BASIC UNDERSTANDING OF GENOME EDITING
THE REPORT

Project led by Genetic Alliance UK and the Progress Educational Trust
Supported by the Wellcome Trust

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EXECUTIVE SUMMARY AND KEY RECOMMENDATIONS

The '**Basic Understanding of Genome Editing**' project was led by **Genetic Alliance UK** and the **Progress Educational Trust** (**PET**), and was funded by the **Wellcome Trust**.

The project centred on a series of workshops and online engagement events held between January 2017 and May 2017, which explored what people think and know about genome editing and its implications.

Participants in the project were drawn from the rare disease and (in)fertility communities. These groups are likely to have a particular interest in the development of genome editing technologies, and are also likely to have an important role to play in this development in future.

The project sought to incorporate participants' voices into the development of language and images around genome editing, and to empower participants to discuss genome editing's current uses and future potential.

Key recommendations

The report of the project's findings contains a number of recommendations aimed at people or organisations wishing to discuss genome editing in public. The report's eight key recommendations are as follows.

1. Use the term *'genome editing'* exclusively. Do not use potentially confusing alternatives such as 'gene editing', 'genetic editing', 'genomic editing', 'genome engineering' or 'genetic modification'.

2. Before attempting to describe or discuss genome editing, ensure that your audience has some understanding of what a genome is. Explain this if necessary.

3. Prioritise explaining the use(s) of genome editing over explaining the mechanism(s) via which genome editing works. Deprioritise the term 'CRISPR' – do not use the term interchangeably with genome editing (as CRISPR is just one possible approach to genome editing), and think carefully about whether and when it is necessary to refer to CRISPR at all.

4. Explain genome editing as straightforwardly as possible, certainly in the first instance. Use simple analogies and metaphors – *'find and replace', 'copy and paste'* and *'cut and paste'* work well, and build on the fact that *'editing'* is already something of a metaphor. Metaphors have their limitations, but they are useful in establishing basic understanding before attempting to go into greater detail.

5. When discussing uses of genome editing, distinguish clearly between:
    - Human and other uses.
    - Current and future uses.
    - Research and treatment.
    - Uses that are currently permitted and uses which would require regulatory change.

    It may also be important to distinguish treatment from enhancement, but refrain from suggesting that there is a settled consensus on what this distinction means and where it lies (as that particular debate is ongoing).

6. When discussing a use of genome editing that relates to humans, take particular care to address whether or not it could (intentionally or inadvertently) affect the human germline – in other words, cause a heritable change to the genome.

7. Be prepared to have to differentiate between genome editing and genome sequencing and/or between genome editing and mitochondrial donation, as these are common areas of confusion. Having made it clear that these are different things, then bring the conversation back to genome editing.

8. Do not expect complete retention after one explanation of genome editing, no matter how well-received the explanation is. The message will need to be repeated multiple times, in order to achieve enduring comprehension.

Further work

There was insufficient time in this project to fully examine all of the issues of comprehension, language and ethics that our participants wished to discuss.

Genetic Alliance UK, the **Progress Educational Trust** and the participants in our project are all keen to deepen this discussion in further work, and to develop a related set of additional resources. The final chapter of our report outlines possible next steps.

1. OVERVIEW AND METHODOLOGY

Overview

The findings of this report are the result of structured and unstructured discussions with participants in the '**Basic Understanding of Genome Editing**' project led by **Genetic Alliance UK** and the **Progress Educational Trust** (**PET**), and funded by the **Wellcome Trust**. These discussions involved participants reading and responding to articles, looking at and responding to images, watching and responding to videos, completing surveys, giving their own presentations, hearing from and questioning genome editing experts, and participating in other engagement exercises.

Participants in the project were drawn from the rare disease, genetic disease and (in)fertility communities. These groups are likely to have a particular interest in the development of genome editing technologies, and are also likely to have an important role to play in this development in future. The project sought to incorporate the participants' voices into the development of language and images around genome editing, and to empower participants to discuss genome editing's current uses and future potential.

The project centred on a series of day-long workshops. Five separate workshops were held in total, but as detailed below, individual participants only attended a maximum of three. Participants belonged to two distinct groups which attended an initial workshop separately, were brought together for a second workshop, and then attended a third and final workshop separately again.

Articles discussed by participants were drawn from news and comment pieces published over the preceding two years (2015/2016), representing a wide range of publications and perspectives. Prior to each workshop, each participant was assigned a different article to read and to discuss.

Partway through each workshop, an invited expert gave their own perspective on genome editing and then responded to questions and comments from participants. Topics covered by experts included a general introduction to genome editing, a more detailed exploration of the difference between somatic and germline genome editing, and the ethical challenges associated with genome editing. (For details of the five experts who spoke at the workshops, see **Annex B**.)

It was important to add this expert perspective to each workshop, so that participants could seek clarification and resolve areas of confusion. However, it was equally important to do this only partway through each workshop, so that participants' more naïve views and thoughts could be explored and captured beforehand.

During the course of the project, participants were also invited to visit Dr Chris Lord's laboratory at the Institute of Cancer Research, where genome editing is being used to find novel approaches to the treatment of cancer. Several participants took up this invitation.

Participant Groups

There were three groups of participants, referred to in this report as the **Genetic Alliance UK Group**, the **PET Group** and the **Online Group**.

Genetic Alliance UK Group

There were **18** participants in the **Genetic Alliance UK Group**, carefully selected in order to ensure a range of ages, geographical location, disease type, patient/carer status and potential benefit from the technology.

The participants were all affected by, or cared for someone affected by, either an undiagnosed genetic condition or one of the following conditions.

- Breast cancer
- Cystic fibrosis
- Ehler Danlos syndrome
- Epidermolysis bullosa
- Leukaemia
- Muscular dystrophy
- Niemann Pick disease
- Noonan syndrome
- Primary cilliary diskinesia
- Sickle cell
- Thalassaemia

Group members were drawn from England, Scotland and Northern Ireland. This group also had a balanced gender mix, and included representatives of ethnic minorities.

Members of the group identified as being distinct from the general population, and therefore potentially holding distinct views. The group acknowledged that as patients, or carers of patients, they have a vested interest in genome editing due to personal experiences. They have unmet health needs, they are more likely than the average person to benefit from genome editing, and they tend to be correspondingly more engaged and more informed.

PET Group

There were **14** participants in the **PET Group**, drawn from backgrounds relevant to the fertility sector.

The group included an embryologist, a fertility nurse, a former member of the Human Fertilisation and Embryology Authority (the UK's fertility and embryo research regulator), fertility counsellors, patients with personal experience of undergoing fertility treatment, and representatives of patient groups. Participants' areas of expertise included donor conception, multiple births, prenatal testing for fetal abnormality and mitochondrial disease.

Participants in this group varied widely in their scientific literacy. Some had a good grounding in genetics due to their profession or their experience as patients and advocates, whereas others were completely new to thinking and talking about genetics.

Online Group

In order to test and further explore the findings from workshops with the Genetic Alliance UK Group and the PET Group, two online surveys and two follow-up webinars were conducted. Participants in these activities – the **Online Group** – were recruited via Genetic Alliance UK.

These participants consisted of patients and family members affected by rare, genetic or undiagnosed conditions. **86** participants responded to the first survey and **45** responded to the second survey. All respondents were invited to join a follow-up webinar to discuss issues that arose during the surveys.

Workshops

To moderate the workshops, we enlisted two professionals who each had substantial experience and skills in discussion and debate of science as well as in public engagement more broadly. For their details, see **Annex B**.

In addition to the workshop exercises detailed below, there was also exploration of the images that accompany media coverage of genome editing, and whether particular types of imagery aided or impeded understanding. The Genetic Alliance UK Group conducted this exercise during its first workshop, whereas the PET Group conducted this exercise during its third workshop.

Workshop 1

To begin with, the Genetic Alliance UK Group and PET Group met separately. Prior to any structured group discussion, participants' naïve views of the terms *'genome'*, *'genome editing'* and *'CRISPR'* were captured.

Participants were then shown headlines about genome editing which had been stripped of means to identify the source or author. Participants were divided into smaller groups and asked to place the headlines under categories of *'positive'*, *'negative'* or *'neutral'*, according to the connotations of the headlines and the feelings the headlines elicited. Plenary discussions then allowed words and phrases to be picked out and discussed at greater length.

Participants were also given articles to read and then to discuss in smaller groups. The groups were invited to look at the language and metaphors used in the articles, and to discuss which of these they found most helpful. Notes were taken during these discussions, and groups fed back to the room at large.

Workshop 2

The Genetic Alliance UK Group and the PET Group were brought together. This provided an invaluable opportunity to explore where the thinking and comprehension of these two constituencies converged and diverged, and to explore what happened when the two groups mixed and exchanged ideas.

Participants watched an animated film entitled '**What is gene editing and how does it work?**' – available online at https://youtu.be/I5_2c52OPFw – which had been produced by the Royal Society in conjunction with Wellcome Trust. PET also commissioned several scientists and students (who use genome editing in their work) to make their own amateur videos seeking to explain this technology to a lay audience. There was plenary discussion to explore which aspects of these videos participants found helpful or unhelpful.

