The Need for an International Moratorium on Clinical Uses of Human Germline Gene Editing

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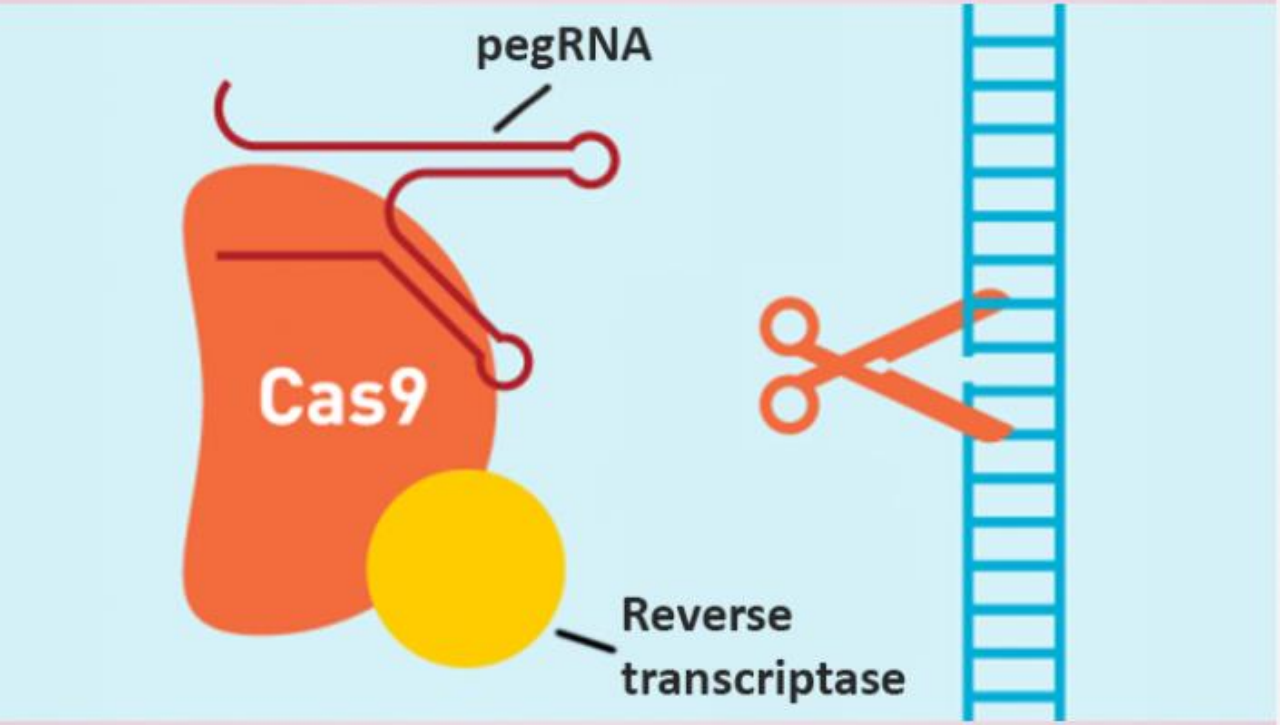
Director, National Institutes of Health

ASGCT Policy Summit
November 6, 2019

Advances in Gene Editing

- Powerful tools rapidly becoming ubiquitous
- Ease, precision of technology makes experiments feasible that were too difficult to conduct using older techniques
- Improvements continue to extend applications – see “prime editing”

https://directorsblog.nih.gov/



Gene-Editing Advance Puts More Gene-Based Cures Within Reach

Posted on November 5th, 2019 by Dr. Francis Collins

There's been tremendous excitement recently about the potential of CRISPR and related gene-editing technologies for treating or even curing sickle cell disease (SCD), muscular dystrophy, HIV, and a wide range of other devastating conditions. Now comes word of another remarkable advance—called "prime editing"—that may bring us even closer to reaching...

