# **The Ethics of CRISPR: What We Can Do vs. What We Should Do**

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Geneticists have known for years that DNA is the biological memory bank. Deoxyribonucleic acid, or DNA, contains all the information that our body needs to perform daily tasks, as well as for growth and development. There are many well-documented genetic disorders that result from incorrect DNA sequences—examples include benign things such as albinism all the way to more hazardous conditions such as cystic fibrosis. Until the last two decades, scientists were without tools to effectively edit any erroneous sequences, and the first two potential methods—zinc finger nucleases and transcription activator-like effector nucleases (TALENs)—proved to have significant faults. They were both inconsistent and lacked specificity. However, the newest genetic editing system, CRISPR Cas9, is a potentially revolutionary scientific advancement.

First recognized in a bacterial immune system, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) are used for directing enzymes to destroy or alter genes. It can be tailored to make changes at specific locations in our massive collection of DNA, known as the genome. The system has already been used in mice to correct the genetic errors implicated in cystic fibrosis and sickle cell anemia (Specter, 2015). It is being investigated to see if CRISPR can reprogram an individual's cells to grow into specific tissues—doctors might be able to grow new, custom nerve tissue and implant it in patients with neurodegenerative disorders (Savell and Day, 2017). While the most obvious applications are found in the world of genetic disorders, CRISPR's potential influence in other areas of biology are profound. For example, a research group at MIT is using CRISPR to create a genetically-altered strain of white-footed mice that are immune to the bacteria that causes Lyme disease. Ticks can only spread the disease after being infected, and mice act as the primary carrier of Lyme bacteria. If scientists release Lyme-immune mice into the environment, they would be able to mate and spread the trait to the population of

mice in the ecosystem. The prevalence of Lyme disease would fall, as the ticks would no longer be as prone to get infected (Specter, 2016).

The applications of this technology, while exciting, bring up normative questions of what ethical responsibility the scientists, doctors, and researchers have when wielding a technology this powerful. Unlike other biotechnologies, CRISPR Cas9 has the capability to fundamentally rewrite DNA on a scale which is unprecedented. If the genetically altered mice are released to fight Lyme, there is no reversing that process. Those mice and any future progeny are fundamentally and irreversibly changed due to human influence. The stakes are even higher as CRISPR is being investigated for potential medical treatments on humans—what are acceptable amounts of tampering in human DNA? Who should have access to these treatments? Should the technology only be used for serious, life-altering diseases, or are auxiliary uses acceptable? For example, would parents using CRISPR technology to select for a certain hair color in a child constitute unethical genetic engineering?

These types of questions have been addressed by prominent medical ethicists in the past—a future with genetically altered humans has captured the public imagination well before CRISPR was a subject of extensive research. Michael Sandel, a philosopher based out of Harvard University, presents an argument against using these technologies for selecting things such as cosmetic traits in humans. Julian Savulescu, an Australian bioethicist at Oxford, proposes that parents are morally obligated to use these technologies to select for traits they think will maximize the utility of their children. The primary works from these philosophers presenting these arguments were written before CRISPR was revolutionizing genetic research. It is important to think about how the technology of CRISPR is developing, as well as how the ideas presented by these philosophers contribute to the normative discussion of genetic editing.

This research has two components. First, an extensive review of the primary and secondary literature on CRISPR takes place. To begin speculating on the normative questions surrounding this technology, it is important to understand how the system works and what kind of applications are likely to become available. Afterwards, an ethical argument on the morally responsible usage of CRISPR is made, specifically with respect to human germline genome editing. This includes comparisons to current situations in the medical field that may provide a foundation for thinking about this novel technology—in particular, the ethical framework of pre-implantation genetic diagnosis. Furthermore, it is necessary to think about how unequal access to this technology could consolidate disadvantage and marginalize certain groups. Principles of Rawlsian justice will be applied to ethical issues associated with CRISPR to give a framework for thinking about risks to social justice stemming from this research. The potential eugenic threat that this technology represents will be discussed as well.

These are important questions to consider as we move closer to using these genetic editing treatments in humans because of the profound nature of the technology. Mistakes in these treatments will not be easily erased or forgotten. An erroneous usage of CRISPR could result in generations of life being affected, unable to do anything about the flawed treatment that is hard coded into their DNA. This work brings together the fields of medicine, biochemistry, genetics, poverty studies, and public health. Thinking about the ways that CRISPR might change the world is exciting—this could be the most revolutionary technology that comes out in this lifetime—but careful consideration of potential ethical hazards must take place as it moves forward.

