This article is licensed under a Creative Commons Attribution 4.0 International License (CC BY 4.0).

Sample Article

Editing destiny - Future of embryo genome editing

Harshitha V| Nrupathunga University |

All data supporting the findings of this study are available in the manuscript and supplementary files

A preprint version of this work is available on bioRxiv:

Harshitha V. 2025. Editing destiny- future of embryo genome editing. bioRxiv. doi.10.1101/2019.12.11.123456

Abstract

This sample article address about the ongoing research of germline human genome editing. The use of CRISPR-Cas9 allows specific gene knockout at molecular level, through this technique various genetic and neurodegenerative diseases like sickle cell anemia, cystic fibrosis, muscular distrophy and various other diseases can be cured and prevent it from passing from generation to generation. Many countries are against this germline editing and it resulted in chaos anf confusion. It disadvantaged the people living in that country by the implementation of first germline editing by He Jiankui. He introduced that genetic diseases can be cured without passing it to the next generation. Various discussions and debates have been undergone even though people had not come up with proper conclusion. All these because; if this therapy had come to public there is a chance of misusing and altering the genes which may create serious problem in the world. So, germline alteration should be made only to treat diseases and not to have designer babies. Lots of surveys and Human Genome Editing (HGE) registory collects information about the pros and cons about this technique and based on people's opinion treatment is provided. Tight regulation of germline editing is made to avoid future consequences. Secondly, this technique has its own disadvantage of leading to mutation and intolerance to some factors in the future.

Introduction

Embryo genome editing is one of the best methods to permanently get rid of genetic diseases. DNA is an instruction manual where we can tailor our genes to our interest and knock down the genes that cause mutation. A movie called *Gattaca* in 1997 which themed about designer babies have came to reality. *He Giankui* [Southern University, Shenzhen, China] One of the famous biophysics researcher, created first ever genetically edited babies. His work on modifying CCR5 gene in embryos by giving a mutation that would make babies immune to HIV. Gene editing is the process where genes can be edited by adding or deleting the nucleotide base pair which helps in functioning or mutation of the gene. The world's first edited genome in the embryo level was done by He Giankui for twin babies. This process raises social, ethical, religious, and cultural aspects about altering human genome at embryo stage, which prevents carrying of genes from generation to generation. And also it points out an important question, will we become more tolerant after editing? Ethical consideration also considers the possible side effects after editing. Various articles and experiments have been performed to give the rightful conclusion for this issue. Also genetic editing creates genetic discrimination between genetic haves and have-nots.

Introduction to CRISPR in germline editing

One of the common genome editing tool is CRISPR-Cas9, which consists of mRNA and a protein. In 2017, U.S. National Academy of Sciences examined both somatic cell and germline genome editing(1.). Examination created a genetic discrimination in the country. OCT-4 is the targeting guide RNA using inducible human embryonic stem cell based system and microinjection of mouse zygotes, specific targeting of gene encoding OCT-4 (4.). OCT-4 gene is responsible for regulation and maintenance of genes in the embryonic stage. It is the type of proto-oncogene where mutation in this gene may cause cancer, germline modification are subjected to threaten human dignity and are invalid. It is the link between human dignity to human genome. These methods which are used in germline editing do not preserve human genome in current state and stops any natural random mutations (5.). There is always a considerable risk of carrying mutations and individual may lose the ability to deal with harsh environmental factors and the immune barrier would be weak. Traditional methods like PGD (Pre-implantation Genetic Diagnosis) and IVF (In-vitro fertilization) works on specific selection of healthy German cell that are fertilized outside the placenta

cultured in labs that are grown upto 32 celled zygote, genetic disorders can be treated by selecting disease free germ cell. However, only limited embryos can be created. These methods allows carry of genetic disorders one or the other way(7.). In order to take this situation under control HGE (Human Genome Editing) Registry Central Database that collects information of clinical trials using HGE editing technologies. It was initiated and collected by WHO International Clinical Trials Registry Platform (ICTRP) on July 2019. WHO Director General was issued with WHO Expert Advisory Committee's recommendation, the regulation of embryo germline editing.

Methods used for Embryo editing

Human germline editing leads to so many consequences, leading to designer babies in the future. Lots of debates and discussions have been undergone to verify people views, their genuine discussion.

1. The committee which is responsible for this issue should propagate treatment in treating genetic diseases which are inheritable and stop creating designer babies.
2. CRISPR is the major tool which is used for editing the embryo genome although such interventions exacerbate social divisions or marginalisation of disadvantaged groups within a country. (14.)
3. No individual scientists have specific warrant to redesign human embryos or design new bacteria or virus. Altering human genome cannot be made without discussing to the affected population(6.).
4. Potential regulations should be made in context of reducing sperm and egg count, reducing the number of zygotes on basis of population crisis. The couples have the right to select an unaffected baby.
5. Genome editing could have unpredictable effects on future generation which is dangerous and ethically unacceptable(7.).
6. Gene editing techniques have an impact on mankind i.e, 6% of births that are altered have serious birth defect which is genetic.
7. Traditional techniques including PGD and IVF involves many embryos to test that goes wasted to get non-carrier disease for embryo(7.).
8. Major surveys have undergone i.e, somatic therapy (64%) and germline therapy (65%) that includes significant birth rate with low level of germline enhancement app;

(26%) with (51%) finding unacceptable and somatic enhancement app (39% with 35%) finding unacceptable (9.).

9. Germline editing may help in eradicating inherited genetic diseases but also causes significant mutation and an individual may loose the tolerance to adapt to new environment or even unable to fight upcoming diseases. This technique if not regulated properly, human population have to face consequences which result in significant downfall of healthy natural births globally. For example, genes responsible for intelligence and individual's strength are altered and designer babies are created that are targeted on particular community or country.

