UTILIZING SCIENCE FICTION TO VISUALIZE ETHICAL ISSUES SURROUNDING HUMAN GENOME EDITING, INFLUENCE ETHICAL REASONING SKILLS IN EDUCATION, AND GUIDE POLICY IMPLEMENTATION

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ABSTRACT

Utilizing Science Fiction to Visualize
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Doctor of Medical Humanities Dissertation by

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CRISPR-Cas9 has revolutionized genetic manipulation in unprecedented ways, as it is an inexpensive, precise, and fast means of editing genes. The CRISPR-Cas9 system has been exploited to alter DNA in various organisms and human embryos. Editing the human genome has the potential to become a reality, thus theoretically enabling scientists to correct disease-causing mutations in human DNA. However, this revolutionary technique has serious ethical considerations. Before employing CRISPR-Cas9 for human medical treatments, the four tenets of biomedical ethics need to be addressed for all stakeholders. Other considerations for moving forward include the influence of societal values and laws governing such practices.

Ethical issues surrounding gene editing in humans are vividly and thoroughly depicted in various works of science fiction. Although the science may or may not be in alignment with current technologies, the social and ethical warnings presented in science fiction are undeniable. Science fiction can serve as a tool to educate future scientists on how to ethically evaluate research projects to ensure ethical standards are met and consider the social impacts discoveries might have. Lastly, science fiction can be a visualization tool in guiding regulations that need to be implemented now while technologies are advancing to prevent ethical violations.

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CHAPTER 1: A REVIEW OF THE LITERATURE: THE SCIENCE AND ETHICAL ISSUES OF CRISPR-CAS9 GENE EDITING

Introduction

Bacteria are able to remove foreign DNA from their genome using CRISPR-Cas systems as a part of their immune response mechanisms (Doudna and Charpentier 2014; Evitt, Mascharak, and Altman 2015; Kick et al. 2017; Komaroff 2017; Lander 2015; Lundberg and Novak 2015; and Qui 2016). By manipulating the CRISPR-Cas system, editing genes has become relatively simple and rapid with high precision and low cost. Single nucleotides or entire genes can be excised or added using this system, thus allowing the ability to excise undesired mutated DNA and insert desired genes or corrected genes (Baker 2016, Baumann 2016, Doudna and Charpentier 2014, Kick et al. 2017, Komaroff 2017, Ormond et al. 2017, Qui 2016, and Smolenski 2015).

CRISPR stands for clustered regularly interspaced short palindromic repeat, which means there are identical segments of DNA that are twenty to forty base pairs in length that read the same forwards and backwards (5'-3' and 3'-5') with unique spacer DNA in between the repeats (Doudna and Charpentier 2014 and Qui 2016). In bacteria, since this is an immune response system, the spacer DNA segments are identical matches for infectious viral DNA (Doudna and Charpentier 2014 and Qui 2016). Cas is short for CRISPR associated genes that encode for the Cas proteins, which are helicases (proteins that unwind the DNA double helix) and endonucleases (proteins that cut DNA by cleaving the phosphodiester bonds between nucleotides). Cas9 in particular is a helicase with two endonuclease sites, thus enabling it to cut both strands of DNA (Doudna and Charpentier 2014 and Qui 2016). In order to use the CRISPR-Cas9 system in human and animal cells, the Cas9 protein is complexed with a synthesized twenty base pair RNA sequence that acts as a guide to find the desired gene through complementary base pairing with DNA (Baker 2016, Doudna and Charpentier 2014, Komaroff 2017, Lundberg 2015, Ormond et al. 2017, Qui 2016). Cas9 is able to unwind the DNA, which allows the RNA to bind to the target DNA, then the endonuclease sites of Cas9 are able to cleave both strands of the DNA at a specific location in the DNA sequence (Baker 2016, Doudna and Charpentier 2014, Komaroff 2017, Lundberg 2015, Ormond et al. 2017, Qui 2016). This is what makes the CRISPR-Cas9 system very precise. Using the CRISPR-Cas9 system, mutated DNA can therefore be excised and if an insertion of DNA is desired, it is added to the CRISPR-Cas9 complex and will be inserted into the DNA after the mutation is removed (Baker 2016, Doudna and Charpentier 2014, Komaroff 2017, Ormond et al. 2017, Qui 2016).

To date, CRISPR-Cas9 has been utilized to eliminate genetic diseases in animal models, as well as successfully editing both human somatic and germline cells (Baltimore et al. 2015; Bauman 2016; Evitt, Mascharak and Altman 2015; Komaroff 2017; Ormond et al 2017; Phimister and Bieniasz 2017; Smolenski 2015; and Zhai, Ng, and Lie 2016). In April of 2015, nonviable human embryos were genetically modified for the first time by a research group in China to cure a blood disorder (Baker 2016; Baumann 2016; Lundberg and Novak 2015; Ormond et al. 2017; Qui 2016; Scott 2015; Smolenski 2015; and Zhai, Ng, and Lie 2016). CRISPR-Cas9 may be the means to eradicate genetic diseases, but with this incredible scientific breakthrough comes issues pertaining to autonomy, beneficence, nonmaleficence, and justice. However, editing somatic cells raises less concerns than germline cells since germline cells affect future generations and not just the individual. Uncertainty of potential harms should not be a hindrance to further research the potential benefits of gene editing to eradicate diseases. But research should be conducted with ethical considerations to ensure experiments are morally acceptable to society. Chapter one will be dedicated to how CRISPR-Cas9 works, applications of CRISPR-Cas9, the ethical debates discussed in the literature, one major unethical use of CRISPR-Cas9, and the current status of laws globally regarding gene editing.

In order to guide ethical considerations, especially for those who might not have a science or genetics background nor a biomedical ethics background, science fiction could be of assistance to aid in the visualization of ethical concerns. Science fiction, whether written literary works or movies, offers invaluable insight into the perceptions that people may have regarding potential technological advances and social issues surrounding those advances. Science fiction writers seem to have an innate ability to creatively imagine what seems fantastical at the time of inception only to predict technologies that become available in the future. Technologies may not come to fruition exactly how the writer envisioned, but the basis for them is evident, nonetheless, through the conceptualization in fictitious works.

In regards to genetics and gene editing technologies, I have read novels and watched movies that range from the ridiculous and completely improbable to the very probable that actually may be a feasible future reality. Exploring novels written from 1896 to 2019 and movies filmed from 1968 to 2019, common themes were evident over multiple decades. Due to the fact that DNA was first identified in 1869 by Frederich Meischer but not really researched until 1944 to the present, some of the early novels only allude to genetics indirectly through scientific techniques of the time or eugenics, which was unfortunately prevalent in the early 1900's.

Listed in chronological order of the original publication dates, the following novels were read as a part of this analysis (chapters two through five): *The Island of Dr. Moreau* (Wells 2004), *Brave New World* (Huxley 1932), *That Hideous Strength* (Lewis 1945), *Friday* (Heinlein 1982), *Beggars in Spain* (Kress 1993), *My Sister's Keeper* (Picoult 2003), the *MaddAddam* trilogy (consisting of *Oryx and Crake, The Year of the Flood,* and *MaddAddam*) (Atwood 2003, 2009, and 2013, respectively), *The Neanderthal Parallax* trilogy (consisting of *Hominids, Humans,* and *Hybrids*) (Sawyer 2002, 2003, and 2003, respectively), *Cowl* (Asher 2004), *Next* (Crichton 2006), The *Tankborn* Series (consisting of *Tankborn, Awakening,* and *Rebellion*) (Sandler 2011, 2013, and 2014, respectively), *2312* (Robinson 2012), *Intrusion* (MacLeod 2012), *The Origin Mystery* Trilogy (consisting of *The Atlantis Gene, The Atlantis Plague,* and *The Atlantis World*) (Riddle 2013, 2013, and 2014, respectively), the *Rise of the Kymiera* six-part series (consisting of *Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) (Turnbull 2017), *Change Agent* (Suarez 2017), and *ReEvolution* (Grant 2019). The films included in this analysis, listed in chronological order of year of release, were *The Blood Beast Terror* (Miller 1968), *The Island of Dr. Moreau* (Steloff 1977), *Brave New World* (Babbin 1980), *The Island of Dr. Moreau* (Pressman 1996), *Gattaca* (DeVito 1997), *Brave New World* (Joyce 1998), *X-Men* (Donner 2000), *Code 46* (Eaton 2003), *Star Trek: Enterprise* season 4 episodes 4-6 (*Borderland, Cold Station 12,* and *The Augments*) (LaZebnik 2004, Brennert 2004, and Sussman 2004, respectively), *Splice* (Hoban 2009), *My Sister's Keeper* (Furst 2009), *Extraordinary Measures* (Shamberg 2010), *The Amazing Spider-Man* (Arad 2012), *The Reconstruction of William Zero* (Burns 2014), *The Perfect 46* (Bonowicz 2014), *Equals*

(Pruss 2015), *Jupiter Ascending* (Hill 2015), *The Titan* (Amel 2018), *Tourbillon* (Ivery 2018), and *Rampage* (Flynn 2018).

Because gene editing is relatively new, this science fiction analysis in chapters two through five is not limited to just gene editing. Each novel and film was evaluated for its depiction of genetic diseases, genetic research, and/or gene editing in correlation with one or more of the four tenets of biomedical ethics: autonomy in chapter two, beneficence in chapter three, nonmaleficence in chapter four, and justice in chapter five. Various issues under each tenet are discussed separately and the scientific feasibility, whether in the present or future, is discussed where necessary. If a novel was adapted into a film (or in some cases, multiple versions filmed in different years), both are discussed as well. Nonmaleficence was the most common tenet of all of the works, which was expected prior to viewing or reading because science fiction often depicts dystopian societies. They are generally social warnings of the pitfalls of certain technologies, which will be substantiated in the analysis of this work.

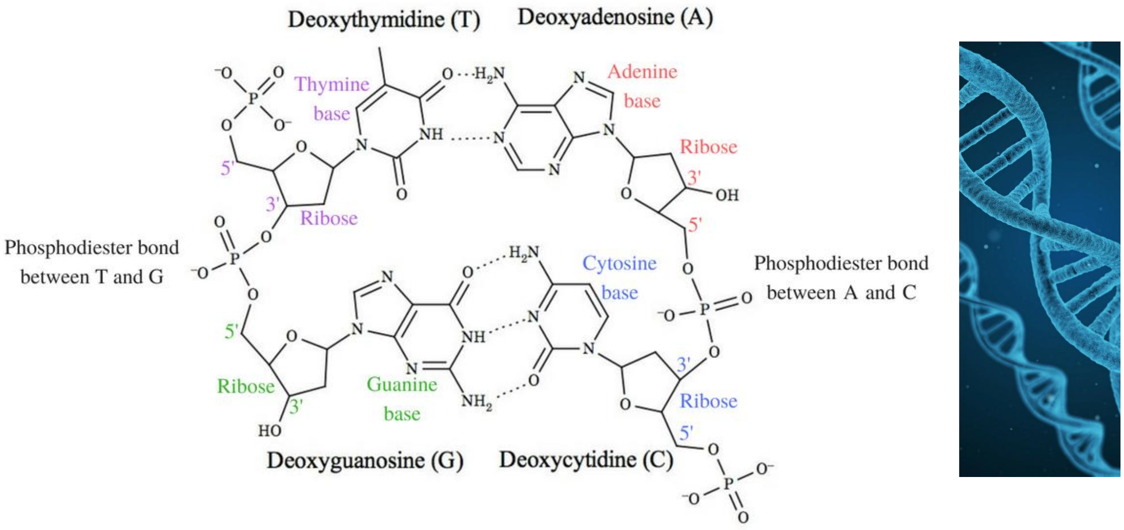
Lastly, chapter six will outline how science fiction in both films and novels can be utilized in an educational setting to promote the understanding of the ethical issues around CRISPR-Cas9. The goal of teaching this subject in a biomedical ethics course would hopefully ensure potential future scientists are capable of ethical decision making, which is often lacking in current curriculum (Yarborough 2019). A section will also be dedicated to describe how a subset of the stories analyzed in chapters two through five can be used to influence policy decision making when updating laws governing CRISPR-Cas9 specifically and gene editing in general. Events in various stories demonstrate negative applications and directions gene editing can go if it is not regulated properly and if moral values are not upheld.

History of Techniques, How Current Techniques Work, and Successful Applications of CRISPR-Cas9 Gene editing

Overview of DNA and RNA

In order to understand CRISPR-Cas9 and what it does, a basic understanding of DNA and RNA is necessary. DNA, which stands for deoxyribonucleic acid, contains a complete genetic code for an organism. RNA, or ribonucleic acid, serves a different function depending on the type of RNA, but RNA strands are much shorter compared to DNA. Another major difference between these molecules is DNA is double stranded while RNA is single stranded.

Nucleic acids are polymer chains of nucleotides and the four nucleotides that are found in DNA are deoxyguanosine-5'-monophosphate (dGMP), deoxythymidine-5'-monophosphate (dTMP), deoxyadenosine-5'-monophosphate (dAMP), and deoxycytidine-5'-monophosphate (dCMP). They are called deoxy- in DNA because they are missing a hydroxyl group, -OH, on the 2' position of the sugar portion of the molecule, which is the sugar ribose, thus the name ribonucleic. In RNA, all of these nucleotides, except for dTMP, exist in their oxygenated form and the "d" is removed from the abbreviation (e.g. dAMP in DNA and AMP in RNA) and deoxy' is removed from the name. Also, the one nucleotide that is only found in RNA is uridine-5'-monophosphate (UMP). They are all simply abbreviated with a single letter: G, T, A, C, and U, respectively. Lastly, the 5' in the name is the position on ribose where the phosphate group is attached. See ***Figure 1****,* which shows the nucleotides in DNA.



A **B**

Figure 1. A shows the structure of the nucleotides found in DNA (the -5’-monophosphate was eliminated from the names to simplify the image). The base and ribose components are labeled, as well as the 5’ and 3’ positions in the phosphodiester bonds, for each nucleotide and they are color coded to indicate which ribose coincides with each nucleotide. Two phosphodiester bonds are indicated as well. Lastly, hydrogen bonds between nucleotides are shown as dotted lines between bases. The molecules were drawn in MarvinSketch and the labels were added in Canva. ***B*** shows a rendering of the double stranded helical structure of DNA. This was a free image downloaded from Canva.

Nucleotides are linked together in nucleic acids to form chains or strands via phosphodiester bonds, which are covalent bonds (electrons are shared between nuclei of atoms to make the bond), that link the phosphate group on the 5’ position on one nucleotide to an oxygen on the 3’ position of the ribose on the next nucleotide (see ***Figure 1)***. In DNA, to form double strands, two separate strands are held together by hydrogen bonds between the bases of nucleotides (adenine, guanine, cytosine, and thymine), which is referred to as base pairing, and form what is called a double helix because the two strands twist to form what looks like a spiral staircase (see ***Figure 1).*** Specifically, A pairs with T due to two hydrogen bond interactions and G pairs with C due to three hydrogen bond interactions, shown as dotted lines in ***Figure 1.*** It is important to note that hydrogen bonds are not actually bonds, but are intermolecular forces, which are attractive forces between molecules. Intermolecular forces are more easily broken than actual covalent bonds because nuclei are just interacting with electrons rather than sharing them. In addition, RNA molecules do rely on base pairing for certain functions and since RNA molecules do not have T, A pairs with U instead.

History of Previous Techniques

After the discovery of DNA, research was dedicated to understanding double strand breaks (DSB), repair mechanisms in various organisms that repair double strand breaks in order to survive, and exploring the possibility of genome editing: the idea that double strand breaks can be introduced on purpose with the goal of changing the DNA at a site-specific location (Doudna and Charpentier 2014). Two branches of research emerged in attempts to perform genome editing and ran in parallel until they merged in 2012: ZFN/TALEN research, which was discovered first, and CRISPR research, which was discovered later, but became the standard method of gene editing due to simplicity of use, precision, and low cost in 2012 (Doudna and Charpentier 2014).

Starting in the 1950's, the earliest attempts to locate DNA sequences and inflict double strand breaks relied on either oligonucleotides (molecules with a short nucleotide sequence) or peptide nucleic acids (synthetic nucleotides) to find the desired DNA sequence combined with a chemical agent that would perform the double strand break, or self-splicing introns (segments of DNA or RNA that do not code for protein) that found desired DNA sequences through base pairing and cut it at that location; these methods proved it could be done, but were not very efficient methods (Doudna and Charpentier 2014). The next breakthrough discovered in the mid-eighties in gene editing was zinc-finger proteins that recognized DNA sequences, but they were not coupled with an endonuclease (FokI) (an enzyme that cleaves DNA at or near a specific site) until the mid-nineties to synthesize zinc-finger nucleases (ZFNs); although ZFNs were capable of locating DNA sequences and cleaving both strands, designing ZFNs to recognize specific DNA sequences was tedious (Doudna and Charpentier 2014). In 2009/2010, researchers determined that naturally occurring site-directing effectors, called transcription activator-like effectors (TAL), could be coupled with the FokI endonuclease (TALEN) to do what ZFNs do, but could be generated and validated more easily (Doudna and Charpentier 2014). Although the process was easier with TALENs as opposed to ZFNs, it was still not easy.

While the discovery and development of ZFNs and TALENs was taking place, simultaneous research was occurring for CRISPR-Cas9. CRISPRs, or clustered regularly interspaced short palindromic repeats, were first described in *E. coli* bacteria in 1987 by a research group led by Y. Ishino, meaning short segments of DNA were repeated and alternated with unique segments of DNA in between the palindromic repeats (they had the same sequence 5’ to 3’ and 3’ to 5’, or forward and backward; see ***Figure 2***) (Doudna and Charpentier 2014, Heidari 2017, and Ishino et al. 1987). It was not until 2005/2006 that the unique spacer DNA was determined to be of viral origin and that *cas* genes were identified, which encode for *cas* proteins that are able to act as helicases (enzymes that unwind DNA by breaking hydrogen bonds), endonucleases, or both (Doudna and Charpentier 2014).

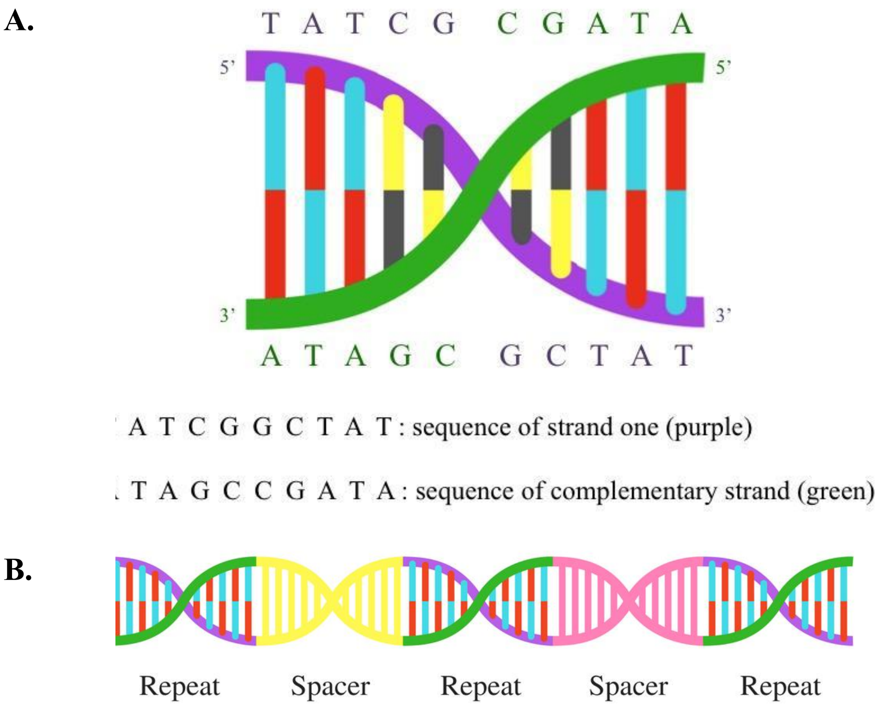


Figure 2. ***A*** demonstrates the palindromic nature of CRISPR genes. The sequence of one strand, colored in purple, gives the sequence of nucleotides. The green strand shows the complementary strand. Both the 5’ and 3’ ends are labeled for both strands. Nucleotides are colored as follows: T is blue, A is red, C is yellow, and G is grey. The DNA clipart is from Canva and the image was modified in Microsoft PowerPoint. ***B*** uses clipart to show how the palindromic repeats contain unique spacer DNA in between them. This image was created in Canva.

These discoveries led to the conclusion in 2007 that CRISPR-Cas systems must be bacterial immune responses to protect them against viral attacks, as the spacer DNA are segments from previous invading viruses enabling the bacteria to recognize future attacks and cut up the DNA of the virus to protect themselves (Doudna and Charpentier 2014). From 2008 to 2012, CRISPR-Cas systems were shown to use RNA as a guide to find specific DNA sequences and that Cas9 was a useful protein to further research because it was a single protein that contained both a helicase domain and two endonuclease domains to induce double strand breaks (Doudna and Charpentier 2014). The major breakthrough that occurred in 2013 was when CRISPR-Cas9 was engineered with a twenty-base pair guide RNA to edit eukaryotic cells and human cells at site-specific locations (Doudna and Charpentier 2014 and Heidari 2017). Since this discovery, CRISPR-Cas9 surpassed all other gene editing technologies in terms of usage, cost, efficiency, and simplicity.

How CRISPR-Cas9 Works

Bacteria utilize CRISPR-Cas systems as a part of their immune response mechanisms to remove foreign DNA from their genome (Doudna and Charpentier 2014; Evitt, Mascharak, and Altman 2015; Komaroff 2017; Lander 2015; Lundberg and Novak 2015; and Qiu 2016). Manipulation of CRISPR-Cas systems, in particular CRISPR-Cas9, has led to a means of editing genes that is rapid and simple that can be done with relatively high precision (although issues with off-target edits, unintended consequences, and mosaicism have been observed) and low cost. CRISPR-Cas9 can be used in cells to excise single nucleotides or entire genes (segments of DNA that encode for proteins and hereditary features, etc.), therefore, undesired mutated DNA can be removed and desired or corrected genes could be added (Baker 2016, Baumann 2016, Doudna and Charpentier 2014, Komaroff 2017, Lanphier 2015, Ormond et al. 2017, Qiu 2016, Sas and Martin-Lawrenz 2017, and Smolenski 2015).

As stated in the previous section, CRISPR stands for clustered regularly interspaced short palindromic repeat, which means identical segments of DNA that are twenty to forty base pairs in length that have the same sequence forward (5’ to 3’) and backward (3’ to 5’) with spacer DNA that has unique sequences in between the repeats (see ***Figure 2***) (Doudna and Charpentier 2014 and Qiu 2016). Since this is an immune response system in bacteria, the spacer DNA segments actually are identical matches for viral DNA that had previously infected the bacterium, which allows the bacterium to recognize and destroy the viral DNA if re-infected (Doudna and Charpentier 2014, Kick et al. 2017, and Qiu 2016). Cas is short for CRISPR associated genes that encode for Cas proteins, which are helicases (proteins that unwind the double helix of DNA), endonucleases (proteins that cut DNA by cleaving phosphodiester bonds between nucleotides), or both. There are two classes of Cas proteins, Class I requires multi-protein complexes and Class II are single proteins, and six types depending on what the enzyme(s) cleave (DNA or RNA); Cas9 is a Class II, type II because it is a single protein that is an endonuclease, which creates blunt end double strand breaks (even breaks with no overhang) as opposed to sticky end breaks like other Cas proteins (5' overhang) (Kick et al. 2017). Cas9 derived from *Streptococcus pyogenes* bacteria is of particular interest due to the fact that it is a single protein that has multiple domains: a helicase domain and two endonuclease domains, RuvC-like (which cuts the target DNA strand) and HNH (which cuts the second DNA strand) (Doudna and Charpentier 2014 and Kick et al. 2017). When using CRISPR-Cas9 to perform gene editing, it is important to note that the only component from bacteria that is used is the Cas9 protein, yet researchers use the full CRISPR-Cas9 name (meaning the CRISPR DNA is not used at all) (Doudna and Charpentier 2014). In other words, CRISPR is a convenient acronym that is easily remembered.

What makes CRISPR-Cas9 so simple to use is the fact that it has been reduced to a two-component system: the Cas9 protein and a single guide RNA (sgRNA), which is synthesized by fusing together mature CRISPR RNA to a trans-activating CRISPR RNA (crRNA:tracrRNA), both of which are necessary for activating the Cas9 protein and recognizing the target DNA sequence (Doudna and Charpentier 2014 and Kick et al. 2017). The crRNA is complementary to the target DNA, which is how CRISPR-Cas9 uses base pairing to locate a specific sequence, and the tracrRNA binds to the Cas9 protein (Doudna and Charpentier 2014 and Kick et al. 2017). In order for Cas9 to cleave the target DNA, a protospacer adjacent motif (PAM) sequence two to five bases in length must be located next to the target DNA sequence because Cas9 will cleave the DNA three bases upstream from the PAM (Doudna and Charpentier 2014 and Kick et al. 2017). Different Cas proteins recognize different PAM sequences and it is a means to prevent cleavage of a bacterium's own DNA, since viral DNA has PAMs and bacterial DNA does not have PAMs (Kick et al. 2017). Therefore, Cas9 can only be used to cut DNA sequences that have a PAM next to it that Cas9 recognizes as invading DNA (Doudna and Charpentier 2014 and Kick et al. 2017).

To put this more simply, in order to use CRISPR-Cas9 in human and animal cells, the Cas9 protein obtained from bacteria is complexed with a synthesized single guide RNA, which is about twenty nucleotides in length, that has complementary base pairing to the target DNA that is next to a PAM. The helicase domain of Cas9 is able to unwind the DNA, which allows the guide RNA to bind the target DNA, then the endonuclease sites (RuvC-like domain and HNH domain) cleave both strands the DNA three bases upstream of the PAM, thus creating a blunt end double strand break. Once the break has occurred, the cell's repair mechanisms take over in an attempt to fix the double strand break, which could be non-homologous end joining (NHEJ) or homology-directed repair (HDR) (Doudna and Charpentier 2014 and Kick et al. 2017). NHEJ essentially uses specific proteins to bring the ends back together without a template strand to copy, but results in gene disruption due to small insertions, deletions, or both in order to link the broken strands back together (Doudna and Charpentier 2014 and Kick et al. 2017). HDR does require a template strand to induce repair, but this is a perfect way to introduce whole new gene sequences into the DNA: donor DNA can be added to the CRISPR-Cas9/sgRNA complex to serve as the template for HDR (Doudna and Charpentier 2014 and Kick et al. 2017). What this essentially means is mutated or undesired DNA can be excised with the CRISPR-Cas9 system and corrected or desired DNA can be inserted in between the double strand break, which utilizes the organism's own repair mechanisms to achieve this.

Successful Applications of CRISPR-Cas9

Manipulating a bacterial immune system to alter the DNA of other non-bacterial organisms may not seem that significant, but it truly is an amazing scientific breakthrough. Scientists now have the means to purposely perform double strand breaks in DNA with a simple two-component system: Cas9 protein and a sgRNA. They can even insert entire genes just by adding a template DNA to the CRISPR-Cas9 system. Subsequently, what does this really mean for genetic engineering?

To date, CRISPR-Cas9 has been used successfully to correct diseases in animal models, including sickle cell anemia (beta-thalassemia) in mice (Komaroff 2017 and Austriaca 2017), a liver-based metabolic disease in mice (Baltimore et al. 2015), cataracts in mice (Doudna and Charpentier 2014), cardiovascular disease in mice (Heidari et al. 2017), Duchenne-like muscular dystrophy in mice (Komaroff 2017), prostate cancer in mice (Komaroff 2017), and human chronic myelogenous leukemia expressed in mice (Doudna and Charpentier 2014). Experiments have been conducted on at least thirty-six organisms, including mice, rats, monkeys, etc. (Doudna and Charpentier 2014 and Smolenski 2015). These gene corrections were done by removing mutated genes and replaced with corrected, fully functioning genes.

Animal models are not the only experiments that have been performed. CRISPR-Cas9 has been used to edit both human somatic and germline cells (Baltimore et al. 2015; Bauman 2016; Ormond et al 2017; Smolenski 2015; and Zhai, Ng, and Lie 2016). In April of 2015, a research group in China was able to cure a blood disorder, beta-thalassemia, in non-viable human embryos through CRISPR-Cas9 genetic modification (Baker 2016; Lundberg and Novak 2015; Ormond et al. 2017; Qui 2016; Scott 2015; Smolenski 2015; and Zhai, Ng, and Lie 2016). Other studies that have had successful edits in human cells include correcting cystic fibrosis in human stem cells (Doudna and Charpentier 2014) and determining which genes in human cells are resistant to HIV by using CRISPR-Cas9 to disable genes and exposing those cells to the virus (Phiminster and Bieniasz 2017). Scientists suspect that CRISPR-Cas9 could be used to treat genetic diseases in humans such as Huntington's disease (Baker 2016, Heidari et al. 2017, and Lander 2015), muscular dystrophy (Hynes et al. 2017 and Komaroff 2017), multiple sclerosis (Lander 2015), and hemophilia (Baumann 2016 and Lanphier 2015). Viral infections like HIV and cancer are also believed to be treatable with CRISPR-Cas9, since there is success in animal models and human cells (Doudna and Charpentier 2014, Heidari et al. 2017, Lanphier 2015, Ormond et al. 2017, and Qiu 2016). Clinical trials are even taking place in China and the US to treat cancer patients for whom chemotherapy has failed by removing T-cells from the patient, genetically modifying the T-cells to recognize cancer cells as foreign, then injecting them back into the patient (Cyranoski 2016, Hynes et al. 2017, Komaroff 2017, and Sas and Martin-Lawrenz 2017).

With this incredible scientific breakthrough comes issues pertaining to autonomy, beneficence, nonmaleficence, and justice, which are described below. However, editing somatic cells raises less concerns than germline cells since germline cells affect future generations and not just the individual. Uncertainty of potential harms should not be a hindrance to further research the potential benefits of gene editing to eradicate diseases. But research should be conducted with ethical considerations to ensure experiments are morally acceptable to society. If gene editing becomes a viable treatment option, then healthcare delivery of this technology must be unbiased, affordable, and accessible to all. Laws may even need to change to accommodate the new technology as well.

An Overview of Ethical Debates

CRISPR-Cas9 and cloning have their own ethical issues falling under the four tenets of biomedical ethics: autonomy, beneficence, nonmaleficence, and justice. Briefly, the working definitions utilized throughout this work are as follows:

1) Autonomy: the right to make decisions without coercion or influence,
2) Beneficence: the obligation to "do good" or provide benefit,
3) Nonmaleficence: the obligation to "do no harm", and
4) Justice: fair, equitable distribution of benefits and burdens (Beauchamp and Childress 2009).

However, through exploration of ethical issues, some overlap will be apparent, especially with regards to autonomy.

Advancements made to Cas9 technologies has sparked debate about how they should be researched and if viable medical treatments are developed, how they should be implemented. Issues pertaining to each tenet are outlined below.

Issues Pertaining to Autonomy

Although the Netflix Original documentary series entitled *Explained* is not exactly a scholarly production, there was an episode that provided a graph that summarized the ethical debates surrounding CRISPR-Cas9 gene editing quite succinctly, which is reproduced below in ***Figure 3*** ("Designer DNA" 2018). The issues of somatic versus germline cells are plotted on the x-axis while the issues of therapy versus enhancement are plotted on the y-axis, which results in four quadrants that represent potential applications of CRISPR-Cas9 gene editing: medicine, curing the patient (somatic cells plus therapy); medicine, curing future generations (germline cells plus therapy); plastic surgery equivalent (somatic cells plus enhancement); and eugenics and designer babies (germline cells plus enhancement). There is a solid line between somatic and germline cells because this distinction is clearly defined by science and ethics, even though there is ethical debate on allowing germline edits. However, the line between therapy and enhancement is purposefully blurred to represent where the science and ethics distinction is not clearly defined and where much ethical debate arises. At this time, most research is dedicated to the first quadrant, curing the patient.

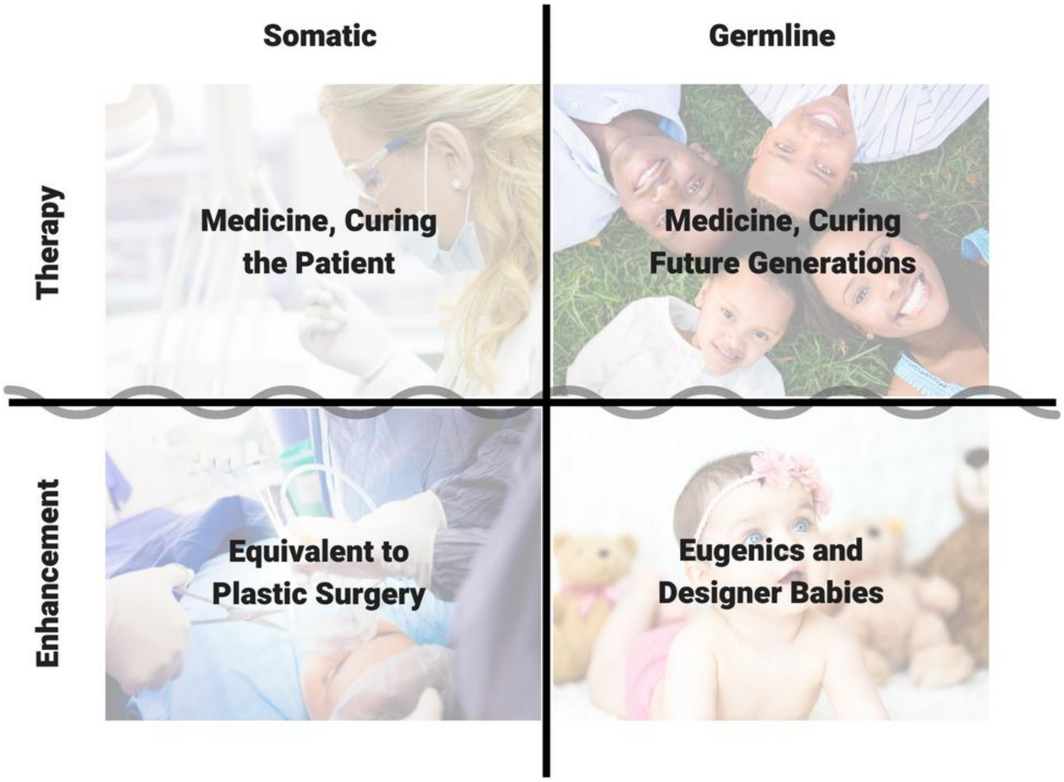


Figure 3. This graph, recreated in Canva, represents a summary of the ethical debates of CRISPR-Cas9 gene editing (adapted from "Designer DNA" 2018). The line between somatic and germline cells is solid and well-defined while the line between therapy and enhancement is purposefully blurred (author's emphasis). The quadrants represent theoretical applications of CRISPR-Cas9.

Autonomy, more specifically in regards to medicine, is an individual's right to either accept or decline medical treatment after being properly informed about his or her medical condition, the benefits of the treatment, and potential side effects. When considering editing human genes as a means of medical intervention, ethical concerns pertinent to autonomy include potentially violating informed consent of future generations and embryos. Since editing somatic cells only affects the individual and editing germline cells affects both the individual and all of his/her subsequent generations, stronger ethical concerns are raised in regards to germline edits (Baker 2016; Baumann 2016; Bosley 2015;

Evitt, Mascharak, and Altman 2015; Harris 2015; Heidari et al. 2017; Hynes, Coller, and Porteus 2017; Lander 2015; Lanphier et al. 2015; Lundberg and Novak 2015; Ormond et al. 2017; Pei et al. 2017; Qiu 2016; Sugarman 2015; Zhai, Ng, and Lie 2016). Many cite lack of informed consent of future generations and embryos as a reason to prohibit germline editing completely, but this argument has not been strong enough to halt all research on germline editing.

