CRISPR-Cas9 in America

the national landscape of gene editing technology

By Carson Viggiano

PREFACE

The Food and Drug Administration's approval of human CRISPR-Cas9 clinical trials in 2017 opened the door to a revolutionary new world of gene editing technology. CRISPR allows for the modification of genes by altering DNA base pair sequences, and holds the potential to treat genetic diseases that, up until this point, have been outside the reach of medicine. In theory, CRISPR could allow researchers to edit out diseases completely—effectively eradicating them. While the technology holds great scientific and medical potential, it has garnered political contention of equal magnitude, and now must navigate a tumultuous national landscape in an attempt to reconcile this divide. For no inconsequential reason is CRISPR-Cas9 a highly polarizing topic. The ethical considerations surrounding the possibility of its misuse are not to be taken lightly. Inherent in this technology is the potential to enable a new-wave eugenics movement.[1] The question, thus, becomes one of setting limitations. May the words of author Hannah Arendt remind us of the deep relationship between ability and

[1] Robert Pollack, (2015, May 22), Eugenics lurk in the shadow of CRISPR," *Science*, https://www.science.org/doi/10.1126/science.348.6237.871-a.

Scaffold is a digital collection of first-year writing curated by the Vanderbilt Writing Studio. To highlight the developing writing processes and learning experiences central to the growth of new college writers, the collection pairs each piece with a recorded reflection from its author. Visit *Scaffold*'s website to listen to the authors reflect, learn more, and tap into this resource for college students and instructors alike.

ethicality. Informed by her years in Nazi-controlled Germany that increased her familiarity with eliminatory eugenics ideology, she remarked: "If it should turn out to be true that knowledge (in the modern sense of know-how) and thought have parted company for good, then we would indeed become helpless slaves, not so much of our machines as of our know-how, thoughtless creatures at the mercy of every gadget which is technically possible, no matter how murderous it is."[2]

CRISPR-Cas9 was not born out of the malicious creative intent to genetically execute bigoted notions of racial, ethnic, religious, and socioeconomic hierarchy. It holds this power nonetheless, and so is potentially dangerous for this very reason. Public input on the ethicality of this technology is critical in determining limitations of design, experimentation, and use. Before this can happen, the highly-technical information that clouds CRISPR-Cas9 must reach the public in an accessible and understandable way. How is it reasonable to expect commentary from citizens on the ethics of science they do not understand? It simply is not. Here arises a dilemma: citizens' informed opinions are critical to regulating science, but are absent to date. Establishing a greater social dialogue surrounding scientific and technological innovation is absolutely critical. But first, the American public has to understand CRISPR—its successes, failures, uses and misuses alike.

EDUCATION AND AN INFORMED PUBLIC

CRISPR is possibly one of the most futuristic and controversial discoveries presented to Americans. It is simply

[2] Gertrud Sandqvist, (2009, April 29), Art and Social Democracy," *Afterall*, https://www.afterall.org/article/art.and.social.democracy.

not acceptable for the public to blindly accept the enthusiasm and reassurance of scientists pursuing the title of "visionaries." Despite promises of its safety and efficacy from the researchers, companies, and agencies, it is a relatively new and unexplored technology. CRISPR-Cas9 is still overwhelmingly experimental, if not conceptual. Ambiguities inhibit its advancement. Medical efficacy and controllability are points of contention. So too are questions concerning the ethics of gene editing. To this end, CRISPR demonstrates, on a major scale, a truth that applies to scientific endeavors as a whole: the component of ethical review is not restricted to the researchers who carry out experiments. Nor is it relegated to the greater scientific community. Politicians and the public alike have a right and an obligation to participate in ethical debates of scientific innovation. Yet, in the sea of technical jargon, it is exceedingly difficult for non-scientists to truly comprehend the necessary vernacular. The conceptual elements here at play are even less attainable. Without understanding the lexicons that enable these technologies—terms like guide RNA, endonucleases, and base sequencing, in the case of CRISPR-Cas9—the processes they describe remain abstract.

