Journal of Clinical and Nursing Research

Research Article

Risks of CRISPR Gene Editing and An Answer to Them

Emily Li（李佳怡）

Pinghe Non-government Schools of Shanhai City

Research Question: What is the potential risks of CRISPR gene editing and how to tackle with these risks?

Abstract: CRISPR gene editing is a technology used to edit genomes of a variety of organisms like bacteria, animals or even human beings. Currently, there are various criticism concerning CRISPR since the technology is still immature. It's important to address these concerns to ensure that CRISPR wouldn't cause harms to the society. The purpose of this investigation is to summarize methods which can be used to solve the risks and ethical issues regarding CRISPR through examining published researches in-depth. To draw a conclusion, scientists can use anti-crispr protein to minimize the off-target effects. For immunity issues, scientists can employ immunosuppressive drugs or to use CRISPR in places where immune system cannot reach. What's more, given both legal and ethical hurdles, the problem of designer babies and bio-weapons are unlikely to happen. Therefore, although there are various concerns regarding CRISPR, scientists are figuring out ways to minimize the risks and to optimize the usage of the CRISPR.

Key words: CRISPR; Off-target effect; Immunity issues; Bio-weapons; Designer baby

Publication date: July, 2020
Publication online: 31 July, 2020
[*]***Corresponding author:*** Emily Li, lijiayi2018@shphschool.com

1 Introduction

Ever since the Human Genome Project changed the world, the technologies of gene editing have brought potential promise and peril to the society. Last year, A scientist in China created two genetically engineered babies. This event has ignited heated a debate among academic fields as well as the general public. Scientists criticized this experiment as "Premature" and "Risky" since the babies may suffer from off-target effects, on-target mutations, as well as various unknown consequences. This prompted me to investigate the various risks of CRISPR gene editing. CRISPR-based gene editing technology generally involves three steps. Firstly, a specially designed guide molecule, usually RNA, finds the target DNA strand. Then, an enzyme, usually a cas-9 protein, cuts off the target DNA strand. Finally, cells will detect broken DNA and repair it. Sometimes, a new strand of DNA is inserted. Through the process of targeting, cutting, and editing, CRISPR gene editing allows researchers to change the genomes of various organisms.

Compared with traditional genetic editing technologies, CRISPR is highly specific and accurate since it is based on complementary base editing (For instance, A pairs with T, C pairs with G). Due to its high specificity and flexibility, CRISPR gene editing has a wide application in real life.

For instance, CRISPR gene editing can be used to treat various diseases. According to NPR, doctors from Hangzhou Cancer Hospital have successfully treated patients with esophagus cancer by using CRISPR. Besides, CRISPR has the potential to treat various monogenetic diseases such as sickle cell disease, cystic fibrosis, and Tay-Sachs disease.

Besides treating diseases, CRISPR gene editing can also be used to protect environment. As is known to all, due to increasing temperature and the devastating effects of environmental pollution, coral reefs suffered from the problem of "bleaching", and nearly half of Australia's Great Barrier Reef has

been threatened to death. Under this circumstance, researchers from Stanford University tried to use CRISPR to edit coral's genes and save them from the brink of death. In addition, CRISPR can be used to create various food such as jointless tomatoes, pest-resistant tomatoes, and drought-resistant corns, greatly increasing the variety and the productivity of crops.

Like other technologies, CRISPR is a double-edged sword. While it may have the potential to treat patients diagnosed with certain diseases, it may also pose significant harms for both the health of the people as well as the whole society if used improperly. Currently, critics claimed that CRISPR editing involves risks such as off-target effects, on-target mutations, immunity issues, and other unknown consequences. The biggest problem with CRISPR editing is unknown effects. Almost all genes have a variety of functions, most of which remain unknown to humans. Therefore, when we edit genes, we might delete genes that are crucial for biological function. For instance According to Scientific American, by deleting sickle cells, it is more likely to get malaria. By deleting the CCR5 gene would make people resistant to HIV, but will also make them 21 percent more likely to die earlier. Thus, it would be reckless for us to forge ahead with CRISPR.

What's more, there are a series of ethical considerations related to CRISPR gene editing. For instance, with gene-editing technology, people may create designer babies that are taller, stronger, and smarter than normal babies, which will widen the gap between rich people and poor people. Some people also suggest that CRISPR gene editing is a violation of the god since when we edit human genes, we are not "Natural" anymore. Also, due to its wide accessibility, CRISPR might be utilized by bad people such as terrorists or criminals. They might create a super-sized virus or bacteria that might threaten human beings into extinction.

2 Risks of CRISPR

In the following part of the report, I will summarize the risks of CRISPR gene-editing technology through the following several aspects: off-target effects, immunity issues, designer babies, and bio-weapon. Besides, I will present methods that can be used to minimize or avoid these risks.