The literature on CRISPR is vast—although the system has only recently been discovered, it is a hot topic in biochemical and genetic research. Having some idea of the

mechanism is important when considering the ethical concerns about the system, so some of the terminology and biological models for CRISPR will be discussed here. The most basic version of the CRISPR model is comprised of two parts. For one, there is a protein called Cas9. This protein acts to cleave DNA, breaking the long structure of our genetic material as scissors would cut a rope (Shalem et al., 2014). The second portion of the system is a piece of guiding RNA. Where DNA is the master copy of all genetic information, RNAs serve the function of transporting that information—if DNA is the genetic cookbook, RNAs are pieces of scrap paper that recipes are copied onto when they need to be transported around. This guiding RNA can be used to do two things. Firstly, it can be used to attract the Cas9 protein. Secondly, it can be designed to localize to incredibly specific locations on DNA, thereby allowing scientists to cut the DNA at any location they see fit (Savell and Day, 2017). The astounding nature of this ability cannot be overstated—each cell in your body has around 3.2 billion locations where the DNA could be cut, and CRISPR allows scientists to cut with relatively high specificity (Toledo and Saltsman, 2017). That being said, the system is not perfect, and discussions of that imperfection are a factor in discussion of ethical issues with CRISPR.

The variation of potential applications for CRISPR is represented within the diversity of research. CRISPR is not only being used to dream of new, novel treatments in the medical field, but the high specificity and ease of application is reforming established research methods. For example, gene research often uses a technique called “genetic knockout”. For scientists to discover what a gene does, they will cultivate a line of organisms that have been genetically altered or selectively bred to have a non-functional version of a certain gene. By examining the outcomes from knocking out this gene, it is possible to determine what the gene is responsible for in a healthy organism. While this is a long-standing research procedure, Korean scientists

have recently used CRISPR Cas9 to knockout genes related to obesity in mice (Roh et al., 2018). CRISPR provides a more effective, specific, and customizable tool for creating these mouse models in obesity research—this is likely applicable to all research that focuses on how metabolic pathways are related to gene expression. Prior to these methods, known as "new wave" gene editing, it could take an entire year to create a successful, genetically modified mouse, and now the process is anticipated to take closer to six weeks (Gupta and Musunuru, 2014).

CRISPR is also shaping up to be a crucial tool in stem cell research. Stem cells are the precursor cells to the tissues we have in our body. Part of the problem with stem cell research is the tendency of these cells to differentiate into different configurations—biologists need the cells to stay in their "stem form" until the researchers decide how they want to manipulate them. Chinese scientists have used CRISPR Cas9 to halt stem cell differentiation, effectively immortalizing the stem cells and allowing the researchers to decide when the cells should continue growing and developing (Hu et al., 2017). The limits of what CRISPR can do is largely restricted by how creative scientists are with the technology. As the science gets better, researchers and doctors will be forced to address the ethical considerations of this work, and some individuals have already considered what responsibilities come with CRISPR.

Due to the vast number of possible applications, this research will choose to focus on a specific type of research and potential medical treatment. One of the most ethically interesting investigations being affected by the development of CRISPR is in an area called human germline genome editing. The term germline refers to cells which are used to pass on DNA and reproduce—in humans, they are referring to sperm and egg cells. The term genome is referring to the entirety of genetic material that any organisms possesses. As such, human germline

genome editing refers to making changes in the beginning stages of human development. Given that CRISPR/Cas9 is a locally applied series of biomolecules, use of CRISPR on humans when they are grown will only allow it to make changes within cells to which that it is administered. This has proven useful to things such as cancer treatment in tumors, showing potentially therapeutic effects by targeting cancer cells with a CRISPR that is meant to stop tumor cells from continuing to grow and proliferate (Yi and Li, 2016). While there are still ethical discussions surrounding this work, there are fewer moral disputes in this vein of research. However, using human germline genome editing means that every one of the trillions of cells in the patient treated will have different DNA due to the treatment. This has already generated discussion about ethical responsibility. A variety of ethicists and scientists are thinking about both what we can do with this technology, and also what should we do with this technology.

In terms of human germline genome editing, it provides a very exciting set of potential applications. Since it is much less expensive and much more efficient than the previous options of zinc-finger nucleases (ZFNs) or the transcription activator-like effector nucleases (TALENs), the research is proceeding at a remarkable pace (Zhang et al., 2017b). By using CRISPR to edit either germline cells or early stage embryos that are only composed of a few cells, it is possible that CRISPR could eventually treat a pre-implantation human embryo for genetic disorders before the individual was even implanted for pregnancy. The targets would be specifically monogenic disorders—or genetic disorders that are only linked to a single gene—such as cystic fibrosis, sickle cell anemia, or Duchenne muscular dystrophy (Hsu et al., 2014). The first paper that showed work where scientists modified genes in early stage human embryos has already been published, and while it asserts that “further investigation… of CRISPR/Cas-9-mediated

gene editing in human model[s] is sorely needed", the results are promising enough that therapeutic treatments in humans are not an impossible goal (Liang et al., 2015).

