

HUMAN GERMLINE GENE EDITING: ENGINEERING AN UNSTOPPABLE TRAIN

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This, then, is the problem: science will not wait for man to catch up. It does not hold itself responsible for the morals or capacities of its human employers. It gives us a fire engine with which to throw water to extinguish a fire; if we want to use the engine to throw kerosene on the fire, it is our lookout. The engine is adapted to both purposes.

— Raymond Fosdick¹

I. INTRODUCTION

Humans: engineers of our own destiny. Science has gifted humanity powers for great good, but also weapons capable of the most unconscionable evils. In that respect, the arrival of human genetic engineering is no different. On one hand, gene editing technology has the potential to cure the world of all genetic diseases. On the other hand, rearranging human DNA to our liking could have unimaginable consequences. To some, the act of genetically modifying human germlines is an unconscionable trespass into the territory of God. However, as grave as the moral and medical risks of human germline engineering may be, science is a one-way train that will stop for no man's conscience. Nevertheless, some limited blockades have persisted in the United States—e.g., bans and moratoria on human cloning.² Rather than playing the role of prison warden and locking away germline gene editing behind closed regulatory walls, the United States should be a diligent steward and teacher of the technology, carefully nurturing its development towards an acceptable future.

This paper will first examine the development of gene editing technology and its application in human cells in vitro. Second, it will examine the current progress in applying gene editing technology in human cells in vivo and what regulations are in place for regulating clinical germline gene editing. Third, this paper will then present the moral and ethical argument for and against human germline engineering. Fourth, this paper will examine the legal arguments for germline gene editing. Finally, this

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1. PETER H. DENTON, *THE ABC OF ARMAGEDDON: BERTRAND RUSSELL ON SCIENCE, RELIGION, AND THE NEXT WAR, 1919–1938*, at 134 (2001).

2. Paul Berg, *Asilomar 1975: DNA Modification Secured*, 455 *NATURE* 290, 290 (2008).

paper will conclude with an argument as to why human germline gene editing research and application should be permitted in the United States in specific circumstances and under a tightly controlled regulatory scheme.

II. BACKGROUND

Although the technology for human genetic engineering has been around for several decades,³ human germline gene engineering has accelerated in the past few years. The first instance of human germline engineering was reported in 2015 by scientists in China.⁴ More recently, in July 2017, scientists at the University of Portland published the first case of genetic modification of human embryos.⁵ Before examining how the United States and other countries have regulated human genetic engineering, it is important to understand how gene-editing technology has evolved and why recent scientific advances have greatly increased its practical application today.

A. THE DEVELOPMENT OF GENE EDITING SCIENCE

Human genetic engineering comprises a multitude of technologies.⁶ For example, genetic modification of human embryos in the United States occurred as early as 2001 when scientists used ooplasmic transfer, the transferring of healthy mitochondria into an infertile mother's eggs to overcome infertility.⁷ For this paper, I will only be examining one specific technique of human genetic engineering: gene editing. Unlike ooplasmic transfer, which injects a set of genes to co-exist with the existing cell's genome, gene editing inserts, deletes or even replaces a target gene.⁸

Gene editing first began with the use homologous recombination ("HR").⁹ Homologous is defined as "having the same relative position, value, or structure."¹⁰ In a genetic context, HR involves the exchange of similar or identical DNA sequences between two similar molecules within a cell.¹¹ When DNA is damaged and double-stranded DNA break occurs, HR repairs the DNA by bringing together homologous or corresponding DNA

3. See Jennifer A. Doudna & Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 *SCI.* 1077, 1078 (2014).

4. David Cyranoski & Sara Reardon, *Chinese Scientists Genetically Modify Human Embryos*, *NATURE* (Apr. 22, 2015), <https://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378>.

5. See Hong Ma et al., *Correction of a Pathogenic Gene Mutation in Human Embryos*, 548 *NATURE* 413, 413–17 (2017).

6. Doudna, *supra* note 3, at 1078–79.

7. Annabel Ferriman, *First Cases of Human Germline Genetic Modification Announced*, 322 *BRIT. MED. J.* 1144, 1144 (2001).

8. See S. Antony Ceasar et al., *Insert, Remove or Replace: A Highlight Advanced Genome Editing System Using CRISPR/Cas9*, 1863 *BIOCHIMICA ET BIOPHYSICA ACTA* 2333, 2335 (2016).

9. See Stewart Scherer & Ronald W. Davis, *Replacement of Chromosome Segments with Altered DNA Sequences Constructed in Vitro*, 76 *PROC. NAT'L ACAD. SCI.* 4951, 4951 (1979).

10. *Homologous*, MERRIAM-WEBSTER ONLINE DICTIONARY, <https://www.merriam-webster.com/dictionary/homologous>.

11. Patrick Sung & Hannah Klein, *Mechanism of Homologous Recombination: Mediators and Helicases Take on Regulatory Functions*, 7 *NATURE REV. MOLECULAR CELL BIOLOGY* 739, 739–41 (2006).

regions and effectively restoring the original nucleotide sequence.¹² In addition, during meiosis—cell division yielding haploid cells—HR can increase genetic diversity by exchanging homologous regions from sister chromatids (one of the halves of a replicated chromosome, joined at the centromere).¹³ In 1979, Stanford scientists took advantage of HR and were able to delete and replace a mutant gene in yeast.¹⁴ Although HR pioneered the field of gene editing, it is not without its shortcomings. HR is extremely inefficient and is either isolated to simple organisms or requires the time-consuming selection of rare-events to achieve homology in more complex animals such as mice.¹⁵ Furthermore, although HR gene editing has been successfully done in animal models, it has been extremely inefficient in human cells.¹⁶

In 1989, scientists made a breakthrough in DNA recombination technology by inducing specific enzymatic breaks in the DNA rather than relying on natural recombination events.¹⁷ In homology-directed repair (“HDR”), an external DNA fragment is used to initiate specific repair at the targeted DNA site.¹⁸ Compared to HR, HDR implements significantly shorter single-stranded DNA inserts.¹⁹ While HDR DNA inserts are easy to design and produce, they too have their own limitations.²⁰ The short DNA inserts are conducive to fixing point mutations—involving a single nucleotide base—but are unable to replace lengthier genes.²¹ Moreover, because the length of HDR inserts is so small, it is prone to off-target editing.²² Lastly, even if HDR-inserts edit the correct site, confirmation of the gene editing requires time-consuming DNA screening protocols.²³

The need for less restrictive site-specific gene editing was eventually addressed by the use of Zinc-fingered nucleases (“ZFNs”) for genomic engineering. In the early 2000’s, scientists discovered that when source-independent nucleases were paired with Zinc-fingered DNA recognition proteins, the complex could cut DNA at almost any point and with more

12. *Id.*

13. *See DNA Is Constantly Changing Through the Process of Recombination*, NATURE EDUC.: SCITABLE, <https://www.nature.com/scitable/topicpage/dna-is-constantly-changing-through-the-process-6524876> (last visited Apr. 11, 2019).

14. *See* Scherer, *supra* note 9.

15. *See* Alvaro P. Reyes & Fredrik Lanner, *Towards a CRISPR View of Early Human Development: Applications, Limitations and Ethical Concerns of Genome Editing in Human Embryos*, 144 DEV. 3, 4 (2017); *see also* Kirk Thomas et al., *High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome*, 44 CELL 419, 419 (1986).

16. Raheleh Heidari et al., *CRISPR and the Rebirth of Synthetic Biology*, 23 SCI. ENG’G ETHICS 351, 352 (2017).

17. *See* Norah Rudin et al., *Genetic and Physical Analysis of Double-Strand Break Repair and Recombination in Saccharomyces Cerevisiae*, 122 GENETICS 519, 520 (1989).

18. *See* Reyes, *supra* note 15, at 3.

19. Kazuyuki Hoshijima et al., *Precise Genome Editing by Homologous Recombination*, 135 METHODS IN CELL BIOLOGY 121, 123–24 (2016).

20. *Id.* at 124.

21. *Id.*

22. *Id.*

23. *Id.*

precision compared to previous HR and HDR techniques.²⁴ While gene editing using ZFNs proved effective in drosophila and mammalian cells, the production of effective DNA binding protein complexes and the confirmation of locus-specific ZFNs was extremely difficult and laborious.²⁵ To the delight of the field, in 2009, a new DNA recognition protein, the transcription activator-like effector (“TAL”), was discovered for gene editing.²⁶ TALs are naturally produced in bacteria, making their production significantly easier.²⁷ By combining TALs to source-independent nucleases to create TALENs, scientists had a cheaper alternative to ZFNs without sacrificing significant editing efficiency.²⁸ Although TALENs provided an effective method of gene editing, the costs of protein design, synthesis, and validation remained generally high.²⁹

Enter CRISPR-Cas9. First discovered in 1987, CRISPRs, or Clustered Regularly Interspaced Short Palindromic Repeats, are naturally found in bacteria and are comprised of short, repetitive nucleotide sequences.³⁰ However, it wasn't until 2005-2007 that their role in the bacteria's natural defense system was reported.³¹ In short, when viral or foreign DNA is detected, the bacteria's natural defense system will cut the foreign DNA into small sequences and then incorporate it into the bacterial genome using flanking CRISPRs. If the same foreign DNA invades the bacteria at a later time, guide RNAs derived from the previously incorporated foreign DNA segments will then recognize and bind onto the foreign DNA. Once bound, CRISPR recruits *Cas* restriction enzymes to cut up the invading DNA. Bacteria utilize three *Cas* systems (I, III & III).³² Although *Cas* I and III immunity pathways require complexes of multiple *Cas* proteins for DNA digestion,³³ it was discovered that type II immunity only requires a single protein, *Cas9*.³⁴ Based on the *Cas9* immunity pathway, scientists were able to engineer a single CRISPR guide RNA (sgRNA) for gene editing.³⁵ sgRNAs are comprised of a single-stranded 5' twenty-nucleotide sequence (for targeting a specific DNA sequence) attached to a 3' double-stranded

24. See Marina Bibikova et al., *Targeted Chromosomal Cleavage and Mutagenesis in Drosophila Using Zinc-Finger Nucleases*, 161 *GENETICS* 1169, 1169–70 (2009); Marina Bibikova, *Enhancing Gene Targeting with Designed Zinc Finger Nucleases*, 300 *SCI.* 764, 764 (2003).