News

Advances in Gene Editing

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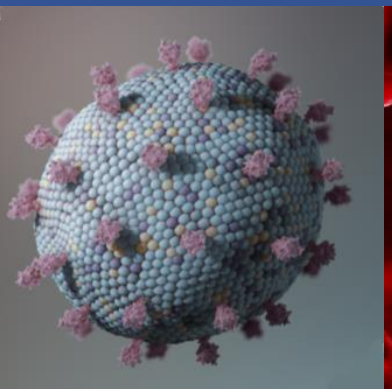
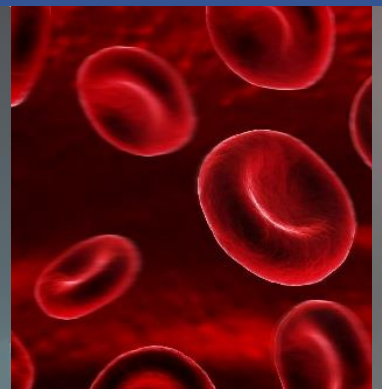
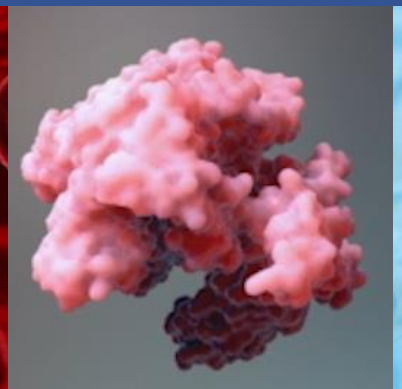
- Improvements continue to extend applications – see “prime editing”
- Multiple Applications
  - Basic Science
  - Gene Drives – the end of malaria?
  - Somatic Cell Gene Therapy – non-heritable

Somatic Cell Genome Editing Program

- *In vivo* human applications require safe, effective delivery of editing tools to *specific cell types* for *specific diseases*
- New NIH program speeds their development, supporting:
  - New delivery systems
  - Expanding repertoire of genome editors
  - Animal reporters & testing centers
  - Assessing unintended biological effects
  - Dissemination & coordinating center