When debating editing somatic cells versus germline cells, those that argue somatic cells should be the focus of initial research insist that the majority of monogenic diseases manifest in somatic cells only, therefore, editing germline cells does not make sense due to the risk of unforeseeable, irreversible harmful effects to future generations (Evitt, Mascharak, and Altman 2016; Lander 2015; Lanphier 2015; Lundberg and Novak 2015; and Ormond et al. 2017). Currently, treatments for some debilitating genetic disease do not exist; therefore, others argue that germline edits may be the only option of research to pursue (Baumann 2016; Bosley 2015; Hynes, Coller, and Porteus 2017; Qiu 2016; and Sugarman 2015). Harris insisted in his article that purposely editing germline cells is not really different from and has no greater risk than the random combination of DNA from germline cells during sexual reproduction, which also has the risk of causing mutations resulting in birth defects (2015). Since these issues have not been completely settled worldwide, the general consensus is germline edits are permissible, but only in non-viable human embryos (meaning embryos that will not be implanted for pregnancy and will be destroyed after a determined time limit, usually forty-eight hours to fourteen days depending on the country of origin) (Baker 2016; Baumann 2016; Ormond et al. 2017; Pei et al. 2017; Qiu 2016; Zhai, Ng, and Lie 2016).

Assuming exploration of gene editing continues and eventually becomes a viable treatment option for genetic diseases, then obtaining informed consent is not actually an issue for individuals who opt for editing of their somatic cells, as individuals have the right to make autonomous decisions to accept treatment. Informed consent has been brought up as an ethical issue because it cannot be obtained from future generations who would be affected by germline editing (Evitt, Mascharak, and Altman 2015; Harris 2015; Hynes, Coller, and Porteus 2017; Ormond et al. 2017; Qiu 2016; Smolenski 2015; and Sugarman 2015). However, there are a few reasons why the validity of this argument is questioned. The first reason is parents currently have the right to make medical decisions on behalf of their children, born or unborn, due to children's inability to make autonomous choices. In order to prevent the passing of genetic diseases to their children, the options available to parents at this time include obtaining genetic testing and selectively choosing an embryo for implantation that is devoid of disease-causing genes. Theoretically, parents could choose to genetically modify their DNA in their germline cells instead, which could be viewed as an autonomous choice made on behalf of their children to eliminate a genetic disease. This would be on par with selective implantation. Therefore, germline editing could be viewed as morally acceptable, as they are acting in the best interest of the child (Evitt, Mascharak, and Altman 2015; Harris 2015; Hynes, Coller, and Porteus 2017; Qui 2016; and Sugarman 2015). If germline gene editing were to become a mainstream treatment option in the future, then a resulting negative consequence could be that parents may need to justify their choice if they decide to not use genetic modification when the probability for inheriting a genetic disease in their children is high (Baumann 2016; Evitt, Mascharak, and Altman 2015).

Additionally, in regards to informed consent, embryos and nonexistent individuals (which would include future generations) are not afforded the same moral status as human beings. In other words, they do not technically have personhood. Some have suggested that multigenerational consent would be necessary to allow germline editing, but clearly, this is impossible (Evitt, Mascharak, and Altman 2015; Harris 2015; Qiu 2016; Smolenski 2015; and Sugarman 2015). Lack of moral status and the impossibility of obtaining multigenerational consent are further reasons why the argument against germline editing solely based on the lack of informed consent from future generations and embryos is questioned. Parents are afforded parental autonomy to make decisions for their children under the assumption that they wish to do what is best for their child (Evitt, Mascharak, and Altman 2015; Harris 2015; Lander 2015; Ormond et al. 2017; Smolenski 2015; and Sugarman 2015). What needs to be agreed upon is if germline editing to correct for genetic diseases is similar or different from other treatment options. Such research would be reliant upon the assumption that parents, doctors, and scientists believe that a future child and subsequent offspring would want to live without a genetic disease.

Issues Pertaining to Beneficence

Beneficence in simplistic terms is the obligation to act in such a way to provide benefit for others. Medically speaking, beneficence would be the obligation to treat medical conditions in order to alleviate suffering. Genetic diseases afflict millions of people and the intent of developing CRISPR-Cas9 is to create a means of correcting genetic mutations that cause disease. Once proven effective, a genetic disease can be eliminated by excising mutated DNA with CRISPR-Cas9, whether one nucleotide or an entire gene, and a corrected gene can be inserted in its place (Baker 2016, Baumann 2016, Doudna and Charpentier 2014, Kick et al. 2017, Komaroff 2017, Ormond et al. 2017, Qiu 2016, and Sas and Martin-Lawrenz, 2017). However, if further research is hindered, the potential benefit of this theory will never be realized.

Because of the current understanding of genetics, CRISPR-Cas9 technology is more likely to be effective in treating monogenic diseases. Categories of monogenic diseases are autosomal dominant diseases (homozygous dominant in one parent) or autosomal recessive diseases (homozygous recessive in both parents), which include beta-thalassemia, hemophilia, Huntington's disease, cystic fibrosis, phenylketonuria, and familial adenomatous polyposis (Baumann 2016; Evitt, Mascharak, and Altman 2015; Hynes, Coller, and Porteus 2017; Lander 2015; Lanphier et al. 2015; Lundberg and Novak 2015; Qiu 2016; Sas and Martin-Lawrenz 2017; and Scott 2015). Researchers even conjecture that cancer and HIV/AIDS can be fought with CRISPR-Cas9, so much so that clinical trials are taking place in the US and China (Cyranoski 2016; Doudna and Charpentier 2014; Kick et al. 2017; Hynes, Coller, and Porteus 2017; Lander 2015; Lanphier et al. 2015; Qui 2016; and Sas and Martin-Lawrenz 2017).

Parents who are predisposed to genetic diseases and who wish to have genetically related offspring have limited options for bearing children. Technologies that are currently available to prevent passing on genetic disorders are prenatal genetic testing, *in vitro* fertilization (IVF), and preimplantation genetic diagnosis embryo selection (PGD), but they are limited in their accuracy (Lander 2015, Lundberg et al. 2015, Sas and Martin-Lawrenz 2017, and Sugarman 2015). Gene editing could be a better, viable treatment option to have children without disease. Without further research, the potential of CRISPR-Cas9 will not be realized.

A complete ban on gene modification, whether somatic or germline, would eliminate any potential for the exploration of CRISPR-Cas9 to cure diseases. For individuals who suffer from genetic disease that have limited or no treatment options, this would eliminate any possible benefits from being discovered, which would in turn violate the tenet of beneficence. There is an obligation to treat patients with what is available if no other cure exists. This is an argument for limiting research to somatic cells only, since most monogenic disease only affect an individual (Baltimore et al. 2015; Lander 2015; Lanphier et al. 2015; Lundberg and Novak 2015; Qiu 2016; Smolenski 2015).

As stated previously, research involving germline edits are recommended to only be performed on non-viable embryos, meaning they cannot be implanted for pregnancy (Baker 2016; Baumann 2016; Ormond et al. 2017; Pei et al. 2017; Qiu 2016; Zhai, Ng, and Lie 2016). As of 2015, the United States and fifteen out of twenty-two Western European countries do not allow human germline modifications, citing that the introduction of genes that cause negative consequences is too dangerous (Heidari et al. 2017, Lander 2015, Lanphier et al. 2015, and Pei et al. 2017). But there is support among researchers that in order to gain a better understanding of genetics, embryonic development, and diseases, utilizing non-viable human embryos to perform germline edits offers a solution to allow for further exploration without jeopardizing the human gene pool and harming people (Baker 2016; Baumann 2016, Bosley 2015; Hynes, Coller and Porteus 2017; Ormond et al 2017; Pei et al. 2017; and Zhai, Ng, and Lie 2016). Unless they are studied, the span of benefits and risks associated with germline editing cannot be fully understood.

Issues Pertaining to Nonmaleficence

Nonmaleficence in its most basic definition is to not do harm to others. Although there are clinical trials occurring in the United States and China that utilize CRISPR-Cas9 to modify somatic cells in cancer patients for whom chemotherapy has not been successful, CRISPR-Cas9 is unable to be used at the moment to cure various diseases as conjectured due to a limited understanding of the human genome (Cyranoski 2016; Kick et al. 2017; Hynes, Coller, and Porteus 2017; Lander 2015; Lanphier et al. 2015; Qui 2016; and Zhai, Ng, and Lie 2016). This means that the safety of CRISPR-Cas9 cannot be ensured because of the harmful side effects observed when using CRISPR-Cas9, which include off-target edits, unintended secondary effects, and mosaicism. Ethicists also warn against moral risks, such as eugenics and enhancements or nontherapeutic applications.

When CRISPR-Cas9 cuts DNA at a different location than intended, this is referred to as an off-target edit and off-target edits occur because only fifteen out of twenty base pairs of the guide RNA has to match in order to bind to the DNA (Ormond et al. 2017, Sas and Martin-Lawrenz 2017). There is consensus that even though CRISPR-Cas9 is the most precise gene editing method, fifteen out of twenty base pair matching is not precise enough to justify human experimentation. However, Doudna and Charpentier (2014) give assurances that research groups are attempting to figure out how to minimize off-target edits to improve the accuracy of CRISPR-Cas9 edits, thus improving the safety of the technique. Unintended secondary effects or consequences are the result of interdependent gene function or polygenic genes: if one gene is dependent on the function of another gene located at a different site and one of those genes is altered, then the other gene also ceases to function properly (Komaroff 2017). Polygenic genes are not mapped well enough to edit them using CRISPR-Cas9 and therefore the risk is too high to justify experimenting on humans (Baltimore, et al. 2015; Baumann 2016; Evitt, Mascharak, and Altman 2015; Qiu 2016). Experiments on embryo modification have shown mosaicism, meaning not all of the cells within the embryo have been modified and therefore the therapeutic effect is low (Baumann 2016, Bosley 2015, Kick et al. 2017, and Scott 2015).

The potential mistakes that can occur with CRISPR-Cas9 gene editing (off-target edits, unintended consequences, and mosaicism) have not entirely been prevented and can have serious effects on embryos (and humans if they are not corrected before use) (Baltimore et al. 2015; Baumann 2016; Doudna and Charpentier 2014; Evitt, Mascharak, and Altman 2015; Komaroff 2017; Lander 2015; Lanphier et al. 2015; Ormond et al. 2015; Qiu 2016; Sas and Martin-Lawrenz 2017; Scott 2015; Smolenski 2015; Sugarman 2015; and Zhai, Ng, and Lie 2016). If CRISPR-Cas9 gene edits were performed on humans in their current state, these mistakes may be irreversible and might not be realized for years, which could have devastating effects on multiple generations if the edits were performed on germline cells as opposed to somatic cells. In order to be used in humans at some time in the future, the risks of mistakes must be reduced or eliminated.

Thus far in this discussion, only therapeutic applications CRISPR-Cas9 have been ethically debated. However, CRISPR-Cas9 has the potential to be developed for non-therapeutic applications, including eugenics, or the belief in preferential genetic selection, and genetic enhancements. For this reason alone, many have either not condoned utilizing CRISPR-Cas9 for enhancements or raise strong ethical objections to gene editing in general (Baker 2016; Evitt, Mascharak, and Altman 2015; Lander 2015; Ormond et al.

2017; Pei et al. 2017; and Sas and Martin-Lawrenz 2017). For instance, genes for eye color and athleticism are well understood, which means they could theoretically be easily edited (Baumann 2016 and Qiu 2016). Others claim the line between enhancements and therapy is not clearly defined, as therapies might have enhancing side effects, or private markets in capitalist societies cannot be controlled to prevent enhancements (Austriaco 2017, Juengst 2017, and Pei 2017).

Along these lines, one of the most frequently mentioned issue cited as an argument against CRISPR-Cas9 gene editing is "designer babies," the concept that in the future, parents would be able to select any characteristic they desired their children to have: eye color, hair color, skin color, hair texture, height, athletic ability, intelligence, etc., in addition to preventing the passing on of disease causing genes (Komaroff 2017; Lander 2015; and Sas and Martin-Lawrenz 2017). Fezza (2017) counters these concerns, stating that how science is often communicated to the populace leads to misunderstanding because of poor language choice and fear of using CRISPR-Cas9 to make "designer babies" is a result of miscommunication. The metaphor that CRISPR-Cas9 acts as a "molecular scissor" and the term "edit" actually imply that such genetic modifications are simple endeavors in the laboratory (i.e. as simple as editing Word documents via cut, copy, and paste commands, for instance) and therefore have led to exaggerated hype around non-existent problems because the technology has not been developed to allow for the creation of "designer babies" yet (Frezza 2017). Regardless, researchers and society both must continue to be cautious that enabling genetic modifications to cure diseases could potentially initiate a slippery slope to eugenics and enhancements if CRISPR-Cas9 is developed enough and this serious ethical decision might have to be made in the future.

Issues Pertaining to Justice

Justice, in regards to medicine, refers to distributive justice, which is equal access to goods and services, as well as equal distribution of burdens to all members of a community. Issues concerning justice surrounding CRISPR-Cas9 include providing access to only the wealthy, violating disability rights, and an unequal burden placed on women due to the need for egg donation for embryonic studies.

In the future, if genetic diseases are able to be treated with CRISPR-Cas9 or babies are able to be born free of genetic diseases, then the cost must be affordable in order to ensure equal access to all. If the cost is too high, distribution of goods and services would not accessible to all, which would violate the tenet of justice (Baker 2016; Evitt, Mascharak, and Altman 2015; Heidari 2017; Hynes, Coller, and Porteus 2017; Kick 2017; and Ormond et al. 2017). However CRISPR-Cas9 technology may be incorporated into medicine, societies worldwide should not allow genetic diseases to become an affliction only to those with low socioeconomic status who cannot afford treatment, the consequence of which would be unshared risk and unequal burden. Further separation into new classes of people would also be a detriment to societies, such as "genetically modified" and "non-genetically modified" people, which may result in one class being viewed as superior over the other (Bosley 2015). Lastly, "designer babies" do not just have implications in regards to nonmaleficence but also justice. Assuming "designer babies" become a reality, if the cost is exorbitant and marketing is targeted to the wealthy, then the poor will be excluded from benefitting from the technology.

Disability rights are not discussed often in the literature yet genetic modifications could very well violate them. Editing out diseases from the human genome gives the impression that disabled people do not have the right to live or perhaps their value in society is lower than able-bodied people (Baker 2016; Hynes, Coller, and Porteus 2017; and Ormond et al. 2017). This would not be equal rights for all. There is fear that tolerance for imperfections will decline over time if parents are given the choice to edit out imperfections (Ormond et al. 2017). Coinciding with the tenet of autonomy, people living with genetic diseases should have the right to accept or decline treatment without discrimination or repercussions. Echoing what was stated under autonomy, assuming genetic modifications become mainstream, laws may need to be enacted to protect parents who choose not to genetically modify their children who have a high risk of acquiring a genetic disease; without this protection, justice and disability rights are not guaranteed (Baumann 2016; Evitt, Mascharak, and Altman 2015). Forcing genetic modifications on anyone, individuals or parents, would be discriminatory and unjustifiable to those who are disabled or afflicted with a genetic disease.

Most often when discussing the rights of those involved in gene editing technology, embryos and children are debated (Werner-Felmayer and Shalev 2015). However, essential contributors to further embryonic research that are often left out of the discussion are women: they are the ones who donate eggs and are therefore the ones who must bear an unequal share of the burden and risks of research through egg donation and perhaps carrying out pregnancies in the future (Werner-Felmayer and Shalev 2015). Women play a crucial role in participating in research, yet shockingly, their rights are rarely mentioned. Their contributions to research should be fairly recognized and should be acknowledged for the risks for which they volunteer if research on gene editing is going to continue, as numerous eggs will need to be harvested from women via a painful procedure (unless eggs are able to be grown from stem cells in the future). Any associated risks to women's health during donation, as well as pregnancy associated with implantation if the technology advances to that stage, must be minimized (Werner-Felmayer and Shalev 2015).

Proposed Solutions to Solve Ethical Dilemmas

The tenants of biomedical ethics conflict when determining how CRISPR-Cas9 technology might be used in gene editing. Because there are risks associated with CRISPR-Cas9 that have not been eliminated, which include off-target edits, unintended secondary effects, and mosaicism, nonmaleficence conflicts with beneficence. Even though it has been demonstrated that CRISPR-Cas9 was used to correct mutated DNA in human embryos and animals, the risks currently do not outweigh the benefits to proceed to treatment of diseases in humans (Qui 2016; Scott 2015; and Zhai, Ng, and Lie 2016). Nonmaleficence also conflicts with autonomy, which is why some argue informed consent is an issue. Since mistakes still occur when editing genes with CRISPR-Cas9, using the technology to edit germline cells that are then used for pregnancy could cause unforeseeable harms to that person and his or her offspring to which he or she did not agree and now has to live with those harms (Baltimore et al. 2015; Baumann 2016; Evitt, Mascharak, and Altman 2015; Lander 2015; Lanphier et al. 2015; Ormond et al. 2015; Qui 2016; Sas and Martin-Lawrenz 2017; and Smolenski 2015). However, parents do have decision making capacity for their children and would make treatment decisions on behalf of their child, thus ensuring that autonomy and beneficence do not conflict by eradicating a genetic disease for their child to ensure higher quality of life. This is only a possibility, though, if the benefits outweigh the harms by improving the effectiveness of CRISPR-Cas9.

Justice also conflicts with nonmaleficence in that if research does not continue in an ethical fashion, class separation could become a reality. If CRISPR-Cas9 technology is not cost controlled, then only the wealthy could have access and then genetic diseases only affect the poor. Another potential class separation would be genetically modified vs. non-genetically modified humans, one of which might be viewed as superior. Lastly, irresponsible research could lead to development of enhancements instead of cures to diseases, which could lead to eugenics and possibly discrimination in society. Those who cannot afford to pay for CRISPR-Cas9 gene edits or those who choose not to genetically modify based on their beliefs could face social harms if protections are not put in place.

Therefore, local and global conversations need to continue to establish guidelines for continued research while considering the tenets of autonomy, beneficence, nonmaleficence, and justice. There is inconsistency in policies in various countries in regards to research on embryos and germline cells in particular. A unanimous consensus may not be feasible due to cultural and societal differences, but there must be some guidelines on which countries can agree. First and foremost, more basic research is needed to understand how genes work and how genetic diseases manifest before CRISPR-Cas9 can be utilized to edit genes to cure diseases. The technology is in an infancy stage and determinations on what to ban and what not to ban cannot be based on fear of uncertainty. Therefore, a total ban is not the answer, but rather clear pathways of research must be established with ethical considerations and proper oversight.

Oversight committees with comprehensive representation should be established and should advise on policies that determine what is acceptable research and what is not. Scientists, ethicists, social scientists, public health officials, clinicians, and the general public should all be included on committees. With every new breakthrough or proposal, policies need to be reassessed (Baltimore et al. 2015; Evitt, Mascharak, and Altman 2015; Hynes, Coller, and Proteus 2017; Lander 2015; Ormond et al. 2017; Sankar and Cho 2015; Sugarman 2015; and Zhai, Ng, and Lie 2016). This ensures beneficence is upheld: research can continue to explore potential cures to debilitating genetic diseases that have no other cure, but are explored in such a way that ethical values are supported.

Basic and preclinical research aimed at gaining a better understanding of genes and genetic diseases must be performed first. This would include experimenting with cell lines, embryos, and animal models, progressing in that order. Continuing to perform edits only on nonviable embryos is a wise decision for the time being, as the technology has not been perfected. Specificity must also be improved, meaning the guide RNA segments must be constructed to ensure better binding to the targeted DNA sequence, thus limiting or eliminating off-target effects (Evitt, Mascharak, and Altman 2015; Hynes, Coller, and Porteus 2017; Ormond et al. 2017; and Scott 2015). If germline editing is going to move forward, animal models proving multigenerational safety and limited side effects must be established before experimenting on humans (Baker 2016; Baltimore et al. 2015; Evitt, Mascharak, and Altman 2015; Ormond et al. 2017; Qui 2016; Sas and Martin-Lawrenz 2017; and Smolenski 2015). If the technology is proven safe and effective in cells, embryos, and animal models, then clinical trials may proceed, followed by postapproval distribution. This research will take many years, but is necessary to ensure safety and effectiveness.

If CRISPR-Cas9 is developed to the point where it can be safely studied in humans, then autonomy needs to be agreed upon in germline cells, meaning stakeholders need to decide if parents have sole decisional capacity or not to use CRISPR-Cas9. Governments need to establish laws to protect citizens from discrimination if they decide not to genetically modify and to ensure equal access to treatment options. Governments also need to establish funding for research since proper regulation and oversight cannot occur if public funds are not utilized and only private funds are utilized. Even though this may not be completely feasible, governments should also enact policies to prohibit genetic modifications for enhancements and restrict gene editing for medical purposes only. All of these suggestions ensure CRISPR-Cas9 is responsibly researched with ethical considerations to satisfy the tenants of autonomy, beneficence, nonmaleficence, and justice.

Legislation Around the World: What is Legally Permissible and What is not

Bans vary around the world in regards to gene editing: some allow edits on embryos and some do not, some allow germline gene edits and some do not, some allow for clinical trials in humans and some do not. What is definitely clear is that there is not a consistent global agreement on what is permissible and what is not. This section will attempt at compiling a brief summary of what is legally permissible, which should suffice for analyzing science fiction for guiding policy implementation in the last chapter.

First, germline edits, which affect not only the individual but all of their offspring, are not entirely banned, but are controversial in many areas of the world and admittedly, they may not be able to be banned entirely throughout the world (Bosley et al. 2015 and Nordberg et al. 2018). Germline edits are banned through legislation or guidelines for reproductive purposes in approximately twenty-nine out of thirty-nine countries studied by Ishii, which includes Canada, Brazil, Australia, the UK, and most western European countries (Ishii 2015). However, countries that have guidelines as opposed to legislation that are amenable are China, Ireland, Japan, and India; the rest have ambiguous guidelines, such as Russia and Argentina (Ishii 2015). An assumption is that the United States has a ban on germline editing, but that is not the case: germline editing (as well as somatic gene editing and gene therapy) is just restricted and research has to be reviewed by the FDA and NIH (Grant 2016 and Ishii 2015). The driving force behind bans is the fear of eugenics, the desire to preserve human dignity, and safety concerns (Nordberg et al. 2018).

China should be addressed briefly separately due to the controversial Jiankui He incident described in the next section. To be clear, China does have a ban on germline edits and embryonic research for reproductive purposes (The Lancet 2018, Normile & Cohen 2018, Wang et al. 2019, and Zhai et al. 2019). The problem lies with the fact that there are not clear penalties defined if this ban is violated (Normile 2018, Normile & Cohen 2018, and Zhai et al. 2019). Many have therefore raised the concern that stricter laws and a clear, regulatory framework with penalties defined for violations need to be established before germline editing continues, perhaps banning it for a five year period until the framework is complete (Cohen 2019, Nordberg et al. 2018, and Wang & Yang 2019). The World Health Organization is already attempting to establish an Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing to address these issues (Cohen 2019).

Smith claims a complete ban on germline editing would be a mistake globally because there are instances where germline editing could be the only option for some couples to conceive (Smith 2019). Some claim that pre-implant genetic diagnosis (PGD), in vitro fertilization (IVF), and assisted reproductive technology (ART) are sufficient for preventing the transmission of genetic disorders. But Smith (2019) points out that PGD is only useful for screening out monogenic disorders, not when both parents are not homozygous for the mutant gene (i.e. neither parent has wild types genes) or if one parent is homozygous for disease inducing gene that is dominant. If parents wish to have children that are genetically related to both of them, then having a donor or adoption are not solutions to their predicament; germline editing may be their only hope for genetically related offspring and limiting such research would prevent parents in this situation from conceiving in the future (Smith 2019). The author made a strong case as to why a complete ban on germline editing globally would be an unethical approach.

In regards to gene editing embryos, political issues have led to strict bans in the US (Blind Baby Maker 2019). Federal funds are prohibited from being used on research for modifying human embryos and embryos cannot be created or destroyed for research (Grant 2016). However, some states do allow for the creation of human embryos with non-federal funds, IRB approval, and approval from a stem cell oversight committee (Ishii 2015). For human embryonic stem cell research, seventeen countries permit the use of surplus embryos from assisted reproductive technology (ART) and fifteen permit the creation of embryos, so long as they are cultured for no longer than fourteen days (Ishii 2015 and Pei et al. 2017). The US, UK, and China are included in the fourteen day embryonic development limit (Pei et al. 2017). Additionally, China requires IRB approval and informed consent from donors (Ishii 2015). Gene editing will never be fully understood if embryonic research does not continue and researchers sometimes cite the fourteen day limit as a hindrance.

Lastly, clinical trials for somatic cell gene editing using CRISPR have taken place in the US and in China for various cancer treatments (Cyranoski 2016, Kick et al. 2017, and Zhai et al. 2016). At this time, both FDA in the US and the EMA in the EU are updating regulations on genetically modified cells to be used for new medicines and therapies, but clinical trials for germline gene editing are strictly banned in Europe (Nordberg et al. 2018).

Jiankui He Shocks the World: The First CRISPR Edited Babies Were Born and the Scientific Community's Reaction

It is important to note that when researching this incident, most of what is available at this time are news articles. While *Science Magazine* and *Nature News* are reputable and the reporters obtained quotes from prominent scientists and ethicists in the field such as Dr. Jennifer Doudna and Dr. David Baltimore, only a few journal articles could be found. The majority of authors condemn the work of Jiankui He due to lacking scientific rigor, transparency, and ethical oversight, in addition to committing fraud and violating the law; but there was one author who supported his work because he claimed He made a breakthrough that the scientific community has yet to appreciate and one author who does not necessarily support He's work, but offers a different explanation as to why He may have pursued impregnating women with gene edited embryos (The Blind Baby Maker 2019, Cohen 2018, Cohen 2019, Enserink 2018, Hoffmann 2019, The Lancet 2018, Mitchell 2019, Normile 2019, Normile 2018, Normile & Cohen 2019, Normile & Cohen

2018, Savulescu & Singer 2019, Wang & Yang 2019, Wang et. al. 2019, Yarborough 2019, Zhai et. al. 2019, and Zhang et. al. 2019).

At the Second International Summit on Human Gene editing in Hong Cong in October 2018 (which I was watching via webcast from the U.S.), Jiankui He announced to the world that a woman had given birth to twin baby girls who were gene edited by He's research team to be HIV resistant (The Blind Baby Maker 2019 and Cohen 2018). According to Wang and Yang (2019), CCR5 (chemokine-related receptor 5) is one of two receptors on white blood cells that the HIV-1 virus uses to infect cells. He theorized that CRISPR-Cas9 could be used to knock out the CCR5 gene in human embryos in attempt to make them resistant to HIV infection, performed these gene edits, impregnated a woman with these embryos, and she gave birth to twin girls in November 2018; however, the evidence is lacking that both girls will actually be resistant to HIV and that the edits were successful (The Blind Baby Maker 2019, Cohen 2018, Enserink 2018, Normile & Cohen 2018, Savulescu & Singer 2019, Wang & Yang 2019, and Zhai et. al. 2019). At the present with the data that is available, it appears that one twin, Lulu, only had one allele that was wild type and one mutant allele making her susceptible to infection while Nana had two mutant alleles, suggesting she is immune to infection via the CCR5 receptor (Wang & Yang 2019). Furthering this, the theory was not scientifically sound because He based his research on knockout experiments in mice that were insufficiently tested (using only four tissue samples and two behavioral tests), the CCR5 knockout he performed is not the only one that is possible, he did not take into account the risk of mosaicism or the introduction of other mutations, and only used one human embryonic stem cell line as opposed to multiple cell lines to prove the edits (Wang & Yang 2019). Without providing details, other authors echoed the lack of scientific validity of He's experiments, citing that risks to safety were not investigated and protocols were not evaluated (The Lancet 2018, Mitchell 2019, and Zhang et. al. 2019).

Clearly, from a scientific standpoint alone, He's research had some serious issues and explains why the scientific community was quick to criticize his work. The National Institute of Health (NIH) in the U.S. and the Association for Science and Technology in China spoke out against He's research, which has also led to an investigation into his unethical practices and a call for legal action against He (Mitchell 2019, Wang et. al. 2019, Zhang et. al. 2019). Addressing legality first, there were Chinese laws that were broken and He is expected to be prosecuted. In China, there is a strict ban on editing human gametes, zygotes, and embryos for reproductive purposes, meaning research can be performed on these so long as they are not implanted into a woman leading to pregnancy (The Lancet 2018, Normile & Cohen 2019, and Wang et. al. 2019). Even though He and his research team violated this ban, there technically is not a defined penalty under the law for violating it, which of course is problematic in dealing with He and potentially others who may violate this in the future (Normile 2018, Normile & Cohen 2018, and Zhai et. al. 2019). However, this was not the extent of his transgressions under the law, which included committing fraud and evading oversight. He avoided oversight by conducting fertilization outside of his university laboratory to evade supervision, raised his own funds for the project, selected a research team who would perform the edits and implantation, did not publish his findings, and faked review documents (Normile 2019, Normile & Cohen 2019, and Normile & Cohen 2018). His practices were fraudulent because in China, it is illegal for HIV positive individuals to receive fertility treatments at IVF clinics; therefore, He and his team utilized non-infected individuals to give blood samples in place of HIV positive research subjects (Normile 2019 and Normile & Cohen 2019). Lastly, he only recruited couples where the father was HIV positive and deceived them by stating on the consent form that the project was involved in the creation of an AIDS vaccine (Normile & Cohen 2018). This also served the purpose of concealing what he was really researching in his laboratory: He was not creating a vaccine but rather was attempting to prove the theory that he could edit out a receptor that allowed HIV to penetrate cells in the embryonic stage and that those embryos were viable. Revisiting the previous paragraph, his theory was not scientifically valid and couples agreeing to the program did not know exactly to what they were agreeing. He even went so far as to offer medical and health insurance and services to the couples and babies in addition to compensation for harms that may arise, which should have been an indication that the research was not substantiated yet (Savulescu & Singer 2019). The average person might not know this is a red flag that the study is not legitimate or legal.

In addition to scientific and legal issues, ethics were also violated through He’s work. Global recommendations have already been made in regards to germline editing, which include forbidding implanting embryos leading to pregnancy because gene editing technology is not advanced enough to prevent off-target edits and mosaicism, thus the safety of such edits is not ensured for clinical applications (Enserink 2018, The Lancet 2018, Wang et. al. 2019, and Zhang et. al. 2019). Some also insist that germline editing should only be pursued to treat diseases where somatic cell editing, PGD, and other preventative measures are insufficient as treatment options; HIV does not fall under one of those three categories (The Blind Baby Maker 2019, Savulescu & Singer 2019, and Wang

& Yang 2019). Ignoring these global recommendations, He put the twins at risk for unintended mutations and potentially other health risks associated with off-target edits or disrupted polygenic gene function, which cannot be determined at this time. Also, the CCR5 receptor is not the only receptor HIV uses to invade cells, therefore the twins are not completely immune to HIV infection genetically speaking, and the risk of HIV contraction can be reduced through other methods like PGD or ART (The Blind Babymaker 2019, Enserink 2018, and Wang & Yang 2019). Performing these edits and impregnating a woman is completely unethical and violates the tenets of beneficence and nonmaleficence, since the girls do not have the intended benefit of being immune to HIV contraction and they may now be susceptible to risks that are unknown.

Other ethical issues were the fact that his research findings and methods were neither transparent nor reviewed for ethical standards. He did not follow the principles of human research because his work did not go through the initial steps of basic research before jumping to a clinical application, nor was his research evaluated and approved by an IRB or equivalent, thus why his research was deemed to have evaded ethical oversight (Mitchell 2019 and Savulescu & Singer 2019). What He was doing in his laboratory was also not transparent. Where he obtained permissions or if he had permissions at all to perform the experiments he did was unclear (Cohen 2018). His methods and findings were not transparent to his patients either, nor did he publish a paper on his findings to support his claim that he was successful (or thought he was successful) at editing embryos to confer HIV resistance (Enserink 2018 and Normile & Cohen 2018). Protocols are in place for a reason for developing drugs and treatments, which are rigorous and could take years, and clinical trials in humans is the last step in proving a drug to be effective. He did not perform sufficient validating experiments prior to human use or consult an ethics review board, which is a violation of the principles of research ethics (Wang & Yang 2019). By not publishing his methods or findings, he did not give the scientific community the opportunity to evaluate them for accuracy, dependability, reliability, thoroughness, or robustness, which is a standard practice.

The issue of lack of transparency also tied into the issue of informed consent. He had couples undergoing his study sign a consent form, but what they signed stated that he was developing a vaccine for AIDS, not that he was performing genetic manipulation on embryos, a process that was not scientifically or ethically validated (Normile & Cohen 2018). He did not inform them of the design of the study, the risks involved in what they were doing, and offered medical and health insurance as incentive to undergo the study (The Blind Baby Maker 2019, Cohen 2018, and Savulescu & Singer 2019). This is outright deception to the couples, as they agreed to one study (developing an AIDS vaccine) but were used in another (germline gene editing of embryos). This, along with not fully describing the risks they were undertaking, is a violation of their autonomous choice because they were not fully informed about the study. The fact that they signed a consent form is completely irrelevant because it lied about what the study really was, therefore, they did not truly give consent. Also, offering health and medical coverage could be viewed as an enticement, depending on the circumstances, since the couple was receiving some monetary compensation for their participation. We do not know if they would have rejected participation if this was not offered. Since Chinese law prohibits HIV positive individuals from utilizing IFV clinical services, the couple may have been desperate to find a means to have children, which may also have influenced their decision to participate and there could therefore be a level of exploitation present. Exploitation could also be an issue if the couple had limited knowledge of science, which also may have prevented them from making an autonomous choice. Regardless of all of these factors and potential factors, they and their daughters now have to live with any consequences that may arise from the deplorable actions of He and his research team. Clearly his research is unethical on many levels, which is why many researchers and ethicists are calling for stricter guidelines, regulations, and laws on germline gene editing (The Blind Baby Maker 2019, Cohen 2018, The Lancet 2018, Mitchell 2019, Normile & Cohen 2019, Wang & Yang 2019, Wang et. al. 2019, Zhai et. al. 2019, and Zhang et. al. 2019).

Only one author, Hoffmann (2019) supported He's work. The reference itself came up as a peer-reviewed journal article, but it is a German journal and I am unsure if that is accurate; therefore, the information in the article may not be reliable. Regardless, Hoffmann offered a differing opinion to the majority. In his article, he was discussing how biotechnology over the last one-hundred years has grown as a field, offering many breakthroughs in medicine and they should be celebrated (Hoffmann 2019). Among those celebrations should be Jiankui He, who was not the first person to edit human embryos, but was the first to impregnated a woman with gene edited embryos (Hoffmann 2019). Hoffmann thinks the public outcry against He is unjustified, but not surprising, since a similar reaction was observed when cloning and artificial insemination were first introduced, which became achievements that led to Nobel prizes (Hoffmann 2019). He also defended He, insisting that he had performed gene edits on over three-hundred embryos prior to impregnating a woman to prove his gene edits were successful and did not result in off-target edits or mosaicism, yet still could not convince scientists that his work met scientific and medical standards (Hoffmann 2019). Therefore, Hoffmann thinks that He's work may receive criticism now, as artificial insemination and cloning did, but later the scientific community will be persuaded and He's work will eventually be viewed as groundbreaking.

This opinion by Hoffmann is the complete opposite of the scientific community at the moment. He's work is certainly not viewed as scientifically valid, groundbreaking, legal, or ethical, as described above. Attitudes about what is ethically permissible may change over time as basic and clinical research further our understanding of genetics and gene editing, as well as rectify safety concerns of CRISPR-Cas systems present right now. As the technology improves, ethical concerns can be reevaluated. Therefore, Hoffmann may be correct that in the future, He's research could be the first step in moving toward human germline editing and recognition for his contributions will follow. Or perhaps not, but this will be revealed in due time.