25. See Doudna, *supra* note 3, at 1078.

26. See Jens Boch et al., *Breaking the Code of DNA Binding Specificity of TAL-Type III Effectors*, 326 *SCI.* 1509, 1509 (2009); Matthew J. Moscou & Adam J. Bogdanove, *A Simple Cipher Governs DNA Recognition by TAL Effectors*, 326 *SCI.* 1501, 1501 (2009).

27. See Doudna, *supra* note 3, at 1078.

28. Jeffrey M. Perkel, *Genome Editing with CRISPRs, TALENs and ZFNs*, *BIOCOMPARE* (Aug. 27, 2013), <http://www.biocompare.com/Editorial-Articles/144186-Genome-Editing-with-CRISPRs-TALENs-and-ZFNs/>.

29. See Doudna, *supra* note 3, at 1078.

30. Yoshizumi Ishino et al., *Nucleotide Sequence of the *Iap* Gene, Responsible for Alkaline Phosphatase Isozyme Conversion in *Escherichia Coli*, and Identification of the Gene Product*, 169 *J. BACTERIOLOGY* 5429, 5429 (1987).

31. See Doudna, *supra* note 3, at 1078–79.

32. *Id.* at 1079.

33. *Id.*

34. Martin Jinek et al., *A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity*, 337 *SCI.* 816, 816–17 (2012).

35. *Id.*

structure for binding to the Cas9 protein.³⁶ In contrast to ZNC and TALEN systems, which require complex and laborious synthesis of different protein complexes for every new DNA restriction site, the CRISPR-Cas9 system only requires a simple change to the twenty-nucleotide guide RNA sequence—providing a significantly easier and more efficient method of precise gene editing.³⁷ In addition, while ZNC and TALEN systems inherently must have DNA recognition and nuclease complexes affixed to each other, the CRISPR system has the flexibility of using a CRISPR-Cas9 complex or separately injecting the sgRNA and Cas9 protein into the target cell.³⁸

B. CRISPR GENE EDITING IN HUMAN CELLS IN VITRO

Starting in 2012, numerous CRISPR studies have shown successful gene editing in human cells in vitro.³⁹ Just to name a few, gene editing has been done in human embryonic kidney, chronic myelogenous leukemia, T-lymphocyte, fibroblasts and pluripotent stem cells.⁴⁰ While gene editing of human somatic cells has been hotly pursued by scientists, human germline gene editing has been embroiled in controversy. In April 2015, scientists in China reported the world's first case of genomic editing in human embryos.⁴¹ The Chinese scientists used the CRISPR-Cas9 system in 'non-viable' pre-implantation, single-cell embryos to edit the HBB mutation, which causes the disease β -thalassaemia.⁴² Their initial findings suggested that CRISPR gene-editing in germ lines would be more difficult than in somatic cells.⁴³ A year later, another Chinese team published another paper detailing the use of CRISPR-Cas9 to make human embryos resistant to HIV.⁴⁴ The scientists also collected non-viable embryos and used CRISPR to introduce a mutation into cell surface protein CCR5.⁴⁵ If successful, the mutated CCR5 protein would prevent the HIV virus from entering T-lymphocytes.⁴⁶ Although a few

36. *Id.*

37. See Perkel, *supra* note 28.

38. Heidi Ledford, *CRISPR Fixes Embryo Error*, 548 NATURE 13, 14 (2017).

39. See Doudna, *supra* note 3, at 1081.

40. See Doudna, *supra* note 3, at 1081; Rafal Kaminski et al., *Elimination of HIV-1 Genomes From Human T-Lymphoid Cells by CRISPR/Cas9 Gene Editing*, 6 SCI. REPS. 1, 2 (2016); Sojung Kim, *Highly Efficient RNA-guided Genome Editing in Human Cells Via Delivery of Purified Cas9 Ribonucleoproteins*, 24 GENOME RES. 1012, 1013–14 (2014).

41. See Cyranoski & Reardon, *supra* note 4 (explaining how 86 embryos were injected with the CRISPR-Cas9 complex. 71 embryos survived and 54 were genetically tested; only little more than half the embryos (28 embryos) were successfully spliced at the target site and only fraction of the spliced embryos incorporated the correct genetic sequence; in addition, there was a high occurrence of off-target gene editing). β -thalassaemia is a hemoglobinopathy somewhat similar to sickle cell anemia. One form is Cooley's or Mediterranean anemia.

42. *Id.*

43. *Id.*

44. Ewen Callaway, *Second Chinese Team Reports Gene Editing in Human Embryos*, NATURE (Apr. 8, 2016), <http://www.nature.com/news/second-chinese-team-reports-gene-editing-in-human-embryos-1.19718> (explaining how, of the 26 human embryos targeted, only 4 embryos were successfully modified; of the 4 embryos successfully modified, not all of the embryos' chromosomes contained a mutated version of CCR5, resulting in a mosaic phenotype).

45. *Id.*

46. *Id.*

embryos adopted the mutated CCR5 gene, only about 15% of the embryos were successfully spliced.⁴⁷ Moreover, in the few embryos actually spliced, not all chromosomes exhibited a modified CCR5 allele—further demonstrating the inefficiencies and off-target risks of CRISPR gene editing in human germ lines.⁴⁸ In March 2017, a third Chinese team published the first CRISPR gene editing paper using viable embryos.⁴⁹ Although the viable embryos performed slightly better than the previous non-viable embryo studies, the scientists still ran into significant issues with editing efficiency and mosaic phenotypes.⁵⁰ Thus, until recently, it appeared that germline gene editing might never reach clinical applications due to varied and significant technical obstacles.

In August 2017, privately-funded scientists from the University of Portland reported the first instance of human germline CRISPR gene editing in the United States.⁵¹ The scientists target a mutation called MYBPC3, which causes hypotrophic cardiomyopathy in adults.⁵² Like the most recent embryo gene editing report to come out of China, the Portland study also used viable pre-implantation embryos.⁵³ However, in contrast to the Chinese studies, which exhibited low splicing efficiency and mosaic or off-target effects, the Portland study reported high gene editing efficiency, low off-target effects, and almost no mosaic phenotypes.⁵⁴ The study attributed its gene editing success to a change in CRISPR application protocol.⁵⁵ The scientists showed that injecting the CRISPR-Cas9 complex during the MII-phase of the oocytes dramatically reduced mosaic phenotypes.⁵⁶ In addition, by injecting the CRISPR guide RNA attached to the Cas9 protein rather than injecting them as separate items, the scientists created a complex that would degrade faster within the cell—thereby allowing “little time for off-target mutations to accumulate.”⁵⁷

The recent advancements of germline gene editing technology are a direct reflection of the progress of gene editing therapies in human clinical trials. On November 15th, 2017, doctors announced the United State’s first attempt at gene editing in a human patient using ZFNs.⁵⁸ Considering the cost and efficiency upside of CRISPR technology compared to ZFNs, it may only be a matter of time before CRISPR clinical trials are also implemented. As the technology for genomic engineering continues to advance, the United

47. *Id.*

48. *Id.*

49. Lichun Tang, *CRISPR/Cas9-mediated Gene Editing in Human Zygotes Using Cas9 Protein*, 292 MOLECULAR GENETICS & GENOMICS 525, 525 (2017).

50. *Id.* at 532.

51. See Ledford, *supra* note 38, at 13–14.

52. *Id.* at 13.

53. Hong Ma et al., *supra* note 5.

54. *Id.* at 413–18 (72.4% (42 of 58) were successfully spliced and of tested embryos exhibited a WT/WT phenotype; only one out of the 58 embryos displayed a mosaic phenotype).

55. *Id.*

56. *Id.*

57. Ledford, *supra* note 38, at 14.

58. *Scientists in Oakland Try 1st Gene Editing In the Body*, CBS: SF BAY AREA (Nov. 15, 2017), <http://sanfrancisco.cbslocal.com/2017/11/15/first-gene-editing-in-body-crispr-oakland/> [hereinafter *Scientists in Oakland*].

States must also develop a regulatory framework to oversee the technical and ethical challenges posed by human germline engineering.

C. U.S. REGULATION OF GENETIC ENGINEERING IN HUMAN SOMATIC CELLS

While federal regulation of genetically modified crops and organisms has been well established for several decades,⁵⁹ the genetic modification of humans has been the subject of more recent legislation. Before examining current United States legislation on gene editing, this paper will first review the history of regulating human genetic engineering.

Recombinant DNA technology, the artificial synthesis of DNA, first began to develop in the early-1970s.⁶⁰ In 1974, amidst growing recognition of the potential benefits and risks associated with recombinant DNA, the National Institute of Health (“NIH”) established the Recombinant DNA Advisory Committee (“RAC”) to oversee public safety concerns about manipulating DNA.⁶¹ At the Asimolar Conference on Recombinant DNA Molecules, the committee addressed the “many unknowns” and “potential biohazards” of recombinant DNA technology, and recommended that research freedom be limited to match the risk of the technology until it was better understood.⁶² A year later, the NIH followed suit and issued guidelines for any recombinant DNA research that wished to receive NIH funding.⁶³

As DNA biotechnology evolved in the 1980’s, the possibility of gene transfer in humans came to the attention of the federal government.⁶⁴ Initially only considered in somatic cells, gene therapy involved using a vehicle, often viruses, to delivery a healthy version of a gene that was defective in a human patient. The viruses could either be delivered directly into the patient (in vivo) or used on cells extracted from the patient (ex vivo) that were later transplanted back into the patient’s body.⁶⁵ In the 1980’s, RAC established a subsidiary agency, the Office of Biotechnology Activities (now known as the Office of Science Policy), to establish regulations for and review all federally funded gene therapy experiments.⁶⁶

For human gene therapy clinical trials, investigators were required to submit an Investigational New Drug Application (IND) to the Food and Drug

59. See generally Luis Acosta, *Restrictions on Genetically Modified Organisms: United States*, LIBR. OF CONGRESS (Mar. 2014), <https://www.loc.gov/law/help/restrictions-on-gmos/usa.php>; JONATHAN TUCKER, FED’N OF AM. SCIENTISTS, *U.S. Regulation of Genetically Modified Crops*, in CASE STUDIES IN AGRIC. BIOSECURITY (2011), <https://fas.org/biosecurity/education/dualuse-agriculture/2.-agricultural-biotechnology/us-regulation-of-genetically-engineered-crops.html>.

