Potential and risks of recent developments in biotechnology

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Speech outline

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The developments in genetic technologies that have led us to where we are

1a. Setting the scene

I grew up in India – a country where many people do not have enough food to eat and where cancer survival rates are among the world's worst. However, I have spent most of my life in the US and UK where people have greater access to food and healthcare and so often have very different priorities and concerns about new technologies.

When considering what we can do with technology we also need to consider what we should do. This is not something that should be decided by a small group of people in a small group of nations because new technologies will affect us all.

We have all heard the promises of biotechnology and specifically genetic technologies – feeding the world, curing disease, even making money. There are people who say there is too much hype – those who would ask, for example, where is the vitamin A-rich 'golden rice' that is meant to prevent blindness? Yet, at the same time, there are those who would point to the fact that in the UK we have a young girl called Layla who is alive because of a last resort experimental gene editing therapy that was used to treat her leukaemia.

Today I want to look at where genetic technologies are now and what they can realistically achieve. I want to ask if we are at the dawn of a new age of biology. I also want to explore where we might go next, how we decide what the next steps should be, and how we might get there.

1b. The history of genetic manipulation

Adapting biology for the benefit of humankind is far from new. There is a long history of it – from selectively breeding and domesticating crops and animals, to using modern biotechnology such as gene therapy in healthcare.

If we look at plants, we know that the domestication of crops by selective breeding began over 10,000 years ago. In the 1800s the father of modern plant breeding, Luther Burbank, developed over 800 new strains of fruits, vegetables and flowers. Perhaps most famously, his blight-resistant Burbank potato was planted across Ireland and widely celebrated for ending the potato famine. Fast forwarding to the 1980s, we have the first genetically modified (or GM) crops grown in the US, and nowadays GM crops are grown on more than 10% of the world's arable land[1].

When it comes to animals, we see a similarly long history of genetic manipulation, usually to make wild animals more desirable to humans. Chickens have been selected to be larger, wild cattle to be smaller, and sheep to lose their bristly outer hairs but not their soft inner hairs (or wool).

Perhaps most striking are cases where the same ancestral species has become domesticated for different purposes, resulting in very different breeds or crops. Dogs, for instance, have been variously selected to kill wolves, dig out rats, race, be eaten, or be cuddled in our laps. When faced with wolfhounds, terriers, greyhounds, Mexican hairless dogs and Chihuahuas, you could easily be forgiven for assuming they were different species. Similarly, *Brassica oleracea* has been variously selected for its leaves (to become cabbage and kale), its stems (to become kohlrabi), its flower shoots (to become broccoli and cauliflower) and its buds (to become Brussels sprouts)[2].

All of this has been done with genetics. But few would refer to these examples as having used 'biotechnology' or 'genetic technology'.

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1c. New tools

Nowadays we have a wider range of tools at our disposal. Advances in science are making genetic manipulation faster, easier and cheaper.

Sequencing DNA in the 1980s cost around US$6,400 per base pair; it now costs between US$0.03 and US$0.10 per base pair[3]. The cost of synthesising DNA – a newer technique – is also dropping steadily, as figure 1 shows.

As well as sequencing and synthesising DNA, we can also edit it. We can cut out single base pairs or large sections or DNA with increased precision. We can insert DNA from other species. And thanks to our increasingly sophisticated understanding of how genes interact with the environment, we can alter gene expression by turning genes on and off.

A genome editing technique called CRISPR/Cas9 is receiving particular attention at present. It involves a molecular system (CRISPR) that guides a protein (Cas9) towards a specific target sequence of DNA. The protein then cuts the DNA at that specific site. CRISPR-based methods are relatively efficient, cheap and easy to use, and allow edits to be made at multiple sites in the genome in a single procedure[5].

The rapidly advancing field of synthetic biology – which has been described as "the design and engineering of biologically based parts, novel devices and systems as well as the redesign of existing natural biological systems"[6] – is also receiving attention and opening up new biological vistas.

FIGURE 1: THE COST OF SEQUENCING AND SYNTHESISING DNA[4]

Price per base of DNA Sequencing and Synthesis March 2016.

