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The New Eugenics: Germ Line Editing and the Future of Genetic Engineering

When thinking about eugenics, we think about racial cleansing and Nazi holocaust killings. There is a negative connotation with the eugenics movement; however, with the advent of modern genetic engineering technology this sentiment is slowly shifting. Ever since cloning became a popular topic of debate, germ line editing and eugenics came back into the bioethics consciousness. Germ line editing is the latest ethical challenge facing genetic engineers. Germ line editing refers to the purposeful genetic manipulation of human embryos. This engineering of the germ line has scientists and ethicists stumped on the right course of action: on the one hand, this technique could help many and "eradicate devastating diseases"[1], but also opens up the door for modifying embryos that could have future consequences as these changes will be passed down to future generations.

If germ line editing is helping people alleviate the risks of passing along harmful alleles in their gametes, then is it eugenics? In order to delve into this question, a definition of eugenics must be set forth. According to the Oxford English dictionary, the definition is, "the study of methods to improve the mental and physical characteristics of the human race by choosing who may become parents."[2] By manipulating reproductive decisions, eugenics allows certain racial or ethnic groups to be perceived as better or

[1] http://www.nature.com/news/ethics-of-embryo-editing-divides-scientists-1.17131
[2] http://www.oxforddictionaries.com/us/definition/learner/eugenics

worse than others—allowing for interesting ethical cases to come to fruition over the past century. Buck v. Bell, one of the most notable eugenics cases in the past century was a United States Supreme Court case, was a case where the court ruled that compulsory sterilization of handicapped individuals (or individuals who were viewed as being unfit), was acceptable under the constitution.[3] This case sparked the negative connotation of eugenics in the United States, because looking back historically, eugenics was used to try to diminish the "feeble minded" population in the country.

In looking into the social philosophy behind eugenics, many journals from the 1930s justify the practice. Many of these justifications are based in economics: parents who have a greater number of children are more likely to be in poverty because they won't have enough resources for the children to be in a higher economic strata[4]. Positive eugenics, promoting certain groups of people to have children, quickly shifted to negative eugenics, eliminating unfit individuals from the population and not allowing them to reproduce. The switch came from "progressive health-reform movements such as prohibition, birth control, and anti-prostitution campaigns were easily transformed into a negative eugenics, the attempt to manage the procreation of those deemed unfit to reproduce.[5]" Negative eugenics is now the most widely studied section of the movement due to the tragedy of Nazi eugenics. Since then, the discussion of eugenics shifted to finding genetic proof that certain characteristics such as an individual's intelligence quota are predetermined by one's genetic makeup. In a review of the history of eugenics, Cullen concludes in *Back to the Future: Eugenics—A Bibliographical Essay* that

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[3] http://www.oyez.org/cases/1901-1939/1926/1926_292
[4] The Development of A Eugenic Philosophy, p. 389
[5] http://www.jstor.org/stable/10.1525/tph.2007.29.3.163 . (p. 165)

"It is not a coincidence that the social and cultural factors that propelled the movement for better breeding in the first decades of the twentieth century re-appeared as the culture wars took place in the last decades of the century. Policymakers, therefore, should more closely examine the scientific and moral assumptions of proponents of genetic determinism and make the distinction between what science can accomplish and what science should accomplish." [6]

Eugenics, be it positive or negative, is now coming into our consciousness again with germ-line editing because it alters the traits that can be passed on to future generations, but also allows adults who could not previously be parents due to the risk of a hereditary disease have a child. So what is immoral about eugenics?

In *What is Immoral about Eugenics*, David Magnus and Arthur Caplan argue that due to the "abysmal history of murder and sterilization", the risk of a slippery slope brings "all ethical arguments in favor of eugenics to an end" (Caplan and Magnus). This paper, written in 1999, notes that it is "important to distinguish between genetic changes undertaken with respect to improving a group or population and genetic change that takes a single individual as its focus."[7]. This argument rests on the foundation that eugenics up until the past decade did not provide individuals to make reproductive decisions due to genetic engineering, and in the past these cases rested on powerful groups coercing others to make specific choices regarding their ability to bare offspring. The paper addresses three common objections to eugenics: coercion, the subjectivity of perfection, and equality. In these three objections, Caplan and Magnus argue that couples have the right to make reproductive decisions about not transmitting devastating genetic diseases if the choice is "free and informed". If this is the case, then they believe that it is not immoral to make reproductive decisions. Secondly, addressing the subjectivity of perfection, they

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[6] http://www.jstor.org/stable/10.1525/tph.2007.29.3.163 . (p. 175)

[7] all references in this paragraph: http://www.bmj.com/content/319/7220/1284

state other decisions that parents make to influence the lives of their children such as the schools that they attend, the values they instill, and the customs they are grown up with.

