Genome Editing: Rigging the Genetic Lottery

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Global Perspectives
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Preface

People have long sought and used scientific knowledge to improve the conditions of human life. Genome editing was hailed the 2011 Method of the Year by *Nature Methods,* and the CRISPR-Cas9 system of genome editing was named the 2015 Breakthrough of the Year by *Science.* The technology has ignited international interest because of insights it may offer into fundamental biological processes and advances it may bring to human health. But with these advances come many questions, about the technical aspects of achieving desired results while avoiding unwanted effects, and about a range of uses that may include not only healing the sick, but designing human beings. It is important now more than ever to consider these questions. Clinical trials using human somatic cells are already underway and more are being anticipated. To help direct the use of genome editing toward promoting human wellbeing, it is important to examine the scientific, ethical, and social issues it raises, and assess the capacity of governance systems to ensure its responsible development and use. This paper examines possible implications for genome editing and provides recommendations for maximized potential. Humans are on the cusp of a gene editing revolution. The question is, are we ready?

Summary of Research Methods

This report provides information on the highly contested subject of genome editing. Conclusions and analyses made within the report are a result of conducted research from a variety of academic sources. These include, The National Academy of Science, The National Academy of Medicine, The Nuffield Council on Bioethics, The Centre of Genomics and Policy, The World Health Organization (WHO), Commission de l'éthique en science et en technologie, non-governmental organizations including the United Nations, scholarly journals and news articles.

Culmination of this report was made possible in large part to the diverse perspectives and insights of the experts involved. I am grateful for the contributions of Dr. Vardit Ravitsky, Dr. Shane Green and Dr. Gronostajski for their willingness to participate and assist my research. In particular, I would like to express my deep gratitude to Dr. Ravitsky for her extensive knowledge and generosity in providing many valuable sources and recommendations.

Information in the report examines genome editing in both a historical and modern context, demonstrating the evolution of gene-editing technology and the current need for effective governance and collaborative action. The purpose of the utilized research methods was to produce a report that reflects objectivity, factual evidence and responsiveness to relevant issues.

Definition

In order to assess the practice of genome editing, it is important to define the scientific concepts and terms that will be employed throughout the paper.

There are roughly 37.2 billion cells in an average human body.[1] There are two categories of cells within eukaryotic organisms. Somatic cells are nonreproductive cells that are present in almost every area of the body, including the skin, liver and heart. These cells are identical to one another and are responsible for basic organism functionality including repair of tissue, protection of internal structures and contribute to the body's major systems. Somatic cells refer to essentially all the cells of the body except for the germline.[2] Germline (reproductive) cells reside in the sexual organs that produce sperm and eggs. DNA present in the germline is heritable, meaning it is passed on through generations.

DNA (Deoxyribonucleic acid) is the genetic material in almost all living organisms. DNA plays a crucial role in directing cell function, providing instruction to build and repair cells and determining amino acid sequences. These sequences of four different sub-units, called nucleotides, determine the expression of an organism's biological roles and traits. Although there is no generally agreed definition of the term 'genome', it is understood that genomes comprise the chemical deoxyribonucleic acid (DNA) or, in the cases of some viruses, the related chemical ribonucleic acid (RNA).[3] More specifically, the genome may be used to refer to the particular sequence of nucleotides in an organism.[4]

Genome editing is the practice of making targeted interventions at the molecular level of DNA or RNA function, deliberately to alter the structural or functional characteristics of biological entities.[5] Genome technologies act like scissors, cutting the DNA at a specific spot. Then scientists can remove, add, or replace the DNA where it was cut.[6] This process can be

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[1]An estimation of the number of cells in the human body. (2013, July 5). *National centre for biotechnology information.* https://www.ncbi.nlm.nih.gov/pubmed/23829164

[2] National Human Genome Research Institute (NHGRI). (2017, March 1). Genome editing. *Genome.gov.* https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-human-genome-research-institute-nhgri

[3] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

[4] ibid

[5] ibid

[6] National Human Genome Research Institute (NHGRI). (2017, March 1). Genome editing. *Genome.gov.* https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-human-genome-research-institute-nhgri

applied to complex living organisms, such as humans and animals, tissues and cells in culture, and plants, bacteria and viruses. The focus of this report will be on the application of genome editing in humans.

There is a diverse range of genome editing technologies. The most widely recognized method within the scientific community is a molecular tool called CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). The process (appendix I) begins with the injection of gene modification particles into the patient. Each particle holds three components that assist the cut and paste process. A guide gene leads the other components in locating the defective gene on a DNA strand. An enzyme in the editing package removes the defective gene through precise incisions. Finally, the healthy gene enters the nuclei to take the place of the mutated gene.

Other forms of genome editing include base editing, gene drives and epigenome editing. Base editing utilizes chemical reactions to create changes to genetic strands as opposed to cutting the DNA into pieces. Gene drives propagate particular genes within a population to influence the transmission of dominantly inherited genes by offspring. An exciting prospect currently being developed by scientists is the method of epigenome editing. Rather than completely deleting genes from individual organisms, this technology will allow scientists to minimize or maximize the prominence of defective genes.

Prospects indicate genome editing technologies will allow wide-scale intervention to occur in all areas of the body, including at the germline or in the human embryo. Genome editing provides long-lasting effects to the DNA as alteration at the genome causes the reproduction of those genes as they divide. Although uncertainty and safety concerns remain, modern technologies have demonstrated increased levels of specification.

Significance

The advent of CRISPR-Cas9 gave rise to emerging scientific and medical opportunities. Since introduction, ethicists have identified the moral, legal and social, and scientific and technological ramifications of genome editing practices. There remains a persistent gap in social consensus and understanding. The line that distinguishes acceptable and inappropriate uses has not been firmly defined. Dialogue and prospective analysis are needed to ensure the benefits of genome editing are maximized while the risks are both limited and acknowledged.

Scientific and Technical Considerations

Although techniques and knowledge of genome editing processes have improved, many hold the view that the current state of knowledge surrounding genome editing is insufficient. There is a wide agreement in the scientific community that, for clinical germline editing, the risk of failing to make the desired change or of introducing unintended mutations is unacceptably high.[7] However, the right to free scientific inquiry holds priority among researchers. The pursuit of scientific knowledge, in general, will contribute to more powerful technologies that can, in turn, give rise to productivity and welfare benefits.[8] It also requires consideration of what might be given up if technologies are ruled out because they are 'wrong' in principle. Professor Doudna, pioneer of the CRISPR-Cas9 system stated in an interview with the Guardian, "I have come to feel that the greatest problem may be fear itself. It is important to understand that the CRISPR technology has the potential to do many beneficial things for society. To reject that technology because we are uncertain of the way it may be used in the future, I think would be a mistake."

Another area of consideration is the ability for the cost, efficiency and versatility advantages of the CRISPR technology to increase rates of experimentation. This may lead to contingent limits on the rate of adaptation to new knowledge within the scientific community (and the relative capacity of ancillary functions such as scientific publishing and peer-to-peer

[7] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5

[8] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

communication), leading to a lack of coordination among research groups and unnecessary duplication of work.[9] On the other hand, competition may lead to increased experimental output and enhanced data quality.

There are also uncertainties surrounding the associated risks of manipulating certain genes and mutations. Replacing particular genetic variants with alternative ones may lead to unintended consequences. While certain genes are known to cause a specific disease, absence of that gene could increase the risk of other diseases. For instance, the gene SLC39A8 decreases a person's risk of developing hypertension and Parkinson's disease, but increases the risk of developing schizophrenia, Crohn's disease and obesity.[10] Sickle-cell mutations also serve an important role in protection against malaria. The gene APOE4 would also not be a good candidate for germline editing because it may confer some protection against liver damage by hepatitis C infection. The unpredictable outcomes of modifying particular genes would put significant health and safety risks on patients.

Medical Opportunities

Healthcare continues to be a pressing issue in society. Increased prevalence of disease creates demand within medical communities to produce new diagnostic and treatment tools. Genome editing allows scientists to change the genetic makeup of individuals that causes or increases susceptibility to disease or infection. Somatic modification is currently being used in the context of gene therapy and clinical trials. Today there are over 10,000 diseases created by mutations in a single gene (monogenic diseases).[11] The use of gene manipulation has been focused on rectifying monogenic diseases containing somatic cells. Using the CRISPR-Cas9 system, researchers were able to edit the CFTR gene responsible for mutations that lead to cystic fibrosis and in the dystrophin gene, in which mutations lead to Duchenne and Becker muscular

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[9] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

[10] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5

[11] WHO. (n.d.). Genes and human diseases. *World Health Organization.* https://www.who.int/genomics/public/geneticdiseases/en/index2.html

dystrophy.[12] Various clinical trials have also tested the effectiveness of the CRISPR system in cancer therapies in which prostate cancer, esophageal cancer and renal cancer were treated. The Recombinant DNA Advisory Committee (RAC) of the US National Institute of Health (NIH) believes that with further advancement and ensured safety of the CRISPR system, additional cancer types including; relapsed refractory multiple myeloma, melanoma, synovial sarcoma, and myxoid/round cell liposarcoma could be treated.[13] There is also evidence that CRISPR-Cas9 could be used to target and disrupt the genomes of viruses directly.[14] Research of the Hepatitis B virus indicates genome editing could control the virus and possibly cure patients.[15] Genome editing technology also poses a promising future for the treatment of hematological diseases (diseases pertaining to blood). Hemophilia is a disorder in which blood doesn't clot normally because it lacks sufficient blood-clotting proteins (clotting factors).[16] Allife Medical Science and Technology Co. (AMST) released a study regarding the potential for genome technologies in the treatment of hemophilia in 2016. AMST stated that they believed the CRISPR system could be applied through the insertion of a corrective FIX transgene into the subject's albumin locus, severely reducing clotting in the liver. Scientists believe similar processes could be applied to the diagnosis and treatment of Sickle Cell Disease, a disease associated with abnormal protein concentration in red blood cells.

While there is currently general acceptance of somatic modification, greater controversy is held in the argument of germline editing. This contention is due to the heightened risk germline modification presents in that the edits would be heritable, and their effects could be multigenerational. Though genetically inherited diseases are rare, collectively they affect a sizable fraction of the population (about 5-7 percent).[17] Some argue that germline editing is

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[12] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[13] Li, H., Yang, Y., Hong, W., Huang, M., Wu, M., & Zhao, X. (2020, January 3). Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. *Nature.* https://www.nature.com/
[14] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[15] ibid
[16] Mayo Clinic. (2019, August 22). Hemophilia. *Mayo Clinic.* https://www.mayoclinic.org
[17] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

urgently needed to stop children from being born with severe genetic diseases. Others point to how transmission of severe disease causing genes is mitigated through existing alternatives. These include, deciding not to have children, adopting a baby, prenatal testing, embryo donors, sperm donors, egg donors or adoption.[18] These options, however, sacrifice the genetic relationship between parents and their children, which is of great importance to many people. This desire is proven by the fact that the majority of prospective at-risk parents will choose to have an affected child over foregoing the genetic relationship.[19] A desirable avenue for many at-risk couples is generally that of in vitro fertilization (IVF) in conjunction with preimplantation genetic testing (PGT). This process identifies affected embryos and discards them to ensure only healthy ones have the potential for fetus production. For a tiny fraction of couples, however, they can not attend to IVF and PGT procedures as 100% of their embryos will be affected. These rare couples may present the strongest case for considering clinical germline editing, because the technology would be their only way to conceive unaffected children who are biologically related to both parents.[20] The parental benefits of having genetically unaffected children are considerable. The technology would alleviate various emotional and financial burdens and allow for the birth of a child that would enjoy better health and an increased life span.

Social Justice

Many concerns arise regarding the threat genome editing poses to social justice. This technology has the potential to exacerbate existing inequalities and further disadvantage groups that occupy positions of vulnerability. The use of genome editing to eliminate the presence of non-life-threatening conditions (i.e. down syndrome) may risk perpetuating stigmatization and negative attitudes towards already marginalized groups and detract from a society that for example, fosters respect and fair treatment for women and people with disabilities.[21] Jackie

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[18] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5

[19] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

[20] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5

[21] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

Leach Scully, a disability advocate, believes genome editing sets us on a "slippery slope" toward intolerance of disability. There is also an argument for the preservation of human diversity, individuality and visible representation. Disability justice and rights scholars have made a range of arguments such as the right to life for people with disabilities, to arguments for the social and emotional value of biological difference, to the value to humankind of conserving disability cultures.[22]

Some note that germline editing has the potential to create a level playing field for those whose traits put their children at a genetic disadvantage.[23] The principle of replacing a disease gene variant with a corresponding, common, nondisease variant, as such change would give the offspring no social advantage would not necessarily experience opposition.[24] Coversly, predictions on the use of genome editing for enhancement purposes continues the argument that genetic modification would make a culturally determined inequality into one that is biological.

There is also a risk that if genome editing becomes an approved and available health care, it would lead to the creation of two classes of citizens: those who have the financial means to use it, and those who do not. Introduction of genome editing has the potential to interfere with established values practiced in global healthcare systems. First, genetic modification would hinder the principle of equal opportunity since it would allow some people to enjoy good health while for others, the range of opportunities available to them would be significantly reduced.[25] While inequality already exists in the form of better nutrition and use of vaccines among the advantaged populations of the world, some critics are concerned about adding yet another, more durable form of superior access to better health.[26]

Another area of consideration is the principle of responsible resource allocation.[27] Widespread application of genome editing into medical practices would be a significant financial

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[22] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[23] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1
[24] ibid
[25] ibid
[26] ibid
[27] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf

investment. The technology has not reached the point of becoming a medical need or meeting a cost-benefit ratio. Expenditures like genome editing risk detracting from other areas of medical and social importance. Some view the technology as another example of a society allocating considerable resources to developing a technology that will benefit only a small minority when this money could be used to relieve the sufferings of millions through already existing technologies. Isaac Mwase of the Kennedy Institute of Ethics Journal further explains, "It is outrageous to discuss genetic enhancements for the privileged in developed countries, when the poor of these same nations and of others around the world lack even rudimentary access to the health-care services needed to ensure basic survival. If the gap between the privileged and the underprivileged continues to grow, wealth-based access to healthcare and future genetic enhancements will threaten the basic structures of society."

