

EMBRYOS AS PATIENTS? MEDICAL PROVIDER DUTIES IN THE AGE OF CRISPR/CAS9

G. EDWARD POWELL III[†]

ABSTRACT

The CRISPR/Cas9 genome engineering platform is the first method of gene editing that could potentially be used to treat genetic disorders in human embryos. No past therapies, genetic or otherwise, have been intended or used to treat disorders in existent embryos. Past procedures performed on embryos have exclusively involved creation and implantation (e.g., in-vitro fertilization) or screening and selection of already-healthy embryos (e.g., preimplantation genetic diagnosis). A CRISPR/Cas9 treatment would evade medical malpractice law due to the early stage of the intervention and the fact that it is not a treatment for the mother. In most jurisdictions, medical professionals owe no duty to pre-viable fetuses or embryos as such, but will be held liable for negligent treatment of the mother if the treatment causes injury to a born-alive child. This issue brief discusses the science of CRISPR/Cas9, the background legal status of human embryos, and the case for considering genetically engineered embryos as patients for purposes of medical malpractice law.

INTRODUCTION

Fernando and Pilar Ruiz hail from the shores of Lake Maracaibo in Venezuela, where almost 1% of the population is affected by Huntington's disease,¹ a rare and incurable genetic disorder.² While Pilar is healthy, Fernando is not so fortunate. Both of his parents died from Huntington's, and Fernando carries two copies of the deadly Huntington's gene. Since inheriting only one copy is sufficient to pass on the disease,³

[†] Duke University School of Law, J.D. expected 2018; Imperial College London, M.Sc. Human Molecular Genetics, 2014; University of Chicago, B.A. Religious Studies, 2013.

¹ *How Common Is Huntington's Disease (HD)?*, HUNTINGTON'S NEW S. WALES, <http://www.huntingtonsnsw.org.au/information/hd-facts/how-common> (last visited Mar. 2, 2017).

² See Sara Imarisio et al., *Huntington's Disease: From Pathology and Genetics to Potential Therapies*, 412 *BIOCHEMICAL J.* 191, 191, 200 (2008) (discussing basic features of the disease and treatment options).

³ *Id.*

Fernando cannot have healthy children, and the couple is distraught over the prospect that Fernando will die childless.

No current technological measures can solve the Ruizes' predicament, but the promise of surmounting this sort of obstacle to bearing healthy children is closer to reality than ever before in the form of a new gene editing technology called CRISPR/Cas9.⁴ The CRISPR/Cas9 technology promises the ability to specifically target and shut down or replace genes in human embryos.⁵ Particular sections of DNA with disease-causing genes can be replaced with healthy copies of the genes, curing some genetic diseases.⁶ Furthermore, unlike contemporary gene therapies performed on adults, CRISPR/Cas9 would alter the germline of its embryonic targets, not just the somatic or non-reproductive-cell DNA: the eventual children of individuals treated as embryos would inherit the healthy, altered gene.⁷ Contemporary gene therapies, which edit the genome to attenuate or cure genetic disease, alter only somatic cell DNA, so the children of gene therapy recipients could still express or carry the disease. But germline editing, if broadly accessible, could eliminate entire genetic diseases. The technology will not be ready for clinical use in human embryos before ethical⁸ and methodological⁹ issues are resolved, but its significant curative potential is already being recognized throughout the scientific community.¹⁰

While the science of CRISPR/Cas9 has been blazing a new trail in therapeutic potential, the development of the law governing the

⁴ See Tetsuya Ishii, *Germ Line Genome Editing in Clinics: The Approaches, Objectives and Global Society*, 16 BRIEFINGS IN FUNCTIONAL GENOMICS 46, 48 (2017) (“[F]urther research will likely make germ line genome editing clinically feasible in the near future.”).

⁵ See NAT'L ACADS. OF SCIS., ENG'G, & MED., INTERNATIONAL SUMMIT ON HUMAN GENE EDITING: A GLOBAL DISCUSSION 1–2 (2015) (describing the promise of CRISPR/Cas9 and the potential applications of human germline editing).

⁶ See *id.* at 2 (discussing cystic fibrosis, sickle cell anemia, and Huntington's disease).

⁷ *Id.*

⁸ Ethical objections involve, for example, concern for the moral status of the embryo, rising inequality, and potential eugenic applications. *Id.* at 4.

⁹ See Rongxue Peng, Guigao Lin & Jinming Li, *Potential Pitfalls of CRISPR/Cas9-Mediated Genome Editing*, 283 FEBS J. 1218, 1223, 1226–27 (2016) (discussing off-target effects, low homology-directed repair rates, and agent delivery difficulties).

¹⁰ See generally Katrine S. Bosley et al., *CRISPR Germline Engineering—The Community Speaks*, 33 NATURE BIOTECHNOLOGY 478 (2015) (compiling expert opinions on the potential and ethics of germline editing).

treatment of preimplantation human embryos has lagged behind.¹¹ Assisted reproductive technologies (ARTs) are regulated much more lightly—and inconsistently from state to state—than the prevalence of their use and the depth of the interests at stake demand.¹² Neither Congress nor most state legislatures are particularly willing to regulate ARTs, as the question of the legal status of the embryo is highly politically polarizing.¹³

One possible method of regulation in the face of legislative inaction is to proceed by the common law. For example, some state courts have applied property law or contract law to novel disputes involving unimplanted embryos created by ART.¹⁴ Such extensions of common law doctrines and statutory law to cover new situations are well-meaning efforts to provide a remedy for unaddressed but wrongful acts.