Along with these exciting possibilities, there come a group of potential concerns. For one, as previously mentioned, the technology is not quite fail proof. It is hard to estimate the efficiency of the system due to the wide variety of targets and different biological settings where CRISPR is being used, all of which contributes to how effective the cutting process will be. The efficiency goes even lower if scientists are hoping to insert their own gene in place of the one that was cut out. The highest efficiency for adding a new gene is reported to be around 30% in human stem cells (Zhang et al., 2017a). While this is an impossibly enormous efficiency compared to older methods, this would not suffice for clinical treatment. In many cases of unsuccessful gene insertion, there is still a successful cut in the DNA, which can pose a threat to the health of that cell. Another worry in the research community of CRISPR is the potential of mosaicism. This would occur if the CRISPR worked successfully in some cells of an embryo and was ineffective in other cells. This creates a genetic "mosaic", and it is unclear what kind of effects this might have on organisms. In one study that used monkey embryos to make genetic knockouts and went on to implant them in females, they saw normal development of the mosaic embryos at the time of publication (Niu et al., 2014).

Another chief concern in the scientific community over CRISPR is the possibility of off-site cuts. Though the technology has proven to be very specific, any off-target CRISPR edits could have implications on the individual who received treatment, as well as any future children of that patient (Cribbs and Perera, 2017). These fears have caught the mind of both scientists and the public at large. American author T. Coraghessan Boyle has recently published a short story "Are We Not Men?" that was inspired by the future he envisioned as possible with CRISPR. The

story involves a character who struggles between having a natural child and a genetically manipulated one—an option that might be plausible sooner than many people anticipate (Treisman, 2016). Most of the individuals who find this technology ethically repulsive are concerned about the potential unforeseen consequences, but they are countered by proponents of the promising beneficence (Cribbs and Perera, 2017).

Currently, there are already international regulations and guidelines associated with human germline editing, and by extension, appropriate usage of the CRISPR system in humans. The regulations take slightly different forms across the globe. From a survey of 39 countries where this research is occurring, there were 29 that were found to ban human germline genome editing; the U.S. is not included in this group (Araki and Ishii, 2014). Many countries also ban the creation of human embryos for research purposes, but researchers in certain countries are allowed access to excess embryos that were created for in vitro fertilization. There have been calls to standardize the research regulations internationally to prevent forming "regulatory havens" where scientists go to do experiments that cannot be performed in other countries (National Academies of Sciences et al., 2017). The consensus is that human germline genome editing is unsafe until more research is done, but that has not stopped researchers in China from using CRISPR in human embryos that were not intended for pregnancy. In the US, the NIH will currently not fund research that involves making changes in human embryos regardless of whether they are bound for pregnancy or not (NIH, 2017). Not all science is being done is funded by government money in the US, however. In addition, researchers in China have been publishing papers for several years now that contain experiments that would likely be considered unethical by regulations in other countries (Liang et al., 2015; Niu et al., 2014; Zhang et al., 2017a).

There are two groups that tend to focus on addressing the ethics of CRISPR. One is the scientists and physicians who are doing the research, and the other are philosophers and medical ethicists. It is important to consider the literature from both sides and think about how each perspective influences the arguments, as well as the reality of how the technology will be used. Geneticists have thought for years about the potential moral hazards that could occur from human germline editing. The presence of CRISPR has already ignited much discussion about what ethical considerations must be measured. The American Society of Human Genetics (ASHG) organized an international work-group that came together recently to make a statement on what they considered an appropriate usage of this technology. In this statement, the scientists see the ethical issues fitting into one of two categories: there are those arising from potential failures, as well as issues that might arise from potential success (Ormond et al., 2017).

The issues arising from potential failures include the risk of harmful side effects from the treatment, as already touched on earlier in this paper. The ASHG, and other groups, make it very clear that any future germline-editing medicinal treatments would need to be carefully weighed against the potential negative side effects (Ormond et al., 2017). When thinking about the ethical issues related to successful germline genome editing, the rhetoric becomes more hypothetical given the inherent technological restrictions that come from the current limits of CRISPR. This category of ethical concern is further subdivided into three groups: impact on an individual, impact on a family, and impact on society. For the individual, there are issues of consent—without being able to communicate with the individual in question who will be treated, it is impossible to know if that person would grow to desire the genetic changes that were made to them as an embryo. The closest analogy to this situation is pre-implantation genetic screening,

but the idea of germline genome editing differs in fundamental ways that make it an uncharted ethical territory (Ormond et al., 2017).

Pre-implantation genetic diagnosis (PGD) and pre-implantation genetic screening (PGS) are two current medical practices that have ethical considerations that overlap significantly with some of the questions with CRISPR based technologies. PGD is used to discover genetic information about an embryo for in vitro fertilization, and it can be used to identify potential harmful genetic disorders so that parents using fertility assistance can choose an embryo that is free of debilitating genetic traits (Sermon et al., 2004). PGS is only used to screen for embryos that have multiple copies of genetic material, which can result in unsuccessful implantation or development, where as PGD refers more broadly to the practice of "checking the genetic make-up" of a child prior to implantation (Brezina et al., 2012). Ethical concerns come into play with PGD, where parents can potentially pick traits that they find favorable in some embryos over others. This provides an indirect comparison to human germline genomic editing, and PGD regulations aimed at counteracting ethical concerns can be compared across different nations to act as a comparison point for potential CRISPR regulations.

