

Acceptance of CRISPR: A Thematic Analysis of Attitudes on Novel Gene Therapies in Undergraduates

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Abstract

The purpose of this study was to examine the attitudes of undergraduate health science students toward somatic cell and germline genetic therapies. To do this, students were presented a choice between using or not using CRISPR gene editing techniques in a hypothetical situation involving a child with Duchenne muscular dystrophy. Additionally, this study investigated whether the choice of supportive or critical supplemental literature would influence a student's final decision and identify any differences in the themes that led to this ultimate decision. After a semester of education and supplemental reading, thirty-three (n=33) students were given a short writing assignment where they were presented with two case scenarios involving their own hypothetical child, who had been diagnosed with Duchenne muscular dystrophy. The scenarios differed in that the first presented students with the option for somatic cell therapy, while the second provided a cure using IVF and germline therapies. The responses were scored to determine the overall support for the use of CRISPR in these situations. A thematic analysis was also conducted to determine what themes were relevant to decision making, and how they may have been influenced by the supplemental readings. The findings show that students were especially accepting of somatic cell therapies, and on average, were also willing to accept the use of germline therapy in this scenario. The two most common themes from students accepting of CRISPR use were to "remove/prevent/treat human genetic diseases and cancer", and to "improve quality of life". The two different types of supplemental literature had no statistically significant bearing on the outcomes of this study.

1. Introduction

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) gene editing is one of the most important recent advancements in biology. CRISPR is a notable advancement for its genetic editing efficacy in all organisms because it functions by using a relatively accurate RNA guide^{1,2}. Importantly, CRISPR, like other methods of genetic therapies, is able to make both somatic-cell and germline genetic edits to living organisms. Successful CRISPR gene editing has occurred in animal models that are highly relevant to clinical applications in humans such as the treatment of various cancers and Duchenne muscular dystrophy.^{3,4} Additionally, there are several recent reports of successful and safe gene editing experiments in humans.^{5,6}

At this juncture, genetic therapies such as CRISPR are capable of quickly reshaping the human genome in ways that were previously impossible.⁷ Additionally, it is reasonable to assume that technological advancement in this area will continue to force the topic into stark relevance.⁸ Due to its revolutionary potential, the use of CRISPR is at the forefront of scientific and bioethical debate.⁹ In 2015, a multidisciplinary committee convened in Napa, California to discuss the future of gene therapies. This meeting resulted in four recommendations. First, the committee recommended that there be no attempts at germline therapies for clinical application in humans due to the potential of problematic ethical and environmental consequences. Two other recommendations were to create forums in which experts are able to provide information and education about these novel therapies and support transparent research that would evaluate

the safety and effectiveness of CRISPR technology in living organisms. Lastly, it was suggested that a group of globally representative developers and users of genome editing technologies should form to discuss a path forward.⁷

The future clinical use of CRISPR in humans will, in theory, be partially shaped by public opinion. Early-stage empirical studies serve to present some of the attitudes held by the general public. An online social media survey, with responses from 12,562 people across 185 countries, showed support for the use of gene editing in children and adults to cure “life-threatening diseases”, with 59.0% of participants agreeing to this application of the technology. Similarly, when questioned about the use of genetic editing to cure “debilitating diseases,” 59.4% of participants agreed. In this same study, 43.3% of participants disagreed with applications that were not medically necessary. Participants who agreed with the non-medically necessary interventions (26.8%) were questioned about the specific non-health related traits they would agree with modifying. Intelligence had the highest acceptance (68.0%), followed by strength or sporting ability (58.4%) and appearance (51.3%).¹⁰ In 11 European and American countries, support is consistently greater for treatment than enhancement.¹¹ The statement, “gene editing for adult enhancement” receives only 26% positive comments. Less than half as many comments on prenatal enhancement are positive (11%). In order of frequency, the negative comments from respondents were: gene editing is “unnatural and messing with nature”, “there is no need” for this type of intervention, there are “risks of unknown consequences”, and it is just “wrong”.¹¹

