2019

AP CollegeBoard

AP® Research Academic Paper

Sample Student Responses and Scoring Commentary

Inside:

Sample H

- ☑ **Scoring Guideline**
- ☑ **Student Samples**
- ☑ **Scoring Commentary**

AP® RESEARCH — ACADEMIC PAPER
2019 SCORING GUIDELINES

The Response…				
Score of 1 **Report on Existing Knowledge**	**Score of 2** **Report on Existing Knowledge with Simplistic Use of a Research Method**	**Score of 3** **Ineffectual Argument for a New Understanding**	**Score of 4** **Well-Supported, Articulate Argument Conveying a New Understanding**	**Score of 5** **Rich Analysis of a New Understanding Addressing a Gap in the Research Base**
Presents an overly broad topic of inquiry.	Presents a topic of inquiry with narrowing scope or focus, that is NOT carried through either in the method or in the overall line of reasoning.	Carries the focus or scope of a topic of inquiry through the method **AND** overall line of reasoning, even though the focus or scope might still be narrowing.	Focuses a topic of inquiry with clear and narrow parameters, which are addressed through the method and the conclusion.	Focuses a topic of inquiry with clear and narrow parameters, which are addressed through the method and the conclusion.
Situates a topic of inquiry within a single perspective derived from scholarly works **OR** through a variety of perspectives derived from mostly non-scholarly works.	Situates a topic of inquiry within a single perspective derived from scholarly works **OR** through a variety of perspectives derived from mostly non-scholarly works.	Situates a topic of inquiry within relevant scholarly works of varying perspectives, although connections to some works may be unclear.	Explicitly connects a topic of inquiry to relevant scholarly works of varying perspectives **AND** logically explains how the topic of inquiry addresses a gap.	Explicitly connects a topic of inquiry to relevant scholarly works of varying perspectives **AND** logically explains how the topic of inquiry addresses a gap.
Describes a search and report process.	Describes a nonreplicable research method **OR** provides an oversimplified description of a method, with questionable alignment to the purpose of the inquiry.	Describes a reasonably replicable research method, with questionable alignment to the purpose of the inquiry.	Logically defends the alignment of a detailed, replicable research method to the purpose of the inquiry.	Logically defends the alignment of a detailed, replicable research method to the purpose of the inquiry.
Summarizes or reports existing knowledge in the field of understanding pertaining to the topic of inquiry.	Summarizes or reports existing knowledge in the field of understanding pertaining to the topic of inquiry.	Conveys a new understanding or conclusion, with an underdeveloped line of reasoning **OR** insufficient evidence.	Supports a new understanding or conclusion through a logically organized line of reasoning **AND** sufficient evidence. The limitations and/or implications, if present, of the new understanding or conclusion are oversimplified.	Justifies a new understanding or conclusion through a logical progression of inquiry choices, sufficient evidence, explanation of the limitations of the conclusion, and an explanation of the implications to the community of practice.
Generally communicates the student's ideas, although errors in grammar, discipline-specific style, and organization distract or confuse the reader.	Generally communicates the student's ideas, although errors in grammar, discipline-specific style, and organization distract or confuse the reader.	Competently communicates the student's ideas, although there may be some errors in grammar, discipline-specific style, and organization.	Competently communicates the student's ideas, although there may be some errors in grammar, discipline-specific style, and organization.	Enhances the communication of the student's ideas through organization, use of design elements, conventions of grammar, style, mechanics, and word precision, with few to no errors.
Cites **AND/OR** attributes sources (in bibliography/ works cited and/or in-text), with multiple errors and/or an inconsistent use of a discipline-specific style.	Cites **AND/OR** attributes sources (in bibliography/ works cited and/or in-text), with multiple errors and/or an inconsistent use of a discipline-specific style.	Cites **AND** attributes sources, using a discipline-specific style (in both bibliography/works cited **AND** in-text), with few errors or inconsistencies.	Cites **AND** attributes sources, with a consistent use of an appropriate discipline-specific style (in both bibliography/works cited **AND** in-text), with few to no errors.	Cites **AND** attributes sources, with a consistent use of an appropriate discipline-specific style (in both bibliography/works cited **AND** in-text), with few to no errors.

AP® RESEARCH
2019 SCORING COMMENTARY

Academic Paper

Overview

This performance task was intended to assess students' ability to conduct scholarly and responsible research and articulate an evidence-based argument that clearly communicates the conclusion, solution, or answer to their stated research question. More specifically, this performance task was intended to assess students' ability to:

- Generate a focused research question that is situated within or connected to a larger scholarly context or community;
- Explore relationships between and among multiple works representing multiple perspectives within the scholarly literature related to the topic of inquiry;
- Articulate what approach, method, or process they have chosen to use to address their research question, why they have chosen that approach to answering their question, and how they employed it;
- Develop and present their own argument, conclusion, or new understanding while acknowledging its limitations and discussing implications;
- Support their conclusion through the compilation, use, and synthesis of relevant and significant evidence generated by their research;
- Use organizational and design elements to effectively convey the paper's message;
- Consistently and accurately cite, attribute, and integrate the knowledge and work of others, while distinguishing between the student's voice and that of others;
- Generate a paper in which word choice and syntax enhance communication by adhering to established conventions of grammar, usage, and mechanics.