CGE
Somatic Cell Genome Editing

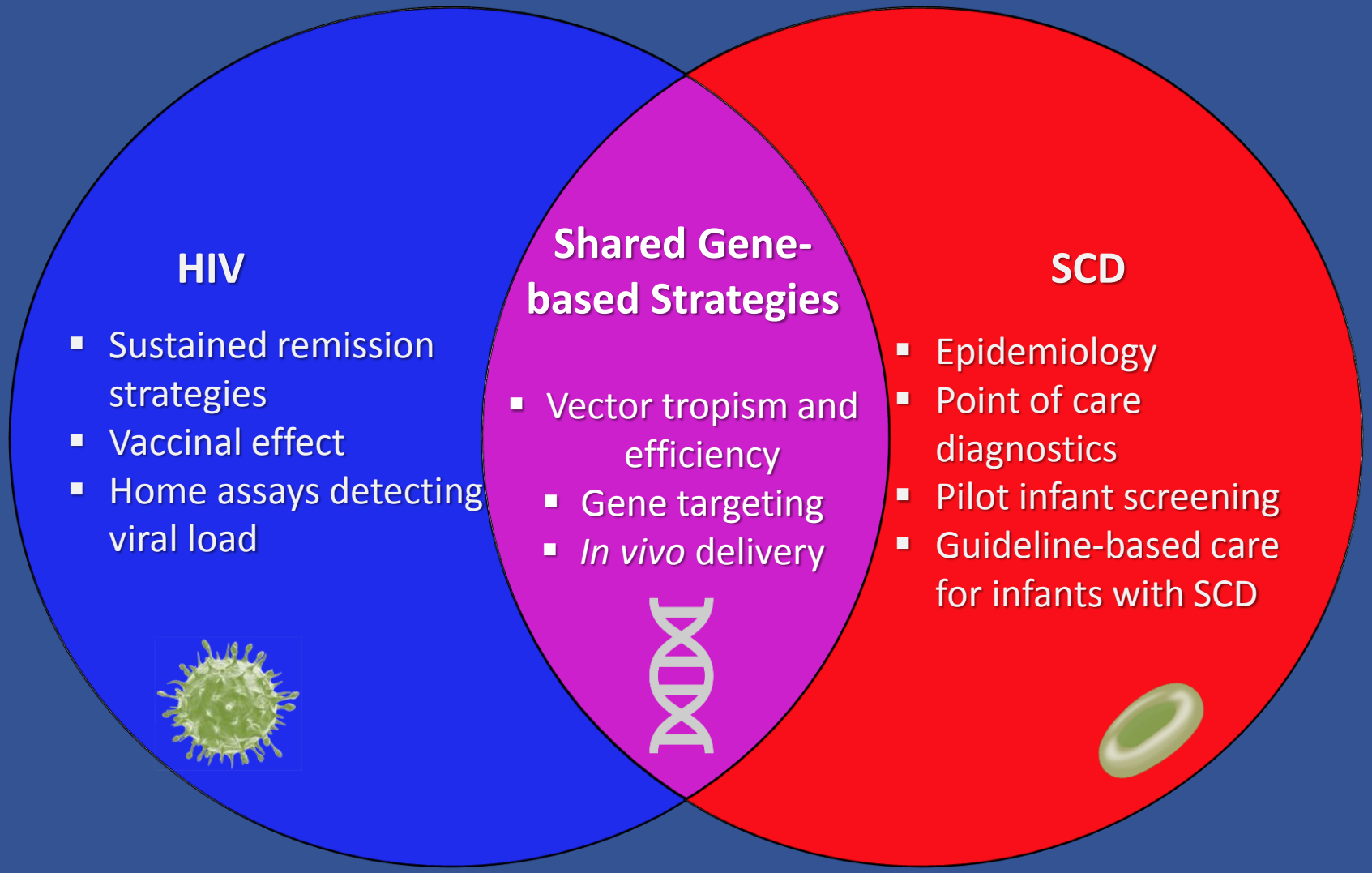
NIH/Bill and Melinda Gates Foundation (BMGF) Cures Collaboration

Will invest at least $200M* over next four years to develop affordable, gene-based cures for HIV, sickle cell disease (SCD)

- Gene-based treatments
  - Dramatic advances in last decade offer extraordinary opportunities
  - However, most treatments are complex, costly … and not yet available for most diseases
  - Potential for *in vivo* gene editing approach holds enormous promise
- NIH/BMGF collaboration will
  - Identify potential candidate cures for HIV, SCD for pre-clinical and clinical evaluation
  - Work with African partners to advance promising candidates to late-phase clinical trials

*All $ amounts in U.S. dollars

Research Focus of the NIH-BMGF Collaboration



Advances in Gene Editing

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  - Gene Drives – the end of malaria?
  - Somatic Cell Gene Therapy – non-heritable
- **Human Germline Modification – heritable**
  - **Profound ethical implications**

On the Ethics of Human Germline Editing in the Era of CRISPR

- 2015:

Intensive basic and preclinical research is clearly needed and should proceed, subject to appropriate legal and ethical rules and oversight.

It would be irresponsible to proceed with any clinical use of germline editing.