Enhancement

The accelerated pace at which genome editing is advancing has caused many to question if society is approaching a future of designer babies. The technology could eventually be used to allow parents to select the characteristics of their unborn child, including physical or psychological traits (eye colour, personality traits, gender, cognitive ability, physical strength).[28] Some believe this prospect is inevitable due to the social pressures and expectations placed on parents and individuals. Many scientific advances in the past have proven this notion including reconstructive surgery (which has led to plastic surgery for aesthetics) and prenatal screening for lethal disorders (which has led to screening of carriers for disease genes and preimplantation screening for nonlethal, even late-onset disorders).[29] In a study published by the New England Journal of Medicine, participants demonstrated support for genome editing in certain circumstances. The majority of respondents indicated that they were comfortable with the use of genome editing in humans to treat disease (i.e. somatic modification) or to prevent a

[28] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf
[29] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

life-threatening or debilitating disease in future generations (i.e. germline modification), but oppose the use of technology to enhance non-disease characteristics (i.e. genetic enhancement).[30]

Precluding access to genome editing technology, however, contradicts aspects of personal and parental autonomy, which value is variant depending on country and culture. Clinical ethics accepts the idea that parents are, almost always, the most appropriate surrogate medical decision makers for their children until the children develop their own autonomy and decision-making capacity.[31] There are others that do not share the view of parental autonomy, and see germline editing as a step toward seeing children as constructed products and an increasing intolerance of their inevitable imperfections and failures to live up to parental expectations.[32]

Eugenics

Many suggest that genome editing is likely to express 'eugenic' views or exacerbate what has been described as 'selection society.'[33] The goal of eugenics is to improve human genetic traits by reducing the reproduction of people with socially undesired traits (negative eugenics) and/or promoting the reproduction of people with socially desired traits (positive eugenics).[34] Manipulating genetics allows individuals to select 'desirable' traits and remove 'undesirable' ones. Notably, Nazi eugenic experiments promoted ethic cleansing through the Holocaust movement and forced sterilizations. Genetic editing combined with cultural values has the potential to move our society towards an "perfect" race, paralleling the Aryan race which the Germans idealized. In an interview with The Guardian, Jennifer Duodna stated, "fairly early on in the development of the CRISPR technology, I had a dream in which a scientist was introducing me to a man in a dark room. When that man turned around it was Adolph Hitler

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[30] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf

[31] US National Library of Science. (2017, August 3). Human Germline Genome Editing. *NCBI.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5544380/

[32] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

[33] ibid

[34] Ishii, T. (2017, January). Germ line genome editing in clinics: The approaches, objectives and global society. *Research Gate.* https://www.researchgate.net/publication/284847889_Germ_line_genome_editing_in_clinics_The_approaches_objectives_and_global_society

asking me to describe to him how the CRISPR technology worked and tell him how it could be useful. That was one of the things that motivated me to begin discussing publicly the implications." Though there has been advancement in social progress and human rights policies, Daniel Kevles, a historian of science at New York University, argues that it does not mean we are immune to going down that path again.[35]

Background

The concept of genome editing is relatively new within the scientific community. Since introduction, knowledge regarding somatic and germline cells has improved, resulting in biotechnological advances in genome editing techniques.

Early attempts at DNA alteration held developmental challenges and limitations in the research that could be done. The first transgenic mice (mice containing DNA from other species) were produced in the mid 1970s.[36] Transgenesis only allowed genes to be added and offered no control over where the genes were added into the subject. In 1989, it became possible to make direct alterations into the genomes of embryonic stem cells. Derived from the inner cell mass of the early embryo, embryonic stem cells have the potential to develop into many distinct types of cell in the body. The technically challenging nature of embryonic stem cell procedures hindered its development and application in clinical trials. The process remains time-consuming, expensive, variable, often highly inefficient, and requires a special skill set.[37]

The first documented gene therapy procedure took place on September 14th, 1990. The procedure was performed on four-year-old patient Ashanti DeSilva, born with the rare genetic disorder of SCID (Severe Combined Immunodeficiency Disease). The disease affected her immune system and caused her to experience increased vulnerability to standard germs and infections. At the time, the probability of children diagnosed with this disease living past the age of 6-7 years old was extremely low. This forced Ashanti to live in an isolated and sterile

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[35] Lewis, T. (2015, December). The major concern about a powerful new gene-editing technique that most people don't want to talk about. *Business Insider.* https://www.businessinsider.com /gene-editing-history-of-eugenics-2015-12

[36] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

[37] ibid

environment, avoid contact with people outside of her family and regularly consume antibiotics. In this procedure, doctors removed the white blood cells (cells responsible for defending the body against disease) from the patient's body. For a two week period, the cells grew in the lab and doctors precisely inserted the missing gene into the cells. Culmination of the procedure resulted in a genetic infusion of the new blood cells back into the patient's bloodstream. Laboratory tests later confirmed that Ashanti's immune system was strengthened by 40%; she no longer experienced recurrent colds and was able to attend school.

Limitations of previous genome editing techniques justified a continued search for alternative gene targeting technologies. In 2005, zinc finger nucleases (ZFNs) were created, leading to the development of transcription activator-like effector nucleases (TALENs) in 2010. ZFNs and TALENs contain a set of 'fingers' that can be designed to identify specific sequences on a DNA strand. Each device attached to an enzyme produces a targeted double-strand break in the genome, activating the cellular repair processes to add new DNA where the breakage took place. This process still presents risk, as there is a chance the break will be made at an unintended point in the genome and it requires considerable effort to design, synthesize and optimise a pair of proteins for every procedure.

The CRISPR technology has been a massive revolution in genome editing. In 2012, it was discovered that a system of defense against antiviral attack found in the bacterium *Streptococcus pyogenes* could be adapted as a programmable system for genome editing.[38] When DNA is damaged as a result of a virus, cellular machinery kicks in to fix the strand that has been damaged. With the CRISPR system, using a protein called Caste9, scientists are able to convince those repair processes to make the desired edit as opposed to natural reconstruction in the case of ZFNs and TALENs. Many scientists who perform genome editing now use CRISPR.[39] By the end of 2014, CRISPR had been mentioned in more than 600 research publications and by June, 2016 this figure had more than doubled.[40]

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[38] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[39] National Human Genome Research Institute (NHGRI). (2017, March 1). Genome editing. *Genome.gov.* https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-human-genome-research-institute-nhgri
[40] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

Initial discovery of genome editing resulted in tremendous excitement and hope within the medical community. Prior to recent developments, gene editing was viewed solely as a healthcare application. Due to this narrow identification of opportunity, genome editing was received positively by those involved. However, as the technology has improved and become increasingly efficient, scientists have recognized ethical concerns and a need for effective regulation.

Experts

The genome editing industry has welcomed many accomplished medical professionals and scientists that have contributed to dialogue and research regarding the implications and technical aspects of genetic modification technologies.

Expert 1: Dr. Richard M. Gronostajski

Dr. Richard M. Gronostajski is a Professor of Biochemistry at the Jacobs School of Medicine and Biomedical Sciences at the University of Buffalo. Dr. Gronostajski is also the director of the Genetics, Genomics, and Bioinformatics Graduate Program and of the Western New York Stem Cell Culture and Analysis Centre (WNYSTEM). From 1985-1992, Dr. Gronostajski served as an assistant professor for Medical Biophysics at the Ontario Cancer Institute at the University of Toronto. Dr. Gronostajski is also a member of both the International Society for Stem Cell Research (ISSCR) and the Society for Developmental Biology (SDB). Dr. Gronostajski's research has focused on analyzing the impact of the Nuclear Factor I (NFI) through the use of mouse embryonic stem cells on brain and lung development. These analyses contribute to an understanding of what factors influence gene differentiation in later development including susceptibility to disease and phenotypic characteristics. After evaluating Dr. Gronostajski's work, an email interview was conducted (appendix III) in which he provided several valuable insights. When asked about his predictions for the future of genome editing, Dr. Gronostajki expressed a similar view to many other experts in that given the current state of knowledge, germline editing should not be an available option within the next 10 years. His main concerns lie in the potential for off target effects and somatic mosaicism. Unintended genetic

modifications as he explained are hard to correct and have the ability to cause serious health related issues. The tolerance for off-target effects in the germline will be much less given that adverse effects can be multiplied across generations. Dr. Gronostajski then introduced the topic of somatic mosaicism. It is possible there may be more than one somatic cell population causing a particular disorder. In the case of genome editing, some cells may be modified and others may not, which fails to remove genetic disease. Dr. Gronostajski also identified alternative applications of genome editing. He noted that modification of fertilizer could be used to promote global health and wellbeing, and that genetically modified organisms might be used to clean up toxic waste in the future.

Expert 2: Dr. Shane Green

As a former director of outreach and lead advisor of GE3LS (genomics-related ethical, economic, environmental and social issues) at the Ontario Genomics Institute, Dr. Shane Green is a qualified expert in the field of genome editing. Dr. Green has a multidisciplinary background in cell and molecular biology, bioethics and global health and development. During his time at the Ontario Genomics Institute, Dr. Green led the implementation of several outreach programs to various stakeholders including researchers, government, teachers, students and the general public. As program leader of the Ethics, Social Impact and Outreach program, Dr. Green participated in the integration of several genomics research projects and served on the board of GE3LS representatives for Genome Canada. Dr. Green stresses the importance that existing regulations against false advertising are enforced, proper certification for profiling labs is maintained, more genetic testing-related information is made available to healthcare professionals, and ways to increase the number of qualified genetic counsellors are sought.[41] When reaching out to Dr. Green, he revealed that he had moved into global health and development and had not been following genomics and gen-ethics closely since his career change. He was able, however, to provide a valuable connection with Dr. Vardit Ravitsky.

[41] Green S., Spear M. (2009, September 9). Getting Personal with DNA: From Genome to Me-Ome. *Journal of Ethics.* https://journalofethics.ama-assn.org/article/getting-personal-dna-genome-me-ome

Expert 3: Dr. Vardit Ravitsky

Dr. Vardit Ravitsky holds a PhD and is an Associate Professor of the Bioethics Programs within the Department of Social and Preventive Medicine at the University of Montreal. Dr. Ravitsky is President of the International Association of Bioethics, member of the Standing Committee on Ethics of the Canadian Institutes of Health Research (CIHR) and of the Institute Advisory Board of CIHR's Institute of Genetics. She is also a member of the National Human Genome Research Institute's (NHGRI) Genomics and Society Working Group. Her research interests in bioethics include genetics, reproductive technologies, health policy, and cultural perspectives. Dr. Ravitsky was able to provide valuable insight and opinions regarding genome editing in a conducted phone interview (appendix IV). An interesting concept Dr. Ravitsky introduced was the connection between human identity and genetics. In the future, CRISPR may begin modifying genes that are genetically complex such as height, intelligence and gender. "From that perspective, CRISPR could open the door to not just fighting against disease but to changing identity," states Dr. Ravitsky. This outlook also relates to the genome editing technique of Mitochondrial Transfer. In this process, conception involves using part of the genome (mtDNA) of a third person.[42] Many ethicists have recognized the potential impacts of three genetic contributors on a child's personal identity including atypical family dynamics and a confused sense of self representation.[43] Another takeaway from the interview was the importance of international harmonization. Without international coordination, she explained there is a potential for medical and scientific tourism. This raises serious health and safety concerns as studies will be carried out in countries with less rigorous scientific oversight and regulation.

[42] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf
[43] ibid

The Role of Control

Control is the power to make all the important decisions about the way that an organization, place or system is run.[44] The question of who holds control over genome editing technologies has not been clearly defined. There is no singular answer as there are many individuals and groups who hold varying levels of influence.

The first level of power is the scientists. When a new technology is introduced, scientists have a desire to push experimental boundaries. A prime illustration of this is the work of He Jiankui. Jiankui is the biochemist who delivered the first humans with entirely genetically modified cells using the Crispr-Cas9 system. He was labelled a "rogue" scientist. Government bodies rushed to assemble expert groups to develop regulatory guidelines that could prevent similar actions from other outliers.[45] There were publicly available guidelines that would indicate He's experiment unsafe and in violation of multiple codes of conduct. Yet He has defended his experiments by arguing that he had 'complied with all the criteria' laid out by those guidelines.[46] It was also revealed that multiple American and Chinese scientists were aware of He's intentions, and allowed him to proceed. Basic research can be applied in uncontrolled ways and by scientists who may not be socialized into the notional global community of responsible researchers.[47] Established guidelines and regulations are dependent on scientists to interpret and implement them into their research practices.

As the prevalence of these technologies increase, government bodies continue to play an active role in the governing process. These bodies are referred to as the second level of power. Many authoritative structures have adopted frameworks that incorporate input from a variety of medical, bioethical and academic communities. Although the government has the final say in approval of policies, laws and regulations, the recommendations of these organizations are vital to the decision-making process. In the United States, governance of enhancement applications

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[44] Collins English Dictionary. (n.d). Definition of Control. *Collins.* https://www.collinsdictionary.com/dictionary/english/control

[45] The Guardian. (2020, March 4). Doctors use gene editing tool Crispr inside body for first time. *The Guardian.* https://www.theguardian.com/science

[46] ibid

[47] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

are controlled by the Food and Drug Administration (FDA), the Recombinant DNA Advisory Committee (RAC), institutional biosafety committees (IBC) and institutional review boards (IRB). These groups all have different roles and influence over the eligibility for citizens to receive such treatments. The RAC provides a platform for somatic enhancement proposals to be made. The IRBs and the FDA are responsible for identifying individual, societal and medical benefits of somatic enhancement procedures as well as the risks to the individual, public health, and environmental safety. IBCs work directly with the government to examine the recommendations of the IRBs and the FDA and apply them to legal contexts. Funding for these enterprises is accomplished through the government as well. These bodies have an important role in developing clear and equitable criteria that is provided to the medical professionals. This level has control over determining the balance between free scientific inquiry and standards for responsible research. Dr. Ravitsky states that "making it a criminal act, people may still do it but they will go to prison which is what happened in China. That is why it is the second level of power because people can still do it but there will be repercussions."