In the United States, there are no regulations concerning how PGD may be used when couples are in the process of an IVF pregnancy. This is a stark contrast to Europe—almost all European countries have some level of regulation (Bayefsky, 2016). For example, Italy has some of the most restrictive laws on the continent. During IVF in Italy, only three embryos can be made, and there was a complete ban on using PGD in 2004. About five years later, the Italian court system ruled the restrictive laws unconstitutional, but PGD is only allowed to be used for interventions with therapeutic purpose, as opposed to social applications such as sex selection (Bayefsky, 2016). In the United Kingdom, there is a government institution called the Human

Fertilization and Embryology Authority which receives applications from individuals who wish to use PGD to ensure that an embryo will not have a serious medical condition. This reserves PGD to be used only for cases of preventing genetic disorders as opposed to using this technology for making social determinants about an embryo. In the US, there are a variety of societies that form recommendations for how to use PGD, but none of these are legally binding. This discrepancy likely arises out of the private insurance market in the US, where the European countries discussed have single-payer systems (Bayefsky, 2016).

For the family, it is argued that the existence of "designer babies" could undermine the unconditional acceptance that parents traditionally hold for their children. If parents view unfavorable traits as things that should have been cut out of the genome when their child was an embryo, there could be negative ramifications to family structure and unreasonable expectations put onto children. Lastly, in terms of the impact on society, there are two major moral questions: one is the potential of eugenics, and the other is concerns about social justice and solidifying inequalities. Eugenics refers to both the "selection of positive traits" as well as the "removal of disease or traits viewed negatively" (Ormond et al., 2017). The ASHG argues that both pose a potential threat to societal values of inclusion and diversity. The statement highlights that part of the uneasy feeling about this technology is conceptual—the idea of humans tampering with the germline can feel like a science fiction becoming reality. They go on to speak about social inequality, and how unequal access to this technology might further solidify disparity, and make genetic disease a function of socioeconomic class in which an individual is born (Ormond et al., 2017).

In addition to scientists gathering to address these ethical concerns, prominent medical ethicists are discussing the potential moral implications of this technology. *The Case Against*

*Perfection,* a book written by Michael Sandel, lays out an argument against using genetic engineering on human subjects. This work goes a step past current ideas about eliminating genetic disorders and goes as far to talk about the possibility of genetic enhancement. In this text, Sandel discusses other arguments against genetic engineering and why they are not convincing. He makes the assertion that saying genetic treatment hurts a child's autonomy is not a convincing argument due to the fact that the child does not have autonomy over what traits they would receive in the absence of genetic treatments, so there is no autonomy to be lost in the first place (Sandel, 2007). Sandel touches on how the speed of CRISPR's development is a factor in the moral conscious of the people when they think about using it on germline humans—he states that "when science moves faster than moral understanding, as it does today, men and women struggle to articulate their unease" (Sandel, 2007). Moving through a series of potential hypothetical genetic enhancements, he tries to understand the core of what moral objection people have to these ideas. He comments on the idea of muscle enhancing genes being used in athletes and denounces the idea that this is wrong because it is not fair—even if the treatments were available to everyone, people would still find them to be disconcerting. He mentions that the idea of "hyper agency" is why individuals find treatments like this to be unsettling (Sandel, 2007).

Sandel goes on in his text to say that genetic enhancements take away the "giftedness of life" in a way that detracts from our humanity. He brings up a similar point as the ASHG and says that these treatments could undermine parental unconditional love—though he also proports that this research occurring is the very result of transformative love that parents have and how it inspires them to instill positive qualities into their offspring. Sandel also brings up eugenics—after a brief history, he mentions that using genetic treatments to try to eliminate traits seen as

unfavorable could result in a evolved eugenic movement, removing communities that might not consider themselves to be disabled (Sandel, 2007). Sandel's arguments come from a communitarian viewpoint. A communitarian philosophy has a strong emphasis on how individuals are affecting by the social networks around them. This philosophy is well-known for its critiques of Rawlsian principles (Bell, 2016), and this interaction will be discussed in more depth when analyzing how Sandel's arguments concerning genetic manipulation fit within a Rawlsian perspective.

An influential counter-point to Sandel's work is Julian Savulescu, a professor of practical ethics at the University of Oxford. His argument is that humans have an obligation to further themselves to the limit of intellect and capability using every tool at their disposal. His position on genetic editing is recognized as a fringe perspective—most individuals do not embrace genetic enhancement with the same ferocity. He brings up a normative argument that compares iodizing salt to genetic treatments. He cites that every year, a billion IQ points are lost due to pregnant women in developing countries who consume insufficient iodine. Each of these fetuses lose 10 to 15 IQ points, but it would "only cost 2 or 3 cents per person per year to iodize salt", therefore we have a moral obligation to save that cognitive ability (Savulescu, 2014a). He extends this logic to genetic enhancements—claiming there is a moral obligation to not only save any utility being lost but do our best to increase traits that society deems beneficial in whatever manner that we can.