Workshop 3

To conclude, the Genetic Alliance UK Group and the PET Group were separated again. Participants were divided into pairs and asked to prepare and present their own explanations of genome editing, drawing upon what they had learned in the preceding two workshops. This provided an opportunity to observe which terminology, analogies and metaphors they alighted on, and whether these were consistent with their preferences as stated elsewhere.

Participants were cognisant of the fact that explanations of genome editing are liable to be pitched differently at audiences with differing experiences and levels of expertise. Participants were therefore asked to imagine an audience to whom they were addressing

their explanation of genome editing, and to explain which audience they had in mind at the beginning of their presentation. (For summaries of participants' presentations, including the imaginary audience at which each presentation was targeted, see **Annex F**.)

2. NAÏVE VIEWS AND EXISTING SOURCES OF INFORMATION

Definitions

At the outset of the first workshop, participants offered their naïve views of what the terms *'genome'*, *'genome editing'* and *'CRISPR'* meant.

Genome

Workshop participants tended to be familiar with the term *'genome'* but unable to explain it. Several participants described having heard terms including *'gene', 'genome', 'DNA', 'exome'* and *'chromosome'*, but did not understand how these terms relate to each other.

The term *'genome'* encompasses all of an organism's genetic material, but this fact was not apparent to all participants, and in fact some participants were uncertain about whether a genome was bigger or smaller than a gene. When asked to describe a genome, participants in the Genetic Alliance UK Group and the PET Group gave answers ranging in scale from from *'our genetic code in its entirety'* and *'set of complete DNA containing the instructions to replicate that organism'* (both of which are broadly correct) to *'a building block of life'* (which is ambiguous at best) and *'a small unit of DNA'* (which is incorrect).

Of **86** participants in the Online Group presented with multiple choice options, **78** were able to indicate that a genome is our genetic code, and **71** that is made up of DNA. **71** out of **86** were aware that the genome contains the information needed to build a human, and that the genome is the same in different cells of the body (the latter may be debatable in some specialist contexts but it is a true statement for general purposes).

However, the confusion about scale that was evident in the workshops was also evident in the Online Group, with almost half of respondents – **37** out of **86** – thinking that a genome is a small unit of DNA. It is worth highlighting that this confusion existed among participants who had long experience of genetic disease and of related treatment. This suggests that the term *'genome'* has not entered popular use with its meaning intact, not even among those who might be considered likely to encounter and use it.

Participants found it challenging to retain new information presented at the workshops, particularly the meaning and scale of the term *'genome'*. Partway through their first workshop, participants heard a presentation by an expert who provided a thorough and well-received explanation of what a genome is. Despite this, in the second workshop **7** out of **25** participants still thought that a genome is a small unit of DNA, and the same number thought that there would be different genomes in different cells of the body.

Genome editing

All workshop participants had heard of *'genome editing'* and most of them had some understanding of what the term means, even if they could not successfully define a *'genome'*. Participants described genome editing as *'extracting some of the DNA (that was faulty) and replacing it'*, or *'editing the DNA to change the characteristics of a thing'*.

Other participants understood that genome editing involved making changes, but described these changes in vaguer terms. Examples included *'putting things in, taking things out'*, *'altering things in our bodies'* and *'an external event done to the genome for greater good'*. Approximately half of the Genetic Alliance UK Group had heard of the term *'cut and paste'* as a metaphor for genome editing. (The merits and demerits of this metaphor will be explored in **Chapter 4**.)

When looking at the Online Group's understanding of genome editing, **54** out of **86** participants had heard about genome editing via media coverage. In a multiple choice survey, the majority of participants were able to identify genome editing as a research tool to edit the genome.

CRISPR

In recent years, CRISPR has become the leading approach to genome editing, but most participants were not familiar with the term. Even those who had heard of the term did not know what it is or what it stands for. Some participants questioned whether CRISPR was a system, a process, a person, or a company.

Participants were interested to learn that the term is an acronym. A few were grateful to learn how it was pronounced, as pronunciation is an important but often overlooked deterrent to engagement with scientific terms. (Further confusion caused by the term *'CRISPR'* will be detailed in **Chapter 3**.)

Applications

Current uses

When asked to highlight where genome editing is already being used, participants were confident – and correct – in stating that the technology is already being used in the laboratory, both in animal models and in human tissues.

However, participants were divided regarding whether genome editing is already being used in a clinical setting, for the treatment of inherited conditions. Some participants thought that there were countries – outside the UK – where genome editing was already being used in this context.

The remainder of participants were unsure whether genome editing was already in use in the clinic, but were inclined to say that the methods were still very new. Some participants thought that genome editing was already being used for the treatment of genetic conditions, and that it had been used to cure conditions such as leukaemia. (This is correct, but such treatments are still experimental and not yet in widespread use.)

Participants from the Genetic Alliance UK Group observed that progress towards a cure or treatment will be at different stages for different conditions. They tended to know – from their experience of genetic disease, and their interest in related research – that research is prioritised in conditions affecting organs and tissues that are more accessible (such as skin and blood), and that treatments are more likely to target single gene disorders in the first instance.

However, there was also evident confusion among participants in the Genetic Alliance UK Group, with the majority believing that genome editing is already in use in the clinic to correct genetic mistakes in human embryos. The PET Group, whose members were more familiar with procedures and laws around IVF and embryology, did not share this erroneous belief.

Potential future uses

There was a sense among participants that genome editing has enormous potential, and that this is just the beginning of the journey. Participants likened this potential to that of the Gutenberg press and the internet.

Despite acknowledging that genome editing has great potential, most participants were pragmatic in recognising that it will take time before it becomes mainstream as a means of treating genetic conditions. Participants in the Genetic Alliance UK Group were aware that gene therapy has existed for more than two decades and has been proposed as the cure for several genetic conditions, but that in most instances this has yet to become a reality. Meanwhile, there was some confusion in the PET Group about the relationship between genome editing and gene therapy (this will be discussed in **Chapter 3**).

Participants discussed at length medical uses of genome editing that might improve the quality of life, or extend the life, of patients. They suggested that in future genome editing would be used to treat genetic diseases (both inherited and non-inherited), autoimmune diseases, mitochondrial diseases, cancers and allergies. They also discussed using genome editing to address infectious diseases – applications discussed included eradicating malaria, developing vaccines, and changing the genome of humans to improve resistance to infectious diseases.

Other applications that were discussed related to biotechnology and agriculture. Participants suggested that genome editing would be useful to increase the yield of crops and thereby improve nutrition in developing countries, and to improve resistance to disease in crops and animals. Lastly, participants suggested that genome editing could be used to change the appearance of vegetables and animals to make them more appealing, and potentially even to create new species.

There was also discussion of adverse consequences of genome editing, with participants discussing how this technology could lead to bioterrorism or the development of a *'super race'*. The potential use of genome editing to enhance more superficial characteristics, such as beauty, was a matter of concern for some participants (their views on these matters will be explored in **Chapter 7**).

Expectations

Participants hoped that genome editing would increase the quality of life for affected patients, without necessarily bringing a cure.

The Genetic Alliance UK Group expected that genome editing would accelerate research, deliver information, and lead to a better understanding of genetic conditions in general and their own condition (or that of the person they cared for) in particular. Some of the participants in this group thought that by improving understanding of genetic conditions, genome editing could help provide a sense of validation that what patients experience (as a result of their condition) is real.

The Genetic Alliance UK Group had a strong awareness of the complexity of genetic conditions, and understood that – even within a range of similar conditions – the symptoms may be different and the same treatment might not apply to all. They expressed some wariness in light of claims previously made for gene therapy, and in light of the unfulfilled promise of cures for conditions such as thalassaemia.

Sources of information

When looking for information on health- or science-related topics, participants reported that they will read news via newspapers (and/or their websites), via other online news sources (such as BBC News), via news aggregators (such as Google), and via social media. Additionally, several members of the Genetic Alliance UK Group said that after reading a

news piece they would then seek out and read primary research sources, failing which a more specialist popular source such as *New Scientist* magazine.

In the Genetic Alliance UK Group, participants' motivation to seek information – and then read more widely and deeply – tended to be their personal health or that of their family. One participant highlighted how their approach to looking for more detailed information had changed after being diagnosed with a genetic condition.

In this respect, the Genetic Alliance UK Group may have been less typical of the lay public than the PET Group. Members of the PET Group were more likely to come across information about genome editing and genomics through casual reading. Several said they would then look up terms they did not understand via Google.

A number of participants explained that their expectations of the quality and reliability of information are set by the source. The more popular and less specialist the source, the more they will bring a sceptical eye to it (even though they may still be interested in it and inclined to read it).