It is also important to note the current control mechanisms within pharmaceutical companies. Pioneers in the genomics industry predict versions of these technologies will eventually become available in the form of off the counter medication. It is important to keep in mind that once a medical product has been approved for a particular purpose and population, the sponsor is limited to marketing it for its "labeled" indications, but individual physicians are free to use their judgment and prescribe the product for other uses and other populations.[48] This model gives physicians significant control over the application of certain treatments and becomes an important consideration regarding the potential for genome editing commercialization.

Dr. Ravitsky explained that the third level of power is the public. In the past, debate on genetic issues has been limited to specialists. The public needs to have a certain level of control and active participation in the future. This is for two main reasons. First, a great deal of research in the academic sector is publicly funded, from the money collected through general taxation. This implies that the money is spent in a way that reflects public priorities and pursues them with

[48] National Academies of Sciences. (2019, January 10). Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop–in Brief. *NAP*. https://www.nap.edu/catalog/25343/second-international-summit

the greatest possible efficiency.[49] The second reason is that the products, practices, processes and tools produced by the application of knowledge gained through research have a direct or indirect impact on the wellbeing and welfare of the public.[50] It is for this reason that the role of the patient is so vital. The magnitude of genome procedures require everyone involved to be fully engaged in the process. On a global scale, governing bodies and institutions have recognized the necessity of providing individuals with an in-depth consent process to promote patient autonomy. The foundation of genome editing practices should ensure there is patients' control over their participation in research.

It has been addressed that genome editing may expand to the consumer level. CRISPR-Cas9 requires skills that can be readily acquired by those with standard degree level skills in molecular biology, which both potentially lowers the cost of deploying it (if it is no longer necessary to have extensively trained specialists) and increases the potential pool of users (this pool might potentially extend to include non-specialists and even amateur enthusiasts).[51] CRISPR toolkits are currently available for purchase for less than $200. As Dr. Ravitsky stated, "we call them 'biohackers' but they are not really hacking anybody, they are just doing things to themselves, to their own bodies, because they do not have patience for the approval processes that we require in society."

To some degree, everyone holds power in the conversation. There is no simple answer as to who should hold control over genome editing technologies. If genome editing is to become a fully integrated technology in medicine and science, cooperation and consensus of all parties involved is essential. Principles of scientific freedom and inquiry are valued within Western societies, however, it is important scientists are held to high standards when handling transformative biotechnologies. Although governments play an important role in accountability and enactment of accountability structures, experts in bioethics and scientists should hold the dominant voice in the conversation. It should not be up to politicians to develop regulations on technologies of which they do not understand the applications or associated risks.

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[49] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[50] ibid
[51] ibid

International Organizations

Genome editing requires the effort of scientific institutions and organizations for contribution to research and effective management strategies. Organizations contributing to the genome editing movement include the National Human Genome Research Institute (NHGRI), the United Nations Educational, Scientific and Cultural Organization (UNESCO) and the Global Alliance for Genomics and Health.

National Human Genome Research Institute

The NHGRI has made significant strides for the genome editing movement. The organization works in research-oriented projects to provide genomic education and investigate social, legal and ethical implications. As a leading authority in the field of genomics, their mission is to accelerate scientific and medical breakthroughs that improve human health. They do this by driving cutting-edge research, developing new technologies, and studying the impact of genomics on society.[52] The defining attribute of the organization is its past involvement in the International Human Genome Project. The Human Genome Project, which had as its primary goal of sequencing the 3 billion DNA letters that make up the human genetic instruction book, was completed in April 2003.[53] In addition to participation in the International Human Genome Project, the NHGRI has participated in research efforts focused primarily on the influence of genomic principles on human health and disease. This research occurs across a spectrum: basic research to shed light on the structure and function of the genome; translational research to decipher the molecular bases of human diseases; and clinical research to establish how to use genomic information to advance medical care.[54] The NHGRI is composed of several branches including Cancer Genetics and Comparative Genomics, Computational and Statistical Genomics, Genetics Disease Research, and Translational and Functional Genomics, among others. The organization's ability to provide expertise in many areas allows it to contribute to diverse research. Current projects the organization is involved with include the Limb Morphology

[52] National Human Genome Research Institute (NHGRI). (2017, March 1). Genome editing. *Genome.gov.* https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-human-genome-research-institute-nhgri
[53] U.S Department of Health and Human Services. (2019, November 5). Human Research Standards. *HHS.* https://www.hhs.gov
[54] ibid

Database, Zebrafish Insertion Collection, Breast Cancer Information Core and the Hydractinia Genome Project Portal.

United Nations Educational, Scientific and Cultural Organization

The United Nations Educational, Scientific and Cultural Organization (UNESCO) is a branch of the United Nations that supports a number of genome editing initiatives. The Universal Declaration on the Human Genome and Human Rights, of which UNESCO subscribes, refers to the principles of dignity, diversity and equality, and supports the concept of the human genome as a symbol of humanity's heritage.[55] In 1993, UNESCO developed the International Bioethics Committee (IBC). Composed of 36 independent experts from around the world, the IBC provides the only global forum for bioethics reflection.[56] The organization has 5 main functions to contribute to bioethic knowledge.

Courtesy of the UNESCO digital library, the IBC states their goals as follows:

1. To promote reflection on the ethical and legal issues raised by research in the life sciences and their applications.
2. To encourage the exchange of ideas and information.
3. To encourage action to heighten awareness among the general public, specialized groups and public and private decision-makers involved in bioethics.
4. To co-operate with the international governmental and non-governmental organizations concerned by the issues raised in the field of bioethics as well as with the national and regional bioethics committees and similar bodies.
5. To contribute to the dissemination of the principles set out in the UNESCO Declarations in the field of bioethics, and to the further examination of issues raised by their applications and by the evolution of the technologies in question.

Rather than participating in action-oriented projects, the IBC provides insight and engages in dialogue to provide recommendations to legal and government bodies. The committee released an extensive report in 2015 providing a reflection of the human genome concerning human rights

[55] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf

[56] UNESCO. (2020, February 6). International Bioethics Committee (IBC). *Unesco.* https://en.unesco.org/themes/ethics-science-and-technology/ibcInternational

and framework for effective management strategies. The IBC stated in the report that they recommend a moratorium on human germline modification until concerns about its safety and efficacy have been addressed.

Global Alliance for Genomics and Health

The final organization is the Global Alliance for Genomics and Health (GA4GH). The GA4GH's mission is to provide a platform for researchers to share genomics and other health-related information. The organization accomplishes this through the integration of over 500+ organizations and members from over 90 countries working in healthcare, research, patient advocacy, life science and information technology. The access and sharing of genomics data is managed through cultivating a common framework of standards and harmonized approaches for effective and responsible genomic and health-related data sharing.[57] These standards are achieved through close attention to the Framework for Responsible Sharing of Genomic and Health-Related Data. The organization states that the core elements for responsible data sharing include transparency, accountability, data quality and security, privacy, data protection and confidentiality, risk-benefit analysis, recognition and attribution, sustainability, education and training and accessibility and dissemination. Notable projects of the GA4GH include the European Genome-phenome Archive (EGA) and the Australian Genomics Health Alliance (AGHA). The EGA provides a wide-scale framework for the sharing of medical experiments and a baseline for establishing patient consent. The AGHA provides resources within Australia to partner organizations for the goal of finding methods to shorten diagnosis times, enable early intervention and provide access to treatment for people with genetic disorders.

[57] Global Alliance for Genomics and Health (GA4GH). (n.d). About Us. GA4GH. https://www.ga4gh.org

Case Studies

Case 1 - China

China is the world's most populous country and is now considered the second largest by land-mass.[58] With close to 1.4 billion citizens, China accounts for almost 20% of the world's population.[59] The nation is located in East Asia and borders Mongolia and Kazakhstan. China is one of the world's oldest civilizations and has been ruled by a centrally controlled government and the Communist Party since 1949. The national language of China is Mandarin and 92% of the population is held by the ethnic group Han. China has the second-largest economy in the world, with a GDP of $6.988 trillion.[60] Despite economic prosperity, China remains a developing country, ranking 85th on the UNDP Human Development Index[61] with 373 million citizens living below the poverty line of USD 5.50 a day.[62]

A defining characteristic of China is its prioritization of education. In 1986, the Chinese government passed a compulsory education law, making nine years of education mandatory for all Chinese children. Today, the Ministry of Education estimates that above 99 percent of school-age children have received a universal nine-year basic education. China has about 400 million students today and investments in education account for 4% of the country's GDP. Education institutions in China reflect an emphasis on competition and achievement. Only a small minority of the most academically proficient individuals can pursue careers in science, technology, engineering and mathematics (STEM). Higher education in China has played an important role in economic construction, scientific progress and social development by bringing up a large scale of advanced talents and experts. Technological advancement in China has significantly influenced the country's approach to genome editing. China has been identified as a leading technological force, creating world-class industries in everything from 5G and artificial

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[58] Overview of China. (n.d.). *U.S News.* https://www.usnews.com/news/best-countries/china
[59] China - Country Profile, Facts, News and Original Articles. (n.d.). *Global Sherpa.* http://globalsherpa.org/china/
[60] ibid
[61] Human Development Report. (n.d.). Inequalities in Human Development in the 21st Century. *CHN.* http://hdr.undp.org/sites/all/themes/hdr_theme/country-notes/CHN.pdf
[62] The World Bank. (2019, December). China Overview. *The World Bank.* https://www.worldbank.org/en/country/china/overview

intelligence to biotechnology and quantum computing. In 2017, Beijing announced its goal of becoming a world leader in AI technology by 2030. In the minds of China's leaders, from Mao Zedong to Xi Jinping, technological progress is not only a means to economic and military prowess but also an ideological end in itself—offering final proof of China's restoration as a great power after decades of struggle.[63]

Traditional Chinese culture embraces Confucianism ideology, in which moral status is entailed by the acquisition of personhood, which begins at a child's birth (rather than at the time of conception). Consequently, traditional Chinese culture is, by international standards, relatively hospitable to responsible human embryo research. It should also be remembered that China has pursued population control as a public policy objective and, until 2015, strongly discouraged multiple-child families. The move to a 'two-child policy' has boosted the market for prenatal genetic screening and testing, which has prevented genome editing in China from facing the same level of social opposition as other nations. The Chinese government has attached great importance to preventing the transmission of genetic conditions and actively encouraged forms of preconception and prenatal screening.[64]

China has become a world leader in genome editing, adopting a highly research-driven approach. Governance of biomedical research and practice in China is centralized under the National Health and Family Planning Commission (NHFPC), which is responsible for laws, regulations, policies and plans related to public health, including the ethical governance of biomedical research and applications. The NHFPC oversees medical practice in state hospitals and medical institutions and holds genome editing research to a number of safety standards and relevant guidelines.

In 2016, the biophysicist He Jiankui launched a project to edit genes in human embryos with the goal of live birth. Seeking to decrease the children's risk of acquiring AIDS if exposed to HIV later in life, Jiankui attempted to inactivate the gene CCR5, which encodes a receptor that

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[63] Buckley, Chris. (2017, October 24). China Enshrines 'Xi Jinping Thought,' Elevating Leader to Mao-Like Status. *New York Times.* https://www.nytimes.com/2017/10/24/world/asia/china-xi-jinping-communist-party.html

[64] The World Bank. (2019, December). China Overview. *The World Bank.* https://www.worldbank.org/en/country/china/overview

HIV uses to enter cells. Two months after Jiankui had announced via media channels that he had created the world's first babies genetically modified with CRISPR: a set of twin girls named Lulu and Nana, the Chinese National Health Commission immediately ordered an investigation. Jiankui began recruiting HIV positive couples for his experiments in March of 2017. The investigation found that Jiankui, "seriously violated" state laws in pursuit of "personal fame and fortune." According to a report from the Xinhua state news agency, he avoided supervision, faked an ethical review, and used potentially unsafe and ineffective gene-editing methods on the children. The Southern University of Science and Technology located in Shenzhen, China where Jiankui conducted his experiments denied having any knowledge of, or affiliation with, Jiankui's work. Following the release of his experiments through an article published by the *MIT Technology Review,* Jiankui was censured by the Guangdong Health Ministry and fired from his university. Hank Greely, a Stanford law and ethics professor, called the experiment, "reckless [because] of a terrible benefit/risk ratio for the baby." Others have called the experiment "monstrous," "unconscionable" and "premature," and 122 Chinese scientists wrote a joint statement denouncing the work. In December of 2019, He Jiankui was sentenced to three years in prison along with a fine equivalent to USD 480,000 after being declared guilty of "illegal medical practices." It was found out after further examination of Jiankui's work that the two girls demonstrated extensive mosaicism in his data. Such off-target edits leave Lulu and Nana and their descendants vulnerable to various cancers and heart disease and has forced the girls to be subject to research and investigation for the rest of their lives.

The work of He Jiankui significantly impacted Chinese researchers and society. The news was an embarrassment to the country and the Chinese scientific community. As a result, discussions of Jiankui's experiments were widely censored by Chinese media to preserve the country's tarnished reputation. Marcus Wang and Stella Fan, wrote that the Jiankui situation contributed to a shift in Chinese media. Science communication now appears overly politicised and there is little evidence of public media debate or engagement. Following the Jiankui news outbreak, censored topics in China expanded from domestic policies and social unrest to less politically sensitive topics, in what seems to be an effort to support China's international political

image as a 'great power.'[65] Jiankui has caused China to be viewed as a country that does not practice international standards, placing many barriers in the way for scientific progress.

Wang Haoyi, a developmental biologist at the Institute of Zoology in Beijing, a branch of the Chinese Academy of Sciences (CAS), resents the image Jiankui reinforced of Chinese research as the 'Wild West.' "All the news is that Chinese scientists did this, not that it's a single person—it's like they're crazy people," says Haoyi. Genome editing discoveries and insights from China are not adopted by other countries as they were before. Collaborative research with other nations has also decreased dramatically. Wei Wensheng, who uses CRISPR tools to study how humans respond to microbial diseases, worries it might be difficult to get approval to use gene editing tools in clinical trials, including using the tool to edit adult cells, which do not raise the same ethical questions as work in embryos as many people do not understand the difference between somatic and germline cells. "The industry will develop at a slower pace, the government will be more cautious with research funds, and private organizations, such as charities and startups, will be less likely to invest," Kehkooi Kee, a Tsinghua University researcher stated. Many Chinese researchers are not engaging in the same experiments they would previously, fearing unwarranted scrutiny and criticism. "The Jiankui incident has forced Chinese researchers to think twice about future projects" says Chen Jia, who studies at Shanghai Tech University.

