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On the Technical and Moral Distinctions Between Germline Genome Editing via CRISPR and Existing Genetic Trait Selection Methods

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M.A. (Hons) University of St Andrews, 2017

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An abstract of

A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of
Master of Arts
in Bioethics

2018

Abstract

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By Naomi Elizabeth Ann Marshall

This thesis explores whether there is a morally relevant distinction between human embryonic genome-editing via CRISPR-Cas9 and existing genetic trait selection methods. Numerous advocates, from academia and the public alike, have argued that utilizing CRISPR to edit targeted genes in human embryos does not differ significantly to legalized genetic trait selection methods – including shopping for gamete donors; and selective implantation of embryos after preimplantation genetic diagnosis (PGD). This thesis will counter their position. I argue CRISPR is not only different in degree but also different in kind to existing genetic trait selection methods owing to the nature of CRISPR's technical intervention. Existing methods involve choosing between embryos, whilst CRISPR entails genome editing. Although current policy on reproductive technologies necessitates considerations on the intents and consequences of each new intervention method, this is insufficient for evaluating a fundamentally different intervention procedure. McKibben's (2003) paper on "designer genes" will be used to introduce three bioethical lenses through which the novelty of CRISPR can be analyzed: debates on the moral status of embryos and germline genomes; persisting personal identity; and making heritable interventions. Rather than evaluating the ethics of CRISPR, which would involve judgement on the intents, techniques, *and* consequences of the intervention, this paper argues for an amendment on the lack of academic attention toward the moral relevance of techniques.

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Acknowledgements

I would like to thank the Robert T. Jones Memorial Trust for their generous provision, which enabled me to pursue this degree.

I would also like to give special thanks to Diana Cagliero and Maximilian Curtis for their endless support.

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Introduction

The CRISPR-Cas9 system—commonly referred to as CRISPR—is a relatively new genome-editing technology. CRISPR has proven "to be much cheaper, easier to use, quicker, and more accurate than other tools for genome editing." (de Araujo 2017) Due to this development, the National Academies of Sciences, Engineering and Medicine—among other scientific bodies—believe genome editing is beginning to "transition from basic research to clinical research applications", and as such, insist now is the time to consider "the full range of its possibilities in humans" (National Academies of Sciences et al. 2017, 3-4). In April 2015, CRISPR was used to edit the genomes of 86 human embryos by a research team at Sun Yat-sen University in China, in a bid to analyze a gene associated with the blood disease beta-thalassemia (Center for Genetics and Society 2018). Although all these 86 embryos were non-viable, de Araujo claimed that this experiment has successfully "sparked a global debate on the ethics of gene editing" (de Araujo 2017, 24).

On the one hand, "the speed at which the science is developing has generated considerable enthusiasm", particularly from within scientific communities and patient populations who "perceive benefit from these advances" (National Academies of Sciences et al. 2017, 4). The "use of GenCRISPR for any human germline modification, including modifying the DNA of human embryos or human reproductive cells" was illegal as recently as 2014 (Zhang et al. 2014). Numerous biomedical engineers working with CRISPR at the time, including Zhang et al. (2014), were becoming increasingly frustrated with stagnating legal developments: their perception was that legislative hesitancy stemmed merely from safety concerns, concerns which they knew were rapidly diminishing with technological progress. In February 2017, "an expert committee convened by the U.S. National Academy of Sciences … offered qualified support for

germ-line editing" (Yong 2017), perhaps offering clout to Zhang et al.'s predictions. Be that as it may, this turn of events has simultaneously caused concern among scientists, ethicists, and the public alike. According to Sandel, developments in the study of genetics—that were precursors to CRISPR, such as mapping the human genome—have left society in "a kind of moral vertigo":

> Breakthroughs in genetics present us with a promise and a predicament. The promise is that we may soon be able to treat and prevent a host of debilitating diseases. The predicament is that our newfound genetic knowledge may also enable us to manipulate our own nature … When science moves faster than moral understanding, as it does today, men and women struggle to articulate their unease (Sandel 2004: 51).

Yet while CRISPR is in many ways "groundbreaking" (de Araujo 2017), the practice of selecting traits of future generations is nothing new. Mukherjee (2016) locates CRISPR as the product of a long history of our human "desire to decipher our manual of instructions". From Galton's eugenic hopes to manipulate inheritance for human benefit (Mukherjee 2016, 72) to the motivation and "success" of the human genome project (Mukherjee 2016, 319): evidently, a precise genetic trait selection method such as CRISPR has been a long sought-after and frequently analyzed dream.

Aims, Objectives, and Research Questions

This thesis is an analysis of what is genuinely new about the CRISPR-Cas9 system. Whereas current bioethical literature is utilizing the limelight over CRISPR to add new urgency to age-old questions—such as the appropriate scope of parental power over children, and unease over the societal consequences of attempting to improve heredity—I will add to this important moral work by exploring the very genome-editing techniques which make CRISPR uniquely troubling. To a great extent, the near possibility of parents editing the genomes of embryos appears frightening not because humans have never before considered intervening in the

inheritance of their children, but because the means via which they can interfere are becoming increasingly technically precise. Accordingly, my research questions will be as follows. First, is CRISPR editing fundamentally different to previous genetic trait selection methods? By which I mean, is there a morally relevant distinction to be found within the process of CRISPR genome editing which warrants treating CRISPR as different-in-kind to existing trait selection methods? If so, my second research question is: what is the morally relevant feature of the technique that makes it different?

This thesis will be structured into four parts: an Introduction, two main Sections, and a Conclusion. This Introduction will continue by clarifying and further justifying my select focus on new techniques. I will then offer an exposition on the minute details of the process of CRISPR along with a description of why this new technology contrasts with existing genetic trait selection techniques. During this account, I will draw on O'Keefe (2015) to demonstrate that there is oftentimes confusion among academics over how CRISPR works, as evidenced in misuse of the language of "editing" and "writing" a genome. This confusion will be used to point to my research problem: that bioethicists are willfully ignorant of technical nuances and the unique ethical dilemmas they raise. This research problem is more fully explored in Section 1, where I introduce and examine various arguments for and against the existence of a morally relevant distinction between CRISPR techniques and existing genetic trait selection methods. In this section I explicitly address my first research question. McKibben's argument, that CRISPR represents a difference in kind rather than degree, will be evaluated as stronger than competing claims. I contest that McKibben's argument is cogent because he paid sufficient attention to the sociocultural assumptions which determine his opinion on the permissibility of intervening with embryonic genomes. Section 2 develops McKibben's approach in order to address my second

research question. I draw on philosophical debates on moral status, persisting personhood, and making heritable changes. My Conclusion reviews the difficulty of finding a consensus on the moral status of germline genomes. Moreover, since my aim is to analyze CRISPR's novelty to inform future evaluations, within my Conclusion I also make recommendations on how my analysis should fit into ethical evaluation and policy decision-making.

Setting Investigation Parameters

To focus this investigation, two practical parameters will be set. First, all genetic trait selection methods under consideration will, hypothetically, be occurring on embryos of comparable ages—specifically, on embryos six days after fertilization or younger.[1] This control parameter is helpful in that it prevents my analysis having to address separate arguments on the timeframe within which abortions, and other methods of embryo destruction, are permissible. Moreover, this early embryo focus means I will be examining the germline phase of human development. As defined by the NCI Dictionary, "Germline DNA is the source of DNA for all other cells in the body. Also called constitutional DNA." (National Cancer Institute 2018) As such, genetic trait selection choices made during germline development will be pervasive throughout the cells of the ensuing-adult's body; and will be heritable to any future offspring.[2] Since a major qualm with genetic trait selection is its heritable aspect—as will be accounted for in Section 2—this germline timeframe is imperative.

My accompanying parameter is that I am focusing my attention on therapy-based interventions alone. Focus on therapy avoids conflating my analysis with the bioethical debate on

[1] Embryos of this age are blastocysts. "The blastocyst consists of 200 to 300 cells and is ready for implantation. Implantation, the process in which the blastocyst implants into the uterine wall, occurs approximately six days after conception." (Gale 2006)

[2] While gene-therapy in adults does involve changing genetic material, the change is in somatic cells – meaning the change will not be present in all cells, nor heritable.

human enhancement. While this bioethical debate *will* serve as a research problem in Section 1, this attention will be subsidiary in that I will demonstrate how enhancement debates distract rather than enrich my focus on permissibility of the act of CRISPR. Furthermore, my focus on therapy is sufficient for an analysis of CRISPR. The reason for this sufficiency lies in the fact that if CRISPR is considered impermissible for medical treatment, it will be considered all the more so for non-therapeutic interventions. These two parameters control variables such that I can focus my analysis on CRISPR.

There is another, fundamental way in which I will be focusing my investigation. I am going to bracket out motivations for CRISPR usage as well as consequentialist concerns, to instead focus on analyzing the moral permissibility of the method of CRISPR itself. Of course, consideration on these intents and consequences is necessary for any complete evaluation of the permissibility of CRISPR. Such considerations include but are not limited to: further stratification of society stemming from unequal access to the technology; unforeseen mutations occurring as a result of the intervention; increasing or reifying discrimination against people with genetic disabilities, particularly in how this pertains to cultural mediation of disease classification; and the impact on human diversity. However, while these considerations are important, they are insufficient for an evaluation of CRISPR, or any genetic trait selection method for that matter. The morality of the act in-and-of-itself must also be addressed; and this is where I will focus my analysis.

Here, in order to clarify this focus and justify the parameters I have set, I draw on Natural Law Theory and theorizations of act-morality. First, consider Natural Law Theory's appreciation of how the intrinsic permissibility of an act is a discrete moral consideration. This moral theory's guideline for moral evaluation—the Principle of Double Effect (PDE)—identifies this intrinsic

permissibility as an integral part of its wider equation. Admittedly, the Principle of Double Effect was purposed for dealing with cases of moral conflict; specifically, it addresses questions over whether one is permitted to bring about something bad in order to bring about something good. One *could* frame an evaluation of CRISPR to fit this deliberative situation.[3] But even beyond this situational framing, suffice to say that this moral theory is helpful to my investigation in that it calls attention to the moral relevance of the act itself. According to Timmons (2013, 83) the formulation of the Principle of Double Effect is as follows:

1. *Intrinsic permissibility*. The action in question, apart from its effects, must not be wrong.
2. *Nonintentionality*. The bad effect must not be intended by the agents.
3. *Proportionality*. There is a proportional grave reason for bringing around the bad effect.

My research question pertains to the first point, on intrinsic permissibility. Namely, is the act of CRISPR intrinsically wrong? Again, I concede that this question—my research question—is not the *only* query which must be addressed for a complete moral evaluation of CRISPR. My contention is simply that it is a *necessary* consideration.

To further underpin my focus on the-nature-of-the-act itself, I turn to Wurzburger's (1994) conceptualization of act-morality as a distinct consideration from agent-morality. Wurzburger argues that moral life "is concerned not merely with what an agent does (act-morality) but also with what kind of a person one is (agent-morality)." (Wurzburger 1994, 67) His distinction speaks to how morally relevant features can be present within "the moral propriety of particular actions" (Wurzburger 1994, 70), specifically within the "intrinsic merits of moral actions" (1994, 72). Again, Wurzburger, like myself, does not deny that morally relevant features can also be found in the consequences of actions—where actions "function as stepping stones to the attainment of moral virtue" (1994, 72)—and in "the virtuous disposition of

[3] Say, if one were to frame the investigatory question as "whether it was permissible to destroy or edit some embryos, so *all* living children were sufficiently cared for."

the agent" (1994, 70). Instead, Wurzburger identifies that morally relevant features within acts themselves are a separate but integral part of a complete moral analysis. Put simply, the means matter just as much as the intents and outcomes.

My reason for choosing to focus on the intrinsic permissibility of CRISPR lies in the fact that there is a gap in bioethical literature on the matter. I am not looking at considerations on intentions and consequences since these matters have largely been wrestled with before, owing to the fact CRISPR has comparable motivations[4] and outputs[5] with existing genetic trait selection methods. What is novel about the technology is its means. On this matter, Sandel made the comment that when faced with new technology, we "reach first for the language of autonomy, fairness, and individual rights. But this part of our moral vocabulary is ill equipped to address the hardest questions posed by genetic engineering", the question of whether such interventions are appropriate in and of themselves[6] (Sandel 2004, 51). Accordingly, this investigation will focus exclusively on fully analyzing the nature of CRISPR genome editing and accompanying moral dilemmas.

Context

i) What is CRISPR?

In accordance with O'Keefe's recommendations on what should be covered in an explanation of CRISPR genome editing (O'Keefe et al. 2015, 5), I will first give a brief account

[4] All techniques under consideration, including CRISPR, involve proactively looking for a known or suspected genetic fault. Although PGD has been known to flag other defects—see how PGD is sometimes used for detective purposes (The Niche 2015)—the use of these genetic trait selection methods to avoid genetic disease requires specific goals and hence comparable motivations.

[5] Those developing the CRISPR technology contest that consequentialist concerns over the safety of the procedure—in comparison to existing methods—are transitory (Zhang et al. 2014).

[6] Admittedly Sandel was here asking whether genome editing technologies represented enhancement. Be that as it may, this quote helps point to how consequences should not be treated as the most pressing moral consideration.

of genes vis-à-vis how they constitute a genome. The biological definition of a gene is that it is "the fundamental, physical, and functional unit of heredity." (Biology Online Dictionary 2017) An extreme simplification of the constituent parts of a gene—derived from my interpretation of information provided by the Biology Online Dictionary—is as follows. The basic structural units of genes are nucleotides. These are compounds made up of a "sugar", joined to a "base" and a "phosphate". Duncan (2018) endearingly calls nucleotides "the ACGTs of life" because a nucleotide is made up of one of four bases: either an A, C, G, or T base.[7] These bases are paired together within the iconic double helix structure of Deoxyribonucleic Acid, known as DNA. A gene is a specific sequence of this DNA. When we talk of your "genetic code"—and how CRISPR changes it—we are referring to the order and magnitude of the ACGT within the DNA.

Mukherjee (2016, 9 & 11) also characterizes a gene as the basic unit of all biological information. He details how "genes reside on chromosomes—long, filamentous structures buried within cells that contain tens of thousands of genes linked together in chains". Mukherjee puts this biological unit into perspective for us:

> The entire set of genetic instructions carried by an organism is termed a *genome* (think of the genome as the encyclopedia of all genes, with footnotes, annotations, instructions, and references). The human genome contains about between twenty-one and twenty-three thousand genes that provide the master instructions to build, repair, and maintain humans (Mukherjee 2016, 11).

In review, there are many base-pairings within the structure of DNA; a gene is a specific chain of that DNA code; genes are organized into chromosomes; and all the DNA in your body make up your genome. This genetic constitution of a person is called their genotype, and the way this constitution is expressed—in how you look and function, even on a cellular level—is called your phenotype (Mukherjee 2016, 74). The *way* genotypes are expressed as phenotypes is too

[7] And sometimes "U" bases are present too. That is, if the nucleotide is within messenger RNA, not DNA. But this starts to delve too deep in genomics, going beyond what is a sufficient exposition for my investigation.

complicated to explain here. But suffice to say, changing a part of your genotype can have drastic and unforeseen consequences on your phenotype. As such, scientists prefer to talk of "genome editing" rather than "gene editing" (Horizon 2018); this phrasing better encapsulates how, if you alter one base-pairing within a gene, this may affect the way other genes are "expressed"—and so you are in fact potentially affecting the entire genome, that is, the entire organism.[8]

To clarify what I mean when I talk about "CRISPR", I draw on MIT and Harvard's Broad Institute. According to this collection of scientists:

> In the field of genome engineering, the term "CRISPR" or "CRISPR-Cas9" is often used loosely to refer to the various CRISPR-Cas9 [and other] systems that can be programmed to target specific stretches of genetic code and to edit DNA at precise locations (Broad Institute 2018).

In other words, "CRISPR" is a shorthand—or slang—for a collection of techniques used to edit genomes. When I use the term "CRISPR", I am referring specifically to the CRISPR-Cas9 genome editing technology.[9] CRISPR itself is technically only a part of this method. It is an acronym, standing for Clustered Regularly Interspaced Short Palindromic Repeats (de Araujo 2017, 24). To translate this acronym into wording a philosopher might understand, CRISPRs "consist of repeating sequences of genetic code"; a code that was originally taken from a bacterial immune system (Broad Institute 2018). These CRISPRs are used within the CRISPR-Cas9 genome editing technology as a "guide" (Doudna and Charpentier 2014, 1077): they enable

[8] Consider that presently "the precise effects of genetic modification to an embryo may be impossible to know until after birth." (Lanphier 2015) This stems in part from the involvement of epigenetics.