Savulescu's gives the name of his key principle behind his arguments "Procreative Beneficence". He argues that parents should "select the child, of the possible children they could have, who is expected to have the best life, or at least as good a life as the others, based on relevant, available information" (Savulescu, 2001). According to his principle, parents are

obligated to test for non-disease traits, and selection based on these traits should be morally permissible even if it "maintains or increases social inequality." He begins with an example of a couple having two embryos that could possibly be implanted. After genetic testing, they find that one embryo has zero known predisposition to disease, while the second embryo will be at higher risk for developing asthma. He makes the case that there is no reason to select the second embryo, given the possible detriment to well-being that could arise from the situation (Savulescu, 2001).

To address counter arguments, Savulescu brings up that opponents to his theory argue that selecting for the embryo without asthma predisposition, you could be selecting against a true genius, such as Mozart. Savulescu's counters with the fact that with the information available to the couple, either child could theoretically be a Mozart-level prodigy, so they are obligated to pick the embryo most likely to have the best life (Savulescu, 2001). He says that this logic continues from disease traits into non-disease traits, including things such as intelligence or memory. In defining the "best life", Savulescu mentions three theories of well-being, including hedonistic, desire-fulfillment, and objective list theories. He claims that using any of them as a measurement, traits such as intelligence or memory increase well-being, and they should be actively sought if that knowledge was available from a pre-implantation genetic diagnosis. Savulescu, however, compares how the morally correct course of action change when one is talking about selection of embryos compared to the potential manipulation of embryos.

In his work from 2001, Savulescu makes a very clear distinction between making a selection based on available information and making an intervention that could possibly cause harm, such as a mutation that goes on to cause cancer later in life (Savulescu, 2001). At this point, he does not present genetic manipulation as a morally permissible action. This is more

than a decade before CRISPR was shown to have promise as a highly effective gene editing system, and the change of viewpoints is evident from a TED Talk interview that took place in 2014 (Savulescu, 2014a). When addressing the potential of increased inequality, he mentions how individuals have argued that prenatal testing for genetic disorders such as Down syndrome discriminates against people with these disabilities in two ways. It makes a statement about the worth of such lives, as well as reduced the number of people with this condition. He argues that this is essentially forcing a child with a disability onto a couple who would otherwise have a healthy child to promote social equality (Savulescu, 2001). He goes on to say that this does not devalue the lives of those with disabilities, using the example that attempting to prevent accidents that would cause paraplegia does not mean paraplegics are less worthy of respect.

Towards the end of his argument, Savulescu addresses why Procreative Beneficence differs from eugenics. He highlights that Procreative Beneficence is focused on the private enterprise of a couple's family and encourages the highest quality of life for the parents and the children. He asserts that eugenics operates on a public interest principle, where the justification for action is based on creating a "better population" (Savulescu, 2001). Savulescu's arguments have utilitarian undertones—he is promoting his argument based on maximizing utility among a population and takes time to claim that allowing genetic editing for some will not lessen the happiness that others experience. Although he wrote a blog post in 2014 that claimed he is not a utilitarian despite being labelled as one, he still uses many components of the philosophy in his writings on genetic editing. His writing in that blog post focused on the idea that he thought full utilitarianism was too demanding, rather than inherently disagreeing with the more general principles (Savulescu, 2014b).

When reading about human germline genome editing and CRISPR ethical concerns, the fear of a new wave of eugenics is constantly being brought up. The eugenics movement started with Francis Galton, a cousin of Charles Darwin, who brought the ideas of his more esteemed cousin to societal values about procreation to Britain in the 1860s (Sandel, 2007). He claimed that it was prudent to "produce a highly gifted race of men by judicious marriages during several consecutive generations" (Tanner, 2012). Parallel to this, he believed that stopping "unfavorable" individuals from procreating would also be important in his quest for creating a better world. While modern readers might find this notion disgusting, it was accepted by the social elite of Galton's time (Tanner, 2012). The sphere of influence of eugenics did not stop with Europe—America was heavily influenced by these ideals. Coercive sterilization was upheld in the Supreme Court *Buck vs. Bell*, in which one of the parties involved was the State of Virginia (Spiro, 2010). While the US was accepting ideals of eugenics for purposes of preventing criminal and mentally-ill individuals from procreating, the same movement was inspiring an ideology of "racial hygiene" in Germany that would go on to influence the Nazi's anti-Semitism. Starting around 1933, "the Nazi state forcibly sterilized hundreds of thousands of people (approximately one per cent of Germany's population)" (Tanner, 2012). Despite the horror of the American public at the Nazi's atrocities, eugenics experienced a slow decline between the 1950s through the 1970s as various laws were repealed and court cases handled that stripped the movement of its legal backing (Spiro, 2010).

