

RESEARCH ARTICLE

The View from the Benches: Scientists' Perspectives on the Uses and Governance of Human Gene-Editing Research

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Abstract

The advent of human gene editing has stimulated international interest in how best to govern this research. However, research on stakeholder views has neglected scientists themselves. We surveyed 212 scientists who use gene editing in their work. Questions captured views on oversight and use of somatic and germline human gene editing for treatment, prevention, and enhancement. More respondents were supportive of somatic than germline editing, and more supported gene editing for treatment compared to prevention. Few supported its use for enhancement. When presented with specific conditions, levels of support for somatic editing differed by type of condition. Almost all respondents said scientists and national government representatives should be involved in oversight, but only 28% said scientists are best positioned to oversee gene-editing research. These results can inform the development of sound approaches to research governance, demonstrating the importance of identifying specific gene-editing uses when considering oversight.

Introduction

The advent of human gene editing has stimulated an explosion of international interest in how best to govern this research.¹ It has generated reports from organizations such as the U.S. National Academies of Science, Engineering, and Medicine (NASEM), professional societies, and international commissions calling for precautionary actions, including a moratorium on heritable gene editing, anticipatory public engagement, and pathways for responsible clinical translation.^{2–7} A critical ingredient of these research governance development efforts has been empirical research documenting the views of different stakeholder groups on the challenges involved. To ensure that the policies they develop are realistic and effective, scientific thought leaders, policy experts, and regulatory bodies depend on a robust understanding of the concerns, interests, and values of those affected by any policies they may develop. Most policy discussions to date have

focused on eventual clinical applications of the technology. So empirical stakeholder research has concentrated on the views of potential “downstream” users such as patients, clinicians, and the public.^{8–12} Particularly understudied in this stakeholder research are the views of scientists who use gene editing in their work. These scientists' views on gene-editing applications will influence their own translational research trajectories and thus will play an important role in establishing the technical foundations for and limitations of the types of human gene editing being contemplated by policy reports. For those involved in the ongoing efforts to develop responsible translational pathways for human gene-editing research, an empirical understanding of scientists' attitudes and goals will be critical to the development of policies that are grounded in research realities. Therefore, we surveyed U.S. scientists whose gene-editing work spans basic bench science to clinical trials. We investigated

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Table 1. Vignettes Describing Applications of Gene Editing

Vignette A: Preventing muscle wasting. The *MSTN* gene produces myostatin, a protein regulating muscle growth. Myostatin inhibition causes muscular hypertrophy and dramatic increases in strength. Gene editing has shown such muscle-enhancing effects in dogs. In patients with severe intrinsic muscle diseases, such as Duchenne muscular dystrophy, gene editing may have the potential to block the myostatin pathway to prevent muscle deterioration.

Vignette B: Preventing neurocognitive impairments. The *PDE4B* gene encodes an enzyme called phosphodiesterase-4B, which is present in the brain and other organs. Gene editing can be used to inhibit the activity of this enzyme. Mice who have received this type of gene editing were able to learn faster, remember events longer, and solve complex exercises better than mice who did not receive this gene editing. Editing *PDE4B* may have the potential to treat and prevent cognitive impairments caused by neurocognitive disorders.

Vignette C: Preventing obesity. The *MC4R* gene regulates food intake by signaling the feeling of being full. A loss-of-function mutation in just one allele of this gene can lead to constant appetite, obesity, and diabetes. Gene editing can be used to amplify the expression of the functional allele of this gene. Mice who have received this type of gene editing maintain up to 40% lower weight than their untreated counterparts. Editing *MC4R* may have the potential to prevent human obesity and its comorbidities.

their views regarding somatic versus germline gene editing for disease treatment and prevention, as well as enhancement. We examined whether scientists' general views on acceptability of human gene-editing applications shift when questioned about specific examples. Finally, we asked about gene-editing research governance. For those involved in the ongoing efforts to develop responsible pathways for human gene editing, our results add to previous reports of stakeholder views and to the development of sound approaches to research governance.

Methods

Survey instrument

We developed survey questions based on the literature on advances in gene editing, prior surveys regarding attitudes toward gene editing,^{9,12} and policy discussions focused on human gene editing.^{1,13} Questions were piloted with several genome scientists with knowledge of or experience with gene editing. Their feedback was incorporated into revisions.

