Part of the conference series
Breakthrough science and technologies
Transforming our future

The CRISPR revolution: changing life

Conference report
Held on 7 March 2018

THE ROYAL SOCIETY

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Introduction

On 7 March 2018, the Royal Society hosted a conference on the subject of genome editing. The conference brought together scientists, technologists and experts from across academia, industry and government, to discuss the rapid advances in genome editing and its potential impact on our society and humanity.

Presentations and discussions outlined the current state-of-the-art use of genome editing technologies, such as CRISPR-Cas9, to understand biological pathways; develop improved agricultural crops and farm animals; to create cellular and animal models of disease; and to develop new therapies. Furthermore, the technical, regulatory and ethnical challenges associated with the wider adoption of this technology were discussed.

This conference is part of a series organised by the Royal Society, entitled Breakthrough science and technologies: Transforming our future, which addresses the major scientific and technical challenges of the next decade. Each conference focuses on one technology and covers key issues including the current state of the UK industry sector, the future direction of research and the wider social and economic implications.

The conference series is organised through the Royal Society's Science and Industry programme, which demonstrates our commitment to integrate science and industry at the Society, to promote science and its value, build relationships and foster translation.

This report is not a verbatim record, but a summary of the discussions that took place during the day and the key points raised. Comments and recommendations reflect the views and opinions of the speakers and not necessarily those of the Royal Society.

Full versions of the presentations can be found on our website.

This event was followed by an evening public panel discussion entitled *The future of your genetic health* which can be viewed on our YouTube channel.

Image: Conference participants networking.

Executive summary

This conference considered the application of genome editing to farmed animals, plants and crops; the use of genome editing and the development of CRISPR-Cas9 therapeutics for human disease; the regulatory case for this technology; and the ethical considerations of genome editing.

Image: The speakers and organisers, from left to right. Bottom row: Dr Mathew Garnett, Steve Rees, Professor Wendy Harwood, Professor Jennifer Doudna ForMemRS, Dr Mohammad Bohlooly, Dr Mark J Robertson, and Professor Helen Sang. Centre row: Dr Charlie F Albright, Dr Andrea Nemeth, and Professor Joyce Tait CBE. Top row: Professor Waseem Qasim, Professor Peter Goodfellow FMedSci FRS, and Dr Sarah Chan.

- CRISPR-Cas9 offers a more efficient and applicable approach to genome editing in comparison to other techniques.
- The opportunities for the use of CRISPR-Cas9 in plants, animals and humans are vast.
- Although genome editing is a well-known concept in the scientific community, it is still somewhat unfamiliar to the general public.
- Regulators should consider carefully when and how to regulate this new technology, to maximise its societal benefits while maintaining expected safety, quality and efficacy standards. Further consideration is required regarding whether regulation should be based on the properties of the final products or the processes by which they were developed.
- The ethical considerations of genetic engineering technologies are wide-reaching, and further public debate is needed between scientists, businesses and government. More public outreach is needed to help the general public understand this technology and its implications.

An introduction to genome editing

Genome editing is the deletion, insertion, replacement or modification of genes in a strand of DNA. It can be carried out by using a variety of DNA targeting tools such as zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), or more recently, clustered regularly interspaced short palindromic repeats (CRISPR). Over the past 50 years, scientists have gained the ability to read, copy, synthesise and code DNA, and with new genome editing techniques, it is now possible to edit DNA in a precise and targeted fashion.

Professor Jennifer Doudna ForMemRS, UC Berkeley, explained that the field of directed genome editing has seen a rapid rise in the number of publications and patents in recent years, indicative of the excitement and opportunity it presents. Companies and start-ups are focussing on applications such as human health, agriculture and animal breeding, and a number of clinical trials are currently underway, the outcomes of which will set the scene for the future of this transformative technology.

The CRISPR-Cas9 system was first developed by scientists studying how bacteria fight viruses. In bacteria, a specific cell pathway allows for fragments of DNA code to be copied from an invading virus to produce defensive RNA that protects the host. These virus fragments, acquired by Cas cleavage proteins, appear in CRISPR sequences of bacterial DNA and correlate to the viruses that infect them.

