OPINION

Toward inclusive global governance of human genome editing

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In recent years, many have considered how best to govern increasingly powerful genome editing technologies. Since 2015, more than 60 statements, declarations, and other codes of practice have been published by international organizations and scientific institutions (1). In particular, the 2018 birth of two twins, Lulu and Nana—whose HIV-receptors CCR5 were altered by biophysics researcher He Jiankui—triggered widespread condemnation from the scientific community, the public, and even legal institutions. Eminent organizations that have opined on the matter include the World Health Organization's Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (WHO committee) and the International Commission on the Clinical Use of Human Germline Genome Editing (the international commission).

When it comes to genome editing technologies, we need to acknowledge and account for very different points of view from researchers and regions around the world. Image credit: Shutterstock/vchal.

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To date, reports have expressed common concerns over various issues in the governance of human genome editing—for example, whether to impose moratoriums on basic research and clinical activities in human heritable genome editing. They have also agreed on some general actions, such as encouraging public input and implementing regulations on preclinical and clinical research in human heritable genome editing—in particular as it pertains to the transparent disclosure of experiments underway and the documenting of protocols and patient consent responsibly.

The ethical implications of genome editing seemingly exacerbate the divergent views among stakeholders, especially those with different cultural backgrounds, ideologies, religious views, and commercial interests.

But although most of the opinions, guidelines, and issues discussed in these reports are noteworthy and defensible, we argue that their effectiveness in guiding global governance is limited. Genome editing technology has grown too quickly, and stakeholders in the debate are too diverse, for current approaches to establish a robust, credible, and lasting regulatory regime. We need to acknowledge and account for very different points of view from researchers and regions around the world.

Seeking a Precedent

Existing governance mechanisms share features with the Asilomar statement in 1975, which is generally seen as providing effective regulation on recombinant DNA technologies (2). Features of that approach include 1) a governance body led by a commission of leading experts from one or a few countries and supported by several influential international and professional organizations; 2) proposed governance tools that are nonbinding; 3) guidelines implemented either through direct regulation and restraining the behaviors of the global research community, or having the guidelines absorbed into government regulations and funding agency policies.

Such a governance model has its merits. Indeed, a small group of leading experts can reach consensus quickly and effectively. And if academic journals and funding agencies adopt and adhere to such guidelines, scientists will follow. In such cases, the strong network of leading experts frequently allows guidelines they produce to influence government regulations (3). For instance, the final statement of Asilomar conference later served as a template for the future recommendation of the NIH Recombinant DNA Advisory Committee (4).

However, we are far from achieving a consensus on critical governing issues related to human genome editing at the global level, as illustrated by the divergence of existing guidelines (1). In the case of moratorium on heritable genome editing, for example, some guidelines (e.g., the one developed by European Group on Ethics in Science and New Technologies) suggested broad prohibition on "gene editing of human embryos or gametes which would result in the modification of the human genome" (5), whereas others (e.g., the one developed by the United States National Academies of Sciences, Engineering, and Medicine Committee) tentatively supported germline editing under certain specified conditions (6). Debate and critiques have continued, especially after the gene editing fiasco spearheaded by researcher He Jiankui (7).

Notably, diverse opinions emerged among the scientific community regarding the moratorium on heritable human genome editing. For instance, some leading scientists, such as Eric Lander (8), called for a global moratorium on clinical use of human heritable genome editing for a defined period of time to enable the development of international guidelines. In contrast, some prestigious researchers expressed objections to such a proposal, arguing that it would be open-ended in duration and could impede scientific research and delay the deployment of life-saving technologies for patients who cannot wait (9).

The global scientific community did engage in fierce debates on how to regulate recombinant DNA technology when the Asilomar statement was developed. However, the current landscape of human genome editing is very different. It renders a global governance model led by a small group of scientists and scientific organizations outdated and counter to an inclusive framework that encompasses views and opinions of a diverse set of stakeholders reaching both inside and outside of academia.