The survey began with general questions regarding the use of somatic and germline human gene editing for disease treatment and prevention, as well as enhancement. We then introduced three hypothetical vignettes (Table 1) to examine views on using gene editing for different types of human conditions: *MSTN* for severe intrinsic muscle diseases (physical ability), *PDE4B* to address neurocognitive impairments (intellectual ability), and *MC4R* to target obesity (a perceived behavioral condition). Respondents were told to assume

that each type of gene editing was found to provide a safe and effective way to treat the condition in humans. They were then asked whether they thought somatic editing of the respective gene should be made available to (1) people with the condition (representing treatment), (2) people at risk for the condition (representing prevention), and (3) people not at risk for the condition (representing enhancement), as well as whether people with the condition should have access to germline gene editing for prevention of the condition in their offspring. The order of the vignettes was randomized for each respondent. Finally, respondents were queried about their perspectives on gene-editing oversight, including an open-ended question about scientists' ability to self-govern. The survey questions reported on in this paper are available in Supplementary Appendix A.

Selection and recruitment of respondents

Our respondent pool was comprised of scientists who were likely to be using gene editing in their work from 69 member institutions of the National Institutes of Health (NIH) Clinical and Translational Science Consortium in the United States. We conducted online searches of each institution's website, targeting departments and research centers that included genetics, translational research, biology, and bioengineering. Within each department or center, we searched faculty webpages using the terms "CRISPR" and "gen," the latter to find, for example, "gene editing," "transgenic," "gene enhancement," and "gene therapy." We verified that these words indicated likely use of gene editing in scientific research rather than, for example, the ethics of gene editing. Scientists whose work involved only gene editing with plants were excluded. We recorded the name and contact information of 1,009 scientists who met our search criteria and emailed them an invitation to take our anonymous Qualtrics survey. This study was reviewed by the Institutional Review Board at the University of North Carolina at Chapel Hill and was determined to be exempt.

Analysis

We examined item-response frequencies and percentages. We collapsed Likert scale responses for the analyses (e.g., "strongly support" and "somewhat support" became "support," and "somewhat oppose" and "strongly oppose" became "oppose"). Analyses were conducted in SAS v9.4 (SAS Institute, Inc., Cary, NC). Percentages that do not total 100.0 are due to rounding. We used McNemar's test to examine differences in the proportion supporting somatic versus germline gene editing for a specific purpose.

Results

We present respondent characteristics, and their views on somatic and germline human gene editing for different uses, using gene editing for different conditions, and on oversight.

Respondent characteristics

A total of 212 scientists completed the survey, representing a 21% response rate. Table 2 presents respondents' self-reported demographic characteristics. Almost three-fourths (72.7%) of the sample identified as men, and two-thirds (67.4%) identified as white. Respondents had a PhD (89.2%), MD (1.9%), or both (9.0%). The most common fields of study included molecular biology (20.4%) and genetics (18.0%). The most common type of gene-editing work included nonhuman animal editing for basic or translational research (49.9%).

Views on different types of human gene-editing uses

Table 3 presents levels of support for different types of somatic and germline human gene-editing uses. For each type, more respondents supported somatic than germline gene editing, and these differences in support were statistically significant using McNemar's test. All respondents were supportive of using somatic gene editing for preclinical research, and 87% were supportive of using germline editing for preclinical research. Most supported using somatic gene editing to treat or prevent disease (91% and 80%, respectively), while less than half supported using germline editing to treat or prevent disease (44% and 40%, respectively). Yet, for both somatic and germline editing, respondents were only slightly more supportive of using gene editing for *treatment* of disease compared to *prevention*. There was minimal support for using somatic or germline gene editing to improve physical or intellectual abilities for non-medical purposes in healthy people (<10%). Across all types of uses for somatic and germline editing, there were no statistically significant differences between respondents whose work includes human gene editing and those whose work does not.

Views on using gene editing for different conditions

When asked in the vignettes about gene editing for specific conditions, support differed by treatment, prevention, and enhancement, and by the type of condition (Table 4). Across the vignettes, there was strong support for allowing people who have the disease to use somatic gene editing for treatment, less support for allowing people at risk of the disease to use somatic editing for prevention, and even less support for allowing people who have the disease to use germline editing for their offspring. Virtually all respondents opposed using somatic gene editing for people not at risk of disease, that is, for enhancement purposes.

