

BLOG POST

The moral implications of genome editing in 300 words?

This year, the Council is starting a new project exploring ethical issues around genome editing. In this post, Dr Peter Mills (<http://nuffieldbioethics.org/about/secretariat/>) sets out some of the issues and questions that might be considered and calls for contributions to the project. To register your interest in being involved or kept informed about this work, please email genedit@nuffieldbioethics.org. (<mailto:genedit@nuffieldbioethics.org>)

edit ('ed.it) *v.t.* Prepare (written material) for publication by correcting, condensing, or otherwise modifying it.

I know a thing or two about editing. My first professional job was as an editor for a venerable London publishing house. Later, on different career tack, I saw how it could be both comforting and seductive to speak of the chemical bases adenine, cytosine, guanine and thymine as the letters of the 'genetic alphabet'. I once visited an exhibition where the letters A, C, G and T were incomprehensibly recombined in minuscule type in 46 heavy, printed volumes that evoked the human genome for me like a bookcase in Borges' library of Babel (http://web.stanford.edu/class/history34q/readings/textualizingscience/library_of_babel.html). Genetics as the language of life, genes as its propositions, and the living organism itself as an argument mounted by nature against entropy and chaos. I have since learned to beware, even to disparage such metaphors; they are not bad metaphors but reasoning with metaphors is an errant and undisciplined pursuit.

The choice of the 'genome editing' rubric is perhaps a little coy. The reference to 'editing' irresistibly invites the comparison with authorship and suggests a more humble corrective. But when genome 'editing' is set not against divine 'authorship' but against aeons of evolutionary 'trial and error' it seems potentially far more influential, and influential far more rapidly, than random mutations and their lengthy embedding through 'natural' selection. That is, after all, its point. So, following the death of the author, we must take the rise of the editor more seriously.

Genome editing with engineered nucleases (<https://www.nuffieldbioethics.org/publications/genome-editing-with-engineered-nucleases>) has progressed relatively rapidly from *Nature Methods* (<http://www.nature.com/nmeth/journal/v9/n1/full/nmeth.1852.html>) 'method of the year 2011' to this year's preeminent, hypercathected technoscientific phenomenon. Cue calls for a voluntary moratorium on human germ-line-altering research (from researchers (<http://www.nature.com/news/don-t-edit-the-human-germ-line-1.17111>) keen to

keep their research interests away from the tarred brushes of public hostility) and on therapeutic applications (from the [International Society for Stem Cell Research](http://www.isscr.org/home/about-us/news-press-releases/2015/2015/03/19/statement-on-human-germline-genome-modification) (<http://www.isscr.org/home/about-us/news-press-releases/2015/2015/03/19/statement-on-human-germline-genome-modification>) among others).

The escape of genome editing from the laboratory into the public sphere – especially following the development of the [CRISPR-Cas9](http://www.sciencemag.org/content/346/6213/1258096) (<http://www.sciencemag.org/content/346/6213/1258096>) system – suggests that contained use, at least in the sense of reserving questions about the use of genome editing for researchers *qua* researchers to address, is no longer possible. This is recognised in recommendations published in *Science* (<http://www.sciencemag.org/content/early/2015/03/18/science.aab1028>) for “a globally representative group of developers and users of genome engineering technology and experts in genetics, law, and bioethics, as well as members of the scientific community, the public, and relevant government agencies and interest groups—to further consider these important issues”. But then, the image of the researcher *qua* researcher is itself a little artificial, a little denatured. The *Science* paper is the product of an [Asilomar](http://www.nature.com/nature/journal/v455/n7211/full/455290a.html) (<http://www.nature.com/nature/journal/v455/n7211/full/455290a.html>) veterans’ club who are self-consciously participants in political and ethical debate as well as in scientific discourse, and they are variously citizens, parents, patients and consumers to boot.

In our 2012 report on [mitochondrial DNA disorders](http://nuffieldbioethics.org/project/mitochondrial-dna-disorders/) (<http://nuffieldbioethics.org/project/mitochondrial-dna-disorders/>) we concluded that it was appropriate to describe cell reconstruction using the techniques we discussed as a ‘germline therapy’. (Policy makers subsequently tied themselves in knots to maintain that this germ line modification was not ‘genetic modification’.) We noted then that a “fuller discussion of the ethics of different kinds of prospective and theoretical germline therapies” (including those acting on the cell nucleus or involving nuclear transfer) would be advisable to underwrite robust policy decisions. The need for such a discussion is now pressing. The Nuffield Council on Bioethics will be taking forward this discussion in a project that will run throughout this year. However, the issues are clearly broader than those relating merely to human embryology.