The past 50 years have made the concerns of advanced scientific advancements become a public concern, as opposed to one solely of the scientific and medical communities. CRISPR is no exception. Reports indicate that more than 48% of American adults are familiar with the technology, while 9% report knowing "a lot."[3] Altogether polling at over 50%, the

[3] Associated Press, (2016, July 26), U.S. public opinion on the future use of gene editing," *Pew Research Center*, https://www.pewresearch.org/science/2016/07/26/u-s-public-opinion-on-the-future-use-of-gene-editing/.

population's widespread awareness serves as a testament to the deepening integration of scientific innovation and public life. However, while CRISPR is widely recognized in social and political spheres across the country, there is minimal understanding of the technical processes that enable the technology. CRISPR is a name, an idea—something Americans readily form opinions about, without actually understanding its mechanics.

Language plays a large role in this disconnect—it is unrealistic to expect citizens to understand the elaborate technical vocabulary used by scientists. The grim reality of public science education in America further contextualizes the public's poor understanding. Only 28% of the public ranks as "scientifically literate"; the term is defined by correctly answering 20 of 31 concepts similar to those published in science sections of newspapers such as the New York Times.[4] Communicating the processes of the technology is critical to accurately informing and educating the American public. Clearly defining the lexicon and mechanisms allows science—particularly its new and unfamiliar ideas—to become a part of social dialogue beyond meaningless names. Uninformed opinions do not contribute much to discussions about the ethics of the science. Rather, it is the prudence of which Hannah Arendt spoke that promises to keep misappropriations of the technology at bay.

SAFETY, EFFICACY, AND RELIABILITY

[4] Associated Press, (2007, February 27), Scientific Literacy: How Do Americans Stack Up?" *Michigan State University*, https://www.sciencedaily.com/releases/2007/02/070218134322.htm.

CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. With respect to CRISPR-Cas9 in particular, the system of gene editing relies on the Cas9 endonuclease and a guide RNA (gRNA). Cas9 is the component that physically alters the DNA base pair sequencing, acting like the deletion key. gRNA is the molecule that finds and indicates the section of DNA that Cas9 will alter. The operation of gene editing can occur in any of three ways—disruption, deletion, or correction/insertion. Disruption effectively inactivates a section of DNA without removing it. Deletion, alternately, is a method that physically removes the faulty fragment of DNA. The two "bookend" segments fuse together upon removal. Often this method is preferable when targeting larger sections of DNA. Lastly, correction, or insertion, is a way of repairing a segment of faulty genes, or even inserting new genes. A valuable way to conceptualize the interactions between these processes is to say that they are pausing, deleting, and rewriting the DNA, respectively.[5]

CRISPR is revolutionary in its potential to prevent, treat, and even cure genetic diseases. Sickle cell disease, β-thalassemia, cystic fibrosis, blindness, muscular dystrophy, Huntington's disease, HIV, and cancer are potential targets for highly-receptive treatment via CRISPR-Cas9.[6] However, the efficacy and timeline of the technology are still unknown. Intellia CEO John Leonard hopes the technology will be commercially available "very, very soon," yet fails to specify a projected release year. A decade, at the very least, is realistic for

[5] Associated Press, (n.d.), CRISPR/Cas9," *CRISPR Therapeutics*, http://www.crisprtx.com/gene-editing/crispr-cas9.

[6] Clara Rodríguez Fernández, (2021, September 09), Eight Diseases CRISPR Technology Could Cure," *LabioTech.eu*, https://www.labiotech.eu/best-biotech/crispr-technology-cure-disease/.

the kind of refinement necessary to make the technology publicly available.[7] To date, only 19 people have been treated using CRISPR. Moreover, blood disorders have been the sole subject in clinical trials, with all 19 of these patients diagnosed with either sickle cell disease or β-thalassemia.[8] The treatments seem to be effective, although only by qualitative and not quantitative standards. Patients with sickle cell disease have not reported experiencing typical episodes of pain, and those with β-thalassemia have not since needed blood transfusions.