"Gene editing technology is really giving scientists, clinicians and entrepreneurs opportunities that, even a few years ago, we couldn't have imagined being in our hands."

Professor Jennifer Doudna ForMemRS, UC Berkeley.

Image: Professor Jennifer Doudna ForMemRS, UC Berkeley.

In designed CRISPR-Cas9 systems (see figure 1), precise DNA scission is carried out by a pre-programmed CRISPR segment, a tracrRNA segment (typically attached to the CRISPR segment to form 'guide RNA') and a Cas9 cleavage protein. The CRISPR segment can be varied to target custom genes of a DNA strand, allowing any desired sequence programmed by the CRISPR code to be cut. This also allows for a number of different sites to be targeted simultaneously using numerous guide RNA molecules. In eukaryotic cells, double-stranded DNA broken by a CRISPR-Cas9 directed incision can self-repair. If DNA or single bases are provided at the break site, the DNA chain will include the new fragment in its repair, a mechanism known as homology directed repair.

In comparison to other established DNA editing techniques, CRISPR is faster, cheaper and more accurate. Alternatives such as ZFNs or TALENs are more complicated to use and less adaptable in the lab. Since its first use, CRISPR-Cas9 has been shown to be applicable in a wide range of organisms, giving researchers a powerful tool to use in previously difficult or impossible scenarios.

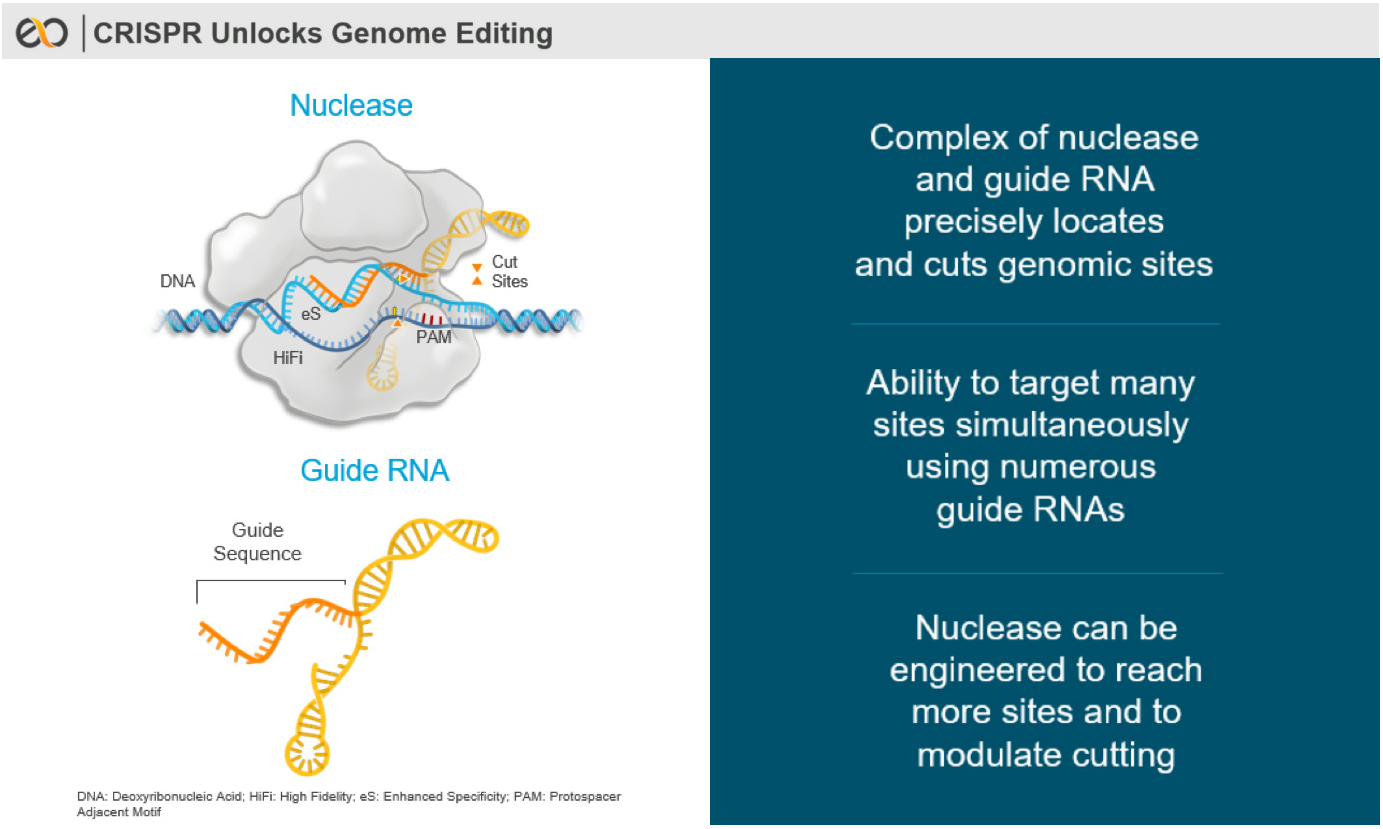
Genome editing by CRISPR-Cas9 is already being developed to treat disease in humans, to modify plants to deal with the impacts of climate change and pathogen-born plant disease, and to halt the spread of viruses in animal populations. It can also be used to edit germline cells in embryos, introducing genetic changes that will be passed onto future generations.

