

General Introduction to Gene Editing

Pascal Borry (KUL)

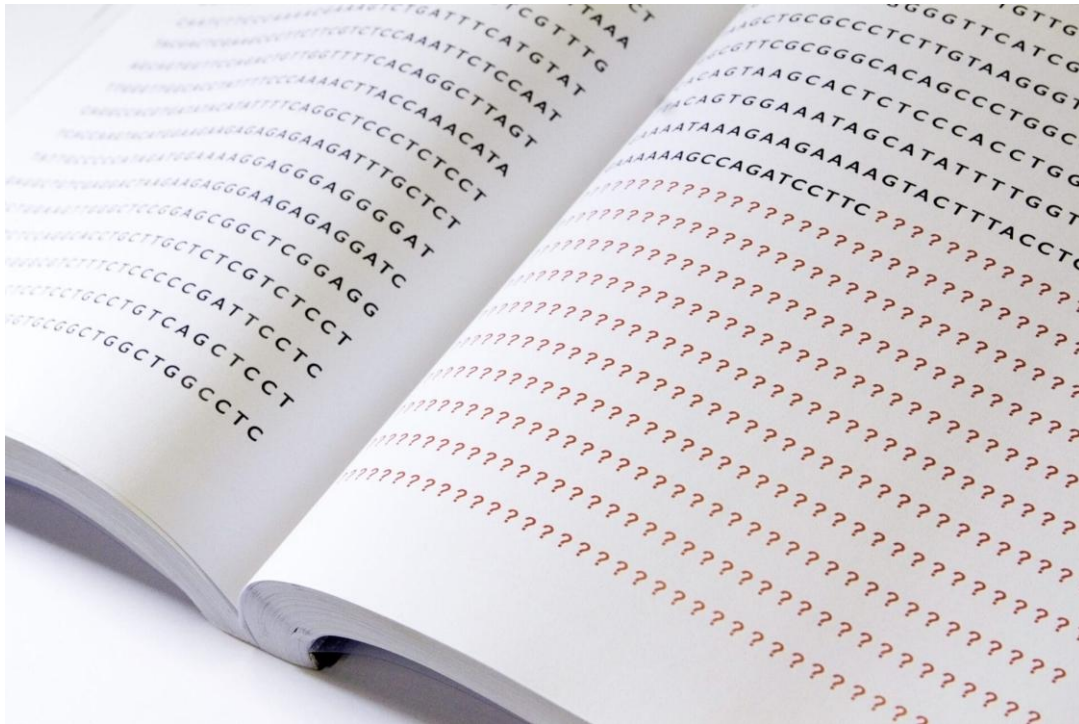


Funded by
the European Union



READING THE GENOME

versus EDITING THE GENOME

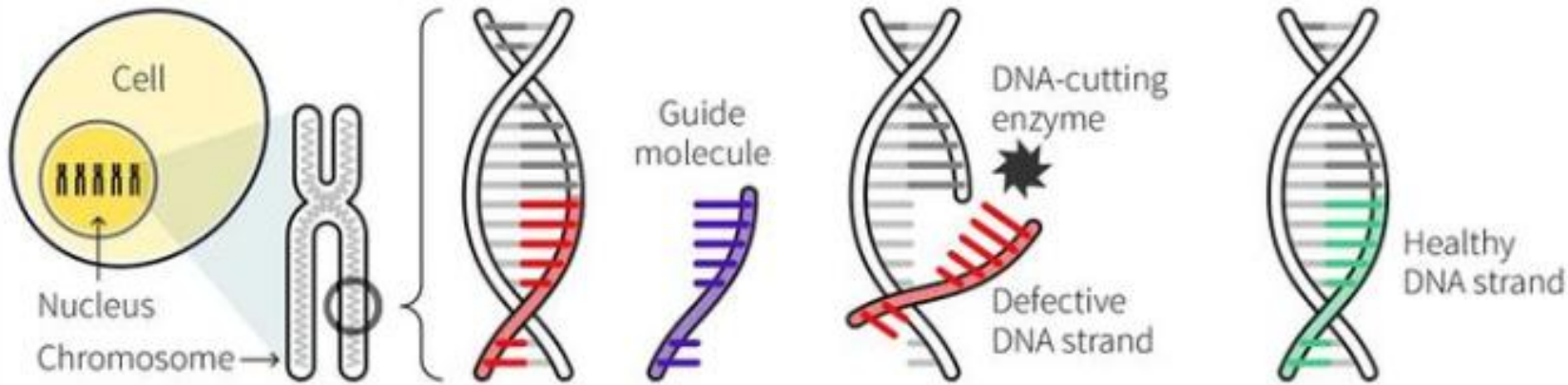


Funded by
the European Union




DNA editing

A DNA editing technique, called CRISPR/Cas9, works like a biological version of a word-processing programme's "find and replace" function.