60. See Mark Jones, *The Invention of Recombinant DNA Technology*, LSF MAG. (Nov. 11, 2015), <https://medium.com/lsf-magazine/the-invention-of-recombinant-dna-technology-e040a8a1fa22>.

61. See Eileen M. Kane, *Human Genome Editing: An Evolving Regulatory Climate*, 57 JURIMETRICS 1, 6 (2017); *Gene Therapy Legislation in the US*, GENETHERAPYNET.COM, <http://www.genetherapynet.com/united-states-of-america.html>.

62. Paul Berg et al., *Summary Statement of the Asilomar Conference on Recombinant DNA Molecules*, 72 PROC. NAT’L ACAD. SCI. 1981, 1981–82 (1975).

63. Recombinant DNA Research Guidelines, 41 FED. REG. 27,902 (July 7, 1976).

64. See Kane, *supra* note 61, at 7.

65. *Id.* at 2, 7.

66. Berg et al., *supra* note 62.

Administration (FDA) for approval from local Institutional Review Boards (IRB) and local Institutional Biosafety Committees (IBC).⁶⁷ Before testing gene therapy products in humans, the FDA requires thorough testing of the technology in laboratories and research animals to prove safety and efficacy.⁶⁸ Once the technology is ready for human application, the IRB reviews such proposals to ensure that patients have been adequately informed of the risks and consented to the procedure.⁶⁹ Before the gene therapy is permitted to be commercially available it must prove its safety (Phase I), optimal dosage (Phase II), and efficacy (Phase III) in human clinical trials.⁷⁰

On August 30, 2017, the FDA unanimously approved the first gene therapy for market use.⁷¹ The gene therapy involves genetically modifying a patient's T-cells and re-injecting them back into the patient to fight leukemia.⁷² Although China and Europe have already approved gene therapies for cancer and inherent diseases, the FDA's landmark approval was a first for the United States and could be a sign of a long line of market-approved gene therapies to come.⁷³ After almost 30 years of without approving a single gene therapy, there is speculation that the FDA could deem a second gene therapy market-ready as soon as this year.⁷⁴

As previously discussed, the use of ZFNs, TALENs, or CRISPR technology in human cells has opened the door to genome editing in humans. Specifically, the successful editing of human pluripotent stem cells allows scientists to engineer any tissue in the human body.⁷⁵ Taking advantage of induced pluripotent stem cell (iPSC) technology, future scientists could reprogram a patient's readily available tissue, such as fibroblasts or peripheral blood mononuclear cells, into pluripotent cells, edit them to fix or introduce a mutation, and then differentiate the cells into a desired tissue for patient transplantation.

67. INST. OF MED., COMM. ON THE INDEP. REV. & ASSESSMENT OF THE ACTIVITIES OF THE NIH RECOMBINANT DNA ADVISORY COMM., OVERSIGHT AND REVIEW OF CLINICAL GENE TRANSFER PROTOCOLS: ASSESSING THE ROLE OF THE RECOMBINANT DNA ADVISORY COMMITTEE 24, 41 (Rebecca N. Lenzi et al. eds., 2014), <http://www.nationalacademies.org/hmd/Reports/2013/Oversight-and-Review-of-Clinical-Gene-Transfer-Protocols.aspx>. Gene therapy is regulated by the FDA in part because it involves biologics and can be used as a drug delivery system. See generally Helen M. Blau & Matthew L. Springer, *Gene Therapy—A Novel Form of Drug Delivery*, 333 NEW ENG. J. MED. 1204, 1204 (1995); Daniel Bobo et al., *Nanoparticle-Based Medicines: A Review of FDA-Approved and Clinical Trials to Date*, 33 PHARMACEUTICAL RES. 2373, 2373–74 (2016).

68. Berg et al., *supra* note 62.

69. *Id.*

70. See *Overview of Clinical Trials*, CENTERWATCH, <https://www.centerwatch.com/clinical-trials/overview.aspx> (last visited Apr. 12, 2019).

71. See Jocelyn Kaiser, *Modified T Cells That Attack Leukemia Become First Gene Therapy Approved in the United States*, SCI. (Aug. 30, 2017), <http://www.sciencemag.org/news/2017/08/modified-t-cells-attack-leukemia-become-first-gene-therapy-approved-united-states>.

72. *Id.*

73. *Id.*

74. *Id.*

75. See *Pluripotent Stem Cells 101*, BOSTON CHILDREN'S HOSPITAL: ABOUT STEM CELLS (Aug. 30, 2017, 2:48 PM), <http://stemcell.childrenshospital.org/about-stem-cells/pluripotent-stem-cells-101/>.

The FDA approved the first clinical trial for human gene editing in 2009.⁷⁶ The clinical trial extracted the patient's own T-cells, genetically modified the T-cell *ex vivo* to prevent HIV infection, and infused the cells back into the patients to restore their immune system.⁷⁷ The treatment has passed both phase I and II clinical trials.⁷⁸ In 2015, the first *in vivo* human gene editing protocol was approved for using ZFNs to correct a liver protein deficiency.⁷⁹ Subsequently, in 2016, the FDA approved another *in vivo* gene editing protocol for the treatment of mucopolysaccharidosis type II (MPS II).⁸⁰ Lastly, on November 15, 2017, a MPS II patient became the first person in the history of the United States to receive an *in vivo* gene therapy treatment.⁸¹

D. U.S. AND INTERNATIONAL REGULATION OF HUMAN GERMLINE RESEARCH

Despite the recent advances in human somatic cell gene therapy, gene editing of the human germline is still facing significant resistance and controversy in the United States. To many, gene editing technology still carries significant unacceptable safety and ethical risks.⁸² Because the effects of germline gene editing are still unpredictable, the area of research has been generally considered taboo in many other countries as well.⁸³ At least at a superficial level, when it comes to altering the genetic code, people drift into an uninformed risk aversion against sharp interferences with Nature and personal identity—as opposed to sexual recombination for hoped-for outcomes.⁸⁴ It is no surprise then that editing gametes or embryos for human

76. See Sangamo BioSciences Announces Plans to Initiate a Second Clinical Trial of CCR5-ZFP Therapeutic to Treat HIV/AIDS, PIPELINEREVIEW.COM (Sept. 23, 2009), <https://pipelinereview.com/index.php/2009092329608/DNA-RNA-and-Cells/Sangamo-BioSciences-Announces-Plans-to-Initiate-a-Second-Clinical-Trial-of-CCR5-ZFP-Therapeutic-to-Treat-HIV/AIDS.html> [hereinafter *Sangamo BioSciences*]; see also *Autologous T-Cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases SB-728 in for HIV*, U.S. NAT'L LIBRARY OF MED.: CLINICALTRIALS.GOV, <https://clinicaltrials.gov/ct2/show/record/NCT00842634>.

77. *Id.* See *Sangamo BioSciences*, *supra* note 76 (T-cells were modified by editing in a mutant CCR5 gene).

78. See News Release, *Sangamo Biosciences Presents Phase 2 Immunological Data from SB-728-T ZFP Therapeutic HIV Program at CROI 2016*, SANGAMO THERAPEUTICS (Feb. 24, 2016, 12:00 AM), <http://investor.sangamo.com/news-releases/news-release-details/sangamo-biosciences-presents-phase-2-immunological-data-sb-728-t>.

79. See News Release, *Sangamo BioSciences Announces FDA Clearance of Investigational New Drug Application For SB-FIX, First In Vivo Protein Replacement Platform Program for Treatment of Hemophilia B*, SANGAMO THERAPEUTICS (Dec. 1, 2015), <http://investor.sangamo.com/news-releases/news-release-details/sangamo-biosciences-announces-fda-clearance-investigational-2> (gene editing to raise the long-term levels of Factor IX in hemophilia B patients).

80. See News Release, *Sangamo BioSciences Announces FDA Clearance of Investigational New Drug Application for ZFN-Mediated Genome Editing Treatment of MPS II*, SANGAMO THERAPEUTICS (June 20, 2016), <http://investor.sangamo.com/news-releases/news-release-details/sangamo-biosciences-announces-fda-clearance-investigational-0>.

81. *Scientists in Oakland*, *supra* note 58.

82. See Edward Lanphier et al., Comment, *Don't Edit the Human Germ Line*, 519 NATURE 410, 411 (2015), <https://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111>.

83. *Id.*

84. See generally BROOK LARMER, OPERATION YAO MING: THE CHINESE SPORTS EMPIRE, AMERICAN BIG BUSINESS, AND THE MAKING OF AN NBA SUPERSTAR (2005).

reproduction has been prohibited in the United States.⁸⁵ This paper will dive deeper into the ethical and practical arguments for and against human germline editing at a later point, but for the purposes of this section, the paper will only examine the regulatory framework that has existed regarding human germline editing.

