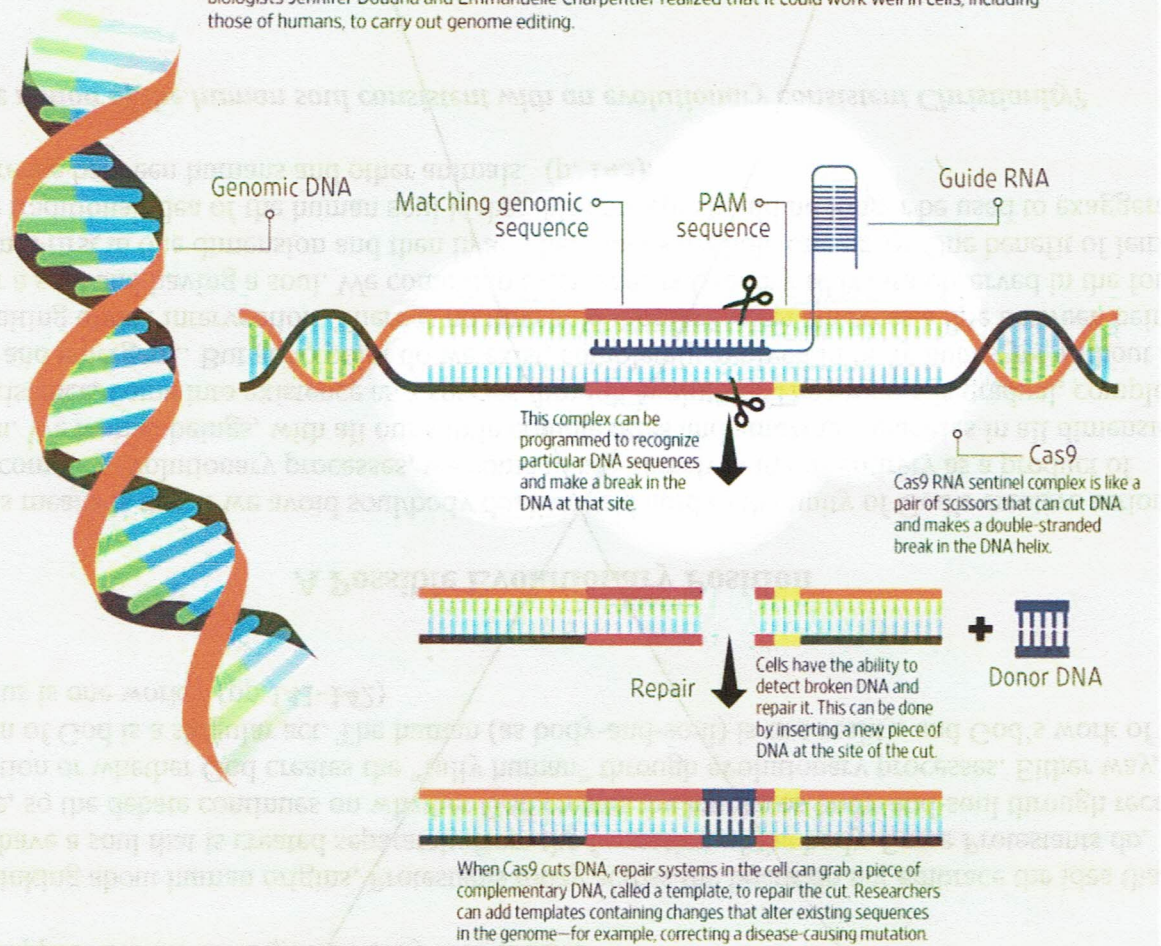


https://www.livemint.com/Politics/kb7XfbE2hT9Sxg74Wola3J/How-genes-are-edited-using-CRISPRCas9.html?utm_source=scroll&utm_medium=referral&utm_campaign=scroll

HOW CRISPR WORKS

CRISPR-Cas9, abbreviated from clustered regularly-interspaced short palindromic repeats, is a hybrid of protein and ribonucleic acid (RNA) which works as an efficient hunt-and-cut system in bacteria. Molecular biologists Jennifer Doudna and Emmanuelle Charpentier realized that it could work well in cells, including those of humans, to carry out genome editing.



● When viruses infect a cell, they inject their DNA. In bacterium, the CRISPR system allows that DNA to be plucked out of the virus and inserted in little bits

into the chromosome of the bacterium.

● These integrated bits of viral DNA get inserted at a site in the bacteria.

