Name: Huong Phan

Prompt: Introduce CRISPR genome editing technology, with a short description of how it works. Discuss at least two pros and two cons of CRIPSR genome editing technology. Finally, give your personal stance on the use of CRISPR genome editing technology and describe why you have chosen this stance.

The discovery of CRISPR in 2012 arguably by Jennifer Doudna and Emmanuelle Charpentier (Houtman 2016; "CRISPR crunch") is remarkable for the genome editing technology's potential to majorly shift paradigms in the treatment of fatal genetic diseases. It is a revolutionary and powerful biological tool that allows scientists to target and cut our genetic sequences at precise intervals (Doudna; Shannon), altering our DNA to be more resistant to fatal diseases such as cancers and HIV-AIDS ("Genetic Engineering Will Change Everything Forever – CRISPR"), and eliminating any inherited genetic diseases such as cystic fibrosis or Tay Sachs disease ("Editing humanity"). However, there is still a long way before this robust mechanism can be legalized for its application in human and other animal's bodies. One of the reasons is that CRISPR is still far from the level of flawless precision: it can target the wrong benign DNA sequences, leading to potentially destructive mutations in the bodies. Nonetheless, its targeting specificity can definitely be improved over time considering the cut-throat rate of biomedical development. The more prominent concerns of CRISPR-Cas9's implementation lies in its prospective socioeconomic impacts, as they would be persistent problems far in the future, while medical concerns would be solved eventually.

Clustered regularly interspaced short palindromic repeats, or CRISPR, derived from what was observed to be a natural defense mechanism of E. coli bacteria against viral infection (Sternberg and Doudna 2015; Doudna; Houtman 2016). As the virus

attacks the bacteria cells repeatedly, the bacteria would develop an immune response by storing the virus DNA between their five-base-pair DNA repeats and producing an RNA that matches the viral DNA to detect the presence the virus DNA and subsequently remove it from the bacteria genome ("Genetic Engineering Will Change Everything Forever – CRISPR"; "RadioLab: CRISPR"), effectively deactivating the virus in bacteria. Scientists have since adapted this mechanism into the concept of CRISPR, which consists of identical DNA sequences separated by "unique spacers sequences", which are actually "foreign genetic elements" (Sternberg and Doudna 2015). CRISPR is also accompanied by a CRISPR-associated or Cas protein, which produces a guide RNA that has the ability to cut out targeted pieces of DNA, usually ones that cause genetic diseases, through "complementary base pairing" (Sternberg and Doudna 2015). Cas9 is the most common type of protein used as it possesses the potency of making double-stranded breaks in the DNA despite having a relatively simple structure of only one polypeptide (Sternberg and Doudna 2015), Together, CRISPR-Cas9 offers a much more specific and simple human genetic engineering tool than its predecessors such as ZFNs or TALENs (Sternberg and Doudna 2015), making it much more attractive. But ultimately, its formidable power lies in its capacity to modify virtually all cells in human as well as animal bodies ("RadioLab: CRISPR"). This means we can modify not only human cells that contain inheritable diseases such as cystic fibrosis, but also animal cells to make them more resistant to contagious diseases such as malaria, preventing them from transmitting these diseases to humans.

CRISPR-Cas9 is a promising and appealing technological endeavor that not only holds great potential for effectively curing numerous diseases in individuals, but also

allows our children of later generations to live in a world free of diseases. Though various drugs have been synthesized to treat genetic diseases, they can only provide palliative treatment as they can address the related symptoms but not the root cause of the diseases, which is a mutation in the DNA (Corn). CRISPR-Cas9, on the other hand, provides an opportunity for people with mutated DNA to correct their DNA in order for their DNA to produce accurate, properly functioning proteins (Shannon). The technology has been proven to be effective in various experiments involving both human and animal cells. For example, it was able to remove half of the HIV virus from mice's cells ("Genetic Engineering Will Change Everything Forever – CRISPR") as well as from infected human cells in the lab (Doudna). It was also shown to be capable of curing sickle cell disease that involves the editing of only a single base pair in human's red blood cells (Corn), and successfully "replacing the CFTR (Cystic Fibrosis Transmembrane conductance Regulator) gene in intestinal organoids" to "restore function of the CFTR" (Shannon). Furthermore, CRISPR-Cas9 can give cancer patients a reason to be optimistic by modifying their immune T-cells to "knock out a gene in the cells" that "encodes a protein called PD-1" in order to develop an immune response against cancer attacks (Cyranoski 2016). Chinese scientists also used CRISPR-Cas9 to experiment on editing human embryos, albeit with low probability of success (RadioLab: CRISPR). But if this technique is further developed to increase its efficacy, we can possibly alter the embryos' heritable germline cells that affect all the following generations, and eliminate some genetic diseases forever.

