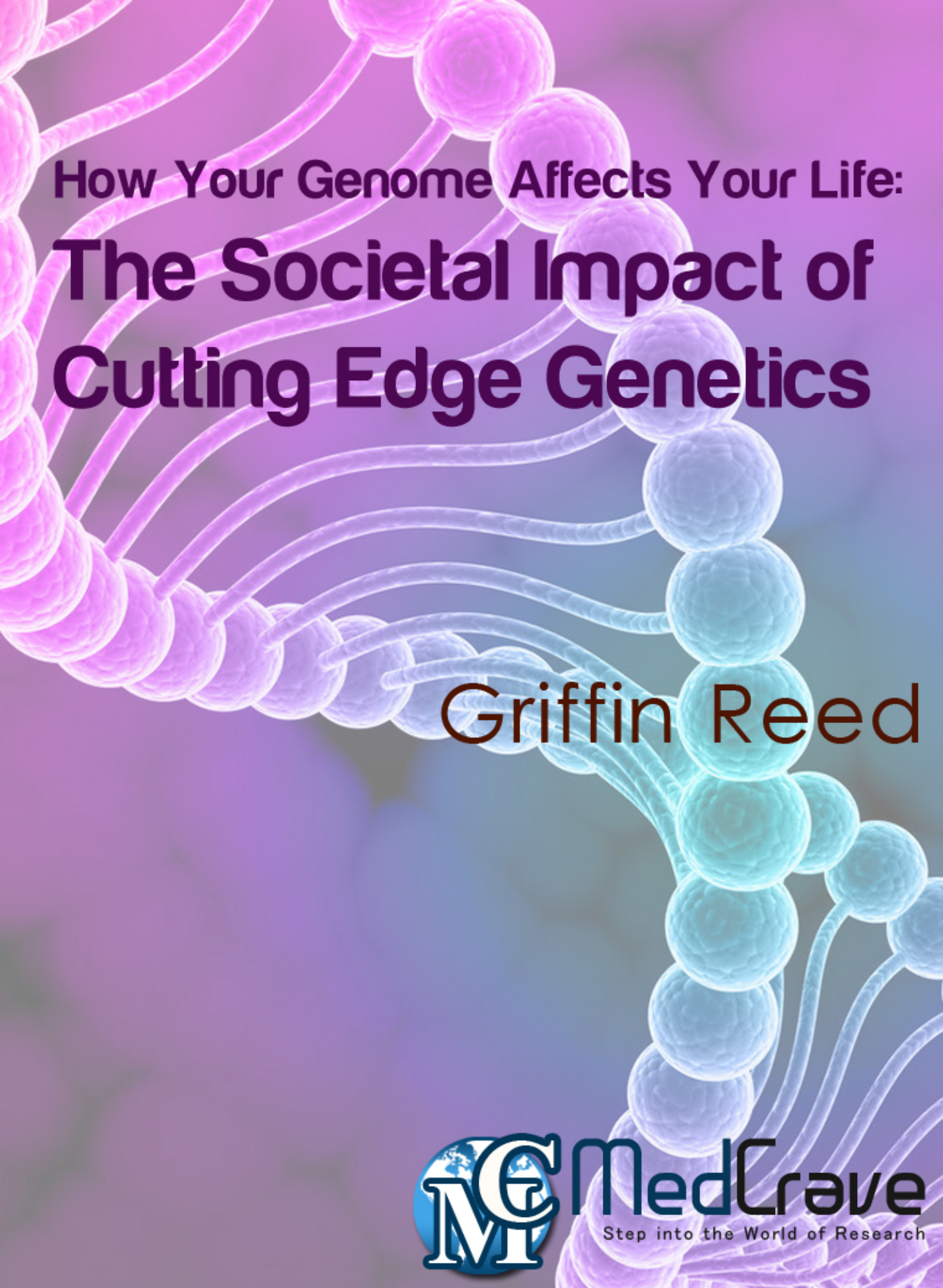

How Your Genome Affects Your Life:

The Societal Impact of Cutting Edge Genetics

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MedCrave
Step into the World of Research

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Abstract

Enormous advances are being made in the field of genetics that enable caregivers to predict diseases more accurately, prevent disease more effectively, and even treat disease by altering defective genes. However, many experts, including those on the Presidential Commission for the Study of Bioethical Issues, are concerned our society may be unprepared for the power that these new technologies bring Gutmann [1]. Three new fields in genetics offering both the most promise as well as the most peril are whole genome sequencing (WGS), epigenetic therapy, and gene therapy. WGS allows for both better diagnostics and better preventative care through genome-wide mutation detection. On the other hand, there are concerns WGS could cause individuals to unwillingly learn about untreatable diseases (such as Alzheimer's or Parkinson's) they are predisposed toward and that individuals could be discriminated against by employers or insurance companies based on their genetic information. Epigenetic advances provide a better understanding of how one's life decisions affect the genes they pass onto their offspring, but with this knowledge may come the obligation to alter one's lifestyle to increase their offspring's quality of life. Gene therapy offers potential cures for previously untreatable or unsatisfactorily managed conditions through the addition, disruption, or editing of genes. Unfortunately, gene therapy is currently a high-risk and expensive treatment option that is available only on a clinical trial basis. My honor's thesis project will consist of three main components. First, I analyze the benefits and dangers of each new technology through a literature review. Second, I determined how an education in genetics alters individuals' attitudes on ethical dilemmas presented by each of these technologies. I accomplished this goal through comparing survey responses of a January-term knitting class with no biology majors, students enrolled in a 100-level biology class, and students enrolled in the BIO-374 Genetics class at Gustavus Adolphus College. The survey includes questions to gauge the reader's acceptance of the technique as a whole, as well as on a variety of ethical dilemmas that arise due to each technique. Third, because education increases acceptance of the three genetic techniques studied in this paper, I recommend public education as a means to increase societal acceptance for these techniques.

