Potential Implications of Genetic Engineering for the LGBTQ+ Community

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Humanity is at an inflection point. Genetic engineering in human reproduction has the power to shape human evolution through the negative selection against genetic disease and disability, and the positive selection of traits like high intelligence, athletic prowess, or even sex, gender, and sexual orientation. Recent advances in genome sequencing, pre-natal screening, big data analytics, and DNA editing through technologies such as CRISPR have fostered great discussion around their use in human reproduction (Isaacson Rules of the Road, 2021). Some argue germline genetic editing is taboo on religious grounds, others that it could reduce genetic diversity and cause unintended evolutionary harm (p. 273), and many, that it could push humanity to new medical, cultural, and intellectual heights (Isaacson Rules of the Road, 2021). But genetic engineering in human reproduction is already occurring. Its effects on our evolution are both now and future. The more humanity understands, the better it can guard against unintended consequences.

The sociotechnical framework of technological momentum looks at the intricate interchange between society and technology and argues that early in a technological system's development, humanity can shape its use but as it matures, the system becomes more deterministic (Hughes, 2000). Hughes notes:

> A technological system can be both a cause and an effect; it can shape or be shaped by society. As they grow larger and more complex, systems tend to be more shaping of society and less shaped by it…shaping (of technology) is easiest before the system has acquired political, economic, and value components (pp. 33-34).

Following Gregor Mendel's discovery of the gene as the unit of heritability and Charles Darwin's theory of evolution by natural selection during the mid-19th century, the idea that humanity could better itself through selective breeding gained traction in Europe and the United

States as eugenics. Eugenics saw its zenith in Nazi Germany's extermination of Jews, criminals, homosexuals, and other "contragenics" during World War II (Plant, 1986; Seel & Le Bitoux, 1995). While the term all but died with their defeat and the atrocities of the holocaust became more widely known, the idea that humanity could better itself through genetics did not.

Rather than selective breeding or genocide of extant groups already born, modern genetic engineering in human reproduction finds its form primarily in pre-natal selective screening for diseases and disabilities such as Down's Syndrome and Tay Sachs and the choice to implant an embryo when using *in vitro* fertilization or terminate a pregnancy in cases of traditional conception. For genetically recessive diseases like Tay Sachs where both parents are heterozygous for the gene that causes it, passive selection against the disease can occur in the decision not to conceive at all. All three methods prevent the genetic cause of the disease from being passed down to future generations in that family's line.

With emergent technologies such as human genome sequencing, big data analytics, and active DNA editing through CRISPR and other technologies, the future holds the promise of not only negative selection against diseases and disabilities, but actively fixing genetic problems *in utero* or *in vitro*, and even positively selecting for traits, as noted above. A significant question arises: what do these technologies mean for marginalized groups whose traits are genetically determined or influenced? This paper focuses on one such group and demonstrates that the technological momentum of genetic engineering could lead to the virtual extinction of the LGBTQ+ community. If this is an uncomfortable topic, it should be, but to shape the future of genetic engineering and the evolution of humanity, this is a question that society needs to answer, and soon.

Genetic Engineering in Human Reproduction

Prenatal Screening

Amniocentesis was first described in the late 1950s (Serr et al., 1955). It is the process of removing cells from amniotic fluid during fetal development. A decade later, it was combined with fetal karyotyping to diagnose Down Syndrome (Palomaki, 1995). In the decades since, amniocentesis has been expanded to diagnose other chromosomal diseases like Taylor or Patau Syndromes and remains the most common type of prenatal screening test. Other methods of prenatal screening have been developed as well: Cell Free DNA screening collects DNA fragments from amniotic fluid and became commercially available in 2011; and Chorionic Villus screening in which villi are collected from just outside the amniotic sac (Carlson & Vora, 2017). All three methods allow for prenatal genetic screening of the fetus. Screening, of course, is only one step in genetic engineering. Unless a change is made to the fetus, then its genes will enter the gene pool and potentially be propagated to its own children.