One last article to discuss regarding the He incident was written by Yarborough (2019) who did not condone He's research, but offered a less harsh explanation as to why he pursued the project other than recklessly implementing a poorly developed theory to satisfy the desire to acquire fame. As stated in many journal and news articles, most authors denounced He's research due to lacking scientific validity, ethical integrity, and/or legal permissibility (The Blind Baby Maker 2019, Cohen 2018, Cohen 2019, Enserink 2018, The Lancet 2018, Mitchell 2019, Normile 2019, Normile 2018, Normile & Cohen 2019, Normile & Cohen 2018, Savulescu & Singer 2019, Wang & Yang 2019, Wang et. al. 2019, Zhai et. al. 2019, and Zhang et. al. 2019). While these claims are legitimate, He did not necessarily pursue this avenue of research with malicious intent, but truly believed he was acting under the tenet of beneficence by seeking a means of preventing HIV transmission in children. But Yarborough (2019) claims that education in biomedical research is failing to equip future researchers with the skills necessary for critically evaluating their work to comply with ethical standards, that merely having a “good” intention is not enough to justify projects and methods. Moral ambiguity sometimes presents itself in research and scientists do not always know how to overcome it and achieve ethical conclusions because they were not taught how (Yarborough 2019). Of course, beneficence is the driving force behind most research, as most biomedical research is geared toward curing some disease. But complying with the tenet of beneficence does not mean all other tenets can be ignored and when an ethical dilemma between the tenets arises, a risk/benefit analysis must be completed to choose the best course of action. CRISPR-Cas systems are very new technologies to edit genes and are not fully developed yet, which means there are many ethical issues surrounding them, but current science curricula do not include training on how to deal with these issues surrounding CRISPR-Cas gene editing and when in the field, scientists often rely on IRBs for review rather than thinking through the ethics themselves (Yarborough 2019). Therefore, it is a very real possibility that He’s training in biomedical research (and most science majors, of course) focused on science and was lacking in ethical training. His ignorance led to violating ethical norms because he was not educated enough in ethical reasoning to know what he was doing was ethically wrong. Again, Yarborough (2019) was not justifying nor condoning He’s research, but provided an alternative explanation: He’s education failed him. With this in mind, Yarborough (2019) concluded that science curricula needs to include courses in liberal arts such as philosophy, history of science, and epistemology, especially in undergraduate curricula, to foster the development of critical thinking and moral imagination to better equip future researchers with the skills to ethically evaluate projects, methods, and results. He might not have pursued impregnating a woman with a germline edited embryo if he was equipped with the capacity to see the ethical implications of his actions.

CHAPTER 2: FILM AND LITERATURE REVIEW: HOW SCIENCE FICTION INFLUENCES PERCEPTIONS OF GENE EDITING AND ADDRESSES AUTONOMY

Introduction

Under the tenet of autonomy, bioethical concerns that arise related to gene editing (as well as genetic engineering and basic genetic research) are issues of self vs. offspring, which could also be viewed as genetic manipulations of somatic cells (self) vs. germline cells (offspring); issues of personhood, as embryos, unborn persons, and future generations would be affected by genetic manipulations performed to germline cells; and decision making capacity, in which informed consent plays a role. Self vs. offspring issues are present in *Beggars in Spain* (Kress 1991) and *Change Agent* (Suarez 2017), as gene edits that were performed at the embryonic stage were heritable. The question of who has rights under personhood was explored in *Brave New World*, both in the novel and films (Babbin 1980, Huxley 1932, and Joyce 1998), *Beggars in Spain* (Kress 1991), *Star Trek: Enterprise* season 4 episodes 4-6 (*Borderland, Cold Station 12,* and *The Augments*) (LaZebnik 2004, Brennert 2004, and Sussman 2004, respectively), *Next* (Crichton 2006), and *Jupiter Ascending* (Hill 2015). Decision making capacity and violations to informed consent were the most dominant issues apparent in the following novels and films: *The Island of Dr. Moreau* (Pressman 1996, Stelloff 1977, and Wells 2004), *Brave New World* (Babbin 1980, Huxley 1932, and Joyce 1998), *Friday* (Heinlein 1982), *Beggars in Spain* (Kress 1993), *X-Men* (Donner 2000), *The Neanderthal Parallax* (Sawyer 2002, Sawyer 2003, & Sawyer 2003) *My Sister's Keeper* (Furst 2009 and Picoult 2003), *Cowl* (Asher 2004), *Tankborn* (Sandler 2011), *Intrusion* (MacLeod 2012), *The Amazing Spider-Man* (Arad 2012), *The*

Atlantis Gene (Riddle 2013), *Change Agent* (Suarez 2017), *Monsters* (Turnbull 2017), *The Perfect 46* (Bonowicz 2014), *The Titan* (Amel 2018), *Equals* (Pruss 2015), *ReEvolution* (Grant 2019).

Issues of Self vs. Offspring or Somatic vs. Germline Cells

Beggars in Spain (Kress 1991)

Imagine the potential of humans if only they did not have to waste hours every day sleeping, but rather could use those hours to learn and work. Nancy Kress did just that in her novel *Beggars in Spain* (Kress 1991). In the story, geneticists claimed that most processes that occur during sleep can occur during wakefulness and sleep is an evolutionary action that no longer serves a purpose in modern society, as man does not have to protect himself from predators by hiding, which was accomplished by sleeping in a secluded place. When the main character, Leisha, was fifteen years of age, one-thousand and eighty-two children were genetically engineered to be sleepless (Kress 1991). Geneticists had only intended to affect the children they edited when they made the edits. However, it was not until the first sleepless child grew to adulthood and had a child with a sleeper that geneticists realized the sleepless gene was the dominant gene over sleep genes. They determined that all offspring of sleepless people would also be sleepless.

This novel demonstrated the very real possibility that if gene editing becomes prevalent, the line between self and offspring is blurred. The sleepless gene was clearly made in the germline as opposed to somatic cells, as the gene was passed on to the offspring of the sleepless. The geneticists did not intend this, yet their actions led to this happening anyway. Because genetics is currently not advanced enough to have mapped every gene and fully understand polygenic genes, editing germline cells could incorporate edits in future generations, whether intentionally or unintentionally, and could have either positive or negative effects on those receiving the gene edits. This is why there is a ban on germline edits on viable embryos being implanted for pregnancy: the downstream effects may not be known at this time. Kress beautifully incorporates this bioethical issue in her novel about genetically engineering sleepless people (Kress 1991).

Change Agent (Suarez 2017)

Change Agent was an action-packed science fiction novel taking place in the not too distant future about an Interpol Geospatial Analysis Specialist in the Genetic Crime Division, Ken Durand, who tracks down illegal CRISPR laboratories and crime syndicates (Suarez 2017). Every tenet of biomedical ethics was touched upon in this novel. In regards to autonomy and specifically somatic vs. germline, two separate instances of this ethical issue were incorporated into this novel. The first instance had to do with germline edits, which would be passed down in future generations of children who were edited in the embryo stage. There was a United Nations approved list of genes that could be legally edited, which included genes for genetic diseases, and genes that could be illegally edited to increase the quality and quantity of life, which required the utilization of black market laboratories (Suarez 2017). Regardless if the edits were legal or illegal, they were heritable because they were made to the germline. Since there was an approved list through the United Nations, one can conclude that there was a global consensus on what edits were acceptable and which ones were not. This will be further discussed in beneficence and nonmaleficence below.

The other instance of this issues arising was when the main character was edited against his will. He was miraculously edited as a full-grown adult, which was thought to be impossible (in reality: it is impossible), as thirty-five trillion cells would need to have their genetic sequence edited all at once (Suarez 2017). A delivery system to achieve this did not exist, or so they thought. On the outside, he was edited to look like Marcus Wyckes, the leader of the Huli Jing crime syndicate, in hopes that he would be arrested and possibly executed in the place of the real Marcus Wyckes. As the story continued, Durand sought the help of a geneticist to confirm his true identity and figure out how to return him to his actual appearance. What he learned along his journey was the Huli Jing had developed a change agent to edit the outside appearance of adults. The reason for developing such an agent was to deceive law enforcement: key members of the Huli Jing kept turning up dead (the Nine Tails), yet the cartel remained active. Durand determined that they were not actually dying, but were editing unrelated adults into the key members so the authorities believed them to be dead. He was able to make this determination because of what happened to him, as he was the only survivor of the transformation.

After connecting with geneticist Brian Frey, they were able to determine that Durand was only edited on the outside (Suarez 2017). All of his internal organs contained his own DNA. Therefore, this large scale edit was only partially completed on somatic cells and only on genes that controlled appearance, which were a duplicate of Wyckes' genes encoding for skin color, build, and chromatophore tattoos. By the end of the novel, Frey was able to acquire the change agent and use Durand's DNA to turn him back into himself.

As described, *Change Agent* addressed somatic vs. germline edits (Suarez 2017). Children received germline edits by being edited in the embryo stage and Durand had somatic cells edited to change his outward appearance into the identity of another individual. Editing the germline is feasible for monogenic genes currently, even though in the novel genetics were further advanced to incorporate quality and quantity of life edits (physical traits, bone density, athleticism, memory, etc.) in addition to eliminating genes for heritable diseases. Editing somatic cells is also feasible, but not currently to the degree Durand was in the novel. At this time it is scientifically impossible to gene edit someone's outward appearance as a full-grown adult, but this imaginative scientific feat provided the basis for a riveting novel.

Issues of Personhood, Including Embryos, Unborn Persons, and Future Generations

Brave New World (Huxley 1932, Babbin 1980, and Joyce 1998)

In 1932, Aldous Huxley published a novel that would continue to be a classical read for generations to come, *Brave New World* (Huxley 1932). This novel was adapted into not one, but two films, with the 1980 film being a very accurate depiction of the novel and the 1998 version a loose depiction (Babbin 1980 and Joyce 1998). It was written before significant breakthrough genetics research, yet portrayed an interesting potential future where humans were no longer birthed, but grown in incubators. They had developed a process called the Bokanovsky Process, which allowed one embryo to bud into ninety-six embryos producing ninety-six identical twins, and the Podsnap's Technique, which sped up the process of egg maturation, to allow for the mass production of people totaling approximately eleven-thousand people in one-hundred and fifty batches in two years time by combining these techniques (Huxley 1932). The reason for the mass production of humans was to have an abundance of Gamma, Delta, and Epsilon classes of people for different levels of labor. The upper classes of people, Alphas and Betas, were still created with one embryo for one person and did more intellectual work. By using this system of non-viviparous procreation, embryos were grown in a laboratory and class was predetermined by hatchery workers (who consisted of Alphas and Betas). Clearly, the manipulation of embryos destined for the lower classes meant they had zero rights under personhood, as they were mass produced into batches of identical twins lacking individuality once born. They were created with only one purpose: to serve the upper classes by doing undesirable manual labor. This class separation will be discussed further under justice.

Beggars in Spain (Kress 1991)

As mentioned above under somatic vs. germline and self vs. offspring, *Beggars in Spain* demonstrated how easily future generations could be affected by gene edits, whether intentionally or unintentionally (Kress 1991). Ethicists argue against germline edits for this reason: editing the germline would mean future generations would be edited without having given consent. Even though future generations are nonexistent people and therefore do not have the same rights under personhood, it is still a concern because they will be born with the edits, yet may not want them. Since the sleepless gene in *Beggars in Spain* was dominant and passed down, all future descendants from the sleepless will also be sleepless (Kress 1991). This may or may not be a desirable outcome and future generations may or may not have wanted to be sleepless (although none of the sleepless had a choice either; their parents chose that for them, which is discussed below under informed consent/decision making capacity). Whether desired or not, researchers forced an evolutionary adaptation into the human race for generations to come. Although fiction, this potentiality seemed very plausible, maybe not with a sleepless gene but rather other genes, and why ethicists offer this warning.

Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and The Augments (Episode 6) (Brennert 2004, LaZebnik 2004, and Sussman 2004)

Although these episodes referenced the eugenics wars, the details of the war were lacking. Via conversations through various characters, the wars took place on Earth in the 1990's when ambitious scientists desired to improve the human race utilizing genetic engineering, but instead caused the deaths of thirty-million people. After the war, genetic engineering of humans was banned because of the mass destruction to the species. Interestingly, the leftover modified embryos were not destroyed, but rather were stored in Cold Station 12 in outer space. The reason for storing the embryos was due to the inability of global governments to reach a consensus on what to do with the embryos once they decided genetically modified humans were a threat to society and could no longer be produced. Storage seemed like the best option as opposed to destruction. It seemed as though the society on Earth at the time valued the potential of life embryos could bring that they felt destroying the embryos would be disrespectful. Even though the historic events are fictional, they allude to current issues surrounding research on human embryos. The non-fictitious global consensus is that genetically modified human embryos should not be implanted for pregnancy because of the uncertainties that surround gene editing. Also, there are people who believe embryos should be afforded the same rights as people under autonomy and should not be experimented on in the first place. These *Star Trek* episodes subtly addressed ethical debates surrounding the moral status of embryos for research purposes.

Next (Crichton 2006)

Michael Crichton's *Next* incorporated too many biomedical issues to discuss, although the format was quite unique by weaving fictional characters, true events, and debunked news articles together into one main story with various side stories (Crichton 2006). The character, Frank Burnet, was based off of an actual person involved in the court case Moore v. Reagents of the University of California where the patient's cells were taken under the guise of routine medical procedures, but were then utilized to create a cell line that the physician sold to a pharmaceutical company amassing a sizeable profit, none of which was given to the patient (Crichton 2006). Burnet stated in court he consulted a lawyer because "'[t]hey were my cells, from my body. I thought I should have something to say about what was done to them,'" (Crichton 2006). The problem was Burnet never signed a consent form authorizing the sale nor commercial use of his cells. The court ruled that Burnet did not actually have the rights to his own tissues because they were considered waste and no longer belong to the individual once they have left the body. Since they are "medical waste", the university and researchers then have the right to do whatever they wish to the tissues, including patenting cell lines and selling them for a profit. Burnet was also not entitled to any of the profits because the tissues no longer belonged to him and the researchers are the inventors of the cell line.

Why did the University of California and BioGen (the fictional company to which they were sold) find the cells so valuable (Crichton 2006)? Burnet's cells produced a large amount of cytokines, which fight cancer cells and are therefore a rare find, and the ruling meant BioGen owned Burnet's cells (Crichton 2006). The problem with this ruling is the lawyers who worked for BioGen twisted the meaning and decided Burnet's cells could be taken from him or his direct descendants (his daughter and grandson) whenever they needed them, forcibly if necessary, as they were walking around with "stolen property" (Crichton 2006). The company hired a bounty hunter who attempted to kidnap the daughter and grandson in order to steal their cells. When taken to court, the judge ruled in favor of the Burnets, citing the previous ruling stated the company owned the cell line from tissue that was already removed and did not grant them the right to harvest cells from any individual just because they own the cell line (Crichton 2006). Any reasonable person can see that the lawyers at BioGen were out of line thinking they did not need permission to collect more cells from Burnet or his relatives. They did not treat Frank, Alex, or Jaime as people with their own bodily autonomy, but rather as bodily tissues from which they could collect cells at any time. The ludicrosity of this family being seen as walking around with "stolen property" is astounding.

Another issue with this is the patented cell line was not actually genetically modified in any way: the company just grew them and sold them. Yet the company was granted a patent for them and the university and BioGen were listed as the "inventors". The patent granted and the court ruling are perplexing, as neither the university nor the company had seemed to invent anything: the cell line naturally synthesized an excess of cytokines and was not therefore due to a genetic modification incorporated by a researcher. BioGen and the university were making three billion dollars in profits by growing more cells they stole from a patient, not because they actually invented a new cell line through research and gene editing. Many would argue it is unethical to not recognize the patient as being a major contributing factor to the company's and university's success and therefore should receive some compensation for having his cells stolen and sold without his permission. Lastly, even though there is an issue here with informed consent, it will not be discussed in the following section because it is not an informed consent issue relating to gene editing.

Jupiter Ascending (Hill 2015)

According to this science fiction tale, humans did not originate on Earth, but rather are descendants from people from a planet called Orous. There were indigenous people on Earth, but humans as they are known today were created by gene splicing the indigenous people with genes from Orous humans and then the genetically modified with Orous genes were allowed to populate the Earth. But according to Orous royals, Earth was just one of thousands of farm planets, a resource for human harvests. The hybrid future generations created were meant to serve one purpose: provide genetic material to produce the ReGenX formula that reversed aging by replacing deteriorating cells with new ones, since genes have an expiration date genetically programmed. It was unclear exactly what genes were introduced into the indigenous Earth population to produce modern humans, but people were completely unaware they were descendants of humans from another planet. Whatever genes the Orous humans spliced into the Earth humans genomes, they affected the entire global population. Their rights were violated under autonomy because their new genes made them ideal resources for genetic material for the Orous to harvest when they believed the time to be right. The Orous royals did not see them as equal humans, but rather just assets designed to generate profit for their business. They essentially did not have equivalent status under personhood as the Orous humans. Under autonomy, all humans should be afforded the same status and rights under personhood because all living humans are persons. The Orous were wrong to genetically modify Earth humans in order to exploit them by treating them as merely bodies from which to take genetic material to synthesize an anti-aging formula.

Issues of Decision Making Capacity and Informed Consent

The Island of Dr. Moreau (Wells 2004, Pressman 1996, and Steloff 1977)

Animals, as they are not humans, do not have the same rights under biomedical ethics, but are still afforded some protection, especially in research. In *The Island of Dr. Moreau*, Dr. Moreau was conducting controversial experimentation on animals by attempting to turn them into humans (Wells 2004 (note: the novel was originally published in 1896, but the eText version published in 2004 was read)). This novel was also adapted into two films; however, the 1977 version was a much truer representation of the novel than the 1996 abomination of a film (Pressman 1996 and Steloff 1977). As genetics knowledge was limited in 1896, Dr. Moreau utilized vivisection and surgery to achieve humanistic appearance and speech while genetic engineering was used in both films. The two major issues with the experimentation implemented by Dr. Moreau was the lack of informed consent, as animals are unable to provide this, and therefore they must relinquish decision making capacity to humans, which Dr. Moreau decided on their behalf for his experiments. In the 1977 film, Andrew (Edward in the other versions) was also injected with the gene editing serum to turn him into an animal against his will (Steloff 1977). Dr. Moreau performed these experiments for his own interests and was displeased when the animals began to revert to their original forms and behaviors, thus rejecting being human and the laws he created to keep the beast people in submission. Interestingly, by rejecting the changes, they were reclaiming their right to autonomy.

Brave New World (Huxley 1932, Babbin 1980, and Joyce 1998)

As mentioned above, in *Brave New World,* hatchery workers were granted decision making capacity by deciding on which batches were made into which classes, although the 1998 version did not go into details about this (Babbin 1980, Huxley 1932, and Joyce 1998). No one had a choice as to which class they belonged in society and therefore had limited options in career paths. Not only were these decisions made at the embryo stage, but they were also conditioned through hypnosis techniques while babies and children to convince them to believe they were happy to belong to their designated class and were constantly fed drugs to make them unable to feel negative feelings. Women were also kept sterile (seventy percent of the female population) or fertile (thirty percent of the population) and were expected to give eggs at the right time to maintain the population (Babbin 1980 and Huxley 1932). Again, this was decided at the embryo stage and they were unable to decide if they wanted to donate eggs or not. These are clear violations of decision making capacity and informed consent. The choice to make decisions for themselves regarding procreation was not given to any individuals.

Friday (Heinlein 1982)

Friday by Robert Heinlein was another futuristic novel involving a combat courier, Marjorie “Friday” Baldwin, who was an artificial person genetically engineered in a laboratory: “My mother was a test tube, my father was a knife” was often quoted by her and other artificial persons (Heinlein 1982). Her job was often dangerous carrying sensitive packages, thus why she was trained in combat in order to guarantee delivery. She had unique genetically engineered abilities that allowed her to excel at her job, which is discussed in the nonmaleficence section. She was also genetically engineered to be reversibly sterile and other APs (artificial persons) were engineered to be just sterile. This violated decision making capacity and informed consent, as APs did not choose if they were to be sterile or not, which did not give them the autonomous choice to become parents. Also, they could be genetically engineered for doxy work, sold, or offered an indentured servant contract when they were adults. As APs, they did not have many career options because by law, they were not viewed as human beings. This type of discrimination will be expanded upon in the justice section. Essentially, they did not have full autonomy over their lives, their reproductive ability, or genetically engineered abilities.

X-Men (Donner 2000), X-Men: United (Donner 2003), and The Last Stand (Donner 2006)

Initially, I debated including cross-genre science fiction and superhero/comic book references, but ultimately decided to add them, as they are popular stories and universally recognized by a wide audience. In these films, two groups exist: humans and mutants. Mutants are endowed with special abilities due to possessing the x-gene, which has unknown origins, but every ability is unique to the individual. This will be described further in the nonmaleficence section. There were a few instances depicting autonomy being violated, mainly, people being edited against their will, mutants being subjected to experimentation against their will, or mutants being administered a cure against their will.

Firstly, in *X-men*, Magneto believes that mutants are the future of the world, not humans (Donner 2000). Humans discriminate against mutants and are sometimes violent toward them due to fear. Magneto grew tired of humans behavior toward mutants, especially since he was Jewish and Holocost survivor. Therefore, he invented a machine that emits radiation that would cause the development of the x-mutation in humans upon exposure, but would not affect mutants, as they already possessed the x-gene. Since his power was the ability to generate electromagnetic fields, he was able to use this machine to amplify his power creating the field of radiation. Magneto was successful at mutating one human, a senator who wished to enact a mutant registration act (just like the Nazis did for the Jewish population during World War II). But the artificially induced mutation was lethal, which Magneto did not discover until later, but ultimately did not care. His plan was to mutate the world leaders who were to gather on Ellis Island and mutate all humans living in New York City, but in order to operate the machine, he kidnapped Rogue. Her ability was to extract the life force of another human or mutant, which enabled her to temporarily use another mutant's ability, thus she could operate the radiation machine in Magneto's place because the amount of radiation needed would kill the operator. This violation of autonomy was two-fold: humans did not choose to be mutated and Rogue did not choose to utilizer her powers to operate the machine and therefore inflict radiation on humans. If she had not been rescued by Wolverine and the X-men team, she and all of the humans infected would have died.

In the second film *X-men: United*, Stiker performed many experiments on mutants against their will (Donner 2003). Striker's son was a mutant who could psychically induce hallucinations in people and mutants. His brain fluid was harvested and developed into a serum, which Striker applied to mutant's necks in order to control them. Jason, his son, was physically handicapped and held against his will in order for Striker and his research team to continuously collect Jason's brain fluid. Wolverine also discovered Striker was the scientist who infused his skeleton with adamantium, an indestructible metal, and gave him retractable adamantium claws as weapons. Wolverine was able to survive the experiment, as well as one other female mutant, due to their true ability: rapid cell regeneration or healing. Stiker insisted that Wolverine volunteered for the procedure, but this could not be verified. Given that Striker was experimenting on and mind controlling other mutants, it is very possible he was not telling the truth to Wolverine. Lastly, Professor Xavier was being mind controlled by Stiker through Jason to use his telepathic abilities to kill all the mutants through the machine, Cerebro. Magneto attempted to force Xavier to then kill all the humans instead. Clearly, Striker had complete disregard for the autonomous decision making capacity of mutants and used their abilities for his own gain.

In the final movie in this series, a cure for the mutant gene was developed (Donner 2006). Rogue, as she was unable to touch anyone due to her power of absorbing life force, was excited for the cure because she longed for physical contact without hurting people. Storm was outraged by the cure and stated the mutant gene cannot be cured because there is nothing wrong with mutants, meaning being a mutant was not equivalent to having a disease. Ultimately, Rogue made the decision for herself to take the cure, which finally enabled her to hold her boyfriend's hand at the end. In contrast, Angel was unsure about taking the cure, but was obviously being coerced by his father. Even displaying an emotional outburst on the medical table prior to being injected, his father continued to try to convince him he would be alright and it would be over quickly. Angel was forced to break free of his restraints and escape through the window. As his name indicates, he possessed wings and therefore could fly. Magneto and Mystique were given the cure against their will, as the military had weaponized it in the form of darts similar to tranquilizers. This demonstrated Magneto's insistence that humans wanted to exterminate them and would find a way to involuntarily administer the cure. Mystique was shot because she stepped in front of Magneto to block the dart. She instinctively chose to protect Magneto in a moment of danger, but she did not truly wish to give up her mutant ability (being able to morph into any person), thus violating her decision making capacity. Magneto was stabbed with several darts toward the end of the movie because he was causing vast destruction in San Francisco in attempts to liberate the child from whom the cure was developed. Wolverine, Storm, and Beast did this to Magneto to stop him from starting a war against humans. As well intentioned as they were, they violated Magneto's right to choose the cure or not.

In addition, Jimmy was the target of Magneto's attack. Jimmy was able to suppress the abilities of other mutants when they were in close proximity to him. He was kept in a medical facility where he was studied and a cure was developed by a research team who analyzed his genes. It was an antibody that suppressed the mutant x-gene. It was never made clear whether this mutant child or his parents agreed to the study or the use of his genes to develop a cure against the mutant gene. Therefore, it is unknown if informed consent and decision making capacity were violated or not.

The Neanderthal Parallax trilogy (Hominids, Humans, and Hybrids) (Sawyer 2002, 2003, and 2003)

This trilogy was a very interesting tale where two parallel universes emerged on Earth after The Great Leap Forward where in one parallel universe, the species *homo sapiens* were endowed with a higher level of consciousness and in the other parallel universe, *homo neanderthalensis* received higher consciousness. The opposite species in either world were extinct: *homo neanderthalensis* were extinct because *homo sapiens* were violent toward other human species and *homo sapiens* in the neanderthal world because they lacked the intelligence to survive. By chance, two neanderthals who were physicists, Drs. Ponter Boddit and Adikor Huld, developed a quantum computer and by accident, opened a portal to the parallel universe where Ponter was transported. There, he met Dr. Mary Vaughn, an expert geneticist specializing in ancient DNA extraction; Dr. Louise Benoit, a physicist studying neutrinos; and Dr. Reuben Montego, a medical doctor. They assisted in teaching Ponter about their world and vice versa. There were very distinct differences, including total population, environmental damage vs. preservation, technology, clothing, lifestyle, existence of religion vs. no religion, sexuality, and justice systems. The neanderthals were much more advanced technologically, medically, and existed in a peaceful world without destroying ecosystems or waging war. Ponter was able to return home when Adikor was able to re-open the portal, then they worked together to open the portal permanently to allow travel between the worlds. They believed the exchange of knowledge would be beneficial to both worlds.

Mary discussed extensively with Ponter and a woman, Bandra, about their system of justice and how they punished criminals. In the neanderthal world, any person who was convicted of a violent crime was sterilized to prevent the transmission of their genes to future generations since they studied genetics extensively and knew that violent behavior had a genetic component. Crimes were rare in recent times because everyone had a companion installed in their arms, which was a small computer that recorded their whole lives and could be accessed in the alabi archives by a judge during a trial or at any time by the individual. However, if a crime was committed, the punishment was also applied to any relative who shared at least fifty-percent of genes with the criminal: parents, siblings, and children. Mary was astounded and insisted that this was a violation of individual rights, arguing that the relatives of the criminal were innocent and being punished for a crime which they did not commit. Ponter and Bandra stated that this process was for the betterment of society as a whole and was not just about individual rights. Everyone benefited from such a process because the entire species is protected and improved. Mary questioned how do they know which traits to eliminate, to which the answer was excessive violence, selfishness, abuse toward children, heritable genetic diseases, and intellectual disability. In contrast, in the *homo sapien* world, humans value the individual's right to procreate. Bandra challenged this, conjecturing that perhaps that value came at a great cost to their society.

Following the tenet of autonomy, Mary is correct: individual rights are being violated by being forcibly sterilized for a crime the individual person did not commit. But if society as a whole has laws in place where this is the punishment and the law was agreed upon by everyone, informed consent may not be violated. Everyone knows the law and by not overturning it, they technically agree to it. Whether the law is just or not is debatable, but the citizens of the neanderthal world are informed of the repercussions of violent crimes. Their society functions very well and is almost completely free of violence; therefore, their people seem content abiding by this law.

Cowl (Asher 2004)

In the novel *Cowl* by Neil Asher, three characters were genetically modified and/or cloned without making the decisions for themselves: Tack, Aconite, and Cowl (Asher 2004). Tack was cloned from the DNA obtained from a CIA agent who had died two-hundred years prior, grown in a vat (probably an artificial womb of sorts), and had a semi-artificial intelligent computer surgically implanted at the base of his skull, thus making him the ideal programmable killer through training and uploading (Asher 2004). He was later modified further to enhance his musculature for martial arts and given cerebral grafts for higher intelligence and reaction times, but was also reprogrammed against his will to make him submissive to Traveler, although this overwrote the programming that made him a heartless killer, thus allowed Tack to experience emotions for the first time (Asher 2004). Aconite and Cowl, who were sister and brother, were genetically engineered by their mother. She wanted to create an exoskeleton for protection, but failed with Aconite who only had tougher skin and legs and arms like a fiddler-crab due to the addition of those genes (Asher 2004). However, she was successful with Cowl who possessed an exoskeleton and lacked eyes and a nose due to genes from a scarabaeid beetle and an aerogel grid sensitive to light radiation fused on the exoskeleton (replacing the need for eyes) interfaced with a semi-AI in the skull (Asher 2004). Their mother unethically experimented on her own children to, in her eyes, advance the human race through genetic recombination research replacing some human genes with animal genes and incorporating the semi-AI interface. Tack, Aconite, and Cowl all had this in common: they were modified with enhancements or a non-human outward appearance without having given consent for any procedures done to them.

Tankborn (Sandler 2011)

Genetically engineered non-humans (GENs) in *Tankborn* by Karen Sandler had very similar issues to artificial persons in *Friday* and were similar to Tack, Aconite, and Cowl in *Cowl* (Heinlein 1982, Asher 2004, and Sandler 2011). GENs were also genetically engineered with abilities to assist in specific types of work, such as manual labor, child care, technology, etc., and were sold at the age of fifteen to households where they would work for the rest of their lives. This was achieved by splicing animal genes into their human genes. Female GENs were also made sterile and therefore did not have the option to bear children.

If a human child was born with an abnormality, then the parents could choose to have the child genetically altered and placed in the tank to regenerate before the age of four, obviously having sole decision making capacity to make healthcare decisions for their children. This part is actually acceptable under the tenet of autonomy. However, if the edits were too extensive or not what they expected, the parents could discard the child and allow them to become full GENs. The main character, Kayla, was a GEN who was once human: she was born without arms and was modified with animal DNA to grow exceptionally strong arms.

Lastly, if enforcers decided GENs were uncooperative or broke laws, they could have their entire memories and personalities erased and replaced, since GENs also had computerized sub-neural networks with a dermal interface, and they could be monitored on the grid at any given moment. This society did not allow the GENs to have any decision making capacity over their lives, whether or not to procreate, or their genetic engineering, and they certainly did not have the ability to consent or dissent to any procedures done to them.

Beggars in Spain (Kress 1991) and Change Agent (Suarez 2017)

Already mentioned in the sections above, parents had the decision making capacity in *Beggars in Spain* and *Change Agent* to edit their children in the embryonic state (Kress 1991 and Suarez 2017). In regards to making edits that provide health benefits to the child, this is actually acceptable under autonomy. In *Beggars in Spain*, being sleepless had other beneficial side effects, such as higher intelligence and no depression (Kress 1991). But whether being sleepless alone is a medical benefit warranting edits is a bit unclear; therefore, allowing parents to make such an edit might not be acceptable under the tenet of autonomy. In *Change Agent,* making the decision to edit children to prevent a heritable disease was legal and the main character had made the decision with his wife to edit their daughter, Mia, to prevent her from being blind (Suarez 2017). This was an acceptable decision to make, as her parents were providing medical benefit by making such a decision. However, the black markets were offering the opportunity for designer babies and enhancements, which is not necessarily acceptable for parents to decide. This will be elaborated on in the nonmaleficence section.

A twist of parental decision making capacity was seen with Dr. Brian Frey who had achondroplasia, which is one type of dwarfism. When he met Ken Durand, during their first conversation he stated that achondroplasia was easily correctable in vitro through a simple modification to eliminate the mutation in the third receptor of the growth factor gene (Suarez 2017). But his mother was unable to even make the decision to have the edit, as it was not on the UN list of approval. Therefore, in words less crude than his exact ones, he has had to endure a life where his height only allows him to reach people's waists. Although he was relatively healthy otherwise, he insinuated that having a form of dwarfism hindered his social and professional life. The people who approved the UN list must have deemed that achondroplasia was not a debilitating genetic disease. But Dr. Frey had a point: his mother was not able to make the decision for him before conceiving or during pregnancy to prevent the development of achondroplasia because that edit was illegal since it must have been viewed as cosmetic or an enhancement. He was not able to make the decision as an adult to not have the disease either. Based on his statement, if he was able to make the decision himself, he would have chosen to be edited. He nor his mother had the decision making capacity to alter his disease state.

My Sister's Keeper (Picoult 2003 and Furst 2009)

My Sister's Keeper by Jody Picoult explored a clear violation of parental decision making capacity, which was adapted into a relatively accurate film in 2009 (Furst 2009 and Picoult 2003). Anna's sister, Kate, was diagnosed with acute promyelocytic leukemia and Anna was born to be an allogeneic donor, meaning a perfect genetic match to her sibling, through pre-implantation genetic diagnosis (PGD). The extent to which Anna was expected to donate will be discussed in nonmaleficence, but in summary, her parents essentially used her to harvest whatever they needed for Kate: cord blood, blood cells, bone marrow, and stem cells. In order to survive, Kate would need a kidney next, which would hinder Anna's quality of life. Her parents expected her to just give her kidney to her sister, but she no longer wished to donate any of her body parts when she reached the age of thirteen (eleven in the film). The conflict was as a minor by law, parents give consent on their children's behalf and have decision making capacity for medical procedures. Even if Anna protested, they could sign the documents giving doctors and the hospital consent for her. Therefore, she sought the assistance of a lawyer to sue her parents for medical emancipation and the rights to her own body. Anna and her lawyer, Cambell, won her case and he was declared her medical power of attorney for more difficult decisions, as her parents were deemed unable to make decisions in Anna's best interest and were only capable of making decisions that prolonged Kate's life. The ending is where the stories deviated quite a bit: in the novel, Anna was declared brain dead after a car crash and Cambell made the decision to donate Anna's kidney to Kate, which allowed Kate to live a fairly normal life; in the film, Kate died in the hospital of renal failure and Anna lived a normal life (Furst 2009 and Picoult 2003). Ironically, the lawsuit was rendered moot in the novel because Anna died unexpectedly and she did what she was genetically created to do: save her sister.

Intrusion (MacLeod 2012)

The fix: one pill that could correct any genetic mutation in a baby's genome in utero when ingested by the mother and worked by turning genes on or off, repairing a stretch of code, or turning a mutated allele back to wild type; but it was also designed to avoid germline cells, therefore rendering the effects non-hereditary (MacLeod 2012). The fix, an invention in the novel *Intrusion,* probably sounds pretty amazing (MacLeod 2012). Taking place in the United Kingdom in the not too distant future, society had clearly changed in that women’s rights were infringed upon: women were driven out of the workplace under the guise of protecting their health (fourth hand smoke leaking from walls could endanger pregnancies), wore ring monitors to track their health and ensure they did not drink or smoke when pregnant, and were regularly visited by the Health Center when they were pregnant. Before the ring monitors, women of childbearing age were required to perform monthly pregnancy tests to obtain certifications in order to be served alcohol. Hope, the main character, did not take the fix during her first pregnancy and did not wish to take the fix during her second. The nurse who visited her home multiple times and her doctor at the Health Center continued to pressure her to take the fix, as there was a recent court case that set legal precedent forcing them to align their policies with the decision and insurance companies would raise premiums if patients did not take the fix because risk of disease increases. There was a conscience exemption under the law, but it was only for religious objection. Hope was unable to articulate why she did not want to take the fix, nor why it pained her knowing she could be forced to take it if her objection escalated to court, but I can: her autonomous choice to accept or decline a medical procedure, regardless of the medical benefit, was being taken away from her by her doctor, the nurse, and an oppressive government. She was being coerced, harassed even, by unexpected visits at her home by the nurse to take a medication she did not want to take, which is a direct violation of informed consent. Coercion is unacceptable and unethical under the tenet of autonomy. Also, the fact that only a religious exemption was accepted under the law is unethical as well. Hope argued multiple times with various people that she should not need a religious reason to say no and forcing mothers to take the fix is unethical. Frankly, she was correct. No one needs a reason beyond “no” and they do not owe an explanation to anyone. In the end, she did take the fix, not because she felt defeated, but because she promised herself she would if she and Hugh survived interrogation after being accused of terrorism (which was a chain of events that all stemmed from not taking the fix) and because she wanted to eliminate from the genome a gene from Hugh that enabled him and their son, Nick, to see tachyons (particles that move faster than light and therefore move backwards in time, which allows precognition, i.e. seeing the future) due to a rhodopsin mutation (MacLeod 2012). Ultimately, she did not think the world that tortured her husband deserved the mutation in the gene pool.

The Amazing Spider-Man (Arad 2012)

There have been multiple movies made in the last decade or so on the origin story of Spider-Man based on the comic book series by Stan Lee, but this movie in particular stood out, as genetic research was a central theme (Arad 2012). Oscorp was performing cutting edge genetic research in herpetology, which is the study of crossing genes across species, in hopes that cures for diseases or deformities could be developed, such as utilizing genes from zebrafish or lizards to regenerate limbs (Arad 2012). The inspiration for such research was from Dr. Connors, as he was missing an arm and was motivated to eliminate weakness and deformities to create true equality among people.

