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The CRISPR Twins: What's all the Fuss About?

Prof. Kevin Behrens

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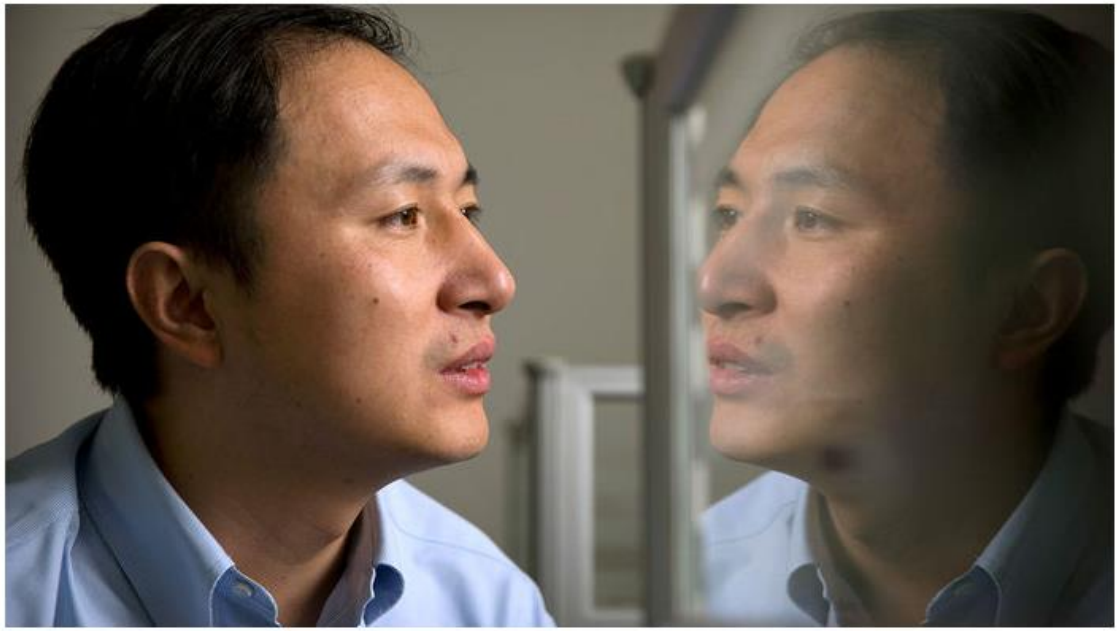
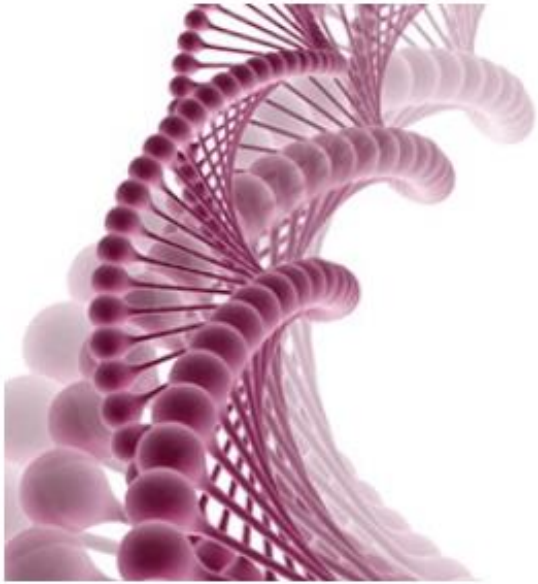


He Jankui told The Associated Press that he carried out his experiment to protect the twin sisters from HIV infection later in life. MARK SCHIEFELBEIN/AP PHOTO

CRISPR bombshell: Chinese researcher claims to have created gene-edited twins

By Dennis Normile | Nov. 26, 2018 , 1:10 PM



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
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What is Human Genome Editing?

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What is Human Genome Editing?

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- A form of genetic engineering
  - Improvement over old genetic engineering techniques that randomly inserted genetic material into the genome of a host
    - This genome editing is able to target specific location in the host's DNA to make an insertion, deletion, modification or replacement
      - Analogy: snipping off a piece of a film strip and splicing a new piece in its place
        - Tools like CRISPR/Cas9 enable the targeted editing of the genome

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Some Applications of Human Genome Editing

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Some applications

1. Basic research
2. Editing of DNA of somatic cells for therapeutic purposes
3. Editing of DNA of germline (reproductive) cells

Some Applications of Human Genome Editing

1. Basic research

- Can help us to understand the biology underlying diseases – which can lead to better management and treatment
  - Research done on human cells in a laboratory, without inserting edited genes into human targets can enhance our knowledge of how genome editing could be used for therapeutic purposes in humans

Some Applications of Human Genome Editing

2. Editing of DNA of somatic cells for therapeutic purposes

- Most of the cells in the human body are somatic (non-reproductive) cells
  - Typically, these cells can be taken from adults, and molecules can be modified in a laboratory, and re-inserted into a person
    - It is possible to edit targeted genes associated with specific diseases or conditions to correct the genome of particular patients to slow or halt the progress of a disease
      - Some possible targets are sickle cell anaemia, thalassemia, immune deficiencies