Whole Genome Sequencing

Background

Whole genome sequencing (WGS) is the determination of the order of nucleotide bases in an organism's entire DNA sequence. The nucleotide sequence can then be used to generate a list of all gene variants that determine the unique characteristics of an individual such as their risk for developing certain diseases or the rate at which they metabolize medication. This genetic information is useful because it allows doctors to prescribe preventative medication for high-risk individuals or the correct dosage of a medication, ultimately resulting in better patient outcomes and less money spent on reparative measures. The cost to sequence the first human genome was estimated to be about 2.5 billion dollars, much of which was due to the large amount of computing required to process and store the information of six billion DNA bases per human genome. However, with the rapidly increasing speed of computers, breakthroughs in storing large amounts of data, and advances in next generation sequencing reactions, whole genome sequencing (WGS) is technically possible at the large-scale and costing around $1,000 per test, much more affordable Herper [2]. Clinical WGS is already being utilized in some institutions such as the Mayo Clinic in Rochester, MN Briggs [3]. There are still some biological problems that occasionally hinder the application of WGS. Variants of genes that encode for important proteins are not always damaging but may simply be a rare, benign polymorphism that leads to false-positive identification. This issue will become less common as more genomes are sequenced and more of these polymorphisms are identified. Additionally, the interplay between an individual's genome and environmental factors can cause reduced penetrance and variable expressivity of a genetic trait. These two phenomena occur when an individual with what is normally a deleterious mutation does not develop the disorder, or develops reduced symptoms of the disorder. Because these factors make damaging mutations appear benign, they also make it difficult to pinpoint which variant is disease-causing.

Ethics

The ethical discussion surrounding WGS is currently centered on the issues of unwanted knowledge, privacy, and childhood screening. The most common example of obtaining unwanted knowledge occurs when an individual is surprised to learn they are at risk for an untreatable disease (e.g. Alzheimer's) or if they inadvertently derive information about their own genome from the results of a blood-relative's genetic tests. Knowing about the *possibility* of contracting serious, untreatable conditions may lead to negative psychological consequences such as anxiety or depression with no actionable insights. In these cases, WGS may do more harm than good. Relative to privacy issues, there is concern that knowledge about an individual's genomic information could be used to discriminate against them by either health insurance agencies or employers. Technically, the Genetic Information Non-discrimination Act (GINA), the Affordable Care Act (ACA) and other state-specific laws make this behavior illegal, but these policies do not apply to life insurance or long-term care insurance. There is also concern that these laws are not always followed. In the words of one genomic-privacy proponent, "I can imagine in a job situation, it's expensive to take on someone if they're ill. And you can always get rid of people for other reasons. I assume that's going on." Gutmann [1]. Furthermore, WGS brings about legal problems of privacy in other areas of science. For instance, in 1951, the first immortal human cell line was cultured from Henrietta Lacks' cervix Skloot [4]. In 2013, the genome of this cell line was sequenced and published without the consent or permission of anyone in the Lacks family Landry et al. [5]. A similar problem was experienced again when a group of families affected by Canavan disease provided a researcher at the University of Miami with tissue samples to develop a genetic test that was meant to be available to the public at large. The researcher patented the gene sequence associated with Canavan disease in these families and commercialized the test. In 2003, a federal court ruled in favor of the researchers, denying the subjects claims of ownership to their genetic material Greenberg V [6].

Childhood screening is one of the most controversial applications of WGS. Most experts agree WGS is advisable when children have symptoms suggesting genetic disease Mayer [7]. The questionable use of childhood screening is on asymptomatic children. On one hand, there is the possibility that early WGS in asymptomatic children can detect childhood-onset diseases that are difficult to treat once symptoms appear. Additionally, early testing adds the benefit of detecting non-paternity, which, despite its mixed social consequences, can be a significant problem in standard genetic testing. On the other hand, early WGS runs contrary to established norms which advice against genetic testing of asymptomatic minors because this testing reveals information that may not be clinically useful or wanted until adulthood. Furthermore, WGS conducted during infancy opens the door to the possibility of genetic discrimination, loss of privacy, and negative psychological impacts without allowing the individual any agency in the process Borry et al. [8]. False-positive diagnoses should also be considered as a costly and potentially dangerous possibility of non-essential genetic testing Fujimoto [9].

Epigenetic Therapy

Background

Epigenetics is the study of trait variation caused by changes other than those in DNA sequence. There are three common types of epigenetic modifications, all of which alter the level of gene expression. The most common is cytosine methylation which makes the affected area less likely to be expressed Bird [10]. Second, histone acetylation is a modification that promotes the chromosome to adapt an open conformation conducive to increased expression Szyf [11]. RNA interference is a third modification in which RNA molecules bind to DNA at specific sites and inhibit

gene expression Schafer [12]. The two major causes of epigenetic modifications are environmental toxins and dietary factors. Environmental toxins are more controlled by social policy, whereas diet is more controlled by individual behavior. While the list of factors impacting the epigenome is constantly evolving, air pollution Liu [13] and smoking Pembrey [14] are examples of environmental modifiers which play a role in asthma and weight gain. Furthermore, excessive alcohol intake is a dietary modifier that has been linked to cancer Choi [15]. Epigenomic modifications not only affect the acting individual's health, but can also be passed down to the next generation Kaati [16].

The future for the application of epigenetic in the clinic is promising. First of all, because epigenetic changes are intrinsically reversible Tompkins [17], the opportunity exists to target harmful modifications with drug treatments. In fact, there are already four epigenetic drugs that have been approved by the Food and Drug Administration and hundreds more in clinical trials Mack [18]. Epigenetic modifications also have the potential to act as markers for disease risk and early diagnosis. The use of epigenetic markers to detect diseases is still limited, but one epigenetic colorectal cancer marker is 70% accurate Shi [19].