Peter Parker developed his spider-like superhuman abilities by being bitten by a spider at Oscorp Industries that had been genetically modified to spin extremely strong webbing for commercial purposes called tinsel string (Arad 2012). Genes from the spider were transferred to him through the bite, thus enabling him to scale buildings and move with extreme agility, by incorporating those genes into his own. He was not upset in any way to have gained these abilities, but technically he was edited without consent. However, no one is to blame for this as it was an accident and Oscorp cannot actually be accused with a violation of autonomy. Peter did wander into laboratories where he was not authorized to be and therefore the bite was his own fault, which releases Oscorp of liability.

In the herpetology experiments performed by Dr. Connors and his research team, genetic modifications in animals were affected by a rate of decay where they rejected the gene edits and reverted back to their original selves and sometimes displayed violent behavior. His colleague warned that the injections were not ready for human trials and the research was to end. Dr. Connors could not accept this failure and in desperation began experimenting on himself by injecting lizard DNA. He was able to regrow his arm, but only temporarily. Therefore, he continued to increase the dosage, which led to negative side effects, including a lizard appearance, violent behavior, and a split personality (Arad 2012). Dr. Connors was warned by his colleague that the experiments were failing in animal models, which satisfies informed consent. He invoked his right to make decisions for himself and decided to be his next test subject regardless, which is his right to make despite leading to negative consequences. Where he violated informed consent and decision making capacity was when he decided to make the gene editing serum into an aerosol spray that would infect the entire city, thus mutating everyone into a “perfected” version of themselves. Luckily, while working with his girlfriend, Gwen, who happened to be Dr. Connor’s intern, Spider-Man was able to neutralize the serum with the antidote from Gwen and thus saved the city from being mutated with lizard DNA against their will. Dr. Connor was also saved when he received the antidote, but seemed to still experience hallucinations as an after effect.

The Origin Mystery Trilogy: The Atlantis Gene, The Atlantis Plague, and The Atlantis World (Riddle 2013, Riddle 2013, and Riddle 2014)

There were two main issues in the Origin Mystery Trilogy regarding autonomy: the recruitment of Indonesian children for a clinical trial and what was called the "euthanasia protocol" as a solution to the Atlantis plague (Riddle 2013 and Riddle 2014). Firstly, Dr. Kate Warner was conducting a study on autism at the Autism Research Center (ARC) in Jakarta by engineering gene therapy retroviruses as a cure (Riddle 2013). One-hundred and three children were enrolled in the study and two of the children showed great progress after administering drug ARC-247 (Riddle 2013). Dr. Warner was being investigated after these two children were kidnapped (a research competitor was behind the kidnapping), during which the police questioned the fact that the laboratory had legal guardianship of the children. This was an ethical question because it seemed that no one had agreed to the adoptions and the laboratory appeared to own the children, which the police interpreted as ill will on Dr. Warners part, insisting she must be conducting experiments on Indonesian children that were not permissible in her home country. When she explained, she revealed that she attempted to recruit children for the drug trial by contacting parents directly, but very few people invited to her seminar attended. She realized there was a cultural and language barrier occurring, so she began to visit small villages. Culturally, people in the villages were ashamed to have children who did not obey or respect their parents, which would result in reduced chances of marriage for their other children if people in the village knew they had a "problem child". Therefore, they tied them up in their homes to hide them or left them in a shelter in the jungle where they died unable to care for themselves. Dr.

Helms, her research colleague, insisted lying to parents to children enrolled in the study was unethical despite the tragic social norms or lack of understanding of the trial. Dr. Warner retorted that allowing children to be left in the jungle to die or living as prisoners in their home was a greater ethical injustice. Dr. Helms later conceded to Dr. Warner's argument, but she forced him to resign for questioning her ethics.

One can see the conflict here: Dr. Warner was unable to convey the truth of her experiment to the parents of the children because they did not even understand that the children had a disease, autism, that affected their behavior, which was misperceived as disobedience. Rather than seek medical attention, the parents hid the shameful children. Under autonomy, this appears to be a violation of informed consent because the parents were incapable of understanding their children's conditions or the potential treatment Dr. Warner was offering. They could not make a proper decision regarding the trial due to lack of knowledge. However, Dr. Warner thought the abuse of the children often leading to their deaths was by far a more egregious violation of ethics. Therefore, she adopted them, enrolled them in the drug trial, and had a staff that properly cared for them. The laboratory had proper living conditions and in her eyes, she had saved them from a life of neglect and cruelty. Most would agree that she made the correct ethical decision.

Secondly, the euthanasia protocol was an ethical issue. In this story, the Atlantis gene was given to humans through retroviruses thousands of years prior by two Atlanteans, Janus and Isis, who were attempting to advance the human race and ensure their survival on Earth. The Atlantis gene affected brain wiring, which caused the Great Leap Forward in history, thus enabling humans to develop religion, advanced tools, and survival skills necessary to survive the Toba Catastrophe (a volcanic explosion resulting in prolonged winter). People with the activated Atlantis gene were able to survive certain radiation exposure and the plague that swept the Earth, killing ninety percent of the infected population (Riddle 2013). Of those that survived, half experienced a devolution: unable to speak, lack of social skills, etc.; the other half experienced an increase in problem solving skills or physical strength, but at the cost of losing empathy. Essentially, the plague was causing another wave of changing human's brain wiring, but those unable to adapt to the changes died. Researchers had developed a semi-cure, Orchid, and was programmed via a subdermal implant running an algorithm, Symphony, to individualize treatments by predicting gene expression and synthesizing enzymes to combat the virus. But Orchid was failing and an actual cure was needed. Dr. Warner, with assistance, had found Adam, the original human with the full Atlantis gene. Janus, who had been resurrected through Atlantean technology, was attempting to use Adam's genes to cure the human race by devolving them back to the stage before the Great Leap Forward, i.e. when he and Isis had interfered with evolution. Dr. Warner had another idea: create a hybrid Atlantean-human genome that would stabilize the genetic changes made. She was successful at curing everyone.

But the euthanasia protocol was in place in case Dr. Warner was not successful and was about to be implemented. Embedded in the Symphony algorithm was a protocol that would inflict a swift death unto anyone with the implant. The idea was to end the suffering of the infected if a cure was not found quickly. However, in a reaction to a rogue group gaining contol of food processing plants, the United States military wanted to use the euthanasia protocol after the cure had been delivered to eliminate those who could not fight in a war. The fact that the protocol was there in the first place was a violation of informed consent because people with the implant did not know it was there. They agreed to the implant to receive Orchid and may have decided differently if they had known about the euthanasia protocol. Also, deciding to activate the protocol after the cure was administered was a violation of autonomy because this was not a group of people deciding on physician assisted suicide for a terminal disease, it would actually be a mass murder of people deemed to be physically "weak". The population had already been severely decimated by the plague and the marines were suggesting eliminating a significant amount more insisting it would ensure the survival of the "strong". Thankfully, the director of the CDC did not allow this to happen, as he felt it was immoral.

The Perfect 46 (Bonowicz 2014)

The Perfect 46 was a movie that seemed very realistic (Bonowicz 2014). A company had developed a website utilizing an algorithm that could determine if a couple was genetically compatible to guarantee their children would not be born with a genetic disease. Couples could give consent to have their DNA from a government database analyzed for a match. A later iteration worked like a dating service to find genetic matches. People complained that their marriages ended over the service. However, the CEO of the company reiterated that the website was just providing a service and people were not forced to use it. People could do what they wanted with the information: have children or not with someone who is compatible or not. Ultimately, the decision was still theirs to make. At one point, about seventeen hundred babies were born free of genetic disease, but a glitch in the algorithm resulted in pairing three-hundred and eight couples who were incompatible, resulting in the births of twenty-four children with Tay-sachs disease (Bonowicz 2014).

The question arose how much responsibility did the company have, since the parents were informed of the process and had the decision making capacity to use the information they were given. This movie demonstrated the reliance on technology in the pursuit of eliminating genetic diseases and the pitfalls of such technology. However, despite the unfortunate error in the algorithm, autonomy was not violated, as parents gave informed consent to use the service and the decision to procreate with the information provided to them was still theirs.

Equals (Pruss 2015)

People in *Equals* were, most simply put, drones existing, not truly living, in a dreadfully boring world swathed in white everything (clothing, decor, buildings, walkways, etc.) called the Collective (Pruss 2015). Everyone was genetically edited somewhere between conception and birth to not have emotions of any kind. The reason was the Collective believed that civilizations of the past were defective, as they allowed their emotions and base desires to rule their existence. Without emotions, they were genetically superior and productive members of society, focused on their work and allowing the Collective to run smoothly. It was made very clear through conversations between characters and announcements made over loudspeakers everyone should have their genes that control emotions shut off in order to be equals in society. However, some people experience Switched On Syndrome (S.O.S.), which occurs when the gene silencing malfunctions. Infected people are expected to take inhibitors to slow the disease state, which are an emotional suppression treatment. Eventually, the disease takes full effect and those infected are taken to the DEN (Defective, Emotional, Neuropathy) Facility where they are contained with electro restraint until they opt for a pain free death, i.e. commit suicide.

The problem was people did not have a choice to be gene edited or not. Informed consent was not even a consideration because everyone was edited prior to being born. There were no parents to make the decision for their child, as women were given a conception summons when they were to be artificially inseminated and then returned to work after giving birth. Everyone was gene edited without a choice to be emotionless. If the gene silencing did not take effect in adulthood, they were immediately issued inhibitor drugs and expected to take them. When the inhibitors failed, they were forcefully taken to a "treatment facility" until they decided to kill themselves. Along those lines as well, touching and coupling was strictly prohibited. People found having sex are also immediately taken to the DEN for treatment. The Collective society was very restrictive controlling most aspects of people's lives and prevented people from deciding if they wished to experience emotions or not.

When a cure was developed, people living with SOS were not forced to take it as soon as it was offered. Soon after the cure was announced, the main character, Nia, received a conception summons. Naturally, she was afraid during the physical examination, they would discover she had SOS, had been living with it undetected for some time, and would force the cure on her. She and Silas were in love and admitted they did not want to live without emotions, as that was an unnatural existence. They decided together that they would not take the cure and would leave the Collective. During the conception summons, Nia tested positive for being pregnant. As she was not artificially inseminated, the doctor knew she must have been living with SOS undetected and was having relations with someone. She was dragged to the DEN, but friends assisted in her escape, giving her the identity of another woman who had committed suicide the night before. This is how they faked Nia's death so she could return to Silas. When their friends (who all had SOS) were caught, they were all given the cure against their will. In the meantime, Silas was told by the gate attendant at the DEN that Nia had committed suicide. Devastated, he attempted suicide by climbing the top of a building. Ultimately, he decided to take the cure instead, as he could not bear living without her and did not want to die either. He also did not want the cure forced upon him, so he opted to take it voluntarily to dull the pain of losing Nia before the Collective decided for him. The fears of Silas and Nia were not unwarranted: the cure was not forced upon people with SOS at first because of the high volume of patients seeking the cure, but their fears were confirmed when their friends were cured after having been caught helping Nia escape the DEN. Escape from the Collective was the only way to ensure Nia would not have the cure forced upon her or her unborn child. She and Silas took their decision making capacity back from the Collective by deciding to leave.

Rise of the Kymiera six-part series (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) *(Turnbull 2017)*

Rise of the Kymiera was one story stretched over six short books that was a dystopian society in which resources were limited after the S.I.D. infectious plague wiped out much of the human population (Turnbull 2017). The infection itself was intriguing because it would lay dormant for years awaiting the presence of foreign DNA, which would be incorporated into the genome of the person. People could absorb animal DNA or infectious

DNA, which would result in strange physical mutations, painful transformations, infections, and loss of mental clarity. Death was inevitable and the transformation process was gruesome; therefore, the Purity organization would euthanize infected people, who were called freaks.

However, there were a group of teenagers who were conceived through IVF under the direction of Dr. Newman. His clinic was just a front for him to perform genetic experiments. The issue with their conception was the fact that Dr. Newman performed genetic edits to the gametes without informing the parents of what he had done. This was a direct violation of decision making capacity and informed consent: the parents sought assistance in conceiving a child and Dr. Newman performed his experiments without their knowledge or permission. What he did was incorporate animal DNA into the gamete genomes and programmed the DNA to develop the mutations around the age of sixteen to seventeen. Chloe, the main character, had bat DNA edited into her genome, which caused her bones to be very light, develop wings, have enhanced hearing, and gave her the ability to “see” with sound vibrations like bats do (i.e. sonar capability) (Turnbull 2017). Thankfully, his edits were different than the S.I.D. infection, since the edits were stable and the teenagers did not lose their mental capacity or experience painful transformations.

Utopia Genetics, the largest genetics research company in the story, were interested in Dr. Newman’s work, as he was able to seamlessly merge foreign DNA with host DNA, thus enabling the edits to be stable, and was also able to trigger them at certain times. No one else had successfully done this prior or after and the company wanted to replicate his work. Under the guise of being philanthropic, they donated expensive medical equipment to schools to assist in screening for S.I.D., but were really gathering genetic data to find

Dr. Newman's subjects. The instruments were connected to Utopia Genetics servers without the school's knowledge. This is also a violation of informed consent because neither the school nor the students gave consent to have their DNA analyzed by the company. In addition, they violated consent by kidnapping teenagers with Dr. Newman's edits and performing experiments on them without their permission. Researchers pushed their abilities to the extreme with more strenuous and invasive experiments. Previous "assets" died during their experiments to understand Dr. Newman's work. At Utopia, the teenage women were not even viewed as people, but rather as specimens to be studied and understood. If they refused to cooperate, they were to be killed. By the end of the story, they managed to evade their captors by working together and combining their abilities in order to escape.

The Titan (Amel 2018)

The Titan was another story that involved the splicing of animal genes into humans, but as fully grown adults and not embryos (Amel 2018). The reason for performing gene editing on the group of soldiers who volunteered for this procedure was to attain traits that would allow them to adapt to the different conditions of the moon, Titan, because Earth was becoming increasingly uninhabitable due to climate change and war. They needed to be able to withstand colder temperatures, swim in the water, and consume less oxygen, essentially. In this film, the tenet of autonomy was violated because the characters were not given informed consent. They were told the procedures were experimental and they would have their genes edited, which involved a certain amount of risk. But they were edited differently to what they agreed: the incorporation of animal genes was never specified and remained a secret to them. Only two members of the group survived all of the edits via injections and surgical procedures, but one was killed because she murdered her husband. Other members died during various stages of the experiment because they could not adapt to the genetic changes or they were killed due to violent behavior. Only the main character, Rick, was sent to Titan to explore. When the soldiers agreed to the experiment, they did not understand that most of the group would not survive the procedures and the depth of the risk was not fully disclosed. The professor leading the research group admitted that at the beginning, there was no means of knowing what the subjects would become because nature itself was unpredictable and people evolve in different ways (Amel 2018). If the professor had been honest about the risk and exactly what would be done to the volunteers, perhaps most would have declined to participate.

ReEvolution (Grant 2019)

ReEvolution was another tale that was very realistic in nature and specifically involved CRISPR research (Grant 2019). Aspects of this story are true in regards to reality: the United States, China, and other countries are performing research on CRISPR and competing for breakthroughs with the technology. Interestingly, in the story, a computer programmer named David was able to write a predictive algorithm to eliminate or minimize unintended off-target edits, which is a prominent ethical issue regarding CRISPR. John, David, and some laboratory technicians were making significant progress in developing CRISPR to cure baldness and possibly slow aging at the U.S. based start-up company, Algogene. By hacking the company’s email, other companies were very interested in their developments, especially a Chinese based company, Xian Corp.

However, an ethical issue that arose here that did not correlate to any of the current issues with CRISPR was violating anti-competition laws and industrial espionage. Briefly, John was given results from a director at Geneteka who, along with his colleagues who performed the initial research, were tired of the company making millions of dollars off of their discoveries but seeing very little of those rewards themselves. Anti-competition laws prevented them from publishing and patenting their findings; therefore, they asked John, a researcher fresh out of graduate school, to start his own company and present the research as his own. The money made from Algogene would be funneled to the director and his colleagues. The Xian Corp then began pushing for a buyout of Algogene in order to obtain the algorithm developed by David. They enlisted airport security to attempt to steal the software when John traveled to China, offered them $5.5 billion dollars for the company when the theft failed, then intended to withhold the second installment after they received the algorithm during the turn over of assets. Although these issues are clearly violations of ethical research practices and are illegal, they still occurred. They were worth mentioning even though they do not directly correspond to any of the issues relating to CRISPR.

Where the story violated autonomy specifically was the company Xian Corp was performing experiments on human subjects, claiming they gave consent for the experiments. John asked this question, as his company was U.S. based and testing on humans was illegal, and did not want to be criminally charged. In Chinese culture (according to the novel), researchers had an obligation to explore the genetic code to improve the lives of children, the future, advance the country and mankind; not performing the research would be equivalent to social negligence. Some people volunteered because they were willing to sacrifice for the good of the country overall. However, through some further investigation, John discovered this was not the case. The human subjects had not given consent to be gene edited with CRISPR. The lead researcher at Xian Corp was open that the subjects were criminals and poor people, but were fulfilling their duty to country. The company was also injecting CRISPR into poor people in the countryside away from the majority of the population where they could hide what they were doing. People, even children, were dying painful deaths from the experimental injections. Some researchers were appalled by these experiments, but feared for their own lives and did not report the violations. The issue here is not just lack of consent, whether informed or not, but the incorrect invocation of utilitarianism. Xian Corp head researchers claimed they were helping advance their country, which would provide overall good for the people. They also did so by ignoring Kantism, which states the end does not justify the means. Under autonomy, it is not justifiable to exploit the poor or criminals in addition to performing experiments on people without their consent. It is also unacceptable to advance the use of CRISPR by any means possible in order to provide the "most good". Xian Corp and their investors, who backed the research and demanded results with complete disregard for anyone who was harmed, were egregiously wrong to perform CRISPR edits on human subjects. Sacrificing the lives of poor people and criminals for a better understanding of gene editing is completely insupportable and unethical.

Conclusion

This set of stories demonstrates a wide variety of portrayals of violations of autonomy. In order to frame perceptions surrounding autonomy and the possible pitfalls of pursuing CRISPR gene editing, the following stories that best demonstrate these issues were *Beggars in Spain* (Kress 1991), *Change Agent* (Suarez 2017), *Brave New World*

(Huxley 1932 and Babbin 1980), *My Sister's Keeper* (Picoult 2003 and Furst 2009), *Intrusion* (MacLeod 2012), the *Rise of the Kymiera* series (Turnbull 2017), and *ReEvolution* (Grant 2019).

One concern about CRISPR is the issue of self vs. offspring, which differentiates edits performed in somatics vs. germline cells. This issue was only seen in two novels, *Beggars in Spain* (Kress 1991) and *Change Agent* (Suarez 2017). Children who were edited in the embryo stage passed down any edits to their offspring, which researchers may or may not have known in the story. People fear passing genes down through future generations when germline cells are edited that may not be beneficial due to mistakes made, thus removing the autonomous choice of future generations. Thankfully, the edits performed in both of these stories did not cause health problems, but the fear is they could. These stories may assist in providing positive perceptions of pursuing germline gene editing.

The three best stories for demonstrating the issues of personhood (the rights of future generations, unborn persons, and embryos) were *Beggars in Spain* (Kress 1991), *Brave New World* (Huxley 1932 and Babbin 1980), and *Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5),* and *The Augments (Episode 6)* (Brennert 2004, LaZebnik 2004, and Sussman 2004). In *Beggars in Spain*, future generations were sleepless due to the dominance of the sleepless genes of their gene edited parents (Kress 1991). This removed their autonomous choice completely, as they acquired the genes from their parents. In *Brave New World,* embryos were manipulated to be mass produced to continue the growth of the labor classes (Huxley 1932 and Babbin 1980). No one had a choice into which class they were placed and embryos seemed to have little regard under personhood. In *Star Trek: Enterprise,* embryos were actually shown some respect under the tenet of autonomy (Brennert 2004, LaZebnik 2004, and Sussman 2004). Since governments on Earth could not decide what they should do with the gene edited embryos after the eugenics wars, the decision to freeze them in cold storage demonstrated that they were treated with some modicum of respect for the potential for life rather than just destroying them as if they were research waste. This set of stories could be used to show that edits that can be passed to future generations in germline cells should be considered carefully and should have medical benefit, not necessarily enhancements or advantageous edits. They also show that perhaps embryos should be offered some protection under autonomy, as research techniques could lead to nefarious uses and gross manipulations.

Decision making capacity was best described in *My Sister's Keeper* (Picoult 2003 and Furst 2009), *Intrusion* (MacLeod 2012), and *Change Agent* (Suarez 2017). Decision making capacity lies with parents for children, which was shown in all of these stories, yet was presented very differently. In *My Sister's Keeper*, Anna was edited to be a genetic match for her sister in order to donate blood, cells, bone marrow, etc. to her sister to treat her leukemia (Picoult 2003 and Furst 2009). This was her parent's decision to make, but as time continued, their expectations for Anna to donate increased and they wanted her to donate a kidney against her will. This was a gross violation of Anna's autonomous choices and begs the question that creating a child to be a genetic match for a sibling is unethical itself. In *Intrusion,* the government claimed that taking the fix was not mandatory, yet healthcare professionals continuously coerced Hope to take it, thus violating her decision making capacity as a parent to edit or not edit. In *Change Agent,* parents were allowed to gene edit embryos to treat genetic diseases legally from an approved United Nations list, but people with money illegally edited their children to have enhancements (Suarez 2017). The first scenario is acceptable under autonomy, the second is not. Combined, these visual representations give a clear picture to all of the concerns regarding decision making capacity and show how people's fear that their autonomous choice to edit their children could be removed or legally mandated. However, without any legal guidance and punishment for violations, gene editing could take us into a future we do not wish to enter.

Lastly, violations of informed consent were demonstrated in the *Rise of the Kymiera* series (Turnbull 2017) and *ReEvolution* (Grant 2019). In *Rise of the Kymiera,* parents had sought help conceiving at a fertility clinic, but the doctor had performed edits to which they had not consented (Turnbull 2017). Even though scientifically gene splicing humans with animal DNA to provide enhanced abilities is unrealistic, the fear that clinicians and/or researchers might perform edits not approved by the parents is a realistic possibility and cause for fear. One might even compare this story to the Jianku He situation in China. In *ReEvolution,* researchers performed gene edits on humans without their consent and inflicted great harm onto these unwilling participants (Grant 2019). The events of this story portrays the need for caution: if CRISPR ever advances to where clinical trials on humans becomes a necessity, informed consent must be given from all participants and there should be strict laws in place enforcing this. Since this story took place in China, it shows the need for some form of global consensus on what is permissible to edit and to perform on humans.

CHAPTER 3: FILM AND LITERATURE REVIEW: HOW SCIENCE FICTION INFLUENCES PERCEPTIONS OF GENE EDITING AND ADDRESSES BENEFICENCE

Introduction

Only one issue under beneficence is ever mentioned when discussing CRISPR gene editing: the obligation to treat debilitating genetic diseases. Theoretically, if CRISPR is developed to the point where it is proven to be a safe, effective treatment for genetic diseases, then researchers have an obligation to exploring and perfecting it. We would limit ourselves if all research into gene editing were halted just because potential abuses are possible. Genetic diseases can be debilitating to those unfortunate enough to have them and CRISPR could be the remedy to ending human suffering from these diseases. Various works of science fiction portrayed futures where heritable genetic diseases were preventable due to gene editing or genetic engineering in addition to curing infectious diseases and cancer. Some stories even included the means to prevent or slow aging, even though aging is a natural process and not technically a disease state, but in doing so alleviates symptoms that accompany the aging process. This could be argued as a benefit or a violation depending on how it is argued or the reason for such a process. Stories that demonstrated the obligation to treat genetic diseases or preventing the susceptibility to infectious diseases were *Brave New World* (Huxley 1932), *Friday* (Heinlein 1982), *The Neanderthal Parallax* (Sawyer 2002, Sawyer 2003, & Sawyer 2003), *Star Trek: Enterprise* season 4 episodes 4-6 (*Borderland, Cold Station 12,* and *The Augments*) (LaZebnik 2004, Brennert 2004, and Sussman 2004, respectively), *Extraordinary Measures* (Shamberg 2010), *Tankborn* (Sandler 2011), *2312* (Robinson 2012), *Intrusion* (MacLeod 2012), *The*

Amazing Spider-Man (Arad 2012), *The Atlantis Plague* (Riddle 2013), *The Perfect 46* (Bonowicz 2014), *Change Agent* (Suarez 2017), and *ReEvolution* (Grant 2019).

The Obligation to Treat or Correct Debilitating Genetic Diseases

Brave New World, Friday, and Tankborn (Heinlein 1982, Huxley 1932, and Sandler 2011)

When discussing gene editing, most would argue that research should be explored because we have the obligation to treat a disease or illness if we have the means to do so. Interestingly, in science fiction, people are not just modified to not have heritable genetic disease, but are also created with resistance to other illnesses, such as infections diseases, cancer, and aging, which reduces health complications even though technically aging is not a disease. There were three novels in which genetic engineering was used in this way: *Brave New World, Friday,* and *Tankborn* (Heinlein 1982, Huxley 1932, and Sandler 2011). Specifically in *Brave New World,* people were genetically modified to be immune to all diseases and aging (Huxley 1932). One could argue, though, that creating people who physically maintained the age of thirty throughout all of adulthood was equally due to aesthetics, not just to minimize health issues associated with age. Eliminating aging through genetic manipulation and medicine provides benefit to everyone in society, but still defies nature and is therefore a questionable practice. But preventing diseases definitely provides benefit and improves quality of life. Also, since people were grown in incubators and not birthed, women no longer had to face the risks associated with pregnancy and birth (Huxley 1932). This could be seen as a benefit in some respects.

There were many parallels observed in *Friday* and *Tankborn*, as seen in the previous chapter regarding autonomy and chapter five regarding justice, as well as beneficence: Artificial persons (APs) in *Friday* and Genetically Engineered Non-humans (GENs) in

Tankborn were genetically engineered to be immune or resistant to infectious diseases (Heinlein 1982 and Sandler 2011). This definitely provides benefit to APs and GENs and improves quality of life. APs in *Friday* were also created to be free of genetic diseases and cancer in addition to resistance to infectious diseases (Heinlein 1982). Another benefit observed in *Tankborn* was Trueborns, if born with a physical abnormality, could be genetically edited and put in the same tank in which GENs were grown to heal, so long as the edit was performed before the age of four (Sandler 2011). For example, Kayla, the main character, was born without arms and had her arms grown this way. The downside to this was if parents rejected their children, then they were transformed into GENs.

The Neanderthal Parallax trilogy (Hominids, Humans, and Hybrids) (Sawyer 2002, 2003, and 2003)

In the Neanderthal parallel universe, people did not live in fear of crime or falling ill to debilitating genetic diseases. The Neanderthals had developed over centuries strict selective breeding and practiced sterilization of violent criminals. They also conserved resources by produced a new generation only every ten years by natural family planning, which they practiced by men and women living separately twenty-six days a month and copulating only when “two become one” four days a month: for nine years, “two become one” occurred during the menstruation cycle when women were infertile and for one year “two become one” occurred when women were fertile. Because all of the women lived together, their menstrual cycles were in sync and these days could easily be determined.

Bandra and Ponter both explained this to Mary in attempt to foster her understanding of their world: generally speaking, most of the “bad” genes were eliminated from the gene pool through selective breeding. For example, they had determined that violence has a genetic component and to prevent the passing down of these violent genes to offspring, they sterilized the person who committed the crime and anyone who shared fifty percent genetic similarity to the criminal. As explained in autonomy, Mary viewed this as a violation of a person's autonomous choice to procreate, especially to the relatives of the criminal, as they were innocent. The Neanderthals did not agree: their philosophy was to place higher priority to the needs of the community rather than the individual.

Ponter and Bandra also insisted that evolution could not occur if bad genes are not purposefully eliminated. Mary asked the question how do the Neanderthals choose which genes to eliminate from the gene pool. Bandra stated it was simple, "Excessive violence. Excessive selfishness. A tendency to mistreat children. Mental retardation. Predisposition to genetic diseases," (Sawyer 2003). Therefore, the purging of genes did not just apply to violent behavior, but also diseases: the Neanderthals had eliminated heritable genetic diseases this way. As a side effect, they also bolstered the population's intelligence, which they also believed greatly benefited society. Their goals were to eliminate suffering of the population as a whole, ensure a high quality of life, ensure the safety of everyone, and ensure everyone was a productive member of society. Their methods may be questionable under other tenets, but their desire to provide benefit is apparent. Those who support the exploration of CRISPR research have the same idea: preventing the transmission of heritable genetic diseases from the gene pool benefits society and alleviates hardship.

Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and The Augments (Episode 6) (Brennert 2004, LaZebnik 2004, and Sussman 2004)

The Augments were a group of genetically engineered humans who were raised by a scientist who stole embryos from cold storage after the eugenics wars that took place on Earth in the 1990's. Their "father" stated that they were stronger, smarter, free from sickness, and had double life spans compared to non-genetically engineered humans (Brennert 2004). The fact that they were stronger and smarter would be considered a violation of nonmaleficence since these would be considered enhancements. Doubling a person's life span could be considered an enhancement or it could be considered a benefit, as decelerating aging would delay the onset of health issues related to aging. Medicine often has the goal of prolonging life, but there is a balance between maintaining quality of life and forcing someone to endure health problems longer. Most would probably argue a longer life, so long as it was of high quality, would be beneficial and desirable. Despite a doubled life span being inconclusively acceptable or unacceptable under beneficence and enhancing people with higher intelligence and strength being unethical under nonmaleficence, what is beyond debate a benefit is being genetically modified to be free of illness. Although what type of illness could be interpreted, as the show did not elaborate: infections diseases, cancer, and/or heritable genetic diseases. Being free from all of these would be extremely beneficial.

Extraordinary Measures (Shamberg 2010)

Extraordinary Measures was not a science fiction film, but rather a drama based on a true story (Shamberg 2010). This movie was worth including in this analysis because it was an excellent visualization of the hardships individuals and families face when living with a debilitating genetic disease, thus supporting the idea that gene editing should be explored because it could lead to a potential cure for genetic diseases, even though the cure used in the film was a drug and not a genetic edit. The main character, John Crowley, had two out of three children born with Pompe disease, a form of muscular dystrophy, where the life expectancy was nine years. They were both wheelchair bound and had less than one year to live, according to doctors, and required $40,000 a month in healthcare costs (Shamberg 2010). John desperately searched for research that could help his children, which led him to Dr. Richard Stonehill. John was able to raise funds for Dr. Stonehill's research, but he was bought out by a bigger company. One of their drugs showed promise and they began a trial on infants, citing the disease was more likely to be treated at a younger age. However, Dr. Stonehill proposed a clinical trial involving siblings with the same disease, but this resulted in John being fired from the company to eliminate a conlift of interest. The drug proved effective by reversing the enlargement of their internal organs, slowing the disease progression, and saved their lives. This movie, although it did not involve curing the disease through gene editing, depicted the application of the tenet of beneficence. John never ceased his mission to find and assist the funding of research that could help his children. By insisting his children be enrolled in a clinical trial with the assistance of Dr. Stonehill, they both felt ethically obligated to ensure Megan and Patrick received treatment because one was discovered. Not giving them the drug would have been a violation of beneficence.

2312 (Robinson 2012)

In relation to this analysis, the description of *2312* stated that augmented humans populated other planets in the solar system, but lacked details about what these augmentations were and how they were created (Robinson 2012). But there were a few technologies worth mentioning that had beneficial applications of gene editing and manipulation, even though they were not the main focus of the novel. Cancer was cured by first identifying the mutations with parallel DNA sequencing, then dissolved with gene therapies (chemo and radiation) targeted at the cancer and telomerase manipulation involving monoclonal antibodies, avimers, or designed proteins for recognition (Robinson 2012). Aging is caused by unrepaired DNA damage and therefore they determined how to repair this damage to make humans live much longer to allow for space travel. Lastly, they also figured out how to regrow amputated limbs using pluripotent stem cells (Robinson 2012). Curing cancer and regrowing limbs would definitely be fruitful applications of medical therapies derived from gene editing and these therapies seemed widely and readily available in the story, thus satisfying the tenet of beneficence.

Intrusion (MacLeod 2012)

Along those lines, the fix in *Intrusion* was also a readily available cure to correct genetic anomalies in pill form (MacLeod 2012). It also provided immunity to childhood illnesses. When Hope protested to taking the fix, her nurse, Fiona, stated the following: “You can’t have people dodging an obligation just because they don’t feel like it,” (MacLeod 2012). This seemed to be the attitude of society as a whole and that a mother who did not take the fix was putting her child’s health at risk, yet the only exemption legally accepted was a religious one. According to all tests, Hope’s baby was perfectly healthy and she insisted she did not need the fix. A sociology researcher, Geena, and her associate, Maya, who was a human rights activist, brought up the fact that some mutations are advantageous and eliminating a beneficial mutation would be an acceptable medical reason to not take the fix. Maya insisted the increased pressure to take the fix was not to convince those resisting to take it for their own good, but rather to protect the unborn, justifying their actions because the unborn only had the state to stand up for them (MacLeod 2012). England and Scotland were developing a legal stance that a mother would be declared unfit if she did not take the fix without good cause because it would be equivalent to child neglect (MacLeod 2012). The issue here is the only "good cause" recognized was religious objection. Maya's point was also fair, that some mutations were beneficial (like the one Hugh and Nick had in their rhodopsin that allowed them to see tachyons). And lastly, if a treatment is available for a disease, one is obligated to administer it, but in *Intrusion*, Hope was having a child that was already free of genetic diseases according to her tests. The coercion to take the fix was unjustified because it was in conflict with her autonomous choice and the state was choosing the unborn child's rights over the mother's right to reject medical treatment, as well as negating her decision making capacity to do what she thought was right for her child.

The Amazing Spider-Man (Arad 2012)

Dr. Connors and his team at Oscorp were performing herpetology research, which is the study of cross species genetics. The theory behind their research was diseases could be cured through transgenic gene splicing. On a tour with other interns, the students laughed when they heard Dr. Connors state this. Peter did not laugh, but rather offered the example of crossing human DNA with zebrafish DNA, which would give humans the ability to regenerate and heal themselves. This type of cure would be revolutionary, as it would eliminate deformities and foster equality, according to Dr. Parker and Dr. Connors. At the time of the tour, results from the mRNA sequencing data was showing that the decay algorithm was still problematic, meaning the genetic edits reverted and were rejected by the host subjects (mice). Since the research team could not rectify the issue, the research was to be terminated and would not move to human trials. This was the correct decision and ethical approach. Dr. Connors could not accept failure and therefore injected himself with lizard genes. He was able to regrow his missing arm, just as the mice did. But when the decay occurred, the limb fell off and he began to experience a split personality and aggressive behavior. Had the research been successful, the company would have had an obligation to provide such a cure. But the cure in its current state was unsuccessful at stably splicing genes and would cause more harm, i.e. would violate nonmaleficence. Even though it was his autonomous choice, Dr. Connors should not have pursued self-experimentation with a gene editing injection he knew would only work temporarily due to instability.