The comparisons have already been made between the possibilities that CRISPR presents to the attitudes of the eugenics movement. In a paper on the history of human germline editing, Morange asserts that CRISPR "debates cannot be understood independently of previous attempts to improve human reproduction" (Morange, 2017). After highlighting the versatility of the

system, Morange goes on to point out that the two main objectives of the eugenics movement were articulated as follows: “to prevent the transmission of bad genes that were no longer eliminated by natural selection because of the social and medical care given to the individuals affected by resulting diseases. The second was to increase human cognitive and social abilities” (Morange, 2017). Those who are resistant to the development of CRISPR in human germline genome editing likely share concerns over the resemblance of these goals to the potential applications of the novel technology. These moral qualms have been present for much longer than the past few years, however. Geneticists have been writing about genetic discrimination for decades, and a particularly influential article from 1992 raised concerns about genetic counseling. Genetic counseling is when prospective parents seek medical advice about potential genetic disorders that the couple might be vulnerable to given the genotype of each individual (Billings et al., 1992). These concerns would only be exacerbated in the face of CRISPR’s possible applications.

The speed at which CRISPR is progressing makes it imperative to begin thinking about these issues. There are already examples of scientists in certain areas of the globe being criticized for their work on CRISPR. The Chinese research group that applied CRISPR to human embryos had their paper rejected from two major scientific journals for ethical concerns. When a third publisher finally printed the research, it received significant backlash from the scientific community and the public (Cribbs and Perera, 2017). It is crucial to start a discussion about what is an appropriate use of CRISPR. This includes discussing what ethical principles dictate the specific treatments that should be allowed, in addition to thinking about how this system affects principles of justice. The current regulatory environment must be considered, and stances from medical ethicists and scientists about the permissibility of these technologies need to be

compared for their alignment with social justice values. Preimplantation genetic testing will be used as a comparison model for these ethical debates as well—the similarities and the differences of these two medical treatments will be juxtaposed as a method of seeing what established ethical principles can be transferred to this new CRISPR technology.

In addition to this, the question of how CRISPR might promote a new wave of eugenics needs to be considered. Looking at historical attitudes towards eugenics and how this movement has manifested itself over the years will be vital for understanding how a reappearance of this ideology might look moving forward. It is important to think about how eugenics often results in human rights violations for those who are marginalized by society, as those in poverty often are. This gives further insight into how we need to treat these technologies as they advance and become potential medical treatments.

This analysis contains three main components. To start, the realistic implications of this technology on the future of healthcare are discussed. Secondly, the two sides of the ethical arguments of CRISPR are compared through the lens of a Rawlsian theory of justice, to see if one argument lines up more consistently with this philosophy which acts as one of the dominant methods for thinking about poverty issues. The degree to which CRISPR represents a potential eugenic system will be discussed, along with how this technology might disproportionately affect people of a lower SES. Lastly, there will be a significant comparison between PGD regulations across different countries and how they might inform what the landscape for CRISPR management in the future.

The literature review of the biological and biochemical experiments involving CRISPR gives insight to the future potential of this technology. It is important to have a detailed understanding of the limitations to CRISPR to make sure there is productive discussion of moral

concerns. This will allow for relevant issues to be addressed instead of imaginative, if somewhat captivating, situations. As CRISPR stands now, there is real promise for it to be an effective enough system to be able to do things such as human germline editing, but the technology simply is not good enough yet. There need to be better guarantees concerning off-target effects—the potential dangers of having unintended cuts in human embryonic DNA can not be understated. Extensive research will need to be done to ensure there is not a hazard to the embryo when undergoing these treatments. When these treatments do arrive to mainstream medicine, it is likely they will be limited in scope based on the type of disease they are trying to treat or the mutation they are attempting to insert.

Both Sandel and Savulescu address the idea of creating genetically altered humans that have been modified genetically to enhance their intelligence. While these ethicists craft arguments that make for excellent juxtaposition on the issue of CRISPR, it is important to note how feasible it would be to use CRISPR technology to implement that hypothetical. Even if the CRISPR system was perfectly tailored and could be guaranteed to make the changes that were desired by geneticists in human embryos, the issue is introduced of whether scientists would know which changes to make. There is evidence for genetic, inheritable components of intelligence, and genome-wide association studies (GWAS) have been performed to discover which genes are important for cognitive function. However, there have been almost no reproducible studies that show a correlation between genetic expression and cognitive ability. The exception to this is the *APOE* gene, which is associated with a more rapid decline in cognitive function throughout life as opposed to any "boost" in intelligence (Deary, 2013). More often, complex traits such as memory, temperament, or intelligence are thought to be influenced heavily by environmental factors in addition to genetic inheritance (Saudino, 2005). On top of

the interplay between the genes and the environment, complex traits are often polygenetic, meaning that they are influenced by myriad genes within the genome, and each gene only would make small contributions to the overall phenotype of the organism (Deary, 2013).

This caveat is important to keep in mind when discussing the ethical arguments to these issues. While it is possible to imagine a future where large, sweeping behavioral changes are possible by the editing of a few genes, the field of behavioral genetics would need to make large advancements before this would be possible. However, there are some characteristics, such as eye color, muscle strength, or perfect vision, that could become targets for genetic manipulation in the near future (Morange, 2017). As the scientific community moves closer to these goals, it would be valuable for both sides of the ethical debate about human germline genome editing to be examined through a lens of Rawlsian ignorance. While there are a variety medical, economic, religious, and cultural factors that need to be considered in the debate over genetic editing, social justice has a significant role in these debates. Introducing a Rawlsian "veil of ignorance" principle could help inform how decisions about morally permissible genetic editing should be made to ensure these technologies are socially just.