Even before the advent of gene editing technology, human germline research has been tightly regulated. In response to public apprehension regarding embryonic stem cell research in the early 1990's, the Dickey-Wicker amendment, continuously renewed since its insertion into the appropriation bill in 1996, bans federal funding for research comprised of creating, discarding or destroying embryos.⁸⁶ Human germline editing was then launched into the forefront of scientific community in 2015 when a team in China announced the world's first case of human germline editing using CRISPR to correct a genetic mutation causing β -thalassemia, a recessive hemoglobin disorder, in pre-implantation embryos.⁸⁷

The response of the United States government was swift. The White House almost immediately issued a statement condemning gene editing of the human germline,⁸⁸ and Congress held several hearings to discuss gene editing technology.⁸⁹ At the end of the fiscal year in 2015, Congress approved an amendment to the year's appropriation bill—prohibiting all federal funding of human germline research.⁹⁰ Specifically, the amendment prohibited federally funded “research in which a human embryo is intentionally created or modified to include a heritable genetic modification.”⁹¹ Shortly after, the NIH explicitly announced that no federal funding would be appropriated for gene editing of human germlines.⁹² Moreover, the RAC would continue to deny review for any applications for human germline research.⁹³ Of note, while federal funding and support is strictly prohibited for gene editing of the human germline, there are currently no repercussions for privately funded human germline research.⁹⁴ As discussed before, a recent study on gene editing using viable human embryos was completed in the United States using private funds.⁹⁵ Some

85. See Julie Steenhuisen, *U.S. Scientists Urge 'Serious Consideration' of Gene Editing in Human Embryos*, HUFFINGTON POST (Feb. 15, 2017), https://www.huffingtonpost.com/entry/us-scientists-urge-serious-consideration-of-gene-editing-in-human-embryos_us_58a48664e4b03df370dc6fcf.

86. See Kane, *supra* note 61, at 13.

87. See Cyranoski & Reardon, *supra* note 4.

88. John P. Holdren, *A Note on Genome Editing*, WHITE HOUSE: BLOG (May 26, 2015, 10:40 AM), <https://obamawhitehouse.archives.gov/blog/2015/05/26/note-genome-editing>.

89. See, e.g., *The Science and Ethics of Genetically Engineered Human DNA: Hearing Before the Subcomm. on Res. & Tech. of the H. Comm. on Sci., Space, and Tech.*, 114th Cong. (2015), <https://www.gpo.gov/fdsys/pkg/CHRG-114hhrg97564/pdf/CHRG-114hhrg97564.pdf>.

90. *Id.*

91. Consolidated Appropriations Act, Pub. L. No. 114-113, § 749, 129 Stat. 2283 (2015).

92. Sara Reardon, *NIH Reiterates Ban on Editing Human Embryo DNA*, NATURE (Apr. 29, 2015), <https://www.nature.com/news/nih-reiterates-ban-on-editing-human-embryo-dna-1.17452>.

93. Kathi E. Hanna, *Germline Gene Transfer*, NAT'L HUM. GENOME RES. INST. (Mar. 2006), <https://www.genome.gov/10004764/germline-gene-transfer/>.

94. See Ledford, *supra* note 38, at 13–14.

95. *Id.*

constitutional considerations regarding state and federal regulation of the private sector are discussed later in this paper.

Although there are no signs that the United States will change its policy towards genetic engineering of the human germline, other countries have already officially adopted human germline research to some capacity. The extent of human germline research allowed varies greatly from country to country.⁹⁶ For example, voluntary self-regulation treaties have been signed by multiple countries, but each country ultimately has its own specific regulations for embryo research.⁹⁷ Three countries, China, Sweden and the United Kingdoms, have already sanctioned gene-editing experiments on human embryos for research into early human development.⁹⁸

No country is pushing human germline gene editing research harder than China. It is fitting that the country that first broke the glass door on gene editing in human embryos would be leading the way for the controversial field. Human germline editing research has been able to thrive in China in part because of how ethical research laws are (or better yet) not enforced. For example, in 2015, when China reported the first case of human germline editing, its Guidelines on Human Assisted Reproductive Technologies stated that “using human egg plasma and nuclear transfer technology for the purpose of reproduction, and manipulation of the genes in human gametes, zygotes or embryos for the purposes of reproduction are prohibited.”⁹⁹ However, the 2015 study was likely able to proceed because such administrative research guidelines are considered “soft law” and not thoroughly enforced.¹⁰⁰ Today, any Chinese university or hospital can freely conduct clinical trials for gene editing technology with approval from their own ethics commissions and do not require approval by China’s federal government.¹⁰¹ Interestingly, it also seems that China is equally willing to support gene editing research for fixing disorders as opposed to human augmentation. For example, while one Chinese study gene edited embryos to correct the mutation for β -thalassemia,¹⁰² another Chinese study enhanced an embryo to give it genetic resistance against HIV.¹⁰³ With other countries following China’s lead, one wonders whether it is inevitable that the United States will eventually join the fray.

96. See generally Rosario Isasi et al., *Editing Policy to Fit the Genome?*, 351 SCI. 337 (2016) (providing global maps of national standards on genetic research).

97. See COUNCIL OF EUR., EUR. TREATY SERIES, No. 164, CONVENTION FOR THE PROTECTION OF HUMAN RIGHTS AND DIGNITY OF THE HUMAN BEING WITH REGARD TO THE APPLICATION OF BIOLOGY AND MEDICINE: CONVENTION ON HUMAN RIGHTS AND BIOMEDICINE 1, 4, 9 (1997).

98. Ewen Callaway, *Gene-Editing Research in Human Embryos Gains Momentum*, 532 NATURE 289, 289 (2016), <https://www.nature.com/news/gene-editing-research-in-human-embryos-gains-momentum-1.19767>.

99. Lauren F Friedman, *These Are the Countries Where It’s ‘Legal’ to Edit Human Embryos (Hint: The US Is One)*, BUS. INSIDER (Apr. 23, 2015, 2:15 PM), <http://www.businessinsider.com/china-edited-human-genome-laws-2015-4>.

100. *Id.*

101. Cho Jin-young, *China Benefits Most from Genome Editing Technology Developed by S. Korea, US*, BUSINESSKOREA (Oct. 20, 2017), <http://www.businesskorea.co.kr/english/news/sciencetech/19614-genome-editing-china-benefits-most-genome-editing-technology-developed-s>.

102. Cyranoski, *supra* note 41.

103. Callaway, *supra* note 98.

III. THE ETHICS OF GERMLINE GENE EDITING

Although the technological shortcomings of germline gene editing technology may be overcome sometime in the future, the ethical controversy regarding “designing humanity” will always remain. It is not the first time our society has wrestled with the idea that mankind is using science to trespass into the realm of intelligent design. In the 1980’s, the same fear prompted the enactment of the Dickey-Wicker amendment and prohibitions on research comprising the creation or destruction of embryos.¹⁰⁴ Although the Dickey-Wicker amendment remains in effect today, the controversy surrounding embryonic stem cell research has significantly subsided compared to when it was at its apex.¹⁰⁵ One could argue that germline gene editing research should be allowed in a limited capacity and like embryonic stem cell research, will be generally accepted over time. However, this argument grossly oversimplifies the differences between embryonic stem cell and germline gene editing research. Although both kinds of research can be done concurrently, they are in principle very different: stem cell research doesn’t necessarily involve germ line editing, although it can include it. While existing pluripotent embryonic stem cell lines are able to differentiate into any type of human tissue, they almost certainly cannot be matured in a laboratory to form a full-fledged human being.¹⁰⁶ Viable gene-edited embryos, on the other hand, may readily grow into an actual human being if implanted into a surrogate mother. Therefore, while embryonic stem cell research is historically limited in its capacity to design a human being, germline gene editing faces significant questions regarding whether it is ethical to tread into the territory of intelligent design.

A. EUGENICS

Eugenics is the idea of systematically applying genetic selection in humans.¹⁰⁷ Negative eugenics teaches “breeding out” negative or unwanted characteristics (e.g. the Huntington’s Disease mutation); positive eugenics promotes desirable genetic traits (e.g. inheritable resistance to Malaria).¹⁰⁸ While proponents for eugenics might argue that it would only be used as a positive tool for fixing some of society’s greatest problems (e.g. inheritable disorders), critics of eugenics would argue that the application of eugenics is not governed by such a bright-line rule. The controversy surrounding eugenics involves the ambiguity regarding what defines a negative or positive characteristic. There are some clear candidates for negative eugenics, such as a Tay-Sachs Disease—a fatal heritable disorder that results

104. Ann A. Kiessling, *The History of the Dickey-Wicker Amendment*, BEDFORD RES. FOUND. (Aug. 24, 2010), <http://www.bedfordresearch.org/the-history-of-the-dickey-wicker-amendment/>.

105. See generally *Sherley v. Sebelius*, 689 F.3d 776 (D.C. Cir. 2012); R. Alta Charo, *The Case of Embryonic Stem Cell Research*, N.Y. TIMES (May 28, 2015, 6:45 AM), <https://www.nytimes.com/roomfordebate/2015/05/28/scientists-curbing-the-ethical-use-of-science/the-case-of-embryonic-stem-cell-research>.

106. Guido de Wert & Christine Mummery, *Human Embryonic Stem Cells: Research, Ethics and Policy*, 18 HUM. REPROD. 672, 674 (2003).

107. See Teddy Ellison, *Why Genetics Is Crispr Than It Used to Be: Helping the Novice Understand Germ Line Modification and Its Serious Implications*, 26 S. CAL. INTERDISC. L.J. 595, 597 (2017).

108. *Id.*

in severe mental retardation and death by the age of eight-years-old.¹⁰⁹ But what about the genetic profile for Down Syndrome patients? Individuals with Down Syndrome experience mental retardation, but can live functional adult lives. Or what about the gene for lactose intolerance? When deciding what sort of genetic conditions deserve eugenic treatment, one must face the difficult, if not impossible task of making value judgments on each disorder.¹¹⁰ Depending on the subjective view for each person, what may be considered an unacceptable characteristic to one individual may be acceptable to another. Therefore, genetic conditions are less likely to fall neatly into rigid categories and more likely to rest in a spectrum ranging from clearly unacceptable disorders to controversial attributes. As one moves along the spectrum away from unanimously dreadful diseases, the room for disagreement increases.