However, as treatments like CRISPR/Cas9 become available, the inadequacy of these patchwork efforts as an overall regulatory regime for the ART industry¹⁵ will become more apparent. CRISPR/Cas9 promises the first therapy intended to cure disease in human embryos, aimed at allowing those embryos to develop into disease-free members of society. This course of therapy, unlike the ARTs that have come before it, treats the embryos (not just the parents) as patients. The proper basic legal principle to govern embryonic treatment with CRISPR/Cas9 ought to be the same that governs other doctor-patient relationships.

I. SCIENTIFIC BACKGROUND

A. *A Quick Introduction to ART and Human Genetics*

Every human begins his or her life as a single cell, a union of sperm and egg called a zygote.¹⁶ After the egg is fertilized, the new zygote divides, each of the two new cells divides, and so on; at this point, the entity is called a cleavage-stage embryo.¹⁷ After a few days, the embryo implants in the uterine wall, as its cells continue to divide and specialize

¹¹ Catherine A. Clements, *What About the Children? A Call for Regulation of Assisted Reproductive Technology*, 84 IND. L.J. 331, 331 (2009).

¹² Jennifer L. Rosato, *The Children of ART (Assisted Reproductive Technology): Should the Law Protect Them from Harm?*, 2004 UTAH L. REV. 57, 64–65 (2004).

¹³ *Id.* at 73–75.

¹⁴ Gregory A. Triber, *Growing Pains: Disputes Surrounding Human Reproductive Interests Stretch the Boundaries of Traditional Legal Concepts*, 23 SETON HALL LEGIS. J. 103, 104 (1998).

¹⁵ *Id.*

¹⁶ T.W. SADLER, LANGMAN'S MEDICAL EMBRYOLOGY 10 (12th ed. 2012).

¹⁷ Fernando J. Prados, Sophie Debrock, Josephine G. Lemmen & Inge Agerholm, *The Cleavage Stage Embryo*, 27 HUM. REPROD. (SUPPLEMENT 1) i50, i50 (2012).

into various tissues.¹⁸ At the end of its eighth week of life, the embryo becomes classified as a fetus and remains so until birth.¹⁹

ARTs are used to create zygotes outside the mother's uterus and implant them within it, often because conventional reproduction is unavailing.²⁰ The most common procedure is *in vitro* fertilization (IVF): a fertility doctor extracts egg cells from the patient or a donor, fertilizes them in the lab with sperm cells from the sperm donor, allows the embryos to grow, and deposits them in the patient's uterus in the hope that at least one will successfully implant and develop into a healthy baby.²¹ Techniques used to supplement traditional IVF include intracytoplasmic sperm injection (ICSI),²² a way to compensate for low male fertility by injecting the sperm directly into the egg, and preimplantation genetic diagnosis (PGD), a technique for diagnosing genetic disease in embryos so that only healthy embryos can be implanted.²³

The adult human body is composed of trillions of small cells, and (with a few exceptions) every cell contains all the genetic information that the zygote contained.²⁴ This information is encoded in deoxyribonucleic acid, or DNA, a double-stranded molecule arranged in a double helix conformation.²⁵ Each strand consists of a series of sugar molecular units stuck to one another in a chain, with one of four nucleotide bases—adenine, thymine, cytosine, or guanine, commonly abbreviated A, T, C, and G—attached to each sugar unit, sticking out toward the other strand, and meeting another base in the middle.²⁶ The bases pair up according to a specific pattern—A bonds only with T, and C with G—due to their respective chemical bonding properties.²⁷ The strands are considered

¹⁸ SADLER, *supra* note 16, at 38–39.

¹⁹ *Id.* at 96.

²⁰ Noah Baron & Jennifer Bazzell, *Assisted Reproductive Technologies*, 15 GEO. J. GENDER & L. 57, 57–58 (2014).

²¹ *Id.* at 58–59.

²² *Id.* at 59.

²³ *Id.* at 91–92.

²⁴ *A Brief Guide to Genomics*, NAT'L HUM. GENOME RES. INST. (Aug. 27, 2015), <https://www.genome.gov/18016863/a-brief-guide-to-genomics>; Rose Eveleth, *There Are 37.2 Trillion Cells in Your Body*, SMITHSONIAN: SMARTNEWS, <http://www.smithsonianmag.com/smart-news/there-are-372-trillion-cells-in-your-body-4941473> (last updated Oct. 24, 2013).

²⁵ ROBERT SCHLEIF, *GENETICS AND MOLECULAR BIOLOGY* 22–23 (2d ed. 1993).

²⁶ *Id.* at 22.

²⁷ *Id.* at 22–23.

complementary: each strand acts as a template to make a copy of the other, allowing each cell to replicate itself accurately.²⁸

A typical human cell's DNA is contained in 46 chromosomes, arranged in 23 homologous pairs; one chromosome in each pair is inherited from each parent.²⁹ Each chromosome contains stretches of DNA, called genes, which instruct other cellular mechanisms to produce certain proteins, which do the work of the cell.³⁰ Changing the sequence of the gene—for instance, replacing one base with another, or deleting or inserting bases—will often change the function of the protein.³¹

DNA instructions are read by a protein called RNA polymerase, which creates a single-stranded transcript of the gene out of ribonucleic acid, or RNA.³² RNA, like DNA, consists of a sugar backbone and a sequence of bases; an RNA transcript of a DNA sequence consists of a complementary sequence, which binds strongly to the template DNA sequence.³³ This transcript then travels to the ribosome, the cell's protein factory, which creates the encoded protein.³⁴

When DNA-copying mechanisms miscopy a gene, by changing, adding, or deleting bases, the changes in the encoded protein can cause it to function incorrectly.³⁵ Any individual mutation occurring in a single adult somatic cell will often be harmless; in fact, adult cells accumulate a large number of mutations steadily over time.³⁶ But if the mutation is present in a gamete—a sperm or egg cell—every cell of the person who develops from the mutated cell will have this germline genetic mutation, which could cause a genetic disease.³⁷ Germline genome editing could solve this problem entirely by replacing a diseased gene with a healthy copy in an embryo.³⁸

²⁸ *Id.* at 2.