HOW THE TECHNIQUE WORKS



A cell is transfected with an enzyme complex containing:

-  Guide molecule
-  Healthy DNA copy
-  DNA-cutting enzyme

A specially designed synthetic guide molecule finds the target DNA strand.

An enzyme cuts off the target DNA strand.

The defective DNA strand is replaced with a healthy copy.

Sources: Reuters; Nature; Massachusetts Institute of Technology



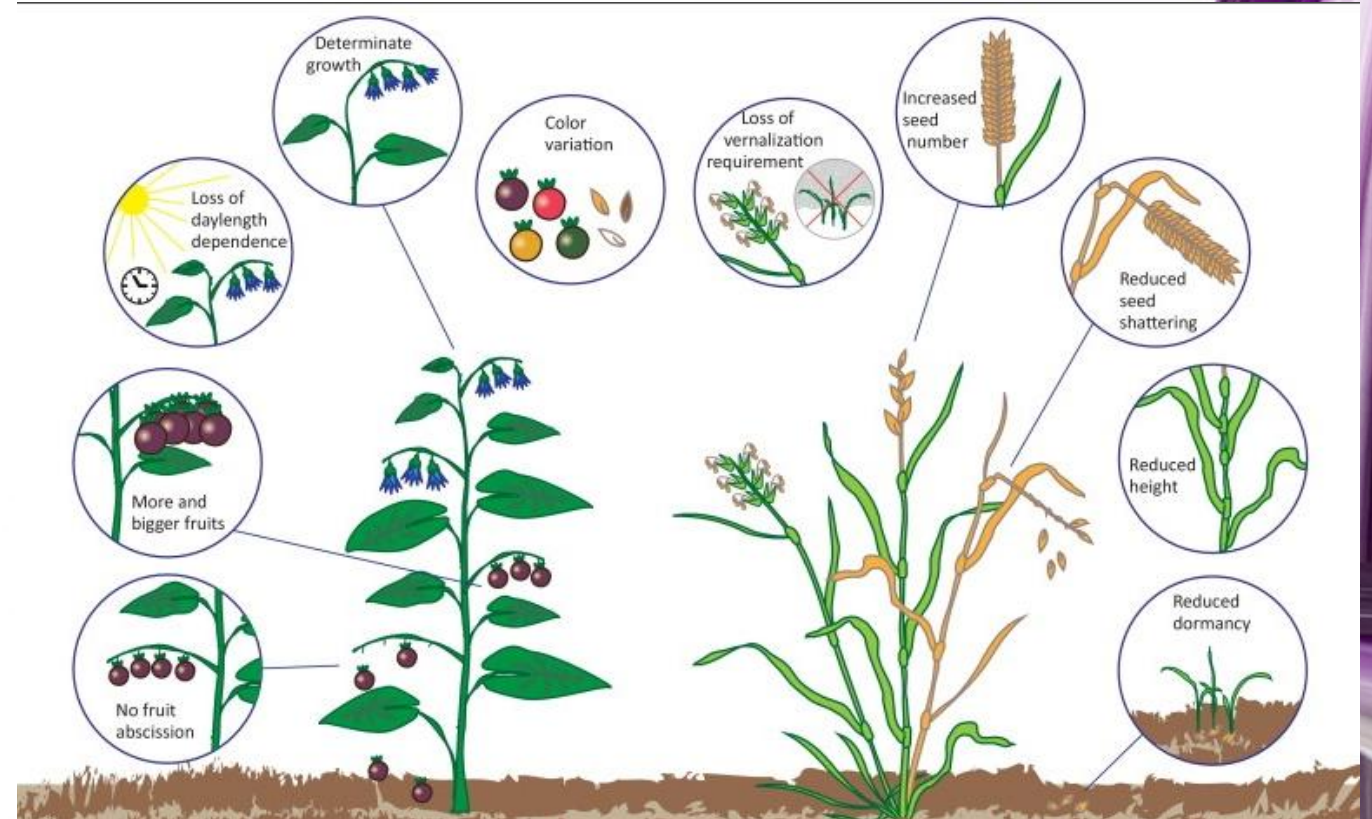
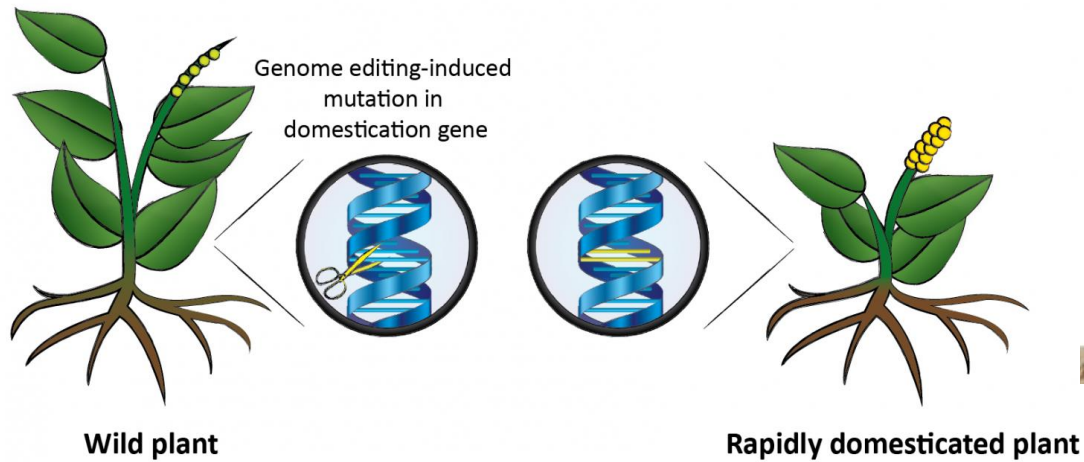
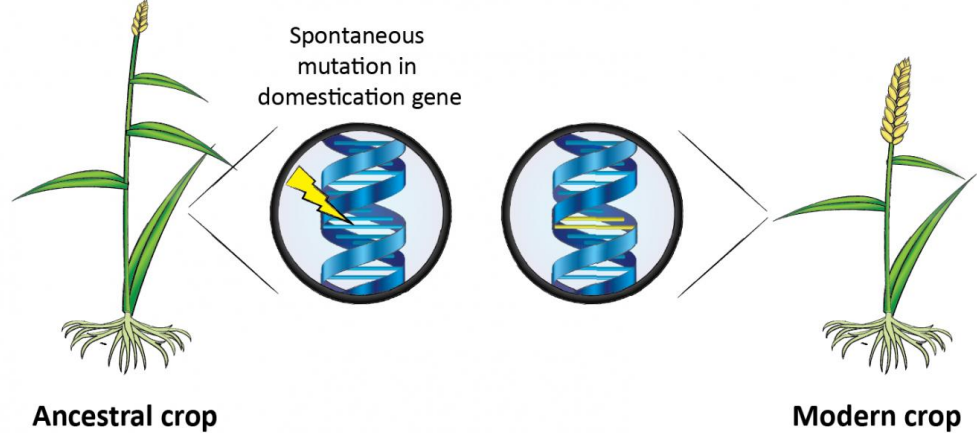
Power of CrispR-Cas editing