The Origin Mystery Trilogy: The Atlantis Gene, The Atlantis Plague, and The Atlantis World (Riddle 2013, Riddle 2013, and Riddle 2014)

Due to strange circumstances, Dr. Kate Warner possessed the memories of a deceased Atlantean scientist, Isis. She was a baby in utero when her mother was placed in an Atlantean resurrection chamber and being the only living body in the chamber, Isis' memories were passed to Kate from an archived backup on the spaceship. Isis, along with her partner, Janus, were experimenting on early humans by gene editing administered through retroviruses in attempts to speed along evolution. Due to imminent threat of another civilization determined to assimilate all intelligent life, another Atlantean, Ares, performed edits of his own. Both edits were intended to ensure Earth humans survived, but against different threats. In the present time, Earth humans were experiencing a drastic die off from the Atlantis plague due to the inability to assimilate the genetic changes. Those that did survive either devolved to a state prior to the Great Leap Forward (Isis and Janus' original edit) or evolved to possess greater strength, intelligence, and problem solving skills but less empathy. Janus left behind a computer chip in Adam, the original human with the full Atlantis gene, that he claimed contained code for a cure; but Kate realized that his "cure" would cause all humans to digress to a stage before their original interference, which meant they would lose religion, communication, art, etc. that were all a result of the Atlantis gene and the Great Leap Forward. Kate and her companions agreed this would be a travesty and there must be another way to cure humans of the plague. By writing a new genetic code, Kate was able to incorporate all of Janus, Isis, and Ares' Atlantean edits with the human genome into one stable hybrid genome. She was able to transmit a new algorithm containing the genetic code to everyone's subdermal implants, which synthesized enzymes that would perform gene edits and stabilize the Atlantis genes. Her algorithm had a one-hundred percent cure rate. Kate felt the obligation to cure the human race from the Atlantis plague and did not see a devolution as an ethical solution. Removing everything that makes humans human would have been cruel; therefore, she was determined to find the cure that prevented further death from the plague while keeping the Atlantis gene edits in tact. This also meant that those that had devolved as a side effect were also cured, bringing them back to where they were before the plague had spread. Devolving humans to a stage prior to the

Great Leap Forward would have protected them from a Serpentine invasion, but taking away the gift of evolution was not the beneficial course of action.

The Perfect 46 (Bonowicz 2014)

The creators of the website Perfect46.com in *The Perfect 46* had the goal of completely eradicating genetic diseases within a few decades (Bonowicz 2014). They did not eliminate genetic diseases through gene editing, but rather through selecting genetically compatible partners. They were not curing diseases, but breeding them out of existence to ensure couples had the healthiest children possible. The CEO even claimed that his website was preventative healthcare and reduced the costs of insurance, as seventeen-hundred children were born free of disease (Bonowicz 2014). In this regard, the website with its genetic matching algorithm seemed to be successful in preventing the births of children with genetic diseases, which many would claim provides significant health benefits to many people, improves quality of life, and reduces the demand on healthcare services. However, one could claim that this practice is simply a technological spin on eugenics. This will be further discussed in nonmaleficence.

Change Agent (Suarez 2017)

Change Agent, taking place in the future year 2045, claimed to have figured out how to use CRISPR specifically to edit embryos in vitro to correct lethal heritable genetic diseases, including, but not limited to, cystic fibrosis, sickle cell anemia, hemophilia, muscular dystrophy, and Huntington's disease (Suarez 2017). There was a United Nations Treaty on Genetic Modification, which contained an approved list of edits that could be performed to correct for these diseases. Any genetic disorder that was not on the list was not considered a debilitating disease. There was an entire scene dedicated to a conversation between Ken Durand and his daughter, Mia, who was genetically modified to ensure she was not blind due to Leber congenital amaurosis (Suarez 2017). He explained the legal edits were those that cured illnesses, thus making sure humans were born as they should be. Suarez envisioned a future where CRISPR germline gene editing was a readily-available, effective application to prevent the spread of genetic diseases. The list above is actually an accurate list of diseases currently being researched to be cured by CRISPR editing. He was also ambitious in his confidence that CRISPR would be ready by 2045, only twenty-six years away from now. But the future he envisioned also had established global laws governing what edits were legal and illegal, thus attaining a global consensus on ethically acceptable germline edits that were only meant to cure disease, which is not the current state of matters in 2019, as germline edits are still predominantly banned or restricted. This future he described is not completely implausible, though. Assuming CRISPR is further researched to ensure efficacy and safety, having the means to cure diseases is an obligation under beneficence. Research on CRISPR is certainly heading in the direction of Suarez's story.

ReEvolution (Grant 2019)

Unintended consequences, off-target edits, and mosaicism are issues of concern under nonmaleficence and are discussed in detail in chapter four. CRISPR would be deemed safer to use if these issues could be eliminated or minimized and various research is dedicated to solving these issues. In *ReEvolution,* a computer programmer had developed a predictive algorithm that could determine if a particular CRISPR guide RNA would cause off-target edits (Grant 2019). Other companies researching CRISPR conjectured that this algorithm would be the key to solving complications with gene editing and were interested in buying AlgoGene to obtain the algorithm for their own research. Cures for genetic diseases could never be implemented without first solving the issue of off-target edits, which this algorithm promised to do. Many advocates for CRISPR research insist developing treatments for debilitating genetic diseases is an obligation that must be fulfilled; the algorithm would enable CRISPR to fulfill the tenet of beneficence by advancing research in order to ensure the safety of genetic cures.

Conclusion

A significant number of the stories mentioned above had means of genetic manipulation to impart immunity to infectious diseases, cancer, and decelerated the aging process. As there are many forms of infectious diseases and cancer, I would assume this would be a tremendous scientific feat. Or perhaps genetically modified human's immune cells were altered to have a broader range of foreign recognition. Regardless of the means, prevention of infectious diseases and cancer would be of great benefit to society if it were feasible through gene editing.

Decelerating aging, although it provides benefits of negating symptoms related to aging (higher susceptibility to infection, mobility loss, memory loss, etc.), is not treating a medical ailment directly. I am sure many people dream of being younger and living longer in general. Quality time is precious while alive because life is finite and we know this. But the negative side to significantly prolonging life for everyone is a strain on resources and philosophically perhaps a loss of meaning of life because the definition of finite is altered.

Since negating aging has benefits and negative aspects, whether gene editing should be utilized to slow aging is not a simple answer and should be carefully considered.

Even though it was not science fiction, the story that best illustrated and allowed the viewer to emotionally experience what living with a genetic disease is like was *Extraordinary Measures* (Shamberg 2010). I cannot imagine anyone watching this film who would not be moved by the difficulties of the children and their parents. Even though the term beneficence was never outright used, the determined father in pursuit of a cure is the epitome of the definition. Anyone without a biomedical ethics background would be able to grasp this tenet while viewing this film.

Intrusion and *Change Agent* were also powerful stories to demonstrate beneficence (MacLeod 2012 and Suarez 2017). The fix and CRISPR were used to treat every genetic disorder in their respective story. Even though the technology as it stands today is not nearly that powerful, having a cure for every genetic disorder is a lofty goal, but the stories seemed realistic in their perspectives for creating such a cure. The conversation between Ken and his daughter, Mia, about whether using CRISPR is ethical can easily be referenced to demonstrate why CRISPR research should be explored (Suarez 2017). The dialogue was very relatable regardless of someone's educational or professional background.

Although beneficence is the briefest tenet explored in science fiction, it is the main reason to pursue gene editing. Violations to autonomy, nonmaleficence, and justice are serious concerns, as well as using CRISPR for non-medical purposes. But these fears should not cloud the central focus of medical research: curing diseases to alleviate suffering. Fears of violating other tenets should be used to ethically guide research to ensure beneficence is met.

CHAPTER 4: FILM AND LITERATURE REVIEW: HOW SCIENCE FICTION INFLUENCES PERCEPTIONS OF GENE EDITING AND ADDRESSES NONMALEFICENCE

Introduction

Nonmaleficence was the predominant biomedical issue portrayed in science fiction. Issues of concern include off-target edits, unintended consequences, mosaicism, designer babies, enhancements (non-medically related edits), and eugenics. To simplify these issues, some were grouped together as one category, as they were similar or related: one category for off-target edits, unintended consequences, and mosaicism; and one category for designer babies and enhancements. Eugenics was kept as a separate category, even though it could relate to designer babies, because it had to do more with eliminating unwanted genes and creating a superior race as opposed to just picking desirable physical traits in children. At times, gene editing was utilized for nefarious purposes in general and did not necessarily correlate exactly with any one category. Therefore, the violation of nonmaleficence was matched as best as possible if the occurrence simply just caused harm.

Stories that depicted off-target edits or unintended consequences (no story depicted mosaicism as an issue) were *The Island of Dr. Moreau* (Wells 2004, Stelloff 1977, and Pressman 1996), *Beggars in Spain* (Kress 1993), *X-Men* (Donner 2000), *The Neanderthal Parallax* trilogy (consisting of *Hominids, Humans,* and *Hybrids*) (Sawyer 2002, 2003, and 2003, respectively), *Star Trek: Enterprise* season 4 episodes 4-6 (*Borderland, Cold Station 12,* and *The Augments*) (LaZebnik 2004, Brennert 2004, and Sussman 2004, respectively), *Next* (Crichton 2006), The *Tankborn* Series (consisting of *Tankborn, Awakening,* and *Rebellion*) (Sandler 2011, 2013, and 2014, respectively), *The Amazing Spider-Man* (Arad

2012), *The Origin Mystery* Trilogy (consisting of *The Atlantis Gene, The Atlantis Plague,* and *The Atlantis World*) (Riddle 2013, 2013, and 2014, respectively), *The Reconstruction of William Zero* (Burns 2014), *The Perfect 46* (Bonowicz 2014), *Equals* (Pruss 2015), the *Rise of the Kymiera* six-part series (consisting of *Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) (Turnbull 2017), *Change Agent* (Suarez 2017), *The Titan* (Amel 2018), and *ReEvolution* (Grant 2019).

Designer babies and/or enhancements were seen in *The Blood Beast Terror* (Miller 1968), *Friday* (Heinlein 1982), *Beggars in Spain* (Kress 1993), *Gattaca* (DeVito 1997), *My Sister's Keeper* (Picoult 2003 and Furst 2009), the *MaddAddam* trilogy (consisting of *Oryx and Crake, The Year of the Flood,* and *MaddAddam*) (Atwood 2003, 2009, and 2013, respectively), *X-Men* (Donner 2000), *The Neanderthal Parallax* trilogy (consisting of *Hominids, Humans,* and *Hybrids*) (Sawyer 2002, 2003, and 2003, respectively), *Star Trek: Enterprise* season 4 episodes 4-6 (*Borderland, Cold Station 12,* and *The Augments*) (LaZebnik 2004, Brennert 2004, and Sussman 2004, respectively), *Splice* (Hoban 2009), the *Tankborn* Series (consisting of *Tankborn, Awakening,* and *Rebellion*) (Sandler 2011, 2013, and 2014, respectively), *2312* (Robinson 2012), *The Amazing Spider-Man* (Arad 2012), *Jupiter Ascending* (Hill 2015), the *Rise of the Kymiera* six-part series (consisting of *Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) (Turnbull 2017), *Change Agent* (Suarez 2017), *Tourbillon* (Ivery 2018), *Rampage* (Flynn 2018), and *ReEvolution* (Grant 2019). Interestingly, a common method for endowing enhanced abilities was derived by splicing animal DNA into human DNA. Scientifically, this is not currently feasible, but makes for interesting and entertaining science fiction by satisfying the imagination that humans can be enhanced in such away. Lastly, stories that contained eugenics were *Brave New World* (Huxley 1932), *That Hideous Strength* (Lewis 1945), *Code 46* (Eaton 2003), and *The Perfect 46* (Bonowicz 2014).

Just as a side note, some stories also took place in dystopian societies, which included societies that were post-apocalyptic or post-war. This meant that the Earth was practically destroyed, had limited resources due to wars, or societies were just downright oppressive. If a society was deemed unfit or unpleasant in which to live, it was categorized as dystopian for the purpose of this analysis. Such stories were *Brave New World* (Huxley 1932, Babbin 1980, and Joyce 1998), *Gattaca* (DeVito 1997), *Code 46* (Eaton 2003), *Cowl* (Asher 2004), *The MaddAddam Trilogy* (*Oryx and Crake, The Year of the Flood, and MaddAddam*) (Atwood 2003, Atwood 2009, and Atwood 2013), *Tankborn* (Sandler 2011), *2312* (Robinson 2012), *Intrusion* (MacLeod 2012), *The Origin Mystery Trilogy* (*The Atlantis Gene, The Atlantis Plague, and The Atlantis World*) (Riddle 2013, Riddle 2013, and Riddle 2014), *Equals* (Pruss 2015), *Rise of the Kymiera six-part series* (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) (Turnbull 2017), and *The Titan* (Amel 2018). Dystopian societies do not technically fit in with the issues under nonmaleficence regarding gene editing, but were more the result of systemic issues that developed due to misuse of gene editing.

Issues of Off-target Edits, Unintended Consequences, and Mosaicism

The Island of Dr. Moreau (Wells 2004, Pressman 1996, Steloff 1977)

Dr. Moreau in *The Island of Dr. Moreau* claimed he was helping the a beast people he created become men and women by altering their outward appearance to be more human and erasing their animal instincts (Pressman 1996, Steloff 1977, and Wells 2004). He believed his research would advance mankind and he was just mimicking nature by shaping the animals to his will, but he admitted he never thought about the ethics of his research (Wells 2004). In the 1977 film, Moreau asked the question, can we change the destiny of what an embryo becomes, since embryos of animals and humans look the same (Steloff 1977). As an outside observer, Edward/Andrew could see there was no clear benefit to this research and questioned Moreau's intentions. Moreau even admitted that the process of transforming the animals into humans, whether by vivisection in the novel or genetics in the films, regressed over time. In the 1996 film, Montgomery administered hormone shots to control the regression and moods of the animals while Moreau maintained their submission through a remote controlled implant that electrocuted them (Pressman 1996). In all three versions of the story, the beast people were clearly mentally distressed fighting their animal instincts and eventually rebelled against Moreau; both Moreau and Montgomery were killed, but Edward/Andrew escaped the island. Changing animals into humans had no clear medical benefit, the transformation process was painful, and the beast people were abused by Moreau. The unintended consequence in this case is the regression and rejection of the animals becoming human. Also, the beast people were not fully transformed, therefore, mosaicism must be occurring in the films: not all of the cells were incorporating the genetic edits (Pressman 1996 and Stelloff 1977). This was not explicitly stated, but obviously happening. Moreau's experiments were a gross violation of nonmaleficence, as he was certainly causing harm to animals/the beast people.

Beggars in Spain (Kress 1991)

As mentioned under autonomy: somatic vs. germline, the geneticists in *Beggars in Spain* did not know when they made the sleepless edit, that the sleepless gene would be dominant and every child born from a sleepless person would also be sleepless (Kress 1991). This was one example of an unintended consequence of a gene edit. Another example occurred when a sleepless person died in a car crash and was studied. What they discovered during the autopsy was he was in perfect health and showed he was ageless on the inside due to the lack of organ degeneration that would normally be observed, which meant the lifespan of the sleepless people was unknown (Kress 1991). Susan, one of the geneticists, said to Leisha,, "[Y]ou're going to get called superman, homo perfectus, who-all-knows what. Immortal," (Kress 1991). Clearly, this unintended consequence was due to polygenic genes: altering the genes that affect sleep had effects on other genes that affect aging. The tenet of nonmaleficence warns about unintended consequences that could have a negative health impacts due to polygenic gene interactions because they are not well-understood, but the unintended consequences in *Beggars in Spain* did not cause ill effects; rather, they caused what could be argued to be positive health effects (Kress 1991). Whether or not this is a violation of nonmaleficence is not definitive, since the unintended consequences did not actually cause harm.

X-Men (Donner 2000)

In this film, Magneto had the desire to make more mutants by utilizing a machine that emitted radiation to inflict genetic mutations on humans. He believed humans had feared them and inflicted violence on mutants for far too long in addition to believing that mutants were the next step in human evolution. To test his machine, his team kidnapped a senator who was outspoken about legislating a mutant registration act, thus forcing all mutants out in the open and divulging what their mutant abilities were. After having survived the Holocost, Magneto was against the passing of this act. When he used the machine to genetically edit the senator, he was successful at creating a mutant and providing an enhanced ability (the senator was able to become fluid-like). However, because of his new ability, the senator escaped his prison and sought the X-men for refuge. While at Xavier's School for the Gifted, the forced mutation led to his death by turning him into a puddle of water. Upon hearing this, Magneto did not care that his machine killed humans. He attempted to genetically modify the world leaders at a summit on Ellis Island. Thankfully, the X-men were successful at thwarting his plan.

The unintended consequence here was the fact that the mutation inflicted on Senator Kelly led to his death due to instability of the edit. It was unclear in this movie how mutants were endowed with their naturally occurring mutations, but by creating the x-mutant gene in humans through radiation was not a viable method to genetically edit humans. Magneto had a complete disregard for human life and was not concerned in the least that an artificially derived x-gene caused death as a side effect. Nonmaleficence was clearly violated by Magneto and his use of his radiation machine.

The Neanderthal Parallax trilogy (Hominids, Humans, and Hybrids) (Sawyer 2002, 2003, and 2003)

After falling in love, Mary and Ponter decided they were going to be bonded (the Neanderthal term for married) and wanted to have a child. Due to technically being different species of humans, their chromosomes did not perfectly match, which would make conception difficult (Neanderthals had twenty-four chromosomes and Homosapiens had twenty-three chromosomes). Vissan was a geneticist who had invented a codon writer that could write any desired genetic code. Even though they had eliminated most genetic disorders through selective breeding, errors in the genetic code could still be randomly made through natural procreation. Her desire was to eliminate randomness in gene selection. However, it was banned in the Neanderthal world because people who had been sterilized as a punishment for a crime could still used the codon writer to procreate, which defeated the purpose of the punishment. Vissan had chosen to live alone in the wilderness away from civilization because she was upset that her invention would not be used to benefit society. But this codon writer was their only hope of having a child to ensure their set of chromosomes matched, so they sought Vissan's assistance.

Vissan was able to use her codon writer to program a DNA sequence that combined their chromosomes and selected the traits they desired for their child without mistakes: a daughter who could stay with Mary when two were not one in the Neanderthal world but with a Homosapien's appearance so she would not look out of place in the Homosapien's world. In the end, they ultimately decided to eliminate the God gene as well (a Homosapien genetic trait that predisposed humans to believe in God). They also decided on eye color and a few other traits. To work around the ban, they brought the codon writer to the Homosapien world, as it was not banned there.

Mary and Ponter had entrusted the wrong person to sneak the codon writer to the Homosapien world: Jock. Jock thought the Neanderthal world was far better off than the Homosapien world, as they did not have environmental pollution and overpopulation. He saw this as an opportunity to start over. Therefore, he uses the writer to design a virus that recognizes Neanderthal DNA only to wipe them out, thus enabling Homosapiens to claim their universe. He was not successful, as a scientist working for him realized what he was doing and altered the virus to recognize Homosapien male DNA only instead, thus protecting the Neanderthal world from invasion by men.

This is not directly an unintended consequence or off-target edit, but demonstrates how gene editing technology in the wrong hands with the wrong intentions can lead to abuse of the technology. The codon writer was invented with the intention to prevent the transmission of undesirable genes, possibly disease causing genes, and mistakes that could be made in random gene selection during procreation. But one ill-intentioned person decided to use it to inflict genocide by genetically engineering a deadly virus targeting specified DNA. The level of evilness of this act cannot even be put into words. This is a cautionary tale that could be used to demonstrate the necessity of protective laws governing how CRISPR and other gene editing tools can be legally used.

Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and The Augments (Episode 6) (Brennert 2004, LaZebnik 2004, and Sussman 2004)

During a conversation with Malik, Soong was explaining to him that around the time of the eugenics wars, geneticists had made great strides in correcting genetic mistakes in the human genome, but did not know how to fix all of them. For instance, augments like Malik and his siblings were modified to have double the lifespan, increased strength, and higher intelligence, but this resulted in aggressive behavior and hubris that geneticists did not know how to prevent at the time. Therefore, after "rescuing" more embryos from Cold Station 12 (i.e. stealing), Soong was further modifying them to eliminate the aggressive behavior with his knowledge of genetics, which was more advanced than previous geneticists. However, Malik did not agree with Soong's assessment that aggressive behavior was a design flaw and therefore questioned who decides what is a defect in humans.

Although Malik had a point in questioning who determines what is a genetic defect and what is not, Soong was correct in his assessment that aggressive behavior that accompanied the augmentations to strength, intelligence, and lifespan was an undesirable unintended consequence. Malik appeared to lack empathy toward humans and felt justified in releasing a virus that would kill them in an act of revenge for being ostracized. Feeling a desire to murder people and acting on it is unacceptable. Having the means to correct this unintended consequence and not do so would have been a violation of nonmaleficence and ethically unjustifiable on Soong's part. Attempting to kill Soong for editing aggressive behavior out of the embryos was also clearly wrong of Malik and proved Soong's point.

Next (Crichton 2006)

As stated in the autonomy section, *Next* contained numerous biomedical issues (Crichton 2006). Firstly, a transgenic chimpanzee was created by a geneticist who was researching what genes influence communication issues that manifest in autism, since chimpanzees are able to communicate without language similar to people with severe autism (Crichton 2006). He inserted his genes into a chimpanzee embryo intending to study it before it was carried to term, but the mother was quarantined during an infectious outbreak and gave birth to a "humanzee" named Dave who had some human-like features and could talk (Crichton 2006). The experiment itself was unauthorized and illegal since primates too closely resemble humans and transgenic animals tend to have health issues. The researcher and his family attempted to assimilate him into school by falsifying claims that he had a genetic disorder, but Dave struggled to learn and exhibited chimpanzee behavior when threatened. Similar to *The Island of Dr. Moreau,* Dave struggled to be a human, but dissimilarly, he did not reject the idea of being a part of a family (Wells 2004). The outcome of an experiment by transplanting human genes into an animal embryo clearly led to the unintended consequence of a live, transgenic animal. But incorporating human genes into an animal, even one so closely related to a human, had several outcomes that could not have been known and should not have been attempted without proper authorization.

Also in *Next,* BioGen was studying a rat retrovirus carrying what they called a maturity gene that theoretically accelerated mature behavior which they believed could assist in curing neurodegenerative diseases where the maturation pathways were disrupted (Crichton 2006). One of the laboratory technicians took the retrovirus out of the laboratory accidentally and his drug addicted brother inhaled it thinking it was a recreational drug, after which he ceased using drugs and put his life back in order. The technician administered the retrovirus to one other person who also was addicted to drugs. For a time, they both seemed to be cured and the company thought they had stumbled upon a major discovery that would make substantial profits. Then all of the rats in the study died prematurely, the second person aged very quickly then died of a heart attack at the age of twenty-one, and his brother was aging rapidly in the hospital with his imminent death nearing. Clearly this violated nonmaleficence because the rat retrovirus was administered to people before proper animal studies were completed to prove the safety, efficacy, and mode of action of the treatment. The gene did not just affect behavioral mechanisms in the brain, but also aging mechanisms. The technician and the BioGen company are responsible for the deaths of two people because they did not follow proper research protocols.

Briefly, four more issues of misuse of genes, genetic testing, and gene therapy were discussed in *Next* (Crichton 2006). One issue was how the patent system allows for the patenting of genes by companies or universities, which prevents them from being properly studied for drug development because other companies or universities might not be able to afford the exorbitant licensing fees to obtain the genes from the company of ownership. The second issue was the use of genes in legal battles to excuse poor behavior, such as a pedophile claiming he could not control his behavior because he had the “novelty” or thrill seeking gene, as well as a drug addict tracking down and suing the man who anonymously donated sperm for inheriting genes that cause drug addiction. There is no scientific evidence that one gene alone is responsible for behavioral patterns, but this did not stop lawyers from trying to win court cases with such logic. The third issue was using genetic analysis to prove someone had genes for a debilitating genetic disorder and therefore would be an unfit parent in a custody battle. The fourth issue was the use of gene therapy to attempt to cure terminal patients, which only had a three percent success rate and about six hundred people were killed due to failed gene therapy, one case described was a twelve year old girl (Crichton 2006). The deaths, however, were not reported in detail because of “trade secrets”. With the advancement of research allowing genes to be further understood and therapies developed, the results of such research are being misused for ill intentioned purposes or are being implemented without enough research being done. Also, the applications of gene therapy described in *Next* are premature, as they are leading to a significant amount of deaths (Crichton 2006).

Tankborn and Awakening (Sandler 2011 and Sandler 2013)

GENs (Genetically Engineered Non-humans) in the *Tankborn* trilogy were not supposed to get sick, as they were genetically engineered to resist infection and they healed rapidly (Sandler 2011 and 2013). However, a disease called scratch was fatal to GENs and seemed to surface unanticipatedly. Another seemingly unrelated event was the increase in the distribution and selling of a drug called punarjanma, which healed ailments and diseases in Trueborns. Kayla discovered that a geneticists, Akhilesh, genetically engineered the disease scratch in GENs because when GENs heal, the infection produces punarjanma, which can then be extracted while GENs are in the tank. Punarjanma was described to be a viscous yellow liquid. Essentially, GENs were genetically altered to be infected with scratch with the purpose of manufacturing the drug, punarjanma. Akhilesh was using GENs as drug factories and thus was exploiting them to further benefit Trueborns.

The GENs were already not granted many rights in society. They were the lowest class, were genetically engineered to have a specific set of skills, and were sold as slaves to the Trueborns who could afford them. Trueborns did not even see them as humans, which is clearly apparent in Akhilesh's creation of scratch for the purpose of manufacturing punarjanma. GENs sole purpose in life was to serve Trueborns. Akhilesh is an example of a researcher with ill intentions who used his position at GAMA (Genetic Augmentation and Manipulation Agency) to convince others to approve his research with false pretenses (he claimed he was trying to restore GENs' ability to procreate) and his knowledge of genetics to further manipulate GENs to produce a healing drug for Trueborns. This is an example where Kantianism was not followed: the end, creating a drug to heal diseases, did not justify the means of turning human beings into factories. This story demonstrated a nefarious unintended consequence: allowing gene editing research without clearly defined guidelines could lead to unethical uses of the technology if placed in the wrong hands.

The Amazing Spider-Man (Arad 2012)

At Oscorp, the company had decided not to move transgenic gene splicing experiments to human trials because the problem of the decay rate algorithm had not been solved in animal trials, which meant gene edits reverted over time. Dr. Connors, a geneticist at Oscorp, could not accept the termination of his research project and was desperate to prove his gene edits could work. He was missing an arm and decided to inject himself with the gene editing serum and lizard genes that allowed the regeneration of limbs. At a lower dose, his arm did regrow, but only temporarily. He continued to increase the dosage to make it work permanently, but this is not what happened. Upon increasing the dosage, an unintended consequence developed: he did not just regrow his arm, but also turned into a lizard from head to toe, complete with green scales, yellow eyes, a tail, talons, and sharp teeth. Still, every time he reverted back to his human self. What also occurred unintentionally due to the conversion back and forth from human to lizard was the development of a split personality, which caused him to act out violently and believe gene editing everyone in New York City was a brilliant idea.

It is important to note that such transgenic manipulations are not currently feasible. This may be blatantly obvious, but I am stating it to be clear. The premise behind the research, using animal genes for healing and giving them to humans, is interesting, has medical benefit, and has the best of intentions. But Oscorp deciding not move to human trials was the correct ethical decision to make, as the gene editing serum had negative side effects and was not a permanent cure. Dr. Connors had the right to autonomously choose to use the gene editing serum on himself, but the risks outweighed the benefits. Dr. Connors in the end was fortunate his intern developed an antidote to cure him and stop the aerosol version of the serum from gene editing the citizens of New York City.

The Origin Mystery Trilogy: The Atlantis Gene, The Atlantis Plague, and The Atlantis World (Riddle 2013, Riddle 2013, and Riddle 2014)

The first unintended consequence that occurred in this trilogy was the result of the Great Leap Forward, which was caused by endowing Earth humans with survival genes. The problem was Isis and Janus were attempting to save humans from dying out, but their gene edits worked too well. Humans' brain wiring was affected more than they anticipated, which allowed for the development of religion, art, fashion, and the building of better tools. Isis and Janus anticipated this would eventually happen, but not for thousands of years more. Unintentionally, they also assisted Homo Sapiens too well, as Homo Sapiens wiped out all other species of humans on Earth to ensure their survival.

In addition, Ares and Isis had performed their own genetic manipulations on Earth humans: the Atlantis gene, which was intended to be the ultimate survival gene. Sentinels were a species of sentient beings determined to assimilate all intelligent life forms throughout the universe. Atlantis had already been destroyed by the Sentinels. Within the genetic code of the Atlantis gene was the means of destroying them when they attempted to assimilate a human from Earth who could resist them. However, the Atlantis gene caused a great plague when it was activated and millions of people were killed. The Atlantis gene was unstable in many people. Dr. Warner was able to design and distribute a cure to stabilize the gene, which was successful at saving many remaining lives. David, Dr. Warner's partner, was the one who was able to resist and stop the Sentinels. In the process, Ares' plan may have saved the Earth from Sentinel assimilation, but did so through mass destruction and death.

Ares believed the Sentinels were the greater threat and did not want to see any more planets with intelligent life assimilated by the Sentinels. Earth humans were nothing but pawns in a chess game played by Ares vs. the Sentinels. Ultimately, Earth was saved. But saving the planet came at a great cost. A large portion of the population was lost in the plague. Another means that did not decimate the population would have been a more ethical, better course of action.

The Reconstruction of William Zero (Burns 2014)

William Blakely was a geneticist working on creating proxies or clones in *The Reconstruction of William Zero* (Burns 2014). His research used telomerase protein to create an RNA template to create an embryo that grew to a mature adult in fifteen months, meaning the telomere age of the clone was different than the actual age. He cloned himself at home, which meant the clone's telomere age was thirty-six and his actual age was six months. In the laboratory, his team was cloning dogs. He was not just making exact copies of a genome, though, to create the clones. He was using gene editing to manipulate the telomeres to force the embryo to become a fully-grown adult of a certain age in a short amount of time. The clones, generally speaking, were an exact physical likeness, but seven out of ten clones developed brain tumors and lived less than a month (Burns 2014). By researching telomeres, one would think the goal would be to extend lives, since telomeres shorten over time and affect aging. But this research was using telomeres to make specimens older faster. The potential medical benefit of researching genes to make clones that matured to a particular age quickly is unclear, especially since the clones were riddled with health problems and one clone of William was mentally unstable. William Blakely's research was causing more harm than benefit, therefore violated nonmaleficence.

The Perfect 46 (Bonowicz 2014)

In *The Perfect 46,* again, utilizing the website did not eliminate diseases by editing genes, but rather by breeding them out (Bonowicz 2014). As mentioned in autonomy, about seventeen hundred babies were born without genetic diseases by using the website (Bonowicz 2014). However, a glitch in the algorithm led to the pairing of three-hundred and eight genetically incompatible couples, twenty-four of whom had babies born with Tay-sachs disease that results in painful, premature death by the age of five (Bonowicz 2014). This was most certainly an unintended consequence, as the software was designed to pair compatible couples. An investigation revealed that the company nor any particular individual was at fault for the glitch. Even though 99.95% of clients were unaffected, the 0.05% affected are people and not inanimate objects. To those twenty-four couples, even though the mistake was not due to human error, the consequences were devastating, as their children died and they had to suffer the emotional trauma accompanying the loss. This was a prime example that when people begin to meddle with genetics, unintended negative consequences are always a possibility.

Equals (Pruss 2015)

Every person in *Equals* was genetically modified at the embryonic stage to eliminate emotions (Pruss 2015). The reason was that they believed humans made emotionally charged decisions that negatively affected society, started wars, etc., thus making them defective. Eliminating emotions in turn eliminated conflict and violence. The upside to his was no one was afraid of being attacked while walking alone, women were not afraid of rape or sexual assault, theft was not a problem, and crime was not observed. At first glance, this may seem appealing and in many ways, it is.

However, some people experienced SOS: Switched On Syndrome where the gene suppression stops working. People begin to experience feelings and sensory functions become active again. This leads to "symptoms" of depression, difficulty concentrating, impulsivity, touching, and even coupling. Even though no one in the film can explain why gene suppression fails in some people, I started to conjecture that perhaps mosaicism is to blame. When gene edited in the embryonic stage, not all cells received the edit. Therefore, in some cells, genes that control emotions are turned on. When more cells have the gene turned on vs. off, then the suppression fails. This was not confirmed in the film, but is a possibility. Or an environmental factor caused an epigenetic effect that turned on suppressed genes.

Philosophically, the issue here is that the gene suppression of emotions is not treating a debilitating disease. Nature is being defied and everyone had removed what makes people inherently human. The world was completely white: architecture, clothing, decor, everything was white, white, white and therefore devoid of interest, expression, and individuality. Everyone was a drone going to work, working all day, then spending time alone in one's apartment until bedtime. Even watching someone commit suicide by jumping off of a building elicited zero emotional response. One person said, I hope they find someone to cover his work. Empathy is clearly lacking here. No one was really living life. Humans are supposed to be social beings and there was no socialization at all other than cordial, brief interactions at work. The unintended consequence of removing emotions to prevent violence and promote equality was the complete loss of a life well lived. People were just existing in a boring world working until they die. Those who had SOS admitted that experiencing emotions was how humans were supposed to be. Silas and Nia agreed that now that they had found love in each other, they did not want to give it up. But the only way to live together was to leave, which is what they did.

Rise of the Kymiera six-part series (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) *(Turnbull 2017)*

The gene edits made to embryos at Dr. Newman's fertility clinic actually did not contain any mistakes or off-target edits. This was why Utopia Genetics wanted to study the young women who were gene edited by Dr. Newman to figure out his technique in order to replicate it, as he was able to seamlessly incorporate animal DNA into human DNA without any issues. Essentially, his experiments were successful at creating transgenic humans without becoming "freaks": they did not lose their mental clarity or become infected with an S.I.D. infection. The issue actually was the fact that he violated autonomy by performing edits without the informed consent of the parents. Also, the genetic modifications were time released, so the young women underwent a transformation around the age of sixteen or seventeen years of age. A concern of gene editing typically mentioned is a mistake that is unrealized for years, perhaps becoming apparent in pubescent years of life. Dr. Newman's edits did not contain a mistake, as they were intentionally delayed until puberty. But the adolescent women did not know they had been gene edited and when they suddenly developed unexplainable abilities and changes to their bodies, it was a bit of a shock because they did not know what was happening to them. Then they were kidnapped and forced to undergo scientific testing, furthering their confusion. Lastly, it was unclear if Dr. Newman knew exactly how the gene edits would manifest once the animal genes were expressed during puberty. Lucy grew tough skin like a turtle; Melinda could generate electricity like an eel; Vanessa had canines and sharp hearing like a fox; and Chloe grew wings, had lighter density bones, and could use sonar like a bat. The reader was left to conjecture whether or not these were the intended outcomes or not. If not, then nonmaleficence was definitely violated.

The Titan (Amel 2018)

In the movie, *The Titan,* there were a few instances of unintended consequences (Amel 2018). The premise of the movie was to use gene editing to modify a group of soldiers in order to adapt to the climate on the moon, Titan. At first, the edits seem to work: the soldiers could withstand colder temperatures more easily. But as the film progressed, people began to die due to rejection of the gene edits, which caused asphyxiation or internal bleeding, or they became violent, killing their spouses, and had to be eliminated so they would not be a further endangerment. The procedures became progressively riskier, starting with injections then moving to invasive surgery, and had negative side effects in all but two subjects, but one of the two who survived until the end murdered her husband and was killed as well. The reason for the violent behavior was due to being edited with animal genes, of which they were unaware when they signed on. The animal genes were intended to provide them with abilities that would assist with their survival (enhanced sight, lower body temperature, non-verbal communication, etc.), but violent behavior and untimely death were unintended consequences of the edits. The principal investigator of the research later admitted there were no means of predicting the outcomes, as nature itself is unpredictable, but he also treated the research group as more of an asset or investment than actual human beings (Amel 2018). He did not seem to care that the group was essential sacrificed to determine how humans could be edited with animal genes and his ulterior motive was to create a new race of humans.

ReEvolution (Grant 2019)

Once in China, John was starting to learn more about Xian Corp from a researcher, Li Ming, who was appalled by some of the experiments being performed on people. John had also stated to the lead researcher, Tan, that performing gene editing on humans was illegal in the United States. But Li Ming informed him that wealthy people who wanted ailments cured and their lives prolonged funneled money into research that was not published and the private sector that kept results from the public. They did not care if the results caused harm to test subjects, they just wanted to see progress for their own selfish desires.

As mentioned earlier, Tan was traveling to impoverished communities in the countryside to test CRISPR applications. After being given an injection of CRISPR that was supposed to boost intelligence, a man began to hallucinate, suffered from intense headaches, became psychotic, then eventually died of a stroke. Another young boy was given an injection to increase muscle mass, but succumbed to a painful liver cancer and died. These were just a few examples of many instances. Li Ming was not alone in his disgust for the treatment of these people. John snuck into a restricted research area and observed what he thought to be many unwilling participants in cages suffering from side effects of CRISPR injections, one of them being Li Ming who was obviously taken there to be silenced.