Word Count: 4,910

Abstract

Since 2012, with the arrival of the gene editing system called CRISPR-cas9 (Clustered Regularly Interspaced Short Palindromic Repeats), the advancements in genetic engineering has been continuously growing at an increasingly high rate. CRISPR-cas9 has the power to be inserted into a human cell and change or eliminate genetic mutations in our DNA sequences. With this new advancement to genetic editing, several diseases long thought to be incurable can now be cured. Although, as with any new medical advancement, the general problems it will create will be introduced. This is due to the fact it proposes a shift outside the norms of our current practices in medicine. For the purpose of this research paper, two significant issues at the forefront of its use will be addressed; the dangers/harms it will bring to health safety of humans and its negative effect on modern socioeconomic trends. Through utilization of reported experimental lab results of genetic researchers, the potential dangers of the CRISPR-cas9 system will be supported. Furthermore, a correlational methodology of research to quantify the effect CRISPR-cas9 will induce on our current socioeconomic trends demonstrated the negative toll it may have on our current health care inequality gap. Conclusively, while these are significant underlying consequences of the CRISPR-cas9 system, finding ways to overcome them will aid us in properly taking advantage of the promising future it holds in medicine.

Introduction

"If I cross a tall plant with a short one, would there be a plant of intermediate size? Would the two alleles—shortness and tallness—blend?" (Mukherjee, p.49). Dating back to 1850s, Gregor Mendel, father of genetics, asked these very question amidst his experiments working with breeding pees. While Gregor Mendel himself would note the slow progression of these experiments, it is through them our understanding of what a trait and ultimately what a 'gene' is would develop. In the "Missing Science of Hereditary section of his book, "The Gene," Siddhartha Mukherjee goes to expound on the extensive process of Mendel's experiments including their significance, failures, and successes. Mendel's work with pea plants guided him in discovering the fundamentals of inheritance and the effect of this on gene expression. He believed that his experiments implied that parents each supplied one allele to be passed down in each generation with dominant alleles being overexpressed and recessive alleles being under-expressed (Mukherjee, p.52).While Mendel's work was not appreciated in his time, his principle of inheritance provided a template to explain the unknowns of medicine and move past theoretical claims/myths to explain what we didn't know. For instance, his work paved way to explain questions such as: why did the expression of one gene happen in one generation but then not be expressed in another? Or why did one offspring have a disease and the next offspring didn't when they were both from the same mom and dad?

Since Mendel, and the many geneticists who could come after him, modern genetics has been focused on the recent developments of gene therapy and CRIPSR-cas9. Whilst, our acquired knowledge from Mendel's discoveries, they provide the core foundation to these recent developments. Gene therapy is an experimental technique that allows doctors to treat certain genetic disorders by being able to insert the correct copy of a gene into a patient (NIH.gov, 2019).Contrarily, CRISPR-Cas9 is a "technique that allows for the highly specific and rapid

modification of DNA in a genome" (whatisbiotechnology.org, 2012). What is so different between the two? The arrival of gene therapy arose during the 1960s and 1970s and was first used in the 1990s to cure a girl with a congenital disease called adenosine deaminase (Mandal, 2019). From there, gene therapy is simply "like a car with mechanical problems, and has a history of jerking to life and then quickly stalling" (Labant, 2019). It isn't until decades later that the arrival of CRISPR-cas9 would go to jump-start gene therapy stunting and changing the course of genetic modification research.

Being here for such a short time, CRISPR-cas9 is still under major development and research as it remains a relatively novel concept in medicine. Thus, it was 'premature', critics say, when late November last year, a Chinese scientist in China used human embryos modified with the gene-editing technique, CRISPR-cas9 to create HIV free twin girls. It has become the first known case of human germline genetic modification. The scientist is said to have use CRISPR-cas9 to make changes in to the CRR5 gene (gene that allows HIV to infect cells in the immune system) of day old embryos. Sixteen of these embryos had this CRR5 gene edited and eleven of them were implanted into women before the HIV free twin girls were achieved As the father is said to have been HIV positive and not the mom, the chances of it getting passed down to unborn child is rare. Moreover as the parents wanted to avoid HIV infection, scientist Jennifer Doudna, a biochemist at the University of California points out there are already alternative ways to have prevented infection that are effective. For instance, washing the sperm of the infection to prevent HIV. "Why would you use this instead of an already established approach?" (Doudna, 2018).

Ultimately, as demonstrated by the results of the Chinese Scientist, CRISPR-cas9 would allow for that precise change to the mutated gene eliminating it from the gene pool that current

preventive practices does not. This is because it can target mutated genes and change the path of the disease by eliminating faulty genes completely. Specifically, an RNA is created with short guide sequence that binds to a specified target sequence in a genome and binds to the cas9 enzyme (NIH.gov, 2019). This modified RNA identifies the DNA sequence and cuts at the specific target site (Figure 1). Once the DNA is cut, researchers use the cell's own DNA repair machinery to add or delete pieces of "genetic material, or to make changes to the DNA by replacing an existing segment with a customized DNA sequence" (NIH.gov, 2019). It is through this process that researchers at Izpisua Belmonte at the Salk Institute for Biological Studies in San Diego, were able to conduct a research that led to the curing of blindness in mice. The results of this research show the promising future of CRISPR-cas9 and its potential to help eventually cure diseases such as cystic fibrosis, certain cancers, heart disease, and so forth (NIH.gov, 2016). In brief, CRISPR-Cas9 allows for the replacement/fixation of mutated genes or making diseases more self-evident to the immune system. This means there is now the ability to prolong, heal, and save so many lives that are shortened and destroyed by diseases that for so long medical professionals have not been able to completely understand let alone cure.