- Can be applied to any cell type (plant, bacteria, human)
- Precisely target any region of the genome
- Efficiency is very high
- Can be applied in a living cell/organism
- No trace is left behind
- Tools are simple to prepare and accessible to all scientists



Genome editing to breed better plants:
e.g. the development of crops able to
withstand global warming ?

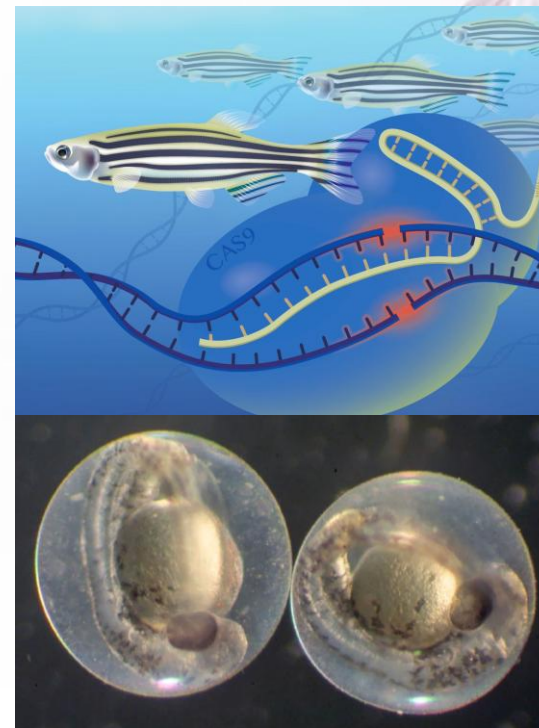
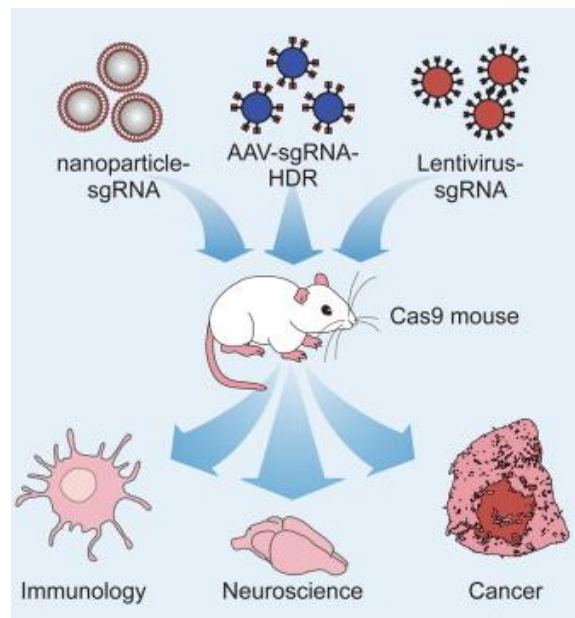
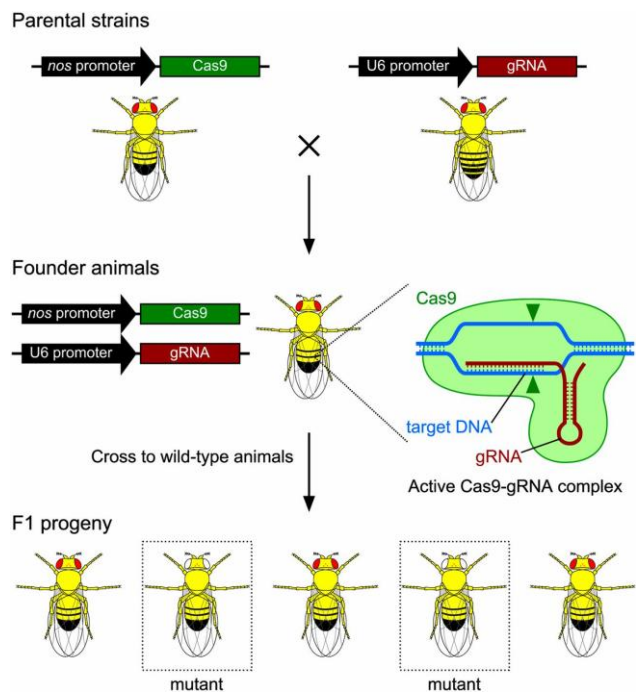
IEWS



Funded by
the European Union

(Slide courtesy Hilde Van Esch)

CrispR/Cas enables scientists to model normal function and disease in all different species



Funded by the European Union

(Slide courtesy Hilde Van Esch)



An Ethical Overview of the CRISPR-Based Elimination of *Anopheles gambiae* to Combat Malaria