Despite the apparent success of CRISPR-Cas9, there are multiple issues that demand attention. High risk and contraction of infections accompanied painful and lengthy treatments. A small clinical sample size fails to reflect larger-scale efficacy. Long-term success and side effects are unknown, with treatments ending as recently as late 2020.[9] These doubts are not to deny the potential CRISPR-Cas9 holds, but rather to underscore the overwhelming uncertainty that clouds the technology. Concerns regarding the medical efficacy and safety of CRISPR-Cas9 are not only relegated to its long-term effects. The predictability of each experiment or treatment has also proven problematic in recent years. A 2020 study at Columbia University found that CRISPR made unintended changes in the chromosomes of human embryos.[10] Of 40 embryos fathered by

---

[7] Ian Thomas, (2021, July 02), CRISPR gene-editing treatment could reach patients very, very soon : Intellia CEO," *CNBC*, https://www.cnbc.com/2021/07/02/crispr-gene-editing-could-reach-patients-very-soon-intellia-ceo.html.

[8] Heidi Ledford, (2020, December 08), CRISPR gene therapy shows promise against blood diseases," *Nature*, https://www.nature.com/articles/d41586-020-03476-x.

[9] Ibid.

[10] Amy Dockser Marcus, (2020, October 29), Crispr Gene Editing Can Lead to Big Mistakes in Human Embryos," *Wall Street Journal*,

a donor with colorblindness, scientists used CRISPR on 37 embryos (keeping three embryos for controls) in an attempt to edit out the mutation of the EYS gene located on chromosome six. The technology removed base pairs than what scientists had intended, and "about half" of the 37 embryos lost significant portions—or even the entirety—of chromosome six.[11]

What is an approximately 50% success rate reflects both the unreliability and unpredictability of the technology. These unintended edits have huge consequences when dealing with something as exigent as genetic sequencing. Even more a cause for concern, mistakes in CRISPR's performance have not been consistent; experiments are revealing that the expressions of its malfunctions are different each time.[12] It is exceedingly problematic for the technology to make different kinds of mistakes, each with different functions and effects. The variability alone causes a host of challenges for scientists to identify and correct the issue. These failures in medical safety—let alone efficacy of the procedures—demonstrate the scale of sheer conjecture that surrounds CRISPR-Cas9. The gene editing technology available today simply does not perform as it has been advertised. For the American public to form opinions about ethicality based on skewed portrayals of the science is fruitless and dangerous.

---

https://www.proquest.com/docview/2455567675?parentSessionId=3JorfD9RfwMGGEPCFim2afflSlbF%2BtnlePiRPlCnrpU%3D&pq-origsite=primo&accountid=14816.

[11] Ibid.

[12] Shaui Jin et. al, (2019, April 19), Cytosine, but not adenine, base editors induce genome-wide off-target mutations in rice," *Science*, 364(6437), https://www.science.org/doi/10.1126/science.aaw7166.

UNDERSTANDING THE THREAT OF EUGENICS AND MISUSE

Besides the lack of medical conclusiveness, questions of CRISPR's ethics surround its potential for misuse. By nature, the technology is enmeshed with America's history of eugenics. The gene editing enabled by CRISPR-Cas9 borders on the selective reproduction of the country's destructive eugenics movement. Equal to the technology's opportunity for disease treatment is the potential for "designer babies"—children with traits chosen selectively by the parents.[13] There is a very fine line between using CRISPR to edit out mutant genes with the potential to become active diseases, and choosing superficial traits like eye color, height, and intelligence. Even more dangerous, the distinction of what constitutes a "disease" that can be edited away. Disability advocates fear that CRISPR creates an opening for eugenics-like practices to resurface. Individuals with conditions like Down syndrome and Fragile X syndrome could become systemic targets of genetic modification.[14] While it may seem unimaginable that science could so blatantly enable this type of discrimination, it is a reality with which America is all too familiar. This type of disability-based eugenics was, at one point, not only practiced, but legalized. The 1927 ruling in *Buck v. Bell* upheld the Virginia Eugenical Sterilization Act, which sanctioned sterilizations of

[13] Henry T. Greely, (2021, April 21), Stanford s Hank Greely on CRISPR People and Designer Babies," *Stanford Law School*, https://law.stanford.edu/2021/04/21/stanfords-hank-greely-on-crispr-people-and-designer-babies/.