Ethics

Since the early 1980s, there has been increasing awareness about the correlation between living near environmental hazards and economic status US General Accounting Office [20]. The environmental justice movement that motivated this research also drove the formation of several organizations dedicated to pursuing environmental justice such as the Environmental Protection Agency and the National Resource Defense Council. Although environmental inequality still exists, it is possible that new knowledge of epigenetic mechanisms linking environmental toxins to adverse health effects could influence the public to support the environmental equality movement. Individuals could support this movement by either cleaning up these toxic sites or moving people away from these sites. Another ethical issue that arises with Epigenetics is intergenerational equity. Since there is now evidence that lifestyle choices affect the quality of life for one's offspring, there may be an obligation of parents to base lifestyle choices on the consequences for their offspring. Additionally, social policies may need to be updated to reflect the evidence that certain products can be harmful to offspring through an epigenetic mechanism. For instance, many smokers continue smoking on the basis that their decision to smoke only affects their own health (if measures are taken to avoid exposing others to secondhand smoke). However, it is currently impossible to protect offspring from receiving the harmful epigenetic modifications associated with smoking. Since smoking is now known to harm unborn children, in a similar but less dramatic way than alcohol, society might consider either requiring warnings of epigenetic modification on tobacco products or making smoking illegal both in pregnant women and in general Pembrey [14]. Experts suggest that society consider the following factors when making lifestyle decisions that have epigenetic consequences Rothstein [21]. First of all, the severity, duration, and reversibility of the transgenerational modification should be considered to determine the costs associated with this modification to both the actor and their offspring. These must then be weighed against the sacrifices made to avoid this modification. For example, a poor family may have to accept less expensive housing near environmental toxins in order to afford food, but tobacco use would likely not outweigh the associated negative effects under any circumstance.

Gene Therapy

Background

Gene therapy is a new treatment strategy with the potential to cure genetic disorders as well as some types of cancer - those caused by oncogenes or defective tumor suppressor genes - by editing genes. The two most common forms of gene therapy are the addition of a functioning version of a non-functional gene or the disruption of harmful genes that produce damaging proteins El-Aneed [22]. A third, newer type of gene therapy, clustered regularly interspaced short palindromic repeats (CRISPR), works by editing dangerous genes into benign forms Carroll [23]. These results are accomplished by transplanting DNA or RNA into cells through a vector, which can be either viral or nonviral. Viral vectors have more efficient transfection but are more expensive to produce at the large scale and more likely to elicit an immune response than their non-viral counterparts.

Gene therapy can be carried out on either somatic cells or on germline cells. Somatic cell gene therapy affects only the patient that undergoes the procedure, not any of their offspring whereas germline gene therapy modifications are heritable because functional genes are inserted into the individual's genome in cells that produce egg or sperm. The germline treatment could be more effective for treating developmental diseases because it acts earlier than its somatic counterpart; however there is concern surrounding both the lack of knowledge about risks to future generations and that this therapy may be used to genetically modify children for non-medical reasons. Until recently, germline gene therapy has been considered too risky and not well understood enough to attempt; however, on February 1st, 2016, a United Kingdom regulatory body gave a London-based research lab the go-ahead to edit the genomes of human embryos in a fertility-related study, but not for the embryos to be implanted Callaway [24]. Gene therapy still has three main obstacles to face in its implementation. First is the issue of cost. At $1.6 million per treatment, the most popular gene therapy drug which treats abnormal fat digestion, Glybera, is unaffordable for most Burger & Hirschler [25].

The second hurdle is the riskiness of gene therapy. Three people have already died in US gene therapy trials, but it is

worth noting that one of these deaths was unrelated to the therapy [26-28]. Gene therapy is dangerous for a number of reasons. One danger is that viral vectors that deliver the genes can regain their pathogenicity. Additionally, DNA can accidentally be inserted into and disrupt a tumor suppressor gene, causing a tumor to be formed Woods et al. [29]. The third obstacle is the biological limitations of gene therapy. Specifically, gene therapy is short lived because current techniques cannot stably introduce the therapeutic DNA into the genome, so patients require multiple treatments Takehara et al. [30]. Furthermore, because the immune system has an enhanced response against antigens it has seen before, repeated treatments of gene therapy are often less effective. At present, gene therapy has only been attempted as a treatment option in monogenic disorders. The treatment of polygenic disorders is unlikely to be attempted until there is a reliable monogenic treatment protocol.

Ethics

Somatic cell gene therapy (SCGT) raises few new ethical questions because it only affects the individuals who choose to undergo the treatment. Therefore, as long as the individual can weigh the risks against the benefits and is free to make his or her own decision, the ethics of SCGT is no different than for any other medical procedure. One ethical question that arises from SCGT is whether the individual has been accurately informed of the treatment risks because SCGT is still highly experimental and scientists may overestimate the degree to which they understand the risks of experimental procedures. Experts in gene therapy also debate whether this technique should be used strictly for medicinal purposes or if it should be allowed for personal enhancement as well. On one hand, elective procedures for enhancing the body already exist in the forms of plastic surgery and hormone therapy. However, the American Association for the Advancement of Sciences (AAAS) suggests that the use of gene therapy be limited to the treatment of clear-cut diseases as its use for enhancement purposes would serve to widen the social inequality gap between the wealthy and the poor Frankel & Chapman [31].

Unfortunately, some difficulty arises with the AAAS recommendation because the word “disease” is subjective. Life-threatening conditions like cystic fibrosis and Tay-Sach’s obviously qualify as diseases, but less serious ailments like color blindness fall under question. The main issue raised by this argument is determining who has the authority to classify genetic traits as disease-causing or not. Asperger’s syndrome is one such trait whose disease status is contested by those who see it as a valuable form of neurodiversity. These advocates are concerned that the classification of Asperger’s as a disease may stigmatize those who choose not to undergo gene therapy to fix it Jaarsma & Welin [32]. It is also important to remember that previous attempts in reproductive interventions, such as the eugenics movement, have generated social injustice against marginalized individuals and the poor. In addition to the ethical issues raised by SCGT, further ethical difficulties come into play when considering germline gene therapy (GGT). The main ethical distinction between GGT and SCGT arises because the former affects the offspring of the individual, who have no agency in the treatment decision. Because GGT also impacts offspring, some argue that even in use for disease treatment and prevention, the medical team and patient should weigh the potential benefits against the risks that not only the individual faces, but also the risks facing all potential offspring. Furthermore, GGT is different from SCGT because it enables the elimination of traits from the gene pool. Genetic variation is valuable because it provides the potential for a population to adapt to new conditions. However, proponents of GGT note that since gene therapy can be used to remove traits from a population, it can also be used to reintroduce traits, provided that the original sequence is recorded.