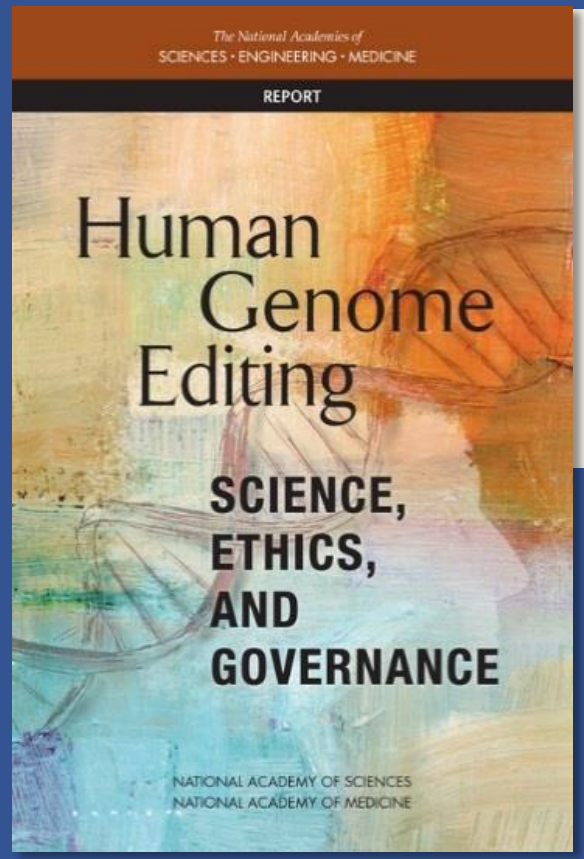
The New York Times

Scientists Seek Moratorium on Edits to Human Genome That Could Be Inherited

By NICHOLAS WADE DEC. 3, 2015

On the Ethics of Human Germline Editing in the Era of CRISPR

- 2015: International Summit on Human Gene Editing
- 2017:

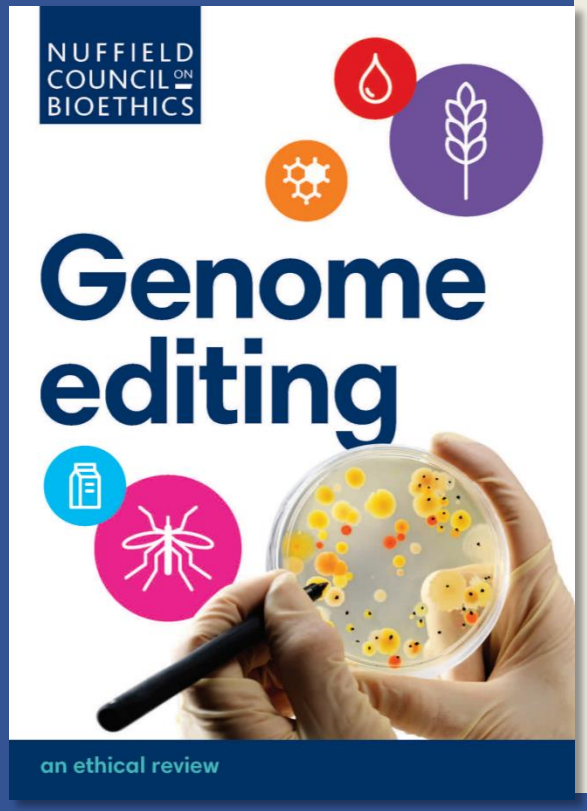


Germline (Heritable) Genome Editing

- Permit clinical research trials only for compelling purposes of treating or preventing serious disease or disabilities, and only if there is a stringent oversight system able to limit uses to specified criteria
- Ongoing reassessment and public participation should precede any heritable germline editing

On the Ethics of Human Germline Editing in the Era of CRISPR

- 2015: International Summit on Human Gene Editing
- 2017: “Human Genome Editing,” U.S. National Academies of Sciences and Medicine
- 2018:



We conclude that the use of heritable genome editing interventions to influence the characteristics of future generations could be ethically acceptable in some circumstances, provided:

- it is intended to secure, and is consistent with, the welfare of a person who may be born as a consequence of interventions using genome edited cells; and
- it upholds principles of social justice and solidarity, i.e. it should not be expected to increase disadvantage, discrimination, or division in society.

On the Ethics of Human Germline Editing in the Era of CRISPR

- 2015: International Summit on Human Gene Editing
- 2017: “Human Genome Editing,” U.S. National Academies of Sciences and Medicine
- 2018: “Genome Editing,” Nuffield Council of Ethics (UK)
- November 2018: Second International Summit on Human Genome Editing

The National Academies of SCIENCES ENGINEERING MEDICINE

NEWS

Second International Summit on Human Genome Editing

On Human Genome Editing II

Statement by the Organizing Committee of the
Second International Summit on Human Genome Editing

"While we … applaud the rapid advance of somatic gene editing into clinical trials, we continue to believe that proceeding with any clinical use of germline editing remains irresponsible at this time."