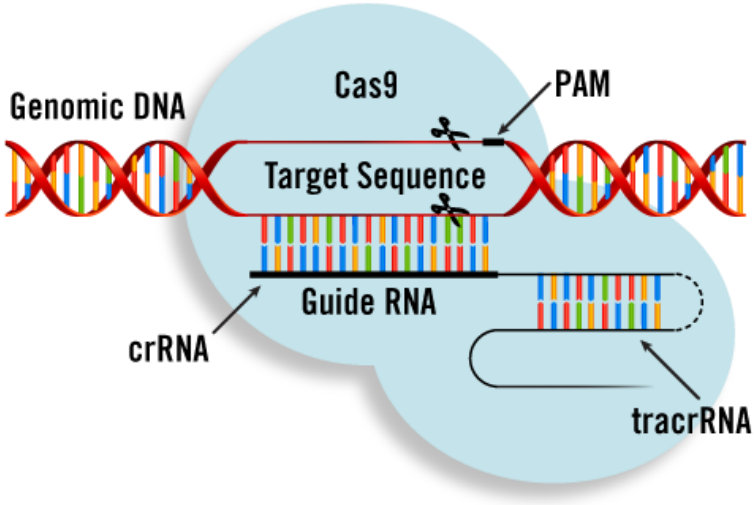


Figure 1: *With RNA guide, CRISPR-Cas9 binds and cuts genomic DNA at the target sequence (Levine, 2017)*

Of course, with any new medical advancement and finding comes the pitfalls that follows. As CRISPR-cas9 supplements our growing move towards a smarter and efficient medical technological industry, it demands testing outside of our traditional boundaries. As a result, "ethical concerns arise when genome editing, using technologies such as CRISPR-cas9, is used to alter human genomes" (NIH.gov, 2019). Hence, the development of CRISPR cas9 provides new advances in the science of genome editing further—it allows us to research outside the realms of medicine that we once thought were impossible. While this upholds many benefits, the implications and issues that are brought with it are concurrently high and must not be overlooked.

Literature Review

One of the biggest aspects that puts the heat on CRISPR-cas9 is the apparent negatives it upholds in the ethicality spectrum of its use. For instance, what happens when a rogue scientist uses CRISPR-cas9 application poorly or for the wrong reasons? Even the Chinese scientist who reportedly cured the twin girls using CRISPR-Cas9, had a hidden agenda as he was found by the Chinese government investigators to have helped cure them "in pursuit of personal fame and fortune" (Belluz, 2019). From there, other questions that arise include: how does CRISPR-cas9 inhibit informed consent of future generations? How can the scientific community account for all its misuses? Are designer babies possible? Thus, several areas of the system's capability are questioned when the use of CRISPR-cas9 is proposed. Although, there are two significant issues that can be delved into to highlight the dire effects that it will have in the prospect of germline editing. These two issues include: the danger it may pose to humans and the limit it will create on current socioeconomic trends.

The Dangers/Imperils of CRISPR-cas9

Primitively, the alteration of the human genome requires that bio technicians hone on in and change the trajectory of the human cell at a fundamentally basic level. Doing this means, that CRISPR-cas9 has the potential to affect unintended gene sequences causing major cell death or transformation. The Interdisciplinary Center for Studies on Bioethics at the University of Chile build on this notion stating that: "the application of CRISPR/Cas9 technique involves risks since it may produce off target mutations, which can be deleterious" (Rodriguez, 2016). A person may walk into a doctor's office thinking they are getting cured of heart disease, for instance, but end up getting a new genetic disease or worst dying from messing with just one, but wrong, segment

of DNA sequence. As Dr.Licholai of Harvard Biotech puts it in blatant terms, “it seems gene editing is going to eliminate all disease. Or kill every last one of us” (Licholai, 2018).

Further concerns on the human ability to manipulate the genetic code transpire when these manipulations are getting passed from one generation to another generation repetitively down the line (Licholai, 2018). We can’t foresee what these genetic manipulations will do and may end up creating unforeseeable alterations that we did not intend on years from now. What if the offspring of genetically modified individuals exhibit foreign diseases? Or what if they have a short life span? These questions and concerns are simply linked to the phenomena where we humans want to believe that we measured the changes we are making to the human genome accurately and precisely one hundred percent. But, even then, there will always be the possibility that we missed something or the technology we used couldn’t pick up changes that we have manipulated for it to react accordingly (Licholai, 2018). However, it must be noted these safety concerns for the CRISPR-cas9 system that have risen purely rely on speculation. To demonstrate any harms that CRISPR-cas9 will cause, it will have to be observed in the lab setting to truly account for these potential damages.

Adverse Effects on Current Socioeconomic Trends

The drawbacks of CRISPR-cas9 are further extended when analyzed through the social and economic lens. CRISPR-cas9, like any current process of gene editing, will further amplify the economic disparity between the rich and the poor (NYU Langone Health, 2018). Studies such as the Whitehall studies published in 1978 that followed British civil servants over many years, are a testament to this notion. “Led by Michael Marmot, PhD, MPH, MBBS, chair of the World

Health Organization Commission on Social Determinants of Health, the studies found a person's relative risk of poor health and disease increased as socio-economic status decreased" (Krisberg, 2016). This trend is further supported by a national health interview survey done in 2011 showing that lower income families tended to have a higher rate of risk for health conditions such as: heart disease, stroke, diabetes, kidney disease, and so forth (Table/Figure 2). The factor that drives this is the growing and demanding expenses of healthcare costs that as you go further down the economic scale, people can't afford.

