BIOS

Liberal arts student impressions of opportunities in gene editing

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Preliminary Report

Liberal arts student impressions of opportunities in gene editing

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Running title: Survey on gene editing

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Abstract. The completion of the human genome project led to advances both in technology and information availability. The potential of gene editing is tremendous. In the foreseeable future, scientists and doctors will be capable of repairing defective genes within humans (as is being done in other species) as a means to treat or potentially eliminate specific diseases. There are ethical dilemmas with the use of this technology, including who decides whether someone can or should be treated and what diseases or traits should be altered. We surveyed undergraduate students from a variety of disciplines about some bioethical issues. With the data collected, we show that in general, students are in favor of using gene editing technology to help cure disease in adults and children, but less willing to support the use in treating cells prior to fertilization. There is less support for altering non-disease characteristics (e.g., hair color, intelligence, or athletic ability), but male students tend to be more supportive of the use of this technology in this area than female students.

Introduction

Modern techniques in the biological sciences impact everyday life, from the presence of genetically modified foods in the marketplace to modern medicines. Providing an understanding of bioethical issues to students should only require a basic understanding of the science behind the issues, but a greater understanding of potential problems and long-term impacts need to be discussed. Current bioethical topics that will have a great impact on humanity in the near future include human cloning, personal genomics, and gene and genome editing.

Following publication of the structure of DNA (Watson and Crick, 1953), scientists have endeavored to gain further knowledge into the role of DNA mutations in disease. Mutations, inherited alterations in the DNA sequence, have been associated with many diseases. More than 3,700 diseases have now been associated with mutations in a single gene (Anonymous, 2017). Knowledge of a single gene that is involved in a human disease provides insight into the involvement of that gene and gene product in the cause and symptoms of the disease, but more importantly provides an avenue into a specialized (gene) treatment for the disease (gene therapy or gene editing). Introduction of a normal, functional gene into the genome, or even as an RNA into the cell, can provide at least short-term benefits for an afflicted individual. Many diseases and traits are influenced by multiple genes and are not yet viable targets for gene editing.

Treating disease using gene therapy involves the delivery of a functional copy of a gene or RNA to a specific cell type or types. Gene therapy treatments have resulted in complications for some recipients, leading to harsher federal regulatory oversight (Hollon, 2000). Safer alternatives are being pursued, such as gene editing.

Gene editing is now possible through a variety of techniques. The use of Zn finger and TALENS technology has been shown to be successful, but has limitations (Gaj et al., 2013). CRISPR/Cas9 technology has been demonstrated to have great potential in gene editing with studies being conducted on a variety of organisms, including on human cell lines (Reyes and Lanner, 2017). CRISPR stands for Clustered Regularly Interspersed Short Palindromic Repeats and uses the associated protein Cas9 (or similar proteins) to direct the cleavage of specific DNA sequences. A guide RNA is introduced to target the cleavage sequence.

Gene editing offers tremendous potential in the treatment of genetic disease as its ability to provide a specific treatment. Using gene editing, a specific DNA sequence that contains a region to be altered, identified through analysis of the individual genome or through sequencing of a region of DNA, can be treated and changed in the laboratory. The cell containing the change is then re-introduced into the individual. CRISPR/Cas9 and related enzyme systems offer the ability to rapidly and specifically alter the genome. While it appears that the specificity for these alterations is fairly high, there is the possibility of off-target modifications (Lin et al., 2014; Schaefer et al., 2017). The impacts of these changes are unknown and there is the potential that these off-target alterations could introduce additional issues in the recipient.

Current uses of CRISPR/Cas9 include editing animal as well as human cells. CRISPR/Cas9 technology has also been used in clinical trials to edit genes in adults to treat cancer. A patient with aggressive lung cancer had some of their immune cells removed, modified using CRISPR/Cas9 technology, and injected back into them with a disabled gene that usually halts the immune system response (reviewed in Cyranoski, 2016). Embryonic and germline gene editing brings up additional ethical issues, however, some research is being conducted. Several groups have reported different accomplishments regarding gene editing. One group reported the treatment of non-viable embryos to alter a gene involved in blood disease (reviewed in Cyranoski and Reardron, 2015). A second group has reported the introduction of a mutation to prevent HIV infection (reviewed in Callaway, 2016). A third group has used CRISPR/Cas9 in viable embryos to begin to study the role of individual genes in early human development (reviewed in Bowler, 2016) The uses of

CRISPR/Cas9 technology are quickly expanding as it becomes less expensive and studied by more scientists.

