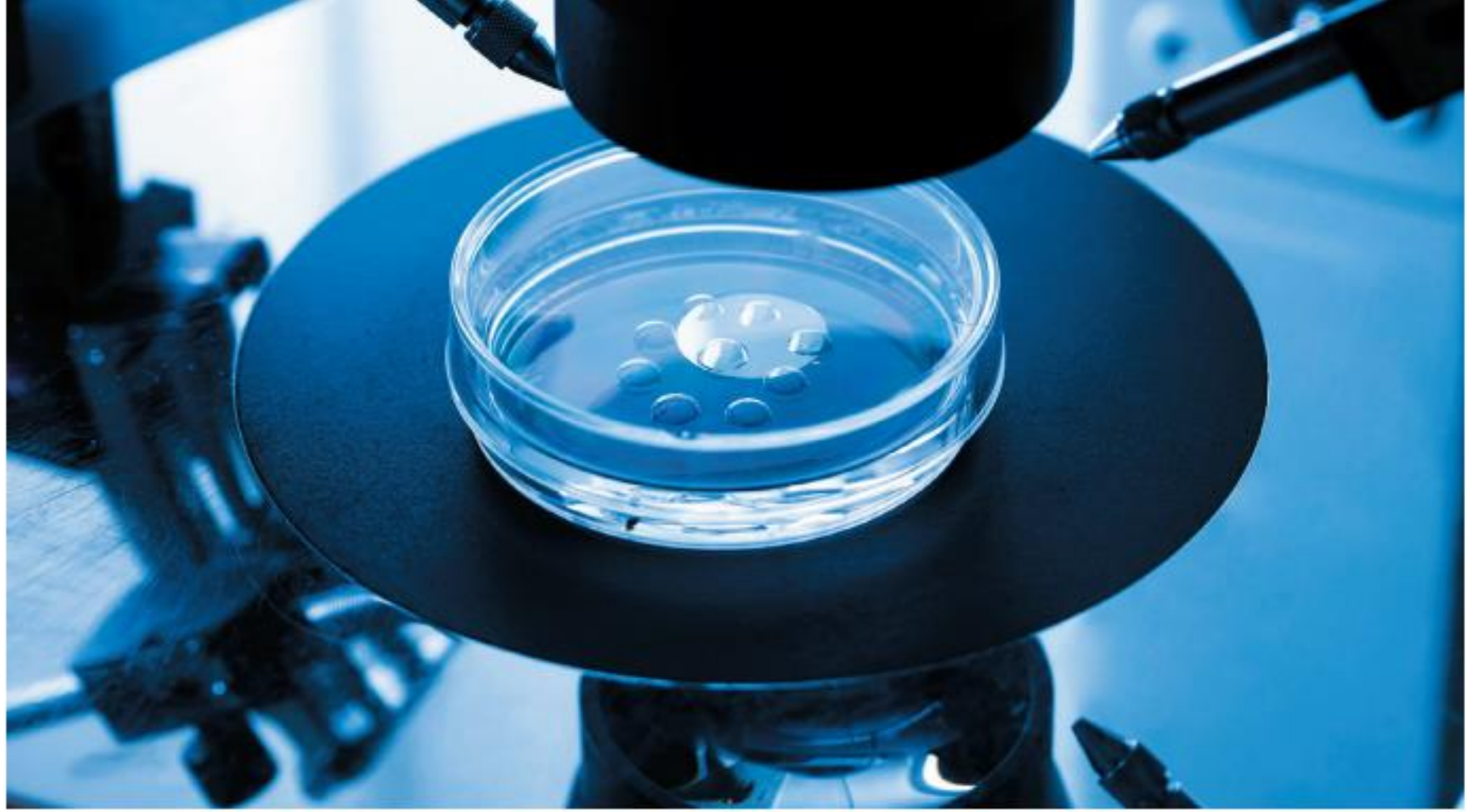
Elements of a rigorous, responsible pathway forward

- Strict independent oversight
- Compelling medical need
- Absence of reasonable alternatives
- A plan for long-term follow-up
- Attention to societal effects

Strict independent oversight

- *Jiankui He* (CHINA) Research approved by the relevant institutional research ethics committee (Allegations of fraud)
  - "Medical Ethics Approval Application Form" submitted in March 2017 to the Ethics Committee of HarMoniCare Shenzhen Women's and Children's Hospital
- *Shoukhrat Mitalipov* (US) Research approved by local IRB
- *Kathy Niakan* (UK) License from HFEA (National oversight)
- *Denis Rebrikov* (Russia) Russian Federation developing policies in this area
- How to ensure "independence" and absence of conflict of interest?
- Is NATIONAL OVERSIGHT preferable? sufficient?