It is important to note that findings gathered via telephone in previous studies contradict many of the opinions found elsewhere. It was reported that 65% of respondents thought that therapies meant to “reduce risk of (a child) developing certain serious diseases” should be illegal. While 83% responded that to “improve their (a child's) intelligence or physical characteristics” should be illegal. These respondents also reported that they do not support the government funding research for reduction of certain serious diseases (51%) or improvements in intelligence or physical traits (82%) in unborn babies. Interestingly, and an argument for the general acceptance of somatic cell therapies, the same study reported that 64% of respondents do support scientific research on developing gene therapy treatments.¹²

The current study was conducted with a group of undergraduate students in an evolution and genetics class to provide more insights about emerging public opinion trends pertaining to the ethical considerations involved in the use of somatic cell and germline gene editing. This is especially relevant in light of the fact that an analysis of 17 public opinion polls, conducted in the United States, over the past three decades show a meager 31% of Americans say they are familiar with gene editing technology, and nearly 69% reported reading or hearing not much or nothing at all on the topic.¹³

In addition to lectures that explained the scientific details of gene therapies, students were assigned a required reading on CRISPR gene editing. Jennifer Doudna’s and Samuel Sternberg’s book, a *Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution*, provides historical context on the early discovery of CRISPR and has a generally supportive stance on CRISPR. In *A Crack in Creation*, biochemist Jennifer Doudna narrates her discovery of CRISPR, and the potential it has for harnessing the power of evolution through gene editing. Her description gives readers the impression that CRISPR either already, or will have the capability, to solve many of humanity’s most intractable problems, and refers to CRISPR as the most promising gene editing technology because of its power and simplicity. Doudna and Sternberg also argue that a large majority of technology is inherently neither good nor bad. Consequently, it is how humans make use of these technologies that determines their aptitude for creation or destruction. In contrast, *Altered Inheritance: CRISPR and the Ethics of Human Genome Editing*, authored by the ethicist Françoise Baylis, offers a bioethical framework with a restrained attitude toward the use of gene editing. Baylis raises many ethical issues that may discourage readers from seeing these novel therapies as net positive for society. Baylis also critically questions the safety of such gene therapies.

The current study is the first known investigation of the effects of gene therapy ethics education on an individual’s decision-making process in a hypothetical case study situation involving CRISPR. It is also the first study to examine the differential effects of supportive versus critical accompanying literature may have on a student’s personal decision-making process regarding the utilization of genetic therapies in a hypothetical case study scenario.

2. Materials and Methods

2.1 Participants

Participants were undergraduate students at a small, public liberal arts college in the Southeastern United States during the Fall semesters of 2018 and 2019. All students were in a course entitled, Genetic and Evolutionary Principles of Health (N = 33, mean age (SD) = 24.8 (8.5) years, 58% female), which was part of the Department of Health and Wellness Promotion curriculum in the university’s Division of Social Sciences. The professor had >10 years of

teaching experience. Three percent of the students were sophomores, 30% were juniors, 58% were seniors, and 9% were post-baccalaureate students. Self-reported religious affiliation included: 15% Catholic, 0% Fundamental Christian, 27% Other Protestant, 0% Eastern Religion, 0% Muslim, 25% None, and 30% Other. On the importance of religion in the students' lives, 52% listed "not important," 6% "slightly important," 15% "moderately important," and 27% listed "very important." This study was approved by the Institutional Review Board at UNC Asheville and written informed consent was obtained from all participants.

2.2 Course description

Genetic and Evolutionary Principles of Health was a three-credit hour course in a Health and Wellness Promotion Department similar to previously described evolutionary medicine courses (e.g., see (Grunspan et al. 2018)). This course taught the fundamental principles of evolution in a mostly human context, with a specific focus on adaptation and maladaptation related to human health and disease. The course examined genetic mechanisms of evolution, the evolutionary history of humans, and how mismatches between our evolutionary history, the bodies we have evolved, and our modern lifestyles affect our health. By considering medicine and public health from an evolutionary perspective, students worked to gain insights into how the human body has adapted to its various environments and why diseases occur. In the final one-third of the course (i.e., last six weeks), this course explored current advancements in, and the ethics of, gene editing, with a particular focus on CRISPR. This course consisted of lectures, group discussions on the readings, weekly quizzes on the lectures and readings, and weekly student presentations on readings. Students in the Fall 2018 semester (N = 15) read and discussed Jennifer Doudna's and Samuel Sternberg's book *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution*.¹⁴ Students in the Fall 2019 semester (N = 18) read and discussed Francoise Baylis' book *Altered Inheritance: CRISPR and the Ethics of Human Genome Editing*.¹⁵