[9] There are numerous "nuclease mediated genome editing" techniques like CRISPR-Cas9 (Thorne 2015). "What makes CRISPR/Cas unique is that it is far more accessible and easy to implement. Other nuclease-based genome editing technologies such as zinc finger nucleases and TALENs are more complex systems with protein-based recognition domains. With the CRISPR/Cas9 system, all that is required is the widely available Cas9 enzyme and an appropriate guide RNA for targeting." (Perkel 2018) So while CRISPR-Cas9 is different in degree—rather than different in kind—to other nuclease-based genome editing, it will be taken as a representative of this method of genetic trait selection; and contrasted to techniques which choose between untampered-with gametes and embryos.

the technology to get to where it needs to go within the genome so that one can make precise edits. The structure which does the actual "cutting" of DNA within this technique is the Cas-9 enzyme.[10]

This brings us to the focal point of this technology, its so-called "genome editing" capacity (Horizon 2018). Numerous metaphors are used to explain what exactly it is that the CRISPR-Cas9 system does to DNA. Often, if not always, the literature used for bioethical analysis alludes to this technique rather than fully explaining it. Whereas Horizon (2018) characterizes this practice as "editing", Saey (2017) claims that "researchers have been wielding the molecular scissors known as CRISPR/Cas9 to make precise changes" in DNA, while the Broad Institute (2018) talks of how "CRISPR-Cas9 can be used to target and modify "typos" in the three-billion-letter sequence of the human genome". Is the CRISPR technology making "edits" (Horizon 2018), "changes" (Saey 2017), or "modifications" (Broad Institute 2018)? Are all these terms accurate and interchangeable representations of the techniques involved?

In order to answer these questions, I turn to Dr. Chris Thorne's (2015) seminar on the exact processes involved in various genome editing techniques. According to Thorne, who is a specialist in helping labs implement CRISPR, "the process of genome editing relies on using the cell's own DNA repair pathways to elicit changes at a target locus. … The function of these tools is to stimulate these pathways and ideally make changes in predictable ways" (Thorne 2015). Put another way, CRISPR-Cas9 does not itself "write the DNA", but rather uses already existent regulation mechanisms in the cells. Thorne expands that there are two pathways which are used to mediate "the majority of changes", and your choice of pathway determines what you can do with the DNA. One option involves using the Cas-9 protein to cut both strands of the DNA in a

[10] When the target DNA is found, Cas-9 – one of the enzymes produced by the CRISPR system – binds to the DNA and cuts it, shutting the targeted gene off (Broad Institute 2018).

way that will catalyze repair via the *NHEJ* pathway, a naturally-occurring DNA repair process in human cells. This certain kind of cut will mean the code can no longer be read, entailing a mutation which deactivates the gene. This approach is most often used in research. By contrast, using the second pathway allows scientists to introduce new material into the DNA (Thorne 2015), and is thus the method more relevant to my investigation into human germline genome changes. Making "that double strand break in the presence of a homologous donor sequence"—the alternative pathway—allows scientists to "introduce exogenous sequence into the coding sequence; and this can be single base changes, or this can be longer modifications" (Thorne 2015). The important point to note here is that the CRISPR-Cas9 system does not itself write the new code, but rather splices it into the DNA. The code is admittedly written—or naturally occurring—in another scientific process. But it is misleading to say CRISPR itself "writes" the genome when it rather sets up the natural machinery to precisely alter specific DNA sequences.

ii) On Metaphors for CRISPR: Benefits and Cautions

One should not be quick to disparage analogies when explaining this technology. Even Doudna, one of the leading developers of CRISPR-Cas9, used microsurgery as a simile to emphasize the technology's precision in her seminal paper[11] (Doudna and Charpentier 2014, 1077). Analogies and generalizations encourage engagement with the details of the technology. However, this does not mean we should readily accept all narratives on CRISPR, nor should we

[11] On that seminal paper, which was revised in 2014, Perkel explains that "three years ago, Jennifer Doudna and Emmanuelle Charpentier launched a molecular biology revolution by unraveling the CRISPR/Cas system. Their seminal paper, [first] published in June 2012 and cited over 900 times according to Google Scholar, describes a mechanism by which the Cas9 enzyme can cleave any segment of DNA, guided by a short RNA molecule complementary to the sequence of interest" (Perkel 2018). When Jennifer Doudna likened CRISPR to microsurgery in this paper, "that metaphor proliferated across media platforms such as the Washington Post, Discover, and CNN, to name just a few." (Perkel in O'Keefe et al. 2015, 3)

treat them as equally valid. O'Keefe and colleagues drew attention to this matter in a "thought-provoking analysis of metaphors used to discuss CRISPR in lay media, arguing that those currently in circulation fall short of accurately representing the science and fully conveying the ethical complexities of this emerging technology." (Nelson et al. 2015, 60) In their own words, O'Keefe et al. claimed that CRISPRcas9 is "an excellent case for examining metaphor's role in bioethics and public discussion because the technology and the metaphors used to describe it are still emerging" (2015, 3). This subsection will unpack that paper to demonstrate the issue of language misuse within bioethical discussion, and to further refine my focus.

The bulk of O'Keefe et al.'s paper investigates various common metaphors for CRISPR.[12] They found a "range of metaphors describing genomes and CRISPR in popular media", including analogies to blueprint, code, gambling, maps, mechanism, origami, and even war (O'Keefe et al. 2015, 6). Their analysis concluded that "editing"—the most frequently cited metaphor—was unfit:

> In general, editing metaphors used in regard to CRISPR emphasize what is being done to genes, presenting genomes as texts to be edited or genes as targets to be struck, and downplay any ethically troubling implications. "Editing" does not convey a sense of risk or a need for caution. It implies a "mere text" that has an overall vision and a purpose within a bounded set of rules (O'Keefe et al. 2015, 7).

At the same time, O'Keefe et al. demonstrate how this metaphor is truly a double-edged sword, in that "editing" takes on a negative hue when associated with discussions on human embryos:

> The idea of "improving" or "editing" embryos seems to be associated[13] with eugenics... Hence, "editing" applied in the context of "human embryos" inflates concerns about potential misapplications while still downplaying complexity and uncertainty and obscuring its envisioned beneficial applications (O'Keefe et al. 2015, 7).

[12] O'Keefe et al. utilize Lakoff and Johnson's definition of metaphor as "understanding and experiencing one kind of thing in terms of the other" (Lakoff & Johnson 2003, 5 in O'Keefe et al. 2015, 4).

[13] An association which will be unpacked in Section 2.

The paper concludes that there are more appropriate metaphors for conveying the "ethical complexity" of the technique (2015, 8). O'Keefe et al. recommend ecological metaphors as their language of choice, since this comparison "could reflect the broad-ranging effects of modifying genomes and the fact that CRISPR is being used in ways that affect not only organisms but ecosystems themselves" (2015, 8).

O'Keefe et al.'s paper demonstrates how the language we use to describe science is not objective. Similarly, cultural anthropologist Emily Martin accounts for the ways in which scientific narratives actively inform—and are informed by—our sociocultural and political assumptions.[14] O'Keefe et al. and Martin's observations on the subjectivity of scientific description are pertinent to my investigation for three reasons. First, this holds me accountable for my own description of CRISPR vis-à-vis the genome. See how O'Keefe observes that "articulations of how CRISPR works rely on metaphors for CRISPR itself, but also for genetics, since any explanation of what CRISPR does is affected by what larger metaphorical frame is used to describe genomes and genes." (O'Keefe et al. 2015, 5) Even within the contextualization of genes and genomes in this thesis, the sources drawn upon explicitly acknowledged the "storytelling" element of any scientific explanation. For example, I used Mukherjee's *The Gene* to explain how genes are organized within the genome. Mukherjee is a self-identified story teller. He states within the book's first chapter that "this book is the story of the birth, growth, and future of one of the most powerful and dangerous ideas in the history of science: the 'gene', the fundamental unit of heredity" (Mukherjee 2016, 9). Mukherjee's acknowledgement of biological features as "dangerous ideas" appreciates the sociocultural-cum-political dimension of communicating scientific knowledge and scientific technology. As such, my earlier description

[14] Martin examines the conception "story" as told by Western medicine—on the supposedly passive egg and active sperm—and unpacks how the language within this narrative reifies gender norms (Martin 1991).

of CRISPR genome editing technologies is not a "definition of terms" per se. Rather, it is a subjective account, and acknowledging the moral dimension of accounts of scientific methods and techniques is imperative to this investigation.

My second point—on how O'Keefe et al. and Martin's works are useful to my investigation—relates to how their observations underpin my research objective: to expose the ethical problem of academic ignorance toward technical information. To begin with, O'Keefe et al. and Martin's work demonstrates the pervasiveness of misunderstanding: both in public and academic spaces. This is what leads O'Keefe et al. to call "for a multidisciplinary conversation among scientists, bioethicists, and academics studying cognition, linguistics, and rhetoric to begin exploring possibilities for metaphors that accurately capture the complexity of the ethical issues involved in CRISPR." (O'Keefe et al. 2015, 3) Insofar as the act-morality is a discrete moral concern—as was accounted for in the parameters subsection of this Introduction—technical inaccuracies corrupt moral evaluation. Moreover, O'Keefe et al. and Martin's work does more than highlight the convolution which can result from technically imprecise moral debates. It also draws attention to academic misconduct. An academic's language misuse can serve to bolster their position on the permissibility of a new technology. In addition, general disregard toward the techniques might allow authors to hide from morally relevant features within these processes—features which might undermine their position. Kass synthesizes a helpful caution on this matter:

> Accurate description is crucial to moral evaluation. One should try to call things by their right names. One should not encumber thought by adopting fuzzy concepts. And one should not try to solve the moral question by terminological sleight of hand—the way that some scientists today try to win support for cloning-for-biomedical-research by denying that the cloning of embryos is cloning or that the initial product is an embryo. In this area especially the terminological question is crucial, but also hard (Kass 2003, 12).

The third and final point I draw from O'Keefe et al. is that their paper's limitations point to yet another gap in the literature that my investigation must address. O'Keefe et al. focus on linguistic honesty over the uncertainties of the consequences of CRISPR.[15] I contest that this focus is insufficient since ethical issues can arise in the act itself, not just the consequences of the action. In a critique of O'Keefe et al.'s paper, Nelson et al. underpin my assertion that their work is incomplete: the former "identify a need to distinguish between metaphors for what CRISPR is, as a technology, versus what CRISPR does, in applications." (Nelson et al. 2015, 60) As a result, my premise is that it is important for bioethicists to appreciate exactly what happens in various genetic trait selection techniques, since only this level of minute attention to method will allow a proper consideration of the act's permissibility. To ground my premise in a clinical case study, I will now detail a situation that illustrates how different kinds of ethical questions are raised by discrete techniques.

iii) Case Study: The Complexities of "Correcting" the NF1 Gene via CRISPR

This case study accounts for how the techniques involved in CRISPR create unique ethical dilemmas. I will detail exactly what CRISPR-Cas9 would do if it were utilized to remove the genetic disease Neurofibromatosis Type 1 from embryos, then analyze the ethical dilemmas intrinsic to this procedure. An explanation of this disease is first necessary since the pathology of Neurofibromatosis affects the way CRISPR can intervene to alter the DNA of those with the disease. Neurofibromatosis Type 1 is a monogenic disease, meaning it is caused by a change on a

[15] For scientists, bioethicists, and the public, a key question is, "how can our language be honest about the uncertainties in how we will use and develop the technology, and what promise and risk its use holds, without employing terms that trigger gut reaction rather than thoughtful deliberation?" (O'Keefe et al. 2015, 8)

single gene—in this case, on the NF1 gene[16] (Carrieri 2016). Even though the genetic change is limited to this specific gene, Neurofibromatosis manifests as a multi-system disorder (Ratner & Miller 2015). Symptoms include, but are not limited to, progressive disfigurement and disability from tumor growth throughout the nervous system, congenital cognitive differences, bone deformities, and rarer complications, including cancer and blindness (Carrieri 2016). As such, Neurofibromatosis is a useful example of the fact that change in one gene can affect how the entire genome is expressed and thus multiple phenotypes. The exact mapping of the disease onto chromosome 17 (Wallace 1990), and the design of molecular guides to target the NF1 gene (Zhang 2014), has enabled researchers to use CRISPR in Neurofibromatosis studies, such as in recent work on rats to develop therapies for treating Neurofibromatosis-related pain in human adults (Moutal 2017). However, the use of CRISPR directly on humans for "any human germline modification, including modifying the DNA of human embryos or human reproductive cells" has yet to be legalized (Zhang 2014; see also Greenfield 2016).

Although the 'curing' of Neurofibromatosis with CRISPR-Cas9 during embryonic development is hypothetical at present, it is still possible to consider what this intervention would involve, step by step.[17] This intervention would not simply be a matter of "correcting" the gene. Knowing what to change within the gene is a dilemma for two interconnected reasons. First, there is huge genetic variation among Neurofibromatosis sufferers (NORD 2018). When someone has Neurofibromatosis, there is a non-functional mutation *somewhere* within the NF1

[16] This disease is more commonly known as NF1. But since the NF1 gene and the disease share the same name, I will refer to the disease as Neurofibromatosis for clarity.

[17] Whether this removal constitutes disease "treatment" or disease "prevention" depends on one's conviction on the personhood of the early embryo. This will be discussed in Section 3. See also Faust and Mentzel (2012) on the treatment-prevention distinction.

gene. This gene, which all humans have, is one of the longest in the human genome.[18] There is no normal NF1 gene—or even section of gene—common to all people with Neurofibromatosis. One Neurofibromatosis sufferer might have a mutation in one section of the NF1 gene, while another Neurofibromatosis sufferer might have a mutation in a completely different part of the gene. Moreover, there are different types of mutations.[19] Accordingly, it would not be a matter of CRISPR identifying the universal code-marker for the disease, slicing it out, and then inserting a corrected section of the code. Presently—and for the foreseeable future—scientists will not always know whether the whole gene needs to be corrected, or even whether altering one section of the code with CRISPR will lead to an unpredictable effect on another section in the same NF1 gene. This relates to my second point, on why 'correcting' Neurofibromatosis in the genome is difficult: there is also variation within the general population (Friedman 1998). One healthy individual might have a completely different NF1 gene to another healthy individual. This variation raises the question of what kind of "healthy"[20] section of code you insert into the gene as a replacement for what you cut out with CRISPR—presuming, of course, you know where and how much to cut out. And, adding to this complexity, recall that everyone has two copies on NF1—and all other genes—to deal with.

Let us now review the ethical questions raised by CRISPR's hypothetical actions in 'correcting' Neurofibromatosis in embryos. The way CRISPR-Cas9 works means parents would not simply decide whether they want their embryo to have Neurofibromatosis or no-

[18] Because of the length of the gene there is more room for error, so to speak. Consequently, Neurofibromatosis is one of the most common genetic diseases around the world, with a prevalence of around one in 3000 births (The US National Library of Medicine 2018).

[19] A frameshift mutation is the most catastrophic type of mutation and may require the entire gene to be spliced out for a functional variation (Biology Online Dictionary 2018).

[20] It is helpful to talk of "functional" and "dysfunctional" (Horizon 2018) variations of the NF1 gene, the latter of which being a gene which presents as Neurofibromatosis. Talking of healthy and unhealthy NF1 genes is misleading since the constitution of a functional NF1 gene is evidently scientifically complex; as well as being socially problematic (Davis 2013).

Neurofibromatosis. The parents would be required to make *further* decisions over their child's DNA. Specifically, the parents would not only have to decide whether to "integrate a piece of DNA" (Broad Institute); but also, what DNA—or perhaps *whose* DNA—and how much, to integrate. Although CRISPR itself would not "write" the new DNA, the fact that selected DNA would be inserted into the young embryo raises questions of how the new DNA is acquired and what it means to have "foreign" DNA—from another human or otherwise—inserted into a human embryo.[21] These are ethical issues which can only be appreciated when considering the technical details of CRISPR.