[14] Miranda Saunders, (2018, October 07), Disability Rights Activists Raise Concerns Over Genetic Editing for Autism," *The Globe Post*, https://theglobepost.com/2018/07/10/genetic-editing-autism-disability/.

those deemed "feeble minded" in state institutions.[15] On a broader scale, the decision affirmed the constitutionality of a state's right to forcibly sterilize "unfit" individuals. In all, 70,000 Americans were sterilized in the following seventy years.[16]

Selective genetic editing and forced sterilizations are not interchangeable, of course, but both play into the same hierarchical and eliminatory ideology. These practices pursue an ideal in which peoples' worth is contingent on their genetic and intellectual "competence"; and in which the failure to meet these imposed standards means eradicating the decidedly "inferior." The driving justification of the public good also bridges the two practices. *Buck v. Bell* advocated for sterilizations in the name of the "health of the patient and the welfare of society."[17] Proponents of CRISPR, similarly, argue that editing away conditions considered to be disabilities promises a better quality of life for those individuals. The seemingly-benevolent rationales for these procedures do not counteract or nullify their potential destructiveness.

Moreover, Novartis—another medical research and pharmaceutical company—is pricing CRISPR at about two million dollars per course of treatment.[18] Even if it were to be

---

[15] Associated Press, (n.d.), Buck v. Bell," *Oyez*, https://www.oyez.org/cases/1900-1940/274us200.

[16] Adam Cohen, (2016, March 07), The Supreme Court Ruling That Led To 70,000 Forced Sterilizations," *NPR*, https://www.npr.org/sections/health-shots/2016/03/07/469478098/the-supreme-court-ruling-that-led-to-70-000-forced-sterilizations.

[17] Associated Press, (n.d.), Buck v. Bell," *Oyez*, https://www.oyez.org/cases/1900-1940/274us200.

[18] Alison Irvine, (2019, December 16), Paying for CRISPR Cures: The Economics of Genetic Therapies," *Innovative Genomics Institute*, https://innovativegenomics.org/blog/paying-for-crispr-cures/.

made available to the public, only the wealthiest individuals could afford it. The economics of gene editing make plausible a genetically-designed class of rich Americans. The lower-income population, however, faces the brunt of generational and genetic health issues.[19] Classism thus threatens to exacerbate social inequality by withholding CRISPR from specific demographics. To this end, questions of ethics do not pertain only to the bio-physical effects of science technologies. They address ethicality and inequality as it relates to accessibility, economics, race, ability, and social well-being.

CRITICAL SCRUTINIZATION IN DETERMINING ETHICALITY

Proponents of CRISPR argue that gene editing would be restricted to a case-by-case basis. They claim the threat of eugenics and population manipulation is therefore a non-issue. However, it reflects a social desire to "fix" disabled and neurodivergent people, even when applied on an individual level.[20] Mental competency and informed consent are particularly pressing questions. Who decides whether someone can, or *will*, be treated via CRISPR-Cas9? Bodily autonomy rivals mental competence to declare self-determination. Once again, the shadow of eugenics looms near. Creating regulatory legislation demands particularly close consideration of these dilemmas. Even the FDA's mere approval of the first CRISPR

[19] Dave A. Chokshi, (2018, April 03), Income, Poverty, and Health Inequality," *JAMA Network | American Medical Association*, https://jamanetwork.com/journals/jama/fullarticle/2677433.
[20] Steven A. Farber, (2008, December), U.S. Scientists' Role in the Eugenics Movement (1907–1939): A Contemporary Biologist's Perspective," *National Center for Biotechnology Information*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2757926/.

human testing was met with heated opinions. Funding, similarly, is a highly controversial matter. It both reflects and informs the conclusions drawn about the ethics of any given technology. Bankrolling a project is essentially an endorsement of its field of study. In this way, the nation's perceptions of ethicality largely dictate federal involvement in research endeavors. Therefore, the administrations, organizations, and agencies that depend on public approval generally must adhere to the desires of their constituents. An unhappy public means poor approval ratings, lower budgets, and losing re-elections.