2.1 Off-target effects

One of the biggest concerns relating to Gene editing technology is that it may have off-target effects. Just like no archer can hit the target every time, editing the human genome is not one hundred percent accurate. According to Statnews, Researchers suggested that off-target effects will pose a significant threat to people's life as it may disable a tumor-suppressor gene, therefore cause different kinds of cancers such as leukemia.

To understand why CRISPR might have off-target effects, we must understand how it works first. CRISPR-based gene-editing technology has two steps. Firstly, designed RNA finds the target DNA strand. Then cas-9 protein will cut off the target DNA strand. The problem is, there are multiple places on genome may share the same sequence of nucleotides, so the designed RNA can pair with these places one after another and allow RNA to cuts multiple DNA sites besides the target one.

However, some researchers suggested that concerns related to the off-target effects might be overblown. It's true that last year, a study showed that CRISPR gene editing might result in off-target effects. However, several months later, Nature retracted the paper after multiple researchers pointed out the mistakes in this study. In their reassessment article, it is said that, "There was insufficient data to support the claim of unexpected off-target effects due to CRISPR."

Under all circumstances, solving off-target effects is paramount to successfully utilize CRISPR in human. One way to minimize the risks of off-target effects is to utilize the anti-crispr protein. It was reported in the journal Science Advances, researchers from UC Berkeley and UC San Francisco showed that anti-CRISPR proteins can "decrease off-target effects by as much as a factor of four, acting as a kill switch to disable CRISPR-Cas 9 after it's done its job." As the gene-editing technology developed in the future, researchers can create even more innovative approaches to deals with the off-target effects to ensure the safety of the therapy.

2.2 Immunity issues

The first barrier for using CRISPR gene editing is the human immune system which protects human body from viruses, bacteria, and other foreign invaders. Since Cas-9 Protein was derived from the bacteria

that used to infect human bodies, the human body may identify this protein as a kind of "Foreign Invader". Therefore, once the cas-9 protein enters the body, the immune cells may detect this protein and try to destroy it. As a result, CRISPR may not be viable in human as it may trigger immune responses. In fact, according to the research published in the peer-reviewed journal Nature Medicine, 96 percent of the people had immune response against CRISPR and 85% of the candidates had antibodies against it. This means that for most people, CRISPR will be resisted by the human immune system and simply will not work.

The immune response may pose serious health risks to humans, so it's essential to address this issue. According to xconomy, One way to tackle the immunity problem is to utilize immunosuppressive drugs to weaken the immune system, so the immune reaction possibility could be reduced. Besides, Researches can also avoid the immune problem by using CRISPR outside of the body or in places where immune system cannot reach.

3 Ethical issues

3.1 Designer Babies

CRIPSR has always been criticized as a tool to generate designer babies which could bring multiple unknown consequences including a widen the gap between the rich and poor people. According to the MIT Technology Review, even the cheapest gene-editing program costs 3 billion dollars to treat only 7 thousand patients, costing more than 0.7 million dollars for one patient.

Under this circumstance, only rich people can afford gene-editing technology. Thus, they may become healthier, richer, and smarter by introducing desirable genes. Moreover, they may create designer babies who can outcompete other normal babies from the time of birth. On the other hand, poor people cannot gain access to this technology as they don't have money. As a result, CRISPR will exacerbate the problem of discrimination. Parents who don't edit their children's DNA will be looked down upon for not ensuring the health of their children. The subjects themselves may be discriminated against as the gene-edited individuals become aware of their "Edited Identity". It's not too farfetched to think of a future where people have stamps on their IDs indicating whether they're "edited" or not.

Even though the problem concerning designer babies has generated heated debate amount the public, it is currently unlikely to occur in the real world due to both legal and ethical hurdles. Germ-line editing, which means editing human genomes in embryos to create designer babies is currently illegal in many countries. Nowadays, 40 countries have already banned the Germline editing. The teams that do researches on the embryos only let them grow for a few days, with no intention of letting them develop into a baby. Thus, we don't need to worry about this problem since the governments have already banned it. What's more, it's difficult to create designer babies that have desirable traits intrinsically. Researches indeed have identified certain genes that may bestow people with desirable traits. However, "To introduce a novel gene is an issue," said Fredrik Lanner, of Karolinska University Hospital in Sweden. By using current technology, to inset certain genes on pairs of chromosomes would be extremely difficult and complex.

3.2 Bio-Weapons

CRISPR indeed has the potential to treat rare genetic diseases such as Huntington disease or Marfan Syndrome, but people are afraid that terrorist groups or criminals might utilize this frontier technology to harm society.