²⁹ SADLER, *supra* note 16, at 11.

³⁰ *Id.* at 3.

³¹ SCHLEIF, *supra* note 25, at 228–29.

³² *Id.* at 85–86.

³³ *Id.* at 22, 85.

³⁴ *Id.* at 86.

³⁵ *Id.* at 228–29.

³⁶ Francis Blokzijl et al., *Tissue-Specific Mutation Accumulation in Human Adult Stem Cells during Life*, 538 NATURE 260, 260 (2016); see also ANTHONY GRIFFITHS ET AL., INTRODUCTION TO GENETIC ANALYSIS 456 (8th ed. 2005) (“Many point mutations within noncoding sequences elicit little or no phenotypic change . . .”).

³⁷ See GRIFFITHS ET AL., *supra* note 36, at 376–77 (describing the difference between somatic and germline gene therapy).

³⁸ *Id.*

B. How CRISPR/Cas9 Works

CRISPR/Cas9 is a molecular complex consisting of the Cas9 protein and a short RNA molecule.³⁹ The RNA molecule is complementary to a target DNA sequence, which it seeks out and binds to when inserted into a cell.⁴⁰ Once the RNA has bound to the target DNA, the attached Cas9 protein cuts both strands of the DNA molecule.⁴¹ The cell then uses one of two methods to repair the cut.⁴² One method, non-homologous end joining, often inserts or deletes genetic material in the process of repair and is likely to stop the gene from functioning.⁴³ CRISPR/Cas9 can thus be used to “knock out” problem genes. Another method, homology-directed repair, involves the cell inserting some free-floating genetic material into the break.⁴⁴ Introducing CRISPR/Cas9 along with a DNA molecule carrying a gene of interest can thus insert the new gene at the target site.⁴⁵

The CRISPR/Cas9 gene editing technology was developed from a bacterial adaptive immune system, which bacteria use to fight off viral infection.⁴⁶ CRISPRs (clustered, regularly interspaced short palindromic repeats) are short stretches of bacterial DNA, interspaced along the single bacterial chromosome by virus-derived, spacer-DNA sequences.⁴⁷ Several cas (CRISPR-associated) genes, located close to the CRISPR sequences, play different roles in operating or managing the CRISPR adaptive

³⁹ See Kristin Beale, *The CRISPR Patent Battle: Who Will Be “Cut” Out of Patent Rights to One of the Greatest Scientific Discoveries of Our Generation?*, B.C. INTELL. PROP. & TECH. F., Feb. 2016, at 3.

⁴⁰ *Id.* at 2–3.

⁴¹ *Id.* at 3.

⁴² GRIFFITHS ET AL., *supra* note 36, at 472.

⁴³ *Id.*

⁴⁴ See *id.* at 473 (describing homology-directed repair as it typically occurs in nature, where the sister chromatid provides the repair template).

⁴⁵ Beale, *supra* note 39, at 3.

⁴⁶ Luciano A. Marraffini & Erik J. Sontheimer, *CRISPR Interference: RNA-Directed Adaptive Immunity in Bacteria and Archaea*, 11 NATURE REV. GENETICS 181, 181 (2010); see also Richard Warrington, Wade Watson, Harold L. Kim & Francesca Romana Antonetti, *An Introduction to Immunology and Immunopathology*, 7 ALLERGY, ASTHMA & CLINICAL IMMUNOLOGY (SUPPLEMENT 1) 1, 1 (2011) (stating that adaptive immunity is targeted at specific invading pathogens, as opposed to innate immunity, which excludes foreign material in general).

⁴⁷ Marraffini & Sontheimer, *supra* note 46, at 181–82.

immune system.⁴⁸ Some of these genes function to append short sections of foreign DNA, derived from infecting viruses or plasmids,⁴⁹ to the CRISPR site as spacers.⁵⁰ Another of these genes codes for the Cas9 protein, a programmable nuclease⁵¹ that forms a complex with crRNA (CRISPR RNA, transcribed from spacer DNA) to identify and cut foreign DNA at the sequence complementary to the complexed RNA.⁵² When a virus infects a Cas9-equipped bacterium,⁵³ the bacterium first incorporates a segment of viral DNA into its CRISPR site as a spacer, rather than at a more dangerous site for the bacterium.⁵⁴ It then creates a crRNA transcript from the newly incorporated spacer DNA, which forms a complex with the Cas9 protein to identify and cut the DNA of the invading viruses in order to fight off the infection.⁵⁵

While the natural function of Cas9 is chiefly immunity, its laboratory applications are numerous and multiplying.⁵⁶ Since Cas9 can easily be programmed to target any short DNA sequence and introduce a break in the DNA strand,⁵⁷ it has been used to modify the function of numerous genes in many different species and cell types, including various types of human cells.⁵⁸ Even more promisingly, supplementing the process by introducing exogenous donor DNA, which contains a sequence to be inserted, bookended with sequences homologous to those on both sides of

⁴⁸ Devashish Rath, Lina Amlinger, Archana Rath & Magnus Lundgren, *The CRISPR-Cas Immune System: Biology, Mechanisms and Applications*, 117 *BIOCHIMIE* 119, 119 (2015).