India Jane Wise  • Pascal Borry



Funded by
the European Union

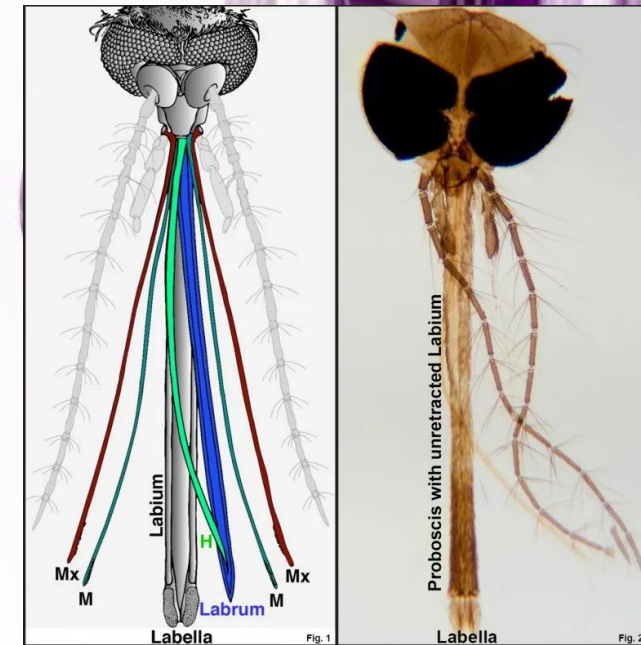


CRISPR-Based Elimination of *Anopheles gambiae* to Combat Malaria

- Malaria is caused by the **parasite** Plasmodium which replicates in, and is transmitted through, female *Anopheles* (Ancient Greek for “useless”) **mosquitoes**—the vectors.
- There are around 515 *Anopheles* species, of which around thirty to forty are deemed important malaria vectors.
- A lot of effort has been put into the development of vaccines that target the parasite, but a vaccine with high efficacy and which provides protection for an extended period of time is not likely to become available soon.
- The decrease in malaria accomplished so far, has therefore been due to major **public health efforts** focused on prevention through the use of insecticides, reduction in breeding sites for mosquitoes, and socioeconomic development



- A gene drive is a **genetic modification that allows certain genes to spread throughout the population by increasing their inheritance rate.**
- When a *doublesex* gene is disabled in female mosquitoes, they develop both male and female organs. Their proboscis turns male, making them unable to pierce human skin and they become **infertile.**
- When the *doublesex* genes were introduced in a caged population of *Anopheles* species, **the population died out after seven to eleven generations.**



- **Biological diversity or biodiversity:** eradication of a species and thus a reduction in biodiversity? The question then follows where to draw the line between morally acceptable and non-acceptable extinction of a species.
- Unicellular organisms are usually not included in life protection programmes: eradication of viruses, SARS-CoV-2, guinea worm parasite...
- The public reaction towards a species' eradication depends mainly on the moral status of the organism as well as the possible consequences that could accompany its eradication.
- Slippery slope?
- Eradication of a species is only permissible if it saves a considerable number of human lives or protects the ecosystem, if there is no other way. Eradication should never be the first option but rather the very last.

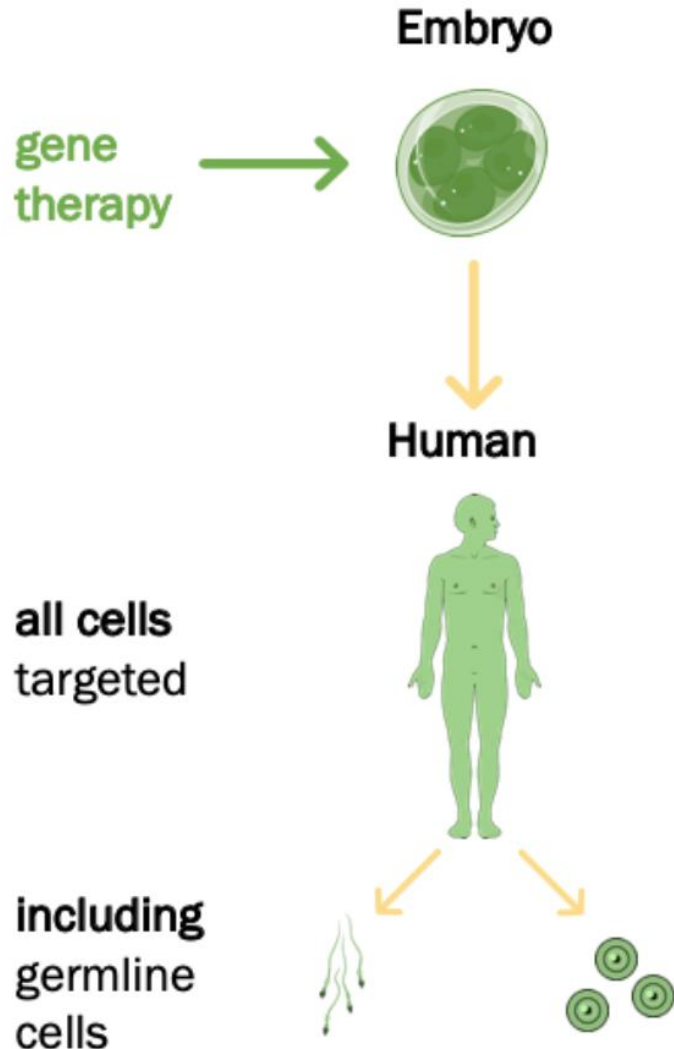
- **Impact on environment:** impact on eco-system (e.g. ecological dependency (pollination, food cycle))?
- **Precautionary principle** emphasizes preventive decision-making in order to protect public health or the environment when there is a plausible risk
- However, a strict interpretation of the principle implies that “regulatory approval should not be granted until all possible or theoretical risk and safety issues are scientifically resolved, regardless of societal needs and potential benefits” (World Health Organization 2014). This has been heavily criticized due to its innovation-hindering effects, since proving complete safety is close to impossible.
- The negative impact of malaria is too substantial to never allow any risks in trying to combat it.