When the Asilomar statement was put forward in 1975, there were around 30 authors who had related scientific publications, far fewer than the 140 participants who attended the Asilomar meeting. Moreover, although the total number of authors grew to around 900 in 1978, more than 70% of their affiliated institutions are based in the United States. In other words, the recombinant DNA research community was much smaller and far less diverse, making it relatively easy for the Asilomar conference to reach a consensus and then convince others in the community to agree.

Today, the scientific community is very diverse geographically and culturally. Between 2012 and 2018, there were more than 8,000 publications on genome editing, carrying the names of more than 36,000 authors. Around 4,000 institutions across 94 countries/regions in all major continents are involved in the field of genome editing (see Table 1). The ethical implications of genome editing seemingly exacerbate the divergent views among stakeholders, especially those with different cultural backgrounds, ideologies, religious views, and commercial interests.

Survey Insights

To investigate further, we conducted a global online survey with the corresponding authors of human genome editing-related publications. We sent out questionnaires to 3,326 authors and received 201 validated responses. We do note limitations for our

Table 1. The global distribution of publications, countries/regions, institutions, and authors for recombinant DNA (1972–1978) and genome editing (2012–2018)

	Recombinant DNA				Genome editing			
	Publications	Countries/regions	Institutions	Authors	Publications	Countries/regions	Institutions	Authors
Africa	2	1	2	3	49	16	~40	~120
Asia	31	3	11	~90	2,932	28	~1,300	~12,000
Europe	121	10	~60	~250	2,367	33	~1,400	~9,300
N. America	335	3	~110	~580	4,093	7	~1,100	~15,000
Oceania	2	1	1	3	233	2	~110	~700
S. America	0	0	0	0	97	8	~90	~300

Publications in the areas of recombinant DNA and genome editing vary widely by region. For details on the search strategy implemented for this table, see the *SI Appendix*.

survey, including the potentially biased opinions of corresponding authors and a relatively low response rate (6%). Nevertheless, we gleaned some insights into researchers' attitudes toward current guidelines and their opinions regarding basic and clinical research of human somatic and germline editing and enhancement research. We also asked for their preference for global governance models in this field.

Specifically, we selected five representative governance guidelines developed by the most authoritative institutions and asked the scientists about their familiarity with these guidelines. Around 40% of the respondents said they had never heard of them, and less than 20% said they had read the guidelines in detail. More importantly, we find very different attitudes toward some crucial issues. For instance, around 30% of respondents wanted to see a moratorium on even basic research in the field. Some 56% disagreed with this idea, and 14% were neutral. There were important regional differences. For instance, scientists from North America and Europe were the least conservative and tended to disagree with imposing moratoriums. Those from Asia were more likely to take a neutral stand, whereas those from other regions (e.g., Africa and South America) were more conservative, tending to agree with the need for a moratorium.

For our part, we believe that a global moratorium is not warranted, but that it is necessary to impose certain restrictions on the research and on clinical trials directed at human genome editing. However, the question of when and how the restrictions should be implemented requires discussions on a global scale and consensus among a broad range of stakeholders from different regions.

That group of stakeholders includes many based in or working with the private sector, which makes the context for global governance quite different from that of the Asilomar period. In the 1970s, most of the scientists engaged in recombinant DNA research were working in public institutions; today, many scientists working in genome editing have conflicts of interest over intellectual property or act as advisors for commercial companies (10). These conflicts are not systematically declared in the guidelines they produce.

Involving the Public

Public engagement is also extremely important, as some existing efforts appreciate. For example, the international commission recommends that "extensive social dialogue should be undertaken before a country makes a decision on whether to permit clinical use of heritable human genome editing" and recognize the efforts by civil society on the global level "to promote international cooperation on approaches to responsible development" (11). We agree with the commission's suggestion that organizations like WHO and the United Nations Educational, Scientific and Cultural Organization (UNESCO) take the responsibility to evaluate and make recommendations. In particular, we appreciate the new framework developed by the WHO committee (12), which highlights the role of various tools, institutions, and processes for the governance of human genome editing.

