Scientific Scissors

User Guidance Notes

BIOCHEMICAL SOCIETY

British Society for Gene & Cell Therapy

The rapid improvement in genome editing techniques, namely the introduction of CRISPR-Cas9, has reignited many old debates about the moral aspects of biotechnology. Whilst many of these issues have been present in the public sphere for some time, the rate of technological advancement means that as a society we need to have an open and frank conversation about how we should move forward, and what sort of world we want to live in.

Scientific Scissors is a hands-on activity aimed at informing and debating about the applications and ethics of genome editing.

Introduction

Depending on your audience, there will likely be a large variation in people's familiarity with genome editing. For some, they will have never heard of the term and they will need more context for it to make sense.

Start out by finding what prior knowledge your visitors have. One way to do this is by showing a model or a picture of DNA and asking if they know what it is. If they do know, ask them what they know about DNA. What does it do? Why is it important? This will give you a good idea of where to begin. Avoid introducing your activity as "all about genome editing" because if they have never heard of this before it can be a bit intimidating.

One way to talk about DNA is to compare it to a set of instructions for building a living thing. Sometimes the instructions contain mistakes called mutations – this causes disease. We can now correct these mistakes. Apart from correcting mistakes to treat disease, we also have the ability to change the instructions in order to change a characteristic of the living thing.

The information flyer provides some of the basic information needed to understand CRSIPR Cas9.

Equipment

Applications cards

Information flyer

Washing line (2-3 m)

Retort stands (or similar to hold washing line)

Table clamps to secure retort stands

Clothes pegs or paper clips

Model or picture of DNA (A template for an origami DNA model can be found **here**.)

A Jenga set (labelled as shown with a sequence on the outside end and a gene on the top)

A pair of tongs labelled Cas9

A bowl to contain gene paper slips

Paper slips labelled with genes

The ethical card game

Set up a washing line, labelled at one end with “Yes, this is a great idea!” and at the other with “No! Don’t do this.” (or similar). Use clothes pegs or paper clips to attach the application cards onto the line. It’s a good idea to start off the activity with a few cards already in place, to give people the idea of what is expected.

Each card contains an application of genome editing, a benefit, and a risk of each use. Visitors to the stand are asked to read a card, ask any questions they have about it, have a brief discussion about it and then place it on the line depending whether they think it is a good idea or a bad idea (or somewhere in between.) Remember, when discussing the application, it is important to discuss the potential benefits and risks as well as the ethical dimensions.

Visitors can move cards they think are in the wrong place, add new cards to the line, and remove cards (there are likely to be too many cards to have them all on the line at once). Whenever they move a card, ask them to explain why and what their thinking is.

At this point it is a good idea to present the other point of view. Try not to do this in an antagonistic way; make it clear that this isn’t necessarily your opinion, but that you are playfully being devil’s advocate. Try questions such as:

- But what if…?
- What about in the situation that…?
- Where would you draw the line for…?
- Is that different to…?
- How do you feel about…?

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Remember, your role in this discussion is to provoke debate, not to start arguments! People will vary in how much they are willing to be challenged, so prepare to be adaptable and try to read your audience.

The “Genetic Jenga” game

In this game, the blocks represent genes. Each block should be labelled on its outside edge with a short length of DNA code (we went with three letter groups to keep it simple). On the top of each brick, you can name a gene. For younger audiences you could write a characteristic, but be aware that few characteristics are solely attributable to genetics and even fewer to a single gene. Each block should be different.

In a bowl have some slips of paper, each one with a gene and the corresponding piece of code. Pick a gene out of the bowl – this is now the gene you are targeting. Explain that Cas9 – your “Scientific Scissors” can be programmed to find that exact piece of code and cut the DNA at that point.

Use a pair of lab tongs, labelled Cas9, to “cut” out the targeted gene. Use the tongs to “knock out” the gene. The visitor can leave this gene inactive by leaving this gap, or they can replace the gene with something else. This is a good opportunity to explain how “knock outs” help us study what genes do and inserting new material can help cure disease or confer different characteristics to the organism.

It is important to note that in reality, Cas9 makes a single cut across both strands of the DNA. The cell will repair this cut, but imperfectly meaning this gene will no longer work. This is what is meant by a “Knock-out”. Cas9 does not remove a whole section like in this game. You can explain this limitation of this particular model, but reiterate that the key point is that we can target particular sections of DNA, we can “Knock-out” genes and we can insert new genetic material.

Discuss how some genes might be connected to other genes – pulling out one might affect others, just like in Jenga, and that the more changes we make, the more likely things are to go wrong! You can also discuss off-target edits – cutting at the wrong gene.

Some visitors will need more information about what DNA is and how it works. It may be worth showing an example of transcription and translation – either in video or via a model. This would be a good opportunity to explain that the over-simplified view of “the gene for…” is not really particularly accurate and that the functions of most genes are far more complex.