Discussion and conclusions

The term *'genome'* is not especially well known or understood. Participants agreed that explanations of what a genome is should be presented alongside explanations of what genome editing is. When, in their third workshop, participants gave their own presentations explaining genome editing, many of them found it useful to begin by explaining in some detail what a genome is (see the summaries of their presentations in **Annex F**).

Members of the Genetic Alliance UK Group reported that knowing what a genome is makes them feel better able to understand their own diagnosis, and to understand research into their condition. Promoting wider understanding of what a genome is will equip the public to formulate and express their views on genome editing.

Improved understanding of what a genome is will also have benefits beyond genome editing, for public understanding of genome sequencing and various areas of genomics-related medicine and research. This is much-needed, at a time when genomics is becoming increasingly central to medicine (as discussed in the recent *Generation Genome* report from the UK's Chief Medical Officer).

KEY RECOMMENDATION

Before attempting to describe or discuss genome editing, ensure that your audience has some understanding of what a genome is. Explain this if necessary.

Failure to understand the term *'genome'* is not necessarily an impediment to understanding the term *'genome editing'*. Indeed, people may already have a decent grasp of what *'genome editing'* entails without understanding the word *'genome'*.

Nonetheless, people's understanding of genome editing will become more robust if they first receive a brief explanation of what a genome is. This explanation may be difficult for them to retain, and may therefore need to be repeated.

KEY RECOMMENDATION

Do not expect complete retention after one explanation of genome editing, no matter how well-received the explanation is. The message will need to be repeated multiple times, in order to achieve enduring comprehension.

Overall, participants expressed a degree of optimism and excitement about genome editing, even at an early stage of this project when their more naïve views were being captured. They believed that genome editing has the potential to be a game changer, while recognising – as one participant put it – that we are *'a split second after the big bang'* and it is too soon to make detailed predictions.

3. TERMINOLOGY AND REFERENCES

Need for consistency

This project explored different terminology and references, to assess whether they were liable to aid or to impede participants' understanding of genome editing. A key finding was that consistency of language is essential.

The current proliferation of synonyms or near-synonyms for genome editing – *'gene editing'*, *'genomic editing'*, *'genome engineering'*, and so on – was a cause of confusion among participants, and lowered their confidence. They could not be certain whether these terms referred to the same technology, or to different technologies.

Two of the expert speakers who gave presentations in workshops remarked that *'genome engineering'* had evolved as a legitimate term of art among scientists, who were therefore liable to use the term unthinkingly even when discussing genome editing in public. We would urge scientists to refrain from doing this.

Meanwhile, the term *'genetic modification'* is liable to cause particular confusion if used in relation to genome editing, as the term has traditionally implied the introduction of foreign (transgenic) DNA into an organism (as in *'GM crops'* and *'GM food'*). Editing the genome of an organism does not necessarily involve introducing any foreign DNA.

Using the term *'genome editing'* consistently and exclusively was found to be the best way to improve understanding. An added advantage of this term is that it has wide scientific applicability. Even an edit to a single gene (or part of a gene) in an organism can be said to change an entire genome, and can still involve an entire genome being searched by a guide molecule.

Putting CRISPR in its place

The CRISPR approach to genome editing has, perhaps understandably, been a prominent focus of media coverage since it was first pioneered in 2012. But participants found the term *'CRISPR'* more difficult to grasp than *'genome editing'*.

Moreover, participants were confused by the tendency to use CRISPR as a synonym for genome editing. This problem is best illustrated by one of the most celebrated uses of genome editing in the UK, which was mentioned in several of the articles discussed – namely, the successful use of genome editing to reverse advanced leukaemia in a one-year-old baby in 2015.

This treatment did not actually involve CRISPR at all, but rather employed the earlier genome editing approach TALENs. One participant in the PET Group formed the misapprehension that this celebrated use of TALENs was not actually genome editing, technically speaking.

The term *'CRISPR/Cas9'*, which is often used interchangeably with *'CRISPR'* and *'genome editing'* alike, left participants even more confused as to where the distinctions lie (and if indeed there are any meaningful distinctions). 'Cas9' is the nuclease most commonly used in the CRISPR approach to genome editing, but it is not the only nuclease that can be used (for example, work is ongoing with the alternative nuclease Cpf1) and it may yet be superseded in future.

Despite the enormous impact of CRISPR, it would be helpful to take a step back and question whether and when CRISPR needs to be mentioned during public explanations of genome editing. By way of analogy, public discussion of genome sequencing does not tend to involve discussion of the method of sequencing or other such detailed mechanics.

Avoiding confusion with other technologies

Genome editing is easily confused with other genetic and reproductive technologies that have recently been the focus of sustained public attention. Participants across all three groups were liable to confuse genome editing with two other technologies in particular – mitochondrial donation and genome sequencing.

This confusion was profound, and poses a serious challenge. For example, a majority of respondents in the Online Group – **30** out of **45** – thought that genome editing was the research tool behind the 100,000 Genomes Project (a major genome sequencing project, initiated by the UK government, which involves no use of genome editing at all). Almost half of respondents in the Online Group – **21** out of **45** participants – thought that genome editing was a technique that could address mitochondrial diseases by creating a 'three-person baby' (this is a description of mitochondrial donation, not genome editing).

It must be emphasised that participants in this project – across all three groups – were more likely than an average member of the public to have encountered and thought about genome sequencing or mitochondrial donation. Despite this, they still struggled to distinguish these technologies from genome editing.

Finally, some participants in the PET Group thought that genome editing was a new name for gene therapy, and asked why the name of the technology had changed. This is yet another potential source of confusion – genome editing is not synonymous with gene therapy, but it can be used as one possible approach to gene therapy (among others).

Unhelpful terminology and references

Bacteria

The CRISPR approach to genome editing was adapted from a naturally occurring mechanism used by bacteria as a defence against invading viruses. A significant proportion of media coverage and popular explanation of genome editing draws attention to this fact.

Although this fact was of interest to some participants, and was perceived to have some positive connotations – as it shows CRISPR to be a natural phenomenon adapted for human use, rather than a completely alien technology – on the whole participants thought that this knowledge did not enhance understanding, and that it could distract from more important information.

Furthermore, mention of the bacterial origins of CRISPR is liable to encourage confusion about the chronology of genome editing. CRISPR was first discovered in bacteria in 1987, but was not adapted for use as an approach to genome editing until 2012. Meanwhile, in a parallel history, genome editing existed before the CRISPR approach was developed – the term applies to technologies dating at least as far back as the mid-1990s.

Knowing this complex history is not a priority for those seeking to achieve a basic understanding of genome editing, and there is a risk that it could present barriers to understanding.

'Discarded' embryos

The PET Group was angered by a reference to *'discarded embryos'* in a newspaper article about researchers editing the genomes of human embryos. Several participants thought that this was misleadingly and insensitively worded – *'surplus embryos'* would have been more appropriate – and all agreed that it should always be made clear that IVF patients had given explicit consent for these embryos to be used in research, where they are highly valued.

There was concern that careless wording could distress IVF patients who had asked for their surplus embryos to be destroyed, who might form the misapprehension that the embryos had been used in experiments instead. Human embryos are only available for research due to the benevolence of fertility patients (and fertility professionals), and care must be taken with terminology in order to maintain this goodwill.

Designer babies

Most participants disliked the term *'designer babies'*, which has long since entered popular use whenever any technology is discussed that involves intervening in human reproduction in an attempt to influence characteristics of the resulting child. Many participants associated the term *'designer'* with consumerism and fashion, implying selection of trivial characteristics. Some participants thought that the term connoted a commodification of babies and children.

Participants expressed disapproval of the way the term *'designer babies'* taints valuable medical progress, by insinuating that it is some sort of lifestyle choice. This reaction was stronger in the PET Group, whose attitudes to the term ranged from weary acceptance – they thought the term lamentable, but had given up discouraging its use – to fierce dislike.

A minority of workshop participants, predominantly in the Genetic Alliance UK Group, thought that the term had more positive connotations and conveyed a positive notion of precision. Even so, they thought that *'aspiration'* might be a more appropriate concept to associate with such babies than *'design'*, as different prospective parents might aspire to achieve different things with such technology (not least the absence of particular inherited diseases in the child) and the technology may or may not realise their aspirations (it is not guaranteed to succeed).

This positive interpretation of the term was also apparent within the Online Group, where a much larger proportion of participants – **38** out of **43** – thought that *'designer babies'* has some merit as a well-understood and useful term, even if it is a suboptimal term. It is interesting to note that participants in the two groups recruited through Genetic Alliance UK's networks appeared to be more comfortable with the term.

Upgrade

Similar disagreement surrounded the use of the term *'upgrade'* in relation to genome editing. For some participants this term evoked benevolent improvement, whereas for others it conveyed an offensive sense of commodification – in the words of one participant *'we're talking about people, not phones'*.

Discussion and conclusions

Inconsistency of terminology around genome editing is unhelpful and a source of confusion. The term *'genome editing'* should be used exclusively wherever possible.