2.3 Assessment

All participants completed a short writing assignment at the end of the semester asking students to share their perspectives on the use of CRISPR for gene editing in a case study involving a hypothetical child with Duchenne muscular dystrophy (DMD). DMD is an X-chromosome linked genetic disease that affects approximately 1 in 3,600 males. The case scenario put the student in the role of parent of a 10-year old boy who began experiencing loss of motor function and was diagnosed with DMD at the age of 4 years. The case was set in the near future, in a hypothetical time when both somatic and germline gene editing by CRISPR are available and FDA-approved for the treatment of DMD. The first part of the case study presented a scenario where *somatic* gene editing by CRISPR is legal, efficacious, and paid for by insurance companies and asked students to consider whether they, as the hypothetical parents of the child with DMD, would be open to somatic gene editing and to justify their answer. The second part of the case study presented a scenario where *germline* gene editing by CRISPR is legal, efficacious, and paid for by insurance companies and asked students to consider whether they, as the hypothetical parents of the child with DMD, would be use to germline gene editing and to justify their answer. In addition, students were asked to write responses to the following four open-ended questions about their attitudes toward CRISPR gene editing: 1. Please describe your thoughts and feelings about genome editing/CRISPR, 2. Do you think it is ever acceptable to do gene editing? If so, under what circumstances? 3. Do you have ethical concerns about genome editing/CRISPR? If so, what are they? 4. What would you like to see as the future of genome editing/CRISPR?

2.4 Analysis

Two reviewers were tasked with independently scoring the students acceptance levels of CRISPR intervention for both the somatic gene editing and germline gene editing scenarios using a 5-point Likert scale, in which 1=Strongly disagree, 2=Moderately disagree, 3=I don't know or no opinion given, 4=Moderately agree, or 5=Strongly agree. Interrater reliability was calculated for these ratings. On one student response, the two reviewers' scores differed and a third reviewer resolved the tie.

Next, a thematic analysis was conducted on the student responses to the four open-ended questions about attitudes toward CRISPR gene editing. The first step of the thematic analysis was for all three reviewers to individually read all student responses and independently identify themes. The following themes were agreed upon by the three reviewers: remove/prevent/treat human genetic diseases and cancer; improve quality of life; agricultural

improvements; gene drive (eradication of malaria-carrying mosquitoes); re-creation of extinct species; CRISPR used in research to determine the function of genes and proteins; CRISPR use in antibiotic research; cost-benefit analysis of CRISPR use is necessary; distinction between somatic versus germline editing; CRISPR use must be for medical necessity; concerns about abuse of gene editing technology; concerns about “designer babies”/human enhancements; concerns about off-target/side effects; concerns about creation of superior soldier/military/bio-weapons; thorough testing on safety and efficacy needed/slow science; concerns about the creation of gene gap/socioeconomic divide/should be equitably accessible; regulation/oversight needed; concerns about eugenic uses; concerns about who provides informed consent; concerns about loss of diversity; global debate and consensus is required; religious views; safeguards needed to protect egg donors; and concerns that CRISPR is unnatural and will affect natural selection. The three reviewers then independently re-read the student responses and identified when the above themes were mentioned. If a student mentioned the theme at least once in their responses to any of the four open-ended questions a score of “1” was recorded for that theme in the student’s response. The total number of mentions was summed for each theme and averaged across the three reviewers.

Table 1. The percentage of student responses that mentioned each theme, averaged across reviewers.