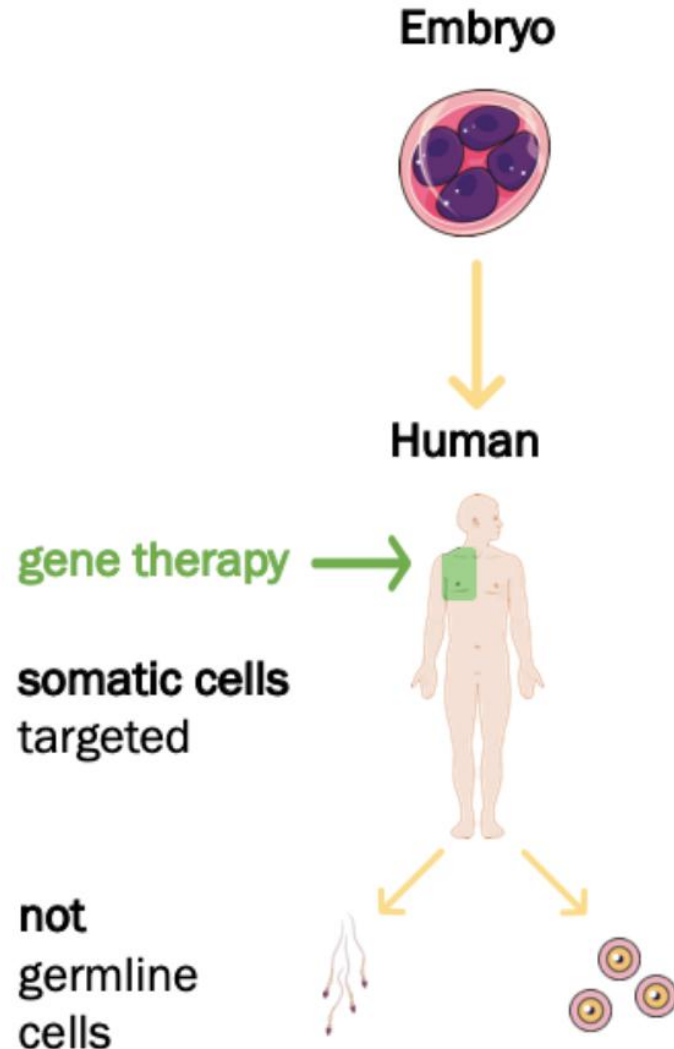
- It should be evaluated whether the funds that are directed towards new biotechnological techniques would not be put to better use by investing in other areas, such as **socioeconomic development**. (Malaria is also connected to poverty)
- **Ethical engagement with the community** in places where the mosquitoes are released remains necessary.



Germline Gene Therapy



Somatic Gene Therapy



- In 2018, He Jiankui announced that he had genetically modified twin babies to make them **resistant to HIV**.
- Widespread criticism from the scientific community and the public due to ethical concerns and the lack of transparency and oversight in the research.



Funded by
the European Union

NEWS | BIOLOGY

After last week's shock, scientists scramble to prevent more gene-edited babies

Claimed creation of CRISPR-altered twins triggers calls for international oversight

4 DEC 2018 • BY JON COHEN



For his talk at last week's summit, He Jiankui was accompanied by security guards because of threats. ANTHONY KWAN/BLOOMBERG/GETTY IMAGES












- “At the summit's end, the organizing panel, concluded that He's experiment was irresponsible, violated international norms, failed to meet ethical standards, did not have a sufficient medical justification, and lacked transparency.” (Science)
- “Even if the modifications are verified, the procedure was irresponsible and failed to conform with international norms,”
- “an inadequate medical indication, a poorly designed study protocol, a failure to meet ethical standards for protecting the welfare of research subjects, and a lack of transparency in the development, review, and conduct of the clinical procedures.”
- National Academies of Sciences, Engineering, and Medicine. 2019. Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop—in Brief. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25343>.



COMMENT | 13 March 2019

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.