KEY RECOMMENDATION

Use the term *'genome editing'* exclusively. Do not use potentially confusing alternatives such as 'gene editing', 'genetic editing', 'genomic editing', 'genome engineering' or 'genetic modification'.

CRISPR should not be used as a synonym for genome editing, and should be de-emphasised when explaining genome editing. Similarly, CRISPR/Cas9 should not be used as a synonym for the CRISPR approach (or for genome editing in general), and should be de-emphasised even further.

This advice may appear counterintuitive, at a time when CRISPR has become such a prominent buzzword. Terms which encompass CRISPR while being broader than CRISPR – for example, *'RNA-guided genome editing'* (see 'Targeted genome engineering in human cells with the Cas9 RNA-guided endonuclease', Cho *et al*, *Nature Biotechnology*, January 2013) – have not as yet found widespread traction. Nonetheless, de-emphasising CRISPR is important if we are to furnish people with an understanding that will still serve them well in light of future possibilities.

A proposed non-CRISPR approach to genome editing called NgAgo recently foundered – its developers retracted their key paper in *Nature Biotechnology*, after other researchers were unable to replicate their findings – but it remains possible that in future, a new non-CRISPR approach to genome editing will succeed. People need to be equipped with a form of understanding that can withstand such developments.

KEY RECOMMENDATION

Prioritise explaining the use(s) of genome editing over explaining the mechanism(s) via which genome editing works. Deprioritise the term 'CRISPR' – do not use the term interchangeably with genome editing (as CRISPR is just one possible approach to genome editing), and think carefully about whether and when it is necessary to refer to CRISPR at all.

Those who discuss genome editing in public should anticipate and be prepared for genome editing to be confused with mitochondrial donation and genome sequencing. In order to clarify how genome editing is distinct, they should ensure they have some rudimentary knowledge of these other technologies and can explain them succinctly.

Note that some revision may be in order, even for experts and experienced science communicators. Mitochondrial donation in particular is a complex topic, involving different aspects and approaches which are easy to get confused.

While it is important to be able to clarify what these other technologies involve and what distinguishes them from genome editing, it is equally important not to become so distracted by them that discussion of genome editing is derailed. After clarifying the relevant differences, the discussion should then be steered back to genome editing.

KEY RECOMMENDATION

Be prepared to have to differentiate between genome editing and genome sequencing and/or between genome editing and mitochondrial donation, as these are common areas of confusion. Having made it clear that these are different things, then bring the conversation back to genome editing.

'Designer babies' is a contentious term whose use should not be encouraged, but which will continue to arise during public discussion of genome editing. People discussing genome editing in public should be prepared to field questions about so-called *'designer babies'*, and should be prepared to add context and nuance – in terms of what is scientifically possible, in terms of what is permissible, and in terms of whether a distinction needs to be made between treatment and enhancement. (The last question will be explored in detail in **Chapter 7**.)

Wherever possible, respect should be paid and acknowledgement should be given to fertility patients who have consented to their embryos being used in research. Care should be taken with the terminology used to describe these embryos.

4. ANALOGIES AND METAPHORS

Metaphors for the genome

Participants who most successfully grasped and conveyed the meaning of the term *'genome'* at the outset of this project already tended to use their own metaphors. For example, they likened the genome to an entire recipe for an organism, a picture of a whole living being, a roadmap, or a shopping list.

The well-worn metaphor of the genome as text – a book – came up repeatedly. This metaphor complements well the fact that the nucleotide bases in DNA are often referred to as letters – as indeed it should, since the whole notion of *'genome editing'* (as a way of describing the deliberate alteration of selected DNA sequences in living cells) has emerged precisely from these sorts of metaphors. *'Editing'* is itself already something of a metaphor.

Expanding on the theme of a written volume, the genome as an instruction manual was considered helpful by participants – even more so than *'blueprint'*, a term which participants thought was not universally understood. One participant also described DNA as a script, with different theatre companies staging very different productions of *Romeo and Juliet* even though the script is more or less identical (and is certainly always distinguishable from *Hamlet*).

The genome as simply *'a set of genetic instructions'* was also popular. In some of the participants' own presentations (see Teams 4 and 5 in the Genetic Alliance UK Group in **Annex F**), this metaphor was developed into instructions for assembling a LEGO set. The extended metaphor is rich, because a LEGO set can also be mis-assembled (in which case it might not work as intended, or might fall apart) if the instructions either contain a mistake or are misinterpreted.

While exploring these sorts of metaphors, one member of the PET Group questioned whether a genome *contains* information or *is* information. This is a rich and subtle scientific (and philosophical) question, and indicates a high level of thoughtful engagement with the topic.

In more specialist discussions of the genome, distinctions are made between *'information'* and *'instructions'*, and the picture is complicated still further by portions of the genome whose function (if there is one) is either obscure or unknown. Our workshops did not reach that level of detail, but it was gratifying to see participants develop some of the conceptual tools that might in future enable them to do so.

Genome editing as word processing

'Find and replace', 'copy and paste' and *'cut and paste'* were the preferred metaphors for genome editing among all participants across all three groups, as well as being among the most commonly used metaphors in the media coverage that participants examined.

Again, these metaphors build on a well-established tradition of analogising genes to the written word – only this time, word processing technology is specifically evoked, as distinct from the printed word. As one participant said, it *'works like the find and replace function on a word processor, first locating the gene to be edited, then making the necessary change'*.

When using these metaphors, attention does *not* need to be drawn to the fact that the analogy is with word processing. In fact, *'word processing'* as an explicit concept was alien to

younger participants – the ubiquity of information and communications technology means that the fact words can be processed (and edited – found, replaced, copied, cut and pasted) is now considered natural and taken for granted.

Metaphors have their limitations, and are by definition imperfect. While we are confident in recommending *'find and replace'*, *'copy and paste'* and *'cut and paste'* as the best metaphors to use, at the outset of an explanation of genome editing, we acknowledge that they have potential shortcomings. We will briefly examine these as they pertain to the CRISPR approach.

To begin with, there is a risk of overstating the ease and accuracy with which genomes can be edited at present. As CRISPR is used and refined, it undoubtedly brings major improvements relative to earlier genome editing approaches. At the same time, however, CRISPR is not necessarily easy and accurate by the standards of popular frames of reference. Researchers must still employ great care, diligence and skill in order to put CRISPR to productive use.

There are some ways of adapting word processing metaphors, in order to clarify that genome editing may be fallible. For example, one of the articles discussed by participants analogised off-target effects to an imperfect search function, that is liable to confuse the words 'CUSTARD' and 'MUSTARD'.

This idea complements another metaphor which is already in use, and which was employed by one of the experts who gave a presentation to workshop participants – namely, the use of misspelt and similarly-spelt words as metaphors for nonsense mutations and missense mutations. These are useful strategies to keep in mind, but it is best to begin with word processing metaphors in their simplest form in the first instance.

Another important aspect of CRISPR that these metaphors perhaps fail to convey is the fact that a cell's own DNA repair mechanism is enlisted in the genome editing process. But despite such shortcomings, *'find and replace'*, *'copy and paste'* and *'cut and paste'* were the most popular metaphors among participants, and were found to be most useful. When participants were asked to prepare and present their own explanations of genome editing, these metaphors appeared in some form in every single presentation.

On the theme of information technology, *'programming'* and *'reprogramming'* were also mentioned as possible metaphors, sometimes in connection with *'satnav'* (a metaphor discussed below). However, these terms did not meet with much enthusiasm from participants. Furthermore, *'reprogramming'* is a term which already has a specific and quite separate meaning in biology (in relation to epigenetic modifications which involve *no* change in DNA sequence), and so it is probably best avoided in any case.

Genome editing as satnav and/or scissors

Besides word processing metaphors, the metaphors most commonly encountered in media coverage of genome editing were *'satnav'* and *'scissors'* (sometimes *'molecular scissors'* or *'genetic scissors'*).

Here, the *'satnav'* represents the guide molecule that directs a nuclease to the relevant part of the genome, and the *'scissors'* represent the nuclease which cuts DNA at the required site in the genome. These metaphors were received favourably by many participants, but not to the same extent as *'find and replace'*, *'copy and paste'* and *'cut and paste'*.

A drawback of the term *'satnav'* is that it is not universally used in English-speaking countries. Meanwhile, *'scissors'* were thought to convey the destructive aspect of genome editing without conveying the constructive aspect – the *'cut'* without the *'paste'*. There was also confusion about how abstract this metaphor is supposed to be, with questions about whether the relevant molecule actually resembled scissors.

Another drawback of using scissors as a metaphor was pointed out by participants after watching a researcher-made video about the use of genome editing in animal research – namely, the fact that depicting animals in close proximity to scissors is disturbing (not to mention misleading). Finally, the fact that satnavs and scissors do not tend to be used together in real life makes them an awkward metaphorical pairing.

Popular culture as metaphor

Some metaphors for genome editing, or for the results of genome editing, draw upon popular culture – for example, superheroes and their superpowers. Metaphors can also blur with reality, in media coverage of hypothetical whimsical uses of genome editing to create mythical beasts such as unicorns or dragons.

