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AQ

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Indefinite Disinformation:

The Political Capital of Fear

INCLUDING: JULIAN BURNSIDE | PROF WENDI ROGERS | DR DAVID TUFFLEY | DR AINSLEY NEWSON

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A ROUGH CLIMATE FOR MIGRATION

BEING HUMAN: Genome Editing

ETHICS IN THE INFORMATION AGE

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A WORD

In a world of lightning fast information, where competition for resources now occurs on a global scale, where innovation is progressing faster than any other time in human history: is the slow, considered application of ethical principles still relevant? Or do ethics burden the already self-regulating principles of the free-market with impractical philosophy?

Welcome to a truly bumper issue of AQ. In this year's Special Edition we look at what role ethics still has to play in our lives, from climate change, to medicine, through to the depths of the internet.

How does the concept of ethics play into our everyday, where is it critical that ethical standard remain enforced and where have we let our ethical responsibilities be usurped by politicking and fear?

We are very lucky to have Julian Burnside QC returning to the pages of AQ, providing a long, hard look at the last 15 years of Australia's border policy. The piece is a powerful reminder of how far we have strayed from the Aussie values of the fair go that we, perhaps wrongly, still wear as a badge of national pride.

In recent years the field of genome editing has been thrown open by the development of simpler, cheaper and more accurate methods of altering the DNA of any living organism. Prominent bioethicists, Dr Ainsley Newson and Dr Anthony Wrigley walk us through the issues in an area of science that could fundamentally change the idea of what it is to be human.

Australia's two biggest political footballs continue to be 'refugees' and 'climate change'. But what happens when the two become one, and we begin seeing climate-refugees, those that have been pushed off their land by rising sea levels and extreme weather patterns? How will Australia react, and should our ethical responsibilities to these people begin *before* they even leave their home country?

We also examine whether ethics can or should be applied to IT and the internet, investigate the balancing act between ethics and innovation, and take a look at the history of Australia's political party Think Tanks.

It's an exciting issue that I hope will entertain as well as challenge. Share your thoughts via our Facebook (@AQAustralianQuarterly) or Twitter (@AQjournal).

Grant Mills
Editor

NOTES FOR CONTRIBUTORS

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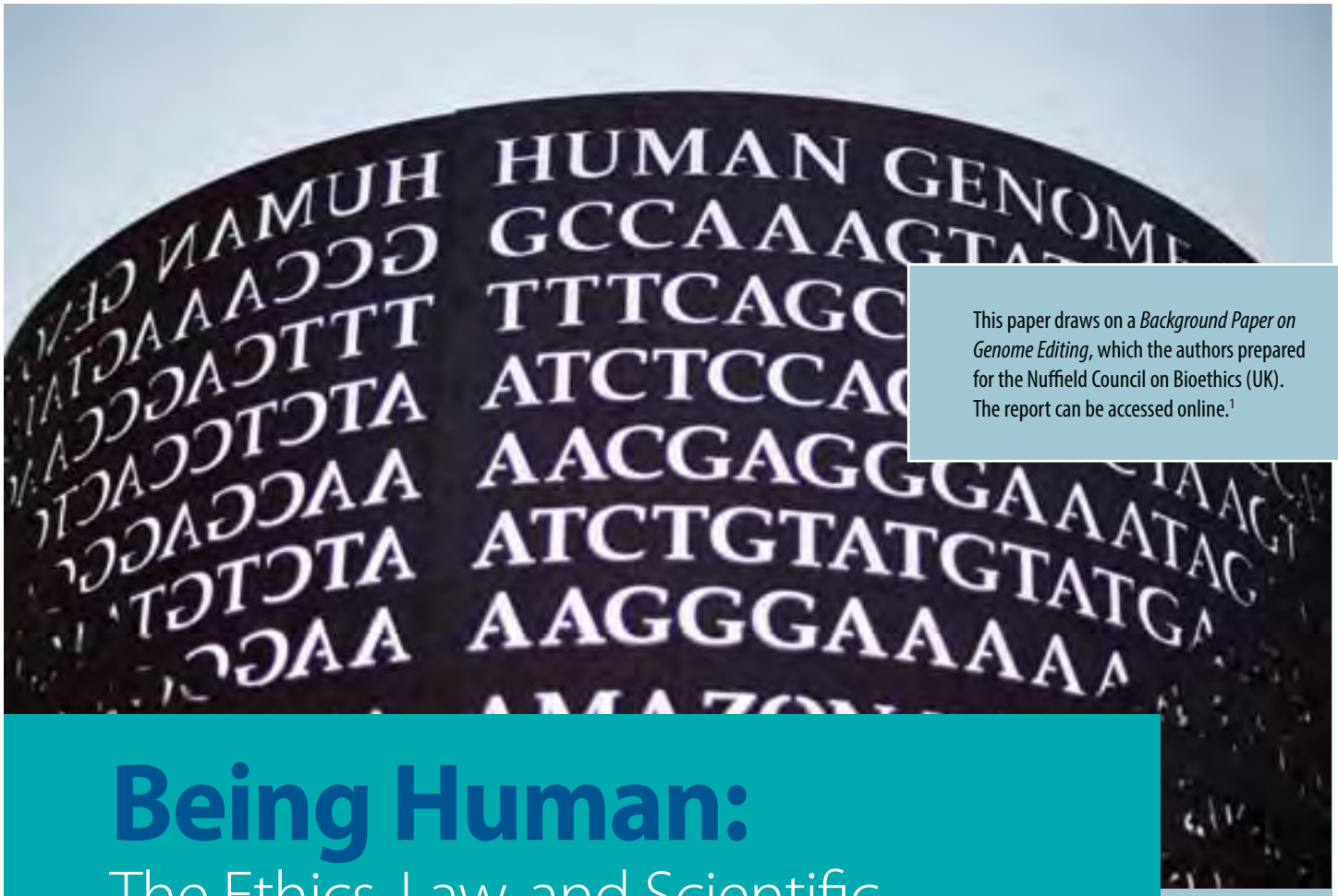