⁴⁹ Plasmids are free-floating molecules of DNA that bacteria can absorb and incorporate into their own genomes.

⁵⁰ Rath et al., *supra* note 48, at 119–20.

⁵¹ A nuclease is a type of protein that cuts nucleic acids such as DNA.

⁵² Rath et al., *supra* note 48, at 121.

⁵³ Viruses are made of protein and genetic material. They infect bacteria by injecting their genetic material into the bacterium. This material gets incorporated into the bacterial genome, which then instructs the cell to make more copies of the virus. These new viruses can leave the cell and infect other bacteria. Craig Pringle, *Overview of Viral Infections*, MERCK MANUALS, <http://www.merckmanuals.com/home/infections/viral-infections/overview-of-viral-infections> (last visited Apr. 23, 2017).

⁵⁴ Rath et al., *supra* note 48, at 119.

⁵⁵ *Id.* at 120.

⁵⁶ *Id.* at 125–26.

⁵⁷ See Alex Reis, Breton Hornblower, Brett Robb & George Tzertzinis, *CRISPR/Cas9 and Targeted Genome Editing: A New Era in Molecular Biology*, 2014 *NEB EXPRESSIONS*, no. 1, at 3, 4. Wild type Cas9 creates double strand breaks in target DNA. Modified forms of Cas9 can create single strand breaks or bind to DNA without creating a break. *Id.*

⁵⁸ Rath et al., *supra* note 48, at 126.

the Cas9-induced break, results in homology-directed repair inserting the donor sequence at the site of the break.⁵⁹ The core of Cas9's therapeutic promise is this ability to make breaks, at essentially any site in the genome, that donor DNA can fill.

C. CRISPR/Cas9 Potentially Allows Editing Embryos in Clinical Medicine, but Hurdles Remain

The CRISPR/Cas9 system promises to be the first gene-editing platform with enough specificity, efficiency, and development potential to become a clinical gene therapy for human embryos.⁶⁰ Prior to the development of CRISPR/Cas9, the most effective gene-editing technologies—zinc-finger nucleases (ZFNs) and transcription-activator like effector nucleases (TALENs)—required redesign of the DNA-protein interface for every new target, making them expensive to develop for specific gene sequences.⁶¹ CRISPR/Cas9 is different: since the Cas9 protein remains constant between uses, and only the guide RNA needs to be changed to target a new gene, the system is much cheaper to use and experiment with than the older alternatives.⁶² This reduction in price has democratized gene-editing technology and prompted a flurry of research activity, leading to numerous improvements and additional uses for CRISPR/Cas9.⁶³

The most controversial use to which CRISPR/Cas9 has been put to date occurred in 2015 in China, where researchers tried to use the

⁵⁹ See *id.* A sequence is homologous to another if the two match or nearly match. Essentially, this feature allows any “insertion, deletion, or change in [DNA] sequence” nearly anywhere in the genome. *Id.*

⁶⁰ See *id.* (claiming that CRISPR/Cas9 “could be used to alter DNA in human embryos to prevent non-complex hereditary diseases”); see also Jennifer A. Doudna & Emmanuelle Charpentier, *The New Frontier of Genome Engineering with CRISPR-Cas9*, 346 *SCIENCE* 1258096-1, 1258096-4 (2014) (“CRISPR-Cas9 represents an efficient tool to edit the genomes of human cells.” (citations omitted)); Anna Zaret, Note, *Editing Embryos: Considering Restrictions on Genetically Engineering Humans*, 67 *HASTINGS L.J.* 1805, 1808 (2016) (“With [CRISPR/Cas9] it is increasingly likely that embryos will one day be edited and used to create genetically modified humans.”).

⁶¹ Doudna & Charpentier, *supra* note 60, at 1258096-3.

⁶² Ishii, *supra* note 4, at 3.

⁶³ See Doudna & Charpentier, *supra* note 60, at 1258096-3. Clinical trials for therapies created with the *in vitro* use of CRISPR/Cas9 are currently underway, and more are planned. Sara Reardon, *First CRISPR Clinical Trial Gets Green Light from US Panel*, *NATURE* (June 22, 2016), <http://www.nature.com/news/first-crispr-clinical-trial-gets-green-light-from-us-panel-1.20137>.

platform to edit the genomes of human zygotes.⁶⁴ Though the zygotes used in the study were terminally defective and would not have developed beyond the blastocyst stage in any case,⁶⁵ the study prompted an outcry from the worldwide scientific community. Many scientists called for a global moratorium on clinical editing of human embryos until the international community settled on regulatory guidelines.⁶⁶

Despite the limited efficacy of the first attempt to edit human embryos, the scientific community remains largely convinced that the CRISPR/Cas9 system will develop into a clinically useful tool for germline editing.⁶⁷ The rate at which gene editing fails or goes awry, introducing unforeseen and harmful changes in the genome of the targeted cell, is still far too high to introduce CRISPR/Cas9 into clinical use in embryos just yet.⁶⁸ But the speed of technological improvement, which comes from the sheer number of scientists working with and tweaking the cheap and easy-to-use system, promises to improve this rate over time.⁶⁹ Whether the regulatory environment will be ready for clinical embryo editing, or whether it will repeat the missteps of prior attempts to regulate ARTs, remains to be seen.