Some participants – particularly in the PET Group – thought that using popular culture in this way risked trivialising genome editing, and obscured the fact that possible treatments for debilitating diseases were at stake. Other participants found popular culture more useful, in that they thought it made for memorable and relatable metaphors.

One participant referred approvingly and enthusiastically to the superhero Spider-Man (who was referred to in some of the media coverage) as *'the ultimate genetically modified human'*, and said they had used this as a way to explain genome editing when they were explaining their involvement this project to their partner.

Other cultural landmarks that made frequent appearances in media coverage were the famous science fiction novels *Frankenstein* and *Brave New World*, which are still widely used as metaphorical shorthand for the perils of playing God. Participants did not tend to find these references helpful, associating them with fear. One participant remarked that such references elicit *'a Pavlovian response'*.

Alternative metaphors

Other metaphors were explored and experimented with during the course of this project. The amateur videos by scientists and students, which were commissioned by PET and shown to participants, included some novel metaphors – one such metaphor involved cooking ingredients, while another involved the use of boarding passes in an airport. However, participants found these metaphors confusing.

Two participants devised a novel metaphor when they gave their own presentation, using their outfits (clothes and accessories) as a metaphor for their genomes, and exchanging shoes as a metaphor for making changes to their genomes (see Team 4 in the PET Group in **Annex F**). Other participants thought that this novel metaphor worked in its intended context (the presentation was aimed at an imaginary audience of 10-year-olds, who might require very rudimentary and engaging metaphors if they are to understand something of genome editing) but it is questionable whether the metaphor would work well outside that context.

Discussion and conclusions

'Find and replace', 'copy and paste' and *'cut and paste'* are the best metaphors to use when seeking to promote basic understanding of genome editing. They are imperfect – as are all metaphors – but they build usefully upon existing metaphors that are well-established, and they can be built upon in turn.

KEY RECOMMENDATION

Explain genome editing as straightforwardly as possible, certainly in the first instance. Use simple analogies and metaphors – *'find and replace', 'copy and paste'* and *'cut and paste'* work well, and build on the fact that *'editing'* is already something of a metaphor. Metaphors have their limitations, but they are useful in establishing basic understanding before attempting to go into greater detail.

'Satnav' and *'scissors'* have some merits as metaphors for aspects of genome editing, but we do not recommend using them in the first instance. That said, because these metaphors have already been used fairly widely, people who wish to explain genome editing should be aware of them and prepared to engage with them if necessary.

Popular culture may be a useful springboard to engage with different audiences. However, there is a risk that this could be perceived as trivialising the uses and potential of genome editing, especially in relation to serious disease. For this reason, metaphors which draw upon popular culture should be used with caution.

5. APPLICATIONS

Key distinctions

Genome editing has a vast range of current and possible future uses (unlike, say, mitochondrial donation, which was developed specifically to avoid the transmission of mitochondrial disease in humans). Throughout our workshops, participants highlighted the importance of making clear distinctions between applications of genome editing.

All participants thought it important to know whether the uses being described were currently happening or might happen in the future, and whether the uses were part of a research scenario or a clinical scenario. Above all, they thought a clear distinction should be drawn between genome editing in humans on the one hand, and genome editing in animals, plants and microorganisms on the other hand. Some of the videos shown to participants switched rapidly between these different categories, or sought to address several of them simultaneously, and this caused confusion.

Across all workshops most discussion focused on human uses, and this reflected the interests of participants. Those in the Online Group – who considered the question of distinctions in the abstract, rather than in the context of a discussion (surveys of the Online Group were conducted prior to webinars) – were more intent on hearing about non-human uses of genome editing, as part of a wider context. But even there, some participants said they preferred to receive information about genome editing that was restricted to human applications only.

Within human applications participants wanted clear distinctions between current and future uses, between research and treatment, and between uses that are currently permitted and uses which would require regulatory change. The distinction between the use of genome editing for treatment and for enhancement is less of a priority, as that distinction is more complex and contentious (as will be explained in **Chapter 7**).

The missing distinction

There is a distinction in genome editing that is thought to be of vital importance in science, ethics, law and policy, which we expected would arise spontaneously during the course of workshop discussions. This was not the case.

We refer to the distinction between somatic genome editing (which results in changes that are *not* heritable by the next generation) and germline genome editing (which results in changes that *are* heritable by the next generation). There was negligible awareness of this distinction among the participants in the Genetic Alliance UK Group and the PET Group.

The distinction did not occur to participants, even when workshop moderators attempted to steer discussion in a direction that would bring it to light. One of the experts who spoke in our workshops was asked to focus on this distinction, but even after this, the distinction was mentioned only fleetingly by participants during workshop discussions.

Priorities

When asked to consider the sequence in which they would find it most useful to receive information about genome editing, participants thought that the highest priority should be given to an explanation of what genome editing is (in tandem with an explanation of what a genome is). After this, they sought an explanation of current and future applications of genome editing. Finally, they were interested in ethical concerns (as will be discussed in **Chapter 7**).

This sense of priorities was consistent across all three groups, and was reflected in participants' own presentations during the third workshop.

Discussion and conclusions

The degree of detail that might be covered when explaining how genome editing works will depend on the audience. Any explanation must include a clear set of distinctions and priorities from the outset. Given how challenging it can be to explain and understand applications in humans, other uses may warrant little more than a passing mention.

Our participants were undoubtedly interested in ethical and regulatory aspects of genome editing, but they were keen to acquire a grounding in what genome editing is and how it could be used before holding forth on such issues. The distinction between using genome editing for treatment or for enhancement is best deferred until other, more scientifically and ethically straightforward distinctions have been established.

KEY RECOMMENDATION

When discussing uses of genome editing, distinguish clearly between:

- Human and other uses.
- Current and future uses.
- Research and treatment.
- Uses that are currently permitted and uses which would require regulatory change.

It may also be important to distinguish treatment from enhancement, but refrain from suggesting that there is a settled consensus on what this distinction means and where it lies (as that particular debate is ongoing).

Participants were not interested in focusing on the distinction between somatic and germline genome editing. However, this distinction is – and will most likely remain – central in science and regulation. Around the world, it is currently the case that germline genome editing in humans is either prohibited or deprecated (unless it is confined to a research context using human embryos).

It is possible that the somatic/germline distinction is simply of less concern to the public than tends to be assumed. The latest research into public attitudes to genome editing in the USA ('US attitudes on human genome editing', Scheufele *et al*, *Science*, August 2017) finds no significant difference between public support for somatic and germline genome editing, provided that genomes are being edited for treatment purposes and not for enhancement

purposes. This contrasts with the view often expressed by specialists that germline genome editing is more ethically problematic.

When it comes to clinical applications, two opposing factors that are ultimately of paramount importance to specialists and the general public alike are risk and benefit. The distinction between these two factors does not necessarily map neatly onto the distinction between the germline and the soma.

Whatever the reasons for our finding, it indicates that proactive work is required to explain the somatic/germline distinction to the public, and to explain why the distinction is considered so important by specialists.

KEY RECOMMENDATION

When discussing a use of genome editing that relates to humans, take particular care to address whether or not it could (intentionally or inadvertently) affect the human germline – in other words, cause a heritable change to the genome.

6. IMAGES

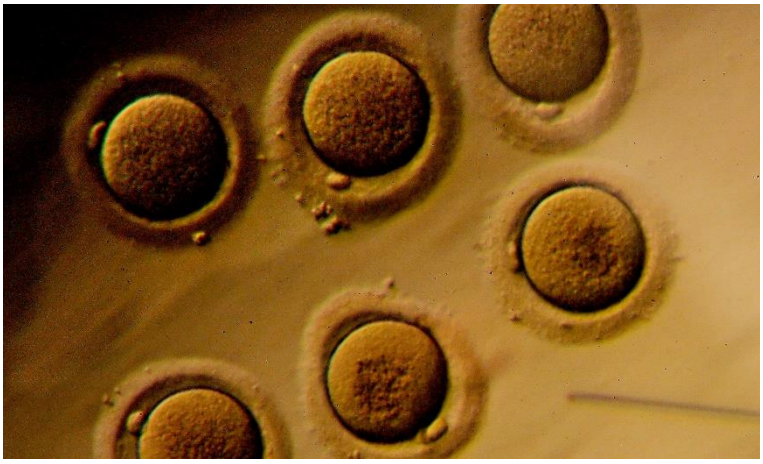
Workshops explored images that accompanied media coverage of genome editing. Two different approaches were used – the Genetic Alliance UK Group assigned images to a *'positive/negative/neutral'* system that was also used for media headlines, whereas the PET Group assessed the same images using a consequential image exploration method.