Placing this case study in context, it is troubling to think that this Neurofibromatosis removal application of CRISPR is—surprisingly—a *less* question-raising intervention compared to some hypothetical alternative disease-correction scenarios. Consider sickle cell disease, where genetic faults can be homozygous or heterozygous (Pasvol 2009). Should parents only intervene in one allele—to prevent disease expression—or should the second allele be subject to CRISPR in order to remove all traces of the trait? Once attention is drawn to the minutiae of the technique itself, the moral dilemmas invoked by the *process* of CRISPR-Cas9 genome interventions become clear and troubling. These dilemmas are overlooked by O'Keefe et al. and completely ignored in bioethical discussions which speak of "gene editing" in the abstract, detached from any technical awareness.

iv) Existing Genetic Trait Selection Methods

Here, at the concluding subsection of this Introduction, some existing genetic trait selection methods—against which CRISPR is being considered—will be introduced. First, there

[21] And the dilemma of an error of insertion [see p20]; given that NF1 is so long, which parts will be selected for excision, and what if those parts are insufficient to prevent Neurofibromatosis?

is Preimplantation Genetic Diagnosis (PGD). According to the National Center for Biotechnology Information, PGD is "generally defined as the testing of pre-implantation stage embryos or oocytes for genetic defects" (Geraedts and De Wert 2009). This testing is most often performed so that a parent may implant only the embryos which test negative for the genetic defect being investigated (American Pregnancy Association 2018). One practitioner of the technique details the process involved in PGD as follows:

> Using PGD, anywhere from one to a few cells (depending on embryo stage) are plucked from early human embryos for genetic analysis. In this way, almost any genetic disease imaginable… can be detected. Right here in Davis and Sacramento, for example, the local fertility clinic called California IVF offers PGD for testing for a huge number of genetic diseases[22]… Embryos lacking genetic disease can then be used for pregnancies (The Niche 2015).

It is important for my investigation to note that this process involves selection between embryos, rather than proactively trying to improve any one embryo. A technique tantamount to post-PGD IVF implantation, in its reliance on the selection of existing genetic material, is shopping for gamete donors. This sensationalized and often ineffective approach relies on acquiring, through donation or consumer purchase, an ovum or sperm from a genetic disease-free donor (ESHRE 2002; Grady 2006). All these selection-based approaches allow limited control to parents. Consider that if both parents were homozygous carriers of a genetic disease, selection-based methods would mean they would have to outsource genetic material, and so could not become biological parents of a disease-free child.

A different approach is therapeutic abortions. A therapeutic abortion, by definition, involves ending a pregnancy where tests indicate the resulting child will be born with "severe abnormalities"; or ending a pregnancy to protect the health of the mother (Winchester Hospital 2018). Consideration on this practice could enrich my investigation. Therapeutic abortions do not

[22] They cite Neurofibromatosis Type 1 on their sample list of diseases they can identify.

necessarily involve choosing between embryos, since the affected-adult could choose to never risk pregnancy again. In other words, selective abortions are different to other genetic trait selection techniques because they rely on choosing *whether* to develop genetic material, rather than choosing *which* genetic material to develop. Be that as it may, this practice does not fall strictly within the parameters of my investigation since the intervention typically occurs between 5 to 12 weeks after fertilization (HCA 2018; C.S. Mott Children's Hospital 2017). As such, when referring to alternative methods to CRISPR, I will not be including therapeutic abortion.

Some ask, "why would anyone even try human gene editing in the germline given the existence of the very powerful, already proven safe technology of preimplantation genetic diagnosis (PGD)" (The Niche 2015), along with the availability of numerous other relatively safe approaches. As has been documented in this Introduction, CRISPR could allow genome changes with a precision impossible in the methods detailed in this subsection. Be that as it may, beyond this improvement in the degree of precision, CRISPR represents the opportunity to work with existing material rather than shopping for; choosing between; or choosing whether to develop embryos. This divergence in methodology raises the question of whether CRISPR represents a genetic trait selection technique which is different in kind to existing methods. The following section will explicitly address this question. While referring to this Introduction's exploration of the unique ethical questions raised by CRISPR's technique, it is now pertinent to evaluate arguments over whether CRISPR's innovative strategy represents a morally relevant distinction.

Section 1: Literature Review – Evaluating Arguments on the Presence of a Morally Relevant Distinction Between Genetic Trait Selection Techniques

This section introduces and begins defending the main argument of this thesis, that there are not only technical but also moral differences between varying methods for selecting genetic traits in children; specifically, that there is a morally relevant distinction between germline genome editing via CRISPR and methods which involve selecting between already existing genetic material. The section opens with a preface that explains what is meant by a morally relevant distinction and highlights that such distinctions are not given but contested, which raises the question of how one argues for the presence of morally relevant distinctions between genetic trait selection methods. To address this question, the remainder of the section will evaluate literature on enhancement—which contains arguments both for and against the presence of a morally relevant distinction between such techniques—by judging each argument's determinacy,[23] external support,[24] and consistency[25] according to Timmons' evaluative standards for moral arguments (2013). In doing so, I will explore reasons to side with the argument that there is a morally relevant distinction between techniques. Since these arguments are situated within the related-but-discrete body of literature on enhancement, before any evaluation of arguments can occur, this enhancement literature will be critiqued as a convoluted debate—which itself demonstrates the importance of moral attention to technical differences.

A) What Are Morally Relevant Distinctions?

[23] Understood as the argument being able to yield a moral verdict about the morality of a practice.
[24] Understood as the argument being supported by nonmoral beliefs.
[25] Understood as the argument yielding consistent results.

Before an investigation into whether there is a morally relevant distinction can occur, it is pertinent to account for this thesis' working definition of "morally relevant distinctions"—which are also known as "relevant differences" for moral reasoning (Richardson 2013, Section 2.3). For the purposes of this investigation, it will be assumed that when one attests there is a morally relevant distinction, one claims there is a morally relevant feature which makes the critical difference to a moral evaluation. To start unpacking this definition piece by piece, it is first important to clarify what we mean here by "moral". Without diverging into a complete evaluation of definitions of morality, it is helpful for this investigation to draw on Beauchamp and Childress' (2009, 2-3) observation that "[morality] refers to norms about right and wrong human conduct that are so widely shared that they form a stable social compact."[26] Their point highlights that there are variations between—and pluralisms within—moralities. This means that claiming the presence of a morally relevant distinction is contentious. Certain features of actions might make a moral difference to some moralities but not to others. To illustrate, Childress et al. (2002, 171) explain that much moral argumentation "will hinge on which similarities and differences between cases are morally relevant, and that argument will often, though not always, appeal to general moral considerations". Examples of this moral work include but are not limited to philosophers claiming certain considerations are more morally relevant than others (Richardson 2013, Section 2.3: Childress et al. 2002, 171), and philosophers arguing over how best to "isolate" morally relevant differences (Richardson 2013, Section 2.3).

Owing to the fact morally relevant distinctions are not self-evident, we must demand a convincing defense to underpin any claim of a morally relevant distinction. Allowing a distinction to function unquestioned as a morally relevant distinction is dangerous. Consider that

[26] Beauchamp and Childress distinguish "morality" from the term "ethics", they claim that the latter term is a way of examining moral life (2009, 1).

Nazis in the Third Reich believed there was a morally relevant distinction between Jews and Aryans regarding who should be allowed to survive in society. Their distinction was of course abhorrent insofar as it is morally irrelevant within the "common morality".[27] A less dramatic example is given by Rollin when he states:

> If two of my students have the same grades on exams and papers, and have identical attendance and class participation, I am morally obliged to give them the same final grade. That one is blue-eyed and the other is brown-eyed may be a difference between them, but it is not morally relevant to grading them differently (2009).

Rollin expands that "a morally relevant difference between two beings is a difference that rationally justifies treating them differently in some way that bears moral weight." (2009) The bulk of the following subsection will hence be spent developing my argument—by means of evaluating a debate—to justify my claim that there is a morally relevant distinction between CRISPR and other genetic trait selection practices.

There are two final points I would like to make on morally relevant distinctions. The first is that within morally relevant distinctions, there are certain "features" (Gert 1999)—of actions or things—which warrant the distinction. According to Gert, a morally relevant feature is "a feature that if changed could change whether some impartial rational person would publicly allow" certain practices (Gert 1999, 16). Morally relevant features point to philosophical questions over why there is a morally relevant distinction. To illustrate this point, look to how there is a morally relevant distinction between someone who is alive and someone who is dead regarding treatment of the human body: the morally relevant feature is life, which arguably necessitates a certain level of respect not present in death. A complete justification of this distinction would require an analysis and evaluation of the philosophical conception of life. As

[27] By which I mean "all persons living a moral life know several rules" which constitute a set of universal norms called the common morality (Beauchamp & Childress 2013, 3). And I contend such rules include the rule not to kill, especially via an ethnic genocide.

such, analyzing morally relevant features is essential to a complete evaluation of new technologies such as CRISPR. While this section will explore the persuasiveness of various arguments on whether a morally relevant distinction is justified, this investigation will merely provide the tools for the all-important task of evaluating the nature and implications of this distinction's morally relevant feature. Part of this all-important task will begin in Section 2.

The final point I would like to make is on how features can lie in facts, but the two are discrete. Gert contrasts morally relevant features to morally relevant facts. He writes that "specific facts count as morally relevant considerations only insofar as they are instances of more general facts that would be understood by all rational persons." (Gert 1999, 16) I contest that Gert is here talking about uncontestable facts which are relevant to certain bioethical cases. Consider that it would be wrong to give a cancer patient a certain chemotherapy drug if, from biomedical knowledge, it is known that this chemotherapy drug is ineffective against the patient's form of cancer. This technical information, on the chemotherapy drug's efficacy rate in treating certain cancers, is relevant to a moral evaluation because it better informs medical decision-makers. However, it is not the source of moral deliberation, in and of itself, because the information is understood and accepted uncontested "by all rational persons" who understand the chemical effect of chemotherapy drugs in the human body (Gert 1999, 16). To give another example, consider that Jehovah's Witnesses do not deny, or contest, the efficacy of a blood transfusions in certain medical situations. Their moral qualm is in the permissibility of using foreign blood products, a moral dilemma stemming from the significance of blood within their theological ontology, which determines their shared morality. We can characterize the fact from the feature as such:

i. *Morally relevant fact*: Blood transfusions are an effective component of the medical treatment of severe infections, liver disease, and leukemia.

ii. *Morally relevant feature* (according to Jehovah's Witnesses): The involvement of blood.

Because Jehovah's Witnesses believe "the life of all flesh is the blood thereof" (Norfolk 2013, Section 12.2), it is morally impermissible to them to accept a blood product from another. The feature that incorporating foreign blood is involved in a medical procedure is the more morally relevant element to consider for this religious group.

The interrelationship between morally relevant *features* and morally relevant *facts* is important to clarify when looking for morally relevant differences in new technologies. While facts on CRISPR may be exciting, mere admiration for innovation cannot distract from or convolute my investigation into whether there are morally relevant features within the process. Put another way, I am not merely asking what is scientifically new, but whether there are features within these new scientific techniques which enable the argument that there is a morally relevant difference—between CRISPR and other genetic trait selection methods—within the editing process itself. The new facts are that precise genome editing is now possible in the germline of human embryos. The task at hand is to look for morally relevant features within those new facts.

B) Enhancement Debates as the Research Problem

According to Sandel (2004), "enhancement employs medical means for nonmedical ends—ends unrelated to curing or preventing disease or repairing injury". In other words, enhancement is not the treatment of pathology, but the act of making someone *better* than well. Bioethicists and other academics writing on enhancement debate the definition of enhancement (Daniels 2000), what practices are included within this catchment, and whether and when enhancement is permissible (Kamm 2005). It is no surprise that genetic trait selection methods

have not gone unnoticed within this debate. The practice of enhancing children is bitterly contested, a discourse which largely focuses on the enhancement of future children's genomes. Some, like Savulescu and Kahane (2009), argue that couples have an obligation to enhance their future children through the selection of favorable genetic traits. They argue for the existence of the "principle of procreative beneficence", and characterize this principle as such:

> If couples (or single reproducers) have decided to have a child, and selection is possible, then they have a significant moral reason to select the child, of the possible children they could have, whose life can be expected, in light of the relevant available information, to go best or at least not worse than any of the others[28] (Savulescu & Kahane 2009, 274).

On the other side of this debate, academics including Sandel (2004, 57) write fervently against the use of genetic trait selection to enhance future children. I will not be taking a stance on the permissibility of enhancement. As prefaced in the Introduction, the purpose of this investigation is to analyze the use of CRISPR for medical—not enhancement—purposes. However, I will utilize this bioethical debate over enhancement as a starting point. Within this debate, arguments are often unwittingly made on whether there is a morally relevant feature present within CRISPR's new technique of genetic trait selection. These arguments will serve as the source material for my evaluation, so that I can investigate the presence and nature of any morally relevant distinctions.

An assumption which will color my evaluation of these arguments is that enhancement debates represent a research problem. I argue that these debates can be improved upon; that they are confused and unfocused because they inevitably touch on, but do not pay sufficient attention

[28] This is according to Savulescu and Kahane's own metric. They set these standards based on their argument, that: if parents cannot have any child whose life is worth living, they shouldn't have any; if parents can select, they have reason to select a child with a good enough life; parents should select the child with least expected suffering, loss of opportunity or happiness; and that parents should select first for most expected autonomy, not wellbeing (2009). Savulescu and Kahane can accordingly be judged as utilitarian thinkers living in a society that values autonomy.

to, the details of technical differences and their potential moral relevance. Admittedly, my intention to argue *for* the relevance of technical distinctions biases my reading of the debate's clarity. As such, I will draw on observations made by Joseph Roberts (2014) to externally underpin my assumption that enhancement debates can here function as a research problem. Roberts evaluates the utility and relevance of the "moral work" performed in enhancement debates and concludes that the approach taken by academics within the debate hinders "clear ethical analysis" (2014, 1). He laments that:

> The enhancement debate would be clearer if [arguments on the definition of enhancement] were abandoned allowing the discussion to centre on the relevant ethical problems which enhancement may or may not raise (Roberts 2014, 10).

Unfortunately for this investigation, Roberts does not explicitly detail what "relevant ethical problems" need addressing. He merely continues that "the use of this distinction depletes precious scarce research resources by sidestepping the relevant distinctions and by generating independent problems such as the problem of excessive medicalization." (2014, 10) But suffice to say, Roberts' cynicism on the productivity of these debates offers independent clout to my assertion that enhancement debates are a research problem insofar as they omit relevant discussions.

I will now follow up on Roberts' evaluation by accounting for why attention to technical detail enables discussion on a relevant distinction. Roberts' approach to evaluating the enhancement discourse involved demonstrating that debating the enhancement-treatment distinction was not only irrelevant to determining the permissibility of enhancement, but also impossible without raising further questions. Rather than joining Roberts in a problematizing quest, I will here expand on his observations by offering a constructive account for *why* these debates have become so unfocused: I argue that the convolution of this unfocused debate stems

from its lack of attention to technical differences in enhancement methods. In other words, *when academics believe they are clashing over enhancement debates, oftentimes they are instead disagreeing over the significance of techniques.* On either side of the enhancement debate, regardless of the definition of enhancement utilized, there are assumptions which pollute the focus of argument. Kass (2003) claims the very reason why enhancement debates are important is because they:

> [Get] us beyond our often singular focus on the "life issues" of abortion or embryo destruction, important though they are, to deal with what is genuinely novel and worrisome in the biotechnical revolution… the new science-based power to remake [humans] after our own fantasies (Kass 2003).

Kass is mistaken here, insofar as he does not appreciate that all literature on enhancement is imbued with "life issue" assumptions. Kass ignores how such assumptions act as confounding variables for transparent and productive debate. It is evident that assumptions—such as whether the embryo is identical to the adult it has the potential to become; how one ascribes personhood to a genome; and the perceived artificiality of technological interventions—all inform perceptions on enhancement's permissibility. Clarifying these assumptions is thus of the utmost importance—not just to enhancement debates, but to any moral evaluation of technologies like CRISPR. To attempt to address this research problem, my next subsection—which involves evaluating arguments from the enhancement debate—will test various arguments to see how far each author acknowledges and understands the intrinsic relevance of these assumptions to any debate on new technology. Accordingly, it will be demonstrated that focus on techniques, and their significance, forces invaluable introspection into our own "life issue" assumptions; including introspection into how these assumptions determine one's position on the permissibility of certain technologies.