Adopt a moratorium



Embryos cultured as part of *in vitro* fertilization can be screened for genetic diseases.

Adopt a moratorium on heritable genome editing

CORRESPONDENCE · 13 MARCH 2019

NIH supports call for moratorium on clinical uses of germline gene editing

Carrie D. Wolinetz & Francis S. Collins

We strongly support Eric Lander and colleagues' call for an international moratorium on clinical uses of human germline editing. We also welcome the proposed process that nations could consider in the future to determine whether necessary conditions to lift the moratorium have been met.

RELATED

Adopt a moratorium on heritable genome editing

This is a crucial moment in the history of science: a new technology offers the potential to rewrite the script of human life. We think that human gene editing for reproductive purposes carries very serious consequences — social, ethical, philosophical and theological. Such great consequences deserve deep reflection. A substantive debate about benefits and risks that provides opportunities for multiple segments of the world's diverse population to take part has not yet happened. Societies, after those deeper discussions, might decide this is a line that should not be crossed. It would be unwise and unethical for the scientific community to foreclose that possibility.

The European Society
of Human Genetics

Response to ‘Adopt a moratorium on heritable gene editing’

03/27/2019

The past year has seen many developments in the field of gene editing, both in somatic and in germ line applications. Editing the germline means that changes will be made in every cell in the body and will be inherited by future generations. While carrying out such editing in a research setting is important for a greater understanding, clinical germline editing leading to a pregnancy carries considerable practical and ethical risks, at least at present.

The announcement of the birth of twins in China, following a procedure of germline gene editing performed by Dr He Jiankui, has attracted the attention of the international media, as well as raising serious concerns in the scientific community, and the Chinese authorities also condemned these procedures as being illegal in the country. A few scientists in the USA were informed about the intentions of Dr He Jiankui both before and during the course of his experiments. However, formal reports to ethics committees or other relevant institutions were never made.

Now clinical germline gene editing has taken place, and the scientific community worldwide has been shaken and is questioning its responsibilities.

ESHRE News and Statements

22 March 2019

Moratorium on Gene Editing in human embryos

ESHRE supports the call for a moratorium on the use of CRISPR/Cas9 nucleases in the human embryo for clinical applications (Nature 567, 165-168 (2019)). This powerful genetic tool can be programmed easily to facilitate the correction of genetic mutations seamlessly and at high efficiency. Although the technology is already revolutionizing preclinical biomedical research, multiple independent reports have raised awareness that the CRISPR/Cas9 system can cause unexpected alterations to genomic DNA resulting in potentially damaging mutagenic events.

Firstly, the nuclease can cause mutation to the genome at closely matched sequences to the target gene, so called off-target mutations. Secondly, recent reports have shown that the enzyme can also cause unexpected large deletions and rearrangements at the actual target site, which could have considerably larger mutagenic effects . Lastly, when applied within the fertilized zygote, the persistence of the enzymes after the first cell-cleavage event can lead to a mosaic outcome, where different cells within a single embryo would harbour different mutations. The downstream consequences of non-specific mutagenesis off-target, genomic rearrangement on-target, and unpredictable mosaicism, are clearly hard to predict but have considerable potential to limit the safety of the CRISPR/Cas9 system for therapeutic intervention.

IRDiRC
INTERNATIONAL
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CONSORTIUM

IRDiRC supports the call for a moratorium on hereditary genome editing

17 MARCH 2019 BY SCIENTIFIC SECRETARIAT IRDIRC

"We call for a global moratorium on all clinical uses of human germline editing — that is, changing heritable DNA (in sperm, eggs or embryos) to make genetically modified children".