Examples like these typically raise questions of the societal implications of genome editing, including the modification of humans. Recent trials in large mammals and human embryos have led to wider public attention and show that scientists across the world are on the cusp of important breakthroughs that demand discussion now.

See our animation *What is gene editing and how does it work?*

FIGURE 1

The mechanics of CRISPR.



Courtesy of Editas Medicine.

Genome editing in farm animals

Professor Helen Sang of the Roslin Institute, The University of Edinburgh, discussed the opportunities and challenges of applying genome editing in farmed animals, where CRISPR-Cas9 is still only in the early stages of development.

The farming industry is currently underpinned by the selective breeding of animals to improve desirable and heritable characteristics in future generations. For example, thanks to selective breeding the chicken has undergone a 79% increase in meat produced per tonne of feed from 1950 to 2014[1]. This can have knock-on effects, such as reducing the amount of arable land needed to grow animal feed.

As the genome of major farm species has been better understood, the use of genome editing has become more common, and fewer animals are required in a breeding system to see genetic change (compared to selective breeding). Genome editing can be used to move beneficial gene alleles between breeds and species and to realise characteristics that are currently challenging for genetic selection.

Examples include:

- The genetic dehorning of dairy cows. Horns are normally burned out, therefore this alternative avoids distress and costs.
- Resistance to porcine reproductive and respiratory disease virus in pigs, which causes pain, affects reproductive abilities, and costs $650 million/year to the US pig industry[2].
- Resistance to the infectious pancreatic necrosis virus in Atlantic salmon.

Image: Professor Helen Sang, The University of Edinburgh.

"In animals, we're really at the beginning of thinking about how we can use CRISPR-Cas9 technologies and what we want to do."

Professor Helen Sang, the Roslin Institute, The University of Edinburgh.

1. Tallentire, C.W., Leinonen, I. & Kyriazakis, I. Agron. Sustain. Dev. (2016) 36: 66. https://doi.org/10.1007/s13593-016-0398-2
2. Neumann, E., Kliebenstein, J., Johnson, C., Mabry, J., Bush, E., Seitzinger, A., Green, A., Zimmerman, J. (2005) Assessment of the economic impact of porcine reproductive and respiratory syndrome on swine production in the United States. Journal of the American Veterinary Medical Association 227:3, 385-392

Image: Steve Rees, AstraZeneca.

Farm animals can also be used to model human disease, especially those whose size allows for longitudinal studies and high-resolution region specific imaging. By introducing specific mutations that cause the same genetic changes observed in humans, disease can be studied and applied to drug development and testing, eg. Batten disease in sheep.

Several future challenges face the use of CRISPR-Cas9 technologies in farm animals, namely:

- Concerns regarding animal welfare, exploitation and sustainable agriculture.
- Public perception of genetic modification in food stocks.
- Appropriate food labelling.
- Global regulation, including whether products or processes should be regulated.