The goal of this survey was to gain insight into the understanding and support of gene editing by undergraduate students in varying disciplines at a liberal arts university. Overall, there was strong support for the use of gene editing technology to assist with disease treatments in adults and children and less support for editing an embryo's genome. Fewer students were in support of gene editing being used to enhance an individual (control physical features, improve intelligence or athletic ability), however males were more likely to support enhancement for intelligence or athletic ability.

Methods

A survey was designed to gather demographic information and personal opinions regarding the use of gene editing on treatment of life threatening or debilitating diseases in adults, children and prior to fertilization (demographics questions are in Fig. 1; survey questions are in Fig. 2). Participants were also asked about the use of gene editing for physical, intelligence and athletic enhancements. The survey was first performed in a freshman biology course (Fall 2016) and then distributed on campus from February 1-24, 2017 via a Qualtrics survey and was restricted to Bradley University students. To maintain anonymity, demographic questions that received fewer than 5 respondents were pooled into a more general category. The survey questions and distribution had previously been approved by the Bradley University Committee on the Use of Human Subjects in Research (CUHSR 67e-16).

Results and Discussion

Over the sampling window, 124 undergraduate students participated in the spring Qualtrics survey (an additional 56 freshman biology students participated in a pilot survey in the fall of 2016 as part of a class, this pilot data is not shown). These students were primarily in the College of Liberal Arts and Sciences (including natural sciences). Students were not asked to provide information regarding specific majors or their academic year within the University. Students were asked demographic questions to determine gender and religious beliefs (Fig. 1). A basic introduction to the survey (Fig. 2a) and the survey questions (Fig. 2b) are shared.

Female and male students had a similar perspective on the favorability for using gene editing to treat adults and children with life threatening or debilitating diseases (>80% support) while the number of individuals supporting the use in embryos dropped (around 60% for life threatening diseases and 70-80% for debilitating diseases) (data not shown). Students identifying themselves as Christian similarly favored the use of gene editing in adults and children, but only about 50% supported the use in embryos (Fig. 3). The reduced support for gene editing pre-fertilization was expected from the respondents identifying themselves as Christian or other religions (59.7% - 74 of 124) as compared to those that identified as non-religious (30.6% - 38 of 124) or preferring not to respond (9.7%) (Fig. 3). There was not a substantial difference when looking at students based on groupings of their major classification (natural sciences, health sciences/nursing, or other).

Students were asked about the use of gene editing in non-disease related instances – physical alterations (e.g. eye color, hair color), improved intelligence or improved athletic ability. The majority of students (65.5% of 116 participants who responded) were not in favor of using gene editing technology to alter non-disease related traits (Fig. 4). However, some differences were observed. First, more males were in favor of using gene editing to improve intelligence or athletic ability (both in the general population of respondents and in the separate freshman biology majors survey). The differences in opinion for alterations of intelligence or athletic ability were not observed when religious beliefs were analyzed, although students identifying as non-religious did support the use of this technology for increasing intelligence more than the other groups.

Students were also asked if they had additional questions regarding this topic. This open-ended question provided some insight into what the respondents thought of the potential use of gene editing, but also provided some insight into their understanding. The survey was geared towards gaining knowledge without necessarily providing insight into the use of this technology. Students were not led to stories or instances of the use of gene editing, which is an ongoing event. They did provide some insight into their thoughts on the benefits (pros) and potential problems (cons) of gene editing (Fig. 5). While this is not an extensive list, these are issues that are actively being discussed and researched, such as off-target modifications. The unknown, as with any new technology, is somewhat frightening. There clearly are questions that cannot be answered at this time. While some of these will eventually be answered, such as the cost and availability of the technology, we may not have a grasp on other questions for an extended period of time and research (e.g., what are the long-term effects or the impacts on the species). It will be important as scientists move forward to continue to have discussions about this technology and the implications. The use of this gene editing technology in germline cells has been restricted by many governments (Kaiser, 2017), but other research is ongoing.

The ability to edit specific genes within a cell is an important accomplishment that has significant implications for human health in the future. The technology is currently being used in a variety of plant and animal cells with great success. Scientists will be able to provide a treatment potentially for all diseases associated with a specific gene, and tailor the treatment to the mutation of each afflicted individual. The long-term effects of these changes may not be significant in somatic cells beyond disease treatment. However, it is unknown how accurate this method is and what off-site target sequences might be altered. The use of gene editing in germ cells or embryos has potentially greater long-term implications through changing the inherited, altered sequence. In theory, this should only lead to an elimination of a specific disease, but other alterations are possible. The non-disease applications of gene editing provide a greater ethical dilemma which should be thoroughly discussed by scientists and non-scientists. Gene editing could lead to alterations that would be considered positive eugenics (transhumanism), leading to social differences based on either perceived (or visual) differences or based on monetary differences (those who can afford the editing versus those who cannot). Scientists are also developing the technology to edit a larger portion of a genome (creating new chromosomes or possibly even synthesizing a new set of chromosomes). Students, scientists and non-scientists all must be involved in the understanding and discussion of the potential benefits as well as the potential risks for the use of these technologies.