C) Evaluating Arguments

In order to begin defending my proposition that there are not only technical but moral differences between varying methods for selecting genetic traits in children, this subsection introduces and defends McKibben's (2003) convincing argument on why there is a morally relevant distinction between CRISPR's method and a selection-based approach.[29] McKibben's argument will be introduced along with his opposition. In fact, I structure this subsection by evaluating two positions, each composed of input from several authors from bioethical debates on enhancement. From the camp that both techniques are impermissible, Sandel (2004) will represent the opinion that there is no morally relevant distinction between the techniques. Kass (2003) will represent a tantamount view: that there is no relevant distinction between the techniques because they are merely different in degree, not different in kind. Both Sandel and Kass agree that there is a lack of morally relevant distinction, but their argumentative justifications differ. By contrast, McKibben acknowledges the nuance between writing an embryonic genome "like a document" (2003) and choosing between embryos; as such, his position will be evaluated and defended as the most convincing.

To clarify, I am not addressing the arguments on the permissibility of enhancement central to each paper. Rather, I address each author's stance on the moral relevance of new genetic selection techniques. Following an exposition on each author's position on the matter, I explore reasons to side with McKibben's stance. As a measuring stick with which to evaluate each position, I adapt Timmons' (2013) standards for evaluating moral theories. Upon evaluation, I conclude that McKibben successfully isolates a morally relevant feature: that there is, in fact, a difference between *improving* one embryo or *choosing* between embryos, and that

[29] Methods including the selective implantation of embryos after preimplantation genetic diagnosis (PGD).

difference is morally significant. I will argue that McKibben was able to successfully defend his position, more so than Kass and Sandel, because he looked to the *method* of enhancement as well as the intentions and consequences. Be that as it may, I will lament that despite the importance of the distinction McKibben brings up, he does not sufficiently develop *why* this distinction is so important. As such, his success will be taken as a starting point to set up Section 2, rather than as an end to this investigation.

i) Introduction of arguments

In his objection to what he perceives to be enhancement, McKibben (2003) writes—with a tone of disgust—on the process of CRISPR genome editing:

> Instead of making babies by making love, we will have to move conception to the laboratory. You need to have the embryo out there where you can work on it — to make the necessary copies, try to add or delete genes, and then implant the one that seems likely to turn out best.

Despite McKibben's hesitancy toward any parental genetic modification of a child, what is relevant to note is how he nevertheless conceptualizes different kinds of modification. McKibben (2003) follows on from the observation quoted above with a citation of Michael West—CEO of the company Advanced Cell Technology—who states that "[ultimately] the dream of biologists is to have the sequence of DNA, the programming code of life, and to be able to edit it the way you can a document on a word processor." (West in McKibben 2003) McKibben disparages such intervention as crossing a line from parenting to "product development" and makes his attack specifically on "germline genetic engineering [which] is something very novel indeed." (2003) McKibben gives reason for why he thinks CRISPR germline genome editing is "novel" and thus apart from other genetic trait selection methods. He laments that scientists "could not only add, delete, or modify some of [the embryo's] genes … they could also insert artificial chromosomes

containing predesigned genes" (2003). He writes about a hypothetical child who would grow from such an intervention:

> His genes would be pushing out proteins to meet the particular choices made by his parents, and by the companies and clinicians they were buying the genes from. Instead of coming solely from the combination of his parents, and thus the combination of their parents, and so on back through time, those genes could come from any other person, or any other plant or animal, or out of the thin blue sky (2003).

McKibben's anxiety over "particular choices" being engineered—as opposed to choosing between supposedly natural, or at least historically traditional, genomes produced from un-interfered-with parental and ancestral meiosis-cum-conception—speaks to his conceptual distinction between editing an embryo's genome and choosing between embryos.

Sandel, in contrast, does not see any relevant moral difference between selective implantation of embryos after preimplantation genetic diagnosis and germline genome editing via CRISPR. To him, lacking "appreciation of the gifted character of human powers and achievements" represents a part of the impermissibility of enhancement (Sandel 2004); and insofar as both these methods represent that Promethean arrogance,[30] one can infer from Sandel's assertations—that "the problem is not the drift to mechanism but the drive to mastery" (2004)—that he believes there is no relevant moral distinction between mechanisms.

Kass takes a comparable stance. Even though he discusses and disagrees with Sandel's reasoning (2003, 18-19), Kass begins with the same premise: that there is no relevant distinction between methods. He believes that powers—"to prevent fertility and to promote it; to initiate life in the laboratory; to screen our genes, both as adults and as embryos, and to select (or reject) nascent life based on genetic criteria; to insert new genes into various parts of the adult body, and

[30] Where Sandel (2004) writes that "to appreciate children as gifts is to accept them as they come, not as objects of our design or products of our will or instruments", one could see the former undesirable situation as relating to CRISPR editing, while the latter addresses post-PGD selection. He thus categorizes both interventions as a inappropriate ways to approach child-rearing.

someday soon also into gametes and embryos" (Kass 2003, 11)—are all merely technological developments of the same pursuit. One can see this conviction when Kass details his anxiety over the use of genetic selection for "ignoble purposes" (2003, 9):

> Once here, techniques and powers can produce desires where none existed before, and things often go where no one ever intended. So how are we to organize our reflections? One should resist the temptation to begin with the new techniques or even with the capacities for intervention that they make possible. To do so runs the risk of losing the human import and significance of the undertakings (Kass 2003, 11).

Kass insists we should instead begin any evaluation "with the likely ends that these powers and techniques are destined to serve" (2003, 11), and hence, he eschews discussion on technical means. In summation, it is not that Sandel and Kass misunderstand the scientific distinctions between techniques, but rather that they do not perceive such distinctions to be morally relevant to the arguments they are making.[31]

ii) Testing arguments according to Timmons' criteria

In order to evaluate the argumentative reasoning in support of the various authors' conclusions on the moral relevance of techniques, I will draw on parts of Timmons' (2013) standards for evaluating moral theories. To justify this approach, I argue that although each author does not develop their own complete moral theory, they *do* aim to evaluate the permissibility of a collection of procedures—genetic trait selection—while providing a moral justification for their stance. In doing so, they must either effectively utilize more established moral theories, or develop sufficient moral reasoning, such that they create an argument tantamount to Timmons' definition of a moral theory.[32] As a result, it is possible to evaluate

[31] Theirs are both consequentialist arguments: the ends do not justify the means

[32] According to Timmons, "a moral theory has the practical aim of providing a decision procedure for making correct moral judgements as well as the theoretical aim of providing moral criteria that explain the underlying nature of morality." (2013, 12)

these arguments using Timmons' evaluative criteria. Consider that Roberts was interested in the productivity of enhancement debates. (Refer back to Part B of this Section 2.) Owing to this interest, it was appropriate for Roberts to use Timmons' criterion[33] of applicability to evaluate the strength of various contributions to the debates. Accordingly, because I am interested in identifying morally relevant features within an act, it will be appropriate to evaluate them according to their determinacy, which Timmons' characterizes as "pinpoint[ing] exactly what it is about such actions that makes them right or wrong" (2013, 13).

Admittedly, there is a limitation to this approach. Sandel, and to a lesser extent Kass, simply eschew the moral relevance of technical means and continue with their enhancement argument. As a result, there is very little to evaluate in terms of an argument on the presence of a morally relevant distinction. Therefore, in addition to the criterion of determinacy, I will utilize the criteria of consistency and external support, by which I mean: if authors deny the presence of a morally relevant distinction in the means of the act, these authors bear the burden of proof vis-à-vis demonstrating an alternative site of a morally relevant feature. And this alternative *must* be backed with consistent and convincing argumentative reasoning in support of their various conclusions. I feel it is helpful to note that I added the criterion of consistency retrospectively. After seeing that Kass ultimately but unwittingly *does* acknowledge the moral relevance of means, I realized each argument might be idiosyncratically fallible. So, while the criterion of determinacy will be used as the primary measuring stick for my evaluation, other flaws in argumentative reasoning will be used to demonstrate the lack of clarity, and misfocus, which occurs when authors overlook the significance of technical means. I must also make a closing

[33] Although Roberts does not explicitly credit Timmons as one of the refiners of this criterion.

reminder: that I am looking to various authors' acknowledgements of the sociocultural assumptions which are essential to informed debate on new technologies.

iii) Evaluating McKibben

Let me begin my evaluation with an observation that McKibben's argument is externally supported by the 2003 President's Council on Bioethics. The Council asserted that there is a distinction between PGD and CRISPR, noting "a range of [methods for] increasing genetic control, from (1) eliminating the bad ('screening out') … to (3) redesigning for the better ('fixing up') [and arguing that] each activity raises its own ethical questions." (President's Council 2003, 33-34) Of course, the Council is by no means an objective or absolute source on locating morally relevant features. Rather than taking this conviction as an easy end with which to bolster McKibben's position, this section will instead tease out some ethical observations that are mentioned, but not fully developed, by the Council to demonstrate how McKibben's position can be defended as an exemplar of Timmons' criterion of determinacy.

The points raised by the Council can broadly be broken down into two categories: practical and ideological. Regarding the former, the Council offers numerous astute reflections on how each technique offers differing levels of efficacy and accessibility. For instance, the Council notes that PGD-based selection cannot optimize "beyond what the parents have contributed to the fetus" in the same way CRISPR can, and hence CRISPR offers more control for parents to engineer their offspring to exact, and often genetically complex, preferences (President's Council 2003, 35). However, insofar as these observations pertain to consequences rather than means, this is less relevant to my focus than the Council's concern with ideology.

The Council's insight—into how ideology informs preferences in genetic trait selection methods—is made within their second ideological category and is central to demonstrating the persuasiveness of McKibben's argument. Look to how the Council's writing alludes to the interrelationship between ideas and practice. The Council states that: "with genetic screening, procreation begins to take on certain aspects of the *idea*—if not the *practice*—of manufacture" (2003, 53 [emphasis my own]). Where the Council writes on how genome editing techniques might "mean" something to future children,[34] I contest that the authors realize, but do not explicitly state, that people can find meaning in different actions. In other words, their ideology is expressed in their practice. This is an important insight vis-à-vis Timmons' notion of determinacy. Because one's choice of technical method can be an expression of ideology, this choice might signify one's value-based concerns over the very action itself, rather than merely a concern over the consequences of each technique.

To illustrate this nuance, look at an objection given to post-PGD selective implantation. Mitalipov, a scientist working on CRISPR technologies, stated that IVF's inefficiency is a moral issue:

> You have no right to throw away 50 percent of these embryos when you can correct them. It's very 19th-century. Some people say that our work [into CRISPR] is ethically wrong but I think it is ethically right (Mitalipov in Yong 2017).

[34] The Council requests that we look "to the question of what it might mean for a child to live with a chosen genotype: he may feel grateful to his parents for having gone to such trouble to spare him the burden of various genetic defects; but he might also have to deal with the sense that he is not just a gift born of his parents' love but also, in some degree, a product" (President's Council 2003, 53). See also where the Council muses that: "Before one can decide whether these [genome] changes should be welcomed enthusiastically, tolerated within limits, or met with disquiet, one must try to think through what they mean—for individuals, for families, and for the larger society" (President's Council 2003, 45). Admittedly, the Council's wording could be clearer. When they say "mean", I contest that the council is not referring to consequences, but rather the meaning the act imbues, its significance. If they are using this word in the latter sense, it demonstrates that they recognize the relationship between idea and practice.

Mitalipov is not objecting to a notion of enhancement in the abstract, but to this specific technicality of IVF selective implantation. He has a practical preference for CRISPR over selection implantation, which points to his ideology.[35] From this preference in technical difference, Mitalipov is expressing his belief that embryos have moral significance to the extent that they deserve ethical consideration. This is just one example of manifold instances where cultural "life issue" (Kass 2003) convictions inform a preference for—or objection to—either post-PGD selective implantation or CRISPR.

Notably, McKibben appreciates this fact, that broader ideologies can be the morally determining factor in one's conviction on the permissibility of certain technical practices. One can see McKibben's awareness of this determinacy where he acknowledges how his own sociocultural conviction informs his conviction on genetic engineering via CRISPR. McKibben, who is fervently against CRISPR usage, laments that:

> You cannot rebel against the production of [an engineered] protein. Perhaps you can still do everything in your power to defeat the wishes of your parents, but that protein will nonetheless be pumped out relentlessly into your system, *defining who you are* (2003, emphasis my own).

By placing this quote in context within McKibben's 2003 paper, we can see that he does not believe in pure genetic essentialism as implied at the end of the quote. McKibben goes on to argue that CRISPR engineering can take away possibilities of personhood—rather than actively writing one's entire being—and uses a featherless chicken example to illustrate this point.[36] As

[35] This is the President's Council on Bioethics' term. I suggest "sociocultural conviction" is a more helpful term than "ideology".

[36] McKibben draws a comparison with how genetic engineering via CRISPR currently "works to ensure absolute success" in the design of livestock (2003). He cites an example of an Israeli scientist who engineered a featherless chicken, noting that the "engineer was not trying to influence his chickens to shed their feathers because they'd be happier and the farmer would be happier and everyone would be happier. He was inserting a gene that created a protein that made good and certain they would not be producing feathers." McKibben claims germline engineering cannot entirely prescribe who you are, but it *can* rule out possibilities of who you could be. In his metaphor, "You won't grow feathers, no matter how much you want them. And maybe they can engineer your mood enough that your lack of plumage won't even cross your mind." (McKibben 2003)

such, McKibben still possesses a clear conviction on the relationship between genome and personhood, and this informs his objection to rewriting genomes via CRISPR. What we begin to see is a pattern of value-laden and culturally informed convictions acting as conflating variables in discussions on enhancement. McKibben inadvertently acknowledges this phenomenon by recognizing what exactly it is about genetic enhancement that upsets him so. Because of his attention to the distinctions between germline CRISPR editing and post-PGD implantation, McKibben elaborates on, and gives sufficient wordcount to justify, his own presuppositions on the moral significance of genomes. But others, like Sandel, often do not stop to consider these nuances, to detrimental effect on the determinacy and overall foundations of their arguments.

iv) Evaluating Sandel

Sandel's argumentative reasoning is flawed in three ways. First, his appeal to appreciating the giftedness of the natural has no determinacy. Sandel is an advocate of Natural Law Theory,[37] and appealing to the determinacy of "the natural" is arguably a pillar of this moral theory: "the idea that there is an objective set of moral principles based in human nature is central to natural law theory." (Timmons 2013, 72) However, Sandel's argument pertains to a heavily critiqued branch of natural law theory known as the "physical interpretations of natural law" (Wijngaards Institute for Catholic Research). Various authors claim this approach misinterprets the determination of what is "naturally good." (Wijngaards Institute for Catholic Research) Look to Kelly's remarks as an exemplar of this theory's arbitrary chain of reasoning,[38]

[37] As evidenced in his publication within Robert George's 2001 edited volume on Natural Law, Liberalism, and Morality (Sandel 2001).

[38] "A couple using artificial contraceptive devices at any time are guilty of serious sin because it interferes with nature . . . The reason why the artificial prevention of births is immoral is written into the very nature of the sexual organs and the marital act itself. The sex organs were made by God to reproduce the human race. Only when

and then consider that just because a phenomenon occurs naturally in nature, its existence is not normative. Death and disease occur just as naturally as birth and communality. One of the most fundamental critiques of this approach is accordingly that factual observances on human physiology do not automatically translate into moral determinacy:

> The subject matter we look to—"human actions, practices, habits, dispositions"—are certainly influenced by the 'natural' causes properly investigated by the methods of the natural sciences, including a part of the science of psychology. But the actions, practices, etc., can be fully understood only by understanding their point, that is to say their objective, their value, their significance or importance, as conceived by the people who performed them (Finnis 2011, 3-4).

Along with Finnis and the Wijngaards Institute for Catholic Research, Timmons argues that an "account of the human good is hardly illuminating until we specify something about the essential nature of human beings" (Timmons 2013, 75), and as such, dismisses physical interpretations of natural law theory.