So what are the ethical issues?

It is not clear whether the methods now in use, such as CRISPR-Cas9 system, themselves raise substantive moral issues of a kind that has not been contemplated previously. We have, after all, discussed genetic engineering, gene therapy, germline modification and disruptive innovation before (within crop science, animal breeding, biomedicine and embryology). But they certainly cast them in a stark new light. And the (apparently) relative ease, efficiency and economy of the new systems clearly have the potential to disrupt and reconfigure normative frameworks and practices in the biosciences and biotechnology, and challenge social, legal and regulatory norms. These raise questions that are not simply about

balancing benefits and risks, or surmounting thresholds of safety and efficacy. They are questions about how different practices and outcomes are defined and valued, and how those values align or disturb others to which importance attaches.

Genome editing is significant, perhaps above all, because it connects the different registers of bioethics: the questions about justice, sustainability and public good confronted in relation to fields such as crop breeding, livestock engineering and pharmaceutical development, and those foregrounding individual liberty, autonomy and respect for persons confronted in fields such as human reproduction. The questions before us are: how do we want to use the technologies and what sort of future do we want to bring about with them?

On 22 April we will be holding a scoping workshop with invited participants from a range of backgrounds to flesh out the most important issues and identify the main questions we want to address with regard to genome editing.

We've invited participants each to submit up to 300 words in response to the question: *What are the most important challenges raised by genome editing that the Nuffield Council on Bioethics should address?* We will use the responses as the basis for our discussion at the workshop. We are keen to cast the net as wide as possible so, if you have up to 300 words in response to this question that you could send us, we would like to include those too – just use the comment box below.

Otherwise, if you would like to register your interest in the project, whether to be actively involved or simply kept informed, please email genedit@nuffieldbioethics.org (<mailto:genedit@nuffieldbioethics.org>).

Comments (7)

Krishna Srinivas 31 May 2015

The international dimension of debating moral implications of genome editing is important. As countries can have different standards/regulations for use of genome editing and as it could be used in collaborative projects first map the the guidelines/positions taken by different countries, science academies and professional bodies on ethics of genome editing.

Pete Mills 21 April 2015

I agree with your conclusion about the need to reflect on societal priorities, but I think your criticism is misdirected, as reading below the line 'So what are the ethical issues?' should make clear. The questions have to be about where we go from here rather than why we should have arrived at this point. Genome

editing techniques exist: we are not standing at a point where we can choose to bring about a counterfactual world in which they don't. Nevertheless we still have to ask 'tough' bioethical questions ('what is the morally preferable innovation pathway?') not simply instrumentalise ethics ('how do I perform this innovation 'ethically'?') And there are economic, social and ethical dimensions to this, as well as merely benefits and risks.

Philippa Brice 20 April 2015

I agree that it is less ethical questions posed by the technique itself, as that the amazing potential of the technique makes what were once fairly theoretical questions much more pressing! It is definitely high time to start addressing them, and the Nuffield Council's plans are timely. One of the major difficulties in posing and addressing key ethical issues raised by the prospects of germline modification (with, let us assume, therapeutic or otherwise altruistic intent) is that they are provoked by some complex (indeed, highly ingenious) science, and this makes it harder than ever for non-experts to take a view on realistic risks as well as possible benefits. Whilst the views of researchers, clinicians and prospective patients and families absolutely need to be heard, there is a danger that wider societal views could be quashed, especially since debate tends to become polarised between the strongest views on both sides. The mitochondrial transfer debate saw some worries raised about long-term safety dismissed by proponents as ethical objections 'masquerading' as safety concerns. Are some ethical views and questions more ethical than others? Should we be led by the science on fundamental ethical decisions for society, and are scientific and clinical experts necessarily unbiased in their views whilst others are not? Is it even reasonable to hold safety concerns if experts in a technique say, and indeed firmly believe, that it is safe? If so, perhaps we should be looking to create an even more accessible model of public consultation and dialogue that perhaps sets out a structure of levels of evidence required to balance perceived risks, to serve as a model both for discussion of germline modification and other innovative technologies as they arise. If not, how can this most effectively be addressed?

Silvia Camporesi 10 April 2015

Reflecting on the implications of genome editing itself is the wrong question to ask.