With this opening sentence in a commentary published this week on Nature, Eric Lander and a group of eminent scientists and bioethicists request an international governance framework to address this challenging theme.

IRDiRC fully endorses their call. Sharon Terry, who represents Genetic Alliance in IRDiRC, has co-authored the commentary.

The new technologies of genome editing bear the potential to correct the genetic defects at the root of many human diseases in somatic cells with unprecedented precision and ease; nonetheless, extending application of these tools to the human germline is fraught with serious concerns that cannot be addressed by the scientific community alone.

The proposed moratorium does not intend to ban research to make therapeutic application of genome editing safe and effective, but calls for a five-year time to build an international network allowing the scientific community and national decision makers to address the medical, social and ethical implications of germline genome editing.

IRDiRC strongly supports the proposal by Lander and colleagues, while encouraging continued research to bring genome editing techniques to the safety and efficacy levels required to transform such potential into effective therapies for rare diseases.

Disclaimer: This statement expresses the outlook of the IRDiRC community and does not necessarily represent the official endorsement by individual IRDiRC member organizations. For more information on contents provided on this website see also IRDiRC Disclaimer.

AMERICAN SOCIETY of GENE & CELL THERAPY

ADVOCACY | POLICY UPDATES

Scientific Leaders Call For Global Moratorium on Germline Gene Editing

April 24, 2019

In a letter sent to U.S. Department of Health and Human Services Secretary Alex Azar today, a broad collective of 62 individual scientists, bioethicists, and biotechnology executives, including past-presidents and current board of directors members from ASGCT, across industry and academia called for collaboration on a binding global moratorium on human clinical germline experimentation.

In a letter sent to U.S. Department of Health and Human Services Secretary Alex Azar today, a broad collective of 62 individual scientists, bioethicists, and biotechnology executives, including past-presidents and current board of directors members from ASGCT, across industry and academia called for collaboration on a binding global moratorium on human clinical germline experimentation.

"Although we recognize the great scientific advancement represented by gene editing technologies and their potential value for an improved understanding and possible treatment of human disease, we strongly believe the editing of human embryos that results in births carries serious problems for which there are no scientific, ethical, or societal consensuses," the letter reads. "As a result, we contend that such human genetic manipulation should be considered unacceptable and support a binding global moratorium until serious scientific, societal, and ethical concerns are fully addressed."

World Health Organization

“I have accepted the interim recommendations of WHO’s Expert Advisory Committee that regulatory authorities in all countries should not allow any further work in this area until its implications have been properly considered.”

DG Tedros Adhanom Ghebreyesus July 26, 2019

Moratorium ineffective

You Retweeted

Nathan Letts, PhD @Sciguy999 · Oct 18

Russian '#crisprbabies' scientist has started editing genes in eggs from a deaf woman Rebrikov also told @Nature that he does not plan to implant embryos until he gets regulatory approval. nature.com/articles/d4158... #ethics #genetherapy @ArthurCaplan @HankGreelyLSJU @pknoepfler

Gaetan Burgio
@GaetanBurgio

"Russian 'CRISPR-baby' scientist has started editing genes in eggs from a deaf woman" @NatureNews -> couple of point here nature.com/articles/d4158...

Rebrikov also provided further information about the egg donor and her plans in his most recent e-mail. In September, N+1 had reported that the couple didn't sign a consent form and had backed away from the idea of creating a gene-edited child, citing personal reasons.

But Rebrikov now says that this is only a temporary hurdle. He notes that the woman who donated the eggs has taken a one-month 'pause' while she gets a cochlear implant.

Rebrikov also emphasized that he will not move forward without
ederation. "I will
permission of the

leased a statement
ature. Rebrikov
n, but it will be

Gaetan Burgio @GaetanBurgio · Oct 18

Replying to @GaetanBurgio

Like it or not, 1/ implantation of the edited embryos will happen again. If it is not China, it will be Russia or elsewhere. In my view it is a matter of time 2/ This story demonstrates that a moratorium is ineffective 3/ Global governance seems not to work either

2 2 3

Moratorium : Temporary prohibition

Francoise Baylis @FrancoiseBaylis · Oct 18
Replying to @FrancoiseBaylis
By definition a moratorium is a temporary prohibition. In July 2019 the @WHO DG issued a statement calling on nations to refrain from heritable editing so that its Expert committee on ethics & governance could complete its work.
1 1