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Legends:

Figure 1. Demographics questions for the genome editing survey. The academic focus was based on one of five colleges within Bradley University or subsets of those colleges.

Figure 2a. Brief introduction to genome editing provided to the survey participants between the demographic questions and the survey questions.

Figure 2b. The second part of the survey includes opinion questions.

Figure 3. Respondent answers to gene therapy for a life-threatening disease being repaired in cells prior to fertilization. Of 124 participants, 59.7% identified as Christian or an other religious affiliation, 30.6% identified as not religious and 9.7% opted not to answer.

Figure 4. Respondent positions on non-disease use of gene editing. Position of the respondents are shown: support (blue), neutral (orange), disagree (gray), unsure (yellow). Percentages of respondents are only shown for support and neutral. The top row is organized by gender: males are shown on the outside ring (solid black boxes for percentages), while female respondents are shown on the inside ring (open white boxes for percentages. The middle row shows the responses from a separate survey using freshman biology majors (students enrolled in BIO150, fall 2016) based on responses organized by gender. The bottom row shows the respondents based on identified religious beliefs. The outside ring indicates respondents identifying as Christian (solid black boxes for percentages), the middle ring are students identifying as non-

religious (open white boxes), and the inner ring are students that identified as other religious (gray shaded boxes).

Figure 5. A list of some pros and cons for the use of gene editing.

Figure 1

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In the classroom, the researchers will introduce themselves and state that this survey is voluntary and is part of a student research project. The survey will be introduced briefly to the participants. The demographic information will be collected followed by a brief presentation or reading of the relevant material. The research questions will then be provided to the participants.

Demographics

1. Gender
    a. Female
    b. Male
    c. I prefer not to answer/other
2. Religious affiliation
    a. Christian
    b. Muslim
    c. Jewish
    d. Hindu
    e. Other/prefer not to identify
    f. Not religious
3. Ethnicity
    a. African American
    b. Asian
    c. Caucasian
    d. Hispanic
    e. Other
4. Academic focus*

Figure 1.

Information provided following the initial questions

In 2004, the Human Genome Project allowed scientists to map out the DNA of the human genome (all of the DNA in one of your cells and the instructions for making of an organism and for the functioning of the collection of cells), and now scientists say we will have the ability to edit the human genome in the next ten years. More than 1,000 human diseases are known to be caused by changes in a single gene within your genome. This technology could allow editing of a human genome to cure one or more of these diseases. These diseases may be life-threatening diseases, or diseases that will greatly reduce your quality of life. These repairs could include fixing mistakes that cause sickle cell anemia, common mutations that are associated with breast cancer, changes that lead to cystic fibrosis and other changes. It may also mean editing the genome of embryos so you don't pass your genetic diseases to your children. The technology could also be used to increase intelligence or strength, even choosing the hair and eye color of your children. While there are many useful applications of the technology, it has also raised many ethical questions. While changes made in an adult would not be passed on to future generations, changes made to embryos or gametes may be passed onto future generations.

The technology has not yet been perfected, but the rate of change in the technology has made the use and usefulness of this technology something for all of us to think about.

Figure 2a.

Figure 2b

The following questions are to be delivered and answered after the informational documentation is provided.

To what extent do you agree or disagree with using gene editing to:
Using this technology to cure (repair an error in the genome sequence) a life-threatening disease (such as sickle cell anemia, cystic fibrosis or some breast cancer mutations)

5. In an adult?
    a. Strongly agree
    b. Agree
    c. Neutral
    d. Disagree
    e. Strongly disagree
    f. I still need more information
6. In a child? (same multiple choice answers as in question 5)
7. In an embryo or before fertilization occurs? (same multiple choice answers as in question 5)

If this gene editing technology could be used to prevent a potentially debilitating disease (such as muscular dystrophy, childhood blindness caused by retinitis pigmentosa or forms of dwarfism), would you support the use of this technology?