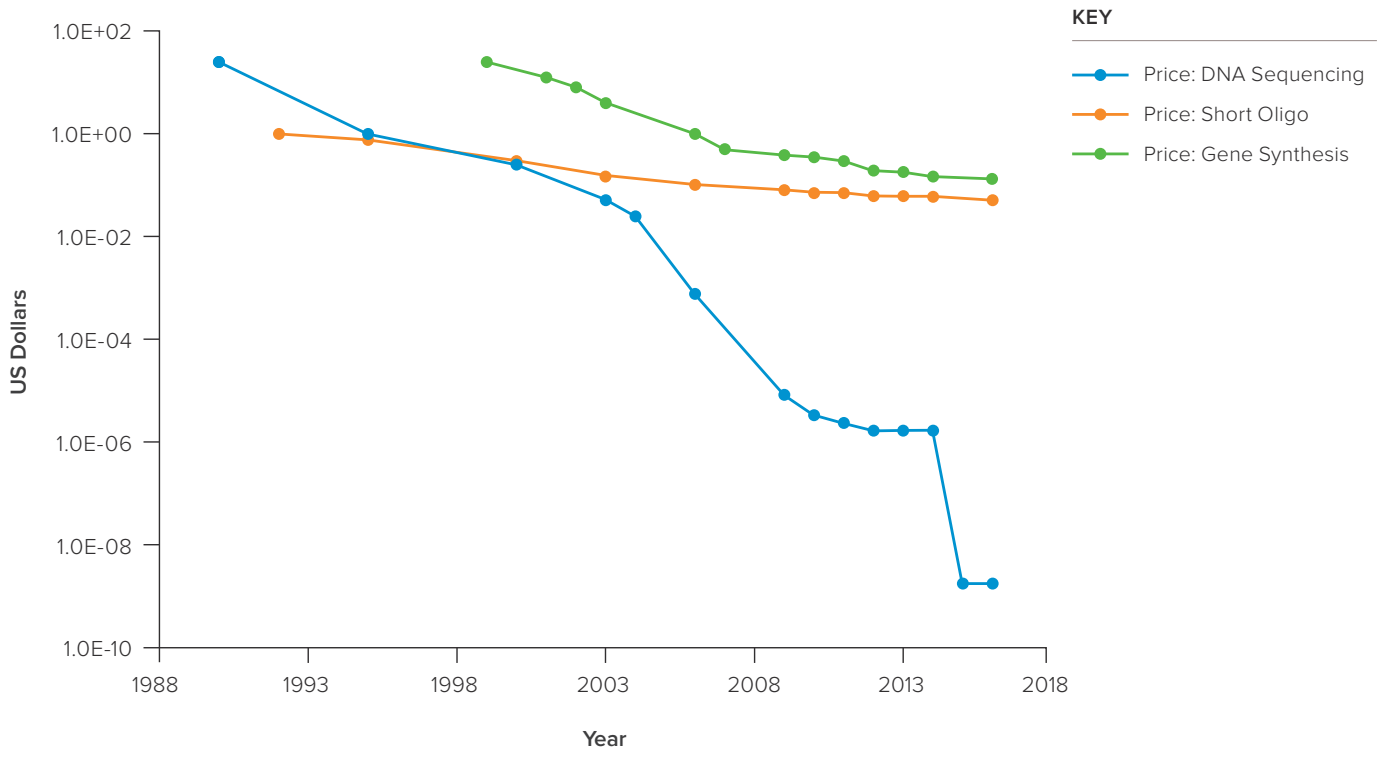

Figure reproduced with permission of Rob Carlson www.synthesis.cc

3. Rob Carlson 2016 On DNA and Transistors, 9 March. (See www.synthesis.cc/synthesis, accessed 12/01/2017)
4. The Royal Society 2015 Sackler Forum 2015, London: The Royal Society
5. Sander, J D, Joung, J K 2014 CRISPR-Cas systems for editing, regulating and targeting genomes. Nature Biotechnology 32, 347-355
6. UK Synthetic Biology Roadmap Coordination Group 2012 UK Synthetic Biology Roadmap. Swindon: Technology Strategy Board

1c.i. New tools for existing purposes

In many instances, new techniques are being used for existing purposes rather than novel ones.

A good example is insulin production for the treatment of diabetes. This was originally extracted from the pig pancreas, which required collection and purification and was an inherently limited supply. In the 1970s, however, the insulin gene was inserted into the *E. coli* bacterium and insulin is now produced in vats of modified *E. coli*; allowing for a clean and consistent supply and removing the need for animal tissue[7].

Another example is vaccine and medicine production. An interesting new development is the use of genetically modified tobacco plants, which act as biological factories and can produce vaccines quicker – up to 2.5 million units of vaccine in a week[8] – and with less waste than traditional methods.

1c.ii. New tools to make new things possible

In the future we could aim for more ambitious targets like trees designed to capture and store more carbon[9], or plants that remove pollution from land[10] or react to explosives to show the location of land mines[11].

But new genetic technologies are already being used to make new things possible.

A recent example was the treatment of Layla, a patient at Great Ormond Street Hospital in the UK, who in 2015 was famously cured of acute lymphoblastic leukaemia. This was made possible by the ability to genetically edit donor T-Cells (a type of immune cell). These cells had new genes added to them so that when administered to Layla they became effectively invisible to a powerful leukaemia drug that would usually have killed them. They were also reprogrammed in such a way that they only targeted and fought leukaemia cells[12].

Although Layla's treatment was experimental rather than part of a clinical trial, the techniques used could potentially be used to treat other cancers, and could mark a turning point in cancer treatment[13].

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1d. A new 'age of biology'?

Despite our long history of genetic manipulation, could our increasing ability to modify microbes, plants, animals and ourselves represent an inflection point in history, or even the dawning of a new 'age of biology'?

We have reached the point where we can not only modify existing life with increasing precision but also create new life from scratch.

A particular breakthrough came in 2010 when a completely synthetic genome was inserted into a closely related host cell and could replicate[14]. The 'synthetic yeast 2.0' project based in Edinburgh is now working to produce a strain of yeast which would be the first eukaryote with an entirely synthetic genome[15]. Figure 2 shows the increasing amount of DNA and increasing complexity of biological forms that we've been able to synthesise over time – right up to synthetic yeast, predicted for 2017.

FIGURE 2: TIMELINE OF THE PRODUCTION OF SYNTHETIC GENES AND GENOMES[16]