"This work represents a deeply disturbing willingness by Dr. He and his team to flout international ethical norms… Lest there be any doubt, and as we have stated previously, NIH does not support the use of gene-editing technologies in human embryos."

U.S. Department of Health & Human Services

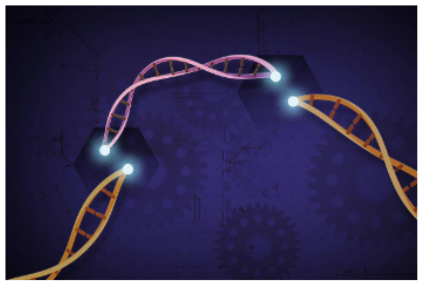
NIH National Institutes of Health
Turning Discovery Into Health

THE NIH DIRECTOR

November 28, 2018

Statement on Claim of First Gene-Edited Babies by Chinese Researcher

NIH is deeply concerned about the work just presented at the Second International Summit on Human Genome Editing in Hong Kong by Dr. He Jiankui, who described his effort using CRISPR-Cas9 on human embryos to disable the CCR5 gene. He claims that the two embryos were subsequently implanted, and infant twins have been born. This work represents a deeply disturbing willingness by Dr. He and his team to flout international ethical norms. The project was largely carried out in secret, the medical necessity for inactivation of CCR5 in these infants is utterly unconvincing, the informed consent process appears highly questionable, and the



CRISPR-Cas9 is a customizable tool that lets scientists cut and insert small pieces of DNA at precise areas along a DNA strand. This lets scientists study our genes in a specific, targeted way. *Image Credit: Ernesto del Aguila III, NHGRI.*

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Parental Genomes Enable Calling *De Novo* Indels, Haplotype to Increase Sensitivity, and Personalized Off Target Hotspot Risk Pool

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November 28, 2018

On the Ethics of Human Germline Editing in the Era of CRISPR

- December 2018: WHO Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing
- 2019: International Commission on Clinical Use of Human Germline Genome Editing–U.S. National Academies of Sciences and Medicine, Royal Society of the United Kingdom

Human Genome editing

WHO establishing expert panel to develop global standards for governance and oversight of human genome editing

14 December 2018 -- WHO is establishing a global multi-disciplinary expert panel to examine the scientific, ethical, social and legal challenges associated with human genome editing (both somatic and germ cell). The panel will review the current literature on the state of the research and its applications, and societal attitudes towards the different uses of this technology. WHO will then receive advice from the panel on appropriate oversight and governance mechanisms, both at the national and global level. Core to this work will be understanding how to promote