Key to achieving these goals is more inclusive engagement of the global scientific community. First, effective public engagement and discussion require basic information on this subject, such as the differences between human genome editing in somatic cells and the germ line. This condition is particularly hard to fulfill in the less-developed regions where access to education and information are more limited. If experts in these regions have more opportunities to engage in global dialogues, they could bring back up-to-date information and various arguments to inform public debates in these countries.

Second, most guidelines and frameworks being suggested by international bodies have no legal authority or jurisdiction. The effectiveness of such approaches therefore depends on national regulators' willingness to voluntarily follow these global rules, creating an enforcement challenge that fails to account for nonadopters. If researchers and representatives of professional institutions from more countries could be involved in global policymaking, they could serve as policy entrepreneurs to inform the national policymakers and provide policy suggestions based on their first-hand experience in the global arena, for a more authoritative local framework. Third, the establishment of stringent global rules requires a high degree of consensus around the worldwide stakeholders. Therefore, inclusive dialogue

and the effort to achieve global consensus within the global scientific community are indispensable.

Toward Inclusive Global Governance

For all these reasons, it is time we go beyond the traditional governance model in the field of biotechnology and draw lessons from broader global governance practices. This can be done in several ways.

First, leading academic journals as well as professional conferences with international influence should serve as more open and inclusive platforms for dialogue on contentious governance issues related to human genome editing. More scientists and experts from less developed countries should be invited to express their views in these journals and speak at international conferences; their opinions need to be seriously considered. Notably, the conference known as CRISPRcon has provided such an inclusive venue for diverse opinions to be shared. There is a silent majority of researchers and stakeholders who have not had the chance to provide meaningful input.

Previous experiences in global governance reveal that ensuring voices are heard is a critical first step towards global governance improvement. One example is the policy-making process of the UN Sustainable Development Goals (SDGs). To generate a consensus on the new set of global sustainable development goals for the period of 2015 to 2030, the UN developed various open platforms for institutions and individuals around the world to provide their opinions. For instance, the UN Sustainable Development Solution Network (UNSDSN) was established to bring together global experts from all regions and all sectors to promote practical solutions for sustainable development (13). They also initiated the UN My World survey to invite voices from around the world into policymaking at the global level (14).

Second, the international professional organizations developing standards and rules for human genome editing should expand their networks to include more historically neglected countries and regions. For example, the international commission is poised to play an important role in the field, but there are only 10 countries' academies of sciences and medicines involved thus far. Efforts should be made to bring in more leading experts from less developed countries; right now, leaders in influential international professional organizations, such as the International Society for Stem Cell Research, are mostly from developed countries. A good model is the World Medical Association, which represents the national associations of physicians of more than 110 countries. Over the years, the association has developed many successful and inclusive standards and rules, including the influential Declaration of Helsinki on research ethics.

Third, public and private funding agencies of science and medicine around the world should work together to initiate collective actions to govern human genome editing. If influential funders could jointly recognize basic principles and standards that strengthen ethical review, accountability, and transparency, large numbers of researchers around the world who have received or wish to receive funding could be incentivized to heed these principles and standards. The Human Genome Project illustrates the impact of funding agencies in forging a community spirit (15). In 1996, the Wellcome Trust sponsored a leadership gathering of the largest labs in the publicly funded genome project coordinated by the NIH. The outcome of this meeting is the famous Bermuda Agreement, in which scientists pledged to release human sequence data "as soon as possible" and submit their data to a public database. Because of the substantial power of these funders, this rule successfully reshaped practice nearly instantly in the field, even without any legal authority (16).

Science is evolving at a feverish pace. Technological development is no longer the purview of a few leading academic institutes and a handful of entrepreneurial forerunners, as illustrated with the rise of CRISPR-based technologies driving the democratization of genome editing. Accordingly, governance by the few for all is no longer appropriate nor acceptable. Each approach suggested above has seen some historical success and has potential to improve governance of human genome editing. We must combine these tools into an integrated network. Standards and agreements independently launched by academic journals, funding agencies, and international professional organizations could mutually reinforce each other. Key individuals and organizations could play the critical role as the bridges connecting different approaches. The global governance of human genome editing urgently needs the wisdom of the entire global scientific community as well as those in related fields and interested members of the general public.

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