8. In an adult?
    a. Strongly support
    b. Support
    c. Neutral
    d. Disagree with its use
    e. I still need more information
9. In a child? (same multiple choice answers as in question 8)
10. In an embryo or before fertilization occurs? (same multiple choice answers as in question 8)

11. This technology could be used to change non-disease, physical characteristics in an individual (such as height, hair color or eye color). In regards to the non-disease, physical characteristics, would you
    a. Strongly support the use of this technology
    b. Support the use of this technology
    c. Be neutral
    d. Disagree with the use of this technology
    e. Strongly disagree with the use of this technology
    f. I don’t know how I feel about this possibility
12. This technology could be used to improve intelligence. Would you support this use of technology? (same multiple choice answers as in question 11)
13. It is possible that this technology could be used to enhance physical attributes, such as strength or endurance to improve athletic capabilities. Would you support the use of this technology for improving athletic capabilities? (same multiple choice answers as in question 11)

14. If it were known that there are no complications with the technology, would you choose to give your offspring any of these characteristics (select all that apply)?
    a. Altering non-disease, physical characteristics (e.g., height, eye color or hair color)
    b. Improving intelligence
    c. Increasing athletic abilities
    d. None of the above

Figure 2b. The second part of the survey includes opinion questions.

Figure 3

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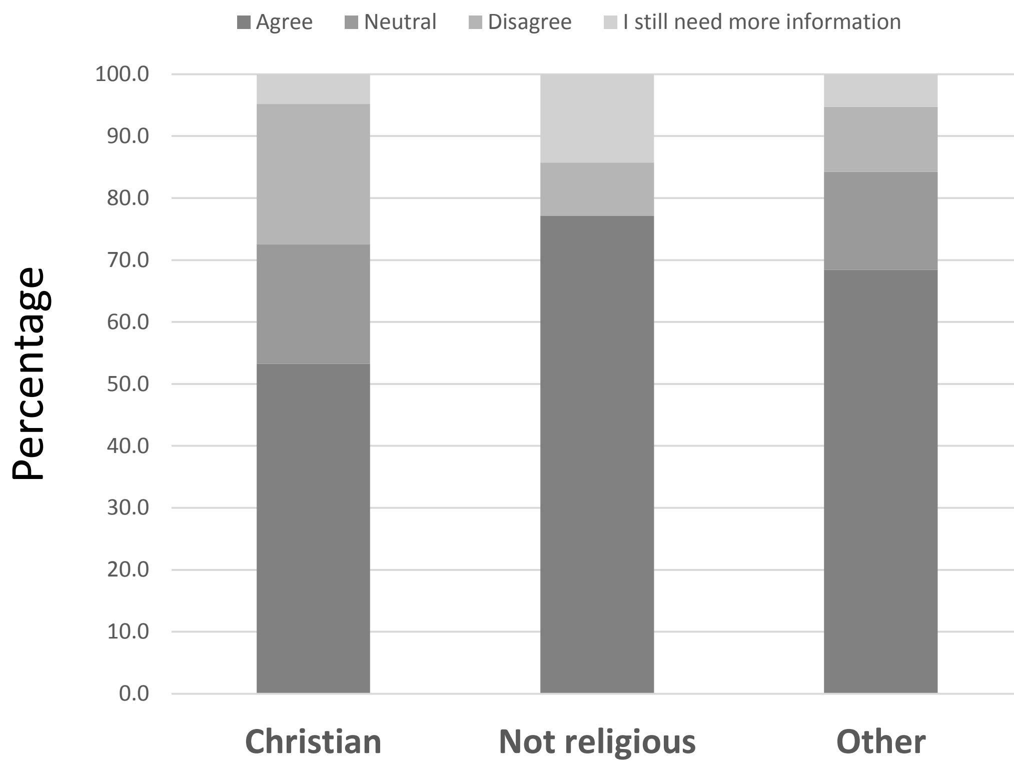

Figure 3.

