THE ROYAL SOCIETY

3 February 2017

Submission to the House of Commons Science and Technology Committee inquiry into genomics and genome editing

Summary

1. Genome techniques are valuable research tools and have wide ranging applications in plants, animals and humans. Considering these applications within a common framework is a helpful way to avoid fragmented or duplicated efforts, to reveal inconsistencies in our approaches to these techniques, and to share learning between different sectors.

2. Regulation of genetic technologies should a) blend the characteristics of a new organism with a consideration of the process by which it was created, b) be adaptable and future-proof for the safe regulation of rapidly emerging areas of science, and c) contribute to a 'web of protection' to help build public confidence regarding biosecurity.

3. Genetic technologies are only valuable if they are developed with public confidence. To make informed choices we need open public debate informed by robust science. The UK has demonstrated leadership in this area through the creation of the Human Fertilisation and Embryology Authority and its process of debate on the issue of mitochondrial donation.

4. The UK's Industrial Strategy should help create an environment that allows for the development and responsible use of these new technologies. This includes investing in infrastructure and developing a proportionate regulatory approach that allows these technologies to be developed rapidly, safely and with public confidence.

Introduction

5. The Royal Society welcomes the opportunity to submit evidence to this inquiry into genomics and genome editing. The Society is the UK's national academy of science. It is a self-governing Fellowship of many of the world's most distinguished scientists. The Society draws on the expertise of the Fellowship to provide independent and authoritative advice to UK, European and international decision makers.

6. This response draws on the Society's previous work, including: the International Summit on Human Gene Editing[1], co-organised by the Royal Society, Chinese Academy of Sciences and US National Academy of Sciences; the InterAcademy Partnership report on 'Assessing the implications of science and technology development for the Biological and Toxin Weapons Convention'[2]; the Society's online resource 'GM plants: Questions and Answers'[3]; the Sackler

---

[1]National Academies of Sciences, Engineering, and Medicine 2016 *International Summit on Human Gene Editing: A Global Discussion*. Washington, DC: The National Academies

[2]InterAcademy Partnership 2015 The Biological and Toxin Weapons Convention: Implications of advances in science and technology. Trieste: IAP

[3]The Royal Society 2016 *GM plants: Questions and Answers.* London: The Royal Society

Forum report on 'Synthetic biology and gain of function'[4]; and previous submissions to the House of Commons Science and Technology Select Committee[5] and Nuffield Council on Bioethics[6].

7. The Society will soon be launching a further programme of work on genetic technologies. This will include public dialogue and international engagement on the use and regulation of a range of genetic technologies. The programme will begin with a framing speech by the President, Prof Sir Venki Ramakrishnan PRS, at the American Association for the Advancement of Science conference on 18 February 2017. This response draws on the content of that speech.

8. There will also be a report on genome editing from the European Academies Science Advisory Council (EASAC) published in early 2017, exploring the societal, ethical, governance and regulatory issues raised by genome editing in humans, animals, plants and micro-organisms.

9. The broad terms of reference for this inquiry mean that a wide range of information is potentially relevant to the questions the Committee wishes to address. This submission touches on and summarises some of these, but is not exhaustive.

Genetic technologies

Background

10. Adapting biology for the benefit of humankind is far from new. Selective breeding and the domestication of crops and animals has been undertaken for millennia, and forms the basis of modern diets and lifestyles. Dogs have been selectively bred for hunting and shepherding and for their desirability as domestic pets. Similarly, the *Brassica oleracea* cabbage has been variously selected for its leaves, stems, flower shoots and buds to become contemporary kale, kohlrabi, broccoli and cauliflower, and Brussels sprouts respectively[7]. All this has been done using genetics, yet the techniques are not generally considered akin to those used to produce modern genetically modified plants and animals.