When such ambiguity exists, there is a greater risk that eugenics may be discriminatory. On one hand, eugenic champions might argue that it is unethical to deprive a mother an opportunity to use gene-editing technology to ensure a healthy child, and that society has a duty to produce healthier offspring.¹¹¹ Negative eugenics could be limited to only clear and obvious cases (e.g., eliminating fatal genetic diseases); positive eugenics could enhance the human race through safe gene editing practices (e.g. increasing resistance to diseases). On the other hand, critics might argue that eugenics sits on a slippery slope and if we allow the possibility of “breeding out” negative characteristics, we will eventually find ourselves back in the 1940s alongside the atrocities of the Holocaust. Critics could also point out that even if society does not descend to such depths, the very concept of eugenics is discriminatory because it suggests that some lives are not worth living.¹¹² If certain racial profiles become associated with diseases, eugenics risks stigmatizing such races.¹¹³ Furthermore, across and within different societies the economic availability of eugenic technology may greatly exacerbate inequality. For example, if the genes for high intelligence are identified and eugenic technology was only available at a high cost, already wealthy families would have a better opportunity to produce genetic “advantages” for their progeny. The ramifications of accelerating social, economic, and political stratification would be difficult to reverse.¹¹⁴ For such reasons, the

109. See Jaime Herndon, *Fatal Genetic Diseases*, LIVESTRONG.COM (Aug. 14, 2017), <https://www.livestrong.com/article/72920-fatal-genetic-diseases/>.

110. See generally Jerome C. Wakefield, *The Concept of Mental Disorder: On the Boundary Between Biological Facts and Social Values*, 47 AM. PSYCHOLOGIST 373, 374, 376–77 (1992).

111. Austen Roxanne Yeager, *The Ethics of CRISPR—Using Human Germline Gene Modification to Prevent Genetic Disease* 1, 4–14 (Spring 2016) (unpublished thesis, Linköping University), <https://pdfs.semanticscholar.org/f4fd/1514b2ad204aa56bd3599a360480da199d5e.pdf>.

112. See *Lives Not Worth Living: The Nazi Eugenic Dream in Our Own Time*, ALETEIA (Sep. 12, 2014), <https://aleteia.org/2014/09/12/lives-not-worth-living-the-nazi-eugenic-dream-in-our-own-time/>.

113. Morris W. Foster & Richard R. Sharp, *Race, Ethnicity, and Genomics: Social Classifications as Proxies of Biological Heterogeneity*, 12 GENOME RES. 844, 848 (2012).

114. See generally DANIEL DORLING, *INJUSTICE: WHY SOCIAL INEQUALITY STILL PERSISTS* (2010).

risk of abuse has been deemed intolerable and eugenics has been mostly rejected in the past several decades.¹¹⁵

On the other hand, one can argue that there is a significant difference between preventing the birth of persons with certain genetic conditions and killing of persons bearing a specific trait. Especially considering the benefits that would come with eliminating unambiguously harmful genetic traits (e.g. Tay-Sachs disease¹¹⁶), the benefits of eugenics may outweigh the risks. Even if one was to accept that eugenics bears a substantial risk of propagating social inequality, is the risk enough to deny the benefits of eugenics to society? Benefits may come at a price.

Regardless of where one stands on the eugenics debate, recent technological advances in gene editing have pumped new life into the eugenics debate. Whereas the historic versions of eugenics revolved around controlling reproductive partners—either by bringing persons together, keeping them apart, sterilization, or gamete selection (as with artificial insemination by donor)¹¹⁷—gene editing refines reproductive strategies by manipulating the very genetic material in any one individual.¹¹⁸

B. GENE DRIVE

One practical application of gene editing in eugenics is the idea of the gene drive.¹¹⁹ The gene drive is a genetic phenomenon whereby certain genes with “‘selfish’ genetic elements”—which provide hereditary advantages— increase the inheritance of the gene in subsequent generations within a population.¹²⁰ The idea is that by using gene drives for advantageous characteristics, scientists can utilize a longitudinal system to address “major biological problems related to public and environmental health.”¹²¹ In practice, a gene drive involves engineering specific genetic traits in a few individuals and propagating the traits throughout the local population through generations of reproduction.¹²² Due to difficulties surrounding engineering an effective gene drive system, gene drives have only been used

115. See Wesley J. Smith, *New and Old Eugenics United by Rejecting Human Exceptionalism*, EVOLUTION NEWS & SCI. TODAY (Feb. 20, 2016), https://evolutionnews.org/2016/02/new_and_old_eug/.

116. *Tay-Sachs Disease*, NAT'L INST. OF HEALTH, <https://rarediseases.info.nih.gov/diseases/7737/tay-sachs-disease>.

117. See Victoria Brignell, *The Eugenics Movement Britain Wants to Forget*, NEWSTATESMEN (Dec. 9, 2010), <https://www.newstatesman.com/society/2010/12/british-eugenics-disabled>.

118. See Amy Maxmen, *Easy DNA Editing Will Remake the World. Buckle Up.*, WIRED (2015), <https://www.wired.com/2015/07/crispr-dna-editing-2/>.

119. Jackson Champer et al., *Cheating Evolution: Engineering Gene Drives to Manipulate the Fate of Wild Populations*, 17 NATURE REV. GENETICS 146, 146 (2016).

120. *Id.*

121. *Id.*

122. See Kenneth A. Oye et al., *Regulating Gene Drives*, 345 SCI. 626, 626–27 (2014).

in a handful of organisms, including yeast,¹²³ fruitflies,¹²⁴ and mosquitoes.¹²⁵ With the evolution of CRISPR-Cas9 technology, however, development of gene drives are becoming increasingly viable. For example, historically it has been extremely difficult to create transgenes in mosquitoes that would be passed on to subsequent generations.¹²⁶ But in November 2015, scientists reported that they had successfully engineered a gene drive in mosquitoes using CRISPR-Cas9, which resulted in inheritance of the mutant gene in 99% of all offspring.¹²⁷ CRISPR-Cas9 technology has been subsequently used to engineer other mosquito gene drives to combat the spread of malaria.¹²⁸

While the idea of using gene drives to eliminate malaria in wild mosquito populations seems promising, the application of gene drives in humans is not so straightforward. One of the gene drive's greatest advantages is also one of its greatest weaknesses—its power to change an entire ecosystem.¹²⁹ Theoretically, once a dominant gene drive has been introduced to favorably bias its inheritance, it will inevitably spread throughout the population unless an accessible off switch is programmed into the gene drive. In mosquitoes, an organism much simpler and more laboratory-tested than humans, such a dramatic genetic change would still have unforeseeable impacts on the ecosystem and the mosquito's long-term survival in the wild. This illustrates both the causal uncertainties and the moral-conceptual “is this a benefit or risk” uncertainties in this field. Even the causal uncertainties aren't purely empirical but have value components (as in proximate cause). In humans, these issues are further complicated in that it would be impossible to test the effects of gene drives on human adults in a laboratory setting. In a perfect scenario, a gene drive without any adverse or off-target effects could be introduced into the human population to battle disease and ubiquitously enhance the human race. Even in such cases, however, would it really be a good idea to drive the same genetic characteristic throughout society? One of nature's best survival tools is genetic diversity.¹³⁰ An advantageous trait one day may be a weakness another day when there are new diseases or different environments. The tug-and-pull between whether a genetic

123. See James E. DiCarlo et al., *Safeguarding CRISPR-Cas9 Gene Drives in Yeast*, 33 NATURE BIOTECH. 1250, 1252–53 (2015).

124. Omar S. Akbari et al., *A Synthetic Gene Drive System for Local, Reversible Modification and Suppression of Insect Populations*, 23 CURRENT BIOLOGY 671, 676 (2013).

125. Valentino M. Gantz et al., *Highly Efficient Cas9-mediated Gene Drive for Population Modification of the Malaria Vector Mosquito Anopheles Stephensi*, 112 PROC. NAT'L ACAD. SCI. E6736, E6741 (2015).

126. See Heidi Ledford & Ewen Callaway, *'Gene Drive' Mosquitos Engineered to Fight Malaria*, NATURE (Nov. 23, 2015), <https://www.nature.com/news/gene-drive-mosquitoes-engineered-to-fight-malaria-1.18858>.

127. *Id.*

128. Gantz, *supra* note 125; see Rob Stein, *To Fight Malaria, Scientists Try Genetic Engineering to Wipe Out Mosquitoes*, NPR (Dec. 14, 2016, 4:20 PM), <https://www.npr.org/sections/health-shots/2016/12/14/504732533/to-fight-malaria-scientists-try-genetic-engineering-to-wipe-out-mosquitoes>.

129. See Stein, *supra* note 128.

130. See generally G. Booy et al., *Genetic Diversity and the Survival of Populations*, 2 PLANT BIOLOGY 379, 383 (2000).

modification is helpful in the short-term or detrimental in the unforeseeable future highlights the blurred “line between diversity and disability.”¹³¹

C. ETHICAL ISSUES WITH THE SAFETY OF GENE EDITING

Regardless of the potential impact of gene editing on diversity or inequality, society is not yet equipped with the technology to safely edit human germlines. Since 2003 and the completion of Human Genome Project, we have fully mapped the DNA of human beings.¹³² However, the knowledge of a human’s nucleotide sequence is a far cry from knowing how genes interact within one another and affect the human physiology. If germline gene modification is likely to have significant medical benefits, is it nevertheless justified if there are still unknown chances that it could have other unintended, adverse consequences as well? Perhaps with some fatal diseases, such as Huntington’s Disease, where a single point mutation causes all symptoms, the benefits of the potential cure may outweigh the safety risks of germline gene editing. In fact, just this year, the U.S. National Academy of Science and the National Academy of Medicine released a report suggesting that such gene editing clinical trials “‘might be permitted, but only following much more research’ on the risks and benefits, and ‘only for compelling reasons and under strict oversight.’”¹³³ Although clinical germline gene editing may be technologically possible in the near future, the state of current gene editing technology does not yet justify the start of clinical applications. The potential benefits of germline gene editing notwithstanding, society has a responsibility to consider the best interests of the potential human life if gene editing still poses significant adverse risks. Currently, there are still too many issues with off-target gene editing (undesired typos in gene editing) and too many questions regarding what unforeseen consequences gene editing may have on future generations.¹³⁴ Gene editing technology and our understanding of genetics will develop in time, but until we can definitively engineer an embryo without significant detrimental effects, there will remain significant questions surrounding medical applications of germline gene editing. Therefore, it is imperative that we support basic science research in human embryos if clinical gene editing treatments are ever to see the light of day.

131. Sarah Ashley Barnett, *Regulating Human Germline Modification in Light of CRISPR*, 51 U. RICH. L. REV. 553, 570 (2017).