CRISPR can also genetically modify animals that causes infectious diseases in human and saving valuable animals to humans out of their impending extinction.

Together with gene drive, CRISPR-Cas9 can bioengineer malaria-resistant mosquitos and release them into the wild so that the trait would spread to all mosquitos, possibly eradicating malaria forever (Reardon 2016; Kahn). It can also rescue imperative animals from extinction (Reardon 2016). Bees, a species that pollinate some of most important plants for human's food consumption, are experiencing a crisis called Colony Collapse Disorder, in which bees keep disappearing and dwindle in numbers ("Colony collapse disorder"). By studying the traits of the healthier "hygienic bees", scientists can use CRISPR to alter bees' behavior into adopting better cleaning habits to resist against diseases. Thus, CRISPR-Cas9 can not only have the ability to treat genetic diseases but also prevent us from contracting dangerous contagious diseases and ensure the survival of animals that are beneficial to human.

However, no matter how powerful the technology is, therapeutic applications of CRISPR-Cas9 would not be happen any time soon due to various medical and socioeconomic concerns. From the medical perspective, it is still far from an infallible tool in curing diseases as it can induce lots of off-target effects and does not correct all mutations in different cells which may lead to mosaicism (Greely 182; Houtman 2016; Lanphier, et al. 2015). Even if CRISPR-Cas9 would be precise enough to target enough DNA mutations accurately, there may still be unpredictable medical consequences of editing germ line cells due to our limited genetic knowledge of epigenetics and interactions between two or more diseases in the same patient (Baltimore 2015; Lanphier, et al. 2015). However, these medical perils could certainly be solved in the future as the genetics field continues to progress at a break-neck speed, and research has already been underway to reduce off-target effects as

much as possible (Sternberg and Doudna 2015). Thus, medical concerns would no longer remain a problem in the future with CRISPR-Cas9's rapid advancements without any signs of staggering.

From the socioeconomic perspective, CRISPR-Cas9 can cause serious social repercussions and widen wealth disparity in the society. It is highly likely that CRISPR-Cas9 could evolve to the extent that allows parents to modify their embryos to have all the traits they consider to be favorable, such as greater intelligence and athletic abilities, which would lead to a slippery slope towards enhancing human and creating designer babies (Baltimore, et al. 2015; "Genetic Engineering Will Change Everything Forever – CRISPR"). If human enhancement becomes the norm in the future, discriminatory treatment against non-modified people is likely to happen (Greely 244), as referenced in the fictional world of the movie "Gattaca" where nonmodified children were denied their life insurance. Family relationships could also be affected, as the parents' hope and confidence that their genetically modified child will automatically grow up with all their engineered traits intact would probably shape their treatment towards the child (Greely 226). They would be more likely to set an unrealistically high expectation for the genetically engineered child if they are not informed of the environmental influence on their child's behavior and abilities. The disappointment would hit harder if the child could not meet their expectations, and it might put a strain on the parents-child relationship. In a broader social context, the upper class would have easier access to genetic editing than the lower class due to their greater financial power. With superior intelligence and appearance, the upper class would no doubt have a greater edge at landing better job deals, leading to an even greater disparity in wealth in the world.