Pregnancy Termination

Abortion is a relatively drastic form of genetic engineering, but it is common world-wide even in cases of non-lethal genetic diseases. It has also been used to implement cultural preference for male children, instead of female. If a child isn't born, or rather, never reproduces, it cannot pass on its genes. Pregnancy termination, then, serves as a method of negative selection against genetic diseases and even sex. As severe as abortion and its toll on families can be, this demonstrates the lengths that prospective parents will take to eliminate suffering in their children, or merely to effect personal and cultural preferences.

The number of pregnancies in the United States screened for Down Syndrome grew from 25% in 1988 to 72% in 2012 (Palomaki et al., 2013). When polled in 2007 about their attitudes

towards abortion in the face of a non-lethal but serious genetic diseases like Down Syndrome (DS), only 20% of Americans thought termination of the pregnancy was permissible ("Public Opinion and the Embryo Debates," n.d.). Yet, even in this contentious environment, of those pregnancies with a positive DS diagnosis in the U.S., 67-72% were terminated (Natoli et al., 2012). In other words, at least 47% of Americans that say they are against abortion in cases involving Down Syndrome, still choose to terminate when presented with the diagnosis in their own pregnancies.

In Europe, the numbers are even larger: 77% in France, 98% in Denmark, and nearly 100% in Iceland choose to abort (Quinones et al., n.d.). In China, up to 95% of families confronted with the prospect that their child will have Down Syndrome terminate their pregnancies (Koetse, n.d.). These numbers are striking, but the elimination of disease and suffering in children are not the only reasons parents choose to abort their pregnancies. Some do so simply to implement a cultural or personal preference.

China's "one child policy" was instituted to combat overpopulation and proved controversial. Although birth and fertility rates both dropped and up to 400 million births were prevented, a cultural preference for male children led to an increase in aborted female fetuses and over 33 million more men in China than women. The number of female babies killed, abandoned, or given up for adoption also increased dramatically while the policy was in place from 1980 to 2016 (*The Effects of China's One-Child Policy | Britannica*, n.d.).

In Vitro **Fertilization**

In utero genetic screening is invasive, as the cells must be taken from inside the mother's womb, but the miracles of modern medicine have allowed conception to occur outside of the mother's body. In 1978, the first human baby conceived through *in vitro* fertilization was born.

Eggs taken from the mother are fertilized by sperm from the father in a laboratory dish. Often, dozens of eggs are harvested from the mother and fertilized, then frozen for long term storage. These embryos can then be thawed later to be implanted in her womb ("History of in Vitro Fertilisation," 2022). In 2012, up to five million infants world-wide were born using "assisted reproductive technologies" (ART) like *in vitro* fertilization (Adamson et al., 2013).

As in prenatal screening, pre-implantation genetic screening is often used during *in vitro* fertilization to prevent children from being born with genetic diseases such as Down Syndrome (Kushnir et al., 2016). Like pregnancy termination, preventing embryos diagnosed with DS and other diseases from being implanted and carried to term is a form of negative selection genetic engineering against disease and disability. As our understanding of genetic influences on traits and behaviors grow, the near future, however, will allow for positive selective screening for traits such as intelligence and athletic prowess. Even still, these forms of genetic engineering do not require active editing of the genome. The big news of the past decade has included technologies that allow for active DNA editing, such as CRISPR.