CRISPR crop opportunities

Professor Wendy Harwood of the John Innes Centre explained that advances in genome editing are also being translated into plants.

Plant breeding relies on variation, therefore breeders need access to DNA sequence mutations in order to change crop characteristics. Gene mutations also allow researchers to determine and confirm gene function.

Sources of genetic variation include:

- Genes from the same or closely related species that can be crossed in.
- Tissue culture induced variation.
- Mutation breeding.
- Gene transfer by genetic modification.
- New breeding techniques, including genome editing.

Traditional plant breeding crosses two closely related species introducing many unwanted genes as well as the required ones, while genetic engineering introduces specific genes into random locations along DNA sequences. In contrast, targeted genome editing allows for specific genes to be introduced, replaced or disrupted at precise locations. CRISPR-Cas9 has been used for targeted gene knock-outs in a number of crops, including barley, brassica, tomato, wheat and potato. The John Innes Centre provides gene knock-out capabilities to the UK research community.

Examples of gene knock-outs in plants include:

- Deletion of the GA4 gene in brassica to reduce fruit dehiscence (pod shatter).
- Targeting of the genes involved in the symbiosis signalling pathway in barley to understand their function and work towards nitrogen fixing cereals.
- Targeted mutagenesis to prevent rice blast disease.
- Knocking out of the gene SP5G in tomato plants to achieve faster flowering and earlier yield.

Image: Professor Wendy Harwood, John Innes Centre.

"There is a huge amount of excitement in the crop research community about the use of CRISPR-Cas9 technologies."

Professor Wendy Harwood, John Innes Centre.

In addition to the production of gene knock-outs, alternative genome editing strategies are being explored to achieve gene insertions and replacements. Early work is proving to be successful in barley, and successive generations are currently being studied to monitor inheritance.

Regulation is important in the wider use of CRISPR-Cas9 modified crops. The United States Department of Agriculture has ruled that it will not regulate a number of CRISPR-Cas9 edited plants, treating them as traditional plants instead of genetically modified variants.

Proportionate and adaptive governance of genome editing

Professor Joyce Tait CBE of the Innogen Institute discussed the role of regulation in supporting the future development of genome editing technologies.

The policy and regulatory landscape that has evolved in the EU since the early development of plant genetic modification serves as an example of the operation of a 'regulatory ratchet', continually adding to the cost and time requirements of the regulatory system and making it increasingly difficult for small companies to innovate independently of large multinationals. Professor Tait argued that inappropriate regulatory decisions are often made too early in the development of new technology, before benefits and risks are clear, and that there can be an unwillingness to adapt the regulatory system proportionally to the emerging properties of the technology. It is also one of the reasons why, in this sector of the economy, most of the innovation arising from publicly funded research is incremental rather than disruptive. Regulation of new technologies being developed using CRISPR-Cas9 and related procedures has the opportunity to learn from this experience, based on a new approach to the Proportionate and Adaptive Governance of Innovative Technologies[3].

Image: Professor Joyce Tait CBE, Innogen Institute.

3. Tait, J., Banda, G. and Watkins, A. (2017) Proportionate and Adaptive Governance of Innovative Technologies: a framework to guide policy and regulatory decision making. Innogen Institute Report to the British Standards Institution. https://www.innogen.ac.uk/reports/1222

CRISPR-Cas9 could lead to incremental innovation that will enable companies to improve on their existing businesses, to make them more efficient or more environmentally sustainable. It could also lead to the development of disruptive innovation leading to major shifts in product types and their place in the market, and potentially to the creation of new industry sectors or radical re-structuring of existing sectors. Tait proposed that:

- The extent to which an innovation is potentially disruptive, and the sectors for which it will be most disruptive, should be early considerations in the choice of regulatory system.
- The final decision on whether there is a need for a legally based regulatory system and the nature of that system, should not be made before the 'proof of concept' stage of product development.
- The focus of the regulatory system should be on the potential benefits and hazards of the final marketed product, not on the process by which it was developed, ie not on CRISPR-Cas9 and related techniques.
- A greater use of standards as part of the development of regulatory systems, can be an important aid to making a regulatory system more proportionate and adaptive, particularly to the needs of disruptively innovative technologies.