11. The science of genetics has advanced rapidly in recent years, providing a wide suite of tools for genetic manipulation. These are faster, cheaper and easier than previous methods, leading to a diversity of potential applications. Sequencing and synthesising DNA is now possible, and techniques such as the CRISPR/Cas9 system allow for very precise genome editing including multiple edits in a single procedure[8]. These techniques, coupled with the rapidly advancing field of synthetic biology, are opening up new biological vistas and expanding the possibilities for redesigning biological systems.

Human health

---

[4] The Royal Society 2015 *Sackler Forum 2015,* London: The Royal Society

[5] The Royal Society 2016 Submission to the House of Commons Science and Technology Committee inquiry into EU regulation of the life sciences. London: The Royal Society

[6] The Royal Society 2016 Submission to the Nuffield Council on Bioethics on Genome Editing. London: The Royal Society

[7] Sauer, J D 1993 Historical geography of crop plants – a select roster. CRC Press: Boca Raton

[8] Sander, J D, Joung, J K 2014 *CRISPR-Cas systems for editing, regulating and targeting genomes*. Nature Biotechnology **32**, 347-355

12. Genetic technologies have been used to improve human health for several decades – in many cases as a way of performing existing functions more efficiently. One example is insulin, which was traditionally extracted from the pig pancreas and purified. By genetically modifying the *E.coli* bacterium, insulin is now produced using a clean, consistent method which no longer requires animal tissue[9]. Methods of vaccine and medicine production have also been refined, with genetically modified tobacco plants producing vaccines more rapidly and with less waste than traditional methods[10].

13. However, genetic technologies within healthcare are also making new things possible. A famous case is that of baby Layla, a patient at Great Ormond Street hospital who was cured of acute lymphoblastic leukaemia[11]. Layla's treatment relied on 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. Although this was an experimental procedure administered clinically, it could lead to a treatment that targets various cancers. A second baby was cured in mid-2016 using the same procedure[12].

14. Layla's treatment involved genetic changes that would not be passed on to future generations. However, there are changes that could be made to the cells that give rise 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 modify embryos for research purposes, although the embryos may only be grown for 14 days. Due to recent scientific advances there have been calls for an extension to this limit in order to enhance our understanding of human embryo development and human disease. In the UK this is tightly regulated by the Human Fertilisation and Embryology Authority[13].

15. Our understanding of genetics is such that we may be able to correct single gene disorders where a known genetic 'error' exists. 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'.

Gene drives – human health and nature conservation

16. Human diseases can also be reduced 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. This means that the gene

---

[9]Goeddel, D V, Kleid D G, Bolivar, F, Heyneker, H L, Yansura, D G, Crea, R, Hirose T, Kraszewski, A, Itakura, K, Riggs, A D 1979 *Expression in Escherichia coli of chemically synthesized genes for human insulin.* Proceedings of the National Academy of Sciences **76** (1), 106-110

[10]Shoji, Y, Farrance, C E, Bautista, J, Bi, H, Musiychuk, K, Horsey, A, Park, H, Jaje, J, Green, B J, Shamloul, M, Sharma, S, Chichester, J A, Mett, V, Yusibov, V 2012 *A plant-based system for rapid production of influenza vaccine antigens.* Influenza Other Respi Viruses **6**(3), 204-10

[11]Reardon, S 2015 *Gene-editing wave hits clinic*. Nature **527**, 146

[12] Page, M L 2017 *Gene editing has saved the lives of two children with leukaemia* 25th January. (See https://www.newscientist.com/article/2119252-gene-editing-has-saved-the-lives-of-two-children-with-leukaemia/ accessed 26/01/2016)

[13] Human Fertilisation and Embryology Act *1990* (UK)

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.

17. Gene drives could potentially be applied to mosquito populations to reduce or eradicate malaria[14]. Despite attempts to control the disease, 200 million cases still exist and half a million deaths are reported annually[15]. 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[16]. Alternatively, a gene drive that reduces the fitness of the female mosquito – for example, by causing sterility – could reduce mosquito populations over time[17]. Both mechanisms are as yet unproven, and the opportunities they present may ultimately be small. In theory, gene drives could also be used to reduce zika, dengue fever and sleeping sickness[18].