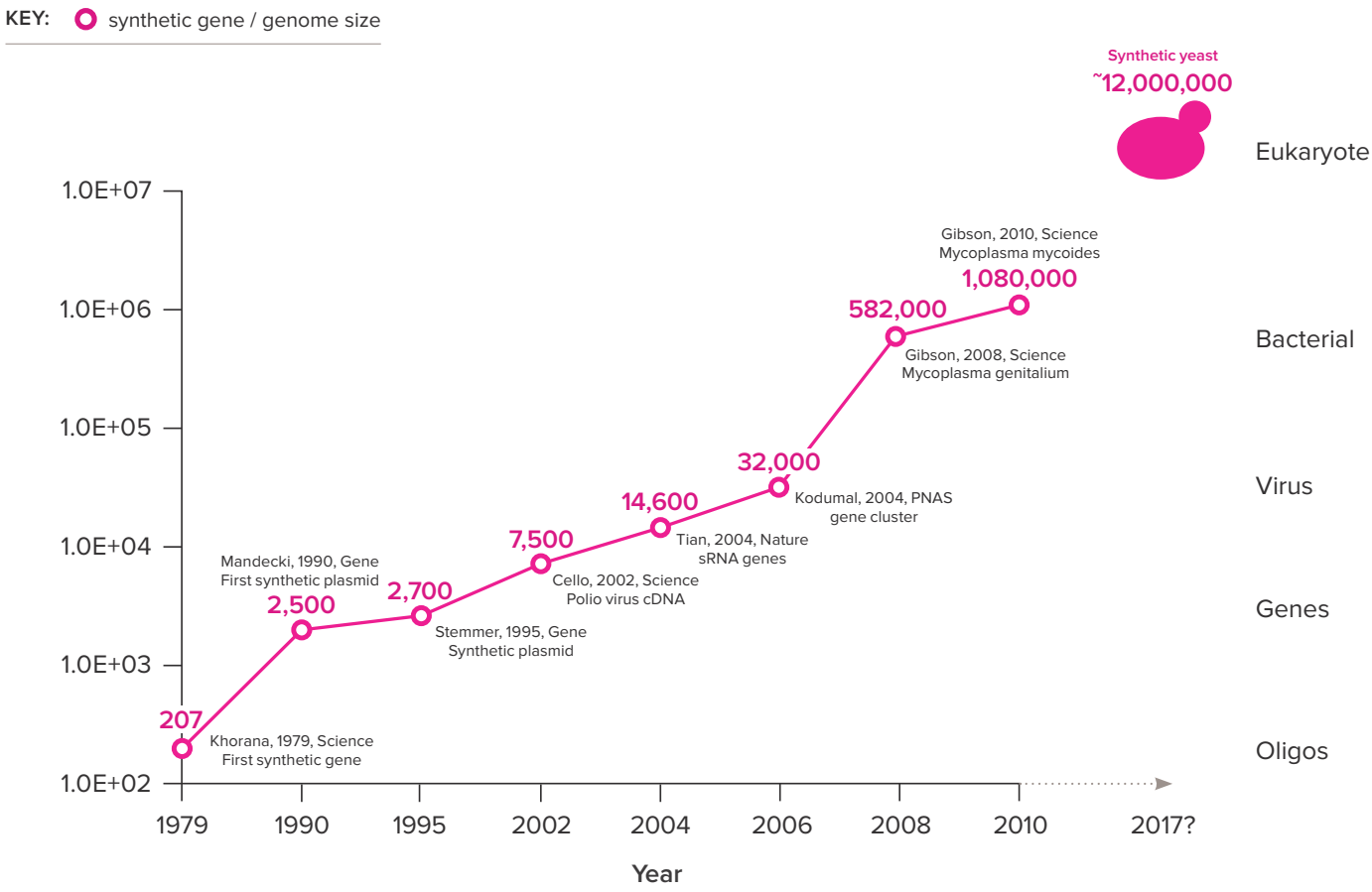

Figure reproduced with permission of Patrick Cai.

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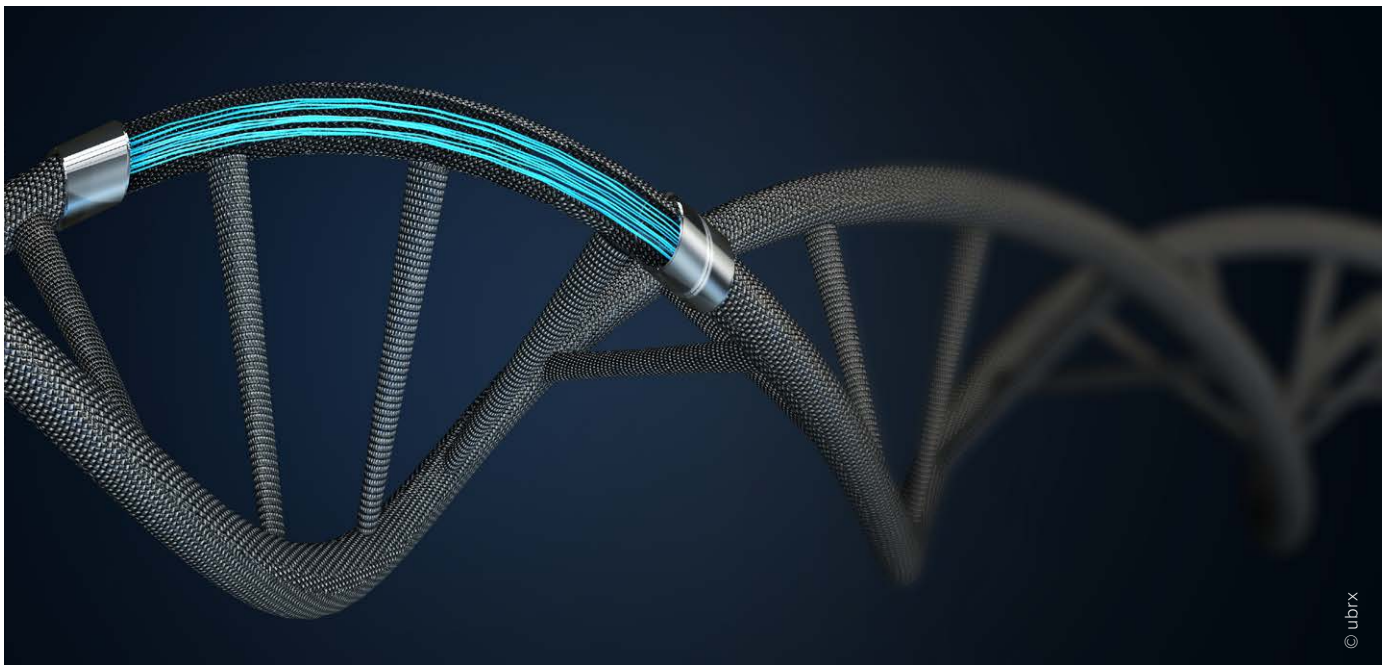

Along with more traditional genetic methods, this sort of work could provide new insights into how genes work and which ones are essential for life. It could also lead to organisms with vastly modified DNA; perhaps containing novel base pairs[17], or new combinations of genes that haven't existed together before. This, in turn, could challenge our ideas about species and what makes something distinctly a grasshopper, orchid or pig.

As genetic science develops even further, we could begin to see applications that go beyond living organisms – such as using DNA to store digital information or to build small machines[18].

All this could mark a change in how we think about ourselves and our relationship with the natural world. As genetic technologies continue to develop, it is important that we discuss how we use them and where we want them to take us. For example, have we moved – or should we aim to move – from observing, preserving and controlling nature to creating, directing and sculpting it and ourselves? Could 'making' biology rather than just affecting or disturbing it draw us into a new relationship with nature[19]?

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The risks and benefits that current developments in genetic technologies present

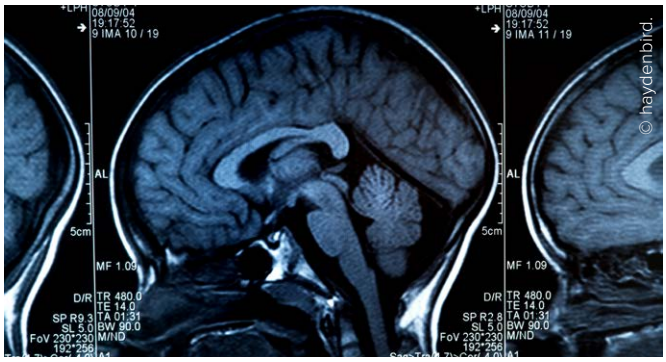
Along with other approaches, these new genetic tools could play a major part in addressing the challenges humanity faces – from tackling human disease to achieving food security, from conserving nature to synthesising useful products. I will consider each of these in turn.