"There is the possibility to have numerous small companies doing interesting things for niche markets that are not of interest to multi-national companies who have conventionally operated in this area."

Professor Joyce Tait CBE, Innogen Institute.

Gene editing immunity

Professor Waseem Qasim of the UCL Great Ormond Street Institute of Child Health discussed ex vivo therapy, the process of collecting cells from patients, engineering them and giving them back to patients to treat their disease.

One commonly transplanted lymphocytic cell is the T cell, which can mediate long-term responses to infections due to their properties of memory and learned immunity. Their interactions with target cells are mediated by major histocompatibility complex (MHC) proteins. Whilst transplanted T cells can fight viruses, protect graft organs against rejection and kill leukaemia cells, they can also attack normal tissue and cause graft versus host disease (GVHD).

Alternatively, T cells can be collected from a patient, taken to the laboratory, engineered using gene transfer vectors, and given back to a patient. T cells are 'reprogrammed' to introduce new receptors that allow them to recognise specific targets in the patient, such as tumours, however this process is expensive, logistically challenging, and quite often not enough T cells can be obtained from patients after intense chemotherapy.

> "There are dozens of gene mutations that can cause inherited disease, and these are now ripe for targeting with gene editing technologies."
>
> Professor Waseem Qasim, UCL Great Ormond Street Institute of Child Health.

Image: Professor Waseem Qasim, UCL Great Ormond Street Institute of Child Health.

Image: Professor Peter Goodfellow FMedSci FRS.

Instead of introducing conventional T cell receptors that rely on an MHC recognition to activate cells, chimeric antigen receptors (CARs) can be used to induce T cell signalling after recognising targets on the surface of leukaemia cells.

Trials to treat leukaemia have been running in the US for over a decade and in some cases have reported remission rates of around 80 – 90% in children and adults.

Alternatively, a single donor's T cells can be genetically edited to treat multiple recipients. Genes are introduced that encode for the CAR proteins so that T cells are armed to recognise leukaemia. Genome editing removes the original T cell receptor, disarming the cell and preventing GVHD, and making the cells invisible to some of the immunosuppression drugs. Using TALENs, this treatment brought two infants with leukaemia into complete remission, now for nearly 3 years. Phase 1 trials are currently underway to test the approach further.

CRISPR-Cas9 also allows for the editing of a range of cell surface targets to either up-regulate or inhibit T-cell activity, and this approach is being applied in traditional CAR treatments. Furthermore, different CRISPR-Cas9 based technologies are also being explored, such as specific base changes that could in theory target a wide variety of pathogenic genomes and correct inherited gene defects.

The first medicinal authorisations have recently been issued and some products priced in the region of $500,000 per patient.

Development of subretinally-delivered CRISPR medicine

Dr Charlie Albright of Editas Medicine discussed the use of CRISPR-Cas9 to treat a rare form of inherited retinal dystrophy, Leber congenital amaurosis 10 (LCA10), the leading cause of inherited blindness among children.

Editas Medicine uses a variety of CRISPR nucleases, DNA delivery options and gene edits to target a broad range of gene sites, allowing them to offer a spectrum of CRISPR-based products that includes genetically edited T cells and hematopoetic stem cells.

CEP290, a ciliary protein that is critical in phototransduction in healthy photoreceptors, is severely deficient or not expressed in LCA10 patients, leading to a failure in protein trafficking. Without the necessary supply of proteins, outer segment discs fail to regenerate, phototransduction does not occur, and vision is severely impaired.

Images of the retina show that LCA10 patients have particularly thin outer nuclear layers of their retinas compared to healthy patients. Repairing mutated CEP290 genes in as little as 10% of these cells should restore protein trafficking and allow for regeneration of the cell layer, thereby improving visual acuity.

The most common mutation in CEP290 is the single base pair mutation IVS26, which can be removed by genome editing. Initial tests on mice suggest that subretinal injections are successfully treating cells, editing every allele exposed to the candidate medicine.