The federal government funds investigations and trials relating to CRISPR through the National Institute of Health. The Somatic Cell Genome Editing program—the first of its kind—launched in 2018 with a preliminary six-year budget of $190 million.[21] Between the 2011 and 2018 fiscal years, the NIH budget jumped by more than 21.9%to about 3.0834 billion dollars. At the peak of its growth, between 2014 and 2015, funding increased by a whopping 213.1%.[22] Expressions of growing concern have met the nation's continued support of gene editing research. In response, the government has devoted more of funding to analyses specifically concerning the ethics and regulatory procedures of the technology. The NIH established the Embryonic Stem Cell Research Oversight (ESCRO) Committee, in compliance with recommendations from the National Academies of Science Guidelines for Human

[21] Rachel Britt, (2018, January 23), NIH to launch genome editing research program," *National Institutes of Health*, https://www.nih.gov/news-events/news-releases/nih-launch-genome-editing-research-program.
[22] Tanya Samazan, (2019, January 04), Government Funding of CRISPR Research and Policy Changes," *Instrument Business Outlook*, https://instrumentbusinessoutlook.com/government-funding-crispr-research-policy-changes/.

Embryonic Stem Cell Research.[23] Yet, these reports are not readily available to the public, as they should be.[24] With taxpayer money funding the NIH, the American public has a right and responsibility to engage in conversation regarding CRISPR. Citizens hold a financial stake in the technology, and given that funding for research continues to increase, citizens must pay greater social and ethical attention.

CONCLUDING THOUGHTS

Scientific exploration is not only a matter of what is physically possible, but also what *should* and be brought safely into fruition. Even if CRISPR-Cas9 was unconditionally reliable—which it is not—the technology inheres within an ethical gray-zone. The ethics of research and experimentation are an integral, guiding force in the field. More importantly, questions of scientific ethics extend beyond the laboratory and into the universities, operating rooms, family houses and Congressional chambers. As discoveries and innovations continue to revolutionize the field, the seemingly impossible becomes tangible. Yet, the unfamiliarity of these advancements creates entirely new ethical considerations. Since its earliest successes, CRISPR has pushed the bounds of comfortable science. Public uncertainty equated to political uneasiness and frenzied funding strategy. Even today, CRISPR is a controversial and unresolved matter in the public eye. Conservative legislation and relatively meek budgets protect against political and economic tumult. CRISPR holds

[23] Associated Press, (2019, January 2019), NIH Intramural Embryonic Stem Cell Research Oversight (ESCRO) Committee," *National Institutes of Health | Office of Intramural Research*, https://oir.nih.gov/sourcebook/committees-advisory-ddir/nih-intramural-embryonic-stem-cell-research-oversight-escro-committee.
[24] Ibid.

tremendous potential for medical advancement as it also does for practices that mirror eugenics. It is unlikely that the debate surrounding its ethicality will find a definitive answer anytime soon; the highly polarizing nature of CRISPR technology may never allow for any real degree of absolutism. However, it is the combination of social and scientific hyper-vigilance that ultimately matters in properly regulating gene editing. Diligent review of scientific ethicality ultimately functions as a type of socio-political regulation that pursues the most benevolent form of research and innovation possible.

BIBLIOGRAPHY

Antonios, Nathalie and Raup, Christina. (2012, January 01). "Buck v. Bell (1927)." *The Embryo Project Encyclopedia*. https://embryo.asu.edu/pages/buck-v-bell-1927.

Associated Press. (n.d.)." CRISPR/Cas9." *CRISPR Therapeutics*. http://www.crisprtx.com/gene-editing/crispr-cas9.

Associated Press. (2019, January 2019). "NIH Intramural Embryonic Stem Cell Research Oversight (ESCRO) Committee." *National Institutes of Health | Office of Intramural Research.* https://oir.nih.gov/sourcebook/committees-advisory-ddir/nih-intramural-embryonic-stem-cell-research-oversight-escro-committee.

Associated Press. (2007, February 27)." Scientific Literacy: How Do Americans Stack Up?" *Michigan State University.* https://www.sciencedaily.com/releases/2007/02/070218134322.htm.