“ If there is a slope from permitting individual choice of one's child's traits to limiting the choices available to parents it is a slope that does not start with individual choice. And if there is a problem of a slope then it must be shown why it is morally permissible for parents to seek betterment after a child is born but why such efforts are wrong if genetic alteration is used. There is nothing terrible about subjectivity in a decision to indulge preferences about the traits of one's child as long as those preferences do nothing to hurt or impair the child.”

This slope is one that aims at allowing individual freedoms in reproductive decisions, and Caplan and Magnus argue is this is no different from making choices about their children’s post-birth lives. This leads to the final objection to the negative impression of eugenics: equality. The authors argue that “allowing parental choice about the genetic makeup of their children may lead to the creation of a genetic “overclass” with unfair advantages over those whose parents did not or could not endow them with the right biological dispositions and traits.” Ultimately, Caplan and Magnus find in their argument that reproductive decisions using genetic engineering are moral so long as they have complete information and are not being coerced. The one objection to the use of genetic engineering to influence reproductive decisions and allow for eugenics to provide a means to control the genetic makeup of their children is how equitable it is. So long as there is equal access to these measures that “enhance our offsprings’ lives, it is hard to see what exactly is wrong with parents choosing to use genetic knowledge to improve the health and wellbeing of their offspring.”

The history of the eugenics movement extended throughout many cultures, geographical areas, and fields of study. Now eugenics cases seem to be quelled by a curtain of shame and feelings that these issues are in the past. Through recent genetic engineering feats in the past decade and a half, many eugenics issues are being revisited. Manipulating the genome in order to solve many human health crises such as sickle cell anemia or tragic genetic diseases is a noble cause, and should be recognized as one. However, scientists must be cautious as to their aims for this new technology. With new germ-line editing techniques developed in the past few years such as the CRISPR/Cas9 mechanism to completely cut out mutated genes and replace them with functional ones, the conversation of eugenics and if we should allow this research to continue comes into the forefront of bioethical discussions.

The example that sparked the entire conversation of germ line editing came from a Chinese laboratory led by Junjiu Huang at University of Guangzhao, when researchers found a "system of molecules called CRISPR/Cas9, known for it's ease of use, to cut DNA in human embryos and then attempted to repair it by introducing new DNA."[8] This new gene editing tool has the potential to add in new genes where there is a non-functional gene producing a faulty protein that causes disease. Huang's results yielded that of the 84 embryos that were subjected to the CRISPER/Cas9 gene editing, only 4 of the embryos "contained the genetic information to repair the cuts." Along with this newly-found data, there was an increasing debate on the safety concerns of these measures. There were additional "off-target mutations" that were unintended results of the research. These unintended consequences are the fear of germ line editing—as a pathogenic mutation could be disastrous as it will continue to be passed on in the germ line.

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[8] http://www.nature.com/news/embryo-editing-sparks-epic-debate-1.17421
4. Ibid

CRISPR/Cas9 provides a unique new strategy for genetic engineering that poses novel ethical challenges. CRISPR/Cas9 gene complexes were originally found in bacteria and archaea, and are critical to these organisms' immune response, allowing them to "eliminate invading genetic material"[9]. There are a few different kinds of CRISPR mechanisms, but the one that is of greatest interests to scientists is that of type II. The CRISPR type II mechanism works by taking small pieces of foreign DNA, cutting it up into segments and incorporating it into it's gene. This is then transcribed. These transcripts are referred to as "crRNA" because they are specific to CRISPR genes. Cas9 is part of the Cas family of proteins that are involved in gene silencing. This is critical for understanding Cas9's function in that it recognizes the target DNA sequence, and through some nuclease activity it cuts the DNA in a double-stranded break, destroying the target DNA. This mechanism is critically important to the topic of germ line editing because through the double-stranded breaks, it can silence the gene by non-homologous end joining. This opens the door for replacement of mutations to occur if there is a homology-directed repair in addition to the Cas9 mechanism to repair the break.

This original discovery of CRISPR/Cas9 pathway introduced a new field of research and there are now new forms that have been engineered to make insertions and deletions without a nuclease. This field of research is now expanded, and recent findings discovered that this genome engineering mechanism can "transmit information from one generation to the next [in] an organism's 'germ line'.". In order to address some of these concerns, a group of professionals from the fields of genetics, law, bioethics, business,

[9] https://www.neb.com/tools-and-resources/feature-articles/crispr-cas9-and-targeted-genome-editing-a-new-era-in-molecular-biology

and medicine came together in a cohort called the “Napa Group”. This group wrote out a set of recommendations that regulate the use of this novel CRISPR/Cas9 technology in order to ensure that it is not used in a potentially harmful or dangerous way.