Survey Experiment

Purpose

Personalized medicine initiatives will heavily employ WGS, epigenetics and gene therapy in future decision making, and these fields are advancing very rapidly (11,897 papers in PubMed for “whole genome sequencing”; 53,079 for “epigenetic*”, and 263,607 for “gene therapy” as of May 21st, 2016). Awareness of this technology at the undergraduate level will be critical for students that intend to enter health professions, which is approximately 50% of Gustavus students. The purpose of this survey experiment is to determine whether participation in an undergraduate biology curriculum influences an individual’s acceptance of cutting-edge genetic techniques for human application. I hypothesize that further education will increase acceptance of genetic techniques because further education will “demystify” the technique. If this hypothesis is correct, I predict that the January-term (non-biology majors) class will have the lowest acceptance of the techniques because they are least familiar with them, the 100-level biology class will have a middle level of acceptance, and the 300-level genetics class will accept the techniques the most because this class is the most educated on the techniques.

Methods

Survey

A survey (Appendix 1) was developed to measure the acceptance of three new genetic techniques with applications to health care choices: whole genome sequencing, gene therapy, and epigenetic based therapy. In addition to overall acceptance of the technique, questions were included to measure response to common dilemmas that occur in each topic such as statement 11 “I would be afraid to provide a sample to a research GenBank because it could reduce the privacy of my life.” This survey (IRB #1516-0011) was administered to three classes, each with

a different degree of integration into the Gustavus Adolphus College biology curriculum: 1) a January-term knitting class, 2) a 100-level introductory biology class, and 3) a 300-level genetics class. Biology majors in the January-term class were excluded so that this class could be representative of non-biology majors. The 100-level biology class was included to represent students who were interested in biology, but who had only completed one class of the biology curriculum. The 300-level genetics class represents students who had completed a large portion of the biology curriculum (at least two years), including part of a course specifically focused on genetics. Additionally, a pre-class and post-class survey was administered to the 300-level genetics class to determine what effect that specific class had on beliefs, but the post-class results were not analyzed due to non-compliance, a small sample size, and low power to detect differences within the class [33-37].

Statistical analysis

To determine the baseline response to each question, the means of each question were calculated along with a 99.5% confidence interval for each question. Mean responses that were significantly different than 3 (the middle score), were further analyzed to draw meaning from the responses. T-tests were used to determine if there was a difference between the male and female responses for each statement. For the univariate class analysis, student responses were first transformed to fit a normal distribution using a stepwise box-cox transformation procedure (equation yielding the lowest test square means was (: Response Score ^ 1.2 - 1) / 1.50633752000753; JMP v10.02, SAS, Cary, NC). Then, ANOVA tests with LSD-post hoc analysis were used to compare the mean agreement response scores of the three classes for each statement. Distribution of the error visualized by plotting the Normal-Quantile plot of the residual values was utilized to check for model assumptions. The purpose of the class analysis was to determine if there is a significant difference between the mean agreement response scores of each class for each question. A similar approach was used for the multivariate analysis that looked for differences between male and females between classes; however, due to time constraints, only statements 2, 13, and 27 were analyzed for effect sizes exhibiting the biggest differences. All analysis was performed in SPSS version 23.0.

Results

Participant demographics

The number of participants, gender ratio, class standing, and percentage of biology majors in each class is recorded in Table 1.

Overall response

Overall, 21 of the 30 survey questions had mean agreement response scores that were significantly different from the neutral response score of 3 (Figure 1).

Conclusions can be drawn from further analysis of these statements (Table 2 & 3). For WGS specifically, students strongly agreed with statements 2 ("*Sequencing an individual's genome to help detect and treat disease is ethical*") and 3 ("*Preventatively sequencing a healthy newborn's genome to help detect and treat disease is ethical.*"). This suggests that respondents think that WGS is ethical for both newborns and adults. Furthermore, a high level of agreement with statement 4 ("*At some point during my life, I would be interested in having my genome sequenced to check for vulnerability to preventable disease.*") indicates interest in participating in WGS testing. However, a neutral response to statement 6 ("*Providing my genetic information would cause me to fear genetic discrimination from employer [refusal to hire, loss of job, etc.].*") and a high response to statement 7 ("*Providing my genetic information would cause me to fear genetic discrimination from health insurance providers [increased premiums, dropped coverage, etc.]*") and a low agreement with statement 11 ("*I would be afraid to provide a sample for a research gene-bank because it could reduce the privacy of my life.*") indicate that respondents would be fearful of insurance companies obtaining their genetic testing information and would be neither fearful nor content with employers obtaining their test results, but would not fear providing their genetic information for research purposes. There was the same mean response both to the true statement, 8 ("*I am aware of federal laws that protect my genetic information from discrimination by employers and insurers.*") and the false statement 9 ("*I am aware of federal laws that prevent insurers and employers from discriminating based on an acquired disease [e.g. Parkinson's, Alzheimer's].*"). Because the students responded similarly on both the true and false statement, it appears that they are not well informed of current genetic privacy protection laws.

For gene therapy, a high level of agreement with statements 13 ("*Altering the genome of a consenting adult to treat a disease should be allowed.*") and 14 ("*Altering the genome of an embryo to treat a disease should be allowed.*") indicate that respondents believe that gene therapy should be allowed to treat disease in both children and adults. However, a low level of agreement with statements 15 ("*Altering the genome of a consenting adult for appearance/performance reasons should be allowed.*") and 16 ("*Altering the genome of an embryo for appearance/performance reasons should be allowed.*") indicate disagreement with gene therapy for non-essential enhancements in both children and adults. A high agreement to statement 17 ("*Doctors would be able to adequately inform me of the risks associated with gene therapy.*") indicates trust in doctors with regard to informing patients on gene therapy. Furthermore, a high level of agreement with statements 18-21 ("*Considering the loss of genetic diversity, treatment of chronic [e.g. color blindness], but not life-threatening diseases [e.g. cystic fibrosis], should be allowed.*"), ("*Gene therapy should be an available treatment option for life-threatening diseases.*"), ("*You have recently been*

diagnosed with a chronic but not life-threatening disease. Given this information, you would be willing to undergo gene therapy as a treatment option."), and ("*You have recently been diagnosed with a potentially fatal disease. Given this information, you would be willing to undergo gene therapy as a treatment option.*") indicates respondents would be interested in gene therapy for both life-threatening and non-life-threatening but chronic disease.