II. LEGAL BACKGROUND

A. *Sources and Circumstances of Liability for Injuries to a Preborn Child or Embryo*

Whatever form of regulation eventually governs fertility clinics' use of gene editing technology ought to compensate children who were injured as embryos through negligently performed gene editing. In all

⁶⁴ David Cyranoski & Sara Reardon, *Chinese Scientists Genetically Modify Human Embryos*, NATURE (Apr. 22, 2015), <http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378>.

⁶⁵ Puping Liang et al., *CRISPR/Cas9-Mediated Gene Editing in Human Trippronuclear Zygotes*, 6 PROTEIN & CELL 363, 363 (2015).

⁶⁶ Edward Lanphier et al., *Don't Edit the Human Germ Line*, 519 NATURE 410, 411 (2015), <http://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111>.

⁶⁷ See Bosley et al., *supra* note 10, at 479; COMM. ON HUMAN GENE EDITING, NAT'L ACAD. OF SCIS. & NAT'L ACAD. OF MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE (forthcoming 2017) (manuscript at 89), <https://www.nap.edu/catalog/24623/human-genome-editing-science-ethics-and-governance> (last visited Apr. 10, 2017) (“[T]he efficiency and accuracy of targeting can be extremely high, and there are sound reasons for believing that off-target effects can be greatly reduced . . .”).

⁶⁸ Cyranoski & Reardon, *supra* note 64.

⁶⁹ See Doudna & Charpentier, *supra* note 60, at 1258096-4 (citing several variants of the technology developed for various applications).

American jurisdictions, a child who is injured prenatally and later born alive can recover tort damages.⁷⁰ Although some older case law seemed to restrict recovery to cases in which the child was injured after attaining viability, the majority of jurisdictions now allow recovery for injuries sustained at any point between conception and birth.⁷¹ Even more, some jurisdictions recognize preconception torts, in which a child can recover even when she had not yet been conceived at the time the tortious breach of duty occurred.⁷²

Courts that have recognized preconception torts have done so by reading the duty requirement broadly, as a public policy determination that liability is appropriate in certain circumstances. One court, recognizing a preconception cause of action for a child injured because of negligent surgery performed on the mother's uterus before the child's conception, employed the following analogy:⁷³

Assume a balcony is negligently constructed. Two years later, a mother and her one-year-old child step onto the balcony and it gives way, causing serious injury to both the mother and the child. It would be ludicrous to suggest that only the mother would have a cause of action against the builder but, because the infant was not conceived at the time of the negligent conduct, no duty of care existed toward the child.⁷⁴

In this case, the child was not only a member of the class of people foreseeably affected by the surgeon's negligence, but also a third-party beneficiary of the doctor-patient relationship.⁷⁵ Finding a duty thus comported with already-accepted principles of tort law.

Courts that have refused to recognize preconception torts have tended to read the duty requirement as something owed to a particular

⁷⁰ RESTATEMENT (SECOND) OF TORTS § 869 (AM. LAW INST. 1979); Matthew Browne, *Preconception Tort Law in an Era of Assisted Reproduction: Applying a Nexus Test for Duty*, 69 FORDHAM L. REV. 2555, 2560 (2001).

⁷¹ Browne, *supra* note 70, at 2560–61. *But see* Andrews v. Keltz, 838 N.Y.S.2d 363, 370 (Sup. Ct. 2007) (disallowing recovery for injuries sustained after conception but prior to implantation, since no duty exists to a pre-implantation embryo).

⁷² See, e.g., Renslow v. Mennonite Hosp., 367 N.E.2d 1250, 1255 (Ill. 1977); Martin v. St. John Hosp. & Med. Ctr. Corp., 517 N.W.2d 787, 789 (Mich. Ct. App. 1994).

⁷³ Martin, 517 N.W.2d at 789.

⁷⁴ *Id.* (quoting Lough v. Rolla Women's Clinic, Inc., 866 S.W.2d 851, 854 (Mo. 1993)).

⁷⁵ *Id.*

person in existence at the time of the breaching act.⁷⁶ Policy rationales for this reading have included a desire not to extend liability to remote injuries, even foreseeable ones. In the medical context, imposing liability could result in conflicts of interest between patients and their potential future children, leading to the practice of “defensive medicine,” in which doctors act to minimize their chance of being sued rather than in their patient’s best interests.⁷⁷

The question of whether embryos or fetuses count as persons, to whom duties in general are owed, is a thorny one. Only one state, Louisiana, recognizes human embryos created through in vitro fertilization (IVF) as juridical persons,⁷⁸ but many other states recognize duties to in utero embryos and fetuses regardless of live birth. For instance, the wrongful death laws of the majority of the states recognize the claims of viable fetuses who die before birth, and a few states recognize such claims for any fetus or implanted embryo, regardless of viability.⁷⁹ No state recognizes a wrongful death claim for an embryo stored outside the body of the mother;⁸⁰ when an Illinois trial court once interpreted the state’s wrongful death statute to include such embryos, the appellate court reversed, reading the legislative history of the statute as restricting its scope to embryos and fetuses in utero.⁸¹

B. When a Medical Practitioner’s Duty of Care to an Embryo or Fetus Arises

In the medical malpractice context, a duty arises from the existence of a physician-patient relationship.⁸² In the fertility clinic

⁷⁶ Browne, *supra* note 70, at 2596–97.