Kass, surprisingly, underpins my claim that Sandel represents this outdated and insufficiently determining branch of natural law theory. Speaking directly to Sandel's 2003 paper, Kass writes:

> The giftedness of nature also includes smallpox and malaria, cancer and Alzheimer's disease, decline and decay… Modesty born of gratitude for the world's "givenness" may enable us to recognize that not everything in the world is open to any use we may desire or devise, but it will not by itself teach us which things can be fiddled with and which should be left inviolate. The mere "giftedness" of things cannot tell us which gifts are to be accepted as is, which are to be improved through use or training, which are to be housebroken through self-command or medication, and which opposed like the plague (Kass 2003, 19).

As such, my evaluation of Sandel's argument is that it lacks determinacy. I contend that Sandel exemplifies Roberts' critique of enhancement debates. Sandel does not "do any moral work" on

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husband and wife unite naturally is the union of sperm possible. Therefore the primary purpose of the marital act is the conception of human life." (Kelly 1958: 47-48)

a morally relevant feature he proposes—appreciating the giftedness of nature—and instead offers "a pseudo-argument … to mask fallacious reasoning and to arbitrarily interrupt the chain of reasons" (Roberts 2014, 10).

Along with this lack of determinacy, Sandel's argument also suffers from insufficient external support. This is particularly evident where he claims that a drive to mastery is a basic wrong. Sandel relies on, but does not give a sufficient account for, his belief that life should be revered not mastered. One could delve into a critique of how Sandel's argumentative reasoning is premised on the existence of a higher power, if not higher goods. Kass saves us the time by disqualifying even the more secular appeal of Sandel's argument. Kass states, "Mastery of the means of intervention without knowing the goodness of the goals of intervening is not, in fact, mastery at all." (2003, 18) Here, Kass contends that Sandel's use of the language of mastery is inappropriate. Insofar as Sandel believes the aim of mastery is the *most* morally relevant distinction,[39] his argument's cornerstone is undermined by Kass' comments.

To avoiding being too dismissive of Sandel's argument, I concede that his 2004 paper does have some worthwhile elements. Sandel offers a compelling cultural critique on the emerging parent-child relationship within a consumer driven context. However, this commentary is ultimately irrelevant to any discussion on genetic trait selection methods since Sandel fails to target his critique to specific procedures. Sandel (2004) states that "the problem with eugenics and genetic engineering is that they represent the one-sided triumph of willfulness over giftedness, of dominion over reverence, of molding over beholding." Without convincingly

[39] I contest that Sandel sees a drive-to-mastery as the morally relevant feature because this drive marks a distinction between enhancement-driven and medically-driven genetic engineering; and Sandel argues against enhancement via genetic selection *whilst* distancing such practices from the treatment of genetic disease—the latter of which he regards as an appropriate medical intervention (2004, 57).

detailing how he believes dominion is *expressed* in any specific genetic trait selection method, he hides in the murkiness of cultural contempt rather than engaging enhancement literature.

This brings me to my third and final critique of Sandel's argument—that he possesses a willful ignorance of technique, which hinders his argument's applicability. Note how Sandel operates with an undeveloped assumption of what mastery looks like. He is dismissive of numerous techniques and ignorant to how, in some ontologies, these techniques *might not* express an impermissible level of control.[40] Moreover, even within his own unacknowledged socio-cultural assumptions, Sandel fails to account for his claim that some methods of parental control are acceptable, while others are impermissible. Much like how there was an ontological distinction drawn by traditional natural law theorists between artificial and natural forms of birth control,[41] Sandel operates under the assumption that new genetic engineering technologies are artificial and thus unacceptable, while post-birth interventions are natural and thus permissible. This claim to a morally relevant distinction is critically and chronically unaccounted for within physical interpretations of natural law.[42] Sandel says he takes issue with drive but not mechanism. This evaluation has aimed to demonstrate that mechanisms are indicative of drives, and thus concludes by asserting that Sandel's argument is incomplete at best. This shortcoming,

[40] For instance, if one believed genes played no significance in determining a child, as will be accounted for in Section 2, then genetic trait selection would not fundamentally affect your beholding of the child

[41] With the advent of new contraceptive techniques, an ontological distinction was forged by Natural Law Theorists between "artificial" and "natural" forms of birth control (Kelly 1958: 47-48).

[42] We must look closer at the "conceptual distinctions" (Finnis 2011, 3-4) drawn between natural and artificial contraceptives. Any appeal to artificiality as a classifier of the unnatural can be undermined. The use of technology, or of manufactured materials altogether, is not unnatural. The human use of tools is ancient. Accordingly, technical medical interventions "cannot be conceived independently of the material body" and its natural modification throughout human history (Cambrosio et al. 2000, 12). In addition, naturally occurring herbs can be used to induce abortion – which is considered unnatural. The kind of material used is evidently a useless way to distinguish between what is natural and what is artificial.

combined with an evident lack of determinacy and a need for further external support, leads me to conclude that his argument is an insufficient alternative to McKibben's.

v) Evaluating Kass

Kass' argument is inconsistent. After opening with the preface that one should resist the temptation to approach an evaluation of genetic engineering with the new techniques (2003, 11), Kass goes on to argue for the importance of attention to means. One can see this transition where he ponders a hypothetical case in which the use of enhancement technology is "safe, equally available, noncoerced and non-faddish" (2003, 16): he argues that even if the consequences were controlled, the technology would still "raise ethical questions, questions that are at the heart of the matter: the disquiet must have something to do with the essence of the activity itself" (Kass 2003, 16). Kass here develops Sandel's concern with what is natural into a more productive discussion over dignity:

> If there is a case to be made against these activities—for individuals—we sense that it may have something to do with what is natural, or what is humanly dignified, or with the attitude that is properly respectful of what is naturally and dignifiedly human. I will come at this question from three directions: the goodness of the ends, the fitness of the means, and the meaning of the overarching attitude of seeking to master, control, and even transform one's own given nature (Kass 2003, 17).

Where Kass acknowledges the significance of "the fitness of the means", one would be forgiven for reading this passage as agreement with McKibben's premise. I admit that Kass' inconsistency lies where he opens by eschewing technicalities before going on to unwittingly acknowledge technique significance via his attention to the ethics of means. However, he does *not* change his argument to truly match McKibben's. Kass pursues the ethics of the acts in order to consider the philosophical distinction between enhancement and medical practices,[43] rather

[43] Kass states he is addressing the ethical questions which arise from "the use of technological means to intervene in the human body and mind not to ameliorate disease but to change and (arguably) improve their normal

than looking to distinctions between genetic trait selection methods. Kass still perceives CRISPR to be different in degree to other genetic trait selection methods, rather than different in kind. By this I mean, Kass addresses CRISPR as a more-effective version of selective implantation and abortion, and as such, does not see CRISPR to be a fundamentally different sort of practice. The President's Council and McKibben perceive CRISPR to be different in kind, and account for the morally relevant feature of this difference.

This ultimate incongruence with McKibben is unfortunate for two related reasons: Kass was close to addressing the relevance of differing trait selection methods, and he is evidently thoughtful in his approach to genetic trait selection methods. Had he focused on establishing the morally relevant feature between genetic trait selection methods, I hypothesize his work would have been more insightful. To demonstrate how close Kass came to McKibben's revelations, look to his writings on enhancement, that "the differing technologically based powers raise different ethical and social questions." (Kass 2003, 10) But here he refers to the various ways one can perform enhancement: through performance enhancing drugs, psychiatric conditioning to enhance morality, hormone therapies, and so forth. Had he applied this framework of analysis to genetic trait selection techniques instead of enhancement, Kass might have been productive in determining a morally relevant feature of CRISPR. In this sense, Kass is another exemplar of Roberts' critique, in that he lets the enhancement-treatment line debate distract his focus from more pertinent discussion. In summation, Kass raises some insightful comments which help inform how one might reach determinacy—specifically, on Sandel's limited determinacy in his use of natural law theory, and the impetus to consider intentions, means, and outcomes as three

workings… What is disquieting about our attempts to improve upon human nature, or even our own particular instance of it?" (Kass 2003, 16)

discrete and relevant moral considerations. Regrettably, he does not himself put forward an argument on the morally relevant facet in genetic trait selection methods and instead diverges into a mere analysis of debates on enhancement. As such, Kass should be taken as an enabler of analysis into CRISPR's novelty, but not as a standalone argument.

D) Section Review

There are some who hold that CRISPR is merely different in *degree*, not different in *kind*, to other interventions. In this section, we have reviewed this stance through arguments put forward by Sandel and Kass. Sandel contested that CRISPR represented an unethical drive to mastery and a disrespect of the "giftedness" of nature. His critique of parental drive was compelling and can be found in other literature (Klipstein 2017; Cavaliere 2018). However, his reliance on an outdated interpretation of natural law theory resulted in his moral argument lacking determinacy. He articulates why he is troubled by parental drives without attaching this concern to any particular technology. Kass' argument, on the other hand, relies on evaluating enhancement technologies via their intents, means, and outputs. While he claims to appreciate the moral significance of means, he addresses CRISPR together with existing technologies *without* giving reason for this group catchment. In both Sandel and Kass' arguments, CRISPR is perceived as merely another development in the drive to control and improve humanity. From selecting a mating partner based on favorable traits to actively changing the genome, these authors read all such actions as comparable in intent and output and thus assume that the means are comparable. A common thread in all such arguments is inattention, or simple ignorance to, the differing ways in which each technology causes these outputs.

The contrasting argument, that CRISPR is different in kind to previous techniques, was represented by McKibben. In his paper, McKibben explored the discomfort he felt toward the new possibility of changing the human genome directly. The argument he puts forward against direct interference in human genomes was underpinned with an account of his understanding of genomes. McKibben specified that the reason *why* he found CRISPR to be uniquely impermissible was that it changed what he saw as an essential part of human nature, the un-interfered-with genome. For as much as it is possible to counter McKibben's reading of the significance of the human genome—which will be explored in the next Section—his argument offers determinacy and transparency because of this attention to interpreting the significance of technical detail.

In review, McKibben's argument that there is a morally relevant distinction between techniques emerges as more cogent than arguments which treat CRISPR as a mere extension of existing techniques. From this literature review, I hypothesize that only in ignorance to CRISPR's technological details can one perceive a difference in degree while denying a difference in kind. Within the scope of this investigation, I cannot prove this hypothesis by conducting an extensive review of all such arguments. But suffice to say, McKibben's technique-focused approach has the determinacy to account for why some find CRISPR more acceptable than existing methods while others find it less acceptable. Meanwhile, Kass and Sandel's argument, which paid little attention to methodological detail, became unfocused and undeveloped in their analyses of CRISPR's technique. As such, I conclude that attention to detail—which correlates with the perception of difference in kind—offers explanatory power over why there is disagreement over the moral permissibility of CRISPR.

In conclusion, although techniques may one day have comparable outcomes in terms of safety and societal consequence, the means to arrive at these goals will remain distinct and thus ethically relevant. There is evidently a technical distinction between post-PGD selective implantation—which involves discarded embryos—and germline CRISPR editing—which involves direct interference in the human genome. McKibben finds this distinction to be morally relevant; and Section 2 will now detail why many others find this distinction to be morally relevant. From this section, I contest that this distinction—regardless of moral conviction—*must* be addressed for any analysis or evaluation of CRISPR to be complete.

Section 2: Identifying the Morally Relevant Feature of CRISPR

Among the papers considered in Section 1, McKibben's stance—that CRISPR's technique warrants a morally relevant distinction—was evaluated as more convincing than Sandel and Kass' arguments. However, this does not mean McKibben's argument is complete or without fault. McKibben's paper helped this investigation demonstrate how attention to technical details correlates with necessary introspection into the assumptions which complicate bioethical discourse. Yet while McKibben should be commended for offering an account of his own assumptions, this account was inadequate in its brevity. McKibben's assumptions on personhood, moral status, and heritability stem from one of many sociocultural understandings of the human embryonic genome. As such, his convictions should be treated as an example of how assumptions inform bioethical reasoning, not as a definitive account of CRISPR's technique, nor even as an argument for why his assumptions should be taken seriously.

This section develops McKibben's argument in two ways. First, I expand on three areas of bioethical literature that were alluded to within his paper: the ethics of making heritable changes; identifying the moral status of embryos and genomes; and questions of continuing personal identity. This literature will help further refine and underpin my premise: that CRISPR represents a morally relevant distinction since its technique involves changing a genome rather than choosing between multiple embryos. Second, I follow up on McKibben's contestable assumptions. As I introduce each of the three areas of bioethical literature—on heritable changes, moral status, and personhood—I will tie in anthropological examples to illustrate various convictions within these discourses.

Incorporating anthropology into this analysis is important. It will allow me to trace exactly how sociocultural assumptions inform philosophical arguments. I contest that

recognizing this relationship between cultural assumptions and ethical convictions is critical to answering my second research imperative of accounting for the morally relevant feature of CRISPR's method. I hold that the morally relevant feature of CRISPR's technology will differ depending on the culture of the philosopher. In other words, the identification of morally relevant distinctions can be culturally mediated. In doing so, my aim is not to make a case for moral relativism.[44] I will not be evaluating moralities and their assumptions but rather noting their variance: rather than identify a single, universal, one-size-fits-all feature, I demonstrate that there is potentially a multiplicity of features relevant for different moralities. To clarify the work I am doing, let me return to the case study of Jehovah's Witnesses I cited in the Introduction. I noted that, to this religious-cum-cultural group, the morally relevant feature of a blood transfusion was the use of blood product, owing to their understanding of the nature and significance of blood vis-à-vis personhood. I did not offer an ethical evaluation of a medical case involving Jehovah's Witnesses. Instead, it was pertinent for my analysis to appreciate that their ontology led to their conviction on the presence of a morally relevant distinction.[45] Likewise, in my analysis of the morally relevant feature of CRISPR's technique, I hold that it is important to recognize that there will be clashing perceptions on the significance of genomes and embryos.

A) Heritability

A facet of CRISPR brought up in McKibben's paper is that changes in DNA will guide "the characteristics of [the resulting child's] children, and their children's children as well … and on into time" (McKibben 2003). This subsection will further explore McKibben's concern to

[44] According to the anthropologist Solomon Asch, "Anthropological evidence does not furnish proof of relativism" (Asch in Vaughn 2017, 14).

[45] According to Vivieros de Castro, sociocultural assumptions are not mere customs, but pertain to extensive and coherent ontologies (Carrithers et al. 2010, 53).

demonstrate that heritability *cannot* be the morally relevant feature which warrants treating CRISPR differently to existing methods. There is evidently much concern over the fact genetic trait selection techniques make heritable changes. Some, like Kass, contend that heritable interventions in genomes allow a disconcerting level of control to parents over their grandchildren and beyond. He writes:

> There are always dangers of despotism within families, as parents already work their wills on their children… Even partial control over genotype—say, to take a relatively innocent example, musician parents selecting a child with genes for perfect pitch—would add to existing social instruments of parental control and its risks of despotic rule (Kass 2003, 16).

Others take Kass' fear of "genetic despotism of one generation over the next" (Kass 2003, 16) and consider this despotism on a societal level. Allowing preferences to be solidified in genomes is troubling due to the continual changing of preferences from one generation to the next.[46] Moreover, Pollack posits that "opening [legislation] to germline modification is, simply put, the opening of a return to the agenda of eugenics: the positive selection of "good" versions of the human genome" (2015, 871).

As troubling as these concerns are, my investigation must ask whether CRISPR would allow such despotism more so than any other existing technology. In response to Pollack's 2015 article on the near possibility of liberal eugenics, Gyngell writes that Pollack's "commentary fails to justify why germline editing deserves to be treated specially." (Gyngell et al. 2015) Gyngell points out that "environmental interventions, such as modified social interaction, have

[46] Medicalization literature has increasingly troubled the catchment of what is considered a genetic disease. Kolb notes that "our discussions about which traits should be preserved or eliminated boil down to our cultural ideas about normalcy" (Kolb & McCoy 2017), an observation drawn from Lennard's (2013) account of how 18th century eugenicists' obsession with population statistics produced the concept of "normalcy". Kolb's argument on the value of genetic difference calls into question the ever shifting distinction between genetic disease and genetic enhancement: "when we understand [genetic disease] from a cultural, social and linguistic perspective rather than solely a medical one, we run into larger questions about what exactly we seek to cure or eliminate." (Kolb & McCoy 2017)

epigenetic effects, modify brain development and can be passed on to the next generation". Moreover, Gyngell specifically addresses my research question by pointing out that the use of CRISPR is in no way different in kind to PGD in terms of the risk of heritable changes:

> Another example [of why CRISPR should not be considered special] is IVF and pre-implantation genetic diagnosis (PGD). PGD requires removing two cells from the 8 cell embryo. It excises 1/4 of the embryo. This could have been much more devastating than gene editing yet it has been proven to be safe. Nevertheless, when introduced it was certainly unpredictable what the effects would be for future generations (Gyngell et al. 2015).