Table 1: Description of survey respondents from the three classes at Gustavus Adolphus College.

Class	Number of Participants (Males, Females)	Class Standing of Participants	Percentage Biology Majors
January-term knitting class	24 (7,17)	First-year (14), Sophomore (8), Junior (1), and Senior (1)	0%
100-level biology class	43 (20, 23)	First-year (39) and sophomore (4)	63%
300-level genetics class	23 (6,17)	Junior (5) and senior (18)	100%

Table 2: Mean agreement response score and conclusion of statements whose mean score was significantly different from the neutral value of 3.

Statement	Mean Response Score	Conclusion
2, 3	4.1, 3.8	Whole genome sequencing is ethical for both newborns and adults.
4, 7, 10, 11	3.8, 3.6, 2.4, 2.5	Respondents are interested in having their own genome sequenced but have conflicting feelings about discrimination or loss of privacy based on results.
13 and 14	4.0, 3.4	Gene therapy should be allowed to treat disease in both children and adults.
15 and 16	2.4, 2.0	Gene therapy should NOT be allowed to for non-essential enhancements in either children or adults.
17	3.9	Respondents trust doctors to inform them on gene therapy.
18-21	3.3, 4.4, 3.4, 4.4	Respondents would be interested in gene therapy for both life-threatening and non-life-threatening but chronic disease.
22	2.4	Respondents unfamiliar with Epigenetics.
23	3.4	Respondents believe environmental factors alter the genome.
24, 26, 27	4.3, 3.8, 3.3	Parents should protect children from negative epigenetic factors and epigenetic treatments should be allowed.
28-30	4.1, 4.2, 3.6	Respondents believe their education affects their beliefs and that they have enough access to it.

A low response to statement 22 ("*Apart from the above information, I am familiar with epigenetics.*") indicates that respondents are unfamiliar with gene therapy. However, respondents still agreed with statements 23, 24, and 26 which all essentially state that epigenetic consequences are real, and people should put forth the effort to avoid them. Additionally, there was a high degree of agreement with statement 27 ("*Drugs that target negative epigenetic modifications should be allowed.*") which shows that people are even willing to allow treatment for a condition they don't really understand. On a different note, the response was neutral to statement 25 ("*I consider epigenetic consequences when making daily lifestyle choices*") which shows that, in everyday life, these respondents don't consider epigenetics, probably because they don't understand what they are.

Table 3: Mean agreement response score and conclusion of statements whose mean score was not significantly different from the neutral value of 3.

Statement	Mean Response Score	Conclusion
1, 12	3.3, 3.1	Respondents neither familiar nor unfamiliar with WGS and gene therapy
6	3.1	Respondents neither fearful nor fearless of fearing discrimination from employer
8,9	2.8, 2.8	Respondents not familiar with laws protecting them from discrimination based on genetic test results
25	2.7	Respondents are neutral with regards to considering epigenetic consequences when making daily lifestyle decisions.

Class comparison

Overall, five of the 30 survey questions showed a significant difference in responses based on class. Because a 95% confidence interval was used, it is expected that 5% of the questions (or 1.5 to 2) would be significantly different based on chance alone. The mean agreement scores from each class generally followed a pattern in which the genetics class had either the highest or lowest mean response score for a statement, the 100-level class mean agreement score was in the middle, and the January-term class mean agreement score was at the extreme opposite the genetics class. This pattern was exemplified by statements 2, 13, 25, and 27. Statement 5 followed a similar pattern, except the January-term and 100-level class mean agreement scores were almost the same (Figure 2).

Notable exceptions to this pattern are statements 8, 9, 15-18, and 26 (ANOVA $p>0.1$ for each of these statements). Additionally, when considering gender, statements 15 and 16 showed a significant difference (t-test $p<0.01$) between males and females with males being more accepting of gene therapy for enhancement reasons than females.

Multivariate analysis (class and gender)

The multivariate analysis showed that there were significant differences between the classes in statements 2 and 27 when taking gender into consideration, but further post-hoc analysis is required to determine specifically which male/female subcategories are different (Figure 3 & 4). The multivariate analysis did not show an overall significant difference between the classes in statement 13 (Figure 5).