Associated Press. (2016, July 26)." U.S. public opinion on the future use of gene editing." *Pew Research Center*. https://www.pewresearch.org/science/2016/07/26/u-s-public-opinion-on-the-future-use-of-gene-editing/.

Britt, Rachel. (2018, January 23). "NIH to launch genome editing research program." *National Institutes of Health*. https://www.nih.gov/news-events/news-releases/nih-launch-genome-editing-research-program.

Chokshi, Dave A. (2018, April 03). "Income, Poverty, and Health Inequality." *JAMA Network | American Medical Association.* https://jamanetwork.com/journals/jama/fullarticle/2677433.

Farber, Steven A. (2008, December)." U.S. Scientists' Role in the Eugenics Movement (1907–1939): A Contemporary Biologist's Perspective." *National Center for Biotechnology Information.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2757926/.

Greely, Henry T. (2021, April 21). "Stanford's Hank Greely on CRISPR People and Designer Babies." *Stanford Law School.* https://law.stanford.edu/2021/04/21/stanfords-hank-greely-on-crispr-people-and-designer-babies/.

Irvine, Alison. (2019, December 16). "Paying for CRISPR Cures: The Economics of Genetic Therapies." *Innovative Genomics Institute*. https://innovativegenomics.org/blog/paying-for-crispr-cures/.

Jin, Shuai et. al. (2019, April 19). "Cytosine, but not adenine, base editors induce genome-wide off-target mutations in rice." *Science*. https://www.science.org/doi/abs/10.1126/science.aaw7166.

Ledford, Heidi. (2020, December 08).“ CRISPR gene therapy shows promise against blood diseases.” *Nature*. https://www.nature.com/articles/d41586-020-03476-x.

Lino, Christopher A., et. al. (2018, May 25). “Delivering CRISPR: a review of the challenges and approaches.” *National Center for Biotechnology Information*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6058482/.

Marcus, Amy Dockser. (2020, October 29). “Crispr Gene Editing Can Lead to Big Mistakes in Human Embryos.” *Wall Street Journal*. https://www.proquest.com/docview/2455567675?accountid=14816&parentSessionId=3JorfD9RfwMGGEPCFim2afflSlbF%2BtnlePiR PlCnrpU%3D&pq-origsite=primo.

Rodríguez Fernández, Clara. (2021, September 09).“ Eight Diseases CRISPR Technology Could Cure.” *LabioTech.eu*. https://www.labiotech.eu/best-biotech/crispr-technology-cure-disease/.

Pfeiffer, David. (1994). “Eugenics and Disability Discrimination.” *Disability and Society,* 9(4). https://www.independentliving.org/docs1/pfeiffe1.html.

Pollack, Robert. (2015, May 22). “Eugenics lurk in the shadow of CRISPR.” *Science*. https://www.science.org/doi/10.1126/science.348.6237.871-a.

Samazan, Tanya. (2019, January 04)." Government Funding of CRISPR Research and Policy Changes." *Instrument Business Outlook*. https://instrumentbusinessoutlook.com/government-funding-crispr-research-policy-changes/.

Saunders, Miranda. (2018, October 07). "Disability Rights Activists Raise Concerns Over Genetic Editing for Autism." *The Globe Post.* https://theglobepost.com/2018/07/10/genetic-editing-autism-disability/.

Thomas, Ian. (2021, July 02)." CRISPR gene-editing treatment could reach patients 'very, very soon': Intellia CEO." *CNBC*. https://www.cnbc.com/2021/07/02/crispr-gene-editing-could-reach-patients-very-soon-intellia-ceo.html.

Uddin, Fathema, Rudin, Charles M., and Sen, Triparna. (2020, August 07). "CRISPR Gene Therapy: Applications, Limitations, and Implications for the Future." *Frontier*. https://www.frontiersin.org/articles/10.3389/fonc.2020.01387/full.

Wu, Katherine J. (2020, October 31). "Crispr Gene Editing Can Cause Unwanted Changes in Human Embryos, Study Finds." *New York Times.* https://www.nytimes.com/2020/10/31/health/crispr-genetics-embryos.html.