18. Gene drives also have the potential to control invasive species populations and therefore conserve native biodiversity. Research is currently underway to control non-indigenous mouse populations[19], and using gene drives to induce a skew in the mouse sex ratio is proving promising. Over time, this should lead to a reduction in mouse populations. Similar techniques are being considered to control other invasive species such as wasps in New Zealand[20] and cane toads in Australia[21].

19. Whilst these developments are promising, gene drives carry considerable risks, and altering a single species could have knock-on for ecosystems. Confinement strategies, safeguards and appropriate governance for the use of gene drives would be critically important[22,23]. Even with safeguards in place, it may be a significant challenge to gain the support of local people who may have concerns about living in the middle of a gene drive experiment.

---

[14]Gantz, V M, Jasinskiene, N, Tatarenkova, O, Fazekas, A, Macias, V M, Bier, E, James, A A 2015 *Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi.* Proceedings of the National Academy of Science of the United States of America **122** (49), 6736-6743

[15]World Health Organisation 2015 *World Malaria Report 2015.* Geneva: World Health Organisation

[16] Gantz, V M, Jasinskiene, N, Tatarenkova, O, Fazekas, A, Macias, V M, Bier, E, James, A A 2015 *Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi.* Proceedings of the National Academy of Science of the United States of America **122** (49), 6736-6743

[17] Hammond, A, Galizi, R, Kyrou, K, Simoni, A, Siniscalchi, C, Katsanos, D, Gribble, M, Baker, D, Marois, E, Russell, S, Burt, A, Windbichler, N, Crisanti, A, Nolan, T 2016 *A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector Anopheles gambiae*. Nature Biotechnology **34**, 78-83

[18]Alphey, L, Benedict, M, Bellini, R, Clark, G G, Dame, D A, Service, M W, Dobson, S L 2010 *Sterile-Insect Methods for Control of Mosquito-Borne Diseases: An Analysis*. Vector Borne Zoonotic Disease **10** (3), 295-311

[19]Cocquet, J, Ellis, P J I, Mahadevaiah, S K, Affara, N A, Vaiman, D, Burgoyne, P S, 2012 *A Genetic Basis for a Postmeiotic X Versus Y Chromosome Intragenomic Conflict in the Mouse*. PLOS Genetics **8** (9), 1-15

[20]Lester, P J, Beggs, J R, Brown, R L, Edwards E D, Groenteman R, Toft, R J, Twidle, A M, Ward, D F, 2013 *The outlook for control of New Zealand's most abundant, widespread and damaging invertebrate pests: social wasps.* New Zealand Science Review **70** (4), 56-62

[21]Australian Academy of Science, 2016 *Gene Drives in Australia*, Acton: Australian Academy of Science

[22] The Royal Society, 2015 *Sackler Forum 2015,* London: The Royal Society

[23] The National Academies of Sciences, Engineering and Medicine 2016 Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty and Alighning Research with Public Values. Washington: NAS

Agriculture

20. Food and nutrition security is a growing global challenge, compounded by a growing population, climate change and the need for crops 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 genetic technologies could also play a part.

21. 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[24]), and crops that are resistant to drought, pests and herbicides. Disease resistant crops are also being developed, including a modified version of matooke, a starchy variety of banana and a 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[25].

22. 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[26], or give them the ability to use nitrogen from the air, like soil bacteria, and no longer require nitrogen fertiliser[27]. However, given the experience of GM crops to date, we should beware of over-stating the potential of new techniques to deliver these benefits.

Regulation

23. Regulatory frameworks for genetic technologies should a) blend the characteristics of a new organism with a consideration of the process by which it was created, b) be adaptable and future-proof for the safe regulation of rapidly emerging areas of science, and c) contribute to a 'web of protection' to support biosecurity and help build public confidence.