Due to off-target edits and detrimental side effects, CRISPR should not have been used in clinical trials involving people. They were experiencing pain and premature deaths as a result of unsuccessful gene edits. Not only were these experiments unethical under the tenet of nonmaleficence, they were an illegal "black ops" research project meant to obtain results by any means necessary. Ethical guidelines and laws were meant to prevent this, especially in the United States and Europe. But some research in China was purposefully hidden and public officials looked the other way. This type of corruption and exploiting poor people in human trials is completely unacceptable and demonstrates why stricter guidelines and laws are necessary on what applications of CRISPR are acceptable.

Issues of Designer Babies and Enhancements

The Blood Beast Terror (Miller 1968)

Although the description of the film stated that the creature in *The Blood Beast Terror* was created using genetics, this was never actually stated explicitly in the film (Miller 1968). Since the professor was a biochemist and entomologist, the assumption will be made that he did use genetics to create the beast that was a cross between a human woman and a death head moth. Professor Mallinger mostly studied moths and wasps, which is most likely the reason he chose to incorporate the death moth into the new species he created. But why he chose to create the cross species in the first place was not revealed. The problem with the moth woman was she was killing men, feeding on their flesh and draining their blood. This is actually not surprising since the death head moth is a blood drinking moth. The strange occurrence was to hunt, she transformed into a human sized moth, then reverted back after feeding. The detective investigating the murders pieced together who the murderer was because like a normal moth, she shed scales from her wings, but much larger. Professor Mallinger was in the process of creating a moth man for her as a mate, but realized she was a murderous terror and burned him before he hatched from the chrysalis. In a rage, she killed Mallinger. Because this was an older film, the acting was entertaining to view. However, even if creating cross species humans that could transform back and forth from animal to human were genetically feasible, there is zero medical benefit to such an application, especially in this case where the beast required human blood for sustenance. This would fall under the category of enhancement and therefore cannot be ethically justified.

Friday (Heinlein 1982)

Friday in the novel *Friday* was an artificial person genetically engineered in the laboratory to have advanced abilities in addition to being immune to cancer and infectious diseases, but was designed in such a way that biologically, she was visually indistinguishable from a naturally conceived human (Heinlein 1982). Her enhancements included elevated strength; quick reflexes; physical endurance; heightened sense of smell, sight, and hearing; the ability to hold her breath for a long time underwater; and superb brain power (i.e. highly intelligent) (Heinlein 1982). Because most AP's were sold as indentured servants for sex work, they were also endowed with perfect bodies and were either sterile or reversibly sterile, Friday being reversibly sterile (Heinlein 1982). In a letter to her after his death, Boss revealed he was her foster father and bought her contract because she was created from ova and sperm from two of his colleagues, his own genes, and genes from other sources stating, "all of you was most carefully selected to maximize the best traits of H. sapiens," (Heinlein 1982). Friday was designed in a laboratory to be perfect, essentially, which violates the tenet of nonmaleficence. She was created with numerous advantageous genetic traits, only two of which had medical benefit: being immune to cancer and infectious diseases. It is also safe to assume she was created free of genetic diseases, as she was completely engineered in a laboratory. Utilizing gene editing and genetic engineering to provide enhancements rather than medical benefit is frowned upon and clearly Friday was extravagantly enhanced. Current scientific methods are not advanced enough to produce an artificial person like Friday, but ethically speaking, society has to decide as a whole if it does become possible, would these types of enhancements be acceptable. The current consensus is no, but as gene editing and genetic engineering technologies advance, so may society's views.

Beggars in Spain (Kress 1991)

Coming back to *Beggars in Spain*, recall that there were intended consequences of which geneticists were aware when they modified the sleep genes, meaning other hormonal adjustments had to be made with other DNA edits to ensure repair mechanisms that normally occurred during sleep occurred during wakefulness, as well as sleepless children were more intelligent, joyful, excelled at problem solving, never experienced depression, and were resistant to illness (Kress 1991). Because of the intended and unintended consequences of editing sleep genes to make people sleepless (the unintended consequences were the sleepless gene was heritable and organ degeneration ceased, thus causing a prolonged life), many claimed the sleepless were unfairly advantaged. All of the sleepless children were highly successful at school and their careers at young ages (in their twenties) due to their enhancements and the sheer fact that they had more hours to accomplish really anything they wished. In the beginning, Leisha's mother also requested that her daughter be tall, slender, blonde, musically adept, and with green eyes; although some of these genes would only provide a disposition toward the trait, such as slenderness or musical acuity (Kress 1991). Not only was Leisha enhanced, she was also a designer baby, as her parents very specifically picked her gender and physical appearance. Enhancements and designer babies are not accepted under the tenet of nonmaleficence.

Gattaca (DeVitto 1997)

Gattaca was a movie well ahead of its time and brilliantly issued a very clear social warning as to the direction society might head if given the chance before gene editing became a real possibility (DeVitto 1997). In this society, most people did not leave having children to chance or nature, but rather, they consulted a geneticist at a fertility clinic. Vincent was conceived the natural way and at birth, he was determined to have a heart defect and was expected to die at the age of 30.2 years (DeVitto 1997). His brother, Anton, was conceived through a fertility clinic and his parents were told by the geneticist that the child would still be theirs, sharing their genes, but the best possible outcome with no predisposition to genetic diseases and they could choose which physical traits they wanted (DeVitto 1997). Fertility clinics were essentially in control of the gene pool and their justification was ensuring parents their child would have the best chance in life by choosing the best genes and performing gene editing in the embryonic stage. They were promoting designer babies, which became a social norm. After watching a few documentaries on CRISPR, I have heard people in charge of fertility clinics state they were inspired by *Gattaca* and the utopian society that was created is something for which to strive. This is not the case: *Gattaca* portrayed a dystopian society (see justice/discrimination/new social classes below) and no one should be inspired by the actions in this film because designer babies are not ethically acceptable.

X-Men (Donner 2000)

Mutants were endowed with superpowers and the x-gene manifested differently in every person. Wolverine/Logan had the gift of rapid healing that enabled him to survive the surgery that grafted adamantium to his skeleton. Magneto had the ability to generate and manipulate magnetic fields. Professor Xavier was a powerful psychic who could read and control minds, as well as track any mutant or human through his invention, Cerebro. Jean had the gifts of telepathy and telekinesis. Storm could control the weather and create lightning. Iceman could (you guessed it) take water molecules from the air and make ice. Mystique had the gift of metamorphosis and could assume the identity of anyone. Rogue was able to drain the life force of anyone she touched, meaning if she held on long enough she could kill them, and if she touched a mutant, she obtained their abilities briefly.

Shadowcat could walk through walls. These abilities are quite incredible and fantastical. It is quite unbelievable that one mutation could generate all of these different gifts.

Except for Senator Kelly who was mutated by Magneto's radiation machine, the x-gene was depicted to be a naturally occurring mutation. This film did not explain how mutants had come into existence. Magneto thought he had built a machine that could emit radiation that caused the x-gene mutation in any human artificially, but the mutation proved to be unstable and led to Senator Kelly's death. He wanted all humans to become mutants, but what enhanced abilities would develop was unknown. Senator Kelly had developed the ability of fluidity, allowing him to turn into water. He died because the last time he turned into a puddle of water, he was unable to turn back into a human. Magneto was not able to mutate any other humans, so it is unclear if every human would have had the same gift as Senator Kelly or if various gifts would have presented themselves like the natural mutants. Regardless, the enhancements would have been short lived due to the artificial mutation being unstable and resulting in death. Clearly, this is an unethical application of gene editing.

The Neanderthal Parallax trilogy (Hominids, Humans, and Hybrids) (Sawyer 2002, 2003, and 2003)

Mary and Ponter decided to have a child after they were bonded (married). But since she was a Homo sapien and he was a Homo neanderthalensis, their chromosomes did not align: twenty-three vs. twenty-four, respectively. This would make conceiving a child naturally risky and could result in a genetic disorder like Down syndrome. Therefore, they sought the assistance of former geneticist, Vissan, who had developed a codon writer that could ensure their genes aligned properly without causing mistakes or genetic abnormalities.

Vissan explained that her purpose in inventing the codon writer was to eliminate the randomness in gene selection during natural conception, which meant the choice of traits inherited by offspring was the “luck of the draw," so to speak. If she could allow the parents to choose the traits they wanted, then the better traits between the two people could be purposefully selected. Vissan assured Mary and Ponter the genetic code of their child would still be fifty percent from each parent, but the optimal combination of their genes would be selected. Mary and Ponter decided on a daughter Homo sapien (twenty-three chromosomes) with hair parted to the side like a Homo sapien, no religious center in the brain like a Homo neanderthalensis, and a few other traits that were not discussed in detail.

Mary had stated that this was not exactly designer babies because they were not adding DNA from outside sources, they were just using DNA from Ponter and herself. But I disagree with her assessment. Some traits were necessary to choose because leaving them to chance could have resulted in mental or physical health problems, as random combination from two species through natural selection had never been done before and the outcomes were completely unknown. For example, not deliberately choosing the genes for religious experiences could have led to a hybrid combination in her brain that could have led to psychosis. Even though they were using their own genetic traits, they were still choosing their daughter’s appearance and physical traits. As Vissan said, they were choosing the “best” traits from both of them. They did not think they were designing their child, but that is exactly what they were doing. However, I do not think that their choices were unethical in this particular case. They were ensuring their daughter would not have health problems by evaluating genes where they did not have genetic overlap and choosing one set to put into her genetic code. It was actually an ethically sound decision to ensure their daughter did not have genetic abnormalities through natural procreation. Not making these decisions could have actually done more harm.

The MaddAddam Trilogy: Oryx and Crake, The Year of the Flood, and MaddAddam (Atwood 2003, Atwood 2009, and Atwood 2013)

The *MaddAddam* trilogy consisting of *Oryx and Crake, The Year of the Flood,* and *MaddAddam* will be treated as one continuous story for the purposes of this analysis (Atwood 2003, Atwood 2009, and Atwood 2013). Crake was a code name for a man named Glenn who was a geneticist and was determined to create ideal humans, or at least what he perceived to be ideal humans, and they were called the Crakers. He spliced genes into humans to create advantageous edits for survival and aesthetics: they all had green eyes, perfect skin with built-in UV protection, and flawless figures; men were beardless; women had no body hair; they all had luminescent eyes that glowed in the dark (using jellyfish genes) and smelled of citrus fruit which acted as a natural mosquito repellent; the men's urine contained chemicals that warded off predators; they could purr like cats to heal bone fractures; they reached adolescence at the age of four; and they were caecotrophs like rabbits to maximize the digestion of food and enabled them to eat leaves (Atwood 2003). Crake also genetically edited the Crakers to have a unique, polygamous mating ritual that consisted of chromophores from an octopus to change a woman's abdomen and buttocks to blue signaling she was fertile, which occurred every three years, and men's genitalia would turn blue in response; then the men would perform a song and dance, she chose four with whom to mate, and her genetically enhanced vulva allowed her to withshand sex until she was pregnant (Atwood 2003). Crake deemed this mating ritual as guilt-free promiscuity (Atwood 2003). As seen in other novels, the Crakers were also immune to diseases. Although the Crakers were a project of just Crake, other BioCorps allowed people to purchase gene splices to customize their children (Atwood 2013). By creating the Crakers, Crake took gene editing to an extreme. The problem with his "perfect" race was they were very innocent and docile, which means they were not violent, but they needed protecting. They did not know how to survive in the world outside of the laboratory forest.

The next major issues in the *MaddAddam* trilogy were bioterrorism and engineered illnesses (Atwood 2003, Atwood 2009, and Atwood 2013). There were many BioCorps that worked on health products, beauty care products, or animal manipulations for food, pets, or organ growth for donation: OrganInc Farms, NooSkins, HelthWyzer, BioDefences, CryoJeenyus, Genie-Gnomes, RejoovenEsense and AnooYoo (Atwood 2003). There were treatments to regenerate/regrow skin to stay looking younger, vitamins that claimed to make you live longer, and animals like pigoons (pigs that could grow multiple kidneys at once) or ChickieNobs (chickens genetically modified to only have a mouth to eat and only produced chicken parts like breasts and thighs) (Atwood 2003). HelthWyzer in particular placed bioforms in their vitamin pills and developed an antidote alongside the bioform so when people became sick, they could only obtain the cure from HelthWyzer, which of course maximized profits from the vitamins and the cures, especially if the illnesses were prolonged (Atwood 2003). No one would argue that the purposeful infection and extortion for medical treatment are completely unethical under the tenet of nonmaleficence. Crake actually invented his own pill that caused the "waterless flood", which decimated most of the population: the BlyssPluss pill, which prevented the transmission of STDs, prevented pregnancy in both men and women, and increased sexual desire, also secretly contained a time-released virus that caused high fever, bleeding from the eyes, organ degeneration, and eventual death (Atwood 2003 and Atwood 2009). Of course he created the vaccine to the virus, but only administered it to a few people. He believed the world was overpopulated and violent, so he made his superior race, the Crakers, to repopulate the earth after wiping out the human population with the BlyssPluss pills. The only people who survived were those who did not take any BioCorps vitamins, BlyssPluss pills, Crake's inner circle who were vaccinated, and the Crakers who were genetically engineered to be immune. Defining his acts as "causing harm" is not nearly descript enough. The waterless flood was an egregiously atrocious act against humanity orchestrated by one man who essentially wanted to play God by shaping the world to his will with his "superior" race.

Cowl (Asher 2004)

As stated under autonomy, Tack in *Cowl* was cloned from a former CIA agent, implanted with a semi-AI computer, and genetically modified as an adult to be the perfect killer possessing superior strength, reflexes, and combat skills in addition to being programmed to carry out his mission: kill Cowl (Asher 2004). He also had modified skin to resist UV damage and polarized nictitating membranes he could blink over his eyes to block sunlight (Asher 2004). Cowl and his sister, Aconite, were genetically engineered by their mother with animal genes, who, like Crake, had the desire to advance the human race (Asher 2004). Cowl possessed an exoskeleton due to beetle genes, which offered protection from attack, and was engineered to be highly intelligent with a semi-AI computer as well, but also had an aerogel grid fused to the exoskeleton so he could “see” without eyes (Asher 2004). Cowl, like his mother, believed himself to be genetically superior to humans, despite their own advancements in genetics. He desired to create more non-humans like himself by going back to the dawn of time to infuse his DNA in the protomix in the seas, theoretically changing evolution to eliminate humans by preventing them from ever existing. In order to determine if he was successful, he dragged people back in time with Tors (scales from his Torbeast) to test their genes, usually killing them in the process of time travel. The Torbeast also fed off of humans during historical events where mass murder would go unnoticed, like war or natural disasters, to avoid timeline disruptions and to drop Tors to pick up victims. This was the reason Traveler modified and programmed Tack: so he would be capable of killing Cowl and would be unable to resist the mission. All of these gene modifications in Tack, Aconite, and Cowl were enhancements, not medical benefits, regardless of the reasons for implementing them and were therefore violations under the tenet of nonmaleficence. Whether or not Cowl was a superior creature is irrelevant; the fact that he and his mother desired to create a “superior” race is also a violation of nonmaleficence.

Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and The Augments (Episode 6) (Brennert 2004, LaZebnik 2004, and Sussman 2004)

The augments in *Star Trek: Enterprise* were humans who were genetically modified in the embryo stage to have advanced abilities (Brennert 2004, LaZebnik 2004, and Sussman 2004). This does not require an extensive explanation: the augments were stronger, more intelligent, had resistance to diseases, and a lifespan that was double compared to a normal person on Earth. The only enhancement on that list that was medically related was the resistance to disease. In most discussions about applications of gene editing, non-medical enhancements are discouraged (Evitt et al. 2015, Hynes et al. 2017, Juengst 2017, Lanphier et al. 2015, Morange 2015, and Qiu 2016). In the show, the eugenics wars between the augments and humans ensued in the 1990's, which led to the death of thirty-million people. As a result, gene editing humans was banned since geneticists at the time had not figured out how to increase strength and intelligence without the accompanying side effect of violent and aggressive behavior. This was probably the best decision since the gene edits were mostly enhancements, not curing diseases, and the augments that were raised by Soong continued to kill people.

Splice (Hoban 2009)

Geneticists Clive and Elsa, who were also spouses who worked together, were combining DNA from various species to develop a new life forms in the hopes that cures for diseases would be discovered (Hoban 2009). Knowing it was an ethical violation and illegal, they began working on a human/animal splice by recombining integrating chimeric plasmids and creating a unique enzyme to enable them to ligate the human DNA to the animal DNA despite the company's objection (NERD: Nucleic Exchange Research Development); they did so because they thought some other company would beat them to it (Hoban 2009). Clive objected, but Elsa fertilized the genetically modified human/animal embryo and placed it in an incubator, which grew rapidly into an infant (Hoban 2009). Dren, their human/animal hybrid, had venom in her tail as a defense mechanism, two sets of lungs: human and amphibious that allowed her to breath air and underwater, a tongue like a reptile, wings, bird-like knees, and a human face. When she was an adult, she seduced Clive, but then because of hormonal changes, transformed into an aggressive male who raped Elsa. Clive and Elsa had determined that the violent behavior and psychological developments could be attributed to disproportionate species identification, i.e. the animal genes (Hoban 2009). In the end during a physical struggle, Dren killed Clive by stinging him with the venom and Elsa killed Dren, but was impregnated during the rape. Their experiment was riddled with ethical issues and illegal acts: cloning humans, using her own DNA in the experiment, prolonging an experiment well beyond the embryonic stage, and covering up what they had done. In the beginning, they claimed they were advancing science, but realized later on they were protecting what they viewed as a child. There was no medical benefit to their experiment, just the desire to confirm that human and animal DNA could be combined to create a new species. It is worthwhile to comment that current genetic techniques are unable to perform a human/animal splice depicted in this film.

My Sister's Keeper (Picoult 2003 and Furst 2009)

In *My Sister's Keeper,* a slippery slope was observed as the expectation for Anna to continually donate tissues increased in risk and quantities (Furst 2009 and Picoult 2003). Anna stated, “When Kate needs leukocytes or stem cells or bone marrow to fool her body into thinking it's healthy, I'm the one who provides them. Nearly every time Kate's hospitalized, I wind up there, too,” and “the only reason I was born was as a harvest crop for Kate,” (Picoult 2003). Anna was only supposed to give cord blood to her sister as an infant, but every time Kate relapsed, Anna was forced to donate something else: lymphocytes three times at the age of five, bone marrow (which she suffered complications and pain from the procedure after being stuck in the bone fifteen times), granulocytes at the age of six, and peripheral blood stem cells (Picoult 2003). Because Kate was in renal failure, Anna's parents expected her to donate a kidney, which would increase her risk for high blood pressure, put her at risk for complications during pregnancy, and would force her to quit playing hockey because she could not risk injuring her remaining kidney in addition to undergoing a major, invasive surgery to remove the kidney. This is a slippery slope because just one donation from Anna led to another, and another, and another, each with increased risk and invasiveness, and each previous procedure justified going a little further the next time. All that happened to Anna was also in conflict with autonomy and beneficence: Anna never consented to any of the procedures, as her parents had decision making capacity due to her being a minor, and none of the procedures gave her any benefit. Also, the ethics committee at the hospital was never consulted on Anna's behalf because Anna was not technically a patient; Kate was their patient. The reason Anna had to endure multiple medical procedures was because she was a perfect genetic match to her sister, purposely conceived to be a donor for her sister. When she refused to donate a kidney, she was forced to take legal action against her parents to protect her autonomous choice. Lastly, Kate did not actually want Anna to donate her kidney because the doctor said she was not strong enough for surgery and she wanted Anna to live her life, but their parents kept insisting because they did not want Kate to die. Nonmaleficence was clearly violated in this story: harm was inflicted onto Anna to benefit Kate.

Tankborn (Sandler 2011)

GENs (Genetically Engineered Non-humans) in *Tankborn* were another example of humans being enhanced with abilities from animal DNA (Sandler 2011). GENs skets (skill sets) were derived from the incorporation of animal DNA to provide adeptness in certain fields of work. Grace was obtained from feline genes, nurturing was obtained from dolphin genes, agility was obtained from cheetah genes, and strength was obtained from elephant or gorilla genes (Sandler 2011). The animal DNA portion was very minute, meaning most of their DNA was human, yet society viewed them as non-humans because of these splices. When GENs died, their genetic material was harvested to make new GENs, including making stem cells from skin, muscles, and organs which could then be used to create artificially grown embryos (Sandler 2011). GENs were not only enhanced, which is already a violation of nonmaleficence, but they were also treated as the lowest class in society and were exploited their entire lives for their abilities, then recycled like inanimate objects. Also, because they had a sub-neural network, they could have their entire identities erased and rewritten if they disobeyed.

2312 (Robinson 2012)

Interestingly, *2312* had humans that were augmented in order to survive space travel and live off of planet Earth, but also adaptations that were unrelated to survival (Robinson 2012). The most crucial augmentation was an extended life past one-hundred years with the oldest person reaching two-hundred years of age, which was achieved through repairing damaged DNA that would normally cause aging (Robinson 2012). Another component to extended lives was bisexual therapies in utero, puberty, and adulthood to make people either gynandromorphs or androgyns, as humans were technically both sexes genetically and hormonally, thus removing societal gender norms (Robinson 2012). They could not determine exactly why bisexual humans lived longer, but the truth of the matter was they did. The main character, Swan had some interesting augmentations: she whistled like a songbird, which was achieved by introducing a bird song node DNA into human stem cells then was inserted into her brain through her nose, allowing it to link to the musical networks already present in her brain; she also purred like a cat because she had feline amygdalan, hippocampal, and hypothalamic cells inserted into her (Robinson 2312). Extending life through repairing damaged or mutated DNA can be viewed as beneficial, as many health issues are caused by aging, and as an enhancement. As stated earlier, even though slowing aging provides health benefits, it defies nature and therefore the practice is ethically debatable. But whistling like a bird and purring like a cat are purely genetic enhancements and therefore frowned upon under nonmaleficence.

The Amazing Spider-Man (Arad 2012)

Spider-Man is a beloved superhero in Marvel™ comics written by Stan Lee. He was endowed with strength, agility, the ability to climb walls, and use webbing to swing around New York City. Prior to becoming Spider-Man, Peter Parker was a nerdy teenager who was very intelligent, especially in science, but otherwise very average. Peter Parker obtained his superpowers through a bite from a spider, which transferred spider abilities to him. In most versions of the story, the spider is radioactive. In this particular film version, the spider that bit Peter at Oscorp was genetically modified to spin biocaplet tinsel string, which was a lightweight but strong cable, instead of regular webbing. Technically speaking, the gene editing tool was the spider itself, which transferred genes to Peter through the bite. Peter took on the secret identity of Spider-Man, complete with a head-to-toe spider costume made of spandex-like material, and used his new powers to fight crime. He even invented a device to shoot tinsel string from his wrists to create his own artificial webbing, which he used to swing between skyscrapers.

Although Peter never intended to be gene edited and his superpowers were unintentionally acquired, he nonetheless was genetically enhanced. The gene edit was also not medically related, which might be argued to be unethical. But one cannot really accuse him of violating nonmaleficence by obtaining non-therapeutic gene editing since the spider bite was an accident. Upon further reflection, Oscorp cannot be accused of violating nonmaleficence either, as the genetically modified spiders were created to spin the tinsel string and not to be a means of gene editing people. The inventors of the spiders (one being Peter’s deceased father) probably did not even know the spiders could transfer genes to other living beings through biting. In addition, Oscorp was unaware that their spider had caused a genetic mutation in a human, since Peter kept this a secret. Having spider superpowers is an unfair advantage, as well as a non-therapeutic genetic enhancement, and should not have occurred. But no one is at fault for causing the mutation in Peter.

Jupiter Ascending (Hill 2015)

Caine Wise was another example of a character who was genetically enhanced by the incorporation of animal genes. He had wolf-like genes spliced into his own genome, which meant he had excellent tracking abilities, agility, and strength. Physically, he had pointy ears, but was considered the “runt” of his “litter”. Personality wise, he and others like him, Lycantants, instinctually needed to be a part of a pack. Caine was forced to be alone because his creators thought the gene edits were not successful and he was sold at a reduced price. People hired Lycantants to track other people, which Caine did for a living. However, because he did not belong to a group, he also had violent outburst and was known for an incident where he attacked and killed members of the entitled class. They claimed there was a defect in his genome engineering, but it was more likely due to rejection by society.

This story did not take place in the future, but was futuristic in tone. Ouros was a much more advanced civilization than Earth. Their scientific and technological capabilities far surpassed those of Earth. Transgenic animal gene splicing in humans is not currently possible, but this fictional advanced society had figured out how to accomplish it. Incorporating animal genes to bestow enhanced abilities is purely science fiction, though.

Tourbillon (Ivery 2016)

Tourbillon was a film that took place in the not too distant future, 2025, where the main character, Daniela, was genetically modified in the year 1932 to have extended life (Ivery 2016). This was achieved by injecting a mutagenic formula that slowed cellular senescence, or deterioration, by deactivating telomere growth repression by a factor of twenty and therefore Daniela aged very slowly and would not die for a long time (Ivery 2016). She was ninety-eight, yet still looked as though she was in her twenties. Other people were modified, but Daniela was the only one who was correctly modified (which was not really explained). There were other characters who conjectured that an antidote could be made that would reactivate telomeres, but needed to obtain the formula from Daniela. Daniela had an interesting thought, which she tape recorded (as she did with many of her thoughts, maintaining a record of her long life): the ecosystem would be damaged if the formula went public because all humans living for hundreds of years would wreak havoc on the Earth (Ivery 2016). That was most certainly a valid fear to have. This movie felt more realistic than some of the others, as Daniela was living a relatively normal life despite her lack of aging. However, one could argue her aging ceasing in her twenties was an unfair advantage and provided no medical benefit (other than not experiencing illnesses due to old age). Many people would probably want a longer life if such an injectable formula existed, but extending life, especially for this long, may not be ethically justifiable.

Change Agent (Suarez 2017)

Even though there were mentions of black market operations in a few instances in the book, there was a rather disturbing scene that explicitly depicted how designer babies could be abhorrently marketed in *Change Agent* (Suarez 2017). There was a United Nations Treaty on Genetic Modification, which contained a clear list on what gene edits were acceptable to perform to correct heritable genetic diseases only; everything else was illegal, but that did not stop "baby labs" from operating illicit businesses offering enhancements, such as extended life, improved memory, intelligence, athleticism, reduced risk of heart disease, etc. (Suarez 2017). Durand and Frey had entered a high-end illegal fertility clinic where the proprietor, Mr. Vegas, demonstrated what gene edits were available by putting on a child fashion show, including touting a fairer skinned, blonde Asian child claiming it was a popular gene edit; a child who had extreme intelligence; and a docile, low IQ child whom he called "worker bee" for performing labor (Suarez 2017). These genetically modified children were a grotesque violation of nonmaleficence and they were expected to prance around on stage marketing their features to wealthy people who observed them in the audience in order to determine if they wanted to buy such edits for their children (or purchase slaves). Mr. Vegas was in the business of making and selling designer babies and his marketing methods certainly emphasized “designer”. He most certainly was not in the business of curing diseases.

Rise of the Kymiera six-part series (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) *(Turnbull 2017)*

Rise of the Kymiera is yet another example where transgenic animal gene splices into humans endowed enhanced abilities. Dr. Newman had perfected this technique of editing embryos at his fertility clinic unbeknownst to parents who used his services, which meant the gene slices did not manifest until sixteen to seventeen years of age. They underwent a transformation when the genes starting being expressed, which left them confused about what was happening to them.

Chloe, the main character, started by losing weight, having incessant hunger, and growing large lumps near her shoulder blades. By the end of her transformation, she had developed wings, low body weight to enable her to fly and leap higher and farther than any human, and enhanced hearing with sonar. She was part bat due to the addition of bat DNA.

Others who had abilities were Melinda, Dog, Jason, Lucy, Venessa, and Delia. There could have been others, but these were the only ones who were known to still be alive. Melinda had eel DNA, therefore, she could generate electric shocks and see electricity flowing in wires, even if they were behind walls. As his name implies, Dog had canine DNA and had enhanced ability to smell and hear, extreme loyalty, and the desperate desire to belong to a family. The DNA that Jason had was unclear, but he had tentacles for a nose (which made him hide his face under a hoodie in public), body fur, and had very speedy movements. Lucy was unique because she just had a human DNA edit, but the gene that was edited led to increased bone density and her skin hardened into a protective exoskeleton. This unfortunately gave her the appearance similar to a turtle. Venessa had been given fox DNA endowing her with sharp canines, sharp hearing, and agility. Her personality was also quite feisty, as would be expected of a fox. Delia had an issue where her skin constantly dried out, forcing her to apply cream multiple times a day and she spent ample time swimming. No one knew what DNA she had, but it could have been some aquatic creature.

Dog was an orphan, Jason was dead according to public records, and Delia's father kept her out of the public eye. Both Dog and Jason worked for Delia's father who was a gang leader. Their lives were very restrictive because of this. Melinda, Venessa, and Lucy had been abducted by Utopia Genetics to be unwilling participants in experiments to understand their genetic edits. Chloe had evaded abduction and was in pursuit of rescuing the young women. Along with Detective Mitchel, Dog, and Jason, she was able to rescue them from Utopia.

In this futuristic, dystopian, post-war, post-plague tale, successful transgenic species gene edits were possible. To reiterate, currently, these types of gene edits are not scientifically possible. It is difficult to believe that splicing animal genes into humans would provide such enhanced abilities as seen in this group of teenagers. When discussing enhancements and designer babies in biomedical ethics, realistic possibilities are physical traits like hair and eye color, increased muscle mass for better athleticism, gender, resistance to health conditions like heart disease or cancer or obesity, and perhaps predisposition to talents like musical aptitude (as described in *Beggars in Spain* (Kress 1991)). However, using gene editing for enhancement purposes is not currently considered ethical.

Rampage (Flynn 2018)

In order to give the film context, the opening credits in *Rampage* provided a few "facts" about CRISPR and that gene editing had been designated as a weapon of mass destruction, but the way they were presented made them seem accurate (Flynn 2018). Yes, CRISPR was first discovered in 1993 and was used in non-bacterial systems in 2012, but it has yet to be used to the extent described to cure diseases and has not been weaponized. Also, people who are not familiar with the technique watching this film would not know the difference. Kate Caldwell was a geneticist at Energyne who researched CRISPR to protect endangered species and find a cure for her sick brother by developing an aerosol delivery system to allow CRISPR to edit every strand of DNA in a host's body, but Energyne stole her research and weaponized it (Flynn 2018). Animal DNA was used to insert favorable traits, such as shark DNA for continual growth of an organism, whale DNA for an advanced growth rate, rhinoceros beetle DNA for added physical strength, cheetah DNA for speed, and bat DNA for bio sonar communication (Flynn 2018). In the film, three aerosol sprays were lost by a research crew in space, but when they fell to Earth, three animals were sprayed and affected: a wolf, an alligator, and a gorilla named George. The three animals grew to a massive size, killed many people, and were terrorizing the city of Chicago. George was given an aggression antidote and was able to assist in killing the CRISPR edited wolf and alligator. This movie catered to the common populace: watching the GCI animated destruction of a city. For once, it was a city other than New York City. Obviously, this was a violation of nonmaleficence: the edits gave advantageous edits (although not to humans) only and the corrupt company, Energyne took an invention meant to be a cure and made it a weapon. The three edited animals who went on a rampage caused ample death and destruction. Story wise and scientifically speaking, this movie was utterly ridiculous. Hopefully people viewing this film are able to recognize it was purely for entertainment purposes only and was not intended to be a science lesson. Let us also hope that CRISPR technologies never advance to the point where a child's favorite video game-turned-into-a-movie characters do not become a reality. We do not need CRISPR genetically modified animals that grow at an unprecedented rate to a massive size with uncontrolled aggression.

ReEvolution (Grant 2019)

Even though in reality the focus of CRISPR research is focused on medical applications, which the main character, John, acknowledged, Xian Corp clearly had other applications in mind. A substantial contributing factor to researching CRISPR to slow aging, increase musculature, and improve intelligence was the funneling of money from wealthy leaders in China to essentially purchase research projects in areas that benefited themselves, an aging population, and assist the military. The benefactors did not care if harms were inflicted on other people so long as CRISPR was used to obtain results that provided what they wanted. They also did not care if research practices were unethical or illegal; results were a priority above ethical practices. All they wanted was to live longer and bolster their military. The end result, no matter how beneficial, does not justify the means. But the wealthy were able to buy the support of certain scientists to appease their self-interests. It does not need to be stated that this is an ethical violation.

At his own company, AlgoGene, he was researching CRISPR to reverse hereditary baldness. Although, the research was not his own: due to anti-competition laws, a lead scientist at Geneteka had offered him the opportunity to use the research as his own. He and his team had already done the research and proved the concept; one of them had already used a CRISPR injection to cure his own balding, even though testing on people was currently illegal in the United States. They were tired of making discoveries that brought in billions of dollars of profit for the company, but hardly saw any of that money themselves. Therefore, they had the idea to give all of their findings to John, allow their computer programmer to work for him at a new company that he would found, then patent the work at the right time for treatment for baldness and the algorithm that predicted where Cas9 would cut, which eliminated off-target edits. They would have investments in the company that would allow them to heavily profit when John sold the company. People would pay a lot of money to not be bald and a CRISPR treatment that was easily applied (topical or injection) would be desirable and profitable. But the algorithm that could predict off-target edits was equally or more valuable, which companies were looking to purchase at large sums of money to advance their own CRISPR research. Xian Corp even committed industrial espionage just to get their hands on it.

Even though their frustrations surrounding the company and top executive profiting from their discoveries, handing their research to someone else to pass off as his own was unethical. Frankly, executives profiting more than the scientists is unethical as well, but perhaps anti-competition laws need amending to address this. A more pertinent issue is baldness, although it can be emotionally devastating, is not exactly a life-threatening condition. Using CRISPR in this way is treating a medically related condition, but should be a lower priority then diseases like sickle cell anemia or Huntington's disease or even cancer. Making profits should not be the driving force behind CRISPR research applications, eliminating the suffering of debilitating genetic diseases should be the focus. But is curing baldness an enhancement? No, it is not. Humans are supposed to have hair and reversing a genetic mutation that causes baldness is technically a cure. Therefore, pursuing a cure for baldness is not unethical, it is just a lesser priority.

Issues of Eugenics

Brave New World (Huxley 1932 and Babbin 1980)

Eugenics, which is the belief that the human race can be "perfected" or favorable traits can be attained (such as blue eyes and blonde hair, i.e. the Aryan race desired by the Nazis) through selective breeding, appeared either directly or indirectly in the following works: *Brave New World, That Hideous Strength, Code 46,* and *The Perfect 46* (Babbin 1980, Bonowicz 2014, Eaton 2003, Huxley 1932, and Lewis 1945). Starting with *Brave New World,* even though children were no longer birthed but were grown in incubators, thirty percent of females were kept fertile so they could give eggs for reproduction later and the rest were sterilized (freemartins) (Babbin 1980 and Huxley 1932). Women who were fertile were solely responsible for taking birth control to prevent pregnancy. As a side note, the more practical solution would have been to sterilize all of the men rather than expect fertile women to take birth control, but the whole story would not have happened if this was the case. Alphas and Betas were grown one egg per person and were conditioned for intellectual work while Gammas, Deltas, and Epsilons were mass produced identical twins from one egg through the Bokanovsky and Podsnap techniques and conditioned for varying levels of labor (Babbin 1980 and Huxley 1932). This is eugenics because the government and hatcheries were in complete control of reproduction and maintaining the population, meaning how many people of each class were grown on a schedule to maintain the proper levels of the labor force. Women were chosen at the embryonic stage who would give their eggs for donation or not, meaning traits could be chosen by selecting which embryos would become fertile and which would be sterile. Because of the class system, intelligence levels were also designated at the time of conception.

That Hideous Strength (Lewis 1945)

Eugenics was occasionally discussed in *That Hideous Strength*, but reading the synopsis of the previous two novels in the trilogy for context, Professor Weston and his associate Mr. Devine (who assumed the new identity of Lord Feverstone in *That Hideous Strength*) attempted to spread the human race to other planets but decided to perfect man on Earth (Lewis 1945). The National Institute of Coordinated Experiments (N.I.C.E.) was taking over Braxton College and had the research goal of using science to recondition the human race, eliminate undesired races through sterilization and selective breeding, and allow those with superior intelligence to live on outside of an organic body, i.e. Man Immortal (Lewis 1945). The N.I.C.E. allowed experimentation on a human, cutting off his head and designing an instrument that allowed that head to speak to prove their theory of living without a body (Lewis 1945). In addition to this, the N.I.C.E. had their own police force, legal team, and reporters to cover up what they were really doing and to control the narrative of their atrocities, which could be likened to the Gestapo and Nazi party (this novel was written during the Nazi regime). The tone of this novel condemned Nazism and eugenics, as the "good" organization prevailed over the N.I.C.E. Characters outside of the inner research team were disgusted and disturbed by the head of Alcasan experiment, which showed a disdain for unethical experiments.