⁷⁷ See *Albala v. City of New York*, 429 N.E.2d 786, 788 (N.Y. 1981) (refusing to find a duty to the later-conceived child of a woman on whom an abortion was negligently performed, resulting in injury to the later child).

⁷⁸ LA. STAT. ANN. § 9:123 (2015).

⁷⁹ See generally Jill D. Washburn Helbling, *To Recover or Not To Recover: A State by State Survey of Fetal Wrongful Death Law*, 99 W. VA. L. REV. 363 (1996) (detailing which states recognize a cause of action for fetal wrongful death).

⁸⁰ See Maria Pellegrino, *Murder in A Petri Dish? The Wrath of Illinois’ Miller v. American Infertility Group: A Push for Legislative Action*, 13 BUFF. WOMEN’S L.J. 137, 137 (2005) (claiming that a wrongful death cause of action for a preimplantation embryo is “without precedent in any jurisdiction”).

⁸¹ *Miller v. Am. Infertility Grp. of Ill., S.C.*, 897 N.E.2d 837, 839, 845 (Ill. App. Ct. 2008). The appellate decision was primarily premised on principles of statutory interpretation (for example, construing the wrongful death statute narrowly due to its derogation of the common law) rather than the policy implications of extending wrongful death liability to preimplantation embryos. *Id.*

⁸² *Johnson v. Thompson*, 650 S.E.2d 322, 323 n.4 (Ga. Ct. App. 2007).

context, before an embryo is implanted, only the mother is generally considered a patient for purposes of this relationship. After implantation, physicians providing prenatal care have a duty to both the mother and the fetus, due to the fetus's presence in utero.⁸³

This limitation on duty would seem to foreclose the possibility of preconception medical provider torts, since every physician-patient relationship requires a patient to exist. As a general rule, if a duty does not exist to a person (or class of persons, of whom the injured party is a member) at the time a wrongful act or omission occurred, the person cannot recover for injuries that the wrong caused.⁸⁴ Despite this traditional limitation, twelve jurisdictions, out of sixteen that have considered the issue, have either found liability for preconception torts or indicated that such liability might be appropriate in some circumstances.⁸⁵ These courts have generally found such liability because it was reasonably foreseeable, in the cases considered, that the as-yet-unconceived children would be harmed by the defendants' breach of a medical duty to another person, the mother.⁸⁶ Some courts have justified this expansion of duty, specifically in the medical context, by analogizing it to third-party beneficiary liability in contract.⁸⁷

While the maternal nexus of duty serves well to compensate the victims of the forms of preconception torts that have been recognized, courts have been reticent to completely unmoor the duty analysis from any specific person in existence at the time of the breaching act.⁸⁸ The courts' unwillingness to recognize either a direct preimplantation duty to human embryos or a theory of third-party harm that does not rely on a breach of

⁸³ See *id.* at 324 (holding that a prenatal care provider had a duty to a fetus "while he was in utero"); *Brown v. Shwarts*, 968 S.W.2d 331, 334 (Tex. 1998) ("[A] fetus can be a patient."). In some jurisdictions, despite the existence of this medical provider duty, breaches are only actionable if the child is born alive. See *HCA, Inc. v. Miller*, 36 S.W.3d 187, 195 n.21 (Tex. App. 2000), *aff'd*, 118 S.W.3d 758 (Tex. 2003).

⁸⁴ *Palsgraf v. Long Island R.R. Co.*, 162 N.E. 99, 99–100 (N.Y. 1928).

⁸⁵ Julie A. Greenberg, *Reconceptualizing Preconception Torts*, 64 TENN. L. REV. 315, 320 (1997).

⁸⁶ See, e.g., *Renslow v. Mennonite Hosp.*, 367 N.E.2d 1250, 1255 (Ill. 1977). *Renslow* involved a case of Rh sensitization, a medical phenomenon causing no injury to the mother but foreseeably harming her future children, caused by medical negligence. *Id.* at 1251.

⁸⁷ See, e.g., *Walker v. Rinck*, 604 N.E.2d 591, 594–95 (Ind. 1992).

⁸⁸ *Renslow*, 367 N.E.2d at 1255; see also *Hegyves v. Unjian Enters., Inc.*, 286 Cal. Rptr. 85, 89 (Ct. App. 1991), *reh'g denied and opinion modified* (Oct. 23, 1991) (suggesting that a duty to not-yet-conceived children can arise out of a special relationship with the mother).

duty to the mother leaves a gap in the law. A breach of duty to the mother before the child is created, causing injury to the child, is compensable, as is a breach of duty to the pregnant mother causing similar injuries to the child. But technologies like CRISPR/Cas9, the use of which would constitute a treatment for the embryonic child and not the mother, fit within neither of these recognized duties.

III. ANALYSIS

A. *Distinction Between CRISPR/Cas9 and Contemporary ARTs Regarding Tort Liability*

Imposing tort liability to regulate ART use has met with several obstacles. The problem to be addressed is that ARTs are risky for the children created and often cause injury to them.⁸⁹ But the unique point in the child's life at which the ART intervention occurs makes applying traditional tort concepts difficult.