● CRISPR allows cells to record over time the viruses that they have been exposed to, so that cells are protected from those viruses.

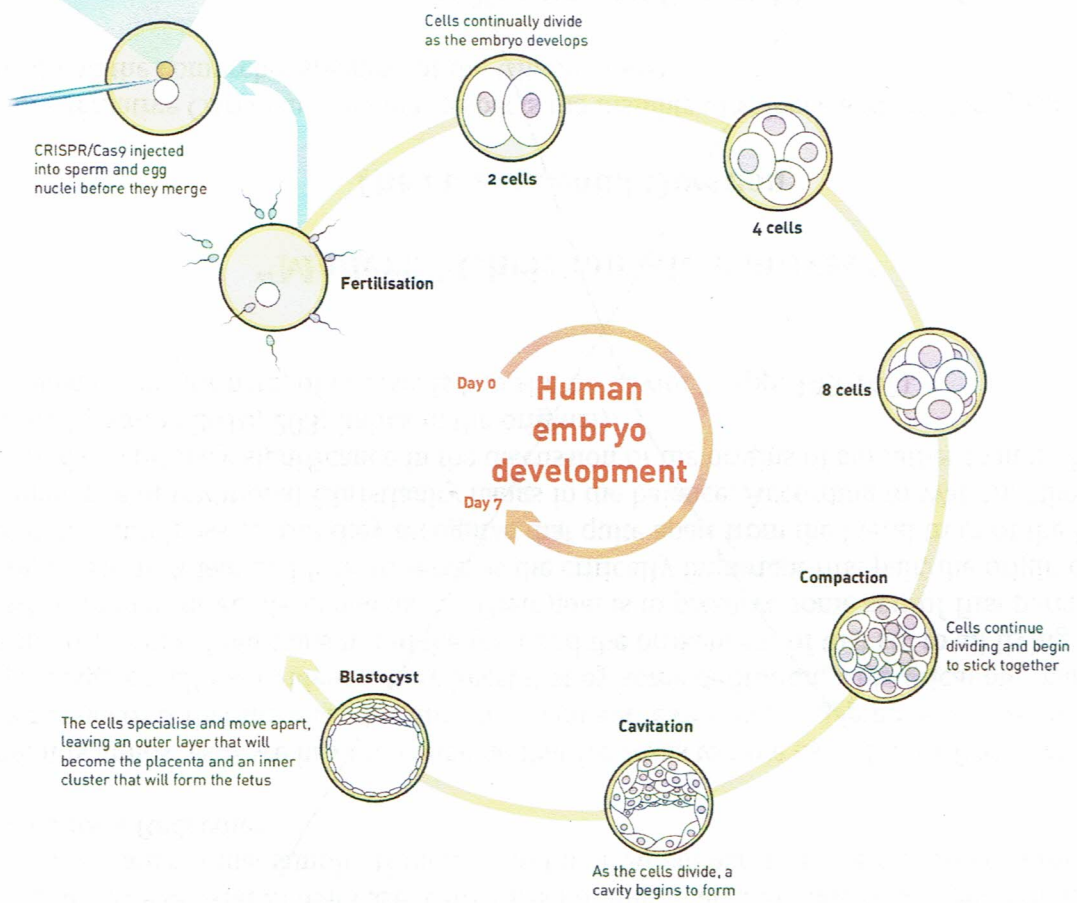
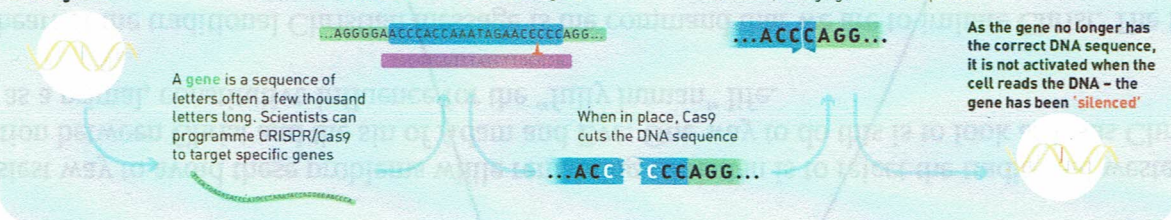
<https://www.rt.com/uk/404050-genome-editing-crispr-ivf/>

CRISPR/Cas9 genome editing

Our genome is the complete DNA sequence found in our cells, containing thousands of smaller sequences called 'genes'

A small guide is programmed to take the Cas9 cutting tool to a distinctive sequence within the selected gene