[Table/Figure 2]

DISEASE OR ILLNESS	ANNUAL FAMILY INCOME				
	Less than $35,000	$35,000–49,999	$50,000–74,999	$75,000–99,999	$100,000 or more
Coronary heart disease	8.1	6.5	6.3	5.3	4.9
Stroke	3.9	2.5	2.3	1.8	1.6
Emphysema	3.2	2.5	1.4	1.0	0.8
Chronic bronchitis	6.3	4.0	4.4	2.2	2.4
Diabetes	11.0	10.4	8.3	5.6	5.9
Ulcers	8.7	6.7	6.5	4.7	4.4
Kidney disease	3.0	1.9	1.3	0.9	0.9
Liver disease	2.0	1.6	1.0	0.6	0.7
Chronic arthritis	33.4	30.3	27.9	27.4	24.4
Hearing trouble	17.2	16.0	16.0	16.2	12.4
Vision trouble	12.7	9.8	7.5	5.7	6.6
No teeth	11.6	7.8	5.5	4.2	4.1

Source: "National Health Interview Survey" (Schiller, Lucas & Peregoy, 2011)

The Congressional Budget Office (CBO) points out that advances made to our medical technologies is a preeminent driver of these increasing healthcare costs that we currently face (Mack, 2016). The founding of our most current advanced gene editing technology is no different and presents a high price tag and will further increase this inequality gap in our healthcare. This first comes with the cost of gene editing within itself and while CRISPR-cas9 is

said to be cheaper than gene therapy by experts, “all forms of gene editing will require a great sum of money” (NYU Langone Health, 2018). “For example, using CRISPR-Cas9 to fix a single point mutation costs $15,000 at Yale, and that’s before the cost of genotyping, which can cost up to $2,000. At Harvard, the rate for the same procedure exceeds $19,000. A point mutation is a very small mutation involving only a few nucleotides, yet it costs this great sum of money to alter” (NYU Langone Health, 2018). Moreover, CRISPR-cas9 also is often dependent on the use of viruses to shuttle its gene editing system into the cells of individuals which is just as expensive as other gene therapies (Kozubek, 2017). These examples of two independent processes consisting of point mutation including the delivery of CRISPR-cas9 through viruses only show the applications of CRISPR-cas9 in the lab and doesn’t even account for the research, development, and production aspect which ultimately determines the cost it will be put at on the market.

Methods

The Dangers/Imperils of CRISPR-cas9

Using a recent experiment showing the inadvertent harm of CRISPR-cas9 conducted by geneticist researchers back in 2018 and published on Nature Medicine, the current dangers of CRISPR-cas9 can be upheld. Initially, before experimentation, these researchers noted that while many cell types are agreeable to genetic engineering, hPSCs, human pluripotent stem cells (self-replicating cells from human embryos or fetal tissue), are difficult to engineer (Ihry et al., 2018). This comes with “reduced efficiencies relative to tumor cell lines or mouse embryonic stem

cells" (Ihry et al., 2018). To overcome this, lines of stable hPSCs were used with the CRISPR-cas9 delivery system in mice in hopes of increasing that efficiency. This method produced an efficiency rate higher than 80%. Despite this produced higher efficiency rate, only a few of the hPSCs actually survived. What had happened? Ultimately, the initiation of this experiment took a different turn as CRISPR-cas9 had caused the amount of these cells to go down killing them off. Due, to this toxicity that CRISPR-cas9 had induced in these cells, researchers decided it was imperative to now study the reason for the toxicity of the system in detail.

To further this mechanism of experimentation, high content imaging and analysis of a concept called, DSB (double-stranded DNA breaks), which are lethal to cells, was induced with the CRISPR-cas9 system. Through this process, cells showed an increase in DNA damage and apoptotic (self-killing) proteins (Ihry et al., 2018). This indicates that CRISPR-cas9 had a higher toxic response to DSBs. The researchers cited causal reasoning algorithms to consistently identify P53 (a tumor suppressor gene that is important in a cell in order to suppress the development of cancer), as one of the top-ranking hypotheses for this. "As these hypotheses are tightly interconnected, further investigation was focused on P53 because of its well-established role in the DNA damage response" (Ihry et al., 2018). Then, through another analysis method, these DSBs induced by CRISPR-Cas9 were shown to have an order of magnitude, triggered a P53-dependent toxic response that reduces the efficiency of engineering (Ihry et al., 2018). "Several groups have demonstrated that multiple cuts induced by Cas9 causes death in transformed cells. The heightened P53-dependent toxic response provides an explanation for the long-standing observation that hPSCs have inefficient rates of genome engineering" (Ihry et al., 2018).