Code 46 (Eaton 2003)

In *Code 46,* couples went to fertility clinics to determine their genetic compatibility because cloning and embryo splitting were so prevalent, therefore they needed to be sure there was not accidental or deliberate genetic incestuous reproduction (Eaton 2003). Code 46 was actually a law that stated humans who had the same nuclear gene set are identical (clones); if a child conceived had one-hundred, fifty, or twenty-five percent of genetic overlap, the pregnancy was terminated; and if the parents knew of the overlap, they would be criminally prosecuted (Eaton 2003). While at a fertility clinic, the main character, William had his genes analyzed to compare against a woman he had met, Mary, to determine why she was hospitalized for a "body issue" and why her memory of him had been erased. He was a fifty percent genetic match for her and Mary was one-hundred percent a match for his mother, meaning Mary was one of twenty-four clones of his mother (Eaton 2003). William admitted he was raised by nurture parents, not biological parents. While he was there, another couple was being evaluated. They were not a genetic match and the geneticist strongly encouraged them to have a baby, since the baby would be highly intelligent because of their genetic compatibility (Eaton 2003). Fertility clinics preventing incestuous combinations of genes is actually a postive act, since incest results in genetic abnormalities. But the clinics would not be necessary if cloning was not so prevalent.

However, even though the scene was brief, eugenics was observed when the geneticist encouraged the couple to procreate to produce a highly intelligent child. This practice encourages selective breeding, in other words. The film did not delve deeper into any other genetic traits that were possibly being encouraged, which would have been interesting.

The Perfect 46 (Bonowicz 2014)

At a dinner party, creator Jesse Darden was pressed by his guests about his website, theperfect46.com, insisting that what he is doing may actually be eugenics (Bonowicz 2014). He explained that he envisioned a future, perhaps ten or twenty years later, where the number of people born with genetic diseases is minimal because his website was able to match people who had the lowest risk of conceiving a child with a heritable disease (Bonowicz 2014). One of his guests asked that perhaps flaws are what make some people brilliant and by eliminating that genetic defect, their brilliance and uniqueness are lost; another guest defended her viewpoint by stating Jesse is trying to manufacture people and the first guest is not interested in doing so (Bonowicz 2014). Of course, Jesse defended his viewpoint insisting he is helping people by ensuring they become who they were meant to be without being hindered by a disease and not changing who they are fundamentally (Bonowicz 2014). The media also started to accuse him of eugenics, especially when the website upgraded to a platform more similar to a dating website rather than just allowing couples to check their compatibility. The problem was people could use the service to not just find someone with whom their genetic combination would not result in a disease, but to also find someone who had desirable traits, essentially selective breeding. Jesse never intended his website to be used in such a way, but his intentions could not stop people from finding a match with whom they thought could produce a child with higher intelligence or a certain eye and hair color, etc. The fact that the website had a glitch that matched incompatible people, resulting in the births and deaths of children with Tay-sachs disease, was perhaps a reminder that eugenics should not be attempted, even with the best of intentions of preventing the spread of heritable diseases.

Conclusion

Significant unintended consequences that appeared in multiple stories were aggressiveness, violence, health defects, and death. This was often related to creating animal/human hybrid DNA edits in order to endow enhancements to the edited. Even though unintended consequences and off-target edits were a separate category from designer babies and enhancements, the issues were interconnected. Increased strength, higher intelligence, heightened senses, impressive agility, and desirable physical traits all are theoretically plausible with CRISPR, but achieving these through splicing animal DNA into the human genome seems unlikely. Science fiction writers seem to be enamored with this possibility, as a decent number of stories contained gene edits through this method: *The Blood Beast Terror* (Miller 1968), *Splice* (Hoban 2009)*, Tankborn* (Sandler 2011), *The Amazing Spider-Man* (Arad 2012)*, Rise of the Kymiera six-part series* (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) (Turnbull 2017), and *The Titan* (Amel 2018). The abilities seen in *X-Men*, such as telepathy, extremely rapid healing, the ability to control the weather, telekinesis, freeze water through touch, generate and manipulate magnetic fields, morph into anyone's physical appearance, etc. are purely fictional, for entertainment purposes only, and most certainly not achievable through CRISPR gene editing.

However, science fiction that is based on more realistic possibilities should be observed more carefully, such as *Beggars in Spain* (Kress 1991), *Gattaca* (DeVito 1997), *My Sister's Keeper* (Picoult 2003 and Furst 2009), The *MaddAddam* Trilogy (Atwood 2003, Atwood 2009, and Atwood 2013), *Intrusion* (MacLeod 2012), *The Perfect 46* (Bonowicz 2014), *Equals* (Pruss 2015), *Change Agent* (Suarez 2017), and *ReEvolution* (Grant 2019). These stories do not just depict nonmaleficence violations, but also include issues under autonomy, beneficence, and justice. Underlying questions they ask are if CRISPR gene editing is pursued, does society as a collective accept designer babies as a valid application? Could gene editing become so widespread that it becomes mandatory, leading to an oppressive society? Could interfering with the human genome lead to forced evolution, which could have negative consequences and a dystopian future as seen in some of these stories? Who is responsible for mistakes made and what kind of retribution will be available? Even with the best of intentions of curing diseases, could opening the door to gene editing allow for all applications to be inevitable?

These questions are serious and valid, but the stories should be used as a guide for making ethical decisions rather than evidence that all gene editing should be halted. With proper precautions, there is no reason to believe that dystopian or oppressive societies are inevitable. What these science fiction stories do is aid in the visualization of the pitfalls of when technology is misused and therefore can serve as a tool on how the pitfalls can be avoided. Even if someone reading or watching science fiction does not know the terminology, one can use emotions that are provoked through this visualization to assist in proper, ethical decision making.

CHAPTER 5: FILM AND LITERATURE REVIEW: HOW SCIENCE FICTION INFLUENCES PERCEPTIONS OF GENE EDITING AND ADDRESSES JUSTICE

Introduction

Justice is another area of great concern when discussing gene editing or genetics research. Four main issues that fall under justice are lack of equal access and affordability, unequal burden of research on women due to egg donation and pregnancy (this happens to be the least discussed issue in research articles), a decrease in protections of disability rights, and the rise of discrimination against new classes of people (genetically modified vs. non-genetically modified). Affordability of and equal access to gene editing were portrayed in *Beggars in Spain* (Kress 1991), the *MaddAddam* trilogy (consisting of *Oryx and Crake, The Year of the Flood,* and *MaddAddam*) (Atwood 2003, 2009, and 2013, respectively), *Intrusion* (MacLeod 2012), *The Perfect 46* (Bonowicz 2014), *Jupiter Ascending* (Hill 2015), and *Change Agent* (Suarez 2017). Most storied portrayed affordability/equal access as an issue where there was actually unequal access and only the wealthy could afford gene edits. But there were a few where gene editing was made accessible at no or low cost to ensure everyone could afford it.

Justice dictates that not just access needs to be equally distributed, but burdens also need to be equally distributed as well among various populations. When only one or a few populations are burdened with taking on research risks, this is ethically unjustifiable. Although not typically discussed, removing the burden of pregnancy on women was observed in a few stories either for procreation or for the development of genetically engineered humans only: *Brave New World* (Babbin 1980, Huxley 1932, and Joyce 1998), *Friday* (Heinlein 1982), *Next* (Crichton 2006), *Splice* (Hoban 2009), and *Tankborn* (Sandler 2011). *Change Agent* (Suarez 2017) was the only story where women were used to harvest eggs for research against their will. Three stories briefly described situations where women needed money and therefore donated eggs for research: *Next, The Year of the Flood,* and *Jupiter Ascending* (Crichton 2006, Atwood 2009, and Hill 2015). Somewhat related to this issue, women were the only sex involved in procreation through artifical insemination in *Equals,* which removes all responsibility of childbearing from men (Pruss 2015). Lastly, this issue most closely resembled the placement of the unequal burden of clinical trials on impoverished people in *ReEvolution* (Grant 2019). The main issue was supposed to be a burden on women, but this issue in *ReEvolution* could not be ignored and best fit here.

The erosion of disability rights was seen in three stories: *Next* (Crichton 2006), *Intrusion* (MacLeod 2012), and *The Perfect 46* (Bonowicz 2014). The issues here would be lack of insurance coverage for refusing to genetically modify one's child, having a genetic predisposition to a disease, or insinuating that people with disabilities have no place in society by pushing for gene editing as a cure for diseases.

Lastly, the most predominant issue under the tenet of justice is discrimination against new classes of society. Some stories discriminated against genetically modified people while others discriminated against non-genetically modified people. *Brave New World* was unique in that genetics determined to what class of society one belonged, but did not necessarily show discrimination (Babbin 1980, Huxley 1932, and Joyce 1998). Discrimination against genetically modified people was the most common in *Friday* (Heinlein 1982); *Beggars in Spain* (Kress 1991); *X-Men* (Donner 2000); *Star Trek:*

Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and *The Augments (Episode 6)* (Brennert 2004, LaZebnik 2004, and Sussman 2004); *Tankborn* (Sandler 2011); *The Atlantis World* (Riddle 2014); *Equals* (Pruss 2015); and the *Rise of the Kymiera* six-part series (Turnbull 2017). Only two stories portrayed discrimination against non-genetically modified people: *Gattaca* (DeVito 1997) and *Intrusion* (MacLeod 2012).

Issues of Equal Access and Affordability

Beggars in Spain (Kress 1991)

In *Beggars in Spain,* only people with at least some financial wealth could afford to have a sleepless child (Kress 1991). This was due to the fact that sleepless children need care twenty-four hours a day and the parents had to sleep at night. To overcome this obstacle, some form of caregiver was needed overnight and only the wealthy could afford to pay a nanny for supervision while parents slept. Leisha's father mentioned that the death of one sleepless child was the fault of the parents because they could not afford to pay a nanny overnight, especially after a divorce left the mother to singly care for their child (Kress 1991). Although this was a very harsh assessment of a tragic situation, he was correct that a single mother who needed to sleep could not properly care for a child who never slept. This also meant he was unfortunately correct in his assessment that raising a sleepless child also required a certain amount of financial freedom to pay for round the clock childcare. This is obviously a violation of justice because not everyone has the financial means to do this.

The MaddAddam Trilogy: Oryx and Crake, The Year of the Flood, and MaddAddam (Atwood 2003, Atwood 2009, and Atwood 2013)

In the *MaddAddam* trilogy, there were many healthcare products and beauty procedures that were available to the wealthy people who lived in the Compounds, which were gated communities surrounding the BioCorps (like OrganInc Farms, NooSkins, HelthWyzer, BioDefences, CryoJeenyus, Genie-Gnomes, RejoovenEsense and AnooYoo) (Atwood 2003, Atwood 2009, and Atwood 2013). Some of the products and procedures were genetically manipulated organisms, some were not. But "gated community" does not really describe the Compounds well: they were more like fortresses, walled in and under high security, separating them from the Pleeblands, which were essentially slums. Compound people really only went to the Pleeblands for entertainment or to market products in establishments where Compound people would go. In the novel *MaddAddam,* one of Crake's researchers stated, "'It was big business, the BioCorps were backing it. People were paying through the ceiling for those gene-splices. They were customizing their kids, ordering up the DNA like pizza toppings,'" (Atwood 2013). Crake was a genius bioengineer at RejoovenEsenese creating custom gene-splices, but only two of his products were marketed: genetically edited children and the BlyssPlus pills (which forced sterilization unknowingly unto the consumers and caused the viral outbreak that decimated the population). His third project was of course the creation of the Crakers, the "perfect" humans. The problem with the class separation (Compounds and Pleeblands) is the products were only affordable for those who had money. Described above under nonmaleficence, the BioCorps also incorporated illnesses into their products and extorted people for the cures. If people in the Pleeblands did manage to purchase vitamins, they could not afford the cures and often went bankrupt or were in massive debt to the BioCorps trying to pay medical bills. This is how Toby lost her parents: her mother took the vitamins, contracted an illness, her father could not pay the debt accrued from treatments, and when her mother died in the hospital, her father committed suicide to avoid debt collection (Atwood 2009). *Oryx and Crake* and *The Year of the Flood* were actually overlapping timelines, telling the story from the perspective inside the Compounds (Jimmy and Crake/Glenn) and from the perspective in the Pleeblands (Toby and the Eden Cliff Rooftop Gardeners) (Atwood 2003 and Atwood 2009). The main point here was lives were very different depending on which side of the wall one lived and products/genetic advancements were only affordable to people in the compounds.

Intrusion (MacLeod 2012)

Another story where services were readily available was *Intrusion* (MacLeod 2012). The fix, the pill that cured all genetic mutations in utero, was available to all citizens in the United Kingdom at no cost to the patient. Therefore, this is actually not a violation of justice in regards to equal access and affordability. The issues with the fix were autonomy and parental decision making capacity, as well as justice regarding disability rights and discrimination (below).

The Perfect 46 (Bonowicz 2014)

The Perfect 46 was actually one of three stories where services were affordable and easily accessible to everyone (Bonowicz 2014). Because the website theperfect46.com was just a website and did not involve any genetic research or laboratory tests, the cost to users was minimal compared to genetic testing, in vitro fertilization, and pre-implantation genetic diagnosis. Their information was obtained from government agencies who had already collected the data through previously performed medical tests. Jesse Darden created the website and computer programmers developed an algorithm that paired people with the goal of eradicating genetic diseases by avoiding dangerous genetic combinations. It was 99.95% accurate in pairing couples and the remaining 0.05% birthed children with Tay-Sachs due to a glitch in the algorithm, but the service itself was inexpensive and easily accessible (Bonowicz 2014). It was as simple as logging on and creating a profile like any social media platform and signing a consent form to have one's genetic data released from a government database. Therefore, this was not a violation of justice. Although, one character accused Darden of attempting to breed a super race of people and enslaving the people who could not afford the service (Bonowicz 2014). Darden refuted these claims, insisted that was never his intention, and the service was not out of reach for the majority of people.

Jupiter Ascending (Hill 2015)

Balem, Titus, and Kalique were siblings descendent from a very wealthy family on Orous. They made their fortune selling the ReGenX formula (also called ReCell or Nectar), which granted immortality by reversing aging. They had figured out how to replace deteriorating cells with new cells, since genes degrade over time. By bathing in the formula regularly, Kalique had reached the age of fourteen-thousand years. However, because of the expense of producing the formula and the high desirability to live longer, only the wealthy could afford ReGenX. Creating a gene editing formula to restore youth that is only available at a high cost is unethical, as this restricts the availability to everyone.

Another issue with ReGenX was the source of the genetic material. One unit of ReGenX was synthesized from one-hundred people. In order to maintain production, Orous needed human sources, which they accomplished by harvesting farm planets, of which there were thousands. They integrated Orous DNA with indigenous people of planets they planned to use as farm planes to ensure compatibility. Earth was one of these farm planets. This is also a violation of justice because humans on the farm planets are being utilized as merely a resource for profit. Balem stated that every human society has a pyramidal structure to justify the family business. However, it is grossly unethical to murder people to harvest their genetic material using the argument that they are less valuable to society.

Change Agent (Suarez 2017)

The last story where gene editing was affordable and readily available was *Change Agent* (Suarez 2017). There were international laws in place that allowed the correction of United Nations approved genetic disorders under the UN Treaty on Genetic Modification (Suarez 2017). Since gene editing for the purpose of curing genetic diseases is equally accessible to all, this is not a violation of justice. However, where the story does violate justice is the black market operations where baby laboratories were catering to the rich, offering beneficial edits that prolonged life, enhanced abilities like intelligence and athleticism, and reduced risk to health problems like heart disease, for a massive profit (Suarez 2017). The wealthy spent small fortunes to give their children every advantage possible and were willing to commit a crime in order to do it. Part of the marketing strategy involved manipulating a parent’s love and insisting performing beneficial edits was a gift passed down to future generations. In the opening chapter, Mrs. Cherian was uncomfortable editing her child in such a way, but her husband stated, "‘Why? Because some bureaucrat says it’s not allowed? Do you really think the wealthiest families are not doing this, my love?’" (Suarez 2017). The wealthy were willing to pay any price illegally to give their children the most advantages possible and seemed shameless about it. The average person could only afford to correct diseases, thus any edits beyond that were financially out of their reach. The system was grossly unfair.

Issues of Unequal Burden on Women in Research

The Year of the Flood (Atwood 2009), Next (Crichton 2006), Jupiter Ascending (Hill 2015), and Change Agent (Suarez 2017)

This issue did not present itself in almost all of the movies watched or novels read. This is most likely because any story involving genetic research, fetuses were grown in artificial wombs or animal wombs: *Friday, Splice, Next, Tankborn* (Crichton 2006, Heinlein 1982, Hoban 2009, and Sandler 2011). Even in *Brave New World,* although not for research purposes, babies were grown in incubators (Babbin 1980, Joyce 1998, and Huxley 1932).

Change Agent was the only story where this appeared, although briefly (Suarez 2017). Gene edits were a large money maker on the black market, but research needed to be done on which genes could be edited for enhancements. The Huli Jing and other gangs kidnapped migrant women who were desperate to escape starvation and war and harvested their eggs for research; any children who were born with deformities during research were discarded at a Budist sanctuary (Suarez 2017). Women were taken against their will to benefit research efforts.

Women donating eggs for research in order to make money for themselves was also very briefly mentioned in *The Year of the Flood, Next,* and *Jupiter Ascending* (Atwood 2009, Crichton 2006, and Hill 2015). In *the Year of the Flood,* Toby was short on funds escaping Compound debt collectors and as a result was rendered infertile during the surgical procedure (Atwood 2009). In *Next,* the daughter of a prominent researcher at the age of sixteen was taking fertility shots to boost egg production to donate them for cash, which was apparently a common practice among teenage girls who were saving money for plastic surgery (Crichton 2006). In *Jupiter Ascending,* Jupiter was going to donate her eggs for money at the suggestion of her cousin for fifteen thousand dollars, ten of which was going to her cousin (Hill 2015). When her uncle discovered this, he reprimanded his son for treating his cousin like a chicken (Hill 2015). These instances were not prominent or terribly important in the stories, but their mention showed how women are misused for research purposes in terms of egg donation. Complications can arise and they put themselves at risk, usually in order to earn money.

Equals (Pruss 2015)

Although not technically a research burden, it is interesting to note that men were no longer involved in procreation in *Equals* (Pruss 2015). Women were summoned for conception duty and then artificially inseminated. In a way this is an unequal burden placed on women, since they are still tasked with pregnancy at the convenience of society rather than the desire to have children. They missed work while pregnant and returned some time after birth. Since children were never viewed in the film, it is difficult to say who was responsible for raising and educating them. Although insignificant to the story, the onus of childbearing was unequally bestowed on women.

ReEvolution (Grant 2019)

The wealthy in China had great influence in research funding, pushing medical research beyond what it should have been for their own desires. In order to advance CRISPR, the Xian Corp needed to perform clinical trials on humans, but laws prevented this and this practice was not favorable in the public eye. To circumvent the law and prying eyes, some researchers traveled to the impoverished country side and began injecting peasants with CRISPR to test the efficacy of gene editing treatments and determine if they caused off-target edits. People were dying horrendous deaths from the treatments and were not willing participants in the study. Tan, the head researcher, insisted when John asked that the people involved were poor or criminals and signed consent forms, but John did not believe this. This is an example of placing an unequal burden of research on poor people. (This did not involve just women, but this category was the most befitting for this issue in *ReEvolution* (Grant 2019).) Not only is it ethically unjustifiable to perform experiments on people without their consent and without sufficient pre-clinical testing, it is also ethically unjustifiable to only test drugs on poor people due to being exploitative.

Issues of Disability Rights

Next (Crichton 2006)

In the United States, health insurance is a private business and full coverage is available through a full-time employment or by paying high premiums individually. In the novel, *Next,* Tom Weller was a young laboratory technician who was dropped from his health insurance after his deceased father was tested for abnormalities and paternity of his youngest daughter (Crichton 2006). John Weller tested positive for a gene that could cause heart disease if expressed and the insurance company decided the son was "pre-ill", therefore dropped him as an insurer (Crichton 2006). This is a genuine fear of an outcome that is entirely feasible if gene editing becomes a viable treatment option in the future. Health insurance companies may decide not to insure people who choose not to genetically edit their children knowing a genetic disease is likely or may charge increased premiums. This practice of not insuring people who have a pre-existing condition, disease, or just happen to have a gene that could cause a disease is unethical.

Intrusion (MacLeod 2012)

To reiterate, women were increasingly being pressured to take the fix while pregnant to correct any genetic mutations in utero and stricter laws enforcing this were being implemented, likening not taking the fix to child neglect; but the only way out of taking the fix was a religious based conscience exemption (MacLeod 2012). This was unfair in and of itself because this disregarded a mother's ability to make medical decisions for herself and her child. But while at the doctor, Hope was pressured by her doctor who cited that insurance companies decide premiums based on risk and probability, as well as the potential for legal issues in the future, and Hope not taking the fix would cause her liability insurance to increase regardless of the fact that all tests showed that Hope's baby was in perfect health (MacLeod 2012). This is another example of fear that deciding not to genetically edit their children, regardless of their reason, could result in lack of insurance coverage or higher insurance premiums in the future. Essentially, insurance companies dictating to patients what treatments they must take and removing autonomous choice (or at least placing financial pressure an opposing choices) to accept or decline medical interventions is unethical.

The Perfect 46 (Bonowicz 2014)

Already described under the section nonmaleficence/eugenics above, a person at Jesse Darden's dinner party argued that eliminating flaws from people, even ones that caused genetic diseases, may be exactly what makes those people brilliant and unique, thus they do not become who they were meant to be and the world suffers that loss (Bonowicz 2014). This is a precise issue under disability rights: by eradicating genetic diseases, society may be indicating that people with disabilities do not have the right to exist. Darden also indicated that eradicating genetic diseases was preventative care and therefore reduced the demand on healthcare, which would appeal to insurance companies because costs would be reduced (Bonowicz 2014). Darden is opening the door for insurance companies to start charging higher premiums for people who chose not to use a website like theperfect46.com to guarantee their children will be free of genetic diseases. Both of these concerns are unjust and perhaps specific protections need to be put in place to prevent insurance companies from taking advantage of people with disabilities or genetic disorders.

Issues of Discrimination and New Classes of People in Society

Brave New World (Huxley 1932, Babbin 1980, and Joyce 1998)

As stated earlier, *Brave New World* had five classes of people (but only four in the 1998 film): Alphas, Betas, Gammas, Deltas, and Epsilons (eliminated in the 1998 film)

(Babbin 1980, Huxley 1932, and Joyce 1998). Clases were determined by hatchery workers at the embryonic stage, as people were no longer birthed but grown in incubators, with the upper classes (Alphas and Betas) born one person per embryo and the lower classes (Gammas, Deltas, and Epsilons) were born up to ninety-six people per embryo (Babbin 1980 and Huxley 1932). To prevent dissent, conflict, and unhappiness, everyone was conditioned throughout their childhood with hypnosis methods and were drugged with soma as adults. The lower classes were made for various levels of labor and the upper classes engaged in more intellectual work. Lenina made a comment to John once that Epsilons were semi-morons who worked vacuum cleaners; she meant other jobs as well, but she was trying to prove a point in that conversation: John did not need to prove love for her by performing manual labor because there were laborers for that (Babbin 1980 and Huxley 1932). Although an indirect comment, there was a level of discrimination here: she was too good and high born to perform any kind of labor herself as a Beta. The level of intelligence declined as the class level declined and Lenina was implying Epsilons in particular were too stupid to do anything other than manual labor. She was correct, unfortunately, because of the incubation and conditioning processes, but no one had any hopes of being in a different class.

Friday (Heinlein 1982); Beggars in Spain (Kress 1991); X-Men and X-Men: The Last Stand (Donner 2000 and Donner 2006); Star Trek: Enterprise Season 4, Borderland (Episode 4), Cold Station 12 (Episode 5), and The Augments (Episode 6) (Brennert 2004, LaZebnik 2004, and Sussman 2004); Tankborn (Sandler 2011); Equals (Pruss 2015); *and*

Rise of the Kymiera six-part series (*Monsters: Purity, Poison, Flight, Abyss, Reasons,* and *Utopia*) *(Turnbull 2017)*

Multiple stories displayed instances of discrimination either against genetically modified people or non-genetically modified people. The stories where genetically modified people were discriminated against are included in this section while the stories where non-genetically modified people were discriminated against are described in the next section. In *Friday,* genetically engineered artificial persons had absolutely zero rights under the law: they could not legally marry humans and labor unions fought to prevent APs from stealing jobs from humans (Heinlein 1982). They were physically indistinguishable on the outside, but if Friday informed people she was an AP, she was often met with disdain and her thoughts revealed APs often hid who they were to avoid discrimination. As tough as she was, all she really desired was to belong and she had to move off planet to assimilate into a family who accepted her for who she was.

The sleepless in *Beggars in Spain* also experienced discrimination and unfair laws, such as scathing letters written in papers stating they were unnatural, a super race, and had an unfair advantage in life to accumulate more wealth and power (Kress 1991). Examples of laws that were put in place were barring the sleepless from competing in the Olympics, citing the genetic alteration was an unsportsmanlike advantage similar to steroid use; denying apartment rental due to disturbing other residents; banning twenty-four hour business from being operated by sleepless because it was an unfair business advantage; and not allowing them to serve on juries because they were not "peers" (Kress 1991). It seemed that the sleepless in the United States experienced the worst discrimination throughout the world.

In *X-Men,* mutants were discriminated against by humans because people were essentially afraid of them due to their unique abilities. In the United States Senate, legislation was proposed that would force all mutants to register themselves and disclose what their abilities were. Those who opposed such laws argued mutants were often met with hatred and violence, therefore, forcing a full disclosure would result in more violence. Magneto, having survived the Holocost, was strongly opposed to legally enforcing a mutant registration. In *X-Men: The Last Stand,* he therefore attempted to recruit other mutants to start a war against the humans since he believed mutants were the future of evolution and held nothing but contempt for humans (Donner 2006).

On Earth, the *Star Trek: Enterprise* society had abandoned genetic engineering of humans because of how many people died in the eugenics wars. The characters were unsure if humans rose up against augments or augments rose up humans during the eugenics wars. Soong explained to the augmented people he raised that humans will always fear them because humans cannot be them (LaZebnik 2004). The creator of augmented humans stated, "Superior ability breeds superior ambition" (Sussman 2004). He was subsequently murdered by an augment, which was a further argument that augmented humans were violent and dangerous, therefore they should not be created.

The GENs in *Tankborn* were very similar to APs in *Friday*: they were not viewed as humans like the trueborns (Heinlein 1982 and Sandler 2011). Society had a caste system and GENs were most certainly the lowest. GENs were essentially genetically engineered, grown in the tank, and then became slaves to trueborns who could afford to purchase them. However, the original researcher, Zul, had a different acronym for GEN: Genetically Engineered Non-natal as opposed to Genetically Engineered Non-human, which meant they were human, just not conceived (Sandler 2011). Trueborns were taught that GENs were happy with their role in society, did not see themselves as individuals, and were given assignments where they would be most content (Sandler 2011). Devak, the grandson of Zul, after spending ample time with Kayla realized what he was taught was not true: GENs were not happy being assigned to jobs for the entirety of their lives and had individuality, feelings, and intelligence, which made her and all of the other GENs human. The enslavement and mistreatment of the GENs was unjustified.

Interestingly, in *Equals,* everyone was created genetically equal through the elimination of emotions, which of course was the intent of this genetic manipulation (Pruss 2015). However, when the gene suppression failed, "infected" individuals were asked to not sit close to everyone or share mugs, even though it was not contagious. Silas experienced this when he was "infected" with SOS (switched on syndrome). Others who experienced emotions to the point where their work was affected or who were caught coupling were sent to the DEN (Defective Emotional Neuropathy facility) where they received emotional suppression treatment consisting of electro-restraint and were offered a pain-free death as an option. Nia ended up there when she tested positive for being pregnant and having stage four SOS. The suppression of emotions was ingrained in this society to the point where a permanent cure, not just a temporary inhibitor drug, was being researched to fix those experiencing SOS. Being "equal" was of utmost importance to ensure society ran smoothly, as emotions caused defects in past civilizations. Even though they were mistreated due to having emotions and SOS, Silas, Nia, and a few other characters did not want the cure: they realized feeling is what humans were meant to do and would rather be outcasts than emotionless drones of the "equal" society.

Lastly, SID infected people in the *Rise of the Kymiera* series were feared and treated like scum (Turnbull 2017). Everyone called them “freaks”. The “freaks” were not genetically edited in a traditional way. A virus infected individuals, but when they were exposed to DNA from other species, that DNA was incorporated into their own genome, although not well. People lost their mental capacity, grew deformities in the form of extra extremities, and/or developed animal features. Because the viral infection was so detrimental, families and contacts of the infected were quarantined for safety precautions, but became outcasts anyway even though after being quarantined they were determined to be clear of the infection. When encountering “freaks”, the Purity killed the infected as a means of preventing the spread of the virus and to end their suffering. A policeman had stated to a suspect in custody, “The rules cease to apply when it comes to freaks,” (Turnbull 2017). This statement implied that “freaks” were not seen as human anymore and were not afforded the same protections against murder under the law.

Gattaca (DeVito 1997) and Intrusion (MacLeod 2012)

Interestingly, *Gattaca* and *Intrusion* were the opposite of the above stories: non-genetically modified humans were the lower class who faced discrimination (DeVito 1997 and MacLeod 2012). In *Gattaca*, the two classes were the Valids (genetically modified) and the Invalids (non-genetically modified) (DeVito 1997). The Valids were designed by geneticists at fertility clinics to be free of genetic diseases and the best traits were chosen from both parents to make the best possible child, which allowed them to be successful in life due to their genetic superiority (DeVito 1997). It was illegal to discriminate against someone for their genetics (called genoism), but during routine drug screenings, employers could perform a DNA test and not hire anyone with genetic issues; Vincent experienced this often as an Invalid and therefore worked as a janitor, unable to attain his dream of becoming an astronaut due to a heart condition (DeVito 1997). In the end, Vincent was able to become an astronaut, but only by assuming the identity of a Valid, Jerome, who was wheelchair bound after an accident, which society would have shunned him had the news of his broken back been discovered.

The discrimination in *Intrusion* was quite different: the faith moms, who did not take the fix for religious reasons, did not want Hope's son to attend nursery because he was a nature child and brought risk of infection, since Hope not taking the fix was for non-religious reasons (MacLeod 2012). Frankly, this did not make any sense whatsoever. Whether for faith or non-faith related reasons, all children who were born of mothers who did not take the fix were equally at risk for infection and disease, yet having certain religious beliefs gave some women a free pass to not take the fix. The state also had legally put in place discrimination against women who wished to have nature children for non-faith reasons because they were pressured by nurses, physicians, and upcoming laws to take to fix against their will, but faith mothers were exempt. Religion as the only means of objection was highly unfair: a woman could claim to follow any religion and the state would leave her alone. Only women who objected for non-faith reasons were deemed "unfit" mothers. In all cases, discriminiation of any kind due to genetics violates the tenet of justice and is unacceptable.

The Atlantis World (Riddle 2014)

On Atlantis, there were two classes of individuals: laborers and intellectuals (Riddle 2014). The intellectuals were not genetically modified to be more intelligent, they just were, but they treated the laborers as a lesser class. Discontented with their lower class status, the laborers rebelled against the intellectuals for equal status. Isis, a geneticist and intellectual, did not agree with the class separation and was in love with one of the laborers. Therefore, she worked on a gene edit to endow the laborers with equal intellectual ability as the intellectuals. Ares opposed here, stating there would always be those who have better abilities and argued who will judge what is genetically superior or inferior (Riddle 2014). He proposed to "rehome" the labor class to eliminate the issue under the Atlantean Equality Act which resulted in the exile of the laborer class to another planet. Clearly, this is not equality. Isis gave the gene therapy to the labor class, which advanced their intellectual ability to the level of the intellectuals and allowed them to rise up against the intellectuals leading to war. In this story, gene editing did not cause class separation. The class separation was already there. But what gene editing did do was eliminate the intellectual distinction between the classes, thus allowing them to be genetically equal. War unneccessarily ensued as a result of class discrimination. Using genetics to separate classes is not beneficial to society and violates the tenet of justice.

Conclusion

Since some uses of CRISPR are being researched in clinical trials for cancer treatments and genetic disorders like sickle cell anemia, legislation on ethically acceptable applications should be put in place sooner rather than later to prevent the violations of justice portrayed in science fiction (Cyranoski 2016, Juengst 2017, and Kick et. al 2017). In *Change Agent,* selling gene edits to the wealthy on the black market was a serious issue that has the potential of coming to fruition, thus having laws and accompanying punishments for breaking those laws is an absolute must (Suarez 2017). Also, protecting people's access to health insurance might require legislation to ensure they are not denied coverage if such treatments are available or preventing denial of coverage if someone decides against gene editing themselves or their children. Situations seen in *Next* and *Intrusion* in regards to health insurance are not desirable (Crichton 2006 and MacLeod 2012).

Researchers must also be careful when recruiting participants in clinical trials or for donation of eggs to ensure the burden of research is not placed on any one particular group of people based on socioeconomic status, gender, race, sexual orientation, etc. Under justice, sharing of burdens is as important as equal access to services. Exploitation of any group is not ethically justifiable, as seen in *ReEvolution* (Grant 2019).

Along the lines of equal access, the protections stated above also apply to disability rights and discrimination. Although most stories depicted discrimination among genetically modified people, the same mistreatment is a possibility for non-genetically modified people. All people should be treated equally under the law. Perhaps protections for genetic modification or refusal of genetic modification needs to be added under anti-discrimination laws that protect people's rights regardless of gender, race, religious affiliation, and sexual orientation, etc. *Gattaca* did discuss an issue here that would be difficult to remedy or prevent: anti-discrimination laws were in place to prevent corporations from using genetic testing upon the hiring process to screen for Invalids, but this did not stop hiring managers from using a "drug test" to screen for genetic abnormalities (DeVito 1997). Even though it was illegal to discriminate against Invalids, corporations found a legal loophole to continue their illegal hiring practices. Even with legal protections in place, preventing all forms of discrimination might not be possible, but this should not hinder enacting protective laws.

Why such discrimination might develop could be the result of fear or misunderstanding. Soong in *Star Trek: Enterprise* succinctly stated that people will always fear the augments (genetically enhanced people who were edited in the embryo stage) because of their power and intellect, which is everything they desire to be yet cannot (Brennert 2004). Friday experienced the same type of fear when she revealed to her family unit that she was an AP (artificial person): they unceremoniously removed her from the family because it was illegal for an AP to marry humans rather than accept her for who she was (Heinlein 1982). When reflecting on this, she admitted in an inner monologue that she had been looking for a place to belong where she was considered equal to a human. Truly, when analysing any story where discrimination occurred against the genetically modified, the driving force was fear of their abilities and differences. In *Intrusion,* the discrimination against the non-genetically modified for non-religious reasons was fear of spreading diseases, which was unwarrented because non-genetically modified children regardless of the reason were equally susceptible to infections (MacLeod 2012). Fear of abilities, differences, or enhancements due to gene editing is not a justifiable reason to mistreat other people. Frankly, not viewing genetically modified individuals as people or human is absurd.

Overall Themes, Comments, and Conclusions Relating to All Tenets

After considering thirty-two stories in the format of novels, films, or both, all of the issues that are a concern for genetic engineering or editing, diseases, and research were well represented. Viewers and readers unfamiliar with the terminology in biomedical ethics may not be able to articulate certain issues, but would have a decent understanding of the issues with this set of stories, as well as the social warnings presented in them. Eighteen common themes that emerged, meaning were definitely present in more than one story, were the following:

1) Germline edits, whether intentional or not, were introduced into the human genome and affected future generations.
2) Informed consent was violated by either performing edits against one's will, by performing edits different than the ones about which the patient was informed, or edits dictate a person's class in society.
3) Parents generally had decision making capacity to edit their embryos/children or not, but this was sometimes violated.
4) Genetic diseases were cured through genetic engineering or editing, as well as selective breeding/eugenics/genetic compatibility.
5) Major unintended consequences of tampering with genes were violent behavior and death.
6) Enhancements provided longer life, higher intelligence, increased strength, increased agility, heightened athleticism, etc.
7) Parents were able to go to fertility clinics and design their ideal child with specific physical traits, which falls under the issues of designer babies and eugenics.
8) Transgenic humans spliced with animal genes or transgenic animals spliced with human genes were created, either leading to violent creatures or super humans.