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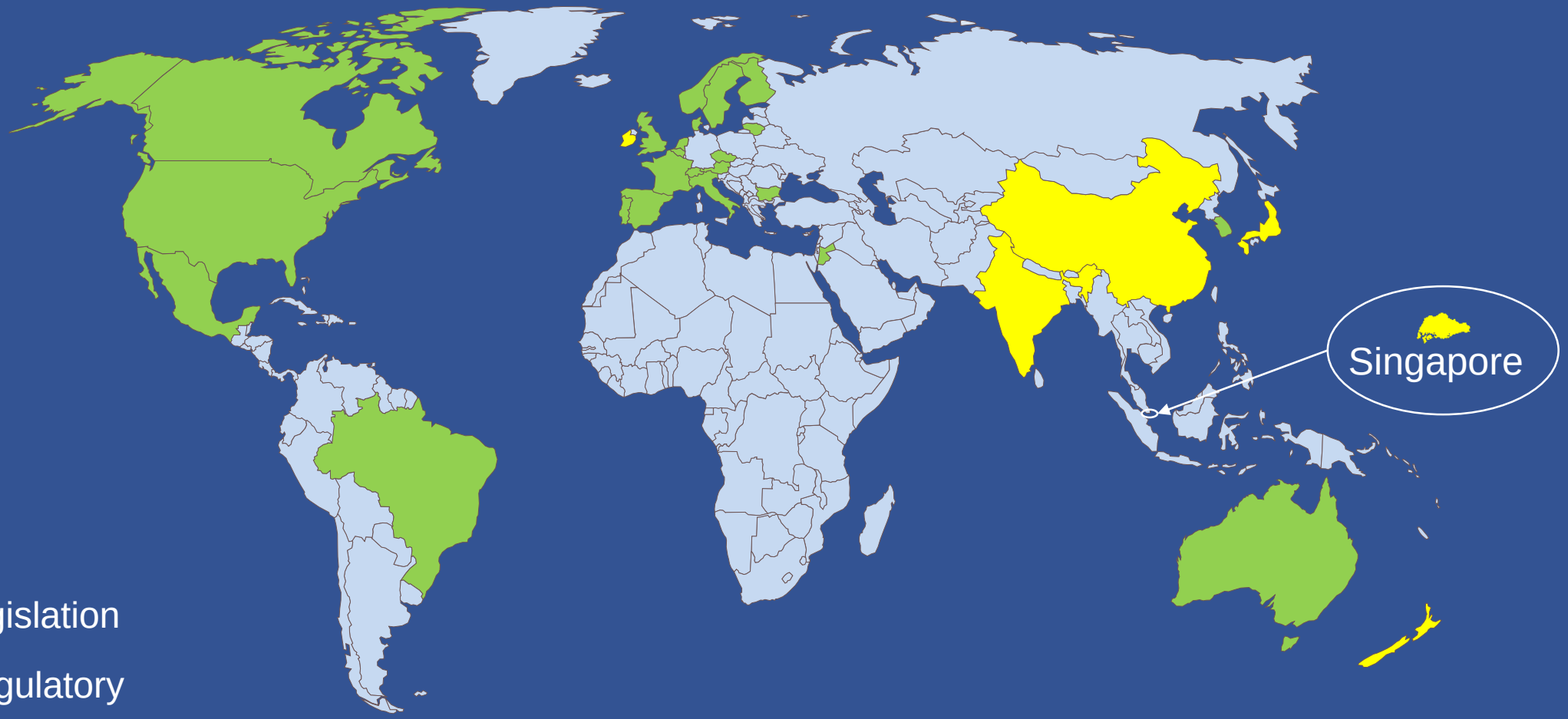
NATIONAL ACADEMY OF MEDICINE AND NATIONAL ACADEMY OF SCIENCES THE ROYAL SOCIETY

May 22, 2019

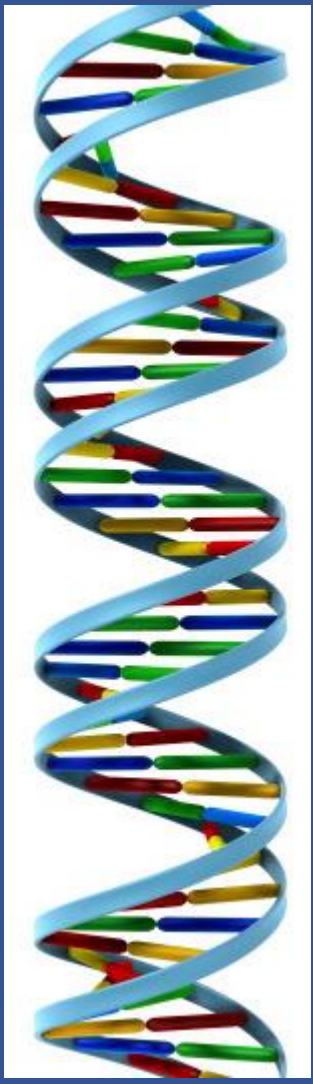
New International Commission Launched on Clinical Use of Heritable Human Genome Editing