CRISPR-cas9's Toll on Healthcare Inequality

To show how the CRISPR-cas9 technology will heighten the current trends of healthcare inequality in our current healthcare system, I decided to utilize the quantitative design of correlational research. Having been recently established in 2012, CRISPR-cas9 is eminently new so the research and data on its application in the clinical setting isn't yet available as it 'legally' remains in clinical trials around the world. In order to combat this, I decided to research for any current medical treatments/procedures currently on the market and in use that had a similar market cap as CRISPR-cas9. My research led me to treatment procedure of chemotherapy. Chemotherapy, established in the mid-20th century, is a chemical drug treatment to kill fast dividing cells (cancerous cells) in the body. It works by interfering with a cancerous cell's ability to replicate, grow, and divide (DNA replication and mitosis). The production cost of the drugs associated with the chemotherapy treatment is roughly $2.7 billion dollars and isn't too far off the production cost of CRISPR-cas9 therapeutics which estimates to around $3 billion dollars (Speights, 2018). Given this slight difference in the production costs of the two, I wanted to see how an already expensive treatment similar in price to CRISPR-cas9 imposes an expense that those of lower income can't afford. My pinnacle goal is to be able to show that if this current treatment is already difficult to afford, CRISPR-cas9 will only do the same and with the advanced techniques it proposes will be unfair to the latter.

To do this, I will as previously stated use the production cost of chemotherapy drugs as a baseline to see how much it has been out on the market for and what patients currently end up paying for it out of pocket. These expenses will be accounted for on a monthly basis along with the total cost on a yearly basis. From there, I will consider the median household income against

the rising costs of these cancer drugs that current research shows. Then, I will look at the national spending on healthcare by income in 2004 and the increasing trend of that data currently. The premise of research for this set of quantitative data will give me the superficial, predicted cost of CRISPR-cas9 when it officially hits the market in later years to attain my pinnacle goal.

Results

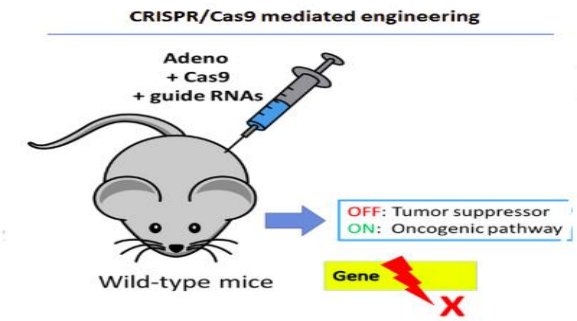
Dangers of CRISPR-cas9 Experiment

While the experiment started as means to increase efficiency in human pluporient stem cells, it would turn into an experiment to demonstrate the problem with the CRISPR-cas9 system. Results of this experiment shows, the toxic response to the CRISPR-cas9 system has important overtones for hPSC-based therapies (Ihry et al., 2018). Moreover, the results of this experiment also unveils with the use of the CRISPR-cas9 system in the mice," P53 inhibition could alleviate toxicity; but it has the potential to increase off-target mutations and poses a risk for cancer" (Ihry et al., 2018). This is because when CRISPR-cas9 worked to increase the efficiency rate of hSPC cells, the p53 inhibition meant that p53 (tumor suppressor) was turned off allowing for this mutated oncogenic (development of cancer) pathway to proceed/occur and thus further raising these concerns (figure 3). This is with the premise, that as previously stated, p53 is essential in suppressing the development of cancer and if it isn't working, is the CRISPR-cas9 system truly efficient?

The researchers of this experiment don't believe so. While not fully discrediting the system, they do believe the results of the experiment can be used to justify that CRISPR-cas9 is

deplorably inefficient. Noted earlier in the experiment, while CRISPR-cas9 did increase hSPC cells' efficiency 80%, it was only a small amount of the cells and killed off other cells utilized in the experiment. Conclusively, the researchers of this experiment state "as hPSC-based cell therapies using genome-edited cells move into the clinic, it will be critical to ensure that patient cells have a functional P53 before and after engineering" (IIhry et al., 2018). Other cell based therapies that utilize CRISPR-cas9 will need to also be monitored occur. While this may be an inconvenience to the CRISPR-cas9 system, it is a measure that will have to be taken before using it on humans.

Figure 3



Source: Rebecca Todd, University of Iowa (2018)

CRISPR-cas9's Toll on Healthcare Inequality Correlational Research

The baseline aspect of data I found yielded that chemotherapy treatment drugs had a production cost of $2.7 billion with CRISPR-cas9 not far behind with a $3 billion production cost. Looking back from 2010 to currently, the monthly estimated out of pocket cost for patients

for chemotherapy was between $10,000-$14,000 and varied within these ranges depending on what the specific treatment drugs the patient was receiving (table/figure 4). Additionally, the variance in price would also occur depending on the level dosage that each patient receives. From there, the yearly (2010 to current) estimated out of pocket cost for patients was anywhere from $120,000-$168,000 (table/figure 4). It is important to note that delineating from these average costs, there have been specials cases in chemotherapy treatments where a patient could end up paying more than $400,000 in treatment costs and beyond. Knowing this, the monthly and yearly out of pocket costs for CRISPR-cas9, will most likely be within these same ranges and if not more.

To accurately quantify the monthly cost of these cancer drugs, the median monthly cost and median monthly household income was found utilizing data from Nature Reviews' Clinical Oncology team. Their results observed this data from 1975 to 2014. Starting with 1975 each median monthly cost of cancer drugs and median monthly household income was averaged out between a four year time span (table/figure 5). To account for current data, I researched the median average cost of cancer drugs from 2015-2018 according to the American Cancer society website. To find the median household income I utilized Nature Reviews Oncology Team's method. Moreover, using the United States Government Census, I attained the median household income for 2015, 2016, 2017, and 2018 respectively. Adding all these numeric together and then dividing the sum of these numbers by 12 (for the total month in a year), I acquired the median household income for 2015-2018 (table/figure 5). In order to visualize the resulting trends of this data, I inputted all of the data information from table/figure 5 onto a google spreadsheet to be uploaded on a graphing software (Datawrapper). The graph that stemmed from this process shows the median monthly cost of drugs continues to rise yearly and skyrocketed this way in the

early 2000s (figure 6). As these drug prices rise yearly, the median household income of Americans has continuously remained below these drug prices except for 1975-2000 when the drugs first hit the market at a cheaper price (figure 6).