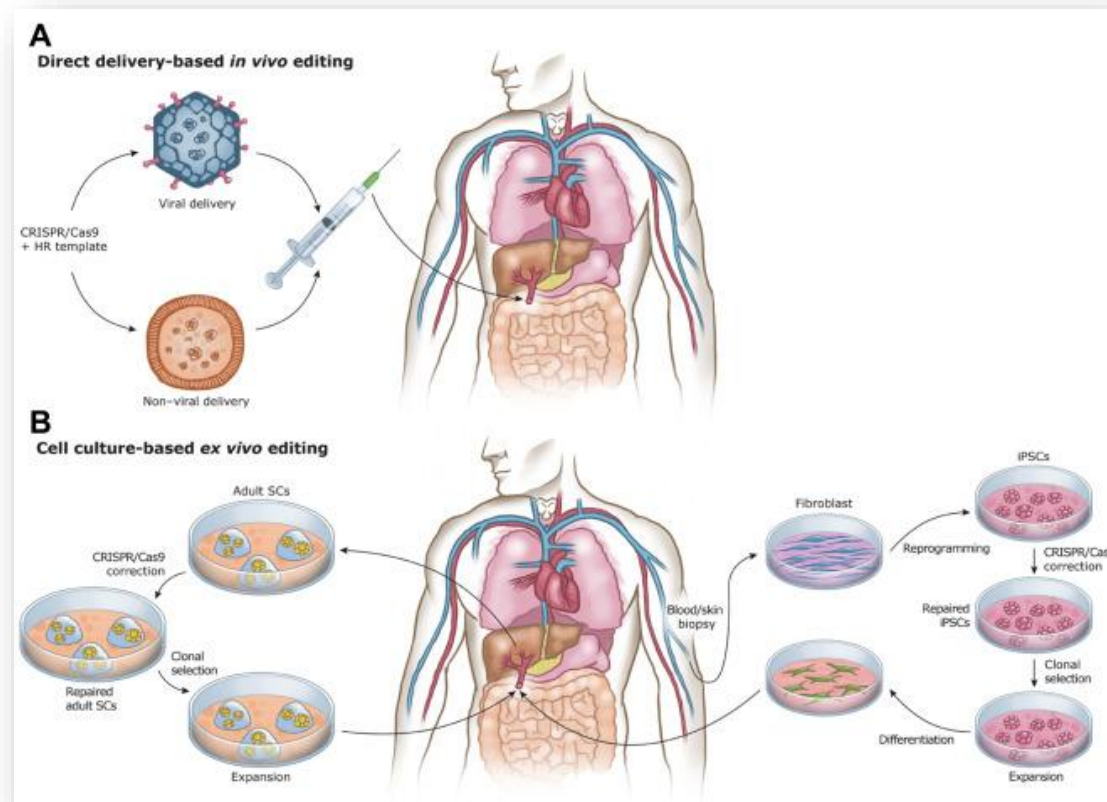
[Eric S. Lander](#)  , [Françoise Baylis](#)  , [Feng Zhang](#)  , [Emmanuelle Charpentier](#)  , [Paul Berg](#)  ,
[Catherine Bourgain](#)  , [Bärbel Friedrich](#)  , [J. Keith Joung](#)  , [Jinsong Li](#)  , [David Liu](#)  , [Luigi Naldini](#) 
, [Jing-Bao Nie](#)  , [Renzong Qiu](#)  , [Bettina Schoene-Seifert](#)  , [Feng Shao](#)  , [Sharon Terry](#)  ,
[Wensheng Wei](#)  & [Ernst-Ludwig Winnacker](#) 



Funded by
the European Union



Somatic gene editing therapy in individuals with rare genetic disorders



In vivo

Genome editing machinery is delivered to the target organ in the body

Ex vivo

Genome editing to modify cells outside the body
 Approach is restricted to diseases affecting the blood or immune system