Francoise Baylis @FrancoiseBaylis · Oct 18
WHO Statement on governance and oversight of human genome editing stipulates that: "regulatory authorities in all countries should not allow any further work in this area until its implications have been properly considered"
1 1

Francoise Baylis @FrancoiseBaylis · Oct 18
The Russian health ministry has since issued a statement saying that it follows the position of the WHO committee: it is too soon to do such experiments. So, seems to me that we have a moratorium, it is just that we can't use the m-word because it offends some.
2

Francoise Baylis @FrancoiseBaylis · Oct 18
As to whether global governance can work, that remains to be seen and may ultimately depend on which scientists and which nation states are open to moral suasion. @LandonGetz @DocDellaire @HankGreelyLSJU @rosario_isasi @CohenProf @pknoepfler @bioethicsjosie @4LOVofScience
3

Julian Hitchcock @julianhitchcock · Oct 19
Replying to @FrancoiseBaylis and @GaetanBurgio
Of course it's ineffective. It does have important totemic value, but no grand international declaration is ever going to prevent something that is already illegal, cheap and easy to conceal. We might as well have a moratorium against the use of controlled drugs.
2 1

Francoise Baylis @FrancoiseBaylis · 21h
There are options for global governance that do not rely on "grand international declarations." Our challenge is to exercise our moral imagination and think about tools and resources that could be effective in high- middle- and low-income countries.
2

"important 'totemic value'"

Voluntary moratorium

Strongly discourages clinical use

COMMENT

Don't edit the human germ line

Heritable human genetic modifications pose serious risks, and the therapeutic benefits are tenuous, warn **Edward Lanphier**, **Fyodor Urnov** and colleagues.

It is thought that studies involving the use of genome-editing tools to modify the DNA of human embryos will be published shortly[1].

There are grave concerns regarding the ethical and safety implications of this research. There is also fear of the negative impact it could have on important work involving the use of genome-editing techniques in somatic (non-reproductive) cells.

We are all involved in this latter area of work. One of us (F.U.) helped to develop the first genome-editing technology, zinc-finger nucleases[2] (ZFNs), and is now senior scientist at the company developing them, Sangamo BioSciences of Richmond, California. The Alliance for Regenerative Medicine (ARM; in which E.L., M.W. and S.E.H. are involved), is an international organization that represents more than 200 life-sciences companies, research institutions, non-profit organizations, patient-advocacy groups and investors focused on developing and commercializing therapeutics, including those involving genome editing.

Genome-editing technologies may offer a powerful approach to treat many human diseases, including HIV/AIDS, haemophilia, sickle-cell anaemia and several forms of cancer[2]. All techniques currently in various stages of clinical development focus on modifying the genetic material of somatic cells, such as T cells (a type of white blood cell). These are not designed to affect sperm or eggs.

In our view, genome editing in human embryos using current technologies could have unpredictable effects on future generations. This makes it dangerous and ethically unacceptable. Such research could be exploited for non-therapeutic modifications. We are concerned that a public outcry about such an ethical breach could hinder a promising area of therapeutic development, namely making genetic changes that cannot be inherited.

At this early stage, scientists should agree not to modify the DNA of human reproductive cells. Should a truly compelling case ever arise for the therapeutic benefit of germline modification, we encourage an open discussion around the appropriate course of action.

EDITING TOOLS

Genome editing of human somatic cells aims to repair or eliminate a mutation that could cause disease. The premise is that corrective changes to a sufficient number of cells carrying the mutation — in which the genetic fixes would last the lifetimes of the modified cells and their progeny — could provide a 'one and done' curative treatment for patients.

For instance, ZFNs are DNA-binding proteins that can be engineered to induce a double-strand break in a section of DNA. Such molecular scissors enable researchers to 'knock out' specific genes, repair a mutation or incorporate a new stretch of DNA into a selected location.