Having knowledge of this data, I wanted to see how those of lower income families specifically are affected by these rising drug costs given the median monthly household income already falls below it. While this specific data could not be found, a national, by income quintile spending on health care statistical data generated by Health Affairs.org in 2004 was utilized to note a probable similar trend. In detail, the table displayed the total average of all incomes and broke it down to incomes of the lowest, 2nd, 3rd, 4th, and highest income quintile (table/figure 7). From the income of each category, the average out of pocket cost spent on healthcare was indicated along with percentage of each quintile's income that went into healthcare spending (table/figure 7). What the results of this chart shows is "families in the lowest income quintile were contributing more than one-fifth of their incomes to support health care spending, almost half of it through direct out-of-pocket payments, while families in all other quintiles were supporting health care spending with a higher family income with a small percentage of it even touched" (Ketsche et al., 2011). While this data is from 2004, this trend still accounts for current healthcare economic trends (Ketsche et al., 2011).

In brief, using a purely relative correlational research, CRISPR-cas9 similar in production cost to Chemotherapy will most likely exhibit a similar price tag as chemotherapy. This is shown as patients pay a high out of pocket cost for chemotherapy drugs across the board while their median monthly household income isn't enough to supplement these prices. Most significantly, of the national average income, people of the lowest income quintile, are shown to already spend more money on healthcare costs than all other higher income quintiles. As most, of their income

goes to typical healthcare costs, they won't be able to afford potential expense of CRISPR-cas9. This is again evident with not being able to afford the treatments of chemotherapy which affects already so many Americans. Thus, as CRISPR-cas9 presents a slightly higher price, it is bound to leave individuals of lower income further behind and/or widen the current economic disparity between rich and poor in our healthcare system. In the end, "you could find wealthy parents buying the latest offspring upgrades for their children. We could see the emergence of genetic haves and have nots, leading to even greater healthcare inequality than we already live with" (Walsh, 2016).

[Table/Figure 4]

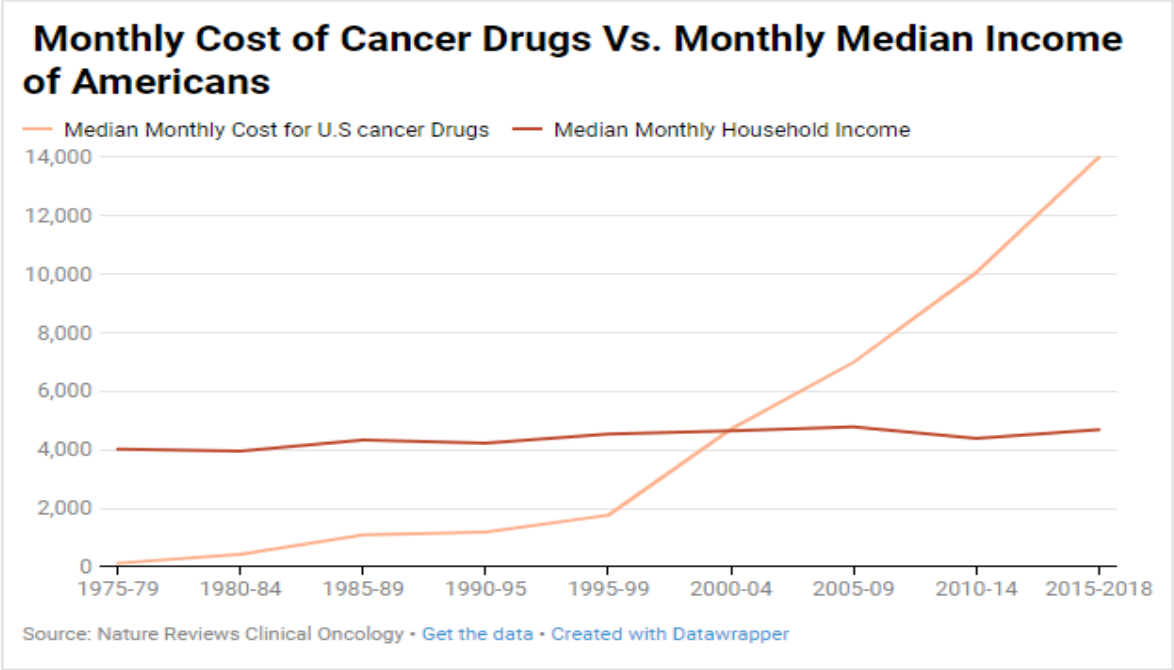
Medical Treatment/Procedure	**Production Cost**	**Monthly Estimated Out of Pocket Cost for Patients (2010-current)**	**Yearly Estimated Out of Pocket Cost for Patients (2010-current)**
Chemotherapy Treatment Drugs	$2.7 billion	$10,000-$14,000 (varies by specific treatment)	$120,000-$168,000
CRISPR-cas9 Therapeutics	$3 billion	?	?