Conclusion

More than 2 genes are responsible for expression of phenotypic traits. 16 genes control eye color. 10,000 different genes play a role in person's maximum height. Genes also consist of DNA repair mechanism (13.); which determines that in order to change one particular trait, we need to alter more than 10 genes depending on type of trait. There are chances of getting mutations due to human error, which leads to cancer. Nearly 40 countries discouraged germline reading. Stakeholders agreed to have public to decide whether it is necessary to opt germline editing. 15 countries in Western Europe banned it. Ongoing debates against PGD, (Pre-implantation Genetics Diagnosis) and HGE on international summit in Washington DC(11.).Moral and religious obligations result in various breakthrough about HGE(11.).

The international summit committee has come up with evolving regulatory framework for gene therapy. Obligations included lack of oversight and transparency. They came up with conclusion that genome editing causes another health problem. However, side effects caused by genome editing may cause new mutation which is not curable in modern genome technology. This has answered the question of tolerance level of an individual who have undergone germline editing.

Reference

1. National Academies of Sciences, Engineering, and Medicine; National Academy of Medicine; National Academy of Sciences; Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations. Human Genome Editing: Science, Ethics, and Governance. Washington (DC): National Academies Press (US); 2017 Feb 14. PMID: 28796468.
   Human Genome Editing: Science, Ethics, and Governance
   https://pubmed.ncbi.nlm.nih.gov/28796468/
2. He J. About Lulu and Nana: Twin girls born healthy after gene surgery as single-cell embryos. 2018. https://www.youtube.com/watch?v=th0vnOmFltc (last accessed September 19, 2020).
3. Robin Lovell-Badge; CRISPR babies: a view from the centre of the storm. Development 1 February 2019; 146 (3): dev175778. doi: https://doi.org/10.1242/dev.175778
4. Genome editing reveals a role for OCT4 in human embryogenesis
   Norah M. E. Fogarty, Afshan McCarthy, Kirsten E. Snijders, Benjamin E. Powell, Nada Kubikova, Paul Blakeley, Rebecca Lea, Kay Elder, Sissy E. Wamaitha, Daesik Kim, Valdone Maciulyte, Jens Kleinjung, Jin-Soo Kim, Dagan Wells, Ludovic Vallier, Alessandro Bertero, James M. A. Turner & Kathy K. Niakan
   Fogarty, N., McCarthy, A., Snijders, K. et al. Genome editing reveals a role for OCT4 in human embryogenesis. Nature 550, 67–73 (2017). https://doi.org/10.1038/nature24033
5. Human dignity and gene editing
   Using human dignity as an argument against modifying the human genome and germline is alogical fallacy Iñigo de Miguel Beriain1,2
   Chair in Law and the Human Genome RG, Department of Public Law, University of the Basque Country (UPV/EHU), Leioa, Spain
   2IKERBASQUE, Basque Foundation for Science, Bilbao, Spain
   https://pmc.ncbi.nlm.nih.gov/articles/PMC6172467/
6. Protecting the Endangered Human:

Toward an International Treaty Prohibiting Cloning and Inheritable Alterations Lori B. Andrews IIT Chicago-Kent College of Law, landrews@kentlaw.iit.edu Follow this and additional works at: https://scholarship.kentlaw.iit.edu/fac_schol

Lori B. Andrews, Protecting the Endangered Human: Toward an International Treaty Prohibiting Cloning and Inheritable Alterations, 28 Am. J.L. & Med. 151 (2002). Available at: https://scholarship.kentlaw.iit.edu/fac_schol/18

7. The moral imperative to continue gene editingresearch on human embryos. Julian Savulescu1,2, Jonathan Pugh1&, Thomas Douglas1, Christopher Gyngell11 Uehiro Centre for Practical Ethics, University of Oxford, Oxford OX1 1PT, UK2 Queensland University of Technology, St Lucia, Brisbane, QLD 4072, Australia& Correspondence: jonathan.pugh@st-annes.ox.ac.uk (J. Pugh)
8. Howard, H.C., van El, C.G., Forzano, F. et al. One small edit for humans, one giant edit for humankind? Points and questions to consider for a responsible way forward for gene editing in humans. Eur J Hum Genet 26, 1–11 (2018). https://doi.org/10.1038/s41431-017-0024-z
9. David Benjamin, Toritz, Cox, Rendall, Chalfre, Platt, and Feng Zhang, Broad Institute of MIT and Harvard, 7, Cambridge Center, Cambridge, MA 02142, USA, MC, Govern, Institute for Brain Research, Department of Brain and Cognitive Sciences, Cambridge, UK. Department of Biological Engineering, Massachusetts, Institute of Technology, Cambridge, MA 02139, USA.
10. Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing https://www.who.int/groups/expert-advisory-committee-on-developing-global-standards-for-governance-and-oversight-of-human-genome-editing/registry#:~:text=Human%20Genome%20Editing%20(HGE)%20Registry&text=In%20accordance%20with%20the%20principles,accessible%20to%20all%20interested%20stakeholders
11. [1] National Academies of Sciences, E., Medicine,. (2017). Human Genome Editing: Science, Ethics, and Governance. Washington, DC: The National Academies Press. https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/ethical-concerns?utm_source=chatgpt.com
12. Suggested Citation:"Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop - in Brief." 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. doi: 10.17226/25343.

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.

https://nap.nationalacademies.org/read/25343/chapter/1

13. White, D., Rabago-Smith, M. Genotype–phenotype associations and human eye color. J Hum Genet 56, 5–7 (2011). https://doi.org/10.1038/jhg.2010.126
14. NASEM. Human genome editing: Science, ethics, and governance. Washington DC: The National Academics Press, 2017. Pubmed