What is more, the concerns raised by Pollack and Kass are arguably concerns over *potential* consequences rather than qualms with the intervention itself.[47] Upon review, while concerns over heritability despotism are serious and should be addressed in greater detail, this matter is not specific or limited to CRISPR. Admittedly, CRISPR changes might be drastically different in degree to PGD-mediated selection – as the latter is limited by what is already there. But a difference in degree is not a difference in kind. Accordingly, the heritable potential of CRISPR interventions cannot be used—as McKibben did—to justify treating CRISPR as different in kind to existing genetic trait selection methods.

B) Moral Status

The presence and degree of moral status in embryos is a question which complicates discussions of CRISPR. I contest that just as "debates about disability rights and the permissibility of eugenics rest in part on theoretical disagreements about the moral status of

[47] A frequently noted concern is that the heritable capacity of this activity raises the stakes for unforeseen consequences. Lanphier notes that "the precise effects of genetic modification to an embryo may be impossible to know until after birth", and as such, "genome editing in human embryos using current technologies could have unpredictable effects on future generations." (2015, 410-411) This point was also noted by the Nuffield Council on Bioethics where the committee wrote that, "intervening in the genome is different [to presently legalized trait selection techniques] in virtue of its role in inheritance and the potential scale, seriousness and unpredictability of effects." (Greenfield 2016, 25-26)

cognitively impaired humans" (Jaworska & Tannenbaum 2018), so too do debates over the permissibility of CRISPR rest in part on theoretical disagreement about the moral status of embryos. In this subsection, I will look at competing accounts over whether embryos and genomes have moral status. If either has any degree of moral status, and has their life ended by the editing or non-implantation, that is some moral reason to not engage in the editing or non-implantation.[48] An accepted definition of moral status is offered by Jaworska and Tannenbaum (2018): "an entity has moral status if and only if it or its interests [matter] to some degree for the entity's own sake".[49] And according to Beauchamp and Childress (2013, 64), "to have moral status is to deserve[50] at least some of the protections afforded by moral norms, including the principles, rules, obligations, and rights" of biomedical ethics. Some argue that only human adults have full moral status, while others claim numerous non-person entities—like the environment—have some degree of moral status.[51]

Where you identify moral status depends in part on which theory of moral status you abide by. Beauchamp and Childress (2013, 65) claim that there are five prominent theories of moral status, and that each "will not, by *themselves*, resolve the main issues about moral status, but that collectively these theories provide us with a general, although untidy, framework". This five-pronged framework includes: theory based on human properties (65); theory based on

[48] This argument emerged from discussions with Dr. Gerard Vong.

[49] Jonathan Crane here noted that "most organisms thus have moral status, as they're interested in their existence for their own sake. If this is so, and if moral status matters morally, it makes it difficult to defend, morally, imposing upon other organisms against their moral interests/status."

[50] "Deserve" is here understood to mean "warrant due considerations" from an examining authority - such as an ethics review board.

[51] On that matter of prioritizing moral statuses in conflict, Jaworska and Tannenbaum introduce two ways to approaching this dilemma. According to their exposé, various utilitarian philosophers claim having moral status means "having one's interests (e.g., the intensity, duration, etc. of one's pleasure or pain) factored into the calculus that determines which action brings about the greatest utility"; while non-utilitarian philosophers argue that moral status lies in the act of considering an entity's interest *even when* it clashes with the overall calculus of net benefit (Jaworska & Tannenbaum 2018).

cognitive properties (69); theory based on moral agency (72); theory based on sentience (73); and theory based on relationships (76). Each of these approaches argue what properties or entities warrant moral status. Respectively for each theory, posited features include: "to be a living member of the species Homo sapiens" (65); capacity to act and give rational reason for your action (69); possessing motives that can be judged morally (72); consciousness in the form of feeling (73); and to be an entity with roles and obligations (77). Beauchamp and Childress "doubt it is possible to resolve definitely all controversies about moral status" (65). However, they do contest that specifying moral status is essential to ensuring "moral coherence", specifically noting the importance of considering the moral status of fetuses (92).

There are arguments that are specific to certain theories of moral status. This is the case in Freeman's argument for children having moral status. He notes that even though children have no "genuine participatory rights"—meaning they cannot act as moral agents—they do have "capacity" in that they have sufficient cognitive properties to express reasons for their actions and desires (Freeman 1997, 4-10). As a result, he concludes by detailing the numerous rights that are given to children according to their moral status. By contrast, an example of an argumentative structure which does *not* rely on any particular theory of moral status can be found in Warren's (2008) investigation into the moral status of the gene. In her work, she contests that genomes do not have moral status. She clarifies that her question:

> … is not whether we can have obligations regarding genes. We obviously have moral obligations towards other human beings regarding what may and may not be done to (parts of) their bodies, including their DNA. The question is, rather, whether we can have moral obligations towards genes, independent of any obligations we may have towards the organisms of which they are, were, or will be part (Warren 2008, 147).

Warren argues that none of the theories of moral status, hitherto introduced, "provides a basis for the recognition of obligations towards *parts* of organisms" (2008, 147 [emphasis my own]). She

expands, “on none of these theories is there a plausible basis for asserting that we can have moral obligations towards part of a human being that are not entirely derivative from our obligations towards the human being.” (2008, 149) Her premise is that DNA, like “tissues and organs”, takes on the specific function of perpetuating the organism it serves, such that DNA—like all other parts of organisms—has “other-directed”, not intrinsic, moral interests (2008, 149). Warren thus concludes that “genes do not have independent moral status” (2008, 147).

A frequent conviction within bioethical literature is that embryos—of the age being considered in my investigation—do not have full moral status, but instead, represent an entity that is owed moral consideration,[52] as Green (2001) and Steinbock (2007) argue:

> This compromise position, between those who think that human embryos are human subjects with all the rights of any other human subjects,[53] and those who think that human embryos are disposable tissue, has been taken by several important official bodies, including the Warnock Committee in Great Britain and HERP in the United States. The HERP report concluded that, while the pre-implantation human embryo ‘does not have the same moral status as infants and children’, it ‘deserves special respect’ and ‘serious moral consideration as a developing form of human life’ (Green 2001: 92).
>
> The challenge, then, is to give content to the notion of respect for embryos: the basis of such respect and what restrictions it imposes on us (Steinbock 2007, 433).

This notion of respect pertains to this investigation’s second research question on how to unpack the morally relevant feature of CRISPR’s method. Does CRISPR’s intervention disrespect the moral status of the young embryo any more so than what is already done through alternative methods of genetic trait selection? Consider the first theory introduced in my account, which holds that “distinctly human properties, those of Homo sapiens, confer moral status” (Beauchamp & Childress 2013, 65). Some proponents of this approach believe “an individual

[52] An entity with partial but not full moral status is owed “moral consideration”, meaning its interests must be carefully considered by an ethical decision-maker.

[53] See Robert P. George and Christopher F. Tollefsen who contest embryos do have moral status in that they have an “active disposition” to become a human being (Symons 2016).

has moral status if and only if that individual is conceived by human parents—or, alternatively, if and only if it is an organism with human genetic code." (Beauchamp & Childress 2013, 65) Since CRISPR can introduce non-human genetic code[54]—most likely artificially produced DNA[55]—into the embryonic genome, some proponents of this theory might contest the resulting adult is in some way less human, and hence disrespects the moral status of the embryo via the diminishment of moral status.

However, as intriguing as this animal-hybrid engineering concern is, defining the disrespect of embryos as creating chimeras is limiting. This definition is idiosyncratic to a specific reading of a specific moral status theory. There remains a need to specify—in more boilerplate terms—what respecting human embryos involves. Many bioethicists draw not on "the strong claim that a human embryo is sacred or inviolable … but the weaker claim that human life in all its stages is worthy of respect" (Steinbock 2007, 436), whereas Macklin (2003) laments how these academics continually fail to specify what a respect for embryos entails. Macklin critiques the frequent reliance on the notion that respect for embryos involves respecting their human dignity. She contests there is hardly any difference between dignity and respect, making such notions redundant. Macklin asks why it is that:

> …so many articles and reports appeal to human dignity, as if it means something over and above respect for persons or for their autonomy? A possible explanation is the many religious sources that refer to human dignity, especially but not exclusively in Roman

[54]Arri Eisen commented here that DNA is DNA; it is not really 'human DNA' or 'rat DNA' or 'bacterial DNA' except in a kind of convenient sense. A particular sequence of ACTGs might be unique to a particular organism, and maybe then we call it 'that organism's DNA', but all living organisms have the same building blocks. It is not as if humans have a unique protein or base pairing which would warrant a distinction between human ACTGs and non-human ACTGs.

[55]Although an unlikely therapeutic use of CRISPR, one should also note the prospect of introducing animal DNA into the human embryonic genome. This has raised some interesting questions on the moral status of chimeras. See that "some philosophers, policy makers, environmentalists and animal rights activists have already expressed deep concern over the widespread use of CRISPR-Cas9… Supporters of animal rights argue that it is morally wrong to create GM pigs to give human beings new kinds of pets or spare human organs. The moral status of chimeras is also unclear." (de Araujo 2017)

> Catholic writings. However, this religious source cannot explain how and why dignity has crept into the secular literature in medical ethics (Macklin 2003).

Rather than seeing dignity as a roadblock to my investigation, a "useless concept" (Macklin 2003), or a distraction from the need to give a secular definition of respect, I wish to pursue *why* this concept proliferates. The prevalence of religious and culturally-specific language is important to note for my analysis: it highlights how there are competing interpretations of the subject matter under consideration. Whether embryos and genomes have moral status—and what it means to treat them with dignity—depends not only on what theory of moral status is being utilized, but also on one's understanding of what embryos and genomes are.

To demonstrate this point, look back to Freeman's (1997) argument that children have moral status because of their capacity. Although Freeman does not consider how to treat embryos or genomes, his argument for how to treat children with dignity depends on his sociocultural understanding of what children are. As such, his helpful analysis illustrates the process of assumptions predicating arguments which I will be unpacking for the remainder of this subsection. Freeman writes about autonomy, which he sees as a privilege of moral status:

> [Autonomy does not] depend on the stage of life that a person has reached. Only human beings are 'persons'. A legal system may attribute 'personhood' to an inanimate entity, a corporation, an idol, a god or even to animals but these do not become 'persons' in the sense used here. What is it, then, about human beings that makes them 'persons'? [It is] a critical competence… a capacity for reasoning (Freeman 1997, 35).

Within his argument, we can see two cultural assumptions which are not universally held: that children are persons, and that only human beings can be persons. Freeman's argument would not work within an ontology that saw non-human entities as persons,[56] nor within an ontology where

[56] According to the anthropologist Willerslev, the Yukaghir people of Siberia understood humans, animals, and spirits to all possess personhood (2007). They did not believe personhood was contained in discrete, autonomous human beings. Instead, souls—which they theorized as the essence of personhood—were understood to be interconnected; expressed in emotions and mirrored in manifest physical bodies.

young children are understood as lacking in personhood.[57] Just as Freeman's argument for the rights of children rests on his perception of children as persons, so accordingly do debates over moral status involve defining entities whose moral status is under consideration. Without getting lost in a definition of respect, it is sufficient to acknowledge that how you should treat the embryo depends on your understanding of what it is.

The remainder of this subsection details a selection of perspectives on what genomes and embryos are—specifically, how they are significant. This detailed account will function as source material for the following subsection, in which I analyze whether CRISPR's intervention constitutes a mistreatment according to various interpretations of *what* you are mistreating. To begin, note Warren's argument on the moral status of the human genome. Warren claims her reasoning does not depend on any one theory of moral status. This claim is justified insofar as she is addressing the defining tenant of moral status—on certain entities not having interests of their own—rather than a feature which warrants moral status. However, her argument *does* rest on a singular and contestable understanding of what genomes are. She herself acknowledges the existence of resistance to her definition of DNA as merely a "part of a person's body" (2008, 148). Be that as it may, Warren dismisses any disagreement, claiming that hers is the "empirical" understanding of genomes (2008, 153). As per Emily Martin's observations (1991)—which were explored in my Introduction—there should be skepticism over any claim that there is an

Furthermore, according to some philosophers, seeing human rights and the autonomy of the individual as the essence of dignity is a "notion that is forced upon more communitarian societies in an act of cultural imperialism" (Weisstub & Thomasma 2001, 317).

[57] The assumption that young children are persons is specific to many Euro-American cultures. To disrupt this assumption, see Scheper Hughes' (1993) work on infant mortality in shanty towns in Brazil. Within her ethnographic fieldwork, Scheper-Hughes noted that mothers would lose their young infants to starvation "without weeping" because the children were not seen as full persons. The health of young sick infants—who did not express a desire to live—did not morally matter as much as the health of older, thriving children. In this context, many infants had no obligation or expectation to live, particularly since they were often perceived to be competing for limited resources with their existing siblings.

objective reading of biology, especially when one is using a biological observation to underpin a moral argument.[58] Unlike Warren, some hold that the genome is sacred, containing the essence of personhood or a soul, and deserves dignity. Others concur with Warren that genomes have no moral status but nevertheless come to this conclusion from religious assumptions of a soul-body duality, while yet others do not see the genome as identical to a particular string of genetic code but do understand the genome as being more than a detachable part of the organism. These three interpretations will now be unpacked.

A radical but prevalent perspective is that the human genome is equivalent to personhood, humanness, even the soul. In an essay entitled, "Is the Genome the Secular Equivalent of the Soul?", Mauron hypothesizes the Human Genome Project is "shaping contemporary ideas about how our genes dictate our humanness." (2001) Mauron traces 20th century ideas of a genetic program[59] to the present day, where:

> The notion that our genome is synonymous with our humanness is gaining strength. This view is a kind of "genomic metaphysics": the genome is viewed as the core of our nature, determining both our individuality and our species identity. According to this view, the genome is seen as the true essence of human nature, with external influences considered as accidental events (Mauron 2001).

On the uptake of people explicitly seeing their genome as their soul, Nelkin (1995) notes that "for some, genes have soul-like, mystical properties", such that DNA is understood to be "immortal", "sacred", "and even at times divine itself." Nelkin, like Mauron, also looked at the cultural influence of the Human Genome Project. Nelkin observed the prevalence of "God talk" surrounding the scientific project. On the successful sequencing of the human genome, Francis

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[58] See also Section 1's criticism of physical interpretations of natural law.

[59] Max Delbrück, a 20th-century pioneer of molecular biology, noted how the notion of a genetic program … had an uncanny kinship with the Aristotelian concept of eidos, the organizing principle inherent in every living thing. Aristotle and medieval philosophers such as Thomas Aquinas regarded the concept of eidos as closely connected with the notion of a forma or "soul," which was believed to shape matter into the recognizable form of a living organism (Mauron 2001).

Collins claimed, "we have caught our first glimpse of our instruction book, previously known only to God"; and Bill Clinton stated that "we are learning the language in which God created life. We are gaining ever more awe for … the wonder of God's most divine and sacred gift." (Nelkin 1995 xix) On such language, Nelkin (1995) commented that "while many biological things are granted emotional and even spiritual importance in popular culture, we know of no other cellular entity that has itself been accorded divinity."