132. *All About the Human Genome Project (HGP)*, NAT’L HUM. GENOME RES. INST., <https://www.genome.gov/10001772/all-about-the--human-genome-project-hgp/>.

133. Jocelyn Kaiser, *U.S. Panel Gives Yellow Light to Human Embryo Editing*, SCI. (Feb. 14, 2017, 11:00 AM), <http://www.sciencemag.org/news/2017/02/us-panel-gives-yellow-light-human-embryo-editing>. See generally George Church, *Compelling Reasons for Repairing Human Germlines*, 377 NEW ENG. J. MED. 1909 (2017); Bryan Cwik, *Designing Ethical Trials of Germline Gene Editing*, 377 NEW ENG. J. MED. 1911 (2017).

134. See Christopher Gyngell et al., *The Ethics of Germline Gene Editing*, 34 J. APPLIED PHIL. 498, 504–07 (2017).

IV. THE UNBORN LIFE'S LEGAL ARGUMENTS FOR GERMLINE GENE-EDITING

With the rapid development of gene editing technology in recent years, the discussion surrounding the legal right to germline gene editing is becoming increasingly important. If gene-editing technology becomes sufficiently safe and effective for clinical application, is there a legal right to germline gene editing? Several scholarly papers have approached the right from the perspective of the parent—specifically looking at whether there is a fundamental right to bodily enhancement/modification, procreation/family formation, or access to medical treatment.¹³⁵ Although such rights are relevant to germline gene editing, this paper will mainly focus on the right to germline gene editing from the perspective of the unborn child and its right to become a person.

First, I will give a brief background on the parent's legal arguments for germline gene editing. I will then examine the legal case for using germline gene editing to treat fatal diseases. Although I concede that there are differences between disorders that cause still-life births, adolescent deaths, and disorders that take effect later in adulthood, for the purposes of this paper I will treat all genetic conditions that lead to certain death as "fatal diseases." Lastly, I will examine whether there is a legal argument for using germline gene editing to treat debilitating, but non-fatal genetic conditions.

A. THE PARENT'S LEGAL CASE FOR GERMLINE GENE-EDITING

Independent of the effects of gene editing on the unborn life, the parent may hold a right to modify his or her body (i.e., the sperm or egg) independent of government interference.¹³⁶ In the context of the parent, gene editing is being used for bodily augmentation rather than disease prevention—fixing a gamete's genetic mutation is not fixing a disease that would affect the parent, but rather the unborn child.¹³⁷ The idea of enhancing one's body using technology has traditionally been associated with drugs and doping.¹³⁸ However, gene editing provides a new alternative that could potentially provide long-term enhancements to the body on a genetic level.¹³⁹ Thus, the same arguments that support a liberty interest in controlling one's own bodily integrity may also apply to choosing to enhance one's body through gene editing.¹⁴⁰

Additionally, one could also argue that the right to reproduction also supports the parent's right to gene editing.¹⁴¹ Since germline gene editing would presumably be applied solely to control the potential health and makeup of the unborn child, is there a significant difference between "careful reproductive mating" (such as choosing the right mating partner) and gene

135. See Ellison, *supra* note 107, at 601–10.

136. See *id.* at 601–05.

137. See *id.*

138. See *id.* at 607–09.

139. See generally James W.B. Bainbridge et al., *Long-Term Effect of Gene Therapy on Leber's Congenital Amaurosis*, 372 NEW ENG. J. MED. 1887 (2015).

140. See Ellison, *supra* note 107, at 607–09.

141. See *Id.* at 609–10.

editing?¹⁴² If gene editing is just an extension of the choice to reproduce, then a parent's right to choose germline gene editing may also be protected by the long-standing fundamental right to procreate and form families.¹⁴³

B. USING GERMLINE GENE EDITING TO SAVE THE UNBORN LIFE FROM FATAL GENETIC DEFECTS

Under current case law, a fetus has no constitutional rights, including the right to life.¹⁴⁴ In *Roe v. Wade*, the United States Supreme Court refused to recognize constitutional rights for the fetus in the course of determining the right to abortion.¹⁴⁵ Writing for the majority, Judge Blackmun stated, "the word 'person,' as used in the Fourteenth Amendment, does not include the unborn."¹⁴⁶ Rather, the Court determined the right to abortion by balancing the State's life interests in the unborn child and pregnant mother, against the mother's privacy interests in controlling her body and having an abortion.¹⁴⁷ However, Blackmun refused to answer when "life" may start, stating that:

We need not resolve the difficult question of when life begins. When those trained in the respective disciplines of medicine, philosophy, and theology are unable to arrive at any consensus, the judiciary, at this point in the development of man's knowledge, is not in a position to speculate as to the answer.¹⁴⁸

Instead, the Court settled on finding a compelling life interest in the unborn child at the beginning of the third trimester,¹⁴⁹ or as subsequently clarified in *Planned Parenthood v. Casey*,¹⁵⁰ at the beginning of fetal viability.

To analyze the unborn life's interest in germline gene editing, it must first be recognized that current germline gene editing research is done in the embryo, not the fetus. As a practical matter, it is easier to gene-edit the few cells of the embryo than it is to edit the thousands of cells of the fetus. Moreover, recent findings suggest that gene editing at the stage of fertilization reduces the risk of mosaic phenotypes.¹⁵¹ Even so, the rapid advances in both gene editing and artificial womb technology suggests that the legal distinctions between embryos and fetuses are beginning to blur.

Progress in reproductive science is beginning to reshape society's perception of the unborn human. Even though the Court refused to answer when human life begins in *Roe v. Wade*, Justice Blackmun did concede that "new embryological data . . . purport[s] to indicate that conception is a

142. *Id.* at 608.

143. *Right to Procreate*, USLegal, <https://civilrights.uslegal.com/due-process-violation/substantive-due-process/right-to-procreate/>.

144. See John A Robertson, *Fetal Personhood and the Constitution*, HARV. L.: BILL OF HEALTH (Aug. 20, 2015), <http://blogs.harvard.edu/billofhealth/2015/08/20/fetal-personhood-and-the-constitution/>.

145. *Roe v. Wade*, 410 U.S. 113, 158 (1973).

146. *Id.*

147. *Id.* at 162–65.

148. *Id.* at 159.

149. *Id.* at 160.

150. *Planned Parenthood of Se. Pa. v. Casey*, 505 U.S. 833, 835 (1992).

151. *Ma, supra* note 5, at 415–18.

‘process’ over time, rather than an event” and that “new medical techniques such as . . . implantation of embryos, artificial insemination, and even artificial wombs” are raising new questions regarding what exactly defines an unborn life.¹⁵² In *Planned Parenthood v. Casey*, Justices O’Connor, Kennedy, and Souter also recognized that “post-Roe neonatal care developments have advanced viability to a point somewhat earlier.”¹⁵³ In the twenty years since *Casey*, reproductive technologies have advanced even further; ‘growing’ a human baby entirely outside of the human womb no longer appears to be a dream, or to some, a nightmare of science fiction.

Assisted reproductive technology (ART) is a well-established and practiced reproductive method in the United States.¹⁵⁴ In ART, an embryo can be created entirely outside of the human body in a laboratory using in vitro fertilization (IVF) techniques.¹⁵⁵ Normally, once an embryo has been created in vitro, it is then transplanted back into a mother’s womb.¹⁵⁶ However, the evolution of the artificial womb suggests that scientists may one day be able to grow a human embryo past the blastocyst stages of development and nurture it into a fetus outside the human body. In April 2017, scientists reported that they were able to grow a 105-120 days old fetal sheep—the equivalent of a 22-24 week old human fetus—in an artificial womb without any developmental abnormalities.¹⁵⁷ Although the scientists conceded that their system could not simply grow a full-fledged fetus from an embryo,¹⁵⁸ the technology may already be present to do so. For example, in 2016, English scientists showed that it was possible to successfully grow a human embryo in a petri dish for up to fourteen days—the legal limit allowed for IVF research.¹⁵⁹ The English study also showed scientists could induce artificial implantation and forcibly cause the embryo to attach to the walls of the petri dish.¹⁶⁰ By combining breakthroughs in embryonic

152. *Roe*, 410 U.S. at 161.

153. *Casey*, 505 U.S. at 835.

154. See generally Whitney Braun, *The History of Assisted Reproductive Technology in Under 1000 Words...*, HUFFINGTON POST (Mar. 14, 2016, 4:30 PM), https://www.huffingtonpost.com/whitny-braun/what-do-christmas-trees-a_b_8851496.html.

155. See *Assisted Reproductive Technology*, MEDLINEPLUS, <https://medlineplus.gov/assisted-reproductivetechnology.html>.

156. *Id.*

157. See Rachel Becker, *An Artificial Womb Successfully Grew Baby Sheep—and Humans Could Be Next*, THE VERGE (Apr. 25, 2017, 5:09 PM), <https://www.theverge.com/2017/4/25/15421734/artificial-womb-fetus-biobag-uterus-lamb-sheep-birth-premie-preterm-infant>.

158. *Id.*

159. See Sarah Knapton, *Human Embryos Kept Alive in Lab for Unprecedented 13 Days So Scientists Can Watch Development*, TELEGRAPH (May 4, 2016, 5:00 PM), <http://www.telegraph.co.uk/science/2016/05/04/human-embryos-kept-alive-in-lab-for-unprecedented-13-days-so-sci/>; see also Paul Tadich, *Artificial, Womb-Free Births Just Got a Lot More Real*, VICE (May 4, 2016, 10:00 AM), https://motherboard.vice.com/en_us/article/nz7ea7/artificial-womb-free-births-just-got-a-lot-more-real-cambridge-embryo-reproduction (at 14-days, the embryo begins to develop its primitive streak; the 14-day embryo termination deadline was set forth by international treaty and voluntarily complied with by individual countries).