2a. Human health

Genetic technologies are already being used to prevent and treat human diseases. I have already mentioned the production of insulin from genetically engineered *E. coli*, the development of vaccines using modified tobacco plants, and promising new cancer treatments.

2a.i. Editing ourselves

Human diseases are often treated by removing cells from the body, modifying them – including now with the CRISPR/Cas9 technique[20] – and returning them to the body. They can also be treated by introducing components that make genetic changes within the patient's body (as with techniques to correct degenerative eye disorders[21] or liver conditions[22]). Monoclonal antibodies (identical copies of antibodies that target specific proteins on the surface of cells) are among the biggest selling medicines on the market today. They are used for treating diseases as diverse as rheumatoid arthritis, Crohn's, Alzheimer's and various cancers[23].



These sorts of genetic changes are not passed on to future generations. But there are changes that could be made to eggs and sperm, or changes that could be made to embryos, which would be passed on to future generations. There is currently a *de facto* international moratorium on genetically modifying embryos that will grow into babies. It is possible to do this for research purposes, although the embryos may only be grown for 14 days. In the UK this is tightly regulated by the Human Fertilisation and Embryology Authority[24].

Our understanding of genetics is such we may be able to correct single gene disorders where there is a known and well understood change in the DNA. However, we do not yet understand the complex interactions that result in multi-gene disorders and produce characteristics like intelligence. Scientific developments in the future have the potential to raise profound questions about the moral differences between treating disease, making cosmetic changes and enhancing human abilities beyond what might be considered 'normal'[25,26].

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2a.ii. Editing vectors of disease

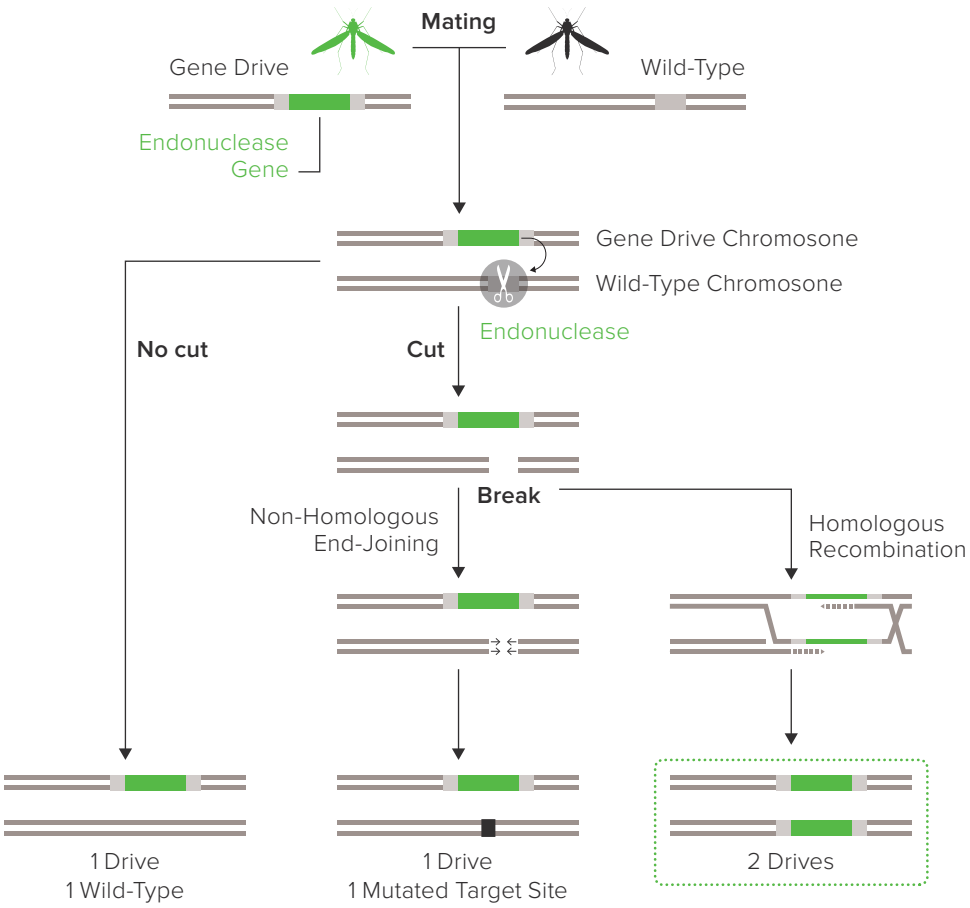
As well as applying genetic techniques to human cells, is it also possible to reduce human disease by targeting animal vectors.

A particularly promising way of doing this could be the gene drive. Gene drives use genetic recombination to ensure that a gene is copied across from one DNA strand to its paired DNA strand, as shown in figure 3. This means that the gene and its associated trait are passed on to all subsequent generations, even if the gene confers a disadvantage on the species. In this way, gene drives force a gene to spread through a sexually reproducing population much more rapidly than natural processes of evolution would.

The insertion of a gene drive into mosquitoes could create an opportunity to reduce or even eradicate mosquito-borne diseases. This could be done using gene drives which make either the female or the male sterile, prevent the transmission of a particular pathogen, shorten mosquitoes' lifespan, or skew mosquitoes' sex ratio[28].

Sterile mosquitoes are already a promising means of decreasing the incidence of malaria, zika, dengue fever and sleeping sickness[29]. However, previous trials have used techniques like x-ray mutagenesis rather than gene drives, and have therefore required the repeated release of swarms of sterile mosquitoes[30].

FIGURE 3: GENE DRIVE[27]



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Malaria is a potential candidate for gene drive technology. Despite efforts to control malaria using bed nets and treatments like artemisinin, there remain 200 million cases of infection and half a million deaths per year[31].

A gene drive that alters the female *Anopheles* mosquito's ability to become infected with the malaria parasite, or one that prevents parasite development within the mosquito, could block malarial transmission without affecting mosquito populations[32]. Alternatively, a gene drive that reduces the fitness of the female mosquito – for example, by causing sterility – could reduce mosquito populations over time[33]. Both mechanisms are as yet unproven, and the opportunities they present may ultimately be small.