- This appears to be a fast (over a matter days) and stable event.
- Editing levels appears to follow the dosage and meets the required therapeutic level.
- The majority of photoreceptors are edited at a 50% success rate.

Tests have now been extended into non-human primates and show similar editing success over a 13 weeks period, this period being longer due to the larger animal size.

Image: Dr Charlie F Albright, Editas Medicine.

"[There are a range of] complexities that go with translating the academic exercise of CRISPR-Cas9 into a therapy for people."

Dr Charlie Albright, Editas Medicine.

Genome editing to create models of disease

The creation of improved cellular and animal models of disease is required to understand disease pathways, to identify and validate novel drug targets, and for the efficacy testing of new medicines during drug discovery. Dr Mohammad Bohlooly from the IMED Biotech Unit at AstraZeneca described the use of CRISPR-Cas9 to create transgenic mouse models of disease for this purpose.

Traditional methods to create transgenic models of disease take over a year due to the timelines for the generation of the transgenic lines and the establishment of colonies of animals for study. Through the use of CRISPR-Cas9, transgenic animal models of disease can be created in weeks and, as a consequence, reduce animal usage. The use of CRISPR-Cas9 also allows the creation of complex disease models containing multiple gene changes.

A transgenic mouse line has been created which expresses Cas9 off a tightly controlled doxycycline inducible promoter system. Following treatment of these animals with doxycycline, Cas9 expression is upregulated in every tissue leading to temporally controlled genome editing. Viral vectors are used to introduce guide RNA into these animals, using local delivery or tissue specific promoters to mediate expression of the guide RNA. This enables temporal and tissue specific genome editing in the adult animal. This technology has been applied to create transgenic mouse models of lung-cancer, enabling new drugs to be tested within four weeks of the creation of the mouse model.

Transgenic models are of use in developing preclinical efficacy models to develop genome editing medicines. Alpha1-antitrypsin deficiency is a genetic disease characterised by a single mutation in the SERPINA1 gene. Patients with this disease suffer from emphysema and lung fibrosis and the disease leads to premature death. Repair of this gene in the liver of patients is expected to lead to a restoration of liver function and the prevention of emphysema. The group at AstraZeneca has been able to use CRISPR-Cas9 to delete the mutant copy of the alpha1-antitrypsin gene in a transgenic model of this disease leading to a reversion of lung fibrosis in these animals. This observation leads to the possibility of developing CRISPR-Cas9 medicines to treat this disease.

Image: Dr Mohammad Bohlooly, AstraZeneca.

"With CRISPR we can rapidly create highly relevant models of disease to help validate new targets and understand the efficacy of new medicines."

Dr Mohammad Bohlooly, IMED Biotech Unit, AstraZeneca.

CRISPR screens for oncology drug testing

Dr Mathew Garnett of the Wellcome Trust Sanger Institute explained that cancer is the second leading cause of mortality in the UK, and 1 in 2 of those born today will be diagnosed with cancer in their lifetimes[4]. It remains a major focus of both basic and clinical research, and in recent years focus has shifted to the development of precision medicine approaches.

The molecular features of a patient's cancer can guide their treatment by using a biopsy or blood sample to perform a molecular diagnostic test. Based on the results of these tests, it may be possible to select the best treatment, improving patient outcomes and reducing toxicity. This process requires a knowledge base, derived from pre-clinical and clinical studies, to interpret existing and new molecular biomarkers.

Examples of molecularly targeted therapies using biomarker-based patient selection that are being used in clinical settings include:

- Germline mutations in BRCA1 and BRCA2 proteins for breast and ovarian cancer patients
- Mutations of ALK genes for a subset (5%) of non-small cell lung cancer patients
- Mutations to EGFR genes for lung cancer patients

In some cases oncology drugs work in relatively small sub-sets of patients for each cancer type (as low as 1%), making the development of these therapies a challenging task. With only 10% of patients currently able to benefit from existing therapies and the rate of FDA approval of new molecular entities falling, new and better drug targets need to be identified.

Image: Dr Mathew Garnett, Wellcome Trust Sanger Institute.