	Average (SD)
Remove/prevent/treat human genetic diseases and cancer	87.9 (8.0)
Improve quality of life	63.6 (26.2)
Agricultural improvements (drought-resistant crops, helping bees/pollination)	10.1 (1.7)
Gene drive (eradication of malaria-carrying mosquitoes)	4.0 (1.7)
Recreation of extinct species	3.0 (0.0)
CRISPR used in research to determine the function of genes and proteins	3.0 (3.0)
Use as in antibiotic research	4.0 (1.7)
Cost-benefit analysis	41.4 (48.1)
Distinction between somatic versus germline editing	39.4 (13.9)
Use must be for medical necessity	53.5 (30.4)
Abuse of gene editing technology	54.5 (23.7)
Concerns about “designer babies”/human enhancements	52.5 (12.6)
Off-target/side effects	42.4 (13.9)
Creation of superior soldier/military/bio-weapons	22.2 (3.5)
Thorough testing on safety and efficacy needed/slow science	40.4 (10.6)
Creation of gene gap/socioeconomic divide/should be equitably accessible	51.5 (3.0)
Regulation/oversight needed	47.5 (24.7)
Eugenic uses	14.1 (3.5)
Who provides informed consent	24.2 (6.1)
Loss of diversity	7.1 (4.6)
Global debate/consensus is required	20.2 (4.6)
Religious views	5.1 (3.5)
Safeguards to protect egg donors	4.0 (1.7)
Unnatural/will affect natural selection	14.1(1.7)

Subsequent quantitative analyses were further conducted on the above themes after stratifying the students by 1) whether or not they were accepting of CRISPR germline editing in the case study scenario and 2) by the book read in class (i.e., Doudna or Baylis). The purpose of these subsequent analyses was to determine if the themes mentioned by students were different between students that did versus did not accept CRISPR for germline gene editing. We also wanted to test whether the two books on CRISPR differentially affected student thinking on the use of CRISPR. Group differences were analyzed with Fisher’s exact test. Statistical significance was set at $p < 0.05$.

3. Results

Interrater reliability on the scoring of acceptance of CRISPR gene editing in the case study scenarios was 0.94, which was determined to be excellent. Students were significantly more accepting of CRISPR use for somatic editing than for germline editing ($p < 0.0001$). All student respondents ($N = 33$) agreed with using somatic gene editing to cure their hypothetical child of Duchenne's muscular dystrophy. However, only 54.5% of students agreed with germline CRISPR to cure their hypothetical child, while 42% disagreed with using CRISPR and 3% did not know or did not share an opinion. There were no differences in acceptance of gene editing when stratified by the book read by the student on CRISPR (i.e., Doudna or Baylis).

The themes that were agreed upon by the three reviewers in the thematic analysis are listed in Table 1 along with the percentage of times they were mentioned in the student responses to the open-ended questions. The most commonly cited themes in favor of CRISPR use were to "remove/prevent/treat human genetic diseases and cancer", mentioned by 87.9% of students, and to "improve quality of life", mentioned by 63.6% of students. Commonly mentioned themes that had a neutral view toward CRISPR were, the need for "cost-benefit analysis", which was mentioned by 41.4% of respondents, and the need to make a "distinction between somatic versus germline editing," which was mentioned by 39.4% of respondents.

Table 2. The percentage of student responses that mentioned each theme stratified by whether the student Agree or Disagreed with the use of CRISPR for germline gene editing.

	Agreed (n=18)	Disagreed (n=14)
Remove/prevent/treat human genetic diseases and cancer	85.2	90.5
Improve quality of life	59.3	66.7
Agricultural improvements (drought-resistant crops, helping bees/pollination)	16.7	2.4
Gene drive (eradication of malaria-carrying mosquitoes)	5.6	2.4
Recreation of extinct species	3.7	2.4
CRISPR used in research to determine the function of genes and proteins	3.7	2.4
Use as in antibiotic research	5.6	2.4
Cost-benefit analysis	40.7	42.9
Distinction between somatic versus germline editing	29.6	50.0
Use must be for medical necessity	53.7	52.4
Abuse of gene editing technology	46.3	61.9
Concerns about "designer babies"/human enhancements	44.4	59.5
Off-target/side effects	50.0	33.3
Creation of superior soldier/military/bio-weapons	22.2	23.8
Thorough testing on safety and efficacy needed/slow science	35.2	42.9
Creation of gene gap/socioeconomic divide/should be equitably accessible	50.0	57.1
Regulation/oversight needed	53.7	35.7
Eugenic uses	7.4	23.8
Who provides informed consent	22.2	26.2
Loss of diversity	0.0	16.7
Global debate/consensus is required	16.7	26.2
Religious views	0.0	11.9
Safeguards to protect egg donors	1.9	7.1
Unnatural/will affect natural selection	1.9	31.0*