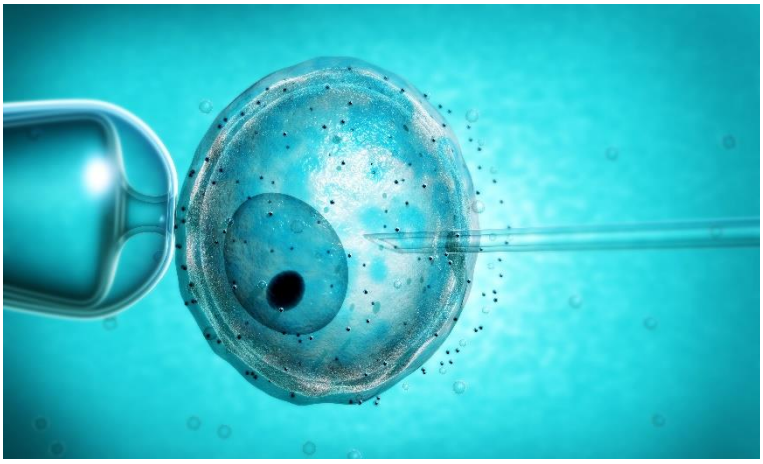
The latter involved participants first examining the image, then having the corresponding image caption revealed to them, and then finally having the headline revealed to them. This allowed responses to the images to be elicited and captured at each stage, to see how the information context affected perception. (Participants' written responses to this exercise can be found in **Annex H.**)

Overall, participants did not find the images below especially useful in terms of advancing their understanding, but they thought that images could add interest and relatability. The PET Group strongly preferred images that related to humans, babies and human embryos and gametes (this may reflect the group's grounding in fertility, or it may be representative of wider trends). The PET Group also preferred photographs over drawings or computer-generated images.

Engaging images

The following images were generally well-received.

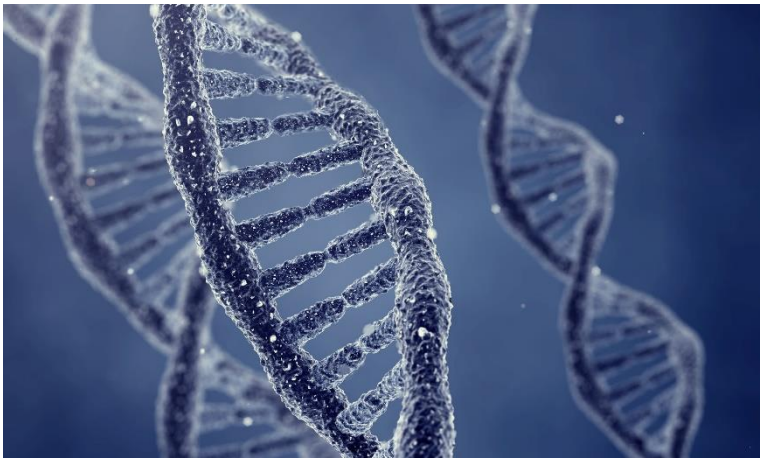


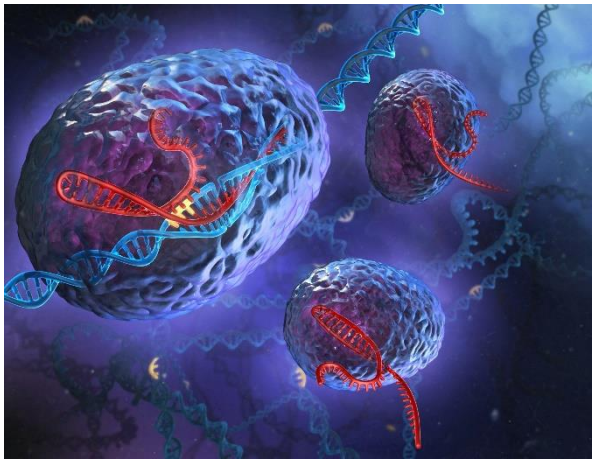


Less engaging images

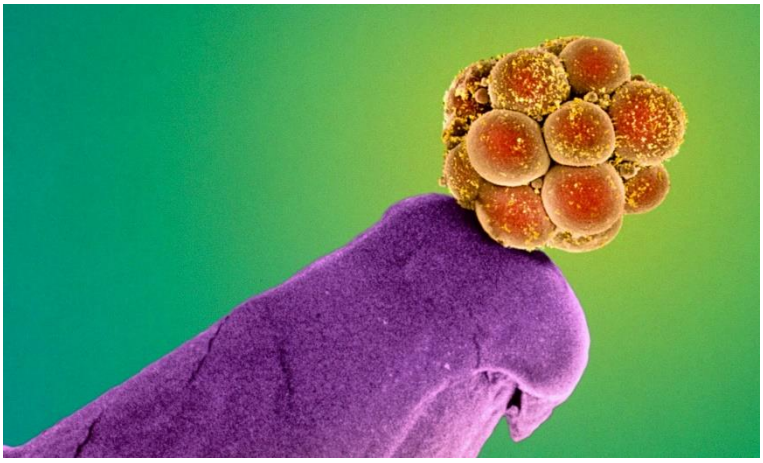
The following images were less popular, eliciting various degrees of criticism.

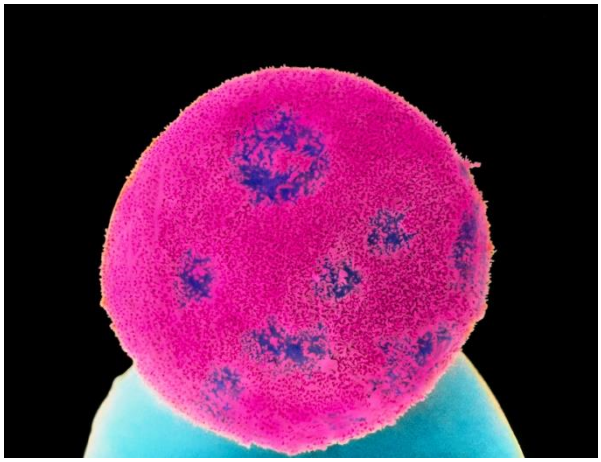
The two images below were unpopular among the PET Group, eliciting associations with *'sci-fi'* and *'teenage boys' posters'* (particularly in relation to their dark backgrounds).



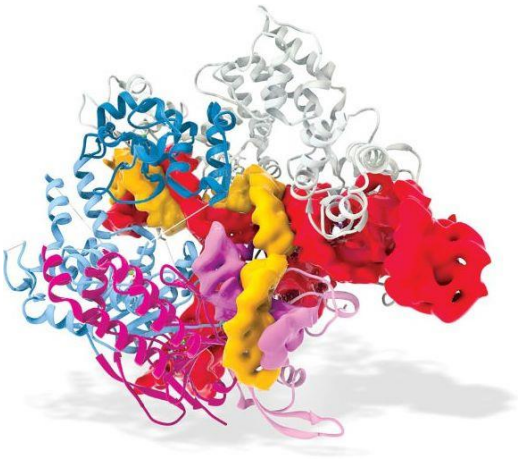


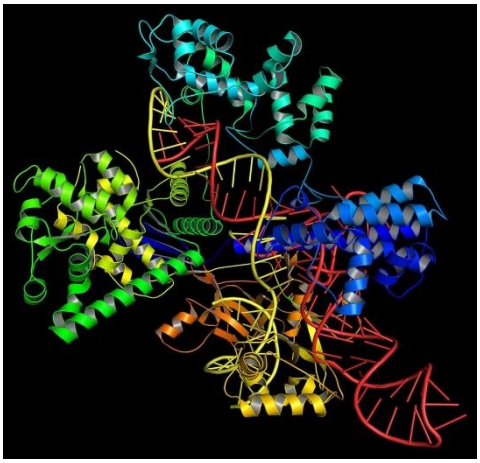
The two images below – electron micrographs with false colour – were confusing to participants. Such images are potentially useful, but only if an accompanying caption details the magnification and the fact that the colour is false (neither of which was indicated in accompanying captions here).





The two images below – computer-generated models of molecular structures – were also thought to be confusing.

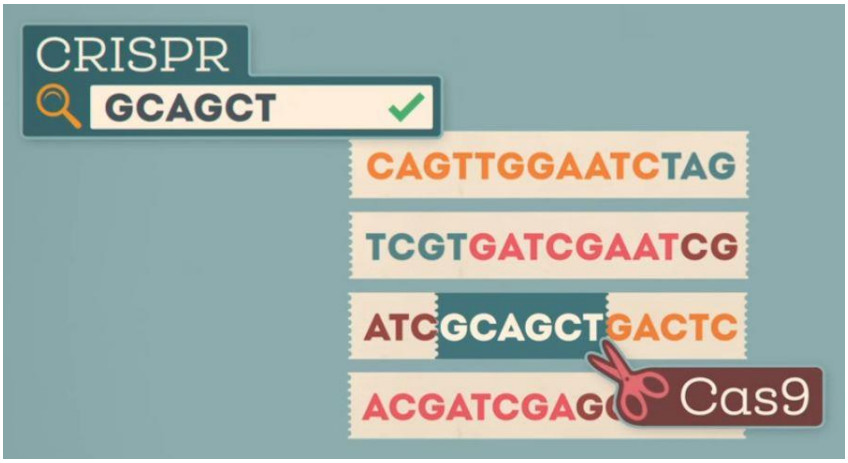




Images featured in animation

Different aspects of the Royal Society/Wellcome Trust animated video '**What is gene editing and how does it work?**' elicited different responses from participants, but one element that was received favourably was the visuals used to explain certain concepts.