Sangamo BioSciences is conducting clinical trials to evaluate an application of genome editing as a potential 'functional cure' for HIV/AIDS[4]. The hope is that

INSIGHTS

PERSPECTIVES

BIOTECHNOLOGY

A prudent path forward for genomic engineering and germline gene modification

A framework for open discourse on the use of CRISPR-Cas9 technology to manipulate the human genome is urgently needed

By **David Baltimore**,[1] **Paul Berg**,[2] **Michael Botchan**,[3,4] **Dana Carroll**,[4] **R. Alta Charo**,[4] **George Church**,[5] **Jacob E. Corn**,[6] **George Q. Daley**,[6,7] **Jennifer A. Doudna**,[8,9*†] **Marsha Fenner**,[4] **Henry T. Greely**,[10] **Martin Jinek**,[10] **G. Steven Martin**,[11] **Edward Penhoet**,[12] **Jennifer Puck**,[13] **Samuel H. Sternberg**,[10] **Jonathan S. Weissman**,[8,9†] **Keith R. Yamamoto**[8,14†]

Genome engineering technology offers unparalleled potential for modifying human and nonhuman genomes. In humans, it holds the promise of curing genetic disease, while in other organisms it provides methods to reshape the biosphere for the benefit of the environment and human societies. However, with such enormous opportunities come unknown risks to human health and well-being. In January, a group of interested stakeholders met in Napa, California (*1*), to discuss the scientific, medical, legal, and ethical implications of these new prospects for genome biology. The goal was to initiate an informed discussion of the uses of genome engineering technology, and to identify those areas where action is essential to prepare for future developments. The meeting identified immediate steps to take toward ensuring that the application of genome engineering technology is performed safely and ethically.

POLICY

The promise of so-called "precision medicine" is propelled in part by synergies between two powerful technologies: DNA sequencing and genome engineering. Advances in DNA sequencing capabilities and genome-wide association studies have provided critical information about the genetic changes that influence the development of disease. In the past, without the means to make specific and efficient modifications to a genome, the ability to act on this information was limited. However, this limitation has been upended by the rapid development and widespread adoption of a simple, inexpensive, and remarkably effective genome engineering method known as clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 (*2*). Building on predecessor platforms, a rapidly expanding family of CRISPR-Cas9–derived technologies is revolutionizing the fields of genetics and molecular biology as researchers employ these methods to change DNA sequences—by introducing or correcting genetic mutations—in a wide variety of cells and organisms.

CURRENT APPLICATIONS. The simplicity of the CRISPR-Cas9 system allows any researcher with knowledge of molecular biology to modify genomes, making feasible experiments that were previously difficult or impossible to conduct. For example, the CRISPR-Cas9 system enables introduction of DNA sequence changes that correct genetic defects in whole animals, such as replacing a mutated gene underlying liver-based metabolic disease in a mouse model (*3*). The technique also allows DNA sequence changes in pluripotent embryonic stem cells (*4*) that can then be cultured to produce specific tissues, such as cardiomyocytes or neurons (*5*). Such studies are laying the groundwork for refined approaches that could eventually treat human disease. CRISPR-Cas9 technology can also be used to replicate precisely the genetic basis for human diseases in model organisms, leading to unprecedented insights into previously enigmatic disorders.

In addition to facilitating changes in differentiated somatic cells of animals and plants, CRISPR-Cas9 technology, as well as other genome engineering methods, can be used to change the DNA in the nuclei of reproductive cells that transmit information from one generation to the next (an