Despite their potential, gene drives carry considerable risks since the broader ecological consequences of reducing or eliminating a species can be uncertain. Confinement strategies, safeguards and appropriate governance for their use would be critically important[34,35]. Once a gene drive is released it may be possible to create a 'reversal drive' which can remove the introduced trait[36]. This might not, however, reverse any changes occurring in the ecosystem in response to changes in the target species. Other potential containment mechanisms include limiting the number of generations over which the gene drive operates in order to partially contain it[37].

Even with safeguards in place, it may be a significant challenge to obtain informed consent from those living in an area where a gene drive experiment is being carried out.

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2b. Food and nutrition security

Another global challenge to which genetic technologies might contribute is food and nutrition security. We are faced with the challenge of creating more, cheaper and safer food against a backdrop of significant pressures on the food system[38]. The global population is climbing towards nine billion, with significant proportions of the current population undernourished or obese. In addition, stresses from climate change mean that food sources need to be more resilient to extreme conditions such as drought and new diseases.

There are many things that could be done, including reducing waste and delivering a more equitable distribution of resources. But given estimated growth in the human population, it's clear that yields will need to improve considerably.

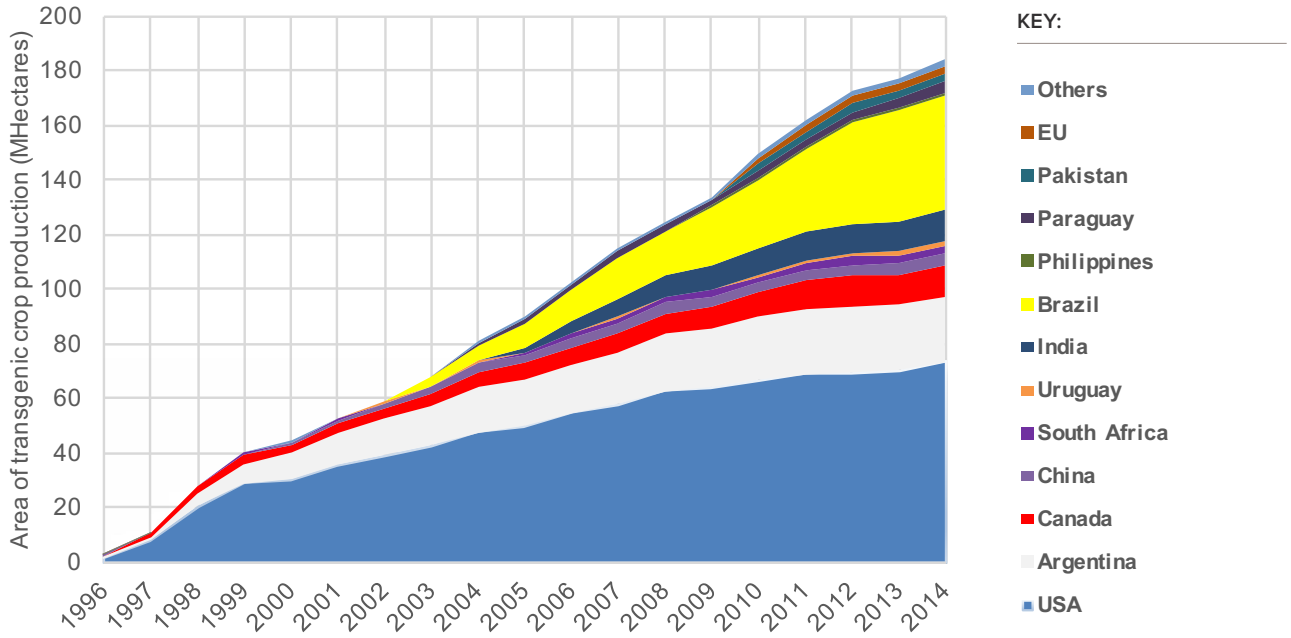
2b.i. Plants

Genetic technologies could offer several ways of alleviating these pressures and meeting future needs. We could produce higher-yielding crops, crops with added nutrients (so-called 'golden rice' with added beta carotene from which the body can make vitamin A is one example[39]), and crops that are resistant to drought, pests and herbicides.

Disease resistance is another desirable feature. A major project supported by the Bill and Melinda Gates Foundation is currently trying to develop a modified version of matooke, a starchy variety of banana and staple food in many parts of Africa. The aim is to create a variety that is resistant to a disease called banana leaf wilt that has been devastating plantations. Within the next few years local scientists hope to have developed a proven wilt-resistant plant by inserting a gene found in red peppers[40].

We have seen a rapid increase in the worldwide acreage of GM crops over the past twenty years, as figure 4 shows. However, progress on many of the anticipated benefits has been slow – not always for scientific reasons.

FIGURE 4: GROWTH IN AREA OF TRANSGENIC CROP PRODUCTION [41]



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While researchers are currently working on things like blight resistant potatoes, in the future new genetic techniques could allow us to redesign crops more dramatically. We could change them from annuals to perennials so they don't need replanting[42], or give them the ability to use nitrogen from the air, like soil bacteria, and no longer require nitrogen fertiliser[43]. However, given the experience of GM crops to date, we should beware of over-stating the potential of new techniques to deliver these benefits.

2b.ii. Animals

When most people think about genetic technologies and food they tend to think of GM crops. But animals are important too.

In November 2015, the US authorities approved the first GM animal for human consumption: a fast growing salmon that contains a growth gene and promoter from other fish[44, 45]. The salmon is not yet available commercially because of problems with identifying and meeting labelling requirements.

There are also possible ways in which genetic technologies could be used to improve animal welfare in farming. Although none has been commercialised[46], they could include growing cattle without horns, thereby reducing the risk of injuries, and making chickens resistant to flu.

42. Melzer, S, Lens, F, Gennen, J, Vanneste, S, Rohde, A, Beeckman, T 2008 Flowering-time genes modulate meristem determinacy and growth form in *Arabidopsis thaliana*. Nature Genetics 40 (12), 1489-1492
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2c. Nature conservation

Another application of genetic technologies which is receiving increasing attention is the conservation of biodiversity. While controversial, and as yet unproven, attempts to resurrect extinct species can tend to grab headlines, the potential use of genetic technologies to reduce or eradicate invasive species could be a more plausible conservation measure.

2c.i. Invasive species

I mentioned gene drives in the context of eradicating vector-borne diseases like malaria and zika. The same technique could be used for conservation – by increasing disease resistance in a species at risk, removing an invasive species, or removing a predator for a protected species.