John Rawls describes a theory of justice that starts by thinking about issues of social and economic inequality behind a "veil of ignorance". From behind this veil, Rawls imagines an individual having the power to structure social and economic systems in a way that would be the fairest, without knowing at what ladder in that hierarchy they will be when the veil of ignorance is lifted. This ensures that an individual does not work to stack the odds of success in their own favor. This leads Rawls to two main principles of justice. For one, "each person is to have an equal right to the most extensive basic liberty compatible with a similar liberty for others". The second principle dictates that "social and economic inequalities are to be arranged to that they

are both (a) reasonably expected to be to everyone's advantage, and (b) attached to positions and offices open to all" (Rawls, 1971).

For the purposes of this work, a Rawlsian veil of ignorance will be applied to arguments made by Sandel and Savulescu about the morality of genetic editing. Sandel argues his stance from how genetic enhancement violates sanctity of life and does not address the component of fairness that Rawls set out to build a framework for thinking about. Savulescu does talk about how genetic enhancement should be allowed despite the possibility of increasing social inequality, but his argument hinges on emphasizing institutional reform over limiting the technology's applications. His arguments also claims that populations will select for genes that maximize well-being, and a society would avoid doing something like selecting too many males because it would be "intolerable" to exist in that environment (Savulescu, 2001). To help elucidate a socially conscious way to think about these moral questions, modified Rawlsian veils of ignorance will be applied to situations involving potential CRISPR usage. The process will proceed through a series of different scenarios that will aim to uncover the morally permissible areas of CRISPR application.

It is important to note that this is not the way Rawls intended for his veil of ignorance to be used. The veil was intended to be used as a tool to determine the social principles that would guide the formation of institutions, and was not originally meant to be applied determining whether or not a hypothetical case is consistent with justice and fairness (Rawls, 1971). Despite this, there are precedents for having Rawlsian justice principles determine how institutions handle specific procedures. Specifically, the organ allocation system in the United States cites Rawl's *Theory of Justice* when they lay out the ethical principles that guide how UNOS (the United Network for Organ Sharing) operates. They state that a "well-known interpretation of the

principle of justice holds that the just or fair arrangement is the one that identifies the worst off persons or groups and arranges social practices so as to benefit that group" in a report published by the UNOS Ethics Committee (2010). This principle allows the justification of giving priority to patients who need an organ immediately to prevent death, even if there is a utilitarian motive for giving the organ to a healthier patient.

The result of having UNOS guided by some pseudo-Rawlsian principles dictates many of the specific practices of the organization. The organ allocation system must carefully balance utility and justice. They must have concern for the amount of good an organ will do when given to a patient, as well as ensuring a degree of fairness in the allocation system. This is a difficult position to be in, but UNOS has been navigating that space for years by considering the two with approximately equal consideration (2010). Despite the United States healthcare system being treated as a market, the organ allocation system works to ensure robust fairness by applying Rawlsian principles when deciding their policy on how to distribute the scarce resource of organs. This acts as a precedent for this paper to use a Rawlsian veil of ignorance to begin informing potential CRISPR policies towards maximizing both utility and justice.

To begin, the case of eliminating a debilitating genetic disorder with CRISPR will be considered, assuming the technology becomes advanced enough to successfully eliminate the problematic gene with 100% efficiency. The alternative option will assume that pre-implantation genetic diagnosis is impermissible, and therefore, choosing to ban the CRISPR treatment runs the risk of being born with a genetic disorder such as cystic fibrosis, which has a prevalence of around 1/3,000 in Caucasians (National Institute of Health, 2012). The individual putting on the veil will be one of the 61,740 babies that is born from an in-vitro fertilization procedure every year (Sable, 2014), and when deciding if it is morally permissible to allow for the elimination of

a debilitating genetic disorder using CRISPR, they would not know which life will end up being theirs. Under these conditions, it seems reasonable that most people would be in favor of CRISPR being used as a human germline genome editing treatment.

Suppose the situation was altered. Rather than eliminating a genetic disorder, CRISPR would be used to enhance the intelligence of every child born from IVF. Someone behind the veil of ignorance might choose to have morally permissible CRISPR enhancement if they were still guaranteed to be born from IVF. However, that answer would likely change if the individual behind the veil was no longer guaranteed to be one of the IVF newborns, and instead might be born as any one of the 4 million U.S. births in a given year. Now, CRISPR no longer represents a way to help ensure equal capabilities among a population. Instead, it represents a threat to that equality. This situation is indicative of Sandel's thinking. The combination of the two suggests that there are morally permissible uses of the technology, but there are boundaries to ethically acceptable CRISPR applications. Savulescu's arguments for the potential of increasing social with genetic enhancement do not find a solid basis under this scenario.