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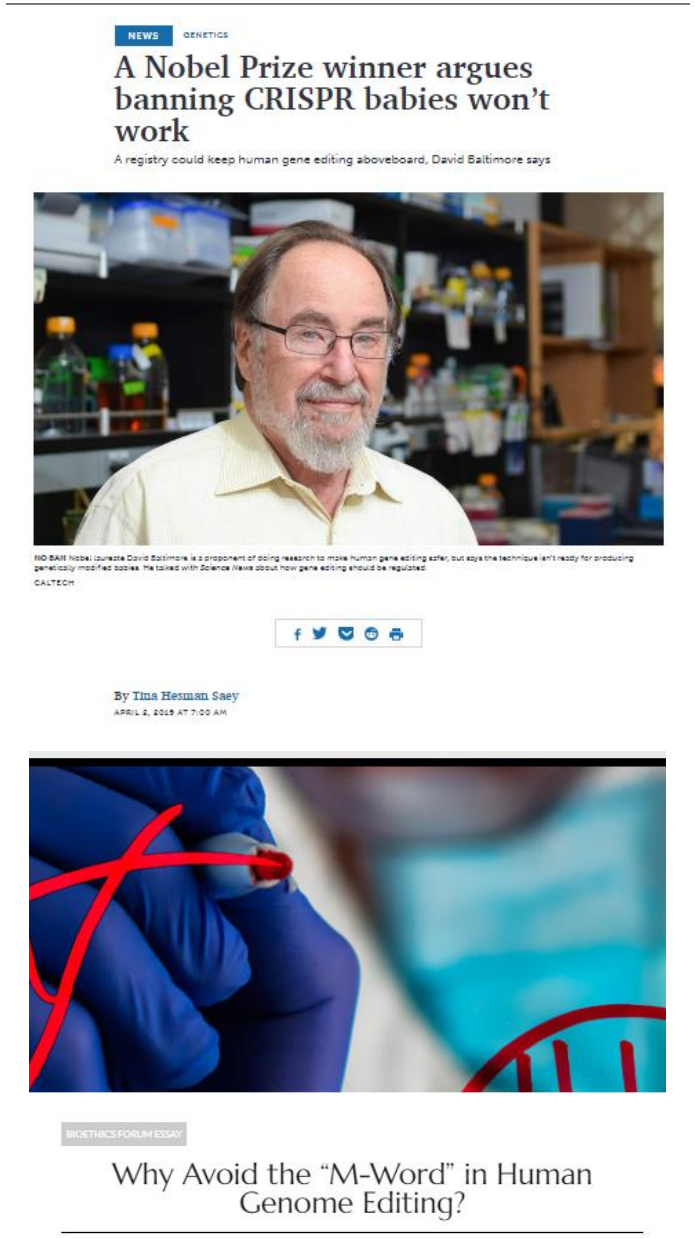
David Baltimore, former president of the California Institute of Technology, helped organize an international group of scientists to discuss use of the Crispr-Cas9 technique on human genes.
Susan Walsh/Associated Press