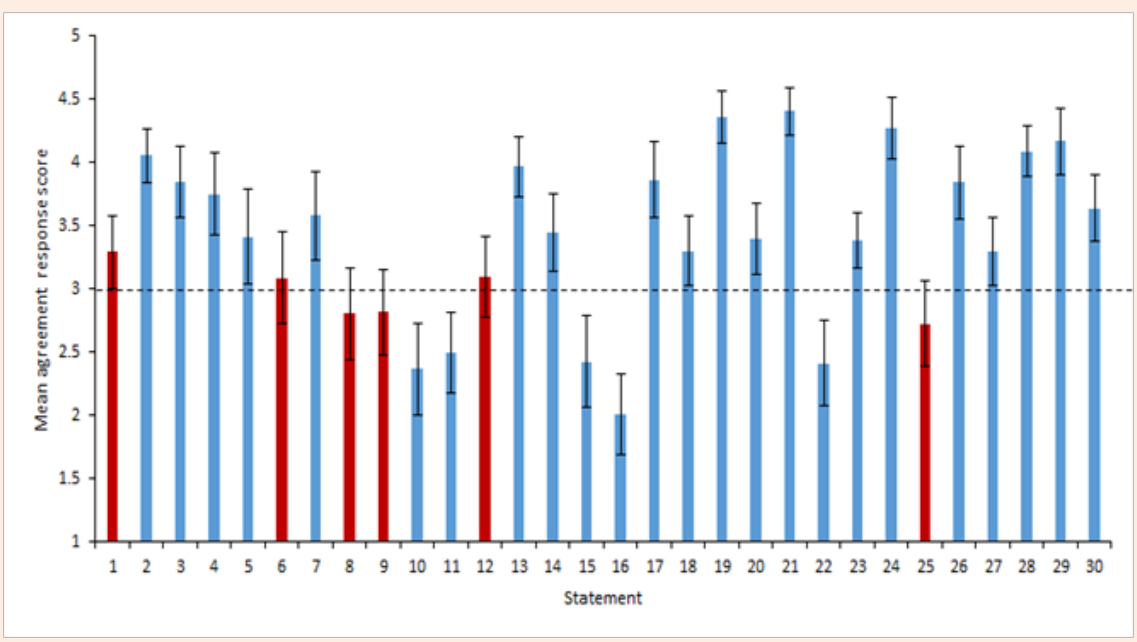

Figure 1: Mean agreement response score ± 99.5% confidence interval for the 30 ethics of genetics survey questions (n=90). Red bars indicate that the average score did not differ significantly from the neutral score of 3 (represented by a dashed line), blue bars did differ significantly from 3.

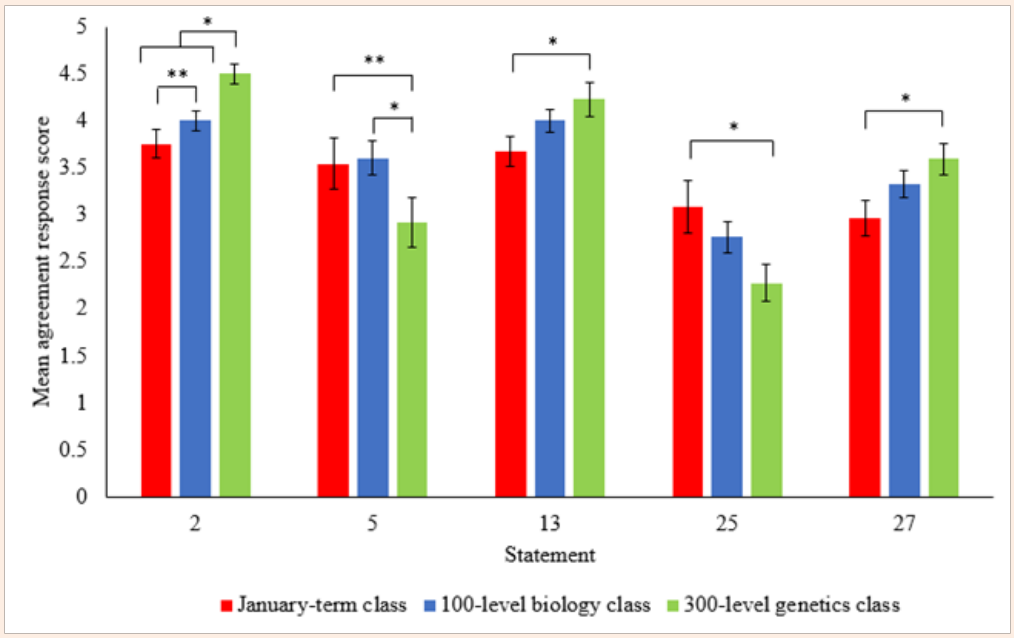

Figure 2: Mean agreement responses to five select questions from the genetic technique acceptance survey for three classes at Gustavus Adolphus College: a January-term knitting class (n=24), a 100-level biology class (n=43), and a 300-level genetics class (n=23). The error bars represent 95% confidence intervals. These statements (other than 5) follow a pattern in which the 300-level genetics class had either the highest or lowest mean response, the 100-level biology class responses had moderate responses, and the January-term class responded on the opposite extreme as the genetics class.* indicates significance ($p<0.05$) and ** indicates borderline significance ($0.05<p<0.1$).

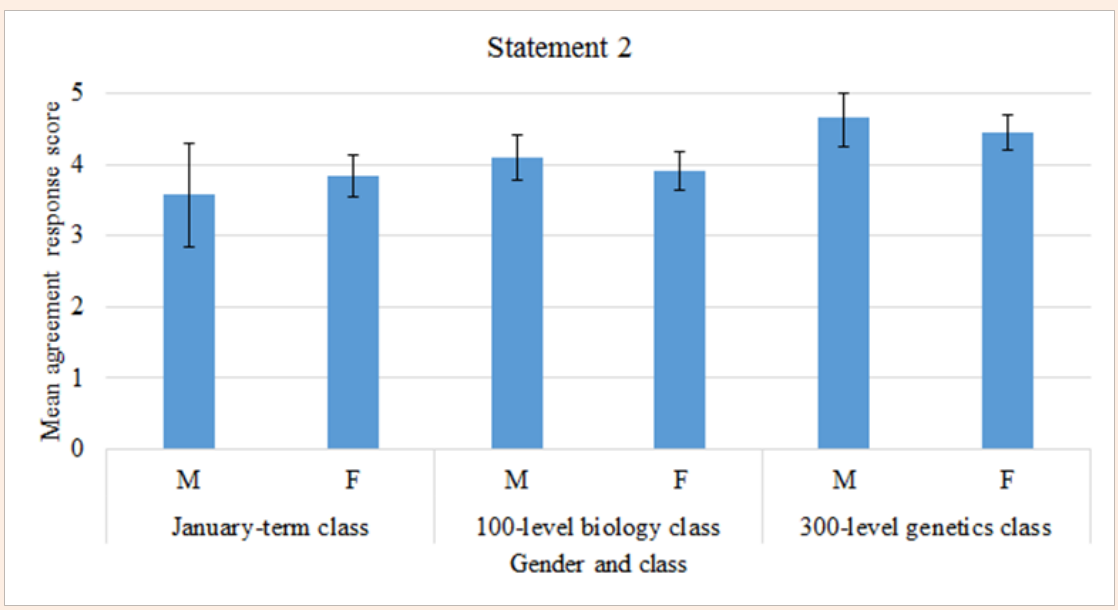

Figure 3: Mean agreement response score to statement 2 ("*Sequencing an individual's genome to help detect and treat disease is ethical.*") for males and females organized by class. The error bars represent 95% confidence intervals. Overall, there was a significant difference between the classes considering the gender interaction, but further post-hoc analysis is required to determine specifically which male/female subcategories are different. (df=5, Two-way ANOVA $F=3.3$, $p<0.01$).