Scientists have been calling for a moratorium to pause and reflect on f germ-line gene editing "until more research is done." References to the best practices set out at the Asilomar conference in 1975 are ubiquitous. But do we really want to replicate an Asilomar today? 40 years ago scientists called the Asilomar conference to discuss the risks inherent in recombinant

techniques. Then they decided to assign different levels of risks to different techniques, and lift the moratorium. The public and society were comforted. But no questions were asked as to why we had the technology in the first place. The only 'how' questions asked were related to how to use the technology. No questions as to why we invested massively in the technology in the first place were asked.

This lack of hard questions seems to me to be the major flaw of bioethics today, which is construed as lagging behind the science, catching up with the science, possibly hindering science. Along these lines, the rhetoric around these discussions is that we should not hinder scientists to continue with their experiments, as that would hinder progress. In our society we have severe issues of social inequalities and have to deal with the catastrophic consequences of climate change. We need to start discussing seriously where we as a society want to put our priorities. This is why we need to engage in discussions rooted in science and technology studies of the coproduction of technology and the moral values intrinsic in it. We need to start imagining the future we would want for ourselves, for our kids and for our planet, and to do so we as bioethicists need to ask tougher questions: Why do we want gene editing in the first place? Who are the actors at play in shaping it? What is the bioeconomy of the technology? Where do we want our priorities to be?

Gene editing offers us the opportunity to reflect on where we want our priorities to be in a society. We should not miss it.

Christoph Then 06 April 2015

All existing life forms emerged from first early cells. Life in its existing forms, but also throughout/during its future evolution, is still in a continuum with its origin some billion years ago. As the philosopher Karl Popper (Popper, 1992) put it: "The first cell is still living after billions of years, and now even in many trillions of copies. Wherever we look, it is there. It has made a garden of our earth and transformed our atmosphere with green plants. And it created our eyes and opened them to the blue sky and the stars. It is doing well." We now have far-reaching technical possibilities to interfere with the "first cell" in its existing and future forms on the level of the genome. Such possibilities cover all kind of living beings, including humans. We can create cells that are substantially different from the "first cell." We can create life that interferes with, disturbs, or interrupts the network and dynamics of current biodiversity and its further development. The future of life can be impacted by economic interests and technological failures to an extent not previously known. In his book, Popper explains that all life is "a search for a better world." Looking at the current options emerging from synthetic genome technologies, it seems a good idea to give the "first cell" a realistic chance to keep on searching for "a

better world” by following its own patterns, dynamics, and networks, which we still do not understand. So how can we protect the genetic integrity of the “first cell”?

Pete Mills 02 April 2015

Thanks for this comment, Huw. I agree that the framing of questions about genome editing is crucially important. But I am sceptical that there is any single, straightforwardly logical way to do this. If, by 'logical' you mean consistent, we have to ask 'consistent with what?' -- there are different, more or less coherent ways of thinking about genome editing and its applications, but none is demonstrably necessary or complete, and all open on to further domains of possible questions. I agree, also, that from a perspective to which I would attach significance, trait-based regulation (as recently asserted by the BBSRC, for example) is more logical/ consistent than process-based. But that doesn't mean that we cannot ask the question whether genome editing is significant in other respects or 'casts them [the familiar moral questions] in a stark new light'. My own thought about this may perhaps seem a little perverse: I would say that it's not really developments in biotechnology that are prompting our interest in genome editing. We have, after all, anticipated these in any number of earlier thought experiments and lines have been drawn as a result; the fact that what was previously imagined is now possible in practice shouldn't, by itself, change that. Rather, I would suggest that it is putative developments in orthodox moral dispositions to certain applications (that may have come about as the result of public debates, for example, around cell reconstruction to avoid mitochondrial disease) that enjoin us to reappraise and open the possibility of new alignments between normative discourses. New framings, or logics, if you will. This is something I would be keen to explore.

Huw Jones 01 April 2015

The most important challenge raised by Genome Editing is to frame the question in a way that is logical. Is it really the specific method used to generate genetic changes that asks the ethical and moral, or is the changes per se that are more important? There are clearly obvious ethical and moral considerations of making heritable changes to the human germ-line regardless of how those changes are made. Should the ethical implications of new crop traits generated by, say, mutation breeding be ignored when the identical genetic change generated by a site-directed nuclease be included? I question the underlying assumption, articulated here, that the process of genome editing somehow carries a fundamentally more significant ethical position than other methods of reverse genetics or of the effects of the genetic changes to individuals and societies.