NEWS GENETICS

A Nobel Prize winner argues banning CRISPR babies won't work

A registry could keep human gene editing aboveboard, David Baltimore says

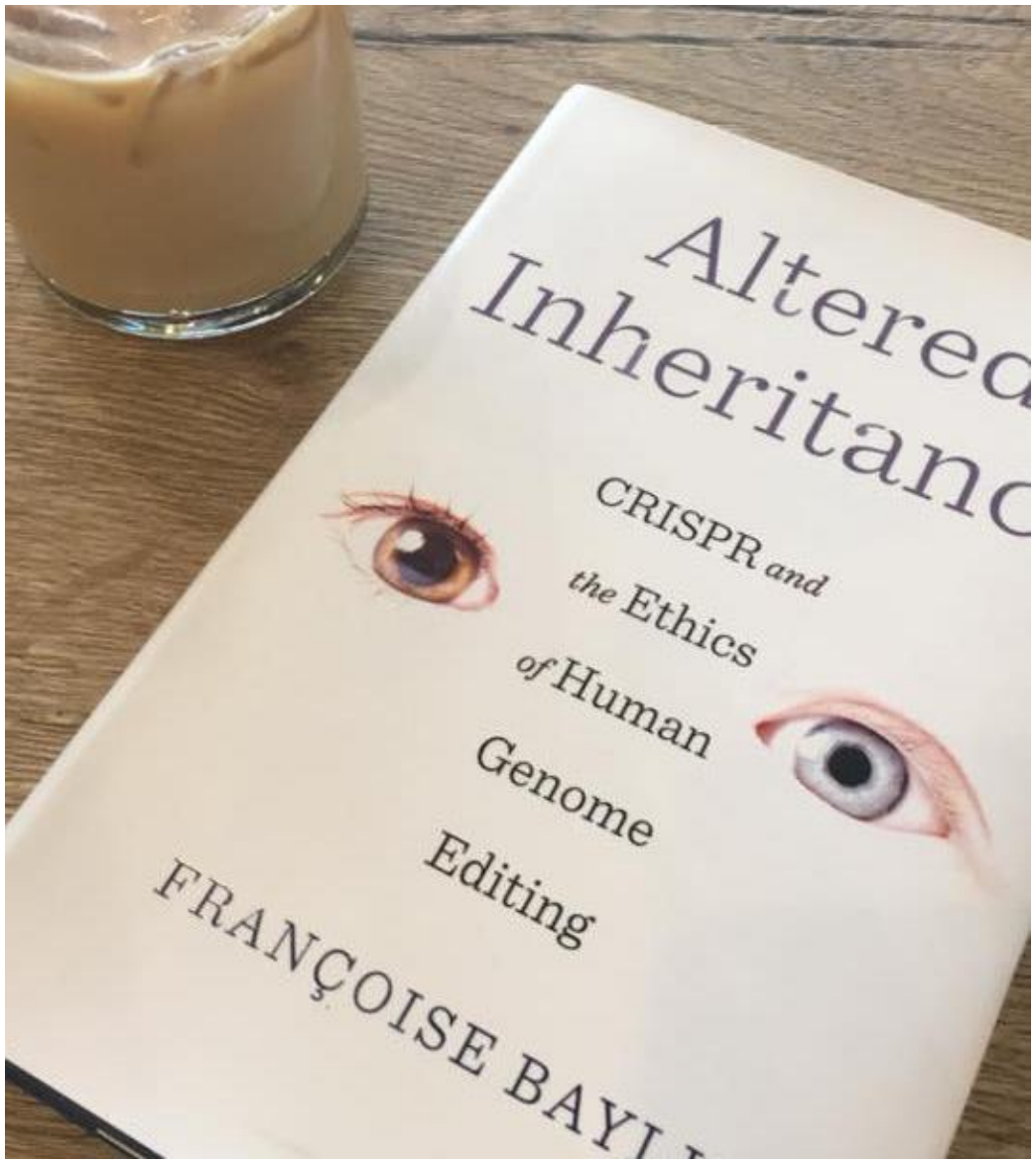
NO BAN Nobel laureate David Baltimore is a proponent of doing research to make human gene editing safer, but says the technique isn't ready for producing genetically modified babies. He talked with *Science News* about how gene editing should be regulated.
CALTECH

By Tina Hesman Saey
APRIL 2, 2015 AT 7:00 AM

BIOETHICS FORUM ESSAY

Why Avoid the "M-Word" in Human Genome Editing?

Statements made after the first summit and the second summit have avoided using the term moratorium. Consciously. Because that word has been associated with very firm rules about what you can do and what you can't do . . . That's what's wrong with a moratorium. It's that the idea gets fixed in people's minds that we're making firm statements about what we don't want to do and for how long we don't want to do it . . . To make rules is probably not a good idea.



"*Altered Inheritance* is a call to action. Fair, balanced, and enjoyably readable, this book provides us with insights into the greatest technical and social challenges of our day and their ethical impact on future generations."

—GEORGE CHURCH, co-author of *Regenesis*

"*Altered Inheritance* argues that the use of gene-editing technology should require significant input from the broad public. This book is extremely timely, addresses a high-interest and important topic, and comes from an influential voice in the gene-editing debate."

—JOSEPHINE JOHNSTON, The Hastings Center

"Informative and thoughtful, *Altered Inheritance* casts the ethically perplexing questions raised by genome editing in a clear, new light. Françoise Baylis asks us to slow down and rediscover our collective moral agency instead of feeling overtaken by the momentum of science and technology."

—PETER MILLS, Nuffield Council on Bioethics

"Incisive and insightful, *Altered Inheritance* wrenches open the laboratory doors behind which science and technology struggle to set a new course for society, for humanity, and for those who are most vulnerable for extinction."

—DONNA R. WALTON, Founder and President, The Divas With Disabilities Project

"Françoise Baylis is a fearless philosopher whose courage is matched by her talent. In this wise, lucid book, she asks exactly the right questions. What kind of world do we want to live in, and how likely is gene editing to take us there?"

—CARL ELLIOTT, author of *White Coat, Black Hat: Adventures on the Dark Side of Medicine*

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