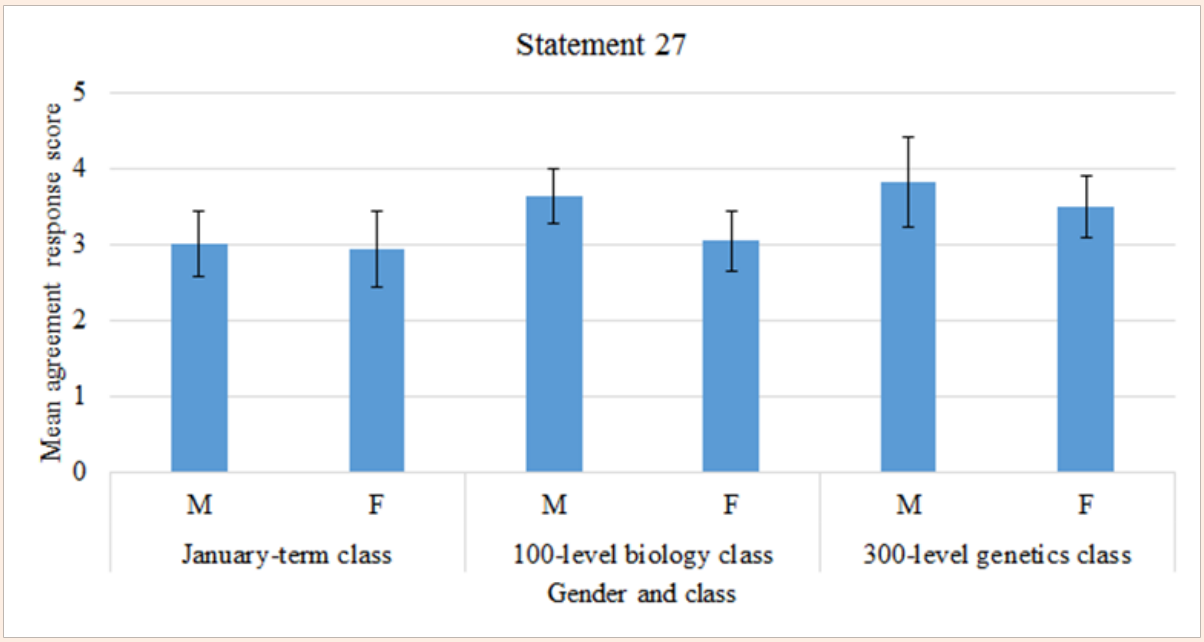

Figure 4: Mean agreement response score to statement 27 ("*Drugs that target negative epigenetic modifications should be allowed.*") for males and females organized by class. The error bars represent 95% confidence intervals. Overall, there was a significant difference between the classes considering the gender interaction, but further post-hoc analysis is required to determine specifically which male/female subcategories are different. (df=5, Two-way ANOVA $F=2.8$, $p<0.05$).

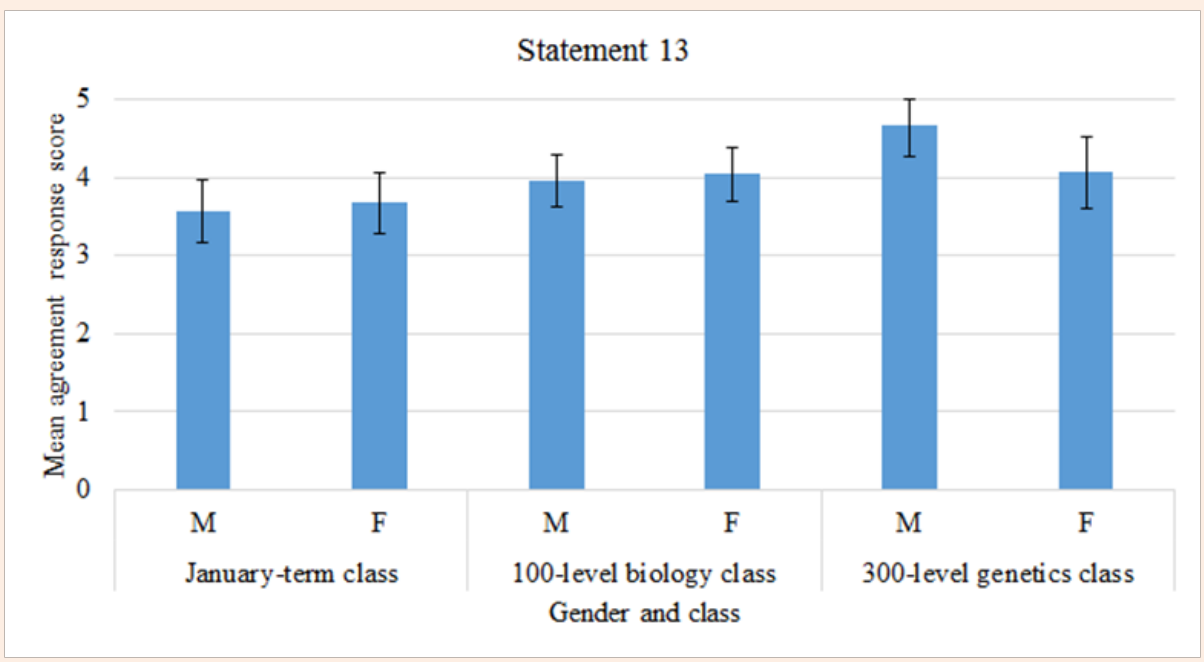

Figure 5: Mean agreement response score to statement 13 ("*Altering the genome of a consenting adult to treat a disease should be allowed.*") for males and females organized by class. The error bars represent 95% confidence intervals. Overall, there was not a significant difference between the classes considering the gender interaction (df=5, Two-way ANOVA $F=1.8$, $p=0.13$).