Before the Jiankui affair, China did have requirements for approval of human subjects in research and regulations concerning ethical genome research. However, it did not have powerful structures to implement those aspirations, or the precedent of taking action against rogue scientists. Following the Jiankui revelations, the Chinese Education Ministry called on educational institutions to strengthen management of scientific research ethics and inspect research involving gene-editing technology. Chinese President Xi Jinping later formed a national medical ethics committee, which is responsible for approving all clinical trials involving high-risk biomedical technologies and includes not only gene editing, but also cloning, cell therapy, xenotransplantation, mitochondrial replacement and nanotechnology. China has added the use of human genomes and embryos into their civil code under the section that ensures a

[65] Gan, N. (2019, February 13). What China's censors did not want people to see in 2018. *Inkstone News.* https://www.inkstonenews.com/society/what-chinas-censors-didnt-want-people-see-2018/article/3000793

person's right to physical well-being, freedom, privacy and dignity. China has continued to pursue efforts to support responsible science and maintain their position as one of the world's leaders in genome editing.

Case 2 - United Kingdom

The United Kingdom (UK) is a constitutional monarchy and parliamentary democracy. The UK remains an economic, political, military and cultural power around the world despite voting to leave the European Union in 2016. The country is a lead trading power and holds the third largest economy in Europe with a GDP of $2.92 trillion.[66] The UK is made up of four nations: England, Wales, Scotland and Northern Ireland. The UK is located off the northwestern coast of mainland Europe, encompassing a total land area of 241,930 sq km and population of 65.1 million in 2018.[67] The majority, 83.7% of the population, live in urbanized areas and account for only a small fraction of the nation's diverse landscape. The country is recognized for ethnic diversity although struggles with issues of immigration, multiculturalism and national identity. The UK has contributed greatly to western culture, primarily through sport, music and literature.

Many factors influenced the progression of genome editing in the United Kingdom. The existence of a nationalised health service since 1948 allows citizens to enjoy equal access to emerging scientific technologies. As a result, the UK has been largely insulated from concerns about social justice and discrimination that affect countries that rely on privatized insurance-based health and care provision. The UK also remains deeply and actively engaged in international processes and institutions. The country is a member of the multiple organizations that govern the international community, including the United Nations and its Educational, Scientific and Cultural Organization (UNESCO) and the Organization for Economic Co-operation and Development (OECD). Active participation and demonstrated commitment to

[66] World Fact Book. (2019, December). United Kingdom. *World Fact Book.* https://www.cia.gov/library/publications/the-world-factbook/attachments/summaries/UK-summary.pdf
[67] BBC. (2017, June). United Kingdom Profile - overview. *BBC.* https://www.bbc.com/news/world-europe-18027954

international processes is of primary importance to the UK to remain a globally important scientific, technological and political entity. UK policies reflect a national prioritization on human rights, those shared by many other Western European civil law countries who explicitly acknowledge values of human dignity as the foundation and principle of their ethical laws. Biotechnology development in the UK is mainly due to the country's investment in scientific productivity. Launched in 2017, the UK's, "Industrial Strategy: building a Britain fit for the future" raised government funding for research in the life sciences sector to cultivate a world-leading scientific base as an important contributor to economic growth. Life sciences is one of the UK's fastest developing industries, with a turnover of USD 64 billion, employing 233,000 people. The UK is often at the forefront of both scientific developments and ethical reflection internationally. The pioneering position of the UK research base in biology and biomedicine has meant that the UK had to confront many ethical challenges before they arrived elsewhere, often having to invent new ways of doing things.[68] The UK's experience and established precedents surrounding biomedicine and transformative biotechnologies has allowed the country to consistently engage in emerging research without the same level of ethical review and extensive approval processes as other countries.

On March 29th of 2017, the British Prime Minister initiated the process of disengaging the UK from the European Union. The role of Brexit has been significant to genome editing progression in the UK. However, the country has not completely retreated into isolationism and forsworn all scientific, economic and geopolitical relationships with European countries. To date, the UK received nearly USD 6.2 billion from European scientific funding grants. UK businesses operating in the European markets still have to follow EU laws post-Brexit due to their European economic dependence. Nevertheless, Brexit has allowed the UK to experience increased flexibility in scientific research. While the UK remains vested in the values and principles of EU law, Brexit has provided the country with an opportunity to fully embrace scientific innovation and CRISPR research. As the UK continues to depart from the EU, it will be necessary for the government to open the market up further to global business and establish an international

[68] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

presence independent from the EU. The country intends to gain economic growth and national recognition through distinguished scientific research and technological innovation, including investment in genome editing as part of future plans.

The United Kingdom has initiated several somatic clinical treatment breakthroughs. As is the case with China, the UK adopted a more permissive approach to germline modifications. It bans such modifications for reproductive purposes but regulates germline research. The UK's approach to human biotechnology is distinctive and, in some ways, unusual compared to that of many other industrialized states.[69] Genome editing procedures are overseen by the Human Fertilisation and Embryology Authority (HFEA). Framework for modification trial approval is guided by the Human Fertilisation and Embryology Act of 1990. The British 'regulatory state' which encompasses the role of an independent regulatory agency, provides the UK with an amendable approach to public ethical problems and the evolving nature of science. The approach functions by statutory prohibition and qualified permission granted through a licensing system. All uses of gametes and embryos outside of the body are prohibited unless carried out in pursuance of a licence and subject to oversight by the regulator, the HFEA. There is a variety of criteria that must be met to be eligible for a license. For example, such research must be found to be 'necessary or desirable' for one or more of several purposes specified in the Act. Since the Act specifies the purposes for which research may be carried out rather than the procedure used, genome editing techniques may be regarded as merely another tool in a scientist's toolbox provided their proposed use falls within the approved statutory purposes.[70] Under the Human Fertilization and Embryology Act 1990, reproductive biomedicine in the UK is controlled at three separate levels. First, statutory provisions guarantee and distinguish circumstances that are prohibited absolutely and subject to criminal penalties. Other procedures may be conducted only under the grant of a license, through a licensing regime that allows the HFEA to determine what licensable activities may be carried out, by whom and in what circumstances. The HFEA assesses potential risks and benefits through evaluating the kind of cells involved (gametes and embryos), the kinds of activities carried out (creating, keeping, using) and the purposes for which

[69] Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf
[70] ibid

those practices are carried out (treatment services or research). Lastly, the HFEA is responsible for oversight of the clinics that are approved, to ensure licensable activities are carried out following license conditions and in conformity with the Authority's statutory *Code of Practice.*

The Council of Europe's *Convention for the Protection of Human Rights and Dignity of the Being with Regard to the Application of Biology and Medicine: Convention on the Human Rights and Biomedicine* (known as the 'Oviedo Convention') is the only international human rights instrument that explicitly addresses heritable genetic modification.[71] The stated objective of the Oviedo Convention is, "Protecting the dignity and identity of all human beings and guaranteeing everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine." The Oviedo convention allows genetic engineering only for preventative, diagnostic, or therapeutic purposes and only when it is not aimed at changing the genetic makeup of a person's descendants, thus precluding heritable genome editing. The convention has been signed by 35 of the 47 member states of the Council of Europe, though only 29 have ratified it. Although the UK has not signed or ratified the convention, the document has influenced national policy decisions and has been taken into account when developing a domestic framework for areas of biomedicine such as patient rights, consent and privacy, the protection of biomedical research participants or living donors and in relation to applications of biomedicine such as genetics. The UK subscribes to similar principles laid out in the convention through voluntary and national codes.

Advancement of genome editing research within the UK has significant impacts that reverberate well beyond the United Kingdom. Through establishing clinical precedents, the UK has greatly informed public debate nationally and internationally. Though the UK has contributed immensely to scientific knowledge and inquiry, the main areas of significance lie in the nation's ability to respond to ethical challenges. In addition to the UK's contributions to human genetic modification studies and research, the biggest immediate opportunity is in agriculture. At present, fungicides spraying is a common practice within the UK, harming biodiversity and producing lots of emissions. Implementation of genome editing in UK agricultural practices would be of

[71] Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf

great benefit to the country both economically and environmentally. Other identified areas of national potential include improving nutrient quality of food, enhancing agricultural yield, improving animal welfare, encouraging biodiversity and bringing back many extinct species.

The UK has managed to accommodate the ethical challenges and social concerns associated with genome editing quite well. The UK has maintained established norms for responsible research and science set internationally. In a 2015 International Summit, the UK along with science and medicine academics from the US and China, called for a pause of some undefined duration in any attempt at heritable genome editing until the relevant safety and efficacy issues had been resolved and broad social consensus had been achieved.[72] The country can attribute its success to the types of individuals assigned to handle genome editing technologies and its associated ramifications. The sector has grown out of a well-organized cadre of practitioners, socialized through medical training and specialism, whose leaders are typically members of a Royal College (the Royal College of Obstetricians and Gynaecologists) and professional membership organizations (the British Fertility Society, the British Andrology Society and the Association of Clinical Embryologists). Reciprocally, elite members of these organizations have been closely involved in governance making (e.g. through membership of the HFEAs board and committees and through setting professional standards).

Case 3 - United States

The United States of America (USA) is recognized as a leading technological force. The USA has the most powerful economy in the world with a total GDP of $19.49 trillion as of 2017. The nation's wealth can be attributed in part to its rich natural resources including coal, copper, lead and uranium in conjunction with agricultural output. However, the country owes the majority of its economic sufficiency to its highly developed industry and infrastructure. The USA has a population of around 329.3 million and experiences an average population growth of 0.8%. Located in Northern America, the USA has a land area of 9,147,593 sq km of which 82.3% of

[72] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

the population occupies urban settlements. The country prioritizes social progress and quality of life for its citizens. Education and healthcare were shown to be above international averages by the HDI census data analysis from 2019. Advanced economic capacities along with investment in areas of human security, poverty, gender equality and environmental sustainability have deemed the US a developed country.

To date, the US has been the most prolific country by far with regard to 'basic' genome editing research.[73] The US has, internationally, the largest federal research budget. In line with many countries, the US has made significant advancements in somatic genome editing research. The National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) produced a report in February 2017 recommending the use of existing regulatory infrastructure and processes to evaluate future basic laboratory research on genome editing and somatic gene therapy involving genome editing. However, The National Institutes of Health (NIH) has stated that it would not provide funding for research involving the use of genome editing technologies in human embryos in which human embryos are, "destroyed, discarded or knowingly subjected to risk of injury or death."[74] Despite an absence of federal funding, embryonic genome editing research has international surpassing quantities of private funding, allowing research to progress at pace. The NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (2016) states that, "the NIH will not at present entertain proposals for germline alterations but will consider proposals involving somatic cell gene transfer." Francis Collins, Director of NIH, noted, "the concept of altering the human germline in embryos for clinical purposes has been debated over many years from many different perspectives, and has been viewed almost universally as a line that should not be crossed." Should heritable genome editing move into clinical investigations, the US Food and Drug Administration (FDA) would have regulatory jurisdiction under the Public Health Service Act and the Federal Food, Cosmetic and Drug Act. It is likely, however, that legality of research and even clinical application would be left to individual states and locals to develop necessary frameworks for ethical standards and safety. Approval of genome editing procedures are subject to a combination of processes

[73] Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf
[74] ibid

(outlined in section 5: The Role of Control). This includes preliminary approval and transparent review by the NIH's Recombinant DNA advisory committee, local institutional review board and local institutional biosafety committee review and a final oversight and approval from the FDA regarding permission of a clinical trial.

Various aspects of American culture have influenced the country's approach toward genome editing. Religious and political affiliation continue to play a large role in American's views toward genome editing. In a 2015 study conducted by Cary Funk, Brian Kennedy and Elizabeth Sciupac, researchers found that the most highly religious Americans would not want gene editing for their baby while the majority of atheists and agnostics demonstrated overwhelmingly support for genome editing. Governance of emerging biomedical technologies requires consideration of how its implementation will fit into the nation's political culture and the way social interests are constituted and engaged.[75] For example, it would be extremely difficult, given the moral divisions in US society over abortion, to implement the kind of regulatory solution that is currently in effect in the UK. This approach does not include public engagement as a guiding mechanism for genome editing management. In states with unifying national ethos, such as Singapore, South Korea or Nordic countries, governance can shape research and innovation more closely than in regionally and socially diverse states, like the US and China, where a range of activities often goes on despite the apparent comprehensiveness of governance arrangements.[76] A country with deep and immobilising moral division between liberalism and Christian fundamentalism and steeped in permanant conflict over abortion rights has effectivley eliminated the potential for any middle ground on which to build societal consensus surrounding human reproduction. This can be attributed to the US constitution and its defence of civil rights and liberties.

Despite national controversy, the general scientific consensus within the US is that CRISPR is worth the risk, particularly to treat serious diseases with few alternative options.[77] In

[75] Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf
[76] ibid
[77] Smithsonian Magazine. (2019, September). Four U.S CRISPR Trials Editing Human DNA to Research New Treatments. *Smithsonian.* https://www.smithsonianmag.com/science-nature/

the past few years, several clinical trials have launched in the United States using CRISPR to treat and potentially cure patients with serious medical conditions. The first US CRISPR trial was conducted in September of 2019 and led by University of Pennsylvania professor of medicine Edward Stadtmauer. The study consisted of genetically modifying patients' own T cells—a type of immune cell that circulates in the blood—to make them more efficient at fighting certain kinds of cancer cells. The trial is scheduled to conclude in 2033, and it will assess both safety (whether the edited T cell treatment leads to any negative side effects) and also efficacy (measured by outcomes such as whether the cancer disappears, the length of remission, and overall patient survival).[78] Since the first trial, many others have been conducted on diseases such as sickle cell disease, lymphoma and hemophilia. Despite a promising future for genome editing in the US, James Wilson, the former director of the University of Pennsylvania center, said in a recent interview: "It's going to be a long road before we get to the point where editing would be deemed safe enough for diseases other than those that have really significant morbidity and mortality."