* $p < 0.05$

There were several themes that focused on unfavorable or cautionary perspectives regarding gene editing. For example, approximately half of the sample mentioned each of the following themes: "use must be for medical necessity" (54.5%), "concerns about abuse of gene editing technology" (53.5%), "concerns about designer babies"/human enhancements" (52.5%), concerns about the "creation of gene gap/socioeconomic divide/should be equitably accessible" (51.5%), and "regulation/oversight is needed" (47.5%). Other important cautionary themes

included concerns about “off-target/side effects” (42.4%), the need for “thorough testing on safety and efficacy/slow science” (40.4%), concerns about the “creation of superior soldier/military/bio-weapons” (22.2%), concerns about who would provide informed consent (24.2%), the need for “global debate/consensus” (20.2%), and “concerns about eugenic uses” (14.1%).

Table 3 presents the frequency of the themes stated stratified by the supporting book read. There were no significant differences in the frequency of themes cited when the sample was stratified by students who read Doudna’s versus Baylis’ book in the course.

Table 3. The percentage of student responses that mentioned each theme stratified by CRISPR book read by the student.

	Doudna and Sternberg (n=15)	Baylis (n=18)
Remove/prevent/treat human genetic diseases and cancer	88.9	87.0
Improve quality of life	64.4	63.0
Agricultural improvements (drought-resistant crops, helping bees/pollination)	13.3	7.4
Gene drive (eradication of malaria-carrying mosquitoes)	6.7	1.9
CRISPR used in research to determine the function of genes and proteins	4.4	1.9
Recreation of extinct species	4.4	1.9
Use as in antibiotic research	6.7	1.9
Cost-benefit analysis	37.8	44.4
Distinction between somatic versus germline editing	33.3	44.4
Use must be for medical necessity	46.7	59.3
Abuse of gene editing technology	57.8	51.9
Concerns about “designer babies”/human enhancements	57.8	48.1
Off-target/side effects	33.3	50.0
Creation of superior soldier/military/bioweapons	26.7	18.5
Thorough testing on safety and efficacy needed/slow science	48.9	33.3
Creation of gene gap/socioeconomic divide/should be equitably accessible	42.2	59.3

4. Discussion

The main goal of this project was to identify overall attitudes and themes held by students in relation to emerging genetic editing in humans. A secondary goal was to determine if assigning different supporting literature would be influential in the decision-making process on CRISPR. The current research gathered qualitative data in the form of undergraduate student responses to short answer questions about attitudes around CRISPR gene editing technologies. Results show that all of the participants were in favor of somatic-cell genetic therapies, while just over half were in favor of germline gene editing. The different books that were assigned had no effect on student views.

By placing students in a hypothetical clinical situation involving a hypothetical child our participants were forced to create a more holistic risk-to-reward scenario based on their own subjective beliefs, understanding of the science, and emotional and ethical views. The findings of the current study support those of McCaughey et al. who showed that participants agreed to the use of somatic cell gene editing to cure life threatening or debilitating disease. Our participants found CRISPR use to be acceptable for medical necessity (54%) while showing concern about the abuse

of gene editing technology (55%) and call for these therapies to be governed by regulation and professional oversight. These concerns align closely with those of Jennifer Doudna and Francoise Baylis, the two authors read in the courses, and many professionals across many fields of study. Conversely, our participant's responses are in direct opposition to the findings obtained by the STAT Harvard Poll from 2016, which showed that a majority of respondents believed that therapies meant to "reduce risk of (a child) developing certain serious diseases" should be illegal. This inconsistency should prompt future inquiry into the opinions held by the larger public.