Discussion

Overall response

Public policy should be at least partially informed by public opinion, and the overall responses to survey questions in this report are representative of the public opinion these genetic techniques. The respondents in this group support WGS (statement 2 response), gene therapy for disease treatment (statements 13 and 14), and epigenetic treatment and disease prevention (statement 27). The public is not in favor of gene therapy for physical or aesthetic enhancements (statements 15 and 16). Further elaboration of overall statement response can be found in Tables 1 & 2.

Impact of education

Statements 2 ("*Sequencing an individual's genome to help detect and treat disease is ethical*"), 13 ("*Altering the genome of a consenting adult to treat a disease should be allowed*"), and 27 ("*Drugs that target negative epigenetic modifications should be allowed*") are all measures of acceptance of their respective techniques. The mean agreement score for each of these statements all increased the further one progressed in the biology curriculum, education does appear to positively influence the acceptance of the three techniques. However, another possible explanation for these trends is that the undergraduate biology curriculum selects against individuals that are opposed to cutting-edge technology like these genetic techniques. A future experiment to resolve this difference could be to perform a longitudinal study in which one set of students was administered this survey periodically throughout their progress through the biology curriculum, which would remove the effect of any selecting factors within the curriculum. If education were shown to increase acceptance of these techniques, an education initiative could be used to make these techniques more accepted by the public.

Agreement with two other statements - 5 ("*I would want to know if I was genetically predisposed to - but may not necessarily develop - an untreatable disease like Alzheimer's or Parkinson's*") and 25 ("*I consider epigenetic consequences when making daily lifestyle choices.*") also both followed the same pattern of having the genetics class agree more than the January-term and 100-level biology classes. The increased agreement on statement 5 may be due to the greater exposure of 300-level biology students to stories of individuals regretting finding out their genetic predispositions due to their subsequent experience of problems like increased anxiety and depression. The results for statement 25 are more complicated to interpret. On one hand, the genetics students are more supportive of epigenetic treatments (see statement 27 results), suggesting that they accept that epigenetics is a real phenomenon. However, on the other hand, the 300-level genetics students are less likely to consider epigenetic consequences of everyday life. Perhaps one reason for this trend is that the genetics students believe that so many factors influence the epigenome that it is futile to try and control them. This could be tested by asking both groups an open ended question of "Why do you or do you not consider the epigenetic consequences of your daily decisions?" and then using key-word tallying to determine trends within the responses.

There were some exceptions to the pattern of the 300-level and January-term classes being separated by the 100-level biology class, where education did not appear to influence the response to these statements. For instance, participation in the biology curriculum had no significant impact on the response to the true statement, 8, a check on knowledge of the genetic information non-discrimination act - ("*I am aware of federal laws that protect my genetic information from discrimination by employers and insurers.*") or the false statement, 9, ("*I am aware of federal laws that prevent insurers and employers from discriminating based on an acquired disease, e.g. Parkinson's, Alzheimer's.*"). Knowing that genetic information cannot be used by health insurance companies or employers to discriminate could make individuals more accepting of whole genome sequencing (WGS) and should be more heavily emphasized in the biology curriculum. Another example where education did not appear to influence participant responses were statements 15 ("*Altering the genome of a consenting adult for appearance/performance reasons should be allowed.*") and 16 ("*Altering the genome of an embryo for appearance/performance reasons should be allowed.*"). It appears that education would not be effective in shaping the public opinion of gene therapy for enhancement reasons.

Impact of gender

Apart from the education factor, gender also influenced opinions on genetic techniques. Specifically, for the mean agreement scores for statements 15 ("*Altering the genome of a consenting adult for appearance/performance reasons should be allowed.*") and 16 ("*Altering the genome of an embryo for appearance/performance reasons should be allowed.*"), men tended to be more accepting of using gene therapy for enhancement reasons. This finding could be partially explained by women being more invested in the fate of their offspring than men or men being more vain than women. This could be tested by asking a group of each gender how often they participate in activities for the purpose of enhancing their appearance (e.g. wearing makeup for women, and lifting weights exclusively for appearance reasons for men). Furthermore, women have been shown to be engaging in less risky behaviors when it comes to healthcare decisions than men, and since gene therapy is currently a risky technique, this mindset may influence acceptance of gene therapy Harris et al. [32]. If policy-makers were looking to make this technique more acceptable, one route might be to increase the safety of this technique.

Multivariate analysis (class and gender)

Further separating the classes to compare the male-female trend between them allowed for a more detailed analysis of what was causing the differences between the classes. The multivariate analysis showed that there were significant differences between the classes in statements 2 and 27 when taking gender into consideration, but further post-hoc analysis is required to determine specifically which male/female subcategories are different.

Conclusion

Each of the new genetic therapies presented in this paper provides some form of ethical challenge that should be considered when determining the policy surrounding its respective technique. Another factor that should be considered is the public opinion of each of these techniques. Overall, students at Gustavus are generally accepting of the genetic techniques examined in this paper (WGS, gene therapy for disease treatment, and epigenetic therapy). Additionally, based on the analysis of responses separated by classes, it appears that education can be a tool for further increasing acceptance of these new technologies (except for gene therapy for enhancement reasons). While the differences in the responses between the classes are likely due to education, a selecting factor within the biology curriculum that weeds out students that are not accepting of whole genome sequencing could be a confounding variable. A future experiment to resolve this difference could be to perform a longitudinal study that followed one set of students through the biology curriculum. In addition to education, gender also appears to play a role on acceptance of gene therapy for enhancement reasons, of which women are less accepting. Increasing the safety of this technique may make it more palatable to women. This study suggests that education and informed consent will play a major role in implementation of these technologies with their increasing complexities of the data itself and ethical considerations arising thereof. Since 50% of Gustavus students are interested in healthcare and the increasing role of these technologies in delivering therapies, there probably needs to be more exposure and discussion based forums at the undergraduate levels surrounding these topics.

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