Figure 4

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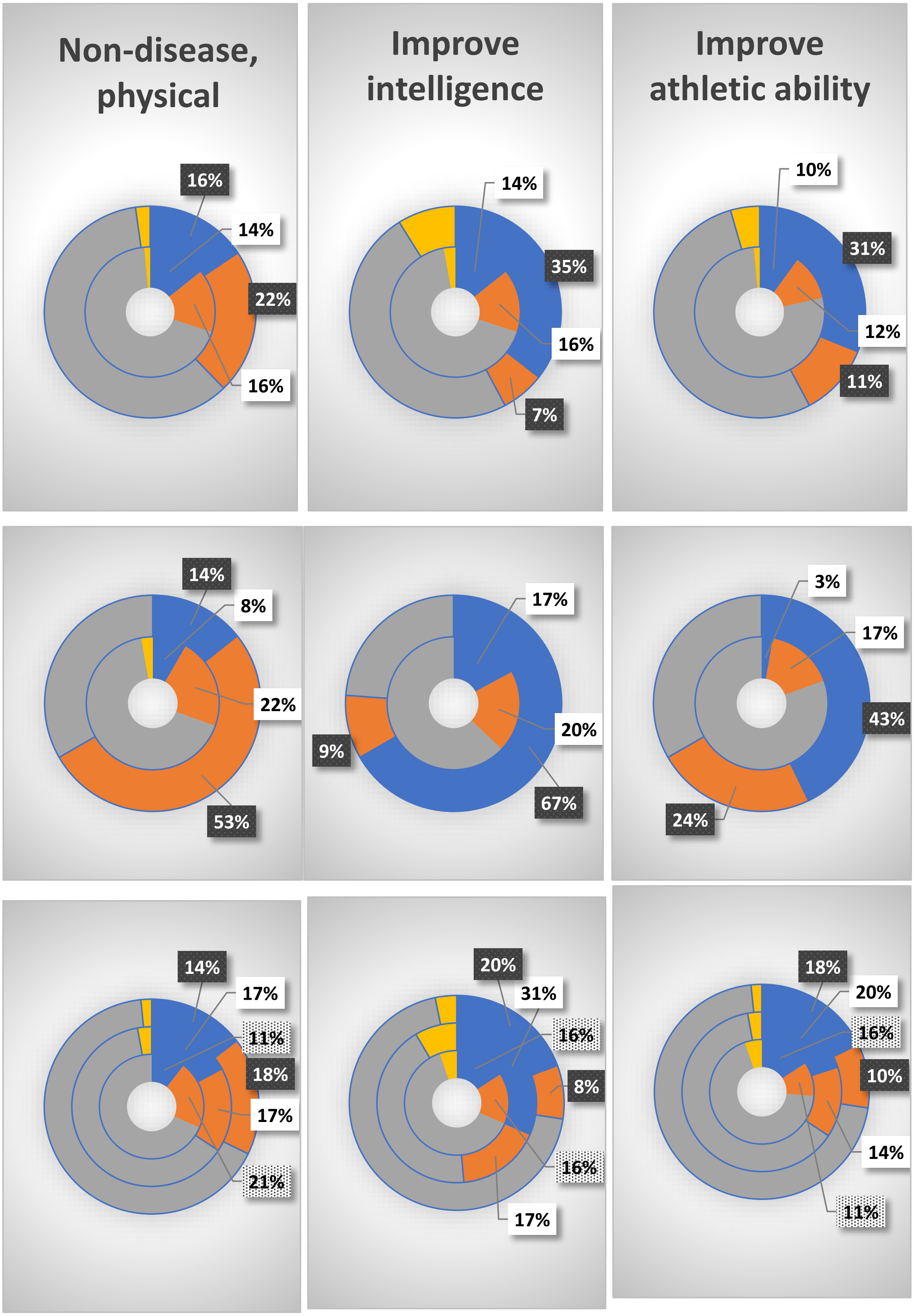

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Figure 5

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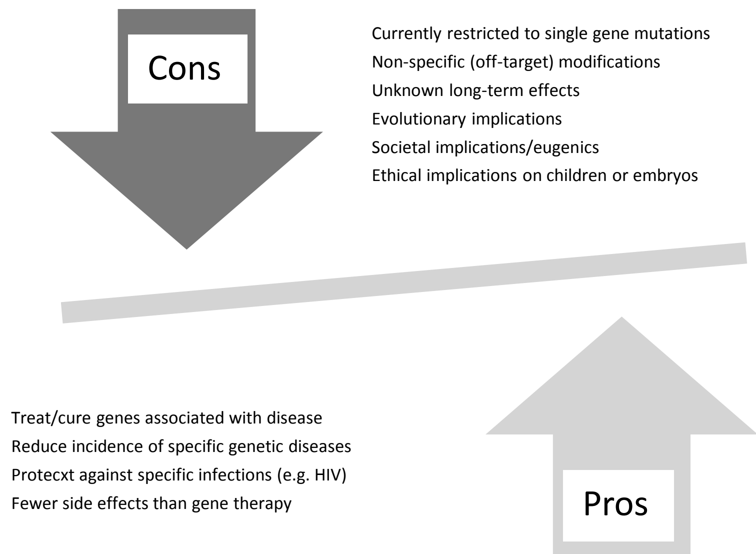

Figure 5.

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