Genome Editing Technologies

CRISPR's use in human reproduction has been contentious. In 2018, a Chinese researcher named He Jiankui shocked the world when he announced that a set of twins had been born. The twins had received a gene meant to confer resistance to HIV via CRISPR edits to their DNA (*CRISPR Bombshell*, n.d.). Walter Isaacson had this to say about Jiankui:

> Chinese officials had designated genetic engineering as critical to the country's economic future and its competition with the U.S., and to that end they launched a variety of initiatives to encourage entrepreneurs and lure back researchers who studied overseas. Jiankui benefited from two of them: the Thousand Talents Recruitment Program and the

> Shenzhen government's Peacock Initiative… Over the next six years, Jiankui's company would receive $5.7 million in funding from government sources (Isaacson, 2021, p. 301)

Jiankui's company developed gene sequencing technology and initially used it to perform genetic screening for diseases in early-stage embryos (Isaacson, 2021, p. 302). But ever ambitious to make history, he then began to pursue the possibility of using CRISPR to make embryonic DNA edits to fight disease, and ultimately succeeded with HIV resistance.

Following the announcement regarding the twins, the world's response was one of near universal condemnation. Scientific consensus exclaimed that Jiankui had been irresponsible; genetic engineering through CRISPR was not yet mature enough for human trials. In 2019, Jiankui was convicted in his homeland of China, banned from reproductive science, fined $430,000, and sentenced to three years in jail (Isaacson, 2021, pp. 315-332).

Technological Momentum

In his book *Hacking Darwin: Genetic Engineering and the Future of Humanity*, futurist and technology political scientist Jamie Metzl makes a compelling argument for the inevitability of genetic engineering in human reproduction (Metzl, 2019). First, he claims, genetic engineering will be combined with big data analytics and humanity's ever-expanding knowledge of the complex interplay between genes and their environment to screen for various traits during *in vitro* fertilization. Big data analytics will serve to provide stochastic probability calculations that genetically influenced complex traits and behaviors will manifest in an individual, based upon their genetic makeup. Prospective parents could genetically screen among dozens to hundreds of embryos and decide which ones to implant based upon which traits they find desirable. In this manner, there are no active edits to embryonic DNA and the baby's DNA is 100% from the parents. Thus, there will be no prospective condemnation as happened to Jiankui.

As noted above, this type of genetic engineering is already used to screen for diseases like Down Syndrome. The near future, however, holds the promise of screening for additional diseases and even traits like intelligence, musical ability, and others as our genetic understanding grows. Many traits and behaviors, of course, are a complex interplay between genes and environment. Using big data analytics and stochastic probability calculations that these complex traits and behaviors will emerge in an individual, CRISPR and other active genome editing technologies of the future will allow doctors to affect those probabilities. Metzl argues that socially sanctioned editing of embryonic DNA through technologies like CRISPR is further down the road, but virtually inevitable once these technologies mature in the not-so-distant future.

Metzl's reasoning is simple and persuasive. If genetically influenced traits such as intelligence are correlated to longer, healthier, wealthier, happier lives – and intelligence is - then it is immoral to withhold genetic markers for these traits from children, if we can add them safely, affordably, and with efficacy (Ali et al., 2013; Arden et al., 2016; Furnham & Cheng, 2016; Metzl, 2019). If we do not confer our children with intelligence and other such genetic traits when we can, then in effect, we are condemning our children to live shorter, sicklier, poorer, and sadder lives. Such reasoning and the strong parental desire to provide children with the absolute best possible chance to thrive will drive eventual social acceptance of genetic engineering beyond mere disease cure and prevention, once the technology matures.

The Genetic Basis of LGBTQ+ Traits

Which LGBTQ+ traits are genetically based and thus, subject to genetic engineering? In short, nearly all of them. First, some definitions for terms used here. Sex refers to anatomical and

biological sex. Gender and sexual identity refer to individual self-identification. While they both influence and are influenced by their respective behaviors, they are distinct from them. Finally, care should be taken to understand that genetically influenced does not mean genetically determined.

Sex

The average human has 23 pairs of chromosomes for a total of 46 chromatids. During mitosis, each pair of chromatids joins at the centromere to form a rough X shape. The 23rd pair is defined as the sex determining set. When the 23rd pair joins together during mitosis to look like an X, then it called XX and the human is genetically female. A genetic male, however, has roughly half of one of the chromatids at the 23rd pair, so when it joins to the other chromatid at the centromere during mitosis, it forms a Y chromosome called XY. An average genetic female, then, is called 46XX, and the average genetic male 46XY.