The basic objections to tort liability in the ART context take three main forms. First is the problem of non-identity: since medical duties are generally owed to persons in existence at the time a breach occurred, no liability to a person would attach to an act, such as IVF, that creates that person.⁹⁰ Second, regardless of what the child's injury is, ART practitioners are not net-liable for it because their negligent act conferred a net benefit, life itself, on the child.⁹¹ Third, creating a duty to persons not yet in existence is properly a decision for a democratically elected legislature, rather than a court.⁹²

A clinical CRISPR/Cas9 gene editing treatment could avoid these limits on liability, due to its differences from currently available ARTs. An example course of treatment for illustrating these differences could comprise IVF, introduction of the targeted Cas9 nuclease and donor DNA

⁸⁹ Rosato, *supra* note 12, at 76. Fertility treatments tend to create multiple births and are responsible for nearly all the especially dangerous, highly multiple pregnancies that occur (for example, the "Octomom."). Alison Stateman, *The Fertility Doctor Behind the "Octomom,"* TIME (Mar. 7, 2009), <http://content.time.com/time/nation/article/0,8599,1883663,00.html>.

⁹⁰ Browne, *supra* note 70, at 2555.

⁹¹ *Id.* at 2555–56. For instance, if a fertility doctor negligently chooses to perform an intracytoplasmic sperm injection, a method of directly injecting the sperm into the egg, rather than conventional IVF, the injured child would have no cause of action, since choosing IVF would have resulted in a different sperm fertilizing the egg and a different person in the plaintiff's shoes. *See id.* at 2587 ("The benefit rule poses an insurmountable challenge to plaintiffs who have the negligent act of the defendant to thank for their very existence.").

⁹² *Id.* at 2556.

sequence to the in vitro zygote, and implantation of the lab-grown, treated embryo.

Regarding the limitations on duty: once the IVF occurs, a unique human organism is created, to which a duty could conceivably attach (for purposes of subsequent medical treatments, like CRISPR/Cas9) without expanding the universe of duty too broadly, e.g., to nonexistent or merely imaginable persons. In fact, such an expansion of duty would be miniscule. Since all jurisdictions recognize a duty to embryos and fetuses in utero, recognizing the same duty ex utero would not require any great leaps of judicial moral philosophy or special legislative policy determinations.⁹³ The only salient difference between embryos currently owed duties and embryos owed this proposed new duty would be the embryo's location—inside or outside of the uterus. The limitations on duty that currently apply to embryos and fetuses, perhaps requiring attainment of viability or live birth before liability attaches, would apply to this proposed duty as well.

Regarding the offsetting-benefit limitation on injury: treatment with Cas9 is a medical intervention designed to improve the health of an already-existing embryo, more akin to surgery performed on a fetus in utero than IVF. Since the hypothetical negligently performed act—gene editing with CRISPR/Cas9—would not be the act that created the embryo, the resulting harm is measured not against nonexistence, but against the outcome in which a non-negligently performed gene edit would have resulted in the child being healthy.

Recognizing a duty that flows directly to the embryo, not merely by way of the mother, is necessary to make negligent gene editing compensable as a tort against the child. Since CRISPR/Cas9 would be a treatment for the embryo rather than the mother and would involve no medical intervention implicating the mother's health,⁹⁴ the physician would be under no duty to perform the procedure in accordance with a standard of care if his only duty were to the mother. The theories of duty that have underlain successful claims of post-implantation or pre-conception torts are not applicable here, since both of those theories

⁹³ Although the duty proposed here would run directly to the embryo, in a break with the derivative-duty regime of the status quo, such a change would not create liability in many additional cases. Due to the ethical questions surrounding germline gene editing, these cases are likely to be rare for quite some time.

⁹⁴ The mother could be harmed by her physician's implanting a negligently edited embryo, which would be a breach of duty. But in that circumstance, the relevant act that the physician could be duty-bound to perform non-negligently would be the implantation, not the CRISPR/Cas9 treatment. Because implantation is a necessary step in embryonic development, the offsetting-benefit limitation on liability could preclude recovery for the child if the duty to the child is derivative of that to the mother.

require a duty nexus running through the mother, who is the patient in the physician-patient relationship. No such nexus exists here; if tort law will compensate the children harmed by negligent genetic engineering, it will do so by finding a duty owed to them directly, which can be breached other than by means of a breach of duty to their mothers.

B. Policy Rationale Supporting a Doctor-Patient Duty to Embryos Treated with CRISPR/Cas9

Finding a duty to edited embryos is consistent with the development of tort duties to unborn children, as well as with tort law's aim of compensation for injuries. Over the last century, courts have recognized that children deserve compensation for injuries, resulting from the wrongful acts of others, that were suffered before their birth.⁹⁵ Some jurisdictions have extended this principle to wrongful acts that occurred before the conception of the child, so long as a duty to the child's mother was breached and injury to future children was foreseeable from the nature of the breach. Therefore, a child who is injured by a wrongful act committed after implantation can recover, as can (in some jurisdictions) a child whose gamete-precursor was still a part of its mother when a certain type of wrongful act, usually reproductive-medical malpractice, was committed. But a child injured as an *in vitro* embryo is barred from recovery at the outset under a strict no-duty rule.

Even in jurisdictions that do not recognize pre-conception torts, drawing the line of liability at implantation rather than conception is arbitrary and outdated. There is no reason to restrict compensation for injuries caused to an embryo, which was in existence at the time of a negligent act, based on whether the act occurred before or after the embryo was implanted. There is an identifiable human organism in both scenarios to whom harm is foreseeable in the event of medical negligence. And such a duty is appropriate as applied to edited embryos intended for implantation. Nothing about the *ex utero* location of these embryos makes their injuries less properly compensable (perhaps assuming the embryos develop into children who are born alive, depending on jurisdiction) than those of embryos injured *in utero*.