[Table/Figure 5]

Year Span	**Median Monthly Cost of U.S Cancer Drugs**	**Median Monthly Household Income**
1975-1979	$129	$4,030.9

1980-1984	$430	$3,965.4
1985-1989	$1,097	$4,336
1990-1994	$1,199	$4,227.1
1995-1999	$1,770	$4,542.1
2000-2004	$4,716	$4,656
2005-2009	$7,000	$4,785.3
2010-2014	$10,059	$4,388.8
2015-2018	$14,000	$4,697.7

Figure 6



[Table/Figure 7]

Income And Spending On Health Care, Nationally And By Income Quintile, 2004

	Income		Out of pocket	
Income group	Average ($)	% of total	Average ($)	% of income
Nationally, all incomes	78,038	100	1,701	2.2
Quintile				
Lowest	13,450	3	1,378	10.2
2nd	34,712	9	1,657	4.8
3rd	56,439	14	1,837	3.3
4th	87,908	23	1,759	2.0
Highest	197,684	51	1,873	0.9

Source: Health Affairs.org, 2011

(Ketsche et al., 2011)

Discussion (Limitations, Solutions, & Future Prospects)

Having now established and substantiated evidence about two of the most significant ethical issues of the CRISPR-cas9 including the dangers/perils of the system and the adverse effect it will have on socioeconomic trends, there are various ways to address these pitfalls. To address, the dangers/perils of the system, scientists have recently proposed adding a switch mechanism to it. The continuous cutting mechanism that CRISPR-cas9 has is one of the biggest proponents that allowed for it to cause the mutation of the cancer suppressor gene in mice. Having a switch mechanism would allow CRISPR-cas9 to only be turned off until it reaches the target site where then and only will it be turned on to go working (Liu, 2019). This would help to decrease the potential of affecting normal, healthy cells that may be around the cell of interest. As a result, you wouldn't have normal cells turning cancerous as shown with the experimentation on the mice. By adding this switch, the CRISPR-cas9 system would justifiably be moving in the direction of a much safer application in the future. In terms of addressing the inadvertent effects CRISPR-cas9 will have on socioeconomic trends, CRISPR-cas9 could first and foremost be much cheaper and affordable as some sources have argued it will be. We could also use an allocation system similar to that of the one which decides who gets kidney transplants among those on a waitlist. Specifically, we could use the aspect of this allocation system where patients who are able to get the CRISPR-cas9 procedure are observed on the basis on how urgent or in need they are of this procedure. This way people who get treated of certain diseases by CRISPR-cas9 aren't solely based on the income they have but rather of severity of disease. Perhaps, this would then tip the scales so we see an increase in genetically viable and healthy low income individuals. Although, truly/greatly addressing the effect CRISPR-cas9 will have on

socioeconomic trends will always remain tedious given how deep our healthcare system has fallen into the inequality gap and the many external factors that coincide with it.

Consequently, there are multiple limitations to both aspects of my methodology utilized in my research for this paper. For the dangers of CRISPR-cas9, it must be noted that these results represent an early onset and stage of the CRISPR-cas9 research as the system remains in clinical trials currently. This means there is plenty of time for adjustments and fixations to be made accordingly before it ever hits the markets. Furthering on, I only utilized the perspective and results of only one experiment that actually showed the indirect cause of cancer in mice. Some outside proponents have argued that that the inhibition of the tumor suppressor gene wasn't significant enough to discredit CRISPR-cas9 in this preliminary stage. Continuously, the limitations of the effect of CRISPR-cas9 on socioeconomic trends was the limited data on it currently. As previously stated, as it has not been 'legally' tested in the clinical lab setting, there wasn't data to accurately suffice my findings. From there, having to use a correlational research methodology to generalize the economic toll of CRISPR-cas9 may be flawed and could have incurred several errors. Lastly, it must be known that correlation does not equal causation. It may be that chemotherapy is on the market right now for a similar production price to CRISPR-cas9 and comes at a high expense; but CRISPR-cas9 may end up doing the opposite of these chemotherapy treatment drugs and may be given at much cheaper prices in the future to come, maybe even alleviating the health care inequality gap.

The prospect of the future of medicine is CRISPR-cas9 as the answer to several diseases and unknowns we still hold in medicine. If we could address both these issues and fix the limitations CRISPR-cas9 currently upholds, it would help to better shape the stature and impact it will bring to medicine in a positive way. After all, it is the promising future/hopes we have for

medicine; and as the biochemist Isaac Asimov once said “the advance of genetic engineering makes it quite conceivable that we will begin to design our own evolutionary progress” (Shukla, 2019).

Citations

Belluz, Julia, “Is the CRISPR baby controversy the start of a terrifying new chapter in gene editing?” Vox.com, Jan. 2019, ttps://www.vox.com/science-and-health/2018/11/30/18119589/crispr-gene-editing-he-jiankui

Doudna, Jennifer, “Chinese Scientist Says He's First To Create Genetically Modified Babies Using CRISPR”, Jan 2018, https://www.wbur.org/npr/670752865/chinese-scientist-says-hes-first-to-genetically-edit-babies

Ihry et al., “p53 inhibits CRISPR–Cas9 engineering in human pluripotent stem cells.”

Nature Medicine, 2018, https://www.nature.com/articles/s41591-018-0050-6.epdf?no_publisher_access=1&r3_referer=nature

J. S., Schiller, J. W. Lucas, and J. A. Peregoy, "Summary Health Statistics for U.S. Adults: National Health Interview Survey, 2011." Vital and Health Statistics 10, no. 256 (2012): 1–207, tables 1, 4, 8, and 12. http://www.cdc.gov/nchs/data/series/sr_10/sr10_256.pdf.