On the Y chromosome, there is a gene called the sex determining region of the Y chromosome, or *SRY*, that when activated during early embryonic development causes a cascade of other genes to switch on and off, and the fetus to develop as anatomically male (Gubbay et al., 1990; Jager et al., 1990; Koopman et al., 1991). That cascade also causes the fetus' testes to produce testosterone that needs to be processed by enzymes so it can bind to the proper receptors on embryonic cells to cause a host of other intracellular signaling cascades that tell the embryonic cells to produce a baby male (Callahan, 2009; Conte & Grumbach, 2011). This delicate dance of genes, hormones, enzymes, and cell receptor signaling cascades all occurs within the first ten weeks of development. As Callahan notes, this is a lot of things that "need to be on time, in place, and ready to go" for a baby male to develop properly.

In addition to 46XX and 46XY females and males, there are people with XXX, XYY, or any number of sex chromosomes. Sometimes there are also 46XX males or 46XY females (Conte & Grumbach, 2011). The *SRY* "master switch", its resulting cascade of genes, hormones, and intracellular signals, plus the number and type of 23rd chromosome must all be perfectly correct and synchronized for sexual organs to develop properly. When these processes have errors, they can lead to the nearly continuous spectrum of genitalia between male and female observed in newborn babies.

Gender

A longitudinal study conducted by Columbia University in 2005 analyzed 46XY babies with severe genital defects who were assigned and raised as female at birth (Meyer-Bahlburg, 2005). They were broken into three age categories: children, adolescents, and adults. The study found that 21% of these children were living as males and 7% of those living as female were clinically diagnosed with gender dysphoria, 9% of adolescents were living as male and 23% had gender dysphoria, and adults were 35% and 18%, respectively. The researchers also noted that 100% of those born 46XY with severe genital defects assigned and raised as male at birth, still identified as male. Further, they added, "Most, if not all individuals (raised female), showed marked 'masculinization' of gender-role behavior…including sexual orientation." In other words, most if not all who were old enough, indicated sexual attraction to females, a behavior that generally pertains to males.

While this study and others do not conclusively establish that gender is 100% genetically determined, as is usually the case with any complex trait or behavior, they do suggest a genetic component (Erickson-Schroth, 2013; Theisen et al., 2018, 2019). Ericson-Schroth notes the following regarding transgender identity specifically,

> A review of the biological studies to date on the etiology of transgender identity hints that genetics and prenatal hormone exposure may play some role in transgender identity development, although a biological model does not appear to account for the entirety of transgender experience.

Theisen et al. found 30 variants in 20 genes of interest among 14 female-to-male and 16 male-to-male subjects who identified as transgender. These genes were associated with neurological development and/or sex steroid metabolism, a common target of the studies in Erickson-Schroth's literature review. Like those studies, Theisen et al. used small sample sizes and the results inconclusive as a result. While these studies suggest a genetic component to gender and transgender identity, they highlight the infancy of scientific research into gender identity, as well as the difficulty inherent in studying groups like the transgender community. Even so, the studies indicate gender is probably genetically influenced, even if the specifics are yet to be identified, and thus, potentially subject to genetic engineering in the future, as our understanding grows.

Sexual Identity

The genetic influence on sexual identity was intimated above in the quote from Columbia University researchers regarding "masculinization" of behaviors and same-sex attraction of 46XY individuals with severe gender deformities assigned or raised female at birth. In other words, these individuals were genetically male, but assigned or raised female and sexually attracted to females. That study is far from the only evidence, however. In the early 1990s, significant press was devoted to the possible discovery of "the gay gene", *Xq28* by Dean Hamer, a researcher at the National Cancer Institute (Mukherjee, 2016, Through the Looking Glass). He had gathered the family trees of 114 gay men and built family trees consisting of 1000 people. He found a strong correlation between gay men and gay maternal uncles, which suggested a gene

on the X chromosome might be responsible. Big data analytics led him to *Xq28*. Subsequent attempts by other researchers to verify the result or find other genetic markers have proven inconclusive, though some have pointed to genes associated with various sex hormones.