Research is currently underway into how gene drives could be used to control non-indigenous mouse populations which threaten native biodiversity on islands across the world. A promising mechanism is a sex-determining gene drive that causes mice to produce more male offspring than female offspring[47]. This takes advantage of a region of the mouse chromosome 17 which has high meiotic drive (meaning it is more likely to be passed on to offspring). Mice can be genetically engineered so that the gene which promotes male characteristics is located on this region of chromosome 17 rather than in its usual location on the Y chromosome. Skewing the sex ratio of multiple generations should lead to a reduction in mouse populations over time.

Gene drives are also being considered as a way of controlling other invasive species, including wasps in New Zealand[48] and cane toads in Australia[49].

We are still learning about the complexity of the relationship between an organism's DNA and its overall functioning and behaviour. More complex still are the knock-on ecosystem effects that could arise from using a gene drive in an invasive species. As with any form of biological pest control, gene drives for this purpose risk opening a 'Pandora's box' of unintended consequences, and any trials in the wild would require containment mechanisms and safeguards.

2d. Synthetic materials

Another application of genetic technologies – and the final one I will mention – is the synthesis of useful materials, including low carbon fuels and industrial chemicals. Fields such as industrial biotechnology and synthetic biology are offering new, more sustainable ways to manufacture products in additional to, or instead of, those traditionally produced by the chemical and materials industries.

One example is the production of acrylic, which is used in a wide range of industrial and consumer products – from paints and adhesives, to nappies and fabric detergents. Although traditionally produced from petroleum, a bio-acrylic is now being developed which can be used in the same ways as petro-acrylic but is associated with a 75% reduction in greenhouse gas emissions[50].

Another promising application is the production of biological batteries. Through studying resilient natural structures such as abalone shells or diatom algae, a team of researchers at MIT have engineered viruses to produce carbon nanowires to serve as battery electrodes. Applying this research to the production of lithium-air batteries holds the promise of drastically increasing power to battery weight ratios. This approach has also been used to build nanoscale biological devices and circuits, touchscreens, fuel cells, catalysts, lightweight, high-strength materials, and to target ovarian tumour cells[51].

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2e. Risk

What can we learn from all these diverse examples – from human health to food security, nature conservation to industrial biotechnology?

2e.i. Perceptions of risk

All change brings risk. But not changing brings risk too.

It is important to recognise that risk is contextual and aspects of it are very culturally dependent. We need only to look at the mix of views on GM crops in different countries and the different rules around human germline editing to appreciate this point.

People are often concerned about why and who, about values of actors, about equity, and about the distribution of risks and benefits for them and those around them[52].

About 15 years ago when GM was just emerging, its main proponents and many of the initial products were from large multinational corporations – even though it was publicly funded scientists who produced much of the initial research. Understandably, many felt GM was a means for these corporations to maximise their profits. This perception was not helped by some of the practices of these big companies, such as introducing herbicide resistant crops that led to the heavy use of herbicides often made by the same companies.

Alternative business models which focus on public interest rather than private gain may be received very differently.

People look at issues through several different lenses, and it is important to debate each on its own terms. Concerns about genetic technologies might relate to globalisation and multinational corporations, or might relate to the safely of a particular application. Both are legitimate concerns, but it can be counterproductive to debate one when the concern is really the other.

2e.ii. Types of risk

Much discussed are the potential catastrophic risks, resulting from intended or unintended action – in particular, that we will release diseases dangerous to humans, plants or animals, or that a biological weapon could be intentionally or accidentally produced.

Harder to visualise, but probably more realistic, are the risks associated with gradual change – that through our choices we unintentionally arrive at a state we didn't want and haven't consented to. Could we reinforce human inequalities through genetic interventions or enhancements in health[53]? Could we reduce biodiversity by trying to increase food security and agricultural productivity?

52. Government Office for Science, 2014 "Perceptions of Risk" in Innovation: Managing Risk, Not Avoiding it (ed. M Peplow). London: Government Office for Science, 93-106

53. Devlin, H, 2016 Kazuo Ishiguro: 'We're coming close to the point where we can create people who are superior to others' 2 December (See https://www.theguardian.com/science/2016/dec/02/kazuo-ishiguro-were-coming-close-to-the-point-where-we-can-create-people-who-are-superior-to-others accessed 12/01/2017)

Where we could go and what we would need to get there

3a. Public debate plus robust science

It is important to recognise that we are not victims to the course of technology; we have choices that will shape its path. Making wise choices on a case-by-case basis requires engagement both with the science and with values and principles. It also requires public debate involving many voices – from scientists, campaigning organisations, industry representatives and policymakers.

To be successful we need public debate and policy decisions to be informed by robust science. The Royal Society has worked extensively with others to promote this, and will continue to do so. For example, we worked with the national science academies of China and the US to co-host the international Human Gene Editing Summit in 2015. We agreed that there was a role for the academies "to take the lead in creating an ongoing international forum to discuss potential clinical uses of gene editing; help inform decisions by national policymakers and others; formulate recommendations and guidelines; and promote coordination among nations"[54].

One example of successful public debate about the issues surrounding new genetic technologies comes courtesy of the UK's Human Fertilisation and Embryology Authority – specifically its process of public debate on the issue of mitochondrial donation. This involved five complementary strands – deliberative workshops, a public representative survey, public meetings, patient focus groups, and an online consultation questionnaire – and showed the various ways of engaging different societal groups to ensure a robust consideration of social and ethical issues raised by scientific advances[55].

Another example comes from the New Zealand Department of Conservation, which has released a strategy for New Zealand to be free of the predators introduced to the islands by humans by 2050[56]. The range of options for achieving this strategy includes gene drives to reduce possum numbers. Several community meetings have been held to discuss the strategy, the challenges associated with implementing it, and the different ways that it could be achieved. Open discussions of a range of technologies in different contexts were important factors in generating public support for the strategy.

54. International Summit on Human Gene Editting 2015 On Human Gene Editing: International Summit Statement, 3 December. (See http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a accessed 13/01/2017)

55. Government Office for Science, 2014 "Ultimately a Decision Has to be Made" in Innovation: Managing Risk, Not Avoiding it (ed. M Peplow). London: Government Office for Science, 137-144

56. Department of Conservation (New Zealand) 2016 Predator Free 2050. Wellington: New Zealand Government

3b. Regulatory systems

Regulatory systems for genetic technologies need to address risks proportionately and apply lessons from responsible and safe innovation in other emerging technologies.