Compared with the old-versioned gene-editing technology, CRISPR is relatively cheaper and easier to obtain. People can buy a set of CRISPR kit from the website. Due to its wide accessibility, people are afraid that CRISPR can also be made into bio-weapons. For instance, bad people may create mosquitos that spread incurable diseases or create super-sized human beings that can destroy the world. It sounds horrible if CRISPR is used as a tool to harm society. However, researchers pointed out that such fears proved largely unfounded. According to James Revill, a Research Fellow with the Harvard Sussex Program, to use CRISPR to harm society is not that easy. To conduct a "simple CRISPR experiment" may be easy, but to develop a bio-weapon that can pose serious effects on society is extremely complex and impossible. The utilization of Gene editing technology requires professional knowledge "beyond the reach of most criminals and terrorists". Therefore, even if terrorists have access to CRISPR,

they are unlikely to turn this technology into fearful bioweapons.

What's more, if someone uses a hammer to smash others, the hammer is not guilty and definitely we will not ban all hammers, as it is a tool. Likewise, if people use gene-editing technology for criminal activities, it is not the fault of gene-editing technology but the people who abuse it. And the solution is not to punish gene-editing technology but to punish the people. We cannot scapegoat CRISPR for the problem that is caused by real criminals.

4 Conclusion

Besides the risks aforementioned, researchers also detected that nucleotides are sometimes lost during the repair process which may cause horrible consequences. Imaging we get a baby without limbs because of gene editing or a baby with three heads, we should always consider the inevitable risks related to this technology before we allow it to be utilized in human, regardless of what potential benefits that the gene-editing technology might bring. Therefore, before the maturation of CRISPR gene editing, governments should keep strengthening legislation in controlling and monitoring germ-line editing as it may cause serious problems that will last for generations.

While many potential risks exist, CRISPR is still a valuable technology with great potential as it offers possible solutions to treat rare genetic diseases as well as various cancers which are incurable nowadays. Currently, 7.9 million children are born with a serious genetic diseases each year. If we use can CRISPR to correct certain genes and restore their normal functions, millions of lives can be saved. No technology will be perfect, I sincerely believe that one day, after addressing all the potential side effects, CRISPR could be used properly to promote the well-being of mankind.

References

[1] Stein, R. (2018, February 21). Doctors In China Lead Race To Treat Cancer By Editing Genes. Retrieved July 13, 2020, from https://www.npr.org/sections/health-shots/2018/02/21/585336506/doctors-in-china-lead-race-to-treat-cancer-by-editing-genes

[2] News Center. (n.d.). CRISPR used to genetically edit coral. Retrieved July 13, 2020, from http://med.stanford.edu/news/all-news/2018/04/crispr-used-to-genetically-edit-coral.html

[3] Weintraub, K. (2019, June 03). Genetic Mutation in "CRISPR Babies" May Shorten Life Span. Retrieved July 13, 2020, from https://www.scientificamerican.com/article/genetic-mutation-in-crispr-babies-may-shorten-life-span/

[4] @sxbegle, S., Begley, S., Writer, A., & Writer, S. (2016, August 09). CRISPR has off-target effects that researchers have been ignoring. Retrieved July 13, 2020, from https://www.statnews.com/2016/07/18/crispr-off-target-effects/

[5] Pre-Existing Immunity to CRISPR Found in 96% of People in Study. (2020, May 29). Retrieved July 13, 2020, from https://xconomy.com/boston/2018/10/29/pre-existing-immunity-to-crispr-found-in-96-of-people-in-study/

[6] Mullin, E. (2020, April 02). Tracking the Cost of Gene Therapy. Retrieved July 13, 2020, from https://www.technologyreview.com/2017/10/24/148183/tracking-the-cost-of-gene-therapy/

[7] What are the Ethical Concerns of Genome Editing? (n.d.). Retrieved July 13, 2020, from https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/ethical-concerns

[8] Report: 8 million born with birth defects yearly. (2006, January 31). Retrieved July 13, 2020, from http://www.nbcnews.com/id/11101963/ns/health-childrens_health/t/report-million-born-birth-defects-yearly/

[9] CRISPR off-targets: a reassessment. Nat Methods 15, 229–230 (2018) doi:10.1038/nmeth.4664

[10] Revill, James. "Could CRISPR Be Used as a Biological Weapon?" Phys.org, Phys.org, 31 Aug. 2017, phys.org/news/2017-08-crispr-biological-weapon.html.

[11] Sanders, Robert, and Robert Sanders. "Anti-CRISPR Proteins Decrease off-Target Side Effects of CRISPR-Cas9." Berkeley News, 10 Oct. 2018, news.berkeley.edu/2017/07/12/anti-crispr-proteins-decrease-off-target-side-effects-of-crispr-cas9/.

[12] Begley, Sharon, et al. "U.S. Scientists Edit Genome of Human Embryo, but Cast Doubt on 'Designer Babies'."STAT, 4 Oct. 2017, www.statnews.com/2017/08/02/crispr-designer-babies/.