Key Messages

Humans have been manipulating genomes of plants and animals for thousands of years via selective breeding.

We can now do it faster and more accurately than ever before by choosing exactly what bit of DNA to change.

We have been able to genetically engineer organisms for many years; a good example is the manufacture of human insulin by bacteria.

New techniques such as CRISPR Cas9 are more precise and targeted than previous methods. Over the last few years, there has been an increase in use of genome editing uses.

There is the potential for genome editing to help us deal with many global challenges; growing more food, making nutritionally fortified foods, producing green energy, producing vaccines, understanding human health and disease, treating epidemics, beating antibiotic resistance, fertility treatment, producing treatments for cancer, and even creating synthetic life.

Correcting faulty genes will help cure certain genetic diseases. This has far-reaching ethical implications about what it is appropriate to treat and how access to this technology is distributed.

There is concern that this could lead to a “slippery slope” allowing cosmetic modification or a two-tier class system of those who can afford to edit their children.

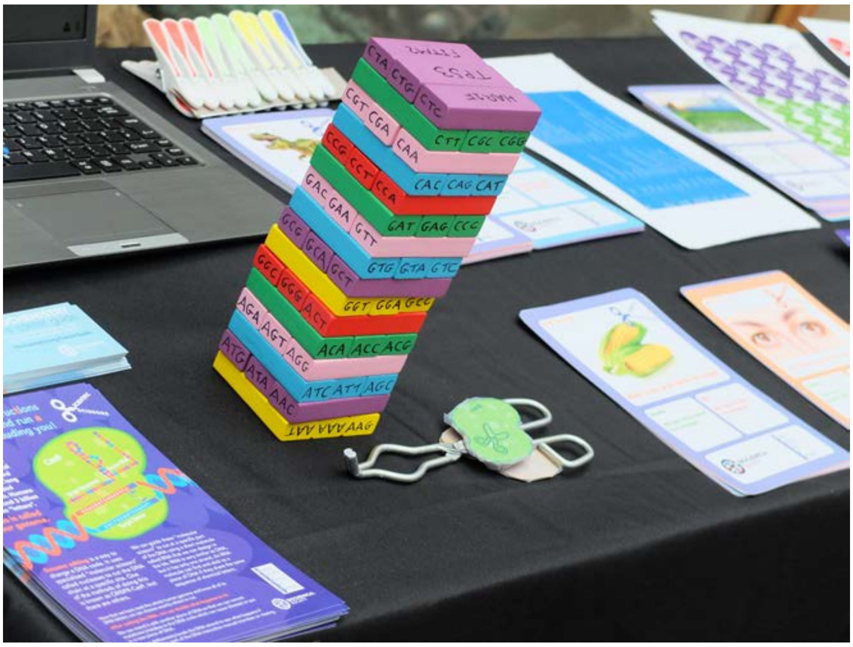
Some people are worried about using Genome editing in humans and food.

They are worried that if we make changes in the germline*, that they will be irreversible.

Since the link between genes and characteristics is rarely straight forward, it is hard to predict what effect changing genes might have.

It is also possible that unintended changes will occur which go un-noticed.

One of the biggest issues surrounding genome editing, is the ease at which we can now make changes. Whilst this will make research much easier, it opens up the door for many potential applications and therapies, which will have safety and ethical issues.



Genome editing is now able to carry out single base substitutions with incredible accuracy. Our game shows how a gene is knocked out, but there is a way to give the cell a template to correct after cutting, like a new set of instructions. However, there is still concern about off-target edits and unforeseen effects. Making DNA edits also have the potential to have unforeseen knock-on effects. Since genes do not work in isolation, it can be very difficult to predict what effects changes might have. On the other hand, mutations and changes in DNA occur naturally and via selective breeding.

The potential for human modification and treatment of disease is now closer than it has ever been. Firstly, it is important to note the difference between somatic genome editing, and germline genome editing. Making changes to the germline mean that the edits will be passed onto any offspring and hence will enter the general population. This means that it would be almost impossible to stop these edits if it was later found out that there was a problem. Somatic edits would not be passed onto any offspring, thereby only affecting that particular individual. This is an important point to highlight when considering with what sort of uses we are comfortable.

Other ethical issues are to think about how this technology will be distributed and who will be able to benefit. There are bound to be economic restrictions to who can access this technology and who can profit from it. It may also result in certain groups becoming marginalised because they either cannot or choose not to use genome editing, in particular certain disabilities and diseases. There are also religious issues, social issues… There are of course benefits as well, including reducing food shortages, helping nutrient deficiencies and treating genetic disease.

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Further reading: -

Nuffield Council on bioethics – Genome Editing

If you could alter the characteristics of future generations, would you do it?

UK Parliamentary report on Genome Editing

Fears vs realities

Slowing Cancer growth

Gene Editing in Food

Use of language in Bioethics