Following the discovery of the He Jiankui CRISPR twin experiment, the US established various governance mechanisms to mitigate the potential for rogue scientific behaviour. Through implementation of extensive and rigorous criteria for approval of genome editing procedures as developed by the NIH and the FDA, scientists and researchers have clarity in which activities are acceptable, contributing to responsible research and scientific accountability. The nation has maintained the position that they will not progress research towards heritable genome editing before all relevant safety, ethical and social challenges are properly addressed and effectively resolved. In June 2015, the United States Congress held hearings on "The Science and Ethics of Engineered Human DNA." The hearings resulted in developing a provision that prevents the FDA from using any of its resources to even consider an application to proceed with clinical trials involving germline modification. Three US senators introduced a bipartisan resolution to encourage international cooperation in regulating human genome editing. The resolution has

[78] Smithsonian Magazine. (2019, September). Four U.S CRISPR Trials Editing Human DNA to Research New Treatments. *Smithsonian.* https://www.smithsonianmag.com/science-nature/four-us-crispr-trials-editing-human-dna-for-new-medical-treatments-180973029/

encouraged the Secretary of State to work with other countries and international bodies to, 'forge an international consensus regarding the limits of ethical clinical use of genome-edited human embryos'. As the world of genome editing moves forward, the US has established itself to lead the way in creating ethical standards for gene-editing research.

Canadian Connection

Canada is divided into ten provinces and three territories that extend from the Atlantic to the Pacific Ocean, covering 9.971 million square kilometers. Canada is recognized as the second largest country by land area in the world, with a population of 37.59 million inhabitants.[79] Canada has been ranked 10th in the world on the United Nations Human Development Index, with a poverty rate of under 10 percent. Canada closely resembles the U.S. in its market-oriented economic system. Canada is considered a developed country due to economic growth, technological infrastructure and commitment to human rights.

In the midst of an active global dialogue about the merits and drawbacks of permitting the editing of human DNA in clinical settings, Canada is an example of a high-profile country that continues to hold a restrictive, statutory approach toward genome editing. “We’re definitely one of the most restrictive in the world right now,” says Dr. Ravitsky. Human genome editing for research purposes and clinical applications is addressed under a combination of the AHRA (Assisted Human Reproduction Act), other Canadian regulation and legislation, and the TCPS 2 (Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans).[80]

The Royal Commission on New Reproductive Technologies was created by the Canadian federal government under Brian Mulroney in 1989 in response to demands for an examination of the use of reproductive technologies. In 1993, the Commission published a report entitled *Proceed with Care*, which recommended a federal ban on several reproductive technologies,

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[79] Statistics Canada. (2018, February). Population and Demographics. *StatCan.* https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/hlt-fst/pd-pl/Comprehensive.cfm

[80] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf

including germline modification. The *Proceed with Care* report led to the 2004 enactment of Canada's AHRA. The AHRA prohibits activities such as human cloning, combining human and non-human genetic tissue, transplanting a non-human embryo into a human being, or creating an embryo for any purpose other than causing a human child to be born.[81] The AHRA states, "No person shall knowingly alter the genome of a cell of a human being or *in vitro* embryo such that the alteration is capable of being transmitted to descendants" (s. 5 (1) (f)).[82] A violation of these remaining parts of the statute can bring a fine of $500,000 or a 10-year prison sentence. The AHRA contained a clause mandating revision every five years, but has not followed through on these promises. There is currently no Canadian or Quebec legislation or guidance (other than the AHRA) pertaining specifically to human genome editing.[83]

In 2016-2017, the CGP (Centre of Genomics and Policy) and the SCN (Stem Cell Network) organized four workshops looking at different aspects of AHRA in order to propose amendments and revisit certain provisions based on the rapid evolution of technology and the changing societal perspectives since 2004.[84] "What [researchers] want to do with human embryos at this point is modify them and see what happens in the very early stages, when you can still grow the embryo in a petri dish — but you can't do that in Canada," says Dr. Janet Rossant, a researcher who uses CRISPR in her lab at Toronto's Hospital for Sick Children. "The Act basically says even if you are not going to put that back into a mother, into the uterus, you cannot even try it because it might have the potential to modify the germ line. That is the interpretation."

While individually rare, genetic diseases collectively affect 1 in 12 or nearly 3 million Canadians. To date, approximately 7,000 rare diseases have been identified and new rare conditions are being discovered each year.[85] It is estimated that as many as half of Canadians

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[81] Chemical Institute of Canada. (2018, April). Canada's CRISPR Conundrum. *Cheminst.* https://www.cheminst.ca/magazine/article/canadas-crispr-conundrum/
[82] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf
[83] ibid
[84] ibid
[85] Critical Care Services Ontario. (2017, March). Rare Diseases Working Group Report. *Health.gov* http://www.health.gov.on.ca/en/common/ministry/publications/reports/rare_diseases_2017/rare_diseases_report_2017.pdf

with rare disorders are undiagnosed. Genetic disorders affect the lives of approximately 500,000 children in Canada. Despite Canada's well structured healthcare system, which prides itself for providing equal access to citizens, Canada as well as other countries have recognized that people with rare diseases systematically experience barriers to accessing health care. The current laws in Canada could be seen to prohibit advancement in a technology that has the potential to improve the lives of millions of Canadians. As a developed nation, Canada has an important role in contributing to scientific progress, and it is not fulfilling that role.

Many experts agree that the current restrictions on genome editing in Canada need revision in order to satisfy Canadians' right to benefit from the advancement of science and allow Canada to contribute to the international scientific community.

Logic of Evil

The concept of evil is complex and often open for interpretation. Evil can be categorized as either natural evil or moral evil. Natural evils do not result from the intentions or negligence of moral agents (i.e. natural disasters).[86] Moral evils do result from the intentions or negligence of moral agents (i.e. Murder and lying).[87] When evaluating the issue of human genome editing, it becomes apparent that both sides of the argument come from a place of moral reason and rationalization. Those who support the practice of genome editing do not necessarily come from a place of evil intent, but rather hold the belief that the technology's benefit to humanity outweighs potential risks and moral opposition. Some believe, to oppose this technology on the basis of fear would be the greatest evil of all.

From the beginning of modern science, the pursuit of scientific knowledge was connected with the idea of moral purpose. The Charter of the Royal Society, the UK's national academy of science contends that the pursuit of knowledge for anything other than to the glory of God the Creator, and the advantage of the human race, is seen as a moral failing. The motivations of

[86] Stanford Encyclopedia of Philosophy. (2013, November). The Concept of Evil. *Plato.* https://plato.stanford.edu/entries/concept-evil/
[87] ibid

scientists are widely variant. Nevertheless, recent research by the Nuffield Council on Bioethics found that more working scientists put 'making scientific discoveries for the benefit of society' as their primary motivation for involvement in science more than any other reason.[88] In addition, there is a notional loan of trust or social 'licence to practice' given to scientists by society.[89] In return for scientific freedom, scientists are assumed to have an implicit responsibility towards society. Professor Robin Lovell-Badge FRS, a leading scientist at the Francis Crick Institute and chair of the Royal Society's genetic technologies programme says, "developments in genetic science are driven by our wish to tackle the many challenges humanity faces, including reducing the burden of human disease. People have told us that they are cautiously optimistic about the potential of the new methods for research and applications, but they are understandably concerned about the risks, and the ethical and social implications.

When asked about her predictions for the future of genome editing, Dr. Ravitsky explained, "I think that the first clinical trials on germline are pretty close. I think between these two camps, the camp that screams the complete ban is going to lose. The forces of enormous clinical potential, pressure from families and patients, a multi billion dollar future and human society's impulse to move ahead will all combine to make genome editing move faster than we thought." Genome editing has already proven to cure various diseases. Studies suggest that many members of the health profession view childhood disability as predominantly negative for the children and their families. Providing a viable means of alleviating financial and emotional burdens would be a reasonable source of rationalization. It is also noted that the research that will make heritable genome editing possible will likely provide insights that will lead to health care interventions for other disorders.[90] The use of the technology to cure monogenetic, serious disorders has not been met with significant opposition. It is when ethicists debate the use of the technology for enhancement purposes that moral issues arise. Nevertheless, there remains logical justification behind the use of genome editing for enhancement purposes beyond the superficial categorization of which it is normally associated.

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[88] Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf
[89] ibid
[90] ibid

Modern transhumanists say that there is a moral obligation to enhance ourselves. These individuals point out that the human body is flawed in that it easily becomes diseased, requires a great deal of sleep, has various cognitive limitations, and eventually dies.[91] They suggest it would make sense to improve the human species by making it more resistant to disease, more moral, and more intelligent. Others argue genetic modification for enhancement is not only permissible, but an essential course of action. Darwin's widely recognized theory of evolution is based on gradual changes to the human species through response to environmental changes. Many suggest that the current rate of environmental change caused by human activity (i.e. climate change) may be too rapid for humans to adapt comfortably, or at all, posing an existential risk. As a species facing a number of potential environmental catastrophes, Darwinian evolution may just be too slow. Conclusions have been made that it is imperative for humans to take rational control of their own evolution at the biological level and to construct a matching morality adequate for this in order to save the future of the human race.[92]

Politics

Research and innovation in biotechnology and biomedicine are now contested intensely in political arenas, demanding both democratic engagement and attention to broader questions of social justice. Politics apply to genome editing through avenues such as the government, media, human rights and the economy.

Government has significant power over genome editing technologies. One area of governmental responsibility is providing democratic governance on matters of public ethics. Democratic procedures offer a plausible solution to, or ways of coping with, the problem of the mutual adaptation of emerging biotechnologies and the normative frameworks within which they are deployed.[93] There is an importance of having an open, effective and inclusive public sphere in

[91] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1
[92] Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf
[93] ibid

which questions about genome editing can be raised and different arguments can be discussed. Politicians are in charge of employing methods where citizens are given the opportunity to express their opinions. Governmental entities also play an essential role in promoting sustainable use and development of genome editing. Governments must employ policies that operate in accordance with established principles and respond to relevant social issues. Governments are left responsible to assess public perceptions of genome editing as they would make political judgments about their citizens views on other complex social issues.[94] This will require transparency, meaning that scientists, regulatory agencies and governments must share relevant information with the stakeholders concerned.

In recent years, media coverage of human genome editing has experienced an exponential increase. Media outlets have associated genome editing with phrases like "editing humanity," "DNA revolution," "eugenics is back," "engineering the human race," and "the end of life as we know it."[95] These terms tend to both reveal the social representations of genome editing and to perpetuate the hype, thereby exacerbating the fears surrounding the technology.[96] Social media influences have been notoriously associated with perpetrating negative stigmatization surrounding body image and societal expectations. Media can be damaging to an individual's self representation and worth. Continued prevalence of media may contribute to an increased social and emotional pressure on individuals to improve their physical appearance, causing them to turn to various enhancement options like genome editing in the future. As well, media coverage of genome editing allows for increased public engagement. When awareness of genome editing is increased, messaging may attract patients and/or willing research participants, spark dialogue or encourage individuals to educate themselves. Publicity lends itself to gain support for funding of genome editing initiatives and put pressure on governments to respond to the wants and needs of their citizens.

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[94] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5
[95] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION
[96] ibid

Conversations surrounding the ethical nature of genome editing have included human rights considerations. The Universal Declaration on the Human Genome and Human Rights suggests that practices like germline interventions could be contrary to human dignity, though the International Bioethics Committee - the UNESCO body responsible for overseeing the functioning of the Declaration - has not decided on the issue. Canada has signed both the Universal Declaration of Human Rights and the International Covenant on Economic, Social and Cultural Rights which promulgate the right for all citizens to "enjoy the benefits of scientific progress and its applications." Application of this right would guarantee scientific freedom as a core principle of liberal democracies and instill the obligation for governments to ensure access to new technologies, while allowing Canadian researchers to be engaged in the international scientific community.[97] Some believe the desire to have genetically related children is a need that engenders certain rights.[98] The Commission de l'ethique en science et en technologie Quebec maintains the position that the "the right to a child" does not exist nor does it believe that the State is bound to meet all the demands for medically assisted procreation.[99] Article 3 of the Universal Declaration of Human Rights proclaims that everyone has the right to life, liberty and the security of person. Disability advocates argue that genome editing violates the right to life of a child with disability and their right to personal autonomy as they are not able to give consent to research participation. As well, article 21 of the declaration emphasizes that everyone has the right of equal access to public service. This would indicate that genome editing must be included in the universally-available healthcare basket in order to uphold this right.

Economic considerations are important when discussing genome editing. Substantial funding is required for genome editing research and clinical trials. The argument against investment in genome editing takes into account that funds directed to one area may take away

[97] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION
[98] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf
[99] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION

from spending in other areas.[100] In addition, if genome editing reaches a point where populations of individuals with genetic disease are severely reduced, companies and programs that provide support and resources for these individuals would not be financially rewarded by this technology. However, some speculate that lower disability populations may increase participation in the workforce and contribute to economic growth. Additionally, many countries have identified opportunities for licensing and commercialization of genome editing technologies as a significant economic contribution to the healthcare, agricultural and infectious disease sectors.

Religion

Religious influences play a large role in a person's view towards genome editing. Many religions are split on their opinions of genetic manipulation. Religious groups are likely to find the idea of redesigning the fundamental biology of humans morally troubling. Other religions have demonstrated an interest in genome editing as a way of preserving human life.

Concerns of genetic manipulation often devolve to the view that the human genome should be treated with a sense of humility and that humanity should recognize the limits of wisdom and science. This outlook is expressed by the term “playing God,” which captures the notion that humans lack a god-like omniscience that would be required to make any changes in the genome safely (and to predict that such changes would actually serve the intended purpose).[101] The argument is based on the premise that the forces of nature and evolution are a better or at least a less problematic source of genome alteration than human intervention.