160. See Sarah Knapton, *‘Artificial Womb’ Breakthrough Sparks Row Over How Long Human Embryos Should Be Kept in Lab*, TELEGRAPH (May 4, 2016, 10:00 AM), <https://www.telegraph.co.uk/science/2016/05/04/artificial-womb-breakthrough-sparks-row-over-how-long-human-embr/>.

development research and artificial womb technology, future scientists may soon be able to grow an embryo past fourteen days for the first time.¹⁶¹

Thus, the project to ‘grow’ a human baby in the artificial womb appears to be more limited by the ethical concerns surrounding ‘growing artificial babies’ rather than the capacity of our current reproductive technology. Considering that scientists can precisely control the conditions of an artificial womb, but not the mother’s womb, it should be safer and easier to ‘grow’ a human baby in an artificial womb once the conditions and protocols for artificial prenatal development have been perfected. Assuming that such technology is achieved one day, is there really a legal difference between an embryo and a fetus in the context of the state’s life interest in the unborn life? I would argue that if artificial womb technology can carry an embryo to birth without changes in prenatal viability, then the embryo and fetus should have equal life interests and the same rights to germline gene editing. Specifically, the State would have a legal interest in protecting the life of the embryo (i.e., the unborn child).

Although the fetus currently has no constitutional rights under *Roe v. Wade*, there are still legal interests that pertain to the unborn life in the context of germline gene editing. For example, long before *Roe*, the unborn life was given legal property rights through the Rule Against Perpetuities.¹⁶² In the years since *Roe*, society has been increasingly willing to recognize other legal interests for the unborn child. For example, today, thirty-six states recognize the killing of a fetus as a form of homicide—up from twenty-seven states just six years ago.¹⁶³ Twenty-four states have also extended legal protections for the unborn life regardless of its stage of pregnancy.¹⁶⁴ In addition, post-*Roe* federal legislation has reflected a desire to protect the life interests of the unborn child. The Unborn Victims of Violence Act (UVVA), passed in 2004, made it a federal crime to cause death or bodily harm to an unborn child.¹⁶⁵ Although the Act does not explicitly name the unborn child as a ‘person’—as recognized under the Fourteenth Amendment—it defines a “child in utero” as “a member of the species homo sapiens, at any stage of development, who is carried in the womb.”¹⁶⁶

Some legal scholars have interpreted the language of the UVVA as rebutting *Roe v. Wade* and supporting constitutional rights for the unborn child.¹⁶⁷ In fact, during the debate of the Act, Senator John Kerry had “serious concerns about [the] legislation because the law cannot simultaneously provide that a fetus is a human being and protect the right of the mother to

161. *Id.* (no studies have been able to successfully grow a human embryo past 14 days).

162. See Gregory J. Roden, *Unborn Children as Constitutional Persons*, 25 ISSUES L. & MED. 185, 187–88 (2009) (“[T]he Rule Against Perpetuities holds that interests in property must vest ‘within a life or lives in being (treating a child in its mother’s womb as in being) and 21 years afterwards.’”).

163. Rachel Warren, *Pro (Whose?) Choice: How the Growing Recognition of A Fetus’ Right to Life Takes the Constitutionality Out of Roe*, 13 CHAP. L. REV. 221, 232 (2009).

164. *Id.* at 237.

165. Unborn Victims Violence Act, 18 U.S.C.A. § 1841 (2004).

166. *Id.* at 1841(d).

167. Amy Lotierzo, *The Unborn Child, A Forgotten Interest: Reexamining Roe in Light of Increased Recognition of Fetal Rights*, 79 TEMP. L. REV. 279, 302–03 (2006).

choose to terminate her pregnancy.”¹⁶⁸ Kerry’s commentary reflects a fundamental difference between abortion and germline gene editing. In abortion, the mother desires the termination of the fetus’s life. A mother’s privacy interests for controlling her body are balanced against the life interest of the unborn child. In contrast, when the unborn child carries a fatal genetic defect, germline gene editing desires to save the unborn child’s life, and to align the unborn child’s life interests with the mother’s privacy interests. Therefore, if a constitutional right to life was recognized for the unborn child, it would necessitate overturning the mother’s constitutional right to abortion.¹⁶⁹ Considering the difficulty in achieving such a constitutional change, it is unlikely that germline gene editing can rely on a fetus’s constitutional rights.

A fetus’s constitutional rights notwithstanding, I argue that a right to germline gene editing could be supported by *Roe*’s existing legal framework. Although I concede that abortion law is not a perfect fit for analyzing the right to germline gene editing—abortion is about ending a life while germline gene editing is about saving one—there is derivative value in applying what we have learned from the history of abortion law. For one, the legal actors for abortion and germline gene editing are the same. Both involve the state’s life interests in the mother and the unborn life, and the mother’s Fourteenth Amendment privacy interests in controlling her body. Therefore, perhaps a test similar to *Roe*’s balancing test for abortion could be adopted for the right to germline gene editing. Unlike the conflicting legal interests in abortion, however, the legal interests in germline gene editing are aligned. First, assuming that germline gene editing technology is eventually perfected, germline gene editing would have minimal impact on the mother’s life. Even under current germline gene editing technology, the editing of embryos and transplantation back into the mother would not pose any health risks beyond what is already found in well-established IVF protocols. Second, the state’s interest in the life of the unborn child would weigh in favor of germline gene editing. Germline gene editing would be used to fix a genetic defect, not terminate the unborn child’s life.¹⁷⁰ Third, the mother’s Fourteenth Amendment privacy interest would also support the right to germline gene editing. Presumably, the mother would pursue germline gene engineering because she wants to save her child’s life. Therefore, when germline gene editing is necessary to save the unborn life, recognizing a right held by the parents and the State against government restriction to germline gene editing under *Roe*’s balancing test would serve all parties involved.

In addition, the legal arguments for using germline gene editing to save the unborn life may also be supported by developments in artificial gestation.

168. B.A. Robinson, *U.S. and Canadian Laws Defining When Human Personhood Begins*, RELIGIOUS TOLERANCE (Apr. 27, 2012), http://www.religioustolerance.org/abo_when1.htm.

169. See Warren, *supra* note 163, at 225–26.

170. An interesting wrinkle in this discussion is what happens when gene editing is applied to the somatic cells of an almost full-term fetus. One could argue that the cells being edited are more akin to an individual human being than to the germline of the mother. However, I would still argue that because the fetus would still presumably be in the mother’s womb, it still applies the same legal arguments (i.e., privacy rights and control over bodily integrity).

As discussed earlier, reproductive technology may soon reach a point where fertilization, gestation, and ‘birth’ can occur entirely outside the human body. If future technologies can reliably ‘birth’ humans without a human mother, should the embryo/fetus held within the artificial womb be considered a “person” as described in the Constitution?¹⁷¹ In general, the judiciary has not had to answer the question of whether an artificially birthed baby is legally distinct from a baby naturally born from a mother’s womb.¹⁷² But if it is accepted that an artificially birthed baby should be his or her own person because it was never completely part of the mother’s body to begin with,¹⁷³ then the constitutional protection of right to life under the Fourteenth Amendment should apply if germline gene editing is necessary to save the unborn child’s life.

C. USING GERMLINE GENE EDITING TO FIX NON-FATAL GENETIC IMPAIRMENTS IN THE UNBORN LIFE

While there are compelling arguments for an unborn child’s right to life, what about an unborn child’s right to a healthy life? When a genetic mutation results in non-fatal impairment, *Roe*’s analysis would not apply because the unborn life (or death) interest is not at stake. What is at stake is the prospect that a living person is doomed to a lifetime of woe. However, if germline gene editing could ensure that the child lives a life without a debilitating non-fatal impairment, does the unborn child still have a legal right to germline gene editing? In general, the unborn life does not hold a constitutional right to be conceived, much less a right to be conceived with good health.¹⁷⁴ Therefore, there is little to no substantially relevant caselaw supporting the right to use germline gene editing to birth a healthy baby by fixing a non-fatal genetic impairment. However, in making the best case for using gene editing to fix non-fatal impairment, this section will look to the wrongful life doctrine—an imperfect, but perhaps insightful comparison.

Like the right to germline gene editing, the wrongful life doctrine “rest[s] to a large extent on the more recent advances in medical and scientific knowledge that makes contraception more practical and make potential fetal injuries and defects detectable prior to birth and even prior to conception.”¹⁷⁵ The doctrine states that:

Tort claims asserted against physicians in which it is alleged that the negligence of physicians failing to diagnose physical defects and anomalies of the fetus deprived the parent(s) of the opportunity to

171. See generally U.S. CONST. (frequently discussing the rights of “the People,” as well as individual “persons”).

172. See *Roe v. Wade*, 410 U.S. 113, 158 (1973); *Planned Parenthood of Se. Pa. v. Casey*, 505 U.S. 833, 835 (1992).

173. The artificially born baby technically would be partially comprised of the mother’s egg, but it would not ever be integrated with the mother’s body when it became a human being (i.e., after fertilization).

174. See Kristen Barrett, *Prosecuting Pregnant Addicts for Dealing to the Unborn*, 33 ARIZ. L. REV. 221, 234 (1991).

175. Catherine Palo, *Cause of Action for Wrongful Birth or Wrongful Life*, 23 CAUSES OF ACTION 2D 55, at §2 (2003).

terminate the pregnancy that resulted in the birth of a severely handicapped child have been termed . . . “wrongful life” when brought on behalf of the child for the harm suffered by being born deformed.¹⁷⁶

Wrongful life claims fall into two categories: (1) claims by normal but unwanted children against their parents or others who were negligent about the child’s birth (also known as wrongful birth); or (2) claims by impaired children that assert that if not for the defendant’s negligence, the parents would not have been precluded from making the decision to abort the pregnancy. In the context of editing a non-fatal genetic impairment, only the second category of claims is relevant.¹⁷⁷

The basis of a wrongful life claim lies with the alleged negligence of the parents or third-party that precludes the parents’ opportunity to decide whether to birth a genetically impaired child.¹⁷⁸ In other words, a wrongful life claim presumes that if the parents or third-party were not negligent, the parents would have known of their unborn child’s genetic defects and deliberated aborting the child, discarding the embryo after pre-implantational diagnosis, or avoided conception altogether.¹⁷⁹ Although wrongful life claims have been considered, courts have generally declined to recognize a cause of action by or on behalf of the child for a birth caused by the defendant’s negligence.¹⁸⁰ To date, only three states have recognized wrongful life as a legal cause of action.¹⁸¹ In one case, the court refused to grant a wrongful life claim on behalf of a mother who sued a physician for failing to test her Down Syndrome child for the disease during pregnancy.¹⁸² The court found that “an impaired life is not worse than non-life.”¹⁸³ In the court’s analysis, it did not recognize the Down Syndrome child as having any “legally cognizable injury.”¹⁸⁴ In another case, where a mother sued a physician on behalf of her child born with severe congenital defects, the South Carolina Supreme Court rejected a wrongful life claim because “a jury collectively imbued with the wisdom of Solomon would be unable to weigh the fact of being born with a defective condition against the fact of not being born at all.”¹⁸⁵

Despite the widespread judicial resistance against wrongful life claims, there are rare cases where courts have allowed an impaired individual to collect damages. In *Turpin v. Sortini*, an impaired child was awarded special damages for extraordinary medical care and training caused by her genetic

176. *Id.*

177. *Id.*

178. *Id.*

179. *Id.*

180. See Kevin R. Costello, *The Limitations of Wrongful Life Claims and Genetic Diagnosis*, L.A. LAW., Apr. 2007, at 14.