While Rawlsian philosophy can help provide a framework for thinking about the social justice principles that would dictate CRISPR usage from behind the veil of ignorance, this does not fully address whether this technology represents a eugenic threat. There has been worry about how advancing genetic diagnostic ability could be contributing to genetic discrimination for decades, even before CRISPR technology was on horizon. In 1992, a geneticist named Paul Billings took a survey of individuals who suffered from a variety of genetic disorders such as Huntington's Disease, Friederich ataxia, PKU and others. These individuals, even if they were leading healthy lives and did not experience any abnormalities in their day to day routines, had trouble finding health insurance and keeping employment (Billings et al., 1992). These negative

externalities could function to solidify inequality and would certainly hinder the socioeconomic mobility of individuals who have irregular genotypes.

There are two ways to think about how CRISPR and genetic discrimination intersect. It could be considered that using CRISPR to reduce or eliminate the amount of genetic disorders is a way to eradicate genetic discrimination. Without the presence of these disorders, there are no distinguishing genotypes that would receive selectively poor treatment. From the opposite view point, CRISPR could be regarded as the ultimate form of genetic discrimination. In the case of using CRISPR to modify a IVF child, the individual receiving the treatment would never get the chance to exist with their natural genome. There is certainly a degree of overlap with the possibility of this procedure and eugenics—both emphasize the elimination of genes labelled as "undesirable". The author Morange mentions that the only time when human germline genome editing might be acceptable is when a genetic disorder is debilitating and dominant—meaning only one copy of a mutated gene is enough to invoke the disorder. But, he goes on to argue that this end can already be achieved through pre-implantation genetic testing, and CRISPR technology represents additional risk (Morange, 2017). This is not entirely free of eugenic risk itself—authors have argued that PGD is a form of selective breeding. On top of that, there has been discussion that the expensive nature of PGD can act as a poverty-sensitive form of eugenics (Han, 2006).

Thinking about how the different systems of regulations imposed internationally on PGD can be an effective way to continue the focus on comparing PGD to the ethical dilemmas of CRISPR. As mentioned previously, the United States has essentially zero regulations on the usage of PGD technologies while European countries are much more heavily monitored. Given some of the overlaps in potential ethical issues between CRISPR and PGD—such as eugenic

threat or solidifying socioeconomic disparities—it can be a useful exercise to extrapolate the regulatory landscapes on PGD to hypothesize what legislation might look like for CRISPR in the future. This hypothetical is not meant to accurately predict the future of CRISPR legislation in any country, but it gives a framework for thinking about what regulations might be able to do to help mitigate ethical problems presented by the novel technology.

If the UK used a "PGG-like" system for CRISPR regulation, they would have a similar ethical oversight committee review application for the usage of any CRISPR treatments. Assuming this committee followed similar principles as the Human Fertilization and Embryology Authority, this could eliminate many ethical issues discussed in this paper. Individuals would not be allowed to select for social traits with CRISPR, nor would be any enhancements be approved. Given the single payer system in the UK, CRISPR treatments during IVF would not be poverty sensitive, either. There is also less concern over a eugenic threat if the procedure requires an active application process and is carefully considered by an ethics committee. If the United States regulatory attitudes on PGD were held constant for CRISPR treatments on embryos, these ethical issues would be unresolved. There could be usage of this medical technology that solidifies social inequalities, and potential moral hazards of genetic enhancement would remain.

There is not a clear answer in the literature about what constitutes the optimal PGD regulation. There are many arguments about the necessity of regulating PGD to prevent the eugenic tendency of the technology. Most sources agree that the answer is not to completely ban these procedures, but that some level of restraint should be exercised (King, 1999). This is a similar attitude that a Rawlsian framework lends to thinking about the usage of CRISPR. It is outside the scope of this project to definitively draw the moral line on these issues, but it is vital

that these issues are considered from a perspective that considers how policies and attitudes will affect populations suffering from poverty. Unequal access to this potentially revolutionary healthcare represents an incredible threat social equality. This opens larger questions about the state of the healthcare system in the United States, which are also beyond the scope of this paper. However, if this technology represents a way to solidify the increasing gaps in socioeconomic status forming in the US, it would be prudent to research how the healthcare system can be changed to better accommodate CRISPR treatments being widely accessible for all citizens, as well as what kind of treatments are ethically permissible.

The development of CRISPR technology is exciting. It represents opportunity that researchers and doctors have strived towards for decades. For the first time in history, a highly accurate genetic editing system seems within reach. The applications extend beyond the situations described here—even if CRISPR does not become involved in human germline genome editing, the technology will hopefully be used to expand biological knowledge and inform research that is used for the betterment of humanity. However, amid this excitement, it is crucial that society thinks about the implications of these novel procedures. Particularly in the case of human germline genome editing, there are profound ethical questions to be considered. The questions are innumerable, and the answers are not currently in perfect consensus across the field—nor are they likely to ever be. Bearing in mind the potential for disease prevention should be coupled with attempting to ensure access to these treatments for individuals experiencing poverty. A dearth of access could be exceptionally harmful for promoting equality of opportunity, and as CRISPR helps to move society towards a healthier future, it is crucial to continue fighting for policy that promotes socially conscious medicine as it relates to this technology.

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