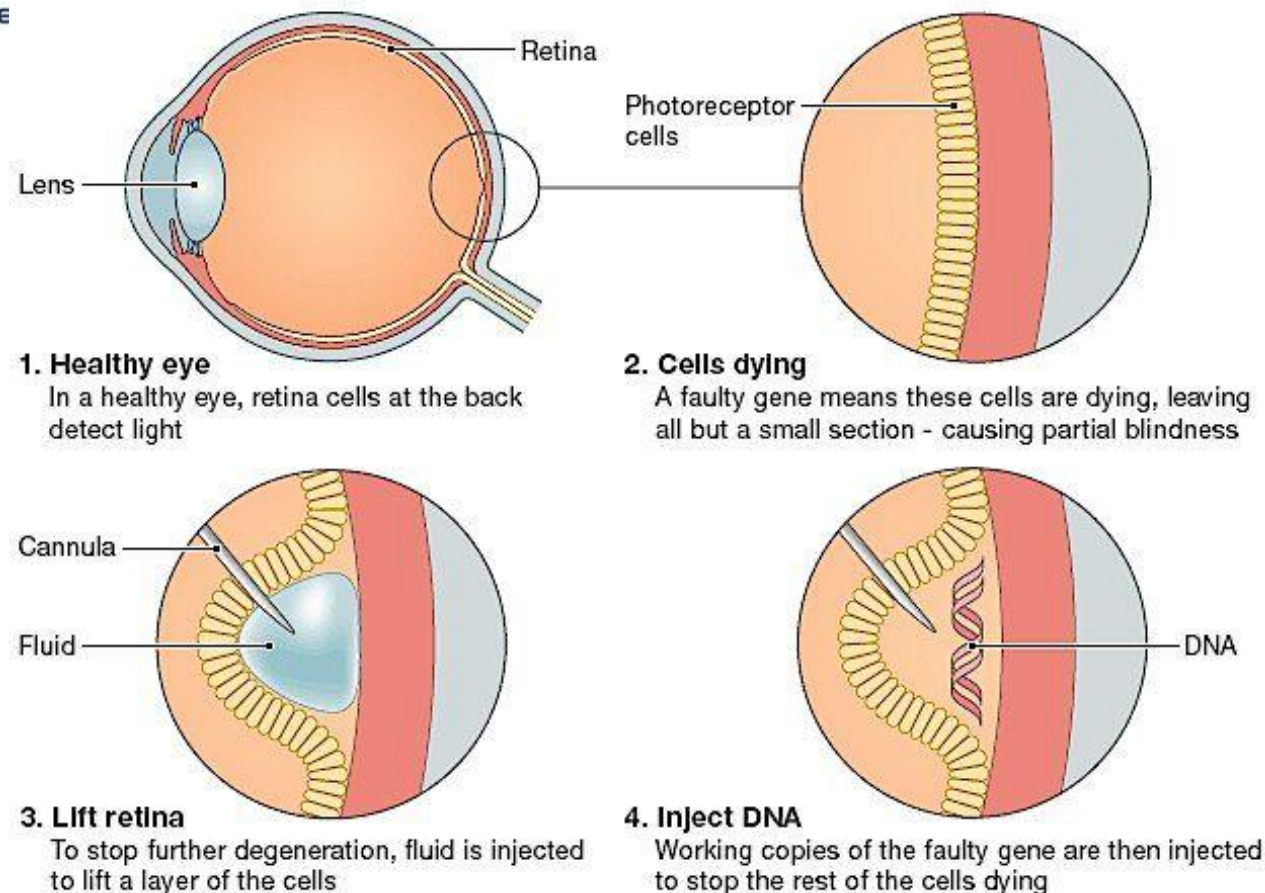
Funded by
the European Union

(Slide courtesy Hilde Van Esch)

- For more than 30 years, gene correction, replacement, and knockout have been in development.
- The major technical challenge is getting the intact gene into the cell using a vector (a kind of shuttle) and placing it in the correct location in the genome.
- The patient's immune system may develop resistance, leading to negative consequences.
- Off target effects



- Leber's congenital amaurosis is a **hereditary eye condition** that typically causes blindness from birth or shortly thereafter.
- In a small number of these patients, **gene therapy** can be used.
- The correct gene is directly introduced into the patient's eye through a modified virus (vector), without any indications of side effects.
- Developing such therapy is extremely expensive due to the need for clinical studies and the small number of patients involved.



- Unfortunately, things do not always go well.
- For example, a clinical study on gene therapy for the congenital immune disorder SCID was successful in nine patients, but in two others, leukemia was detected due to incorrect insertion of the correct genome. As a result, clinical trials were suspended and only resumed later.
- There are ongoing studies in various fields, such as HIV, sickle cell disease, certain cancers, and muscular diseases.



Thank you

Project partners



Funded by
the European Union

Views and opinions expressed are however those of the author(s) only, and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them.

Follow us on social

X: @ChangerEU

LinkedIn: www.linkedin.com/company/changer-eu-project/

Embassy of Good Science: <https://embassy.science/wiki/Initiative:Df0d11b5-2efa-4b58-b94f-6845c6e83b11>

CHANGER Website:



Funded by
the European Union