Legal and Regulatory Prohibitions on Human Germline Gene Editing: The International Landscape



Legal and Regulatory Prohibitions on Human Germline Gene Editing: The International Landscape

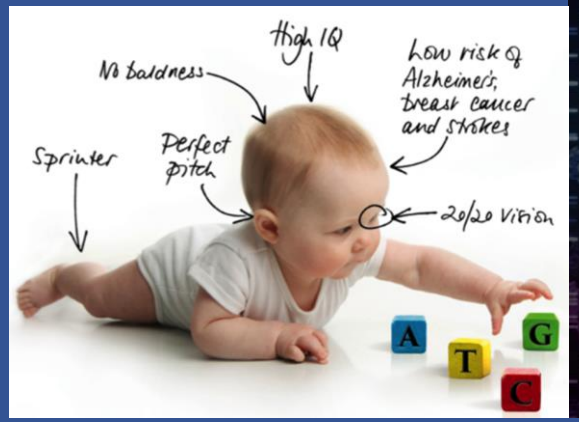
- ~30 countries have legislation or regulations that directly or indirectly prohibit clinical uses of germline editing*
- Prohibitions embedded in several important international instruments:
  - UNESCO Universal Declaration on the Human Genome and Human Rights (1997)
  - Council of Europe's Convention on Human Rights and Biomedicine (1997)
  - European Union Directive on clinical trials (2001)
- Scope of any future clinical applications involving human germline editing usually would require legislation allowing certain procedures



*From HIROs (Heads of International Research Organizations) survey and broader research

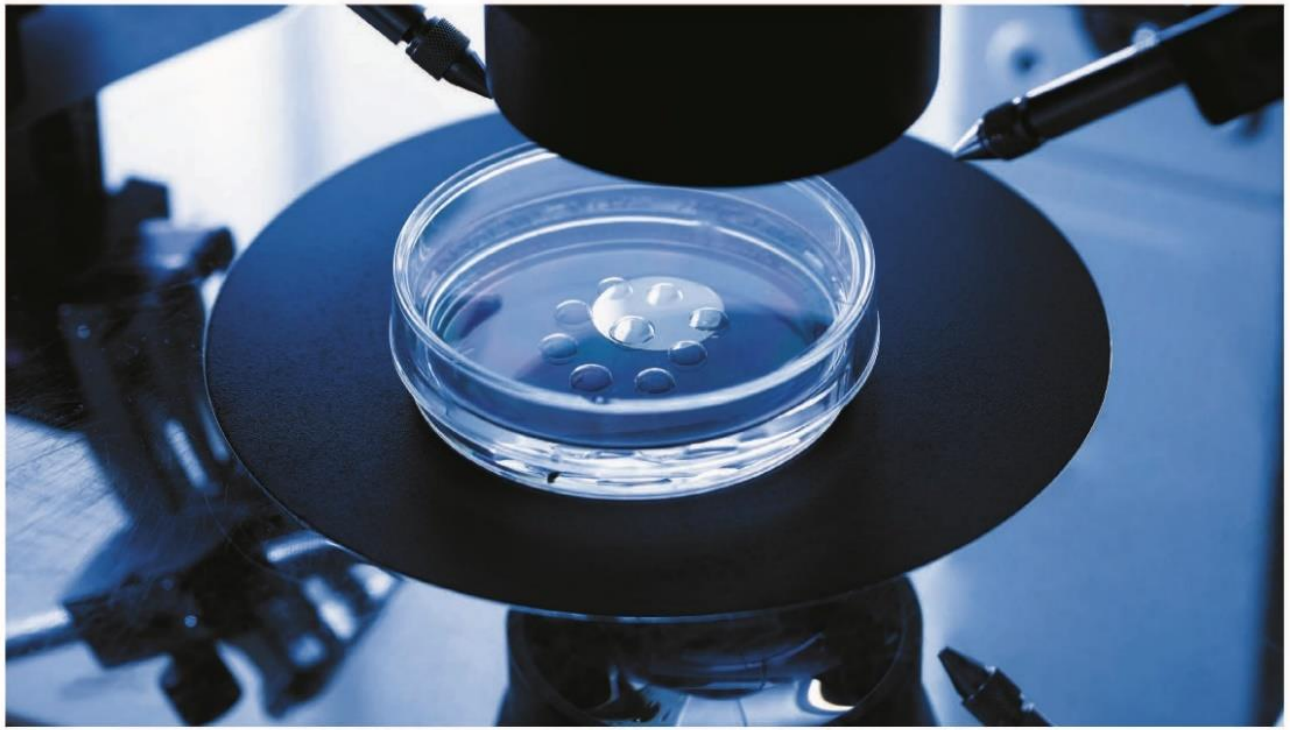
Current Justification for a Moratorium?