This interpretation of the significance of the genome is resisted by many, and not just by biologists like Warren. There are those who contend that humanness, personhood, and souls—variously defined—are entirely unconnected to the genome. First, there are competing cultural accounts. Malinowski (1927), a seminal anthropologist, claimed that for a community from the Trobriand Islands, fathers played no role in producing a child. Austen (1934), an anthropologist who revisited this culture years later, reiterated Malinowski's observation that many Trobrianders did not acknowledge the fertilizing power of semen, consequently denying a genomic account of the creation of persons.[60] In addition, many biological anthropologists are quick to point out that the vast majority of human DNA is shared with chimpanzee DNA; interpreting that our humanness is at the very least not in *all* of our DNA (Marks 2003). In various religious communities, genomes are also understood as unimportant biological parts. The Creation Moments movement attests that, "All our genetic information added together does not define who we are because we also have a soul that has no genetic code" (Creation Moments 2018). Furthermore, there are in fact biologists who have put forward arguments which disagree with Warren's: in *The Selfish Gene* (1976), evolutionary biologist Richard Dawkins

[60] Where the writing of Austen suggests—problematically—that these people were unintelligent and ignorant to science (1934, 105), note that "diverse practices of coming into being" can understand Western medicine while resisting the medicalization of fertilization, gestation, and kinship (Konrad 2005, 52).

conceptualizes genes as mimetic non-sentient entities looking to propagate themselves. Dawkins accordingly sees embryos as divisible from their human carriers.

Apart from those who believe genes are sacrosanct and those who see genes as non-exceptional biological material, others hold that human genomes represent more than non-coding parts but are less than the essence of persons. Such accounts include Liao's theorizations. He describes genes as a "set of physical codes that generate moral agency" and argues that they should not be treated merely as another body part—like an arm, or a heart (Liao 2010). Gallagher notes that Liao addresses Warren's question of "whether human DNA is valuable in itself, or valuable for what it can produce." (Gallagher 2012, 19) According to Gallagher, where Liao sees the genetic basis for moral agency as a sufficient but not necessary "condition for right holding", he identifies DNA as valuable in and of itself: warranting moral status in a way that other biological parts do not. In a similar interpretation, Nelkin (1995, 6) voices skepticism of people being "readouts" of their genes, noting that there are epigenetic and social confounding variables. However, Nelkin does admit that while personhood is not tied to the exact code present at conception, genes do in part determine personal identity vis-à-vis personality traits. Nelkin draws from The Minnesota Center for Twin and Adoption Research, which "has provided percentage estimates of the extent to which certain traits are determined by hereditary: extroversion, 61 percent; conformity, 60 percent; tendency to worry, 55 percent [etc.]" (Nelkin 1995, 9) Nelkin's invocation of twin research is interesting. It points to Green's question: whether the embryo, which is still capable of becoming two or more people, can be said to be a unique individual, for either biological or moral purposes (Green 2001: 31). Where one genome can develop into two discrete humans, this raises further questions about the diversion and persistence of personal identity. This leads into my final subsection, which will explicitly address

what CRISPR's might mean to these various interpretations of genomes. For now, this subsection concludes by noting that there is a correlation between the viewpoint—that embryos have a high degree of moral status—and the conviction that CRISPR-Cas9's method is intrinsically impermissible.

C) Persisting Personhood

A framework which I will use here for identifying the morally relevant feature of CRISPR is considering whether each genetic trait selection method ends the life of the entity in question. This framework interrogates the necessary and sufficient conditions for a person to persist from one time to another: in other words, how does a person continue existing rather than ceasing to exist through change or death? For example, hypothetically assuming the genome is a person with moral status, does the genome-person cease to exist when they have their genome edited? When embryos are discarded because PGD detects genetic defects, the individuals that those embryos would become are being prevented from existing. Does this matter morally? I will develop the reasoning of the three groups of sociocultural assumptions—which were introduced in the previous subsection—to consider how they each might answer these questions.

First, if personhood—or some other essence of your identity—is understood as identical to a particular string of genetic code, then changing or editing the code debatably leads the person who once existed to change into another. On this matter, Olson (2015) refines "the persistence question" by noting that it is not simply asking about continuing existence, but instead investigates the persistence of a person with the same identity:

> When we speak of remaining the same person or of becoming a different person, we mean remaining or ceasing to be the *sort* of person one is. To say that someone would no longer be the same person is to say that she would still exist, but would have changed in some important way. This has to do with one's individual identity in the sense of the who

> am I? question. It is about what sorts of changes would count as losing the properties that define someone as a person. It has nothing to do with persistence through time (Olson 2015).

Olson continues by noting that to answer the question of persistence, "we may want to know whether each of us was ever an embryo or a foetus" (2015). If who we are as people is understood as identical to our embryonic DNA, then changing the genome of an embryo would be understood as changing one person into another.[61] Whether this is more or less acceptable than simply ending the life of a genome-person—say, through discarding the embryo after an PGD diagnosis—is an ensuing question. Regardless of the answer to this secondary question, suffice to say that the morally relevant feature of CRISPR would be its changing of a person from one into another, which is distinct from the choosing between persons involved in PGD.

If embryonic genomes are understood to be insignificant biological parts, then both interventions—CRISPR or PGD—are interchangeable in their significance. Within a sociocultural interpretation of genomes as non-intrinsic parts, the presence of a unique genome within an embryo might not warrant treating the embryo as a person:

> Being a person is most often defined as having special mental properties. Locke, for instance, said that a person is "a thinking intelligent being, that has reason and reflection, and can consider itself as itself, the same thinking thing, in different times and places" (1975: 335). Presumably this implies that something is a person at a given time only if it has those mental properties then. And neurologists say that early-term foetuses and human beings in a persistent vegetative state have no mental properties at all. If anything like Locke's definition is right, such beings are not people at those times (Olson 2015).

Moreover, more than being "not people" at the time of early embryonic development, these embryos could be understood as pre-persons. Whereas others see genomes as a significant part of

[61] Defining what constitutes a "person change" is difficult, particularly in regard to determining what change of biology can truly change a person. Amputation or disease can change a person in terms of their internal experience of bodily existence, and their outward behavior, capacities and appearance – but does this truly change who they are?

determining personhood, those who see personhood as entirely separate from the genetic code might see embryos as not even warranting moral consideration. Persons not yet existing cannot have an interest in coming into being. As such, both CRISPR and PGD would be understood as a preparatory stage to improve the lot of the future person coming into being, much like taking prenatal vitamins or choosing a suitable sexual partner.

For the third and final school of assumption—that genomes represent an important, determining part of personhood—the important question is how we should treat something that is determining but not essential to personhood. The notion that it is impermissible to try and control this determining biological material cannot be the morally relevant feature of CRISPR since both CRISPR and PGD represent changing the parameters of what a person can become. McKibben (2003) laments the power parents will be given with genome editing, power to reduce the range of personhood-defining characteristics their child can possess. However, PGD can theoretically also reduce these options. McKibben develops his argument by pointing out that CRISPR could write in DNA that wasn't naturally occurring, whereas post-PGD implantation does not (2003). But where non-induced spontaneous mutations can also lead to entirely new genetic code, McKibben is left contesting that treating embryos with respect involves non-human-induced interference in the genome. Arguing that the morally relevant feature of CRISPR lies in its artificiality is hard to contest without relying on physical interpretations of natural law theory.

In conclusion, within the three schools of assumptions here analyzed, the most robust way of identifying a morally relevant distinction relies on adhering to the assumption that personhood already exists within the embryonic DNA. If DNA is non-important, then both PGD and CRISPR are preparatory interventions. If DNA is determinant for personhood, then both PGD and CRISPR involve reducing the scope of options, with CRISPR representing a difference

in degree of control, as well as an artificiality which may be disrespectful to the material. However, if personhood is identical to the embryonic DNA, then CRISPR's changing of the DNA—or, for that matter, any environmental change that would cause a difference in gene expression—means transforming one person into another, whereas existing genetic trait selection methods involve discarding many persons to champion the continued development of one person. Within this final catchment of sociocultural assumptions, the morally relevant feature of CRISPR is its changing of one person into another, such that the former person ceases to exist. In summation, when asking, "What does it take for a person to persist from one time to another—to continue existing rather than cease to exist? ... what sort of event would necessarily bring your existence to an end? ... An answer to it is an account of our persistence conditions" (Olson 2015); and this in turn depends on our understanding of the entity under consideration.

Conclusion: Recommendations

This investigation has found that sociocultural assumptions determine whether one perceives a morally relevant distinction between differing genetic trait selection techniques. As posited in the introduction of this thesis, prior arguments have hinged on "which similarities and differences between cases are morally relevant, and that argument will often, though not always, appeal to general moral considerations" (Childress et al. 2002, 171). I have demonstrated that CRISPR's divergence in methodology, from PGD and other selection-based methods, will represent a morally relevant distinction to moralities that hold embryonic human genomes to be in some way sacrosanct. Owing to differing and developing interpretations of the nature of genes vis-à-vis personhood, it will prove difficult to find resolution on the permissibility of emerging genome editing technologies. After all, according to Nelkin, genes are "open to more than one interpretation", and hence discussion on genes must be culturally contextualized to be understood (Nelkin 1995, 8).

Societies, including those within the United States, are continually developing culturally mediated understandings of how genetics relates to personal identity. In 2001, Mauron wrote that "with the imminent publication of the complete sequence of the human genome, often seen as a decisive Promethean step in self-knowledge, the societal and cultural effects of genomics are at the forefront of public awareness." (Mauron 2001) Anthropologists have traced the development of kinship ideology from blood to genes: "'genetic bonds' today seem to hold a similar symbolic value to that of the 'blood bond.' 'Genes' as such seem to be playing an increasingly important role in conceptualizing who is 'connected to oneself'" (Chateauneuf and Ouellette 2017). Moreover, numerous other "social studies have shed light on the social and cultural dimensions of biogenetics and their influence on our way of understanding society, the individual, and his

environment"[62] (Chateauneuf and Ouellette 2017). To look at just one sample of this extensive literature:

> Anthropologist Paul Brodwin (2002) is categorical in his view on the relationship between the development of genetic technologies, society, and the construction of social identities in the contemporary world. As genetics earns greater prestige, historically recognized standards of identity may gain further legitimacy or be overruled by the results of DNA sequencing (Santos and Maio 2011, 19).

From new ideas of "genetic citizenship" (Gibbon et al. 2011), to a questioning of adoptive kinship (Chateauneuf and Ouellette 2017), to disturbing notions that genetic disease lessens personhood (Landsman 2009): the significance of genetics to identity is becoming increasingly divisive.

This division makes writing policy on CRISPR—which involves evaluating various sociocultural assumptions—all the more difficult. The Nuffield Council on Bioethics observed that:

> The requirement to formulate public policy… enjoins an effort to produce a working correspondence between scientific and normative discourses, so that they do not simply 'talk past' one another… Put together, emerging tensions in the correspondence between scientific understanding and social and moral norms, and the difference in relative pace of development raise the stakes for attempts to find a coherent public response at an appropriate level (Greenfield 2016, 26-27).

Previous legal evaluations have determined that genomes represent sensitive, private information, leading to the Genetic Information Nondiscrimination Act of 2008. Presently, various countries—including the United States—are writing legislation on the use of CRISPR in various contexts (GenomeWeb 2017). In this context, the National Academies of Sciences (et al. 2017, 4) noted in their recommendation that "public input and engagement are important elements of many scientific and medical advances. This is particularly true with respect to

[62] Specifically, Chateauneuf & Ouellette (2017) cite the following: Ettorre 2005, Freese and Shostak 2009, Nelkin and Lindee 2004, Tutton 2009, and Shostak, Freese, Link, and Phelan 2009.

genome editing for potential applications that would be heritable—those involving germline cells". The Academies hold that meaningful engagement with the public and various stakeholders "improves policy making" since CRISPR's innovative approach has caused such parties to voice concerns over "whether appropriate systems are in place to govern the technology and whether societal values will be reflected in how genome editing is eventually applied in practice."[63] (National Academies of Sciences et al. 2017, 4)

On the matter of reflecting societal values, I will close my investigation by commenting on the kind of society that sought to develop these genetic trait selection technologies in the first place. I draw on Landsman's (2009) ethnographic research on the construction of motherhood in the USA. Landsman opens with a distinction made in theoretical population biology "between those species whose reproductive strategies rely on investing tremendous resources in each individual offspring and those whose strategy is to spew as many offspring into the world as possible" (Landsman 2009, 38). She claims this lesson in evolutionary theory is becoming weaponized in contemporary American politics, wherein careful, proper parents are seen to be crafting "intensely cultivated fetuses" in opposition to vermin who create "throwaway fetuses". Landsman's thesis is that the drive to create better technologies, which work to create healthy singular offspring, reflects problematic societal values, including: reproduction as subject to individual control and the responsibility of mothers; contempt for poor mothers who make too many children; and the view that good parents seeking one or two healthy children should not be burdened with a disabled child. I argue that she identifies how the intents *and* methods of emerging genetic trait selection technologies express such cultural preferences.

[63] See also the conclusions of the 1975 Asilomar Conference.

The purpose of my investigation has not been to reach a consensus on the moral significance of embryonic genomes, nor to provide an evaluation of the moral permissibility of CRISPR—which would require analysis of the intents and consequences of the practice. Rather, this thesis has demonstrated that a granular appreciation of the techniques involved in genetic trait selection is a necessary part of a complete evaluation of CRISPR. Aside from realizing the unique ethical challenges present within in each method—such as CRISPR requiring parents to make further decisions on their child's DNA—attention to technique forces invaluable introspection into the sociocultural assumptions which pervade moral analysis. Such assumptions are inseparable from bioethical discussions on genome manipulation: one cannot consider how to respect the moral status of a genome without some conception of what this genome is. Moreover, if the method of CRISPR's intervention is found to be intrinsically impermissible by any government,[64] then that is some reason to avoid permitting the intervention: either an outright reason, in a value-based evaluation, or a reason which would weigh significantly into any consequentialist calculus.

While I hope to have enriched deliberation by providing tools for future evaluation, my thesis has also identified questions which need to be further investigated. First, there remains a need to find a way of resolving conflicting interpretations of the significance of genomes. Differing ontologies affect how CRISPR is interpreted, be it as a disease treatment—via turning one disabled person into a healthy person—or as preventative medicine for a person who has yet to come into existence, or even as a medical technique that prevents a particular person from coming into being. Second, my thesis has demonstrated the need for a conversation about human dignity vis-à-vis the involvement of non-natural interventions. A reservation of artificial

[64] For instance, if the morally relevant fact—that CRISPR introduces artificial DNA into the human genome—is understood to be a morally relevant feature by that society.

interventions is insufficient without a justified account of why only nature should be able to interfere in the human genome. For now, my analysis of CRISPR's novelty concludes in alignment with the Nuffield Council's observation:

> Genome editing is a potentially transformative technology, not merely in an economic sense but also in a moral sense, in that it has the capacity both to produce new differences in the world and to provoke new ways of thinking about differences in the world (Greenfield 2016, 26-27).

Bibliography

American Pregnancy Association. "Preimplantation Genetic Diagnosis: PGD." Retrieved June 7, 2018. http://americanpregnancy.org/infertility/preimplantation-genetic-diagnosis/.

de Araujo, Marcelo. "Editing the Genome of Human Beings: CRISPR-Cas9 and the Ethics of Genetic Enhancement." *Journal of Evolution and Technology* 27, no. 1 (2017): 24-42.

Arias, Jalayne J., Jennifer C. Sarrett, Rosa Gonzalez, and Elaine F. Walker. "The Ethics of Prodromal and Preclinical Disease Stages." In *The Routledge Handbook of Neuroethics*, edited by L. Syd M Johnson and Karen S. Rommelfanger, 66-84. New York: Routledge, 2017.

Austen, Leo. "Procreation among the Trobriand Islanders" *Oceania* 5, no. 1 (1934): 102-113.

Beauchamp, Tom L. and James F. Childress. *Principles of Biomedical Ethics*, 7th edition. New York: Oxford University Press, 2009.

Biology Online Dictionary. "Deoxyribonucleic Acid." Retrieved May 21, 2018. https://www.biology-online.org/dictionary/Deoxyribonucleic_acid

Biology Online Dictionary. "Mutation." Retrieved May 21, 2018. https://www.biology-online.org/dictionary/Mutation

Biology Online Dictionary. "Gene." Retrieved May 21, 2018. https://www.biology-online.org/dictionary/Gene

Broad Institute. "Questions and Answers about CRISPR." Retrieved May 16, 2018. https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/questions-and-answers-about-crispr

Cambrosio, Alberto, Margaret Lock, and Alan Young (eds). *Living and Working with New Medical Technologies: Intersections of Inquiry*. Cambridge: Cambridge University Press, 2000.