Interestingly, the differences in supporting literature had no statistical effect on the final decision-making process in these students. Although the point of this study was not to heavily influence one's opinion on CRISPR, perhaps, the results would be augmented by the choice of more strongly oppositional literature, a larger or more diverse sample, or different teaching methods. It is speculated that the classroom discussions were skewed toward a more accepting dialogue, which did contain conversation of many of the same concern's students voiced at the culmination of the study.

Moving forward, it would be prudent to further examine conflicting ambiguities produced by inconsistent results, determine universal themes, and survey overall attitudes toward different types of emerging gene therapies. For example, this study highlights the importance of distinguishing between somatic cell and germline gene editing when surveying opinions on novel gene therapies, and the need for further education on the topic. Here, nearly half (42%) of the participants that were accepting of somatic cell therapy were not accepting of germline therapies. Many students expressed concern that these techniques are unnatural and will affect natural selection suggests that there are high levels of openness when gene therapies are not heritable, and that heritable edits could be seen as potentially dangerous and laden with ethical concerns. Basic education on the topic of CRISPR, while scientifically complex, should be seen as an important component of classrooms and public forums on gene editing. Groups can be familiarized with the most basic concepts and tremendous implications of CRISPR fairly easily. Only then would it be possible to obtain a more precise understanding of public opinion on the topic. Once these fundamental principles of understanding are met, public opinion can be thoughtfully incorporated into the scientific debate at the highest levels.

4.1 Strengths and Limitations

One possible strength of this research design is that the students in this sample were all educated on the risks, benefits, and ethical complications of CRISPR prior to their short answer responses. This basic level of understanding, regarding the landscape of gene therapies, allowed students to make informed decisions on the use of CRISPR. The use of a 5-point Linkert scale allowed reviewers to quantify the qualitative data provided by students in the short answer assignment. By using multiple blind reviews, that produced excellent interrater reliability, the results of this study were reported with a high degree of accuracy. The course that students were enrolled in allowed for all types of discourse between students. There was a high level of engagement in both the 2018 and 2019 sections, and a variety of opinions were discussed. There was also a high rate of short answer assignment completion by students which led to a more inclusive data set.

The limitations of this study begin with the relatively limited sample size and resultant lack of generalizability to the general population. Students who would largely oppose the idea of the use of genetic therapies in humans are doubtful to elect a class that is titled, Genetic and Evolutionary Principles of Health. This would suggest a self-selection bias that may skew the data more toward acceptance than a truly representative sample. Additionally, this sample's median age skews toward a younger individual, and not all religious, cultural, or ethnic identities were included.

Although the three reviewers of the student's short answer questions showed very high interrater reliability, the results reported in this paper are still those of subjective opinions. Although many students were very clear about their ultimate decision, other responses were sometimes vague, or unclear. This would be especially true of the thematic responses, as that data was not a binary yes or no decision. It would be impossible for the reviewers to know the full extent of the student's beliefs without some form of follow-up interview or quantitative data.

Each time a classroom fills with students a culture is formed. Although this class was specially designed to have an open dialogue component, it is still possible that students may have been influenced by their peers, or the instructor during the semester. The students may have felt pressured to agree with the use of CRISPR for unknowable reasons. Finally, the short answer assignment that was given at the end of the semester was not entirely anonymous due to grading requirements of the professor. To control of any bias that may have been caused by this characteristic of the data, the assignment was graded for participation only and made anonymous before being sent to reviewers.

5. Conclusion

There continues to be a significant amount of time and resources dedicated to the advancement of research on the topic of genetic therapies in humans. CRISPR therapies, and others like it, are currently poised to start entering the human genome within the foreseeable future. With great power comes great responsibility, and the continued investigation on the attitudes our civilization has toward novel gene therapies is paramount in understanding what are considered ethical applications. In order to form these attitudes it is essential that the public be informed in the nuances found within these techniques. A point may arrive where the technology has advanced to a point where the only thing that will restrain it is the agreed upon limits set by our species.

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