The question of the proper extent of human intervention in nature has long been discussed in spiritual and religious terms. In the West, where Christian traditions have had the most influence on what is today a more religiously diverse and often secular culture, these ideas are expressed in the debate about which tasks in improving nature are the domain or obligation of humans and which are to be left to God. These beliefs are represented in a variety of traditions,

[100] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1
[101] ibid

including St. Francis' Canticle of Creation and the belief systems across many Native American nations. Conversely, in Jewish tradition, religious texts proclaim that there is an explicit obligation to build and develop the world in a way that is beneficial to people, the role of humans in intervention is seen as a positive collaboration between God and humans, not as an interference with creation.[102]

Judaism offers many tales of people participating in genetic mutation. Stories and parables about people creating synthetic life are mentioned in Jewish texts — notably the Talmud and the Zohar.[103] A guiding principle of Judaism is that human life has infinite value and there is a moral obligation to help heal the sick and prevent disease. In Jewish oral law, the Mishnah, it states that "He who saves one life, it is as if he saved the whole world." Therefore, the use for genome editing to advert disease is received positively for the most part. However, the use of the technology for non-health purposes is met with strong disapproval. Conservative Judaism does not permit several body modifications such as tattoos and piercings.[104] In Judaism the body is recognized as God's creation and enhancement alteration would be viewed as an insult to God's work.

Similarly, Muslims and Buddhists view genetic engineering as just one of many welcome interventions to reduce suffering from disease.[105] Muslims argue God has given humanity the knowledge and skills, and therefore the ability, to develop solutions for harms to our health and genome editing is one of many tools humans should take advantage of in this regard. An additional consideration of Islamic religion is that life is described as being a test including suffering. The Qur'an states, "Believers, fortify yourselves with patience and prayer. God is with those that are patient." This refers to the fact that humans must wait to overcome suffering rather

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[102] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1
[103] Genetic Literacy Project. (2019, November). Religious beliefs shape our thinking on cloning, stem cells and gene editing. *Genetic Literacy Project.* https://geneticliteracyproject.org/2019/11/27/religious-beliefs-shape-our-thinking-on-cloning-stem-cells-and-gene-editing/
[104] NYU Langone Health. (n.d.). Genetic Editing: Ethical and Social Issues. *Med NYU.* https://med.nyu.edu/highschoolbioethics/sites/default/files/highschoolbioethics
[105] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

than fighting it - God's plan will resolve the suffering.[106] Extreme believers of this philosophy disapprove of many modern health care interventions and would view genome editing in a similar light in that it is an unnecessary solution to something for which God already has a plan.

The desire to have genetically related children may arise from a variety of factors, ranging from a wish to see oneself or one's ancestors reflected in the appearance of the children to a belief in the need for a biological linkage in order to satisfy a sense of lineage, continuity, or even some form of immortality.[107] Some people feel they have a religious obligation to have genetically related children. Others see the desire for genetically related children as reifying what some view as outdated notions of kinship and family at a time when adoption, same-sex marriage, donor gametes, surrogacy, and stepparenting are being normalized.[108]

Solutions

Genome editing has the potential to bring about many medical, social and scientific opportunities for humanity. However, with all powerful technologies, there comes an element of risk. Future management of genome editing must encompass a pragmatic approach that identifies the conditions in which genetic modification could be ethically justified and mechanisms that will ensure that these conditions are met.

International Harmonization

One of the main mechanisms to promote sustainable scientific progress of genome editing will be harmonizing regulations among countries and promoting transnational cooperation. Harmonization is usually accomplished through an international treaty or other formal and binding legal instrument, implemented through the amendment of national laws to conform to

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[106] NYU Langone Health. (n.d.). Genetic Editing: Ethical and Social Issues. *Med NYU.* https://med.nyu.edu/highschoolbioethics/sites/default/files/highschoolbioethics
[107] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1
[108] ibid

treaty requirements.[109] An international organization such as the United Nations could be tasked with further standardizing the regulatory framework. This is a necessary course of action for the future of genome editing to prevent medical and scientific tourism. In countries that do not have strict regulations, it is likely clinical trials would be moved to these developing nations. The result could be a "race to the bottom" that would encourage lower standards in nations seeking revenues from medical tourism, as has happened in both stem cell therapy and mitochondrial replacement techniques.[110] This also could cause scientific opportunities to be missed in countries with stringent measures and poses safety risks in areas where scientific oversight is less rigorous. Developing countries where populations are more vulnerable could potentially cause these individuals to be exploited and to agree to take part in clinical trials that expose subjects to significant risk.[111] This also raises the concern that vulnerable populations will not benefit from the outcomes of the research as their countries do not have the resources or infrastructure to apply research findings into their healthcare processes. In addition, citizens' safety will be put at risk as they may be tempted to travel to countries with fewer or no rules in order to satisfy their medical or personal wants and needs. In order for international harmonization, it is important the governance model leaves room for nations to take differing approaches that reflect their distinct history, culture, values and political systems. The criteria for effective global collaboration on genome editing as defined by the National Academy of Sciences includes (1) respect for differing national policies, (2) coordination of regulatory standards and procedures whenever possible, and (3) transnational collaboration and data sharing among different scientific communities and responsible regulatory authorities.[112]

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[109] National Academic Press. (2017, January). International Research Oversight and Regulations. *NCBI.* https://www.ncbi.nlm.nih.gov/books/NBK447261/

[110] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

[111] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf

[112] National Academy of Sciences. (2017, January). Summary of Recommendations and Principles. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

Moratorium

For germline editing in particular, many uncertainties surrounding CRISPR technology remain. In response to the growing interest in proposals for genetic enhancement of humans, many specialists from a variety of fields have called for an international moratorium on heritable genome editing. A moratorium would mean that for a fixed period of time, the use of clinical germline editing will be prohibited. This will give time until further evidence is collected on the safety, efficacy and ethical implications of the technology that is to be regulated.[113] At the first International Summit on Human Genome Editing in December 2015, it was made clear that clinical uses of germline editing should not yet proceed anywhere in the world.[114] However, this statement was not enough to discourage the aspirations of biophysicist Dr. He Jiankui. Therefore, a global moratorium is necessary to ensure there is time to implement strategies to promote general understanding and consensus of the relevant issues and prevent similar situations from occurring. As well, it is argued that such a moratorium would provide opportunities to debate unresolved concerns, to harmonize the definitions of certain terms, to assess the benefits and risks of the technologies as well as develop recommendations for regulations.[115]

Public Engagement and Education

It is vital that the future of genome editing is pursued in collaboration with the general public. Broad consensus for the need to engage the public in the genome editing debate has been clearly expressed in several international statements, reports, committees and summits. As genome editing has the ability to provide humanity with several medical and social opportunities, they must be given an active role in future decisions so the intended benefit to individuals is

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[113] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf

[114] Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. *Nature.* https://www.nature.com/articles/d41586-019-00726-5

[115] WHO. (2019, March). WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing. *WHO.* https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Governance-1-paper-March-19.pdf#page10

maximized. Education and increased familiarity of the technology will encourage public participation in policy decisions, engagement in independent research and ensure research accountability. If citizens are to take part, plain language must be used and, because public opinions are dependent to some extent on the quality of the information provided, it should be as objective and accurate as possible.[116] In order to accomplish the goal of public engagement, many experts suggest establishing an international forum. The ongoing forum would be aimed at discussing the potential clinical uses of gene editing; helping to inform decisions by national policymakers and others; to develop recommendations and guidelines; and to encourage coordination among nations.[117] As genome editing has potential implications for all species, decisions must be informed by diverse interests. The forum must be inclusive and engage a wide range of perspectives and expertise – including from biomedical scientists, social scientists, ethicists, health care providers, patients and their families, people with disabilities, policymakers, regulators, research funders, faith leaders, public interest advocates, industry representatives, and members of the general public.[118]

Attention to Guidelines

An important course of action to prevent instances similar to that of Dr. He Jiankui will be to develop clear and appropriate guidelines. Many experts have recommended that genome editing procedures be viewed as a last resort, given that many proven alternatives already exist. More research is needed before any germline intervention could meet the risk/benefit standard for authorizing clinical trials. When the technical hurdles facing genome editing are overcome, editing to prevent transmission of genetically inherited diseases may become a realistic

[116] Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf
[117] WHO. (2019, March). WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing. *WHO*. https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Governance-1-paper-March-19.pdf#page10
[118] ibid

possibility.[119] Technical and scientific uncertainties remain a pressing concern so guidelines must be largely based on the state of knowledge surrounding the technology. There must also be clearly defined criteria for appropriate application of the technology to cases where there is no alternative.

The National Academy of Sciences recommends that clinical trials using genome editing should be permitted only within a robust and effective regulatory framework that encompasses:

1. The absence of reasonable alternatives;
2. Restriction to preventing a serious disease or condition;
3. Restriction to editing genes that have been convincingly demonstrated to cause or to strongly predispose to that disease or condition;
4. Restriction to converting such genes to versions that are prevalent in the population and are known to be associated with ordinary health with little or no evidence of adverse effects;
5. The availability of credible preclinical and/or clinical data on risks and potential health benefits of the procedures;
6. Ongoing, rigorous oversight during clinical trials of the effects or the procedure on the health and safety of the research participants;
7. Comprehensive plans for long-term, multigenerational follow-up that still respect personal autonomy;
8. Maximum transparency consistent with patient privacy;
9. Continued reassessment of both health and societal benefits and risks, with broad ongoing participation and input by the public; and
10. Reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition.

[119] National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

Regulatory Approach

It is only natural that society's initial reaction towards genome editing is to fear the unknown, often causing the immediate response to be prohibiting access rather than to regulate. Legal experts, bioethicists and scientists indicate that a legal approach toward genome editing is ineffective. In 1982, the Law Reform Commission of Canada noted that criminal law should only be used for "conduct which is culpable, seriously harmful, and generally conceived of as deserving of punishment," and that it should be "an instrument of last resort."[120] In the context of science, criminal prohibitions are considered to be suboptimal policy tools as they are "inflexible, stifle public debate, and hinder responsiveness to the evolving nature of science and societal attitudes."[121] The laws that Canada has established toward genome editing have significantly hindered scientific freedom and potentially caused scientific opportunities to be missed. As genome editing technology is constantly evolving, it is important that there are regulatory frameworks and guidelines in place that respond to the ever changing nature of science. Dr. Ravitsky explains, "I think staying nimble [is important] because technology is moving fast and sometimes the laws are not fully addressing current needs because the laws are written with old technologies in mind." To adopt a regulatory approach, governments must work in conjunction with various organizations to develop a framework that satisfies ethical principles and establishes mechanisms to ensure research accountability.

[120] Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf
[121] ibid

Conclusion

This paper showcases the ethical dilemma concerning genome editing. Advancement of genome editing within medical applications opens the door to broader questions of social justice and the potential for society to revert to eugenic practices of the past. The research within this report highlights validity on both sides of the argument. It is still undecided whether humans should play an active role in genome intervention. The opportunity is clear, however, strategic methods must be employed to guarantee the technology does not fail to achieve its intended purpose or fall into the hands of corruption. With a collective effort and ongoing dialogue, the benefit of genome editing can be maximized and associated risks can be mitigated. The future for genome editing is promising, but it will be up to leading researchers and the public to decide what that future will look like.