Carrieri, Daniele, et al. "Families dealing with the uncertainty of genetic disorders: the case of Neurofibromatosis Type 1." *Sociology of Health and Illness* 38, no. 5 (2016): 753-767.

Carrithers, Michael et al. "Ontology is Just Another Word for Culture." *Critique of Anthropology* 30, no. 2 (2010): 152-200.

Cavaliere, Giulia. "Genome Editing and Assisted Reproduction: Curing Embryos, Society or Prospective Parents?" *Medicine, Health Care and Philosophy* 21, no. 2 (2018): 215-225.

Center for Genetics and Society. "About Human Germline Editing." Retrieved June 6, 2018. https://www.geneticsandsociety.org/internal-content/about-human-germline-gene-editing

Chateauneuf, Doris and Francoise R. Ouellette. "Kinship Within the Context of New Genetics: The Experience of Infertility From Medical Assistance to Adoption." *Journal of Family Issues* 38, no. 2 (2017): 177-203.

Childress, James F., et al. "Public Health Ethics: Mapping the Terrain." *Journal of Law, Medicine & Ethics* 30, no. 2 (2002): 170-178.

Creation Moments. "There Is No Genetic Code for the Human Soul." Accessed June 10, 2018. http://www.creationmoments.com/radio/transcripts/there-no-genetic-code-human-soul

C.S. Mott Children's Hospital: Michigan Medicine. "Vacuum Aspiration for Abortion: Surgery Overview." March 16, 2017. https://www.mottchildren.org/health-library/tw1078

Daniels, Norman. "Normal Functioning and the Treatment Enhancement Distinction." *Cambridge Quarterly of Healthcare Ethics* 9, no. 3 (2000): 309-322.

Davis, Lennard J. "Introduction: Disability, Normality, and Power." In *The Disability Studies Reader*, 4th edition, edited by Lennard Davis, 1-14. New York: Routledge, 2013.

Dawkins, Richard. *The Selfish Gene*. Oxford: Oxford University Press, 1976.

Doudna, Jennifer A. and Emmanuelle Charpentier. "Genome editing: The new frontier of genome engineering with CRISPR-Cas9." *Science* 346, no. 6213 (2014): 1077-1088.

Duncan, David Ewing. "The Next Best Version of Me: How to Live Forever." *Wired*, March 27, 2018. https://www.wired.com/story/live-forever-synthetic-human-genome

ESHRE Task Force on Ethics and Law. "III. Gamete and embryo donation." *Human Reproduction* 17, no. 5 (2002): 1407-1408. https://doi.org/10.1093/humrep/17.5.1407

Faust, Halley S. and Paul T. Menzel. "Introduction." In *Prevention vs Treatment: What's the Right Balance?*, edited by Halley S. Faust and Paul T. Menzel, 1-36. Oxford: Oxford University Press, 2012.

Finnis, John. *Natural Law and Natural Rights*. 2nd edition. Oxford: Oxford University Press, 2011.

Foucault, Michel. "The Politics of Health in the Eighteenth Century." In *The Foucault Reader*, edited by Paul Rabinow, 273-289. New York: Pantheon, 1984.

Freeman, Michael. *The Moral Status of Children: Essays on the Rights of the Child*. Cambridge, MA: Kluwer Law International, 1997.

Friedman, JM. "Neurofibromatosis 1." https://www.ncbi.nlm.nih.gov/books/NBK1109/

Gale, Stephanie. "Prenatal Development." *Healthline*, December 2013. https://web.archive.org/web/20131201081856/http:/www.healthline.com/galecontent/prenatal-development

Gallagher, Christine, M. Consciousness and the Demands of Personhood: Intersubjectivity and Second-Person Ethics. The University of Toledo: The University of Toledo Digital Repository, Theses and Dissertations, 2012. http://utdr.utoledo.edu/cgi/viewcontent.cgi?article=1338&context=theses-dissertations

GenomeWeb. "Senate Committee Holds Hearing on CRISPR Science, Ethical Concerns, Regulatory Approaches." Accessed May 30, 2018. https://www.genomeweb.com/policy-legislation/senate-committee-holds-hearing-crispr-science-ethical-concerns-regulatory

Geraedts, JP and GM De Wert. "Preimplantation genetic diagnosis." *Clinical Genetics* 76, no. 4 (Oct 2009): 315-325.

Gert, Bernard. "Morally Relevant Features." *Metaphilosophy* 30, nos. 1 & 2 (1999): 13-24.

Gibbon, Sahra et al. Racial Identities, Genetic Ancestry, and Health in South America. New York: Palgrave Macmillan, 2011.

Grady, Denise. "Sperm Donor Seen as Source of Disease in 5 Children." *The New York Times*. May 19, 2006. https://www.nytimes.com/2006/05/19/health/19donor.html

Green, R. M. *The Human Embryo Research Debates: Bioethics in the Vortex of Controversy*. Oxford: Oxford University Press, 2001.

Greenfield, Andy, et al. *Genome Editing: An Ethical Review*. London: Nuffield Council on Bioethics, 2016.

Gyngell, Chris, et al. "Editing the Germline - A Time for Reason, Not Emotion." Practical Ethics: Ethics in the News. University of Oxford, 2015. Accessed June 3, 2018. http://blog.practicalethics.ox.ac.uk/2015/03/editing-the-germline-a-time-for-reason-not-emotion/

HCA Healthcare. "Therapeutic Abortion: Surgical." Retrieved May 15, 2018. https://hcahealthcare.com/hl/?/101272/Therapeutic-Abortion--Surgical

Horizon: Inspired Cell Solutions. "Gene Editing." Retrieved May 28, 2018. https://www.horizondiscovery.com/gene-editing

Jaworska, Agnieszka and Julie Tannenbaum. The Grounds of Moral Status. *Stanford Encyclopedia of Philosophy*. Revised January 2018. https://plato.stanford.edu/entries/grounds-moral-status/

Kamm, Frances M. "Is There a Problem with Enhancement?" *The American Journal of Bioethics* 5, no. 3 (2005): 5-14.

Kass, Leon, R. "Ageless Bodies, Happy Souls: Biotechnology and the Pursuit of Perfection." *The New Atlantis: A Journal of Technology & Science* 1 (Spring 2003): 9-28.

Kelly, George A. *The Catholic Marriage Manual*. New York: Random House, 1958.

Klipstein, Sigal. "Parenting in the Age of Preimplantation Gene Editing." *Just Reproduction: Reimagining Autonomy in Reproductive Medicine* 47, no. S3 (2017): S28-S33.

Kolb, Rachel and Dakota McCoy. "Gene-editing tool raises questions about what is 'disease'." *San Francisco Chronicle* (San Francisco, CA), August 3, 2017.

Konrad, Monica. *Narrating the New Predictive Genetics: Ethics, Ethnography and Science*. Cambridge: Cambridge University Press, 2005.

Landsman, Gail H. *Reconstructing Motherhood and Disability in the Age of 'Perfect' Babies*. London: Routledge, 2009.

Lanphier, Edward et al. "Don't edit the human germ line." *Nature* 519, 26 March 2015. https://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111

Liao, Matthew, S. "The Basis of Human Moral Status." *Journal of Moral Philosophy* 7, no. 2 (2010): 159-179.

Macklin, Ruth. "Dignity is a Useless Concept." *British Medical Journal* 327, no. 7429 (2003): 1419-1420.

Malinowski, Bronislaw. *Sex and Repression in Savage Society*. London: Kegan Paul, Trench, Trubner & Co., 1927.

Marks, Jonathan. *What it Means to be 98% Chimpanzee: Apes, People, and their Genes*. Berkeley, London: University of California Press, 2003.

Martin, Emily. "The Egg and the Sperm: How Science has Constructed a Romance Based on Stereotypical Male-Female Roles." *Signs* 16, no. 3 (1991): 485-501.

Mauron, Alex. "Is the Genome the Secular Equivalent of the Soul?" *Science* 291, no. 5505 (2001): 831-832.

McKibben, Bill. *Enough: Staying Human in an Engineered Age*. New York: Henry Holt, 2003.

McMahan, Jeff. "The Morality of Screening for Disability." *Reproductive BioMedicine Online* 10, no. 1 (2005): 129-132.

Merriam-Webster, s.v. "Amoral." Accessed May 29, 2018. https://www.merriam-webster.com/dictionary/amoral

Moutal, A. "CRISPR/Cas9 editing of Nf1 gene identifies CRMP2 as a therapeutic target in neurofibromatosis type 1-related pain that is reversed by (S)-Lacosamide." *Pain* 158, no. 12 (2017): 2301-2319.

Mukherjee, Siddhartha. *The Gene: An Intimate History*. New York: Scribner, 2016.

The National Academies of Sciences, Engineering, Medicine, et al.. *Human Genome Editing: Science, Ethics, and Governance*. Washington, DC: The National Academies Press, 2017.

National Cancer Institute, Dictionary of Cancer Terms, s.v. "Germline DNA." Accessed May 30, 2018. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/germline-dna

Nelkin, Dorothy and M. Susan Lindee. *The DNA Mystique: The Gene as a Cultural Icon*. New York: Freeman, 1995.

Nelson, S. C., J. H. Yu, and L. Ceccarelli. "How Metaphors About the Genome Constrain CRISPR Metaphors: Separating the 'Text' From Its 'Editor'." *The American Journal of Bioethics* 15, no. 12 (2015): 60-62.

The Niche: Knoepfler Lab Stem Cell Blog. "The big blind spot on CRISPR for human embryo editing: PGD." April 24, 2015. https://ipscell.com/2015/04/crispr-versus-pgd/

NORD: National Organization for Rare Disorders. "Neurofibromatosis 1." Retrieved May 19, 2018. https://rarediseases.org/rare-diseases/neurofibromatosis-type-1-nf1/

Norfolk, Derek. "Jehovah's Witnesses and blood transfusion." In *The Handbook of Transfusion Medicine for the United Kingdom Blood Services*. Edited by Derek Norfolk. Norwich: TSO Information and Publishing Solutions, 2013.

O'Keefe, Meaghan et al. "'Editing' Genes: A Case Study About How Language Matters in Bioethics." *The American Journal of Bioethics* 15, no. 12 (2015): 3-10.

Olson, Eric T. Personal Identity. *Stanford Encyclopedia of Philosophy*, 2015. https://plato.stanford.edu/entries/identity-personal/

Pasvol, Geoffrey. "Are Children with Homozygous Sickle Cell Disease Really at a Disadvantage in the Face of Malaria? The Malaria Hypothesis Revisited." *Clinical Infectious Diseases* 49, no. 2 (2009): 223-224.

Perkel, Jeffrey. "CRISPR/Cas faces the bioethics spotlight." *BioTechniques* 58, no. 5 (2018): 223-227.

Pollack, Robert. "Eugenics Lurk in the Shadow of CRISPR." *Science* 348, no. 6237 (2015): 871.

President's Council on Bioethics. *Beyond Therapy: Biotechnology and the Pursuit of Happiness – A Report of the President's Council on Bioethics*. Washington, DC: The President's Council on Bioethics, 2003. https://biotech.law.lsu.edu/research/pbc/reports/beyondtherapy/

Ratner, Nancy and Shyra J. Miller. "A RASopathy gene commonly mutated in cancer: the neurofibromatosis type 1 tumour suppressor." *Nature Reviews Cancer* 15, no. 5 (2015): 290-301.

Richardson, Henry S. "Moral Reasoning." Stanford Encyclopedia of Philosophy, Feb 2013: https://plato.stanford.edu/entries/reasoning-moral/

Roberts, Joseph T. F. "Treating the Enhancement Debate: Irrelevant Distinctions in the Enhancement Medicine Debate." *Kriterion – Journal of Philosophy* 28 (2014): 1-12.

Rollin, Bernard E. "The Moral Status of Animals and Their Use as Experimental Subjects." In *A Companion to Bioethics*. 2nd edition. Edited by Helga Kuhse and Peter Singer, 495-510. West Sussex: Blackwell, 2009.

Saey, Tina Hesman. "CRISPR gene editing moved into new territory in 2017." *Science News* 192, no. 11 (2017): 21.

Sandel, Michael J. "Judgmental Toleration." In *Natural Law, Liberalism, and Morality: Contemporary Essays.* Edited by Robert George. Oxford: Oxford University Press, 2001.

Sandel, Michael J. "The case against perfection." *The Atlantic Monthly* 293, no. 3 (2004): 50-62.

Santos, Ricardo Ventura and Marcos Chor Maio. Anthropology, Race, and the Dilemmas of Identity in the Age of Genomics: A View from Brazil." In *Racial Identities, Genetic Ancestry, and Health in South America*. Edited by Sahra Gibbon, Ricardo Ventura Santos and Monica Sans. New York: Palgrave Macmillan, 2011.

Savulescu, Julian and Guy Kahane. "The moral obligation to create children with the best chance of the best life." *Bioethics* 23, no. 5 (2009): 274-290.

Scheper-Hughes, Nancy. *Death Without Weeping: The Violence of Everyday Life in Brazil*. Berkeley: University of California Press, 1993.

Shaw, Alison. *Negotiating Risk: British Pakistani Experiences of Genetics*. New York: Berghahn Books, 2009.

Steinbock, Bonnie. "Moral Status, Moral Value, and Human Embryos: Implications for Stem Cell Research." In *The Oxford Handbook of Bioethics*. Edited by Bonnie Steinbock. Oxford: Oxford University Press, 2007.

Symons, Xavier. "Personhood and Moral Status: the Debate Continues." BioEdge: Bioethics News From Around the World, 2016. Accessed June 7, 2018. https://www.bioedge.org/bioethics/personhood-and-moral-status-the-debate-continues/11764

Thorne, Chris. "An Introduction to CRISPR Genome Editing." *Horizon: Inspired Cell Solutions*. December 11, 2015. https://www.horizondiscovery.com/resources/webinars/an-introduction-to-crispr-genome-editing

Timmons, Mark. Moral Theory: An Introduction, 2nd edition. Lanham, MD: Rowman & Littlefield Publishers, 2013.

The US National Library of Medicine. "Neurofibromatosis Type 1" Genetics Home Reference. 2018. https://ghr.nlm.nih.gov/condition/neurofibromatosis-type-1

Vaughn, Lewis. *Bioethics: Principles, Issues, and Cases*. Third Edition. New York, Oxford: Oxford University Press, 2017.

Wallace, Margaret R., et al. "Type 1 neurofibromatosis gene: Identification of a large transcript disrupted in three NF1 patients." *Science* 249, no. 4965 (1990): 181-186.

Warren, Mary A. "The Moral Status of the Gene". In *A Companion to Genethics*. Edited by Justine Burley and John Harris. Oxford and Victoria: Blackwell Publishing, 2008.

Weisstub, David N. and David C. Thomasma. "Human Dignity, Vulnerability, Personhood." *Personhood and Health Care* 7, (2001): 317-332.

Wijngaards Institute. "The Physical Interpretation of Natural Law." Wijngaards Institute for Catholic Research: Catholics and Contraception. http://www.catholicsandcontraception.com/physical-interpretation-natural-law/

Willerslev, Rane. "Soul Hunters: Hunting, Animism, and Personhood among the Siberian Yukaghirs." Berkeley and London: University of California Press, 2007.

Winchester Hospital. "Therapeutic Abortion: Medical." Retrieved May 17, 2018. www.winchesterhospital.org/health-library/article?id=101274

Wurzburger, Walter S. *The Ethics of Responsibility: Pluralistic Approaches to Covenantal Ethics*. Philadelphia & Jerusalem: The Jewish Publication Society, 1994.

Yong, Ed. "The Designer Baby Era Is Not Upon Us". *The Atlantic*, August 2, 2017. https://www.theatlantic.com/science/archive/2017/08/us-scientists-edit-human-embryos-with-crisprand-thats-okay/535668/

Zhang, Feng. "NF1 CRISPR guide RNA, neurofibromin 1 CRISPR guide RNA[Human]: gRNA/crRNA for genome editing with WT SpCas9 vector of cas9 protein." *Nat Methods* 11, no. 8 (2014): 783-4.

Zhang, Feng, Yan Wen, and Xiong Guo. "CRISPR/Cas9 for genome editing: progress, implications and challenges." *Human Molecular Genetics* 23, no. R1 (2014): R40-R46.