181. *Id.* Although few wrongful life cases have been recognized in the United States, some wrongful life cases have been accepted in foreign jurisdictions. See Tony Sheldon, *Court Awards Damages to Disabled Child for Having Been Born*, 326 BRIT. MED. J. 784, 784 (2003).

182. *Kassama v. Magat*, 792 A.2d 1102, 1105–06 (Md. Ct. Spec. App. 2002).

183. *Id.* at 1121.

184. *Id.* at 1118.

185. *Willis v. Wu*, 607 S.E.2d 63, 71 (S.C. 2004).

defect.¹⁸⁶ The court held that such damages could only be awarded if: (1) the physician negligently failed to diagnose and warn the parents of the child's genetic defect; (2) the child was born with the defect; (3) the parents were deprived of the opportunity to choose not to conceive the child; and (4) the child required extraordinary medical expenses because of the defect. In essence, wrongful life claims are claims of negligent genetic counseling that result in avoidable healthcare expenses for the child and parents.¹⁸⁷

At a high level, the wrongful life doctrine could perhaps be adopted for germline gene editing. For example, assuming that gene editing technology has been perfected, one could argue that a tort action for wrongful life could be found if: (1) the child was diagnosed with a genetic defect, (2) the physician failed to warn the parents of the defect and gene editing could have fixed it; or the physician warned the parents of the defect and failed to inform them that gene editing could have fixed it, (3) the parents would have fixed the genetic defect using gene editing, and (4) the child require extraordinary medical expenses that could have been avoided if the defect was fixed using gene editing. While courts have rejected wrongful life claims because it is 'impossible' to measure the injury between an impaired life and a non-life,¹⁸⁸ this proposed framework could quantify the legal injury by looking at differences in medical costs between a healthy life without the mutation and an unhealthy life with the mutation. Whereas the practical determinations of damages substantially differ between wrongful life and gene editing cases, one could argue that the conceptual difference between no-life & impaired life (wrongful life) versus impaired life & a healthy life (using gene editing to fix a non-fatal genetic defect) is not all that significant. In such cases, the failure to fix a non-fatal genetic mutation using germline gene editing could be akin to the failure to diagnose the genetic abnormality found in wrongful life cases.¹⁸⁹

The unborn life arguably has a right to using germline gene editing to restore the health that would be forgone by its non-fatal genetic mutation. Society has a duty to act in the best interest of unborn life. If germline gene editing is a readily available cure for a debilitating mutation, is it not medical malpractice by the physician to deprive parents the opportunity to treat the unborn life's medical condition? Even if parents might not elect to fix the genetic mutation, the unborn life might still have a right to germline gene therapy if one accepts that parents also have a duty to reasonably act in the best interest of their child. The law already holds parents legally responsible for the well-being of their children.¹⁹⁰ If the technology provides an

186. *Turpin v. Sortini*, 643 P.2d 954, 965 (Cal. 1982).

187. *Costello*, *supra* note 180.

188. *Id.*

189. The failure to diagnose the genetic abnormality could also be compared to the tort action of failure to treat. See *In re Seiferth* 127 N.E.2d 820 (N.Y. 1955); *In re Sampson*, 323 N.Y.S.2d 253 (N.Y. App. Div. 1971).

190. *But see* Isabel Wingerter, *Parent-Child Tort Immunity*, 50 LA. L. REV. 1131, 1131 (1990) (stating that most states grant parents immunity for tortious actions against their children). See generally Child Abuse Prevention and Treatment Act, 42 U.S.C.A §§ 5101–5119c (1996); Romualdo P. Eclavea, Annotation, *Liability of Parent for Injury to Unemancipated Child Caused by Parent's Negligence—Modern Cases*, 6 A.L.R. 4TH 1066 (1981 & Supp. 1992).

unambiguous cure for their child's genetic disease, such parental legal duties should not be limited by birth, and should extend to the unborn child. Thus, if a parent planning to birth the child is informed that the child has a non-fatal genetic impairment, knows that the germline gene-editing cure is readily available, and chooses not to fix the mutation, then she should be held negligent and in violation of her parental duties.

Although the arguments can be made for using germ gene editing to fix the genetically-impaired unborn life, realistically, it is unlikely that current courts would find a right to such treatment. First, there is little to no caselaw that directly supports an unborn life's right to be birthed with good health.¹⁹¹ Second, even if gene editing advocates look to wrongful life doctrine, the widespread judicial resistance to the doctrine suggests that courts would also be unwilling to impose an obligation to use gene editing to birth a healthy child.¹⁹² Third, fixing an impaired unborn life would not be supported by the state's life interest in the child because the child's life is not at risk.¹⁹³ Perhaps if reproductive technology advances to the point that healthy babies are the uncontroverted norm, the state's interest in the health of a child could eventually replace the state's life interest in the unborn child. Fourth, recognizing a fetus's right to genetic treatments for fixing a non-fatal mutation would place a substantial burden on the medical system.¹⁹⁴ Fifth, courts may be concerned that genetically editing out genetic defects would hurt society's treatment of existing individuals with disabilities.¹⁹⁵ Lastly, the court would have to establish guidelines for what non-fatal genetic abnormalities would fall under the right to gene editing—a tall and difficult task.

V. CONCLUSION

Germline gene editing is a controversial but unavoidable issue facing society today. Although the ethical arguments against allowing germline gene editing are substantial, the United States is causing more harm than good in categorically prohibiting all federally funded research on genomic engineering. In a perfect world, the government could prohibit all germline engineering research on humans until the technology is better understood and developed through less controversial research (e.g., animal studies). However, as evidenced by the international and private domestic research coming out on germline gene editing, the world will not wait for the United

191. Barrett, *supra* note 174.

192. *Kassama v. Magat*, 792 A.2d 1102, 1123 (Md. Ct. Spec. App. 2002).

193. Alternatively, the state could present a legal interest in the unborn child's well-being, but it would likely be weaker than the unborn child's life interest as argued in abortion case law. See generally June Carbone, *Legal Applications of the "Best Interest of the Child" Standard: Judicial Rationalization or a Measure of Institutional Competence?*, 134 PEDIATRICS S111 (2014).

194. See Arlene Weintraub, *Gene Therapy is Booming, But How Will We Manage the Costs?*, FORBES (Dec. 1, 2017, 5:05 AM), <https://www.forbes.com/sites/arleneweintraub/2017/12/01/gene-therapy-is-booming-but-how-will-we-manage-the-costs/#19adea75604d>.

195. MICHAEL H. SHAPIRO ET AL., *BIOETHICS AND LAW: CASES, MATERIALS AND PROBLEMS* 468, 471 (2nd ed. 2003) (labeling genetic defects in a negative light reduces the value of existing disabled persons in society).

States to catch up.¹⁹⁶ Rather than letting the germline gene editing research run wild on the whims of private investigators, the United States should take hold of the reigns and apply strict, but workable regulatory guidelines.¹⁹⁷ Allowing limited germline engineering research does not mean that the government will be allowing the production of “designer babies.” Rather, the federal government could take a similar approach to international embryo research regulations and allow editing of human embryos for up to fourteen days past fertilization.¹⁹⁸ By taking baby steps (pun intended) in germline engineering research, the scientific community can take the time and diligence required to ensure that such research does not result in the kind of Frankenstein horrors dreaded by many.

Assuming that the technology is eventually perfected, there should be a legal right for parents to choose germline gene editing in cases where application of the technology would save the unborn child’s life. By limiting germline gene editing to fixing fatal genetic mutations, the interests of the worried mother, sick child, and benevolent state would all be furthered. Considering that an increasing number of states are recognizing legal rights for the fetus, there will likely be support for the limited application of germline gene engineering. On the other hand, the decisions regarding what non-fatal genetic impairments are worthy of gene editing is more ambiguous and vulnerable to subjective disagreement. By limiting germline gene editing to only fatal mutations, society can avoid controversy and ethical dilemmas that arise from gene drives and genetic enhancement.

Regardless of where one might stand in the ethical argument for germline gene editing, one thing is clear: no matter how we decide to approach germline gene editing, science will continue marching forward—with or without legal oversight.

196. See generally Alex Pearlman, *Scientists Argue the US Ban on Human Gene Editing Will Leave It Behind*, VICE (Aug. 4, 2016, 11:00 AM), https://motherboard.vice.com/en_us/article/nz7dp8/scientists-argue-the-us-ban-on-human-gene-editing-will-leave-it-behind.

197. See generally Meredith Salisbury, *For Genome Editing, Self-Regulation Beats A Government Ban*, FORBES (Jun. 11, 2015, 11:36 AM), <https://www.forbes.com/sites/teconomy/2015/06/11/for-genome-editing-self-regulation-beats-a-government-ban/#4dcf9e641f4c>.

198. See generally Giulia Cavaliere, *A 14-day Limit for Bioethics: The Debate over Human Embryo Research*, 18 BMC MED. ETHICS 1 (2017).