3b.i. Regulating plants and animals

When it comes to regulating the application of genetic technologies to plants and animals, we need adaptable regulatory systems which:

- firstly, blend a focus on the characteristics of new organisms with a consideration of the processes by which they are created;
- secondly, are adaptable and future-proof for safely regulating rapidly emerging areas of science, such as gene drives; and
- thirdly, contribute to a 'web of protection' to support biosecurity and help build public confidence[57].

Very different approaches to regulation exist around the world. In the US and Canada the regulation of GM crops focuses on the characteristics of the crop produced, while in the EU the focus is on how it has been modified[58].

The problem with the latter model is that new characteristics in crops – for example resistance to a particular herbicide – can be achieved in several ways, including through conventional selective breeding and GM. However, resistance generated by GM would be heavily regulated, and hence judged to pose a higher risk, simply because of the way it was introduced. GM crops do not damage the environment or pose any other risk due to the process of their modification. GM is a technology, and it is the resulting product that we should be primarily concerned about and regulate, just as we would any new product.

That said, we are not faced with a binary choice when it comes to regulation – it is not a simple case of 'product versus process'. Moving towards regulation that focuses on the products or characteristics resulting from the application of genetic technologies still requires some understanding of the technique used to create them. This is particularly true as new techniques develop, which may be considered more or less risky[59].

Regulatory systems need to be adaptable and future-proof to cope with new techniques and scientific advances. If it becomes impossible to tell how a characteristic has been introduced, then regulating the method of introduction – or even considering it alongside the end product – will quickly become impractical.

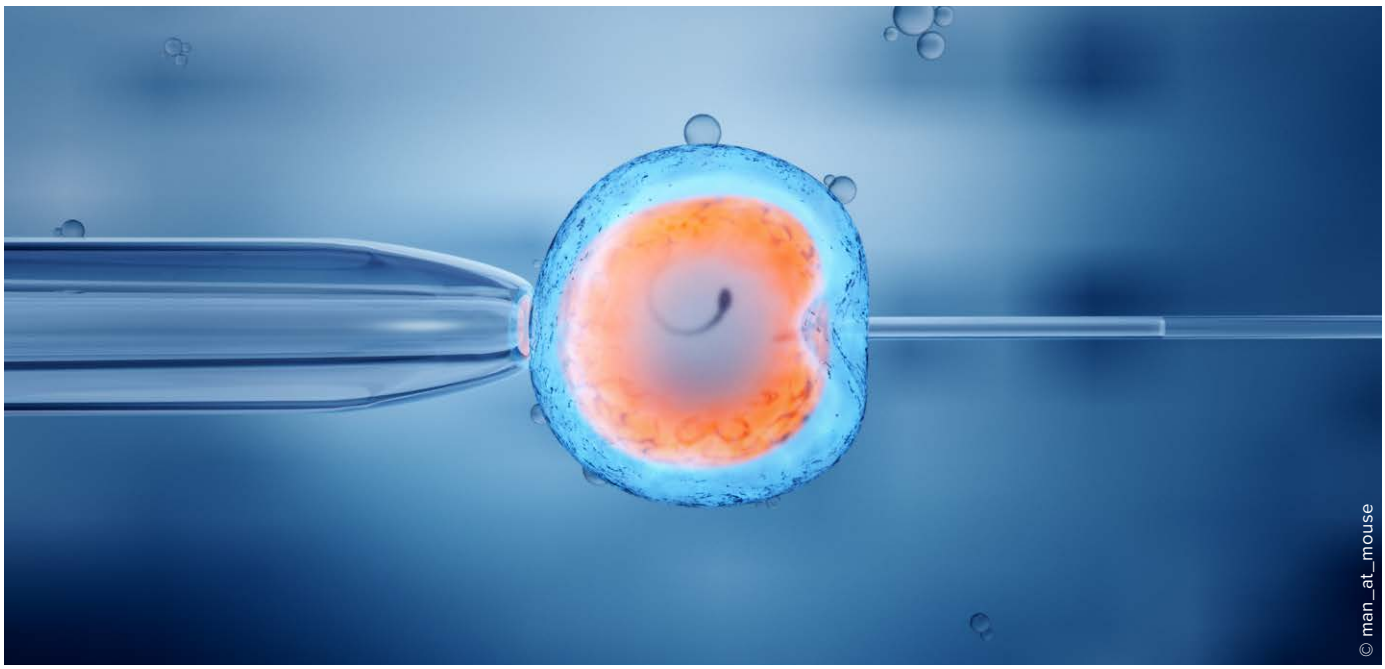
The UK might present an interesting case study in the next few years as it leaves the European Union. In doing that, it may look to reshape the aspects of its regulatory system that apply to the commercial production of GM plants and animals.

No genetically modified animals have been approved for human consumption in the EU, and only a few varieties of commercial crops (mostly maize) have been approved for cultivation. The EU is currently considering whether new techniques – referred to as 'new breeding techniques' and including things like CRISPR/Cas9 and synthetic biology – should be regulated under the GMO regulations. At present, their status and regulation are unclear.

57. The Biological and Toxin Weapons Convention, 2015 Implications of advances in science and technology. London: The Royal Society

58. Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed 2003 (European Union)

59. Kuzma, J, 2016 Reboot the debate on genetic engineering. Nature 531, 165-167



3b.ii. Regulating humans

All human applications of genetic technologies fall under the strict regulation for the development of medicines, governing research on humans or human tissue and new medical procedures.

We still have more to learn about the uses of genetic technologies in humans. Basic research is important in both somatic (body) cells and in the human germline (eggs, sperm and embryos) to advance our understanding of the biological processes underlying disease[60]. Clinical treatment of somatic cells is also showing great promise.

When it comes to the clinical treatment of the human germline – in other words, making changes that would be inherited – it is too early to be confident in using genetic technologies. However, as suggested this week by the US National Academies, developing safe and publicly acceptable ways to prevent future generations inheriting serious genetic conditions could be a realistic possibility[61]. A move in this direction would need to be approached with caution, oversight and public support, but the National Academies have sent a strong signal to scientists to continue advancing our knowledge of what might be possible.