Finding a duty to edited embryos also serves tort law's aim of deterring wrongful acts.⁹⁶ Such deterrence is especially necessary in the brave new world of therapeutic germline editing, where one negligent edit

⁹⁵ Browne, *supra* note 70, at 2560.

⁹⁶ See Edward A. Marshall, Note, *Medical Malpractice in the New Eugenics: Relying on Innovative Tort Doctrine To Provide Relief When Gene Therapy Fails*, 35 GA. L. REV. 1277, 1323–26 (2001) (discussing the level of deterrence necessary to ensure that germ line gene editing is performed with reasonable care).

could lead to generations of inherited disease.⁹⁷ To deny that fertility doctors have any duty of care, when performing a procedure that could introduce entirely new modifications with unforeseeable effects to the gene pool, boggles the mind. Imposing tort liability on fertility doctors who practice gene editing would effectually deter, in the gene-editing context, the reckless experimentation that has been made possible by the veritable Wild West⁹⁸ of unregulated fertility-clinic practice. (Imagine the fertility doctor responsible for the “Octomom” creating designer babies in a petri dish.)

One possible alternative theory of duty for achieving these aims bears addressing: if an ex utero embryo is the property of the parents, injuries due to negligent gene editing could be compensable as the result of a breach of duty to the parents not to negligently damage their property.⁹⁹ This framing avoids the thorny issue of attaching tort duties, which we normally reserve for interactions between persons, directly to human embryos in their capacity as human individuals at an early stage of development.

Despite this benefit, the property framing is an inappropriate response to the problem raised. A claim for injuries sustained due to negligent gene editing is properly the child’s, rather than the parents’. The damages sought are not compensation for the breakage of the parents’ pristine embryo; they are intended to compensate a child who lives with a severe genetic disease or any number of unpredictable maladies due to gene editing gone awry. The duty should be owed to the person for whose benefit the law operates.

The cases in which property law has been applied to human embryos are inapposite, as they have generally involved ownership (or custody) contests between parents, not injuries to children.¹⁰⁰ In these cases, whether the embryos would be implanted at all was subject to adjudication, and thus potential injury to the resulting children was far afield of the issues discussed. In contrast, therapeutic gene editing would always be intended to prepare embryos for implantation, so this context suggests recognizing a duty flowing directly to the tiny human the law is

⁹⁷ Lanphier et al., *supra* note 66, at 410.

⁹⁸ Clements, *supra* note 11, at 347–48.

⁹⁹ See generally Jessica Berg, *Owning Persons: The Application of Property Theory to Embryos and Fetuses*, 40 WAKE FOREST L. REV. 159 (2005) (discussing the role of property law in governing categorization of embryos and fetuses).

¹⁰⁰ See *id.* at 160–61 (listing cases in which property concepts have been applied to embryos).

trying to protect rather than shoehorning embryos into property categories merely to evade an unjust result.

Another alleged benefit of the property framing is its avoidance of conflict with abortion law.¹⁰¹ If embryos are owed duties that resemble those owed to persons, the rationale for preferring a mother's right to an abortion over embryos' and fetuses' rights is supposedly weakened; if embryos are property, no conflict emerges. But the expansion of duty proposed herein would not affect abortion rights, since medical providers already have a duty not to wrongfully harm the implanted unborn children of their patients. Recognizing a duty not to wrongfully harm the conceived, but not yet implanted, unborn child of a patient would not affect lawfully performed abortions at all—all abortions are performed on the mothers of already-implanted unborn children, and abortions that comply with applicable law are, by definition, not considered wrongful acts by law.

Once a duty is recognized, other aspects of tort liability will need to be adapted to the gene-editing context. The need to prove the other requirements of relevant tort law—noncompliance with a standard of care, causation, and damages—will present unique challenges in the germline editing context. Clinical germline editing practice could organically develop a standard of care, as happens with other new medical treatments, if none is set by legislators or regulatory agencies.¹⁰² The effect of any single genetic modification on a person's eventual traits is often indeterminate and highly influenced by environmental factors, so in many cases causation will be difficult to prove.¹⁰³ The proximate cause requirement may also exclude possible multigenerational injuries resulting from harmful germline mutations.¹⁰⁴ It is beyond the scope of this Issue Brief to detail the solutions to these problems, but lines will need to be drawn, as they have been in prior adaptations of tort law to new technological possibilities.

CONCLUSION

CRISPR/Cas9 presents much therapeutic promise, but its use must be regulated to prevent the sorts of experimental dangers that have plagued the fertility industry. If federal and state legislatures are unwilling to step in, tort duties will have to adapt—but only slightly—to cover the children of CRISPR. Performing molecular surgery on a single-celled human

¹⁰¹ See Wendy C. Shaper, *Does a Nonviable Fetus's Right to Bring a Wrongful Death Action Endanger a Woman's Right to Choose?*, 27 Sw. U. L. Rev. 325, 337 (2003) (arguing that attribution of personhood to unborn children undermines abortion rights).

¹⁰² Marshall, *supra* note 96, at 1295–96, 1304.

¹⁰³ *Id.* at 1297, 1310.

¹⁰⁴ *Id.* at 1298, 1326.

being, so that it will develop into a healthy baby, is a different type of medical intervention than malpractice law was created to address, but the timeless tort principles of compensating victims and deterring bad acts require that, if legislatures do not act to protect these children, courts do.