This paper draws on a *Background Paper on Genome Editing*, which the authors prepared for the Nuffield Council on Bioethics (UK). The report can be accessed online.[1]

Being Human:

The Ethics, Law, and Scientific Progress of Genome Editing

Genome editing can be viewed as a disruptive technology – fundamentally changing how scientists alter genomes. Despite the technique remaining imperfect, there is now a real possibility that we can precisely and accurately change almost any part of any genome, including plants, animals, and human beings. The question is, should we?

ARTICLE BY: **DR AINSLEY NEWSON & DR ANTHONY WRIGLEY**

Genetic engineering in itself is, of course, not new – various techniques that allow scientists to modify genes have been around for some time. But the difference with genome editing is that it is simple, cheap, and accurate; thereby opening up the potentials of genetic engineering on a hitherto unseen scale.

Genome editing has a broad range of possible applications in areas such as novel medical treatments, vaccine development,

IMAGE: © Dave Fayram - Flickr

crop innovation and environmental remediation. A variety of approaches fit the genome editing moniker, but the emergence of CRISPR-Cas9 has captured the most attention.

What is CRISPR-Cas9?

Editing a genome involves introducing a change to a chosen target within a cell's DNA. The change can take numerous forms, from introducing a small deletion to effecting a precise sequence change.

There are several methods of genome editing, but CRISPR-Cas9 is currently the easiest to set up and use. The CRISPR-Cas9 technique was first published in 2012,[2] but is based on a knowledge of short DNA sequences found in simple cells; around since the 1980s. "CRISPR" stands for "clustered regularly interspaced short palindromic repeats".

In April 2015, a Chinese research team published the first (albeit not very successful) use of CRISPR-Cas9 in human embryos; with the aim of engineering out the mutation that causes β-thalassemia.

The technique involves two main steps. First, components of a custom-designed nuclease (called an endonuclease) are introduced to a recipient cell, whereupon they self-assemble. This endonuclease then targets and cuts one or both strands of a chosen DNA sequence. Second, the recipient cell's inherent DNA-repair machinery then repairs the cut and in so doing, introduces the designed change. These changes can comprise anything from a single base pair change to the insertion or deletion of whole genes.[3,4]

CRISPR-Cas9 is a very flexible system and can be used without expert protein engineering expertise. The nature of the method also means that several changes can be introduced to a cell simultaneously. Scientific publications using this system are rapidly increasing; with over 800 citations in the database PubMed as at November 2015.