3b.iii. International collaboration

To most effectively manage the risks and benefits posed by advances in genetic technologies, we need to work with international partners to better understand commonalities and differences in national regulatory systems. If, for example, the UK were to reshape its regulatory model for GM plants and animals, it should do so in a way that supports international collaborations from research through to applications, security and trade.

60. International Summit on Human Gene Editing 2015 On Human Gene Editing: International Summit Statement, 3 December. (See http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a accessed 13/01/2017)
61. The National Academies of Sciences, Engineering, and Medicine, 2017 Human Genome Editing: Science, Ethics, and Governance. Washington, DC: The National Academies Press

In matters of security, genetic technologies can both increase the risk of biological weapons being developed and increase our ability to detect and respond to them. International collaboration is essential for building up several different layers of deterrence and protection – from norms within the research community, such as mechanisms for reporting suspicious activity, to appropriate national and international regulation.

The Royal Society has already shown leadership when it comes to international collaboration on these issues; working with the US National Academy of Sciences on synthetic biology and gain of function[62], with the science academies of the US and China on human gene editing; and with the academies of the US and Poland to support the Biological and Toxin Weapons Convention[63].

3c. Exploring inconsistencies and values

New genetic technologies require us to look afresh at profound questions about how we as humans view ourselves and the world we inhabit. They show that we apply very different considerations to the way we produce food and the way we create medicines; that we may think of animals as sources of food or human body parts, as companions, or as elements of 'wild' biodiversity; and that our ideas of what is novel or what is natural themselves change over time. I will briefly consider each of these.

3c.i. Food versus medicine

Examining the range of applications that genetic technologies might have highlights the fact that food and medicine are treated very differently in public debate and policy frameworks. Genetic technologies are generally more accepted in connection with medicine than with food[64].

One illustration of this is the contrast between insulin and vanillin, the substance that gives the vanilla bean its distinctive smell. In a similar fashion to insulin, bacteria have been modified to produce vanillin cleanly and reliably[65]. Before this, commercial quantities of vanillin had been produced using a chemical synthesis process based on a petrochemical by-product.

The difference in the reception of these products suggests, amongst other things, a cultural difference between how medical products are viewed and how food ingredients are viewed. Insulin from GM bacteria has generally been welcomed, while vanillin from GM bacteria has met with resistance and campaigns from organisations, like Friends of the Earth, encouraging people to boycott 'synthetic biology in their food'[66].

FOOD VERSUS MEDICINE

62. The Royal Society 2015 Sackler Forum 2015, London: The Royal Society
63. The Royal Society 2016 Assessing the implications of advances in science and technology for the Biological and Toxin Weapons Convention: meeting summary, London: The Royal Society
64. Connor, M, Siegrist, M 2010 Factors Influencing People's Acceptance of Gene Technology: The Role of Knowledge, Health Expectations, Naturalness, and Social Trust. Science Communications 32 (4), 514-538
65. Barghini, P, Di Gioia, D, Fava, F, Ruzzi, M 2007 Vanillin production using metabolically engineered *Escherichia coli* under non-growing conditions. Microbial Cell Factories 6 (13), 1-11
66. Friends of the Earth 2013 Synthetic Biology Vanillin: not natural, not sustainable, not likely to be labelled, and coming to an ice-cream cone near you. Washington: Friends of the Earth

3c.ii. Animals

A holistic view of genetic technologies also challenges our view of animals, and forces us to question the regulatory frameworks that apply to the laboratory, the field and the wild.

The possible future applications of genetic technologies to animals are wide ranging – from improving animal welfare by breeding flu-resistant chickens; to breeding domestic cats to have hypo-allergenic fur; from creating gene drives to reduce or eradicate pests, invasive species and vectors of disease; to possibly even growing human organs in pigs or other animals. This latter example is particularly controversial since it involves the creation of human-animal chimeras (an area where there has been recent early success[6]) and raises issues about the use of animals for our own ends.

Despite these diverse applications, the regulation relating to animals can be inconsistent even for very similar applications. One example of this in the UK is the fact that researchers covered by the Animals in Scientific Procedures Act (ASPA)[68] need licences to perform laboratory tests on animals. If researchers deal with animals on a farm they still require the appropriate licenses. However, a farmer is able to carry out the same procedures on animals without any licences.

3c.iii. What is natural?

Advances in genetics also challenge public notions of what is natural and unnatural[69], and cast new light on how humans have affected the so-called 'natural' world over millennia.

As mentioned, there is much debate about artificially created gene drives and their regulation. However a naturally occurring gene drive, *Wolbachia*, exists within insect species. *Wolbachia* is not prevalent in *Aedes* mosquitoes, but when infected (naturally or deliberately) with *Wolbachia*, these mosquitoes no longer transmit Dengue fever[70].

Should our perception of the risks associated with gene drives, and their appropriate regulation, be coloured by the fact that a natural analogue exists? Are the traits or outcomes produced by genetic technologies more concerning and less acceptable when they are novel and don't resemble something identifiably 'natural'?

3d. Closing remarks

I hope that I have demonstrated the breadth of genetic technologies and their applications and, by considering them collectively, have provided a new framework for thinking about their risks and potential.

In recent years the idea of globalisation has become increasingly associated with economics, but of course it is not just about flows of capital and labour. Science is global too.

We live in a world where we cannot isolate ourselves from what happens in other countries. We face global problems – hunger, disease and environmental threats do not respect borders. So we should seek to address those global problems on a global stage. That means working together to ensure that the benefits of new technologies – and I personally believe that those benefits can be great – are as widely spread as possible. It also means respecting the needs of people across the globe.

If we are on the verge of a new age of biology we need to go into it with our eyes wide open. The Royal Society will continue to work with others on many of the important issues raised here – through public dialogue and international collaboration – so that science and technology may continue to contribute to safer, healthier, happier lives.

67. Wu, J *et al* 2017 Interspecies Chimerism with Mammalian Pluripotent Stem Cells. Cell 168 (3), 473-486
68. Animals (Scientific Procedures) Act 1986 (UK)
69. Burton, T 2015 Review of research on public perceptions of naturalness. London: Nuffield Council on Bioethics
70. Ye, H Y, Carrasco, A M, Frentiu, F D, Chenoweth, S F, Beebe, N W, van den Hurk, A F, Simmons, C P, O'Neill, S L, McGraw, E A 2015 *Wolbachia* Reduces the Transmission Potential of Dengue-Infected *Aedes* aegypti. PLOS Neglected Tropical Diseases 9 (6), 1-19

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