Table 2. Demographics (N = 212)

	Frequency	Percentage
Self-reported gender		
Men	152	72.7%
Women	56	26.8%
Other	1	0.5%
Self-reported race/ethnicity ^a		
American Indian, Native American, or Alaska Native	1	0.5%
Asian	44	20.5%
Black or African American	4	1.9%
Native Hawaiian/Pacific Islander	1	0.5%
White or European American	145	67.4%
Middle Eastern or North African/Mediterranean	6	2.8%
Hispanic/Latinx	8	3.7%
Other	6	2.8%
Degree		
MD	4	1.9%
PhD	189	89.2%
MD/PhD	19	9.0%
Degree field ^a		
Biochemistry	46	11.3%
Biology	43	10.6%
Cell biology	51	12.6%
Engineering	7	1.7%
Genetics	73	18.0%
Immunology	20	4.9%
Medicine	25	6.2%
Molecular biology	83	20.4%
Neuroscience	9	2.2%
Physiology/biophysics	8	2.0%
Virology	15	3.7%
Other	26	6.4%
Year of degree completion		
1960–1969	3	1.5%
1970–1979	13	6.4%
1980–1989	34	16.8%
1990–1999	44	21.8%
2000–2009	65	32.2%
2010–2019	43	21.3%
Type of gene-editing work ^a		
Human gene editing <i>in vitro</i>	109	30.2%
Human gene editing in clinical application	17	4.7%
Nonhuman animal gene editing for basic or translational research	180	49.9%
Nonhuman animal gene editing aimed at improving animal health or creating better food supply for humans	16	4.4%
Gene editing pathogens, insect vectors, etc., to combat human diseases	19	5.3%
Plants or single celled organism gene editing	17	4.7%
Other	3	0.8%
Funding ^a		
International (e.g., EU funding)	2	0.4%
Federal	181	38.4%
State	35	7.4%
Commercial	27	5.7%
Private foundation	104	22.1%
Institutional	116	24.6%
Other	6	1.3%

Note: Percentages are of those who responded to each question.

^aRespondents could select multiple responses.

Table 3. Support for Different Uses of Somatic and Germline Human Gene Editing

How strongly do you support or oppose using [somatic/germline] gene editing for each of the following purposes?	Percent who somewhat or strongly support		McNemar chi square
	Somatic gene editing	Germline gene editing	
1. To conduct preclinical research (e.g., nonhuman animals, human cells)	100%	87%	27.0**
2. To conduct clinical trials in humans to test gene-editing therapies	88%	38%	105.0**
3. For treatment of disease in humans	91%	44%	98.0**
4. To prevent the onset or symptoms of disease in humans	80%	40%	82.0**
5. To improve physical abilities for non-medical purposes	8%	2%	13.0**
6. To improve intellectual abilities for non-medical purposes	7%	2%	9.0*

** $p < 0.001$; * $p < 0.01$.

Second, for type of condition, 98% endorsed making somatic gene editing available as a treatment for people who have severe intrinsic muscle disease, while the majority supported making it available to those with neurocognitive disorders (87%) or obesity (80%). Similarly, for disease prevention, almost two-thirds (71%) of respondents endorsed making somatic gene editing available to those at risk of severe intrinsic muscle disease, but just over half (54%) endorsed its use for people at risk of neurocognitive disorders, and slightly less (45%) endorsed using gene editing for people at risk of obesity.

This same pattern of support continued when the questions shifted to germline editing, although at a much lower level: support for germline editing in the offspring of people who have intrinsic muscle disease (39%) was higher than for people with neurocognitive disorders (27%) and people who are obese (19%). Lastly, very few respondents ($\leq 5\%$) supported making somatic gene editing available for people not at risk of severe intrinsic muscle disease, neurocognitive disorders, or obesity. There was no statistically significant difference in responses to the vignettes based on order the vignettes appeared.

Views on oversight

We asked respondents who should be included in decision making regarding oversight of gene-editing research, instructing them to select as many categories of people as they wished from a list. Almost all said that sci-

entists (96%) and representatives from national government offices such as the NIH or the Food and Drug Administration (95%) should be included (Table 5). When asked who respondents think is *best* positioned to perform the oversight, national government offices were selected by 48%. Only 28% said scientists themselves are best positioned to oversee gene-editing research.