Appendix

Figure I

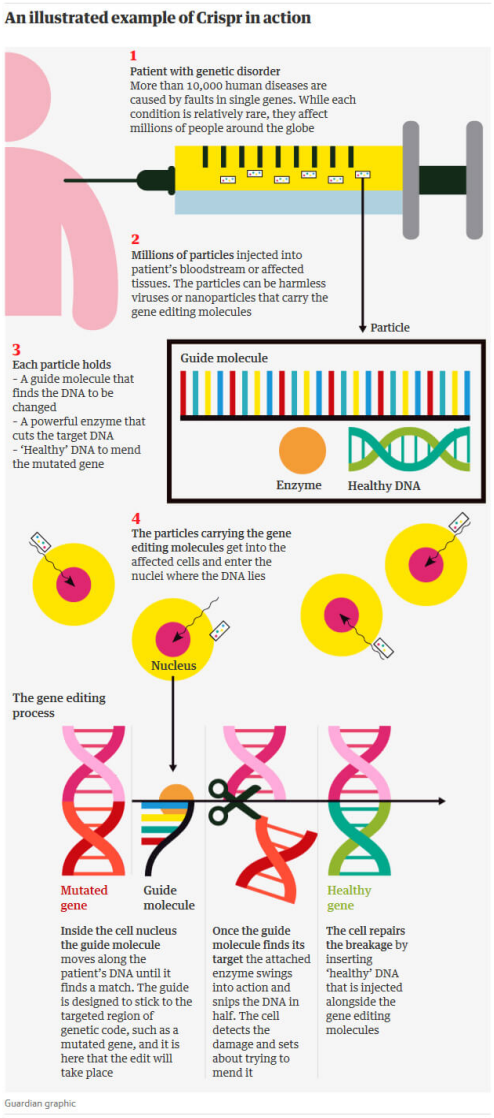

Figure II

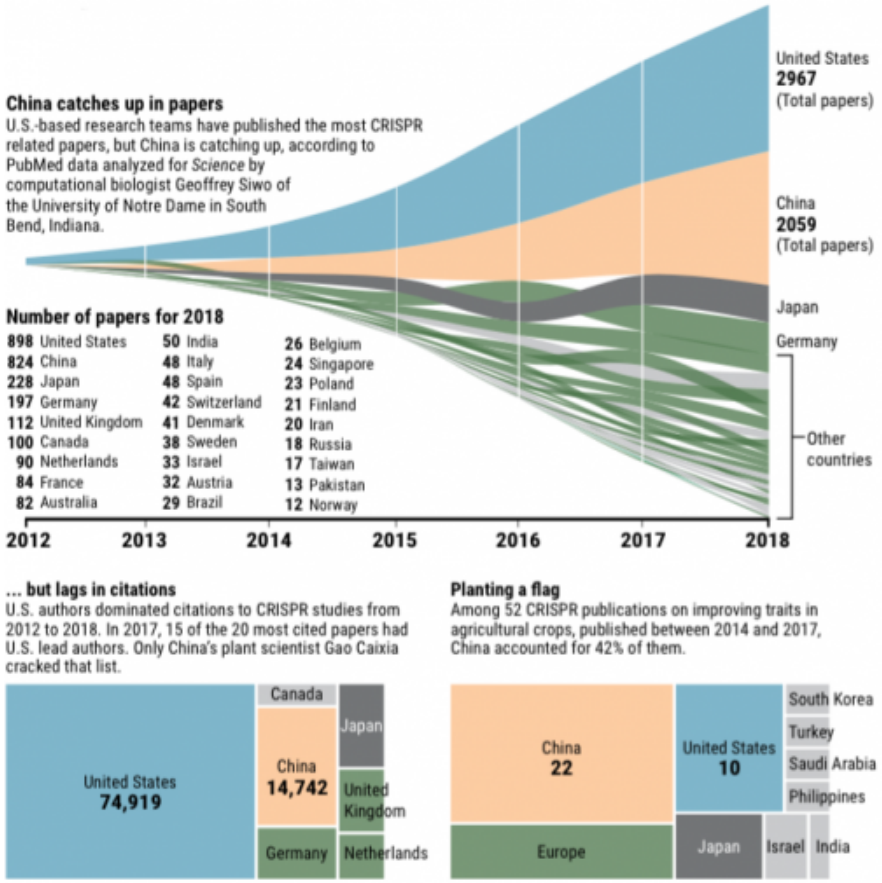

Figure III

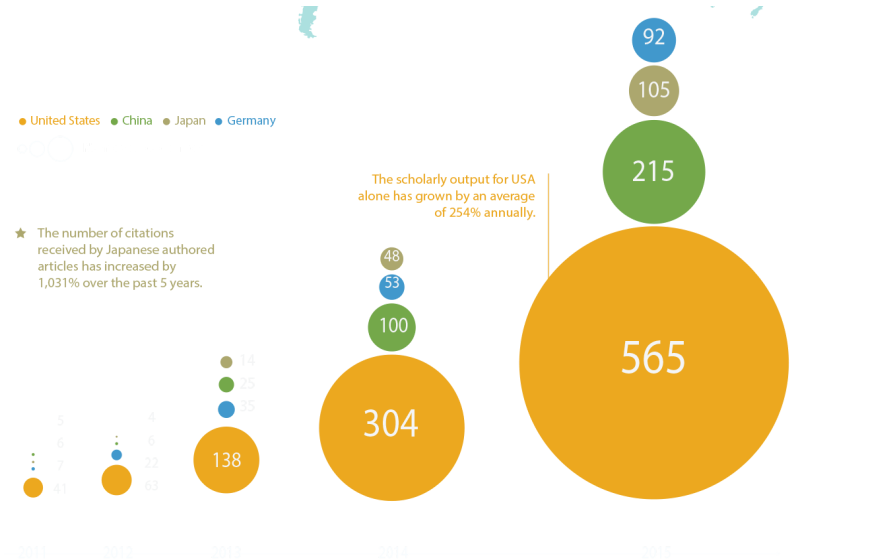

Figure IV - A nuchal translucency scan of CRISPR twins Lulu and Nana

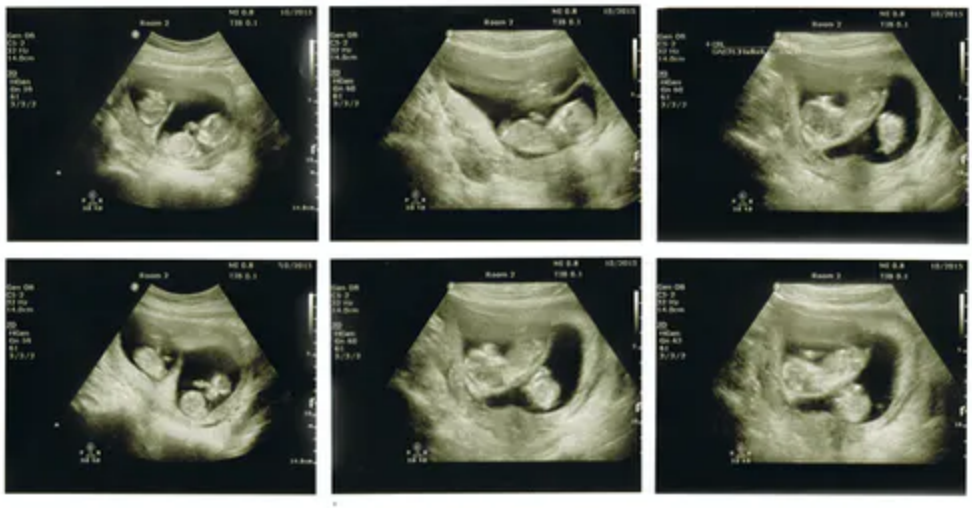

Figure V

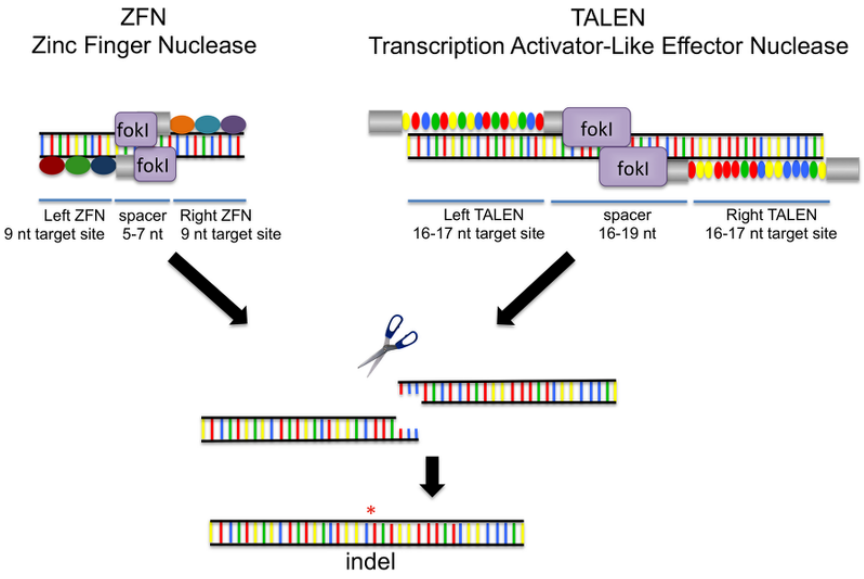

Figure VI

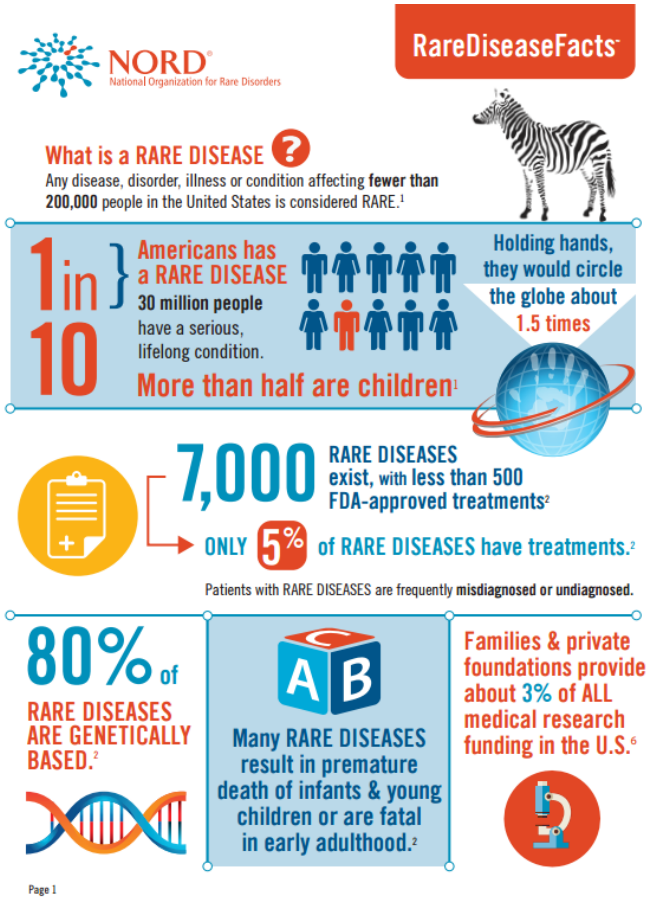

Figure VII - Interview with Dr. Richard M. Gronostajski

How did you get into the field of genomics and what research have you been a part of in regards to genome editing?

I started my career as a biochemist and nucleic acid enzymologist working on a type of protein called a transcription factor. This type of protein binds to specific sites on DNA and controls the expression of multiple other genes in cells. I spent several years identifying binding sites for a transcription factor called Nuclear Factor I (NFI, pronounced nuclear factor one) and asking how they could regulate gene expression by moving them to different places in the genome. While these studies were being done we discovered that what we thought was a single protein, Nuclear

Factor I, was actually a family of proteins which were named Nuclear Factor IA, Nuclear Factor IB, Nuclear Factor IC and Nuclear Factor IX in all mammals. These are abbreviated NFIA, NFIB, NFIC and NFIX. I decided in 1999 that if I wanted to understand what these 4 genes did in animal development that I would need to delete them from the mouse genome and determine what effect this would have on mouse development. So over the next 20 years I made mutant mice that were lacking NFIA, NFIB, NFIC and NFIX and showed that each gene was needed for development of various organ systems in the mouse including the brain, the lungs, the muscles, the skeleton, the teeth and the immune cells of the blood. This was my start at genome editing, creating mice with deletions of the NFI genes.

What is your stance on genetic engineering?

I think that genetic engineering will make it possible to make genetically modified plants and animals that will help feed the world and make the world a better place. For example, it is possible that we could genetically modify pigs so that their organs would be suitable for transplantation into humans to cure heart disease and diabetes. I think that genetically modified organisms could help make the world a cleaner, safer and better place.

In your opinion, how does CRISPR differ from other genome editing systems?

CRISPR is a process that allows more precise and a higher efficiency of genome editing than we had previously. All of the mutant mice that I made were done with an older technology called homologous recombination that took 6-12 months to make a mutant mouse. Similar mice can now be made in 2-3 months which will speed medical research. CRISPR has also been found to work in plants and other animals to make mutants faster than other techniques

What changes have you witnessed in the genetic engineering industry?

Once CRISPR became widely known dozens of companies rose up hoping to create new useful modified organisms. CRISPR has largely eliminated the use of two earlier technologies that had been used to make specific genomic modifications TALENs and artificial Zinc-finger proteins. Companies based on these technologies have largely replaced them with CRISPR.

Do you have any predictions for the future of genome editing?

Over the next 5-10 years I think that we will be curing genetic diseases like sickle-cell anemia and other blood diseases using stem cells from patients that have been modified to cure the disease. I think that genetically modified organisms might be used to clean up toxic waste. It is quite possible that rare genetic diseases of development could be cured with CRISPR editing of cells from patients that suffer from the disease. I think that pigs may be genetically modified to provide needed transplant organs for human beings. Lastly I think that plants will be modified to grow faster using less fertilizer to help feed the world.

Which applications of genome editing would you consider of most value?

All of the ones I listed in Question 5 will be valuable.

What regulations or methods would you propose to ensure this technology is managed appropriately?

Notice that in Question 5 I did not mention what we call "germline" editing of the human genome. These are changes that will be carried into the next generation. Although this is now possible, I don't think in the next 10 years that this should or will be done. While at least 2 children in China have been born with slight genetic modifications, this was done illegally and was not sanctioned by any medical group. I think that germline editing should not be done until we know more about the possible "off target" effects of CRISPR and more importantly, the effects of novel mutations in different groups of humans. This can only be done by further research into the natural variations in genes in human populations over the next 10 years or so. Once these variations are better understood, we may decide that making some specific modifications in the human genome might be worth the risk. For example, putting an extra copy or two of the gene for the p53 protein might make humans resistant to the development of cancer, as has been seen in lab mice with extra copies of p53. But we need to do more research before considering such things and I think that will take at least another 10 years or so. There will likely be trade-offs between positive and negative effects of genetic engineering and these should be decided on, possibly by direct voting on it, by the people who will be affected by it. There is

great interest in modifying human cells to use in cancer therapy using CRISPR, and to cure genetic diseases using CRISPR and CRISPR-modified stem cells.

Figure VIII - Interview with Dr. Vardit Ravitsky

How did you get into the field of genomics and what research have you been apart of in regards to genome editing?

From a very early stage of my career, from my first degree, I was really interested in genetics, especially from the perspective of the interaction with human identity. So from very early on I was interested in the role genetics play in making us who we are. Not just in terms of diseases, so a lot of people are interested in understanding the genetic basis of diseases, and for me the question was much broader. It was also about traits and just in general identity. I think that a lot of human identity is not shaped by genetics. My main interest was understanding what is sometimes called nature and nurture debate. What part of us is nature, and what part of us is nurture? So genetics vs environment, genetics vs culture, this has been my interest for 30 years. My research on gene editing, I am working with scientists on how to use gene editing to cure diseases in a responsible way and I also do a lot of research in bioethics about the social and ethical implications of the capacity to edit human DNA. So the research I have done to develop responsible policies when we are starting to work with a new technology that we have never had before. The way that I see gene editing being related to identity is that at this point, we are thinking of using CRISPR to just cut and change very specific genes that are responsible for very serious diseases. In the future, if CRISPR moves ahead and if we understand better how to do it safely, we may decide to edit many genes at once or try to tackle traits that are genetically complex, such as height. From that perspective, CRISPR could open the door to not just fighting against disease but to changing identity. I think that most people are worried about that potential use of gene editing, more than they are worried about the potential to cure disease. That is where I see a link between my long standing interest in identity and this new powerful technology.

What is your stance on genetic engineering?

My position is that it is a powerful, promising tool and like any other tool that humans have, such as fire, it has to be used a) carefully and b) for the benefit of humans. For the benefit of humans means several things, that it should be safe. Just like fire, we use it to keep warm but then we can burn down a village. So we can use it with the intent of curing disease but we can create other diseases in the process. The issue of what do we use it for, so are we only curing disease or are we designing human beings? Are we only treating certain diseases, or any disease? Thirdly, the issue of justice. So if we are going to use it only on the very rich, what does it mean that as a society we are investing billions of dollars that will only benefit a small minority of people? The use of the tool depends on a bunch of considerations and some of them are ethical and social and some of them are economic. I think moving forward, the tool as a tool is obviously full of promise, and maybe it really is the next big thing in medicine. But moving forward on how to use it for the benefit of people, of society, is a very complex issue that of course I think there is ethical analysis and legal analysis in the development of policy, which is my research.

Who do you believe holds the power and control in the genome editing industry?