In my opinion, this simple but amazing piece of technology should be applied in treatment of diseases, but not enhancement of human traits as it can incur inevitable and probably unresolvable socioeconomic problems. Legally speaking, I believe CRISPR would and should be eventually legalized to some extent. However, the whole idea of determining a child's destiny, a very private matter that apparently requires total respect for parents' personal decision for their future child, seems incompatible with legislation, a restriction on the available choices of alterations parents can make to their child. The legislators will probably meet many obstacles and objections if they decide to ban genome editing for enhancement since this may violate parental rights to make decisions for the child themselves. Instead, I think they can indirectly discourage people from using CRISPR for non-therapeutic enhancements by administering more funds towards research for curing diseases over modifying behavioral traits. Most importantly, I think that we should stop developing CRISPR at a certain point before its power over us becomes out of control. This idea may sound extreme, but I think there would be a tiny chance that CRISPR can one day drive our population into exceeding Earth's carrying capacity and exhausting all its resources. If we give CRISPR the power to cure nearly every disease in the world, our life expectancy would be significantly extended. With potentially much lower death rates in the future, world population will definitely increase at a higher rate than it does now, while Earth's resources will only become more depleted to the point of exhaustion. Nonetheless, to end this essay on a positive note, I have faith in the scientists who have already called a moratorium on clinical application of CRISPR (Doudna) that they will be able to make the right decision on the regulation of CRISPR research for the sake of humanity.

Bibliography

- Baltimore, David, et al. "A prudent path forward for genomic engineering and germline gene modification." *Science*, vol. 348, no. 6230, 3 Apr. 2015, pp. 36-38.
- Doudna, Jennifer. "How CRISPR lets us edit our DNA | Jennifer Doudna." *YouTube*, uploaded by TED, 12 Nov. 2015, www.youtube.com/watch?v=TdBAHexVYzc.
- "Colony collapse disorder." Wikipedia: The Free Encyclopedia. Wikimedia Foundation, Inc., 13 Oct. 2016. Web. Accessed 13 Oct. 2016.
- Corn, Jacob. "The end of genetic disease | Jacob Corn | TEDxBerkeley." YouTube, uploaded by TEDx Berkeley, 18 Feb. 2016, https://www.youtube.com/watch? v=grf3RxryRto.
- "CRISPR crunch." *The Economist*, 20 Feb. 2016, www.economist.com/news/science-and-technology/21693183-row-over-who-invented-new-gene-editing-technique-heats-up-crispr-crunch. Accessed 11 Nov. 2016.
- Cyranoski, David. "Chinese scientists to pioneer first human CRISPR trial." *Nature*, vol. 535, 28 Jul. 2016, pp. 476-477.
- "Editing humanity." *The Economist*, 22 Aug. 2015, www.economist.com/news/leaders/21661651-new-technique-manipulating-genes-holds-great-promisebut-rules-are-needed-govern-its. Accessed 11 Nov. 2016.
- "Genetic Engineering Will Change Everything Forever CRISPR", YouTube, uploaded by Kurzgesagt In a Nutshell, 10 Aug. 2016, www.youtube.com/watch?v=jAhjPd4uNFY.
- Greely, Henry T. *The End of Sex and the Future of Human Reproduction*. Harvard University Press, 2016.
- Houtman, Jacqueline J. "CRISPR/Cas Gene Editing Borrowing Tools from

- Bacteria." *Horizons in Bioscience*, 2016, www.faseb.org/Portals/2/PDFs/ opa/ 2016/FASEB-HorizonsInBioscience-CRISPR-ForWeb%20(2).pdf. Accessed 12 Nov. 2016.
- Kahn, Jennifer. "Gene editing can now change an entire species -- forever | Jennifer Kahn." *YouTube*, uploaded by TED, 2 Jun. 2016, www.youtube.com/watch? v=OI OhvOumT0.
- Lanphier, Edward, et al. "Don't edit the human germ line." *Nature*, vol. 519, no. 7544, 26 Mar. 2015, pp. 410-411.
- "RadioLab: CRISPR." YouTube, link has been removed.
- Reardon, Sara. "Welcome to the CRISPR zoo." *Nature*, vol. 531, no. 7593, 10 Mar. 2016, pp. 160-163.
- Shannon, Stephen. "Can Gene Editing Techniques Like CRISPR-Cas9 Be Used to Replace Mutated Genes in CF?" *Cystic Fibrosis News Today*, 16 Apr. 2015, www.cysticfibrosisnewstoday.com/2015/04/16/can-gene-editing-techniques-like-crispr-cas9-be-used-to-replace-mutated-genes-in-cf/. Accessed 12 Nov. 2016.
- Sternberg, Samuel H., and Doudna, Jennifer A. "Expanding the biologist's toolkit with CRISPR-Cas9." Molecular Cell, vol. 58, no. 4, 21 May 2015, pp. 568-574.