We also asked whether scientists could oversee gene-editing research themselves. Nearly one quarter (23%) said yes, and three-quarters (77%) said no. Those who said “yes” were asked how they envisioned scientists overseeing gene-editing research themselves. Many wrote that they envisioned it taking place “through peer committees” made up of “diverse” scientists. Those who said “no” were asked why they think it is not possible for scientists to oversee gene editing themselves. Of those scientists, many cited “conflicts of interest.” They also said that “health and legal officials” or “experts in ethics” should be involved in oversight, as scientists do not have the training to “see the bigger social picture” or to “address and consider all ethical, financial, societal and political implications.” Others who said scientists could not oversee themselves countered that most actually *could* oversee themselves, but unscrupulous individuals present a problem. As described by one respondent, “I think the majority of scientists have the ability to self-police/self-assess gene editing, however as we’ve already seen, it sometimes only takes

Table 4. Support for Different Uses of Somatic and Germline Human Gene Editing Using Vignettes

In your opinion, should somatic [MSTN/PDE4B/MC4R] gene editing be made available to:	Percent who said definitely or probably yes		
	MSTN (intrinsic muscle disease)	PDE4B (neurocognitive disorders)	MC4R (obesity)
1. people who have the disease?	98%	87%	80%
2. people at risk of the disease?	71%	54%	45%
3. people not at risk of the disease?	3%	4%	5%
In your opinion, should individuals with [condition] have access to [MSTN/PDE4B/MC4R] editing in the germline for prevention of disease in their offspring?	39%	27%	19%

Table 5. Views on Oversight of Gene Editing Research

	<i>Who should be included in the decision-making process about the oversight of gene-editing research? (Select all that apply)</i>	<i>Who is best positioned to oversee how gene editing research should be conducted? (Select one)</i>
Industry representatives	35%	0%
International bodies (e.g., World Health Organization)	76%	15%
Lay people	48%	1%
National government offices (e.g., National Institutes of Health, Food and Drug Administration)	95%	48%
Patients and patient advocates	76%	1%
Religious officials	22%	0%
Scientists	96%	28%
University offices (e.g., Institutional Review Boards, Institutional Animal Care and Use Committees)	66%	6%
Other	6%	2%

one bad actor ... to undermine the entire process and any beneficial progress that has been made. I think we need regulation to make sure bad actors are watched over sufficiently.”

Discussion

Science policy literature on human gene editing calls for policy deliberations to stay “close to the actual science” in the sense of remaining evidence based and in engaging practicing scientists in the planning process.^{14,15} These admonitions reflect the fact that the trajectory of human gene editing will depend in large part on research decisions made by investigators in the field. Thus, the results of our survey offer important data for the ongoing gene-editing governance debates. Five sets of findings, detailed below, seem particularly significant in that regard.

First, our results reveal that more scientists are supportive of human somatic gene editing than germline gene editing, which aligns with results from a previous survey of human genetics professional societies.¹² This finding also aligns with studies of the public,^{10,16} with one exception: Scheufele *et al.* found little distinction between the public’s acceptance of somatic and germline editing,⁸ although their finding may illustrate that members of the public may not understand the differences between germline and somatic editing as others have noted.¹⁰ Despite advances in accuracy and efficiency

that seem to open the door to gene editing as an approach to human germline modification, the majority of scientists surveyed here continue to support this traditional boundary in clinical applications. Scientists *are*, however, supportive of preclinical germline gene-editing research, which may be a step in the pathway to human applications.

Second, attitudes toward different types of uses of gene editing reflect traditional distinctions between applications for treatment, prevention, or enhancement. For somatic and germline gene editing, few respondents supported its use to improve physical or intellectual abilities for non-medical purposes in healthy people. This result aligns with recommendations of policy bodies such as the NASEM and the International Commission that call for priority to be given to treating or preventing severe disease.^{6,7} And it echoes Armsby *et al.*’s finding that genetics professionals are more supportive of therapeutic uses of gene editing than enhancement,¹² as well as previous studies that have found the public to be more accepting of gene editing for treatment than enhancement.^{8–10}