Some Applications of Human Genome Editing

3. Editing of DNA of germline (reproductive) cells

- Involves changing DNA sequences in sperm cells, egg cells or the fertilised egg (embryos)
  - These changes can be inherited by following generations
    - Germline gene editing could allow for disease-causing genes inherited from parents to be modified to prevent the disease being inherited – e.g. sickle cell anemia, cystic fibrosis
      - Could also be used to protect against acquiring diseases: e.g. CCR5 gene of T cells to prevent HIV infection; genes underlying developing heart disease
        - Could be used for enhancement purposes – avoiding cognitive impairment, increasing longevity

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Some Ethical Issues

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Some ethical issues related to Human Genome Editing

1. Safety issues (with editing somatic & germline cells)

- Gene editing is not completely precise – there can be unintended off-target effects. Very significant risk, because we don't know what they might be before they happen
  - Risk of mosaicism (incomplete editing)
    - Genes have multiple functions. We don't know what all of the functions are. Fixing one problem with an edit could create another (even worse) problem

2. Social justice issues

- Could become elitist medicine only available to the rich
  - Rich countries could protect their citizens before others
    - Protection of Intellectual Property through patents could drive prices up
      - Where is the line between disability and diversity?

3. Concerns about Enhancement

- There is a lot of fear around possible uses for enhancement, especially where it would give some a competitive advantage
  - Life extension is ethically problematic – population is already aging and there are fears about how this can be sustainable
    - Is this the start of a slippery slope to a new form of eugenics?

4. Concerns about research with embryos

- Fundamental rejection of embryonic research on the basis of sanctity of life arguments
  - Some also reject research based on the fact that there are always embryos that will be discarded
    - Some countries only allow use of spare IVF embryos

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Ethical issues Related to Germline Editing

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Ethical issues related to germline cell editing

- Main issues relate to the fact that edits can be passed down to future generations
    - Increases risks significantly
        - Safety risks particularly worrying: off-target effects could be inherited
            - Informed consent issues:
                - First modified person cannot give consent, but at least parents/proxies can
                - Later generations cannot consent, nor can their proxies
                    - Will future generations have right to sue/claim compensation?

Ethical issues related to Germline Editing

Ethical issues related to Dr. He Jiankui's experiment

- He did not obtain legitimate ethics clearance
  - His actions were against the law and regulations in China
    - His actions go against global consensus that there should be a (temporary) moratorium on this kind of research
      - Informed consent from future generations is not possible
        - Quality of informed consent of parents is in question
- His choice of targeting an enabler for HIV infection was not in line with general consensus that the first germline editing experiments should focus on genetic disease-causing genes, where a single gene is responsible

Ethical issues related to Germline Editing

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Possible unintended consequences of Dr. He Jiankui's experiment

- May not have worked: "Soon after the announcement of his "success" in November 2018, some experts noted that the likely benefits were smaller than advertised, since He had given neither of the twins that specific gene edit. According to He's own analysis, his CRISPR treatment yielded mutations in CCR5 that had never before been seen in humans — meaning the effectiveness of the edit against HIV infection and its safety were unknown."
  https://www.statnews.com/2019/04/15/jiankui-embryo-editing-ccr5/
  - Recent research in *Nature Magazine* suggests a 21% increase in all-cause mortality rate of individuals who naturally have the CCR5 - delta 32 allele – may expose twins and their descendants to risk
    - Copy-cat research = opening of Pandora's Box

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Current Regulation

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Current regulation

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Global ‘consensus’ position

- Basic research should be allowed, subject to usual ethics committee approval
- Somatic cell editing and implantation should be cautiously allowed, subject to rigorous informed consent and ethics committee approval
- Germline cell editing of embryos for implantation into a womb *would be irresponsible at this time*, at least until risks are better understood and prevented

- Legally: many countries forbid or restrict embryonic stem cell research, anyway

Current regulation

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South African Situation

- Basic research and somatic cell research/therapies are permitted, subject to usual ethics conditions
  - Embryonic stem cells and zygotes: research may be permitted on cells or zygotes less than 14 days old, with written permission of Minister of Health and proper informed consent of donor
    - Basic (laboratory) germline editing might be permitted with ministerial permission
      - Germline editing of viable embryos for reproductive intentions is prohibited

References

- National Academies of Sciences, Engineering, and Medicine 2015. *International Summit on Human Gene Editing: A Global Discussion*. Washington, DC: The National Academies Press. https://doi.org/10.17226/21913.
- National Human Genome Research Institute. 2017. Genome Editing. https://www.genome.gov/27569224/how-is-genome-editing-used/

- National Academies of Sciences, Engineering, and Medicine 2015. *International Summit on Human Gene Editing: A Global Discussion*. Washington, DC: The National Academies Press. https://doi.org/10.17226/21913.
- National Human Genome Research Institute. 2017. Genome Editing. https://www.genome.gov/27569224/how-is-genome-editing-used/

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