Crops

13 Very different approaches to regulating genetically modified (GM) crops have been taken around the world. In the US and Canada, regulation focuses on the characteristics of the crop produced, while in the EU regulation is based on how the crop was modified[28]. This latter model fails to recognise that new characteristics in crops can be achieved using multiple techniques, for example through conventional selective breeding or genetic modification. There is no evidence that a crop is dangerous to eat just because it is GM; 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.

---

[24] Ye, X, Al-Babili, S, Klüte, A, Zhang, J, Lucca, P, Beyer, P, Potrykus, I 2000 *Engineering the Provitamin A (β-Carotene) Biosynthetic Pathway into (Carotenoid-Free) Rice Endosperm*. Science **287**, 303-305

[25] Tripathi, L, Mwaka, H, Tripathi, J N, Tushemereirwe, W K 2010 *Expression of sweet pepper Hrap gene in banana enhances resistance to Xanthomonas campestris pv. musacearum*. Molecular Plant Pathology **11**(6), 721-731

[26] 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

[27] University of Nottingham 2013 *World-changing technology enables crops to take nitrogen from the air*, 25th July. (See https://www.sciencedaily.com/releases/2013/07/130725125024.htm accessed 13/01/2017)

[28] 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)

14 As we move towards regulation which is based on assessment of the benefits and risks associated with a product and its characteristics, the exact form of the regulatory intervention will in some cases still depend on the process by which the product and its characteristics were created. In other words, an understanding of the process used to generate a product or characteristic should help determine the 'right' situations in which to regulate that product or characteristic[29].

15 Regulatory systems also need to be adaptable and future-proof to cope with areas of science that are developing rapidly. If it becomes impossible to tell how a characteristic has been introduced, then regulating the method of introduction will quickly become impractical.

16 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 genetically modified 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.

Humans

17 All human applications of genetic technologies fall under the strict regulation for the development of medicines, governing research on humans or human tissue, or new medical procedures. We still have more to learn about the uses of genetic technologies in humans. It is too early to be confident in using them for clinical treatment of the human germline (eggs, sperm and embryos), but there is promise for the treatment of somatic (body) cells[30]. Research is important in both somatic and germline cells in order to yield important advances in our understanding of the biological processes underlying disease[31].

International Collaboration

24. Working with international partners to better understand commonalities and differences in national regulatory systems is vital to ensure the most effective management of the risks and benefits posed by genetic technologies. If, for example, the UK were to reshape its regulatory model for GM plants, it should do so in a manner that supports international collaborations from research through to applications, security and trade.

25. The 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, and with the science academies of the US and China on human gene editing.

Public confidence

---

[29] Kuzma, J, 2016 Reboot the debate on genetic engineering. Nature **531**, 165-167

[30] National Academies of Sciences, Engineering, and Medicine 2016 *International Summit on Human Gene Editing: A Global Discussion*. Washington, DC: The National Academies

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

26. As with all emerging technologies, public confidence is vital. This requires open debate that considers the science along with values and principles whilst involving many voices – from scientists, campaigning organisations, industry representatives and policymakers.

27. An 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[32].

28. 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[33]. Many disputes about GM crops have been, in part, concerns about multinational companies. 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.

29. 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.

Industrial Strategy

30. The government recently published its Green Paper entitled 'Building our Industrial Strategy'[34], which outlined initial work by Sir John Bell FRS FMedSci FREng on early sector deals in life sciences and genomic technologies. This work should focus on creating an environment that allows for the development and responsible use of these technologies. It will require the right mix of financial instruments, infrastructure, skilled people and a proportionate regulatory approach that allows these technologies to be developed rapidly, safely and with public confidence.

For further information, please contact Becky Purvis, Head of Public Affairs, on becky.purvis@royalsociety.org

[32] 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

[33] 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

[34] HM Government 2017 *Building our Industrial Strategy.* London: Department for Business Energy and Industrial Strategy