The cell stitches the ends back together, but the imperfect process can remove or add letters, changing the DNA sequence



Excerpts from various news sources and scientific journals

From the 2015 International Summit on Human Gene Editing:

<http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a>

“Germline editing poses many important issues, including: (i) the risks of inaccurate editing (such as off-target mutations) and incomplete editing of the cells of early-stage embryos (mosaicism); (ii) the difficulty of predicting harmful effects that genetic changes may have under the wide range of circumstances experienced by the human population, including interactions with other genetic variants and with the environment; (iii) the obligation to consider implications for both the individual and the future generations who will carry the genetic alterations; (iv) the fact that, once introduced into the human population, genetic alterations would be difficult to remove and would not remain within any single community or country; (v) the possibility that permanent genetic ‘enhancements’ to subsets of the population could exacerbate social inequities or be used coercively; and **(vi) the moral and ethical considerations in purposefully altering human evolution using this technology.**”

Draft Ethical Principles for Therapeutic Assisted Reproductive Technologies

He Jiankui, Ryan Ferrell, Chen Yuanlin, Qin Jinzhou, and Chen Yangran

The CRISPR Journal

Published Online: 28 Nov 2018 <https://doi.org/10.1089/crispr.2018.0051>

“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.**”

1. Mercy for families in need (怜悯之心)

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.

YouTube video by Jiankui He, November 25, 2018

"Two beautiful little Chinese girls, Lulu and Nana, came crying into the world as healthy as any other babies a few weeks ago. The girls are home now with their mom, Grace, and dad, Mark... When Mark saw his daughters for the first time **he said he never thought he could be a father**. Now he's found a reason to live, a reason to work, a purpose."

Consent form used by Jiankui He, translated from Chinese

“3. The primary risk of gene editing (DNA-targeted CRISPR-Cas9 endonuclease) is the off-target effect of generating extra DNA mutations at sites other than the intended target. This is due to that the technique can cause nonspecific cleavage, resulting in mutations in non-targeted genomic sites. PGD, whole genome-wide sequencing, amniocentesis and peripheral blood test of mothers in different stages of pregnancy after transplantation will minimize the possibility of substantial injury. **Therefore, this project team is not responsible for the risk of off-target which is beyond the risk consequences of the existing medical science and technology.**”

The CRISPR Baby Scandal Gets Worse by the Day

ED YONG, DEC 3, 2018

<https://www.theatlantic.com/science/archive/2018/12/15-worrying-things-about-crispr-babies-scandal/577234/>

“In an interview with Science, George Church, a respected figure from Harvard and a crispr pioneer, said that he felt “an obligation to be balanced about” the He affair. Church suggested that the man was being bullied and that the “most serious thing” about his experiment was “that he didn’t do the paperwork right.” “[Church’s] comments are incredibly irresponsible,” says Alexis Carere, who is president-elect of the Canadian Association of Genetic Counsellors. “If someone contravenes the rules that we have laid down, we are very justified in speaking out about it. The unfortunate effect of this is that it makes it seem like there is some kind of balance, and George is just in the middle. There is not.”

Carere was also dismayed at the rest of the interview Church gave, where “every sentence was a new ethical maxim that I had never heard of,” she says. For example, Church noted that “as long as these are normal, healthy kids it’s going to be fine for the field and the family.” **But unethical actions are still unethical, even if nothing goes wrong.** Arguing otherwise gives a pass to scientists who blow past ethical norms, provided that they find something interesting. “It’s bizarro-land consequentialist ethics,” Carere says.”

Nature 564, 5 (2018), EDITORIAL 05 DECEMBER 2018

How to respond to CRISPR babies

The claims from He Jiankui that he has used gene editing to produce twin girls demand action. A new registry of research is a good start.

<https://www.nature.com/articles/d41586-018-07634-0>

“Some argue that the circumstances in which germline gene editing would be beneficial, such as to reverse disease-causing mutations that could not be addressed in any other way, are likely to be extremely rare. Nevertheless, given that research and medicine move fast, a clear regulatory system needs to be devised and put in place in case a credible proposal arises. Such a regulatory system should draw on those that already exist to guide the use of gene-editing tools for research into human development, and more broadly govern medical testing of innovative therapies. **But it should not start with the assumption that future germline editing is a foregone conclusion — that is a question for society, not scientists, and one that demands the input of different stakeholders from across the world. Researchers and physicians must ask permission rather than beg for forgiveness.**”