- Safety: risk of unintended mutations (“off-target edits”)
- Medical: are there needs that *only* germline editing could meet?
  - Currently editing would require use of *in vitro* fertilization
  - Genetic diagnosis of embryos would then be needed
  - Why not just implant the unaffected embryos?
  - Mitochondrial diseases are in a different category
- Societal, ethical, moral issues
  - Consent
  - Justice/equity
  - Philosophical
  - Theological



14 MARCH 2019 | VOL 567 | NATURE | 165

COMMENT



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

Adopt a moratorium on heritable genome editing

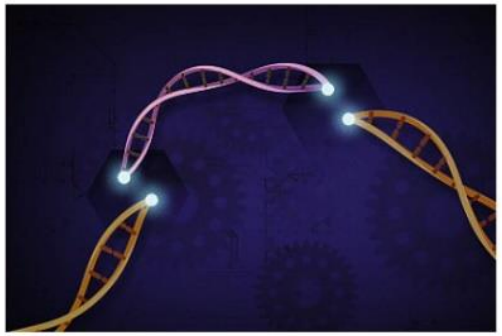
Eric Lander, Françoise Baylis, Feng Zhang, Emmanuelle Charpentier, Paul Berg and specialists from seven countries call for an international governance framework.

THE NIH DIRECTOR

March 13, 2019

NIH supports international moratorium on clinical application of germline editing

Today, leading scientists and ethicists from seven countries have called for an international moratorium on the use of genetic editing to modify the human germline for clinical purposes. The call comes in the wake of irresponsible and unethical research in China, in which twins were born after alterations to their DNA before implantation. This unexpected and unwelcome revelation roiled the scientific community and the general public, and crystalized the need for guiding international principles. Research on the potential to alter the very biological essence of humanity raises profound safety, ethical, and philosophical issues. I expressed NIH's position on the incident in November 2018.



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AMERICAN SOCIETY of GENE & CELL THERAPY

ADVOCACY | POLICY UPDATES

Scientific Leaders Call For Global Moratorium on Germline Gene Editing

April 24, 2019

Dear Secretary Azar,

We write as scientific, industry, and bioethics leaders who are committed to translating the promise of gene editing into medicines to help patients in need, to express our views strongly condemning the recent reports of the birth of CRISPR-edited infants in China and to urge you to take action.

World Health Organization

Statement on governance and oversight of human genome editing

26 July 2019 | Statement | Geneva

"it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing."

Alliance for Regenerative Medicine

The Alliance for Regenerative Medicine Releases Statement of Principles on Genome Editing

WaSHINGTON, D.C. – August 27, 2019

We assert that germline gene editing is currently inappropriate in human clinical settings

nature
International journal of science

NEWS · 18 OCTOBER 2019 · CORRECTION 18 OCTOBER 2019

Russian 'CRISPR-baby' scientist has started editing genes in human eggs with goal of altering deaf gene

Denis Rebrikov also told Nature that he does not plan to implant gene-edited embryos until he gets regulatory approval.

David Cyranoski


We must never allow our
technology to eclipse
our humanity.




NIH... *Turning Discovery Into Health*

www.nih.gov/hope

directorsblog.nih.gov

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