Participants were especially taken with the section depicted below – beginning at the **1:27** mark at https://youtu.be/I5_2c52OPFw – which explained CRISPR using familiar computer icons such as a magnifying glass, scissors and a hand-shaped cursor. This complements well the metaphors recommended in **Chapter 4** – *'find and replace'*, *'copy and paste'* and *'cut and paste'*. (The *'find and replace'* metaphor is actually used in the video's narration.)



Discussion and conclusions

Participants were not averse to imagery. Indeed, they made use of their own imagery when they gave their presentations during their third workshop – more than half of the participants in the Genetic Alliance UK Group availed themselves of a flipchart, while two of the participants in the PET Group used their clothing and accessories as metaphorical props (as was discussed in **Chapter 4**).

However, participants were not enamoured of computer-generated imagery and electron micrographs. Diagrams and infographics were considered helpful, if they were pitched at an appropriate level of detail. The question of how best to develop such diagrams and infographics – so that they are scientifically accurate, but still accessible to the lay reader – was beyond the scope of this project, and deserves exploration in a dedicated piece of work.

The present media environment is not necessarily ideal for the use of diagrams. Journalists writing to tight deadlines about complicated science, as part of a production chain where they may not be in close contact with the subeditor or picture editor, are not always likely to seek appropriate diagrams. There is an important role for scientists to play in seeking to ensure that journalists are supplied with, or advised on, diagrams where they would be helpful.

The popularity of computer-generated imagery and of electron micrographs with lurid colours perhaps indicates an attempt to give articles the 'flavour' of complex science, when there is neither the means nor the inclination to consider whether anything is being conveyed that will aid understanding. Sometimes, an image that looks as though it should be doing the work of explanation – and may be approached with this expectation, by readers who seek understanding – is instead doing more superficial (or even mystifying) work of illustration.

There is nothing intrinsically wrong with images performing a more illustrative role, but as can be seen above, participants expressed a preference for such images to feature people (whether adults or infants). Some images that represented laboratory procedures were well-received, but even these prompted debate among the PET Group about precisely which

cells were being depicted and whether these cells were human or animal. This sort of detail can be helpfully clarified in captions.

7. ETHICS

Freedom to reach moral conclusions

Ethical concerns are often raised in public discussion and media coverage of genome editing. Such concerns arose in various ways during our workshops, and it was always intended that they would be addressed in greatest detail during participants' third and final workshop. However, it was actually during the second workshop – when the Genetic Alliance UK Group and the PET Group were brought together – that one of this project's most striking ethics-related findings emerged.

The finding was prompted by participants watching the Royal Society/Wellcome Trust animated video '**What is gene editing and how does it work?**'. They responded well to many aspects of the video (including the visuals, as was discussed in **Chapter 6**) but the video elicited strong criticism when – beginning at the **2:16** mark at https://youtu.be/I5_2c52OPFw – it began distinguishing between *'positive'* and *'negative'* applications of genome editing.

In its *'positive'* category, the video lists *'radical improvements to human health'* (of which it provides some examples), improvements to crops, and certain specific improvements to animals. In its *'negative'* category, the video lists editing the genomes of human embryos in ways that *'have no bearing on health'*, and then goes on to mention *'designer babies'* and *'designer pets'*. The video also implies that there is something intrinsically *'negative'* about germline genome editing – it is not until it reaches its *'negative'* section that the video notes *'changing an embryo's DNA would not only affect the child but their descendants too'*.

Participants thought the video was dictating to them which applications of genome editing were positive (beneficial, ethical, moral) and which were negative (detrimental, unethical, immoral). Not all participants agreed with the way applications had been categorised – one participant pointed out that they had no particular objection to the idea of genome-edited *'designer pets'*. And even those participants who found themselves in agreement with the video's categorisation thought it presumptuous that their opinions were taken as a given.

Finally, several participants were critical of the video's use of the term *'designer babies'*. As was explained in **Chapter 3**, throughout our workshops the term proved contentious at best and strongly disliked at worst.

Treatment versus enhancement

Ethics was a major focus of discussion in participants' third and final workshop. A majority of participants in both the Genetic Alliance UK Group and the PET Group agreed broadly that using genome editing to avoid, prevent or treat disease was morally defensible. By contrast, a majority thought that using genome editing to enhance the attributes of healthy people was morally dubious.

However, these views were not universally held, and the PET Group was more diverse in its moral perspectives – in both restrictive and permissive directions – than the Genetic Alliance UK Group. Three members of the PET Group expressed varying levels of reservation about using genome editing for treatment (even treatment of serious diseases), while conversely, another member of the PET Group said they were quite happy to consider any applications that might improve quality of life (even if these applications were not medical).

The picture was further complicated by disagreement over how to distinguish between treatment and enhancement, with many participants concluding that the distinction is not clear-cut. One obvious example of a hypothetical use of genome editing that could be characterised as either treatment or enhancement is conferring resistance to infectious disease. Such an application of genome editing might have a similar outcome to use of a vaccine, but it would be achieved via radically different means.

The PET Group explored this uncertainty in some depth via an applied ethics exercise, where participants were presented with different hypothetical applications of genome editing and asked to place them on a grid which had two axes – a treatment/enhancement axis, and an (im)morality axis.

Participants were asked to consider the use of genome editing to achieve each of the following outcomes, all presented with the preceding condition *'Assuming it is 100% effective and safe for mother and baby...'*.

- Ensure child does not have gene for Huntington's disease.
- Ensure child has a reduced risk of developing breast cancer.
- Ensure child will develop into a tall adolescent and adult.
- Ensure child will have lifelong resistance to HIV.
- Ensure child will not be short-sighted.
- Ensure child will not develop dyslexia.

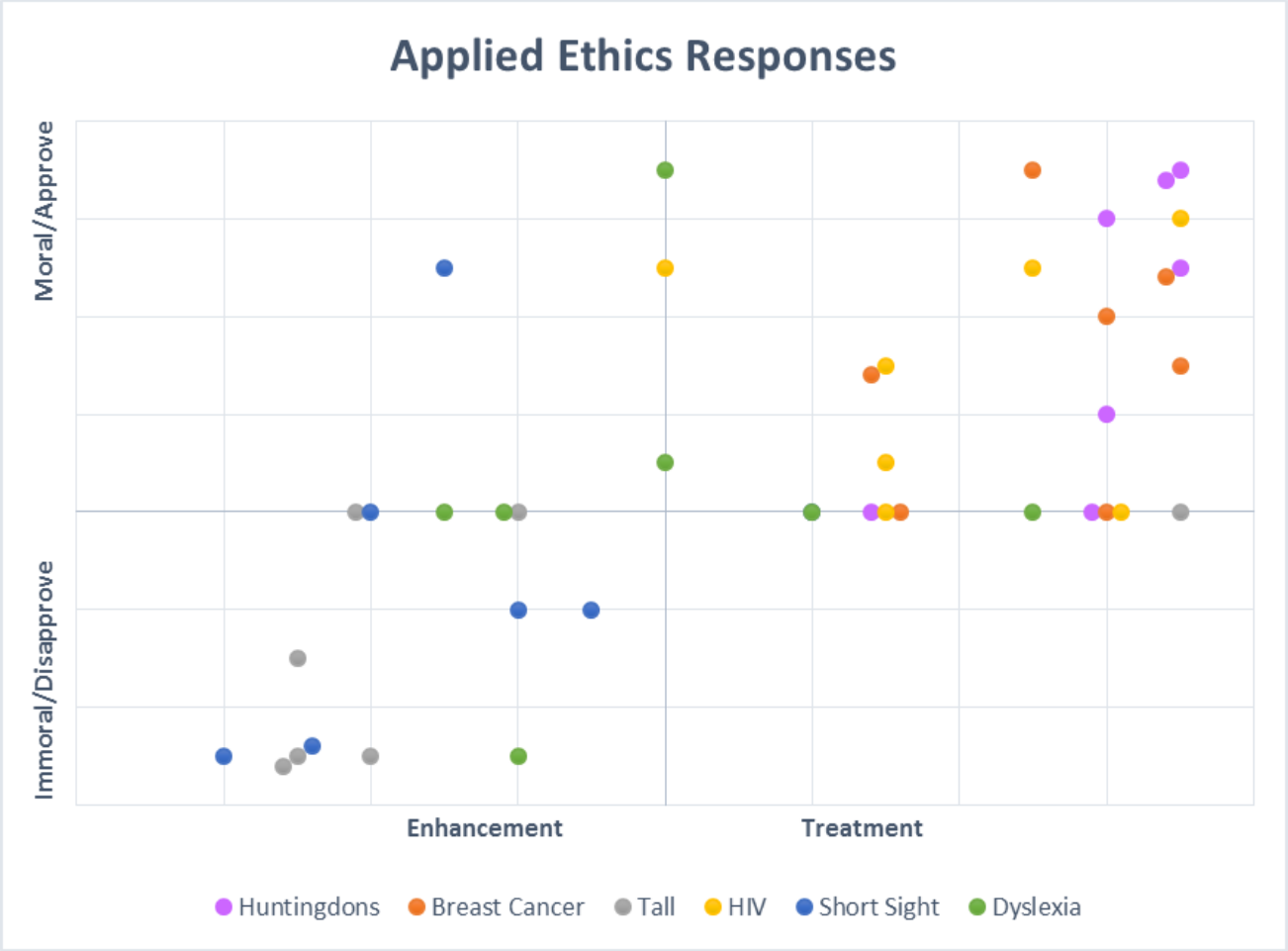
The results of this exercise are visualised overleaf. As can be seen from the fact that the dots tend to cluster along a diagonal line from bottom left to top right, there was a tendency to view enhancement as immoral and treatment as moral. However, this tendency is neither absolute nor uniform. Furthermore, dots of the same colour appear in quite different places, which indicates that there was not a consensus on how particular applications should be categorised.