9) Enhancements were available to the wealthy who could afford them either legally or illegally, depending on the story.
10) Children could be conceived and grown outside of a woman's womb in tanks or incubators.
11) Women's health was endangered by donating eggs for research whether willingly or unwillingly.
12) Classes of society were present: genetically modified and non-genetically modified.
13) Discrimination occurred against certain classes, limiting their choices, occupations, or positions in society.
14) Genetically engineered people were not seen as human.
15) Gene editing or engineering was accompanied with artificial intelligence interfaces to further enhance humans, making them programmable like computers, usually against their will.
16) Computer algorithms assisted in gene editing or genetic matching. They were developed in order to predict off-target edits or genetic compatibility to prevent heritable genetic diseases.
17) The Great Leap Forward affected some species of humans, but not others, changing the brain wiring of humans to endow them with religion, art, fashion, and higher intelligence, thus affecting their ability to survive. The change in brain wiring was genetic.
18) Dystopian societies were a possibility where resources on Earth were limited and people's rights were limited.

Hopefully, the dystopian societies and limitations on rights portrayed in these stories will not be the future if proper precautions are taken. Interestingly, one other theme emerged, although it had nothing to do with biomedical ethics: polygamous relationships, marriages, and/or family units were the social norm in *Brave New World, Friday,* the *MaddAddam* trilogy, *The Neanderthal Parallax*, and *2312* (Atwood 2003, Atwood 2009, Atwood 2013, Heinlein 1982, Huxley 1932, Robinson 2012, Sawyer 2002, Sawyer 2003, and Sawyer 2003). The rest displayed typical monogamous relationships and marriages. Whether or not polygamy contributes to a dystopian society or is a result of genetic manipulations can be debated, but the fact that it was a common occurance was intriguing.

Science fiction can be truly entertaining to watch, but certain scientific experiments or advancements portrayed in them are not feasible, at least not yet. The common viewer or reader may not be able to discern what is possible currently in gene editing and may wrongfully think transgenic humans with super abilities from animal genes could actually be made. Or that a fully-grown adult could be completely genetically modified to be a new person. Or even that fertility clinics have a list that parents can check off boxes on how they want their children to be modified. I would hope not, but personally, I worry about the last one. Although something like green fluorescent protein from jellyfish incorporated into an animal genome to produce glowing eyes has actually been done. It will be interesting to see the future unfold and which advancements conceptualized in these stories will come to pass.

Being one of the most recent works written and specifically about CRISPR, *Change Agent* had an interesting take on world politics that may actually be possible, as well as an accurate assessment of societal views on research in the United States (Suarez 2017).

Having the United Nations draft policy on international law governing the acceptable uses of CRISPR may actually be necessary to allow for the justified prosecution of abuses of CRISPR. Suarez predicted that genetic research would make the most advances abroad for a few reasons: laws prohibited research on embryos because too many people viewed every embryo as a person, lack of scientific knowledge and religious viewpoints fueled these laws, and social media opinions were valued more over scientific facts in peer reviewed journals (Suarez 2017). He is absolutely correct in this assessment and by 2045, maybe foreign countries will make the most headway in gene editing research. In twenty-five years time, I look forward to seeing if these predictions come to fruition.

CHAPTER 6: UTILIZING SCIENCE FICTION TO TEACH ETHICAL REASONING AND INFLUENCE POLICY MAKING

Introduction

To say the least, attempting to convey all of the ethical issues that are of concern to ethicists and even scientists would be a challenge, especially for those who do not have a science or ethics background. Visualization is an important tool for those who do not know the terminology to convey the importance and consequences of implementing gene editing without considering the ethical implications. Through the previous chapters, I have been deeply invested in the analysis of the presentation of ethical concerns surrounding gene editing and genetic research, but I do not expect everyone to have the time to invest to read and watch my selection of stories in its entirety. Therefore, I began to assess the stories for realistic applications that are scientifically possible or probable, for their ability to invoke emotional responses or relatable character connections, for time investment, for multiple conflicting issues, and if the stories were about CRISPR specifically.

Although often told for merely entertainment purposes, I determined that stories that were scientifically absurd were not as useful as teaching tools. By scientifically absurd, I mean stories that involved human/animal gene splices that lead to super abilities. These are not as impactful when trying to convey issues surrounding gene editing when the events transpiring are highly improbable or complete and utter nonsense. Viewers would not be concerned with a downfall of society if the downfall was caused by human/animal hybrids than cannot possibly exist in reality. Prime examples of stories that fall into this category would be *The Blood Beast Terror* (Miller 1968), *The Island of Dr. Moreau* (Pressman 1996 and Steloff 1977), *Cowl* (Asher 2004), *Splice* (Hoban 2009), and *The Titan* (Amel 2018).

Rampage (Flynn 2018) would be another example of scientific absurdity, but it involved animal/animal gene splices.

Emotionally charged movies are critical for conveying issues because people remember and are inspired by what they feel regardless if they can put it into words. Also, if the story feels real, then people would believe that it could become reality. Stories that fall in this category are *Brave New World* (Huxley 1932 and Babbin 1980)*, Beggars in Spain* (Kress 1991)*, Gattaca* (DeVito 1997)*, My Sister's Keeper* (Picoult 2003 and Furst 2009)*, The MaddAddam Trilogy* (Atwood 2003, Atwood 2009, and Atwood 2013)*, Extraordinary Measures* (Shamberg 2010)*, Intrusion* (MacLeod 2012)*, The Perfect 46* (Bonowicz 2014)*, Equals* (Pruss 2015), and *Change Agent* (Suarez 2017). These stories in one way or another invoke compelling feelings of fear, sadness, discomfort, anger, and sometimes even hope. Empathy is a powerful tool to capture people's attention and inspire them to act. One other story that felt very real, but did not necessarily invoke powerful emotional responses was *ReEvolution* (Grant 2019).

There are some stories that were excellent reads, but were trilogies or multiple part series that could be time consuming. If time is limited, although they are worthwhile, thought provoking, and contain significant ethical issues, then the time investment might be too high of an expectation. Students, politicians, or even the general public might not be interested in utilizing their time to read lengthy stories regardless of the payoff. Therefore, these could be mentioned as supplementary materials if someone is truly interested. Examples would be *The Neanderthal Parallax* trilogy (Sawyer 2002, Sawyer 2003, and Sawyer 2003), *The Origin Mystery* trilogy (Riddle 2013, Riddle 2013, and Riddle 2014), and the *Rise of the Kymiera* six-part series (Turnbull 2017).

Multiple conflicting issues are of interest because one story could incorporate several ethical issues surrounding gene editing under multiple tenets. This maximizes understanding while minimizing time investment, i.e. is efficient. Coincidentally, stories with multiple conflicting issues also happen to be emotionally charged stories. Therefore, the stories chosen below for educational purposes and influencing policy changes were carefully selected to obtain the most meaning in relation to time devotion. The goal was to have the most impactful reading or viewing experience to invoke a call to action. Students need to be able to move forward into the world with an ethical understanding and the skills to make ethical decisions, especially if they are going to be future scientists, to prevent ethical violations. Policy makers need to be able to enact policies that allow research to progress, but by ethical means to ensure societal values are upheld and to avoid dystopian scenarios. Science fiction assists in the visualization of these issues and can be utilized in and out of the classroom to accomplish this goal.

Science Fiction in the Classroom: Envisioning Ethical Issues Surrounding Gene Editing and Teaching Ethical Decision Making

Since there are multiple issues under each tenet surrounding the ethics of gene editing, teaching all of them within a course may be challenging to say the least. Gene editing would be one topic among various topics that needs to be covered in most likely about a one to two-week period. When considering this, I asked myself how could I explore the greatest number of issues in a short time frame while enabling students to maximize their understanding of the ethical issues, but still have ample time for discussions, debates, solving ethical dilemmas, and making ethical decisions? What I have learned in the classroom as both the professor and student, as well as from other instructors and best practices, is two methods have proven to be very effective for learning and retention: 1) reflection and 2) active participation. Therefore, my plan encompasses both reflective practices and active participation.

Reflective papers would serve a dual purpose, one purpose being the homework assignment contributing to their overall grade and the other purpose being a preparatory method for upcoming discussions. Since these types of papers are a reflective practice, they do not have to be terribly complicated: one to two pages reflecting on an ethical issue that was apparent, that invoked an emotional response, and what ethical principles determine why a violation took place. For some assignments, ethical principles can be broad and individually chosen by the students. However, for gene editing, the tenets and possibly specific issues will be assigned for the sake of maximizing learning outcomes, which will be accomplished through an active learning technique called the jigsaw lesson.

True to its name, a jigsaw lesson is an active learning pedagogical method that is structured like a jigsaw puzzle. Students are assigned to one group in which they become experts on a particular topic. After they have learned their respective topic, they are then assigned to a new group, the learning group, which consists of one member from each expert group. Each expert member in turn teaches the other members of the group their expertise. Theoretically, after this process, the entire class will have learned all of the topics through discussions within their learning group. The jigsaw requires active participation from every single student, which ensures everyone comes to class prepared for discussion. This type of lesson also pushes maximum accountability for completing assignments and being properly prepared for class. If students do not complete their reading or viewing assignments and reflective papers prior to class, not only will their grades be poor, their classmates will not be pleased. Just to be clear, the goal is accountability and preparedness, not humiliation. But this small level of potential humiliation of being the weak link in a group is hopefully motivation to be prepared to prevent being ostracized by other group members.

In order to cover the maximum number of topics for gene editing and utilize both mediums of literature and film, two jigsaw lessons will be necessary: one jigsaw for literature and one jigsaw for films. The two jigsaw lessons will be structured the same way, four pieces of the puzzle represented by the four tenets of biomedical ethics: autonomy, beneficence, nonmaleficence, and justice. These will be the expert groups. I envision gene editing being a topic taking place later in a semester long course, therefore, students should be quite familiar with the tenets by this point, as well as any subtopics that fall under the tenets. For example, students would already have the knowledge that informed consent, coercion, and decision making capacity are ethical concerns that fall under autonomy. Then the learning groups would consist of one member from each expert group, thus having representation from each tenet covered.

To structure the jigsaw properly, the number of students in the class needs to be considered. Where I currently teach, a single section undergraduate course has a maximum of twenty-four students and a minimum of eight students (this is purely economic in nature because eight students generates enough tuition money to cover the cost of employing the professor). In a graduate level course as a student, the minimum was six students to run a course. With eight to twenty-four students, each expert group will have two to six members distributed appropriately (see ***figure 4***). In a course with eight to eleven students, there will be only two learning groups. Twelve to fifteen students will generate three learning groups, sixteen to nineteen students will generate four learning groups, twenty to twenty-three students will generate five learning groups, and twenty-four students will generate six learning groups. But some tenets will overlap within a group if the number of students does not divide equally. If this occurs, assigning a different issue within the same tenet is a possibility to prevent too much overlap. For example, two issues under nonmaleficence are unintended consequences and enhancements. If there are extra students assigned to nonmaleficence, then one student can explore unintended consequences and one can explore enhancements in the same novel or film in the learning group. Or multiple students can explain together the same issue within a learning group. Either option is acceptable.

If this is implemented in a course where the number of students is less than eight, there will be only one learning group and no expert groups (see ***figure 4***). Rather, individuals will be the experts for their tenets. Since all students will be an expert on a tenet, this is the perfect opportunity to assign a different issue within the the same tenet so everyone has something to contribute to the group if more than one student is assigned to a tenet.

The overall class period would need to be broken into three parts: 1) expert group discussions 2) learning group discussions and 3) entire class discussions. Assuming a standard class time of seventy-five minutes, at the beginning of the lesson, approximately fifteen minutes should be dedicated to the expert groups discussing their respective tenet to ensure they are on the same page before they attempt to teach their learning groups. The learning group discussions will probably encompass the next forty minutes, thus allowing each expert(s) in the group to have ten minutes to teach their tenet to the entire group. Lastly, the entire class will come together for an overall discussion to incorporate or comment on what they learned within their learning groups, which will have the last twenty minutes allotted. This is also the perfect opportunity to discuss other ethical issues within a novel or film that appeared for a tenet that was not assigned and discuss ethical dilemmas that were identified and how to solve them. At the very end, a one to two-minute paper can be written reflecting on an additional issue that made an impression or an emotional response the students might be experiencing or even discuss a topic they may wish to explore further.

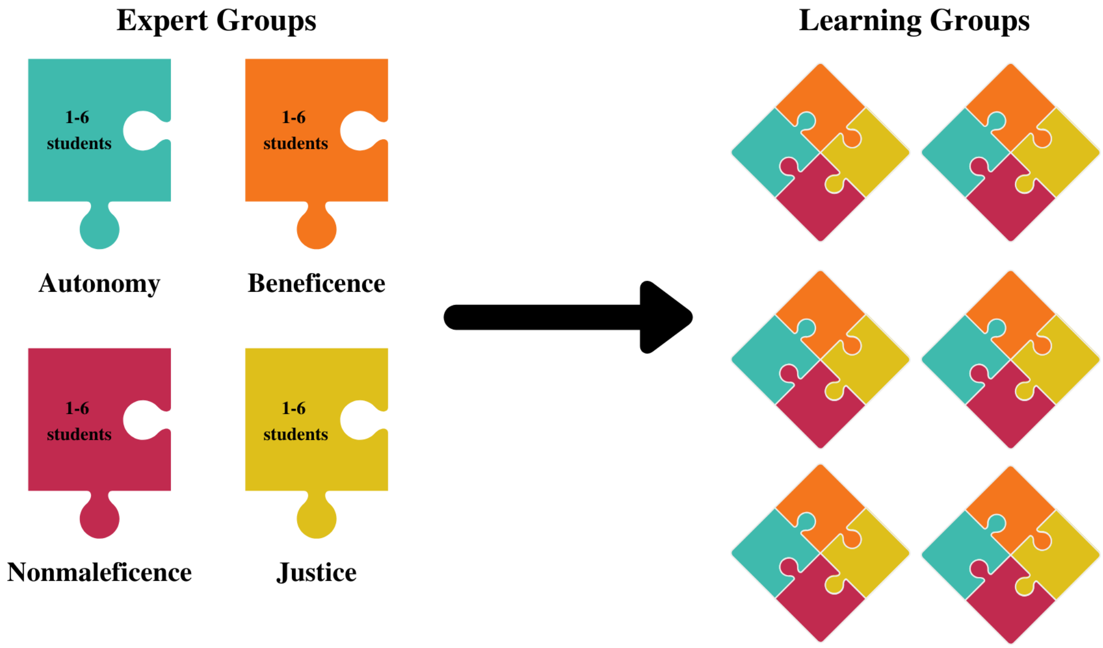


Figure 4. The jigsaw lesson. Students are assigned to their respective expert groups: autonomy, beneficence, nonmaleficence, and justice. They are then assigned to a learning group, ideally one expert per group to teach the members their respective expertise. The number of learning groups varies depending on the number of students.

To encompass all issues regarding gene editing, two lessons will be needed: one for novels and one for films. In an undergraduate course, this would be two lessons occurring on two separate days during the week. In a graduate course, this would be two lessons occurring on the same day, as graduate courses are double lectures that meet weekly. For the first lesson, the following novels were chosen: *Beggars in Spain* (Kress 1991) will demonstrate the tenet of autonomy with the issues of somatic cells versus germline cells and the effects of gene editing on future generations, *Intrusion* (MacLeod 2012) will portray the tenet of beneficence by showing the obligation to treat genetic abnormalities, *Oryx and Crake* (Atwood 2003) will be used to describe nonmaleficence through the issue of enhancements as well as the portrayal of a dystopian society, and *Change Agent* (Suarez 2017) will depict justice via the issue of equal access and affordability. *Change Agent* (Suarez 2017) had the added benefit of being about CRISPR specifically.

To reiterate, the expert groups will be assigned these novels and specific issues on which to focus, but that does not mean there are not other serious ethical issues illustrated within each novel. For instance, *Intrusion* (MacLeod 2012) also had a serious violation of autonomy by denying decision making capacity to mothers through coercion of health practitioners and government officials. But the expert group that reads this novel for its portrayal of beneficence can then bring the violation of autonomy into the large group discussion as an ethical dilemma to be solved. This can also be compared and contrasted with decision making capacity in *Beggars in Spain* (Kress 1991) as part of the larger group discussion. The readers of *Change Agent* (Suarez 2017) may also want to compare the presentation of beneficence through the United Nations approved list of genetic diseases to gene edit to "the fix" in *Intrusion* (MacLeod 2012). The point is there are many comparisons and contrasts that can be made between these stories.

For the second lesson, the following films were chosen: *My Sister's Keeper* (Furst 2009) will illustrate decision making capacity under the tenet of autonomy, *The Perfect 46*

(Bonowicz 2014) will depict beneficence through the obligation to treat and desire to eradicate genetic diseases, *Equals* (Pruss 2015) will serve the purpose of demonstrating nonmaleficence due to unintended consequences and incomplete gene edits in addition to a semi-dystopian society, and *Gattaca* (DeVito 1997) will show how discrimination is a concern under justice. Discrimination was an issue in *Equals* (Pruss 2015), *Beggars in Spain* (Kress 1991), and *Intrusion* (MacLeod 2012) as well, therefore, students can in the larger group discussion compare and contrast how the discrimination was presented in these different stories. Also worthy of discussion would be the degree to which societies were dystopian and whether students would want to live in those worlds or not. Reflecting on why they perhaps might not would impress upon them the importance of ethical oversight not just in research but also in regulations and legislation. The overall theme of enhancements versus treatment could even be a third lesson where students have to choose sides and debate their stance using evidence from any novel or film to support their argument. Somatic cell edits versus germline cell edits could be a debate as well, since there are many arguments for or against germline edits worldwide.

Three issues that were not assigned but still appeared somewhere in these stories were eugenics (*The Perfect 46* (Bonowicz 2014)), unequal burden of research on women (*Change Agent* (Suarez 2017)), and disability rights (*The Perfect 46* (Bonowicz 2014)). If time is available, these can also be discussed.

The selection of eight stories, four novels and four films, covers the main ethical issues: somatic vs. germline edits/future generations, decision making capacity, the obligation to treat genetic diseases, unintended consequences, designer babies/enhancements, equal access/affordability, and discrimination/new classes of people.

The jigsaw lessons also allow all of these issues to be covered without burdening students to read all four novels or watch all four films. They will have time to explore and reflect on their issue individually, then ensure mastery by explaining their issue to their group. Reflection papers, active learning, and self-led discussions promote their understanding of the tenets and how they apply to gene editing. Lastly, the group discussions and debates allow them to practice ethical reasoning by comparing/contrasting issues and solving ethical dilemmas together. Science fiction therefore is the backdrop upon which they gain their understanding by enabling visualization of the issues, evoking emotional responses, and maintaining interest by providing entertaining stories to read and view.

Science Fiction in Politics: Envisioning Ethical Issues Surrounding Gene Editing and Influencing Policy Making

Written by professors at the University of Copenhagen and Lund University, an article was published discussing how legal, ethical, and social concerns intersected with scientific progress of gene editing (Nordberg et al. 2018). Within this article, the following was stated: “Literature and cinematographic works fuel fears and high hopes. The mass media contribute to construction of extremist narratives concerning emerging technology. Major industrial players are portrayed as focusing on short-term economic gain, being over optimistic on benefits, blind to possible negative effects, and with little interest in engaging in an open debate with other relevant stakeholders. Popular culture is rife with alarmism, misperceptions, and dystopian futuristic scenarios that find their way into the policy debate via the discourse of the technology’s opponents. On the other side of the spectrum, we find hyperoptimistic views of possibilities and minimization of risks communicated by proponents of immediate and unlimited use of the technology,” (Nordberg et al. 2018).

While the statements in this article may be true to some degree, the entire basis of this dissertation is utilizing science fiction in a productive manner to convey the ethical issues of CRISPR gene editing in an educational setting and to influence policy making. The stories in the above section and this section were carefully chosen to avoid alarmism, misperceptions, highly improbable dystopian scenarios, minimization of risks, and overly optimistic expectations. To reiterate, unrealistic societal pitfalls or scientific ridiculousness were disregarded for argument in such discussions. The stories included here have substantial value in assisting in understanding genuine and legitimate potential concerns. In other words, realistic aspects in science fiction should be taken seriously and can be an effective tool to visualize and guide ethical decision making.

Firstly, various forms of discrimination were evident in a few stories due to the emergence of new classes of people; either genetically modified people were discriminated against or non-genetically modified people were discriminated against. The genetically modified experienced forms of discrimination in *Beggars in Spain* (Kress 1991), *Friday* (Heinlein 1982), and *Tankborn* (Sandler 2011). While I fully acknowledge the setting in *Friday* (Heinlein 1982) was very futuristic involving space travel and humans being gene spliced with animal genes to provide enhanced abilities in *Tankborn* (Sandler 2011) is scientifically improbable, the degree of animosity and class separation was palpable in their respective stories. I doubt the majority of people would think the disdain and exclusion Friday felt for being an AP or the enslavement of Kayla and other GENs are morally acceptable. The sleepless in *Beggars in Spain* even had laws enacted against them because of their advantage, such as being barred from competing in the Olympics, from owning a twenty-four hour business, from serving on a jury, and even being denied renting an apartment (Kress 1991). *Beggars in Spain* in particular was a very realistic novel that illustrated what genetically modified people might experience if the majority of society believes they have advantages over everyone else (Kress 1991). Such laws are discriminatory in nature and are unjustifiable. Policy makers must be aware of such a pitfall and must be discouraged from proposing and/or enacting such legislation. All three of these stories demonstrate the importance of ensuring genetically modified people are treated fairly under the law.

X-Men was completely ridiculous in terms of people who are endowed with the mutant x-gene would have superpowers, but it was a popular movie that many people would probably have seen and therefore can relate (Donner 2000). Legislators in the United States in this film were shown debating the enactment of a mutant registry disclosing who was a mutant and what their abilities were. Fear of mutants was the driving force behind this proposed law and mutants were opposed because of the violence they experienced from people. Such a registry was likened to the Nazi regime where Jewish people were forced to identify themselves and wear the Star of David for easy identification, which led to the Holocoust. History tells us that any kind of registry to monitor the genetically modified (or any subpopulation for that matter) would be ethically unjustifiable. This kind of discrimination cannot be permitted anywhere in the world, which is the main takeaway from *X-Men* (Donner 2000).

Gattaca (DeVito 1997) and *Intrusion* (MacLeod 2012) demonstrated discrimination in the reverse, but is equally important to addess. Denying employment due to being an Invalid (not genetically modified) was illegal in *Gattaca*, but was subverted through regular drug screening (DeVito 1997). The anti-discrimination laws were not strictly enforced, unfortunately. When screening for drug use, companies should not have been allowed to perform any genetic testing in the process. In *Intrusion,* Hope was confronted by other mothers who did not want to have her non-genetically fixed son enter school for fear of risking the health of other children (MacLeod 2012). These scenes seemed to be very real scenarios and I personally could truly envision this happening in the future. Having only a faith exemption for not taking the fix was discriminatory in nature. Laws and school policies should have protected Hope's son's right to attend and the faith moms should not have been allowed to protest his attendance. Law makers can learn from these stories that it is not just necessary to put anti-discrimination legislation in place, but to determine means for enforcing that law and enacting harsh punishments when it is broken.

Gattaca (DeVito 1997), along with the *Rise of the Kymiera* six-part series (Turnbull 2017) and *Change Agent* (Suarez 2017), provided another warning about which to pay attention: fertility clinics need to have more regulations and their offerings may need to be regularly screened for compliance. Just as a side note, the gene splicing that Dr. Newman performed on embryos in *Rise of the Kymiera* where animal genes provided enhanced abilities can be ignored, as this is scientifically absurd (Turnbull 2017). But what can be taken away from this unethical practice was the need for accountability for performing edits on embryos at a fertility clinic for implantation for which the parents did not give informed consent. Scientists and clinicians should never perform edits to which the parents did not agree or understand, which was an issue already with Jiankui He (The Blind Baby Maker 2019, Cohen 2018, and Savulescu & Singer 2019). *Change Agent* (Suarez 2017) provides a little guidance on this issue by having a globally agreed upon United Nations list of approved gene edits to prevent diseases, which is feasible, but also showed a problematic black market criminal operation. This would suggest new laws against such crimes and accompanying defined punishments would need to be established. Interestingly, in *Gattaca* (DeVito 1997), offering couples the best possible baby by combining the best genes from both parents and allowing them to choose physical traits was not only legal but strongly encouraged; in *Change Agent* (Suarez 2017), edits outside of the UN approved list to correct disease causing mutations that provided enhancements were illegal. Having a globally approved list seems to be a valid approach and violators should be heavily penalized. But if the use of CRISPR for enhancements is inevitable due to wealthy people paying any sum of money to provide an advantage to their children, then perhaps safe, agreed upon enhancements can be offered under strict supervision. Regulations would be preferable to the black market operations.

ReEvolution (Grant 2019), *Change Agent* (Suarez 2017), and *Extraordinary Measures* (Shamberg 2010) all in their own way showed the importance of funding public research. In *ReEvolution*, the private sector in China violated ethics in multiple ways, as people with money poured resources into companies that would produce results by any means necessary and evaded regulations (Grant 2019). It also demonstrated the need to outline and enforce stages of research before attempting human clinical trials. *Change Agent* criticized the United States for not funding embryonic research due to religious reasoning and scientifically ignorant people making decisions, which in the future led to scientific breakthroughs occurring exclusively in foreign countries (Suarez 2017). If the US wishes to be at the forefront of biotechnology and medical advancements, funding public research, including embryonic research, needs to occur. Lastly, *Extraordinary Measures* portrayed the main reason why research is so important: end the suffering of people (Shamberg 2010). If CRISPR could be the answer to curing genetic diseases where PGD and IVF are not suitable options, then such research must continue. Society has an obligation to help those who suffer from genetic diseases.

Intrusion also exhibited the impact on society when mothers have their autonomous choice removed from them (MacLeod 2012). Parents should not be coerced to perform genetic modifications on their child, especially if the probability of disease transmission is low or practically nonexistent. Hope’s child was shown through genetic testing to be free of disease; therefore, the fix was completely unnecessary. Also, the issue of access to healthcare is related: making the autonomous choice to not genetically modify should be respected and health insurance companies must not be allowed to deny coverage or astronomically raise insurance premiums to ensure healthcare is still affordable for those who choose natural reproduction. *Equals* was similar to *Intrusion* in that gene editing was mandatory for everyone: every single person was genetically modified to not experience emotions (Pruss 2015). Not only did this demonstrate that medical applications should be the focus of CRISPR research, but also gene editing should never be made mandatory. Therefore, policy makers should take these stories seriously in that if gene editing ever becomes a viable treatment option for parents, medical practitioners and insurance companies should not be permitted to force people to modify their children. Protections are crucial to uphold autonomous decision making and exemptions should not be restricted to religious reasoning only.

Even though being sleepless had multiple health benefits, the genetic modification in *Beggars in Spain* portrayed why understanding a gene edit thoroughly before performing it in humans is essential to the research process (Kress 1991). The researchers did not know that removing sleep genes and replacing them with sleepless genes was providing an enhancement that was forcing human evolution because they were not somatic edits, but germline edits. Additionally, the sleepless genes turned out to be the dominant genes, meaning all offspring of sleepless people would be sleepless. Unless our collective knowledge of genetics is expanded through research, especially in regards to polygenic genes, a genetic modification could be passed down through generations, whether a positive or negative edit, due to lack of certainty. The warning conveyed here does not necessarily mean all germline edits should be prohibited, but rather understanding gene relationships and edits better through properly funded and organized research should be undertaken before moving forward with editing embryos and implanting them for pregnancy. This story along with others stress the importance of scientific exploration prior to clinical trials then common applications.

Oryx and Crake was a drastic dystopian society taking place after an apocalyptic event (Atwood 2003). The entire population who had not either been given the vaccine in advance or who refrained from taking the Blysspluss pill were wiped out with a deadly, grotesque time released virus. The Crakers were unaffected because Crake had genetically engineered them to be immune. Prior to the Blysspluss pill outbreak, drug companies were regularly in the practice of engineering illnesses that were administered through vitamins and then extorted people for money for the cures that they engineered simultaneously. These practices are gross ethical violations and the warning in this story is to be aware of using gene editing or engineering to develop bioweapons. This is why it is important to define sooner rather than later acceptable applications of gene editing to prevent this type of misuse.

My Sister's Keeper was an emotionally charged story depicting the struggles of a family attempting to save their child's/sister's life (Furst 2009 and Picoult 2003). The major problem in this story, whether watching the film or reading the novel, was that Anna was genetically engineered to be an exact match for Kate in order to donate cord blood in order to put her leukemia in remission. This sounds noble and maybe not that significant, but as the story progressed, the demands from Anna became more painful and invasive, including donating her kidney. Genetically engineering a person to be an organ and tissue donor is just morally wrong. The court granted Anna medical emancipation from her parents, as they were not fit to make medical decisions for her, and she was able to say no to donating her kidney, as she should have been able in the first place regardless of her age. Such practices should be monitored if embryos are gene edited to prevent a situation like this one in fertility clinics and hospitals. Proposals of gene edits should be evaluated by an ethics board before proceeding to ensure parents do not edit for such a reason like Anna's parents did.

In *The Perfect 46,* on the surface, the website to find your genetic match seems like many other matchmaking sites and ultimately harmless (Bonowicz 2014). People seemed to really buy into the concept that genetic diseases could be eradicated through selective breeding, which was what the website was really offering. No one really discussed a true, loving connection, but made a rather considerable assumption that genetics was the perfect means of making a matching relationship. When a mistake in the algorithm led to the inheritance of Tay Sachs in multiple children, leading to the suffering of the loss of a child, the warning against eugenics practices became apparent. Legislation should be ever vigilant to assure medical applications as much as possible. Enhancements may not be entirely preventable, but they should be discouraged.

In *Brave New World,* we really just need to be aware of how advancing technology led to the creation of human factories (Huxley 1932, Babbin 1980, and Joyce 1998). I would assume the majority of people would find such practices appalling and unethical. Societal values also deteriorated into a world of consumerism, superficiality, brainwashing, lacking love, and drug abuse. Genetic engineering should never be used to create clones to maintain the population of certain classes of society.

In agreeance with Norgberg et al. (2018), stories that contain alarmism or misperceptions about transgenic gene splicing imbuing enhanced abilities can be ignored for policy implementation discussions, as this is purely science fiction and therefore the fears generated by them are insignificant. This is not to say that transgenic gene splicing among species is scientifically impossible, but incorporating genes from a spider into a man thus leading to his ability to scale walls and swing from artificial webbing or incorporating lizard genes into a man thus leading to a human sized lizard terrorizing the city are meant to be for entertainment purposes only (Arad 2012). Other similar stories that were not discussed for the same reason that the science was implausible were *Rampage* (Flynn 2018), *Splice* (Hoban 2009), *The Titan* (Amel 2018), *The Island of Dr. Moreau* (Pressman 1996 and Steloff 1977), *Cowl* (Asher 2004), *Jupiter Ascending* (Hill 2015), and *The Blood Beast Terror* (Miller 1968). *Rise of the Kymiera* (Turnbull 2017) and *Tankborn* (Sandler 2011) provided value for other bioethical issues mentioned earlier in this section, such as discrimination and informed consent, but should not be taken seriously in regards to the type of gene edits that were performed (animal genes incorporated in to humans endowed abilities such as enhanced strength and wings to fly). Ignoring these films in particular, the rest offer valuable considerations for policy implementation to continue CRISPR gene editing research without violating ethical principles.

Conclusion

While some scholars have argued that science fiction is fraught with alarmism, misconceptions, and dystopian societies, this argument is not entirely accurate. These three concepts are most likely utilized in science fiction because the ultimate goal is to tell a story and entertain the reader or viewer. However, by being selective with stories, one is able to navigate around alarmism and misconceptions for truly impactful meaning and a reflection on societal values that can assist in understanding significant issues regarding gene editing research. Science fiction is therefore a fruitful tool for teaching ethical problem solving in the classroom as well as guiding policy making.

The stories included in the chapter for educational and policy making purposes were carefully chosen to separate the valid issues from the fantastical, unrealistic elements in science fiction. Even if a story contained farfetched fictional "science" or super abilities, related ethical problems with gene editing were still apparent and therefore should be carefully considered. In an educational setting, two lessons, one incorporating novels and one incorporating films, were developed to encompass the majority of ethical issues surrounding gene editing that are discussed in the literature. Autonomy was covered with *Beggars in Spain* (Kress 1991) and *My Sister's Keeper* (Furst 2009) by demonstrating the issues of germline vs. somatic cell edits, decision making capacity, and the effects of gene editing on future generations. *Intrusion* (MacLeod 2012) and *The Perfect 46* (Bonowicz 2014) described beneficence by conveying the importance of exploring gene editing to eradicate genetic diseases that cause suffering. *Oryx and Crake* (Atwood 2003) and *Equals* (Pruss 2015) were both stories that depicted dystopian societies, off-target edits or unintended consequences, edits to create designer babies and/or enhancements rather than cure diseases, and even bioterrorism. Justice was portrayed in *Change Agent* (Suarez 2017) and *Gattaca* (DeVito 1997) by demonstrating unequal access through black market crime and new class discrimination (genetically modified and non-genetically modified). Each story does have multiple tenets within them, but the structure of these lessons allows for the greatest coverage of issues. However, class discussions would allow for ethical debates, discussion of dilemmas, and comparing and contrasting of the presentation of issues.

The same stories and a few additional stories can be used to influence policy making globally. Policies preventing class separation and discrimination can be visualized and addressed with the following stories: *Beggars in Spain* (Kress 1991), *Friday* (Heinlein 1982), *Tankborn* (Sandler 2011), *X-Men* (Donner 2000), *Gattaca* (DeVito 1997), and *Intrusion* (MacLeod 2012). *Gattaca* (DeVito 1997), *Rise of the Kymiera* (Turnbull 2017), and *Change Agent* (Suarez 2017) can be used to guide the creation, updating, and enforcing of regulations for fertility clinics to determine what gene edits should and should not be offered. Also along these lines, the prevention of eugenic practices was prominent in *The Perfect 46* (Bonowicz 2014). The importance of funding research to seek cures for genetic diseases and understand gene edits prior to implementing them in humans is seen in *Change Agent* (Suarez 2017), *ReEvolution* (Grant 2019), *Extraordinary Measures* (Shamberg 2010), and *Beggars in Spain* (Kress 1991). The necessity to protect autonomous choice to genetically modify or not modify was explored in *Intrusion* (MacLeod 2012) and *Equals* (Pruss 2015). Lastly, preventing misuses of gene editing like creating people to be genetic matches for organ and tissue donations or creating bioweapons were demonstrated in *My Sister's Keeper* (Furst 2009 and Picoult 2003) and *The MaddAddam Trilogy* (Atwood 2003, Atwood 2009, and Atwood 2013), respectively, are also crucial to regulate. Policies, legislation, and laws need to be developed now before gene editing research is explored beyond what society deems ethical. The stories here will enable the visualization of the issues surrounding gene editing and can help define what regulations should be.

The exploration of multiple science fiction works in both literary and film formats offered invaluable insight into perceptions and ethical concerns of gene editing. Whether used in an educational setting to engage students in discussions to build their ethical decision making skills or in discussions in a political or more general setting to influence policy making, science fiction offers understanding through the visualization of positive and negative applications of gene editing to those who do not have a science or ethical background. Without educating future scientists about ethical implications of their research or legislators about the pitfalls of unregulated research, gene editing could violate the tenets of biomedical ethics as well as the moral values of society. Science fiction that contains realistic possibilities should be carefully studied and consulted for guidance regarding ethical considerations surrounding gene editing, especially with the current proliferation of CRISPR-Cas9 gene editing research. The stories chosen in this section accomplished this by selecting the most impactful reading or viewing experience by minimizing time investment, invoking emotional responses, containing multiple conflicting issues, were scientifically possible or probable (if not, the science was ignored and the ethics were extricated), and if they were specifically about CRISPR. Hopefully, by reading and viewing these stories, a call to action would be invoked to prevent ethical violations of the tenets and moral values that are important to society as a whole.

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