Right now I think it is the scientists. The proof of this is that when one person wanted to move ahead, he did it, despite international calls not to do it. The tool is relatively simple to use. So much so that somebody who is not an expert was able to do it on embryos and some people are just injecting themselves. We call them "biohackers" but they are not really hacking anybody, they are just doing things to themselves, to their own bodies, because they do not have patience for the approval processes that we require in society. The real power is in the hands of scientists because anyone can do this. You could buy a CRISPR kit online today for less than $200 and manipulate it at home and inject yourself with whatever you want to try on yourself. It would not be a criminal act, you would be maybe stupid, maybe crazy, but would not be breaking any law. You are only hurting yourself potentially. The power is in the hands of scientists. The second level of power is in the hands of policy makers. By that I include legislators, of course countries have just passed laws that say you are not allowed to do this on the germline. Countries are currently struggling with how to approve clinical trials with somatic cells or CRISPR would be

used on children or adults, not on embryos. So making it a criminal act, people may still do it but they will go to prison which is what happened in China. That is why it is the second level of power because people can still do it but there will be repercussions. When I say policy I do not only mean legislators, I also mean people like me who make recommendations for policy. It is not just those passing laws it is also professional societies who write recommendations and guidelines and people like me who work on expert groups to try to think of how to best formulate this. So it is across the board, it is bioethicists, it is people who write guidelines, all the way to lawmakers. The third level of power is the public of course. You need public engagement and public acceptance in order to move ahead with this. To some degree we all hold some power in this conversation because if this is to become a fully integrated technology is medicine and in science, the public needs to be onboard with this.

What changes have you witnessed in the genetic engineering industry?

Up until 2017, very recently, the general spirit internationally was that we are not ready for germline use. We can move ahead with clinical trials on adults and on children, but we must not touch a sperm, egg and embryo. We are not ready for genetic changes that will be transmitted to future generations. All of the policy statements and all of the ethical analyses on CRISPR said that internationally. In 2017 there has been a shift in the general spirit of the conversation. A few very influential reports were published that said we are not ready, but in principle we have no objection and it all depends on safety considerations and we have to figure out when we do it, not if, when we do it, what genes should we target first? Important bodies around the world started either realizing or got used to the idea. Now the conversation is much more about how to use it and on what genes rather than should we use it, and I am talking about the germline. Some people are still sticking to their guns and saying why this change? Nothing changed, we do not have more data, we are still not ready, we are far from having social consensus, why are we kind of surrendering to the pressure from the scientists and now saying it is okay in some cases, it is still wrong across the board. There is a tension now between bioethicists and policy makers on which stance to take. Complete moratorium? Complete ban? Or a conversation about what are the appropriate first uses of the technology.

Do you have any predictions for the future of genome editing?

Definitely. I think that the first clinical trials on germline are pretty close. I think between these two camps, the camp that screams the complete ban is going to lose. For many reasons, I mean the clinical potential is enormous, the pressure from families and patients because in human society we have this impulse to move ahead. Scientists will argue scientific freedom and patients will argue rights and access to health. Also the economic factors are huge. A multi billion dollar future that is interesting to a lot of people. All of these forces will combine to make it move faster than we thought.

Which applications of genome editing would you consider the most valuable?

There were two reports that were published that were very influential. Both of them are in that new spirit that I mentioned, let's not ban it, let's do it responsibly. One is by the National Academy of Science and Medicine in the US from 2017. The second one was from the Nuffield council on bioethics. These are very thoughtful, deep analyses on the aspects of gene editing and really in-depth reflection on how to move ahead. There was also a very influential recent publication in the Journal of Nature by a group of leading CRISPR scientists and bioethicists calling for a moratorium. These three will give you a whole picture of where the conversation is.

What regulations or methods would you propose to ensure this technology is managed appropriately?

The main thing everyone is talking about is international harmonization. If each country has their own set of rules, some countries will be more advanced and nuanced and others just will not have the resources and the energy to think about this. They will not have regulations and then you get medical or scientific tourism. People go to countries with less regulations to do things that are not allowed in their countries. If these people are vulnerable patients, wanting to have children, then you are suggesting they take more risk by making them go to places that are less regulated. Nobody knows how to do this because I mean look at the Corona virus now even when the threat is imminent we are struggling to find ways to coordinate internationally and this is not an immediate threat to anybody. Everybody acknowledges that international harmonization is the

way to go but nobody knows quite how to do that. At the national level, I think that clarity for researchers is very important. To issue clear guidelines on what is currently allowed or not. In Canada for example, we have a criminal law that says we are not allowed to do this even for research. There is ambiguity in the language of the law. What kind of DNA are we not allowed to touch? What if we never intend to start a pregnancy are we still not allowed to do it? So because the technology is moving fast, sometimes the laws are not fully addressing current needs because the laws are written with old technologies in mind. I think that staying nimble and to issue clarification to existing laws and to publish guidelines. Laws are very heavy tools. From the time a law passes and then you can not change it, it is a heavy tool. I think the way to go with guidelines and regulations that are easier to change that can constantly respond to the evolution of science, and just make sure scientists are clear about what they can and can not do.

Bibliography

An estimation of the number of cells in the human body. (2013, July 5). *National centre for biotechnology information.* https://www.ncbi.nlm.nih.gov/pubmed/23829164

BBC. (2017, June). United Kingdom Profile - overview. *BBC.* https://www.bbc.com/news/world-europe-18027954

Centre of Genomics and Policy. (2018, March). Human Genome Editing Ethical and Policy Considerations. *Genome Quebec*. http://www.genomequebec.com/DATA/PUBLICATION/34_en~v~Human_Genome_Editing_-_Policy_Brief.pdf

Chemical Institute of Canada. (2018, April). Canada's CRISPR Conundrum. *Cheminst.* https://www.cheminst.ca/magazine/article/canadas-crispr-conundrum/

China - Country Profile, Facts, News and Original Articles. (n.d.). *Global Sherpa.* http://globalsherpa.org/china/

Critical Care Services Ontario. (2017, March). Rare Diseases Working Group Report. *Health.gov* http://www.health.gov.on.ca/en/common/ministry/publications/reports/rare_diseases_2017/rare_diseases_report_2017.pdf

Collins English Dictionary. (n.d). Definition of Control. *Collins.* https://www.collinsdictionary.com/dictionary/english/control

Comment. (2019, March 14). Adopt a moratorium on heritable genome editing. Nature. https://www.nature.com/articles/d41586-019-00726-5

Commission de l'éthique en science et en technologie. (2019, February). Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos. *Ethique Gov Quebec*. https://www.ethique.gouv.qc.ca/media/1038/cest_modif_gene_resume_an_acc.pdf

Driver projects. (n.d.). Retrieved from https://www.ga4gh.org/how-we-work/driver-projects/

Fernández, C. R. (2019, March 5). 10 Unusual Applications of CRISPR Gene Editing. Retrieved from https://www.labiotech.eu/tops/crispr-applications-gene-editing/

Friedman, L. F. (2015, April 23). These are the countries where it's 'legal' to edit human embryos (hint: the US is one). Retrieved from https://www.businessinsider.com/china-edited-human-genome-laws-2015-4#ixzz3YXh2b7du

Full Stack Genome Engineering. (n.d.). Retrieved from https://www.synthego.com/blog/gene-editing-nobel-prize

Genetic Literacy Project. (2019, November). Religious beliefs shape our thinking on cloning, stem cells and gene editing. *Genetic Literacy Project.* https://geneticliteracyproject.org/2019/11/27/religious-beliefs-shape-our-thinking-on-cloning-stem-cells-and-gene-editing/

'Genome editing regulations'. (n.d.). Retrieved from https://link.springer.com/search?query=genome+editing+regulations

Greenwall Foundation. (n.d.). Reframing Consent for Clinical Research: A Function-Based Approach. Retrieved from https://www.tandfonline.com/doi/abs/10.1080/15265161.2017.1388448

Hemophilia. (2019, August 22). Retrieved from https://www.mayoclinic.org/diseases-conditions/hemophilia/symptoms-causes/syc-20373327

Human Development Report. (n.d.). Inequalities in Human Development in the 21st Century. *CHN.* http://hdr.undp.org/sites/all/themes/hdr_theme/country-notes/CHN.pdf

International Bioethics Committee (IBC). (2020, February 6). Retrieved from https://en.unesco.org/themes/ethics-science-and-technology/ibc

International Compilation of Human Research Standards . (n.d.). Retrieved from https://www.hhs.gov/ohrp/sites/default/files/2020-international-compilation-of-human-research-standards.pdf

Ishii, T. (2017, January). Germ line genome editing in clinics: The approaches, objectives and global society. *Research Gate.* https://www.researchgate.net/publication/284847889_Germ_line_genome_editing_in_clinics_The_approaches_objectives_and_global_society

Jasonoff, S. (2006). Technology as a site and object of politics, in *The Oxford handbook of contextual political analysis. Oxford University Press.* https://www.oxfordhandbooks.com/view/10.1093/oxfordhb/9780199270439.001.0001/oxfordhb-9780199270439-e-040

Jenks, S. (2000). Gene therapy death. *Journal of the National Cancer Institute.*

https://academic.oup.com/jnci/article/92/2/98/2965013

Kofler, N. (2019, October 22). Gene editing like Crispr is too important to be left to scientists alone | Natalie Kofler. Retrieved from https://www.theguardian.com/commentisfree/2019/oct/22/gene-editing-crispr-scientists

Leather, S., Mills, P. (2005). Regulation of assisted reproductive technology: the UK experience - themes and trends. *London: Taylor and Francis.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4673849/

Lentzos, F. (2015). Dual use in biology and biomedicine. *Nuffield Council on Bioethics.* https://www.nuffieldbioethics.org/publications/dual-use-in-biology-and-biomedicine

Lewis, T. (2015, December). The major concern about a powerful new gene-editing technique that most people don't want to talk about. *Business Insider.* https://www.businessinsider.com/gene-editing-history-of-eugenics-2015-12

Li, H., Yang, Y., Hong, W., Huang, M., Wu, M., & Zhao, X. (2020, January 3). Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. Retrieved from https://www.nature.com/articles/s41392-019-0089-y#Sec19

National Academies of Sciences. (2019, January 10). Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop–in Brief. Retrieved from https://www.nap.edu/catalog/25343/second-international-summit-on-human-genome-editing-continuing-the-global-discussion

National Academy of Sciences. (2017, January). Heritable Genome Editing. *The National Academic Press.* https://www.nap.edu/read/24623/chapter/1

National Center for Biotechnology Information. (n.d.). Retrieved from https://www.ncbi.nlm.nih.gov/

National Human Genome Research Institute (NHGRI). (2017, March 1). Retrieved from https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-human-genome-research-institute-nhgri

National Library of Medicine - National Institutes of Health. (n.d.). Retrieved from https://www.nlm.nih.gov/

Nuffield Council on Bioethics. (2016, September). Genome editing: an ethical review. *Nuffield Bioethics.* https://www.nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf

Nuffield Council on Bioethics. (2018, July). Genome editing and human reproduction. *Nuffield.* https://www.nuffieldbioethics.org/assets/pdfs/Genome-editing-and-human-reproduction-short-guide.pdf

NYU Langone Health. (n.d.). Genetic Editing: Ethical and Social Issues. *Med NYU.* https://med.nyu.edu/highschoolbioethics/sites/default/files/highschoolbioethics

Overview of China. (n.d.). *U.S News.* https://www.usnews.com/news/best-countries/china

Plant Breeding Innovation: CRISPR-Cas9. (n.d.). Retrieved from https://www.isaaa.org/resources/publications/pocketk/54/default.asp

Press, A. (2020, March 4). Doctors use gene editing tool Crispr inside body for first time. Retrieved from https://www.theguardian.com/science/2020/mar/04/doctors-use-gene-editing-tool-crispr-inside-body-for-first-time

Privacy in genomics. (n.d.). Retrieved from https://www.genome.gov/

Read "Human Genome Editing: Science, Ethics, and Governance" at NAP.edu. (n.d.). Retrieved from https://www.nap.edu/read/24623/chapter/8#151

Rees, M. (2003). Our final century: will the human race survive the twenty-first century? *London Heinemann.* https://www.theguardian.com/books/2003/jun/14/featuresreviews.guardianreview10

Richard M. Gronostajski. (2016, December 5). Retrieved from http://www.buffalo.edu/news/experts/richard-gronostajski-faculty-expert-stem-cells-genomics.html

Stanford Encyclopedia of Philosophy. (2013, November). The Concept of Evil. *Plato.* https://plato.stanford.edu/entries/concept-evil/

Statistics Canada. (2018, February). Population and Demographics. *StatCan.* https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/hlt-fst/pd-pl/Comprehensive.cfm

Smithsonian Magazine. (2019, September). Four U.S CRISPR Trials Editing Human DNA to Research New Treatments. *Smithsonian.* https://www.smithsonianmag.com/

science-nature/four-us-crispr-trials-editing-human-dna-for-new-medical-treatments-180973029/

The Guardian. (2020, March 4). Doctors use gene editing tool Crispr inside body for first time. *The Guardian.* https://www.theguardian.com/science

UNESCO. (2020, February 6). International Bioethics Committee (IBC). *Unesco.* https://en.unesco.org/themes/ethics-science-and-technology/ibcInternational

U.S Department of Health and Human Services. (2019, November 5). Human Research Standards. *HHS.* https://www.hhs.gov

The World Bank. (2019, December). China Overview. *The World Bank.* https://www.worldbank.org/en/country/china/overview

WHO expert panel paves way for strong international governance on human genome editing. (n.d.). Retrieved from https://www.who.int/news-room/detail/19-03-2019-who-expert-panel-paves-way-for-strong-international-governance-on-human-genome-editing

WHO. (n.d.). Genes and human diseases. *World Health Organization.* https://www.who.int/genomics/public/geneticdiseases/en/index2.html

World Fact Book. (2019, December). United Kingdom. *World Fact Book.* https://www.cia.gov/library/publications/the-world-factbook/attachments/summaries/UK-summary.pdf

Zehr, E. P. (2019, January 16). Human Gene Editing: Great Power, Great Responsibility. Retrieved from https://blogs.scientificamerican.com/observations/human-gene-editing-great-power-great-responsibility/

Zhang, J. (2015). The credibility paradox in China's science communication: Views from scientific practitioners *Public Understanding of Science.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4595815/