Two participants were unable to complete this exercise, and the reasons they gave for this are perhaps instructive. One of them said they could not accept the proviso *'Assuming it is 100% effective and safe for mother and baby...'* because they did not think safety could ever be proved to their satisfaction when it came to editing the genome. The other participant said that this exercise made them feel uncomfortable, a feeling they ascribed to a *'yuck factor'*.

Freedom of choice

Another major theme that emerged from participants' consideration of ethics was the importance of individual choice. Participants thought it important that patients should be able to choose to receive future treatments involving genome editing, but they also thought it important that patients should have the choice *not* to receive such treatments.

A key question was how best to defend such freedom of choice in different future scenarios. If access to genome editing treatments was not universal, then a two-tier society might emerge. On the other hand, if access to such treatments *was* universal, then different ethical challenges might emerge – questions explored by the Genetic Alliance UK Group included *'Is it wrong to choose not to have genome editing if that possibility exists?'* and (in such a scenario) *'Would the NHS still have responsibility to support that family?'*.



Discussion and conclusions

Participants wanted the freedom to reach their own moral conclusions. They were open to arguments from different moral perspectives but they did not want such perspectives to be presented as though they were unassailable facts, and they did not want such perspectives to be placed on an equal footing with factual explanations of the science of genome editing.

Deferring more focused discussion of ethics until the third workshop paid dividends, enabling participants to acquire a clearer insight into genome editing before they began subjecting it to detailed moral judgement. This was clearly their preferred sequence in which to receive information and arguments about genome editing, and it meant that by the end of the project, they were eager to enter into further discussion of ethics. It is hoped that this enthusiasm can be capitalised upon in follow-up work (as will be discussed in **Chapter 8**)

Our findings on ethics reinforce our view (previously set out in **Chapter 6**) that discussion of ethical implications and legal aspects of genome editing should ideally take place after the audience has a grounding in what this technology is and what it is for.

This may not always be achievable – sometimes, the reason genome editing is being discussed publicly is precisely because of a point of ethical contention. Even so, the more widely and level-headedly the rudiments of this technology can be discussed at the outset, the fewer misconceptions there will be when its ethical dimensions come to be discussed. Furthermore, it is important – for understanding, and also to avoid provoking public resentment – to distinguish scientific fact from moral or ethical opinion.

This approach should be applied to the contentious distinction between treatment and enhancement. There is a commonly expressed view – found in media coverage of genome editing (and other biomedical technologies), and also in key policy documents and pronouncements on genome editing – that enhancement is a morally dubious proposition compared with treatment. While it is true that this view was reflected among (most of) our participants, this obscures the fact that there is not necessarily any consensus on where the boundaries lie between treatment and enhancement.

Explaining the rudiments of genome editing and its applications must be a priority. Once the stage is set for more detailed consideration of ethics, the meaning of and distinction between treatment and enhancement is a rich and worthwhile topic of public debate in and of itself. The outcome of this debate should not be foreclosed.

8. NEXT STEPS

Staying engaged with our participants

As our workshops progressed, it became clear that participants were very engaged with this project. Members of the Genetic Alliance UK Group felt privileged to be part of discussion of this technology, and to have been selected from a much larger group of applicants to take part. The majority of participants attended all three workshops and indicated that they were keen to continue their involvement, with some of them already interested in becoming advocates for genome editing.

Meanwhile, members of the PET Group were keen to learn about the role genome editing might play in the future of assisted reproductive technologies. They all had some knowledge of these technologies, of the history of the technologies (in which the UK has played a leading role), and of the way such technologies have raised fundamental questions about the creation and the beginnings of life. The PET Group wanted to imagine what the next chapter in this medical and social history might contain, now that genome editing has entered the picture. Their curiosity only grew stronger as the project went on.

There was insufficient time in this project to fully examine all of the issues of comprehension, language and ethics that our participants wished to discuss. **Genetic Alliance UK**, the **Progress Educational Trust** and the participants in our project are all keen to deepen this discussion in a further piece of work. It would be beneficial to work with these participants again and learn how their understanding has developed in the interim – in particular what knowledge they have retained, how confident they are in this knowledge, and what they have done with it.

Further resources

There are several resources which it would be helpful to develop from this work, which were not achievable under the auspices of this initial project. These might include the following.

Guidance for journalists

Annex A of this report consists of guidance for scientists who are discussing genome editing in public. It would be useful to develop similar guidance for journalists, tailored to their specific needs and priorities.

A genome editing lexicon

This report explores the most useful terminology to use when discussing genome editing, but stops short of presenting every relevant term together with a concise definition. Such a lexicon would need to be carefully crafted in order to balance expert detail with lay accessibility, while taking account of the latest developments in terminology and of subtleties and disagreements in the way terms are used by experts.

Educational materials and FAQs

Similarly, there is clear scope to develop a basic set of educational materials and 'frequently asked questions' type documents on genome editing – particularly applications in humans – building on the findings of this project and drawing on experts such as those who spoke in our workshops (detailed in **Annex B**).

There is a growing body of materials of this sort already in circulation. There are also initiatives underway to try and synthesise what is most helpful from existing approaches to discussing genome editing, including the Genome Editing Public Engagement Synergy programme run by the National Coordinating Centre for Public Engagement. We plan to engage with and participate in such initiatives wherever possible, and thereby promulgate the recommendations of this report.

Guidance on diagrams and infographics

This project involved exploring different sorts of images that are used in media coverage of genome editing, while assessing people's responses to and interpretations of these images. However, there is a separate piece of work to be carried out looking more narrowly at diagrams and infographics, and developing best practice for visual aids which seek to explain how genome editing works.

Further exploration of the development of stakeholder views on somatic and germline genome editing

Neither the difference between nor the significance of somatic and germline genome editing seemed especially apparent to our participants, even after being emphasised. This is a serious mismatch with the thinking that currently drives scientific and policy developments around genome editing, and it warrants further attention.

One approach might be to explore this area with different participants, to establish whether or not this finding was an anomaly. It is is interesting in this context to consider recent research (discussed in **Chapter 5**) indicating that the American public is as supportive of germline genome editing as it is of somatic genome editing.

Exploring ethics in greater depth

Our final workshop focused on ethical questions, and there was clearly a strong appetite among our participants to explore these questions in greater depth. The Nuffield Council on Bioethics recently sought public and professional views on genome editing in relation to human reproduction, and is due to publish a report focusing on this area. We are eager to contrast our experiences and insights with theirs, and to test their materials and findings with our participants. Similarly, they may have uses for our findings in their work.

Other languages

Many of the recommendations in this report relate to the judicious use of language, and we are acutely aware that such recommendations may not be applicable in other languages – just translating the words *'genome'* and *'editing'*, whether separately or combined, is not a trivial task. We are keen to ensure that the work we carried out with our participants in English is as replicable as possible in other languages. To that end, we would be more than happy to provide advice to anyone hoping to carry out similar work in other languages.

Entering the global conversation

During this project our participants explored media coverage of genome editing covering a period of two years. The two years in question saw genome editing used to reverse advanced leukaemia in a one-year-old baby, used for the first time in human embryo research in China, licensed for use in human embryo research in the UK, and becoming the subject of numerous high-profile policy documents and pronouncements.

Since our workshops concluded, other landmarks have occurred. *Nature* has published UK-led research in which the genomes of human embryos were edited to study gene function (the first time this has ever been done), and has also published US-led research in which a disease-causing mutation was reported to have been edited out of human embryos. These pieces of research have been the subject of high-profile news coverage and discussion around the world.

There could scarcely be a more fruitful time for our participants – people with an established interest in genetic disease, rare disease, (in)fertility, and now genome editing – to not only take stock of the global conversation about genome editing, but also enter into that conversation.