A researcher named Michael Bailey studied homosexuality among identical male twins and found that the concordance was 52%, higher than traits and diseases readily accepted as genetically linked such as Type I diabetes at 30%, and almost as high as height at 55% (Bailey et al., 2016; Mukherjee, 2016). Other studies on identical twins have shown similar results (Bailey et al., 2016; Bogaert & Skorska, 2020). As hinted above, *in utero* exposure and various genes associated with sex hormones may play a role in homo and bisexual identity, as well as epigenetics – chemical tags on DNA that determine which portions of that DNA are active or inactive (Bogaert & Skorska, 2020). While there is unlikely to be an SRY-like "master switch" that conclusively determines sexual identity, these studies show there is at least a strong genetic component that will lend itself to genetic engineering manipulation as our understanding grows.

Societal Attitudes Towards the LGBTQ+ Community

In the past decade, LGBTQ+ rights in the United States have taken momentous steps in basic human rights. The 2015 Supreme Court decision in Obergefell vs. Hodges recognized the right of same-sex couples to marry, 2011 saw the repeal of "don't ask don't tell" which had effectively prohibited LGBTQ+ personnel from serving in the Armed Forces, and in 2020, the Supreme Court ruled that LGBTQ+ workers are protected from discrimination. These human rights victories do not tell the whole story of LGBTQ+ acceptance in American society, however, nor internationally.

In the first three months of 2022 alone, 238 anti-LGBTQ+ bills have been introduced in U.S. state legislatures, whereas all of 2018 saw 41 ("Legislative Tracker," n.d.). Internationally, 38 countries criminalize LGBTQ+ people and 11 countries institute the death penalty (*Map of Countries That Criminalise LGBT People | Human Dignity Trust*, n.d.). FBI statistics now say that LGBTQ+ people are the target of 1 in 5 hate crimes, and that crimes against the LGBTQ+ community are on the rise (Hauck, n.d.). Crime statistics in the United Kingdom also show a recent surge in violence against the LGBTQ+ community (Jones, 2021). These statistics reveal just how tenuous freedom and acceptance are for the LGBTQ+ community in the United States and world-wide. Worse, societal attitudes for many people across the world surpass intolerance and veer into violence.

Conclusion

The advent of genetic engineering technologies and our increasing understanding of the complex interplay between genes and environment have humanity on the verge of species altering evolution. The genetic basis is clear for sex and intersexuality: male, female, and intersex anatomy. While there are unlikely to be genetic "master switches" that act on gender and sexual identity in a deterministic manner, there are strong genetic components to each. With big data analytics, humanity will soon be able to stochastically determine the probability that complex traits and behaviors like expressions of gender and sexual identity will manifest in an individual. With genome editing technologies like CRISPR, those probabilities can be affected. Given the societal attitudes towards the LGBTQ+ community prevalent world-wide, many will use those same technologies to affect the probability against their children becoming LGBTQ+.

Beyond this, however, are decisions to be made concerning the physical and mental health of a prospective child. Most people choose to take the drastic measure of abortion when confronted with a serious, but non-lethal diagnosis such as Down Syndrome, and some, simply because their baby is the wrong gender. Faced with the probability that their child could be LGBTQ+, many parents, if not all, will elect to "fix" the contributing genetic issues to provide their children the best chance to thrive in an often hostile and violent world for the LGBTQ+ community, if the option to do so is safe, easy, and inexpensive. Careful consideration of the technological momentum behind genetic engineering could help mitigate unintended consequences for marginalized groups whose traits are determined or influenced by genetics, like the LGBTQ+ community.

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