The Napa Group’s recommendations were based on the slippery slope argument that is often used in bioethics cases, especially with new technology. The basis of the slippery slope argument is that one use of a certain technology might set off a trend that could be potentially harmful[10]. With the potentials for germ line editing, the group created four suggestions for researchers looking to bring this technology to fruition (these are summarized recommendations): 1. Discourage germ line modification trials to occur in countries with vulnerable populations and with less stringent regulations in order to find mechanisms for “responsible uses” of this technology. 2. Create groups composed of a wide array of professionals in order to fully comprehend the societal, ethical, and medicinal purposes of this technology. 3. Promote “transparent research” of the CRISPR/Cas9 mechanism that will enlighten the scientific community on the safety and potential uses for germ line editing. 4. Get scientists, lawyers, and the public from around the world to assess the status of the technology and potentially create policies to regulate it.

The Napa Committee’s recommendations are based on having public trust in the scientific research for advancement of health. In order to fully understand this, the potential consequences and benefits of this germ-line editing technology as demonstrated with CRISPR/Cas9 must be fully understood. The potential concerns are two-fold: first deals with the safety of the technology, and the second is involved with an ethical issue.

[10] http://www.bbc.co.uk/ethics/introduction/slipperyslope.shtml

This technology isn't proven to be safe or effective to be tested in human trials yet. In the Huang study, there were many off-target mutations that caused great controversy. Any off-target mutations in the human germ line could be catastrophic. The safety of this mechanism is not yet explored. Importantly, germ-line editing alters the genome of cells that will be passed on to an infinite number of future generations, and it is critical that there are no flaws in this technology so that catastrophic events do not occur. Secondly, this technology raises ethical issues pertaining to eugenics. Going off of the morality of eugenics argument that was raised in the Caplan and Magnus article, this technology is only immoral if there are barriers to entry, and there could be a slippery slope in germ-line editing. Especially in countries with lax and or explicit regulations about genetic engineering in humans, this technology must be strictly monitored, and could allow for access to this technological application only to wealthier people—an immoral act according to Caplan and Magnus.

With the concerns of this technology also comes potential benefits. For one, the potential for curing formerly incurable diseases, and answering evolutionary questions about how our planet's species will adapt to the changing environment[11]. There are trials being done with genome editing to create a functional cure for HIV, and could lead to potential cures and better treatments, especially with the personalized medicine movement in cancer research. In mice, the CRISPR/Cas9 mechanism has already corrected genetic defects of a liver-metabolism disorder, and there are other promising future research projects that show future beneficial uses for this technology. The potential benefits of this technology are persuasive enough to continue with this research.

[11] http://www.sciencemag.org/content/348/6230/36.long

How this technology is used in the future and in human applications is for the public to decide.

So should we allow genome editing to occur? These practices have yet proven to be efficient and safe enough to be performed in any human trials, and are a long ways away from these being commonly used. As medicine becomes more and more personalized and precise, as shown by the race for the ability to sequence a full genome for $1000[12], questions of reliability, legality, and ethics come into play. Germ line editing is amongst one of those questions. The CRISPR/Cas9 mechanism in particular is concerning because in the lab it is shown to have silenced genes in full organisms, and replaced non-functioning genes in mice with hereditary liver disease[13]. These findings allow for there to be much greater advances on treatment of genetic disorders that previously had been mysteries for centuries. If this is viewed from a utilitarian point of view, germ line editing could be displayed in two different ways. Utilitarianism works to achieve the maximum amount of good for society. On the one hand, we can view this genetic manipulation as saving families heartbreaking losses from inherited diseases, however, if this technology is used in a fashion that harmed future generations then this could create horrific consequences of a far greater scale than any other negative eugenics movement in history. In the theory of liberalism, one must discern what is a "right". With germ line editing technology, the liberalist view comes into the forefront of people's minds because what society values over other things could greatly influence the outcomes of what becomes of this technology.

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[12] http://www.nature.com/news/technology-the-1-000-genome-1.14901

[13] http://www.sciencemag.org/content/348/6230/36.full

Researchers should be allowed to continue with the research, just not on human subjects (probably ever), and cross the bridge when we come to it of when to allow people with certain mutations to edit their genome. Germ-line editing brings along connotations of both positive and negative eugenics, and in this way it is an issue that needs to be further discussed and debated in order to enable policies to oversee the research to ensure that this novel genetic engineering tool creates positive human benefit, and does not create the headline negative eugenics case of the twenty-first century. With the creation of the Napa Committee, there will be greater oversight of future germ-line editing technology research in a diverse group of lawyers, doctors, researchers, and ethicists from around the world to contribute to creating policies that will allow for this technology to be used for the greatest good. So long as this is the case, germ-line editing has a bright future.

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