4. Cancer Research UK forecast: http://www.cancerresearchuk.org/about-us/cancer-news/press-release/2015-02-04-1-in-2-people-in-the-uk-will-get-cancer, accessed March 2018.

The recent advent of CRISPR-Cas9 provides an opportunity to identify novel drug targets in a new way as its programmable nature can be exploited to investigate gene function in multiple cancers.

- New drug targets are found by performing systematic CRISPR-Cas9 knock-out screens in cancer cell lines (200 of the most common cancers so far out of a library of 1,000).
- The essential genes for cancer growth and development can be identified by using DNA sequencing.
- A systematic and unbiased approach could improve the chances of identifying and prioritising new drug targets.

Results indicate that 1300 genes are required for the fitness of a cancer cell (representing approximately 6% of all genes in the genome), while 503 are 'core essential genes' across common cancers. Pathway analysis shows that these are typically genes associated with cellular processes such as cell division and mitosis. Investigation into how core gene essentialities vary across different cancer sub-types is ongoing, as well as how this links to carcinogenesis processes within each cancer type.

For all of the cell lines screened, complementary datasets such as sequencing data on gene mutations, amplifications and deletions and gene expression are being combined to investigate gene essentiality further. Additional applications for CRISPR-Cas9 screens include modeling drug resistance, the identification of effective combination therapies, and the study of gene regulation.

"This process is just the beginning, a hypothesis generation process, and we are now building confidence in these new targets."

Dr Mathew Garnett, Wellcome Trust Sanger Institute.

Ethics, policy and public perception

The meeting ended with a panel discussion on the ethical considerations of genome editing, chaired by Baroness Helena Kennedy QC. The panelists were Dr Sarah Chan, The University of Edinburgh; Dr Mark Robertson, Science Policy Compass; and Professor Robin Lovell-Badge CBE FMedSci FRS, The Francis Crick Institute.

The ethics of CRISPR-Cas9 editing

- Dr Chan noted that discussions around genetic modification and engineering have, for many years, been considered as a conversation for the future. Due to the fast pace of recent change in CRISPR-Cas9 technologies, a moral and ethical discussion needs to happen now.
- Dr Robertson noted that while scientists might talk about curing sick people, others will see the opportunity to engineer 'perfection'.
- Professor Lovell-Badge argued that although clinicians will be able to prevent genetic diseases, society's consideration of disabled individuals should not and will not change.
- Dr Chan explained that society currently regards it as unethical to not vaccinate children, and when genetic engineering becomes prevalent the same may also be said of its ability to cure genetic disease.
- Professor Lovell-Badge suggested that in the future, humans may have to genetically engineer themselves to survive to deal with issues such as global warming or space travel, and this will shape perceptions of genetic engineering.

Policy implications

- Dr Robertson noted that the applications of CRISPR-Cas9 technology will extend into areas policy makers cannot yet imagine, and that he believes it will be difficult for the regulators to keep up. Research and development mistakes will inevitably occur in the future and if not regulated properly, maverick behaviour could lead to injury and seriously hamper progress in this important area.
- Dr Chan recommended that policy makers should not regulate with a goal of no risk, but policy needs to carefully balance risks vs benefits to assess what is the appropriate level of regulation.
- She also suggested that UK policy makers need to consider international regulation, especially in plant and animal genetic engineering where international borders may not be recognised (eg migrating animals).
- Professor Lovell-Badge explained that different countries across the world have different approaches, and that the UK is in a good position to propagate sensible regulation globally.

Image: The panel members, from left to right: Dr Mark Robertson, Dr Sarah Chan, Baroness Helena Kennedy QC, Dr Robin Lovell-Badge CBE FMedSci FRS.