Third, although our survey distinguished treatment and prevention as distinct uses of gene editing, we found little difference between levels of support of somatic gene editing for these two purposes. This conflation echoes the policy literature^{6,7} and suggests that the medical imperative to combat disease is strong enough to eclipse the ways in which treatment and prevention may differ as translational goals. Scientists’ willingness to embrace preventive goals for gene editing while distancing themselves from enhancement purposes raises a challenge, since in some cases the best way to achieve prevention for progressive or later-onset diseases may be to compensate for an anticipated vulnerability by enhancing another function.^{1,17} Like vaccinations against infectious disease, these preventive uses would be designed for otherwise healthy at-risk people before the onset of clinical disease and might “upgrade” otherwise normal traits. Therefore, they raise important questions about the scope of “prevention,” how “at risk” should be defined,¹³ and how to handle preventive interventions that convey social advantages, which in non-medical contexts would be treated as enhancements.¹⁷

Fourth, different levels of support across the three vignettes raise questions about the ways scientists think about treatment, prevention, and enhancement when contemplating practical applications of gene editing (Table 4). More respondents endorsed somatic gene editing for treatment than for prevention in all three cases. But levels of support for both treatment and prevention differed across types of conditions, with a large majority supporting gene editing for treatment or prevention of

intrinsic muscle disease, fewer supporting its use to treat or prevent neurocognitive disorders, and fewer still supporting its use to treat or prevent obesity. Additionally, while support for gene editing in individuals not at risk of the disease (i.e., for enhancement purposes) remained very low across the three cases, respondents' support of editing each gene in the germline varied in a similar pattern, with the most respondents supporting using gene editing for intrinsic muscle disease and the fewest supporting its use for obesity. Armsby *et al.* have commented that what constitutes a "therapeutic application" needs to be defined,¹² and our respondents echo that through their differential support across the three scenarios.

Finally, in terms of oversight, previous studies and most recent policy reports endorse a relatively democratic view of gene-editing governance, with considerable emphasis on the need for widespread public engagement.^{6-8,18,19} Some reports even suggest that crafting policy definitions for gene editing to operationalize such categories as treatment, prevention, or enhancement fall beyond the scientific community's purview altogether and should be left in large measure to "public dialogues" about the social values at stake.⁶ Although almost half of our respondents endorsed the inclusion of lay people in the development of gene-editing governance, and a majority endorsed including "patients and patient advocates," both groups received negligible support as the best positioned to oversee gene-editing research. Instead, respondents endorsed the scientific community and analogous sources of technical expertise such as national government offices. Yet, perhaps the most striking governance finding was the high proportion of respondents who did not think scientists were capable of self-governance. This lack of confidence marks an important shift from traditional understandings of scientific professionalism,²⁰⁻²² and was likely influenced by the 2018 revelations of Dr. He Jiankui's premature human germline gene-editing experimentation. However, other explanations for this caution should be explored as gene-editing research evolves.

Our survey has limitations. We only surveyed U.S.-based academic researchers. Future studies should explore the views of scientists outside of the United States and academia. Our survey had a 21% response rate, and it is impossible to know whether those who took our survey had different attitudes toward gene editing compared to those who did not take it. The survey was also administered in 2020 during the coronavirus pandemic, which means family obligations or other duties may have prevented some scientists from participating. Additionally, because the majority of our questions offered only closed-ended response options, there

is much to investigate with different research approaches about the reasoning behind scientists' support or opposition to various forms of human gene editing and its governance. Given the dearth of studies that include scientists who use gene editing, we believe our survey, despite its limitations, offers important findings.

Conclusion

This report is important for the ongoing development of human gene-editing research governance in three ways: (1) by amplifying the voice of the growing community of scientists who use gene editing in their work; (2) by illuminating the ways that different kinds of preventive gene-editing applications will complicate the traditional distinction between "treatment" and "enhancement" uses of human gene editing, exposing new governance challenges; and (3) by underlying the need to complement scientific professionalism with other forms of external governance in this domain. Our findings indicate one way forward within any governance strategy. While scientists who use gene editing in their work share the views of other stakeholders on the most appropriate goals for human gene-editing research, their views on where to draw the lines between different therapeutic, preventive, and non-medical applications vary across different cases. This raises important new questions about the considerations being deployed by scientists that take the discussion beyond the simplistic distinctions between "treatment" and "enhancement" that has characterized public discourse and policy in the past and suggests that, at least initially, decisions about oversight may need to be made on a case-by-case basis.²³ Without examining cases, policy makers may not recognize the nuances of what could or should be edited and why, or be able to assess levels of support adequately for gene-editing interventions.

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Supplementary Material

Supplementary Appendix A

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