Ketsche, Patricia, Adams, Kathleen, Kannan, Harini, Kannan, Viji Diane, Wallace, Sally "Lower-Income Families Pay A Higher Share Of Income Toward National Health Care Spending Than Higher-Income Families Do." Health Affairs, Sept. 2011, www.healthaffairs.org/doi/full/10.1377/hlthaff.2010.0712.

Kozubek, Jim. "Who Will Pay for CRISPR?" STAT, STAT, 23 June 2017, www.statnews.com/2017/06/26/crispr-insurance-companies-pay/.

Krisberg, Kim. "Income Inequality: When Wealth Determines Health: Earnings Influential as Lifelong Social Determinant of Health." *The Nation's Health,* American Public Health Association, 1 Oct. 2016, thenationshealth.aphapublications.org/content/46/8/1.1.

Labant, Mary. "CRISPR Jump starts Gene therapy," Pub.org, 2019, https://www.liebertpub.com/doi/pdf/10.1089/gen.39.04.20

Levien, Simon. "CRISPR in the Classroom by Simon Levien." *New Jersey Science Teachers Association*, 2017, www.njsta.org/news/crispr-in-the-classroom-by-simon-levien.

LicholiI, Greg. "Is CRISPR Worth the Risk?" *Yale Insights*, 16 Jan. 2019, insights.som.yale.edu/insights/is-crispr-worth-the-risk.

Liu, Angus. "Adding a 'Switch' to Cas9 to Make CRISPR Gene Editing Safer." FierceBiotech, 11 Jan. 2019, www.fiercebiotech.com/research/adding-a-switch-to-cas9-to-make-crispr-gene-editing-safer.

Mack, Marck. "What Drives Rising Health-Care Costs?" *Gfoa.Org*, 2016, www.gfoa.org/sites/default/files/GFR081626.pdf.

Mandal, Ananya. “Gene Therapy History.” *News*, 27 Feb. 2019, www.news-medical.net/health/Gene-Therapy-History.aspx.

Mukherjee, Siddharta, “The Gene: an Intimate History.” The Gene: an Intimate History, Large Print Press, a Part of Gale, Cengage Learning, 2017, pp. 49–52.

NIH.gov. “Novel Gene-Editing Method Improves Vision in Blind Rats.” *National Institutes of Health*, U.S. Department of Health and Human Services, 13 Dec. 2016, www.nih.gov/news-events/nih-research-matters/novel-gene-editing-method-improves-vision-blind-rats.

NIH.gov. “What Are Genome Editing and CRISPR-Cas9? - Genetics Home Reference - NIH.” *U.S. National Library of Medicine*, National Institutes of Health, 2019, ghr.nlm.nih.gov/primer/genomicresearch/genomeediting.

NYU LANGONE HEALTH. “GENETIC EDITING: ETHICAL AND SOCIAL ISSUES.” *NYU.edu*, 2018, med.nyu.edu/highschoolbioethics/sites/default/files/highschoolbioethics/Genetic%20Editing%20Module.pdf.

Rodriguez, Clin. “Ethical Issues in Genome Editing Using Crispr/Cas9 System.” *Longdom*, 2016, www.longdom.org/open-access/ethical-issues-in-genome-editing-using-crisprcas9-system-2155-9627-1000266.pdf.

Shukla, Ishani Chatterjee. “Types of Genetic Engineering.” BiologyWise, BiologyWise, 2019, biologywise.com/types-of-genetic-engineering.

Speights, Keith. “CRISPR Therapeutics Stock History: The Rise of the World's Biggest Gene-Editing Biotech.” *The Motley Fool*, The Motley Fool, 16 July 2018, www.fool.com/investing/2018/07/16/crispr-therapeutics-stock-history-the-rise-of-the.aspx.

Todd, Rebecca, University of Iowa “Dodd Lab.” *Research | Dodd Lab*, 2018, dodd.lab.uiowa.edu/research.

Walsh, Fergus. “Gene Editing Technique Could Transform Future.” *BBC News*, BBC, 6 June 2016, www.bbc.com/news/health-36439260.

Whatisbiotechnology.org. “What is CRISPR-cas9?” *Whatisbiotechnology, 2019,* http://www.whatisbiotechnology.org/index.php/science/summary/crispr.

AP® RESEARCH
2019 SCORING COMMENTARY

Academic Paper

Note: Student samples are quoted verbatim and may contain spelling and grammatical errors.

Sample: H
Score: 2

This paper earned a score of 2 because the paper is reporting on existing knowledge rather than new knowledge. On page 1 the paper establishes the topic (The purpose of this paper, two significant issues...) as the negative effects of CRISPR and gene editing. There is a narrowing scope, but the focus is not carried through the paper. The paper shifts from the costs of gene editing to the costs of chemotherapy.

This paper did not earn a score of 1 because it does have a narrowing topic of inquiry. There is a stab at a research method that is oversimplified and misaligned (pages 9–12). In the results section the paper continues to discuss components of its method, but that does little to make the method reasonably replicable. The paper's new understanding is not supported by evidence. Although the paper does have a mixture of scholarly and unscholarly sources, they are loosely connected (pages 6–9).

This paper did not earn a score of 3 because the research is not replicable; a variety of relevant scholarly perspectives is not represented, and the writing is less than competent.