Public perception

- Professor Lovell-Badge suggested that success stories can be used to help explain the benefits of CRISPR-Cas9, such as cases where HIV, sickle cell anaemia, and leukemia have been treated.
- Dr Robertson suggested that if a CRISPR-Cas9 mistake does occur, a more established transparent dialogue with the public will result in greater understanding and a better chance of the technology continuing to thrive.
- Dr Chan noted that the best regulation cannot prevent all mistakes, unless the regulation bans the technology completely.
- Professor Harwood was asked "what benefits should consumers be excited about?" She suggested nutritional benefits, reduced toxin levels and plant variations (eg gluten-free), but noted that scientists need to make the cases for changes such as disease and drought resistance in crops that impact food supplies, as they are ultimately a consumer concern.
- Professor Tait suggested that pesticide free crops and the reintroduction of flavour lost due to conventional breeding will also excite consumers, and she predicts smaller companies will work on these disruptive technologies.
- Professor Lovell-Badge explained that many people are concerned with the enhancement of humanity stepping over an undefined boundary for the pursuit of perfection. These stories are portrayed in the media and shape the public's perception. He did note, however, that when the public are engaged they show less concern.
- It was suggested that anxieties stem from the underlying concern that genetic modifications could lead to eugenics. Dr Chan disagreed, noting that eugenics suggests a coercive control of state reproduction, whereas the discussion around genome editing considers a society of individuals shaping overall choice
- Baroness Helena Kennedy QC noted that society is still able to propagate concerning trends itself without regulation. She also noted that public discourse needs to move past slogans such as 'designer babies' to get to the moral heart of what could go wrong.
- Professor Lovell-Badge commented that the individuals he spoke to were primarily concerned with the impact of genetic defects on themselves or their children, and wanted to know when cures would be available.

A recurring question during the conference was "how can scientists better engage with the public and encourage debate around the use of CRISPR-Cas9?"

- Professor Doudna suggested approaches that are accessible by the public, such as the internet (eg 'ask a scientist' forums) or the media and entertainment industry. Scientists can ensure new technologies such as CRISPR-Cas9 are accurately represented in formats, such as television and film, helping to propagate well-understood discussion in the public domain.
- With regards to public reaction to genetic modification of plants, Professor Harwood noted that her approach is to be transparent, explaining her research in the most accessible of ways, eg at public science festivals and in online videos.
- During the panel session, Dr Robertson noted that he is concerned that the general population isn't aware enough or doesn't understand CRISPR-Cas9. He suggested that outreach should focus on schools, educating the public from a young age to tackle the opportunities and challenges that will be with them for the next 50 years.
- Dr Chan suggested the use of digital platforms to engage with the public. She warned, however, that it is important to ensure that misinformation isn't propagated.
- Dr Chan noted that if scientists and policy makers do not engage sufficiently, the public may seek help from private companies who may not always have best patient care in mind. She also noted that the public is well informed, making it harder to refuse treatments.

Image: Conference participants networking.

"The world could be a better place through the application of genome editing technologies"

Professor Peter Goodfellow FMedSci FRS.

"CRISPR gene editing is transforming how scientists understand cell biology. We can look forward to CRISPR transforming human health and wellbeing through the creation of new medicines, through delivering highly sensitive diagnostics, and through improvements in animal health and crop science"

Steve Rees.

Acknowledgements

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Professor Peter Goodfellow FMedSci FRS

Steve Rees
AstraZeneca

Speakers

Professor Jennifer Doudna ForMemRS
UC Berkeley

Professor Helen Sang
The Roslin Institute, The University of Edinburgh

Professor Wendy Harwood
John Innes Centre

Professor Joyce Tait CBE
Innogen Institute

Professor Waseem Qasim
UCL Great Ormond Street Institute of Child Health

Dr Charlie F Albright
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Dr Mohammad Bohlooly
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Dr Mathew Garnett
Wellcome Trust Sanger Institute

Panel members

Chaired by Baroness Helena Kennedy QC

Dr Robin Lovell-Badge CBE FMedSci FRS
The Francis Crick Institute

Dr Sarah Chan
The University of Edinburgh

Dr Mark J Robertson
Science Policy Compass

The Royal Society is a self-governing Fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. The Society's fundamental purpose, as it has been since its foundation in 1660, is to recognise, promote, and support excellence in science and to encourage the development and use of science for the benefit of humanity.

The Society's strategic priorities emphasise its commitment to the highest quality science, to curiosity-driven research, and to the development and use of science for the benefit of society. These priorities are:

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- Supporting international collaboration
- Demonstrating the importance of science to everyone

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