However, despite its simplicity and relatively low cost, CRISPR-Cas9 is not perfect. Problems can arise, such as 'off target' cleavage, which occurs when the endonuclease attaches to and cuts at the wrong site in the DNA helix. There are also concerns that unwanted DNA repair events will occur.

One paper in particular among the increasing literature has led to significant debate. In April 2015, a Chinese research team published the first (albeit not very successful) use of CRISPR-Cas9 in human embryos; with the aim of engineering out the mutation that causes β-thalassemia.[5] If these embryos were implanted (which was not the intention of this work) they could have led to the birth of humans with an engineered germ-line – meaning that the changes could be passed to future generations. The experiment was subject to criticism on both scientific and ethical grounds and soon after, the National Institutes of Health in the United States announced that it would not fund research that used genome editing in human embryos.[6]

Caplan *et al* rightly point out, however, that our examination of ethical aspects of CRISPR-Cas9 should not become too narrow in focus.[7] While genome editing in embryos is ethically significant, issues also arise in other applications: generating transgenic animals; developing novel therapies in humans and releasing genetically modified organisms (GMOs). CRISPR-Cas9 may represent a 'tipping point' for ethics; a point we return to below.

What Role for Bioethics?

The power and precision of this technology means that it's no surprise that everyone involved recognises how its implications could be profound. The issue is getting the balance right between responsible deliberation and governance; and facilitating the development of promising interventions.

Bioethics has historically been a discipline in which philosophers have developed arguments on key concepts or developments in science, health and medicine. Other disciplines, such as law and sociology have also entered the fray, resulting in an ongoing debate over the scope and methods of bioethics and the nature of expertise within the field. Sitting

IMAGE: © Mike Towber-Flickr

alongside academic bioethics is research ethics; or the manner of approving research studies that involve human or certain non-human animal participants; or which involve ethically contested materials such as human embryos.

Writing about CRISPR in August 2015, psychologist Stephen Pinker presented his view on the role of ethics in the genome editing debate, stating that bioethicists should "get out of the way".[8] He was concerned that bioethicists holds up scientific progress (causing harm) and broker moral panic. He criticised bioethicists for mis-predicting the future and over-inflating risks. He implied that ample existing protections and informed consent processes are enough to allow genome editing to safely prosper.

Our take on Pinker's piece and the ensuing debate (of which there was plenty) is that we need to be careful not to tar academic bioethics with the same brush that is used for the definitely imperfect and often cumbersome research ethics process.

Pinker also pitches an unfair stereotype of bioethics; not one that we recognise as representing the discipline. Bioethics is inherent to the development of new technologies. Its role is not one of simply pointing out all the problems with a technology or stating why something shouldn't be done. The challenge for bioethics is to work in collaboration with researchers to scope issues, frame the potential of genome editing as accurately as possible, and to find ways to appropriately facilitate promising research.

The central underlying ethical concern here is one that applies to any application of human genetic modification: **that it may unintentionally change the genome forever.**

Should We Be Worried About CRISPR-Cas9?

The ethics of genetic modification, particularly involving humans, has had an uncomfortable history which has often given rise to a highly precautionary approach to its use. In other words: don't do anything until you know for sure that it will be safe and beneficial. And while genome editing may not present us with any specifically new ethical issues concerning genetic modification – it is in that regard just another technique that allows such modifications to take place – that is not the end of the story.

The important question is not, therefore, whether genome editing raises new questions. Instead, we need to ask whether genome editing warrants further special attention than has already been given to the ethics of genetic engineering in its various forms.

The major concern driving the call for this further attention is a direct result of genome editing's potential for success. As it is so effective and easy to use, there are worries that it may be put into use far too rapidly. This, in turn, will have implications for the ethical debate as the use of the technique may outstrip our understanding of its safety and our window of opportunity to think about whether - and how - it should be controlled.

So just what are the ethical aspects surrounding genome editing? As indicted above, modifying the human genome gives rise to the most concern. The central underlying ethical concern here is one that applies to any application of human genetic modification: that it may unintentionally change the genome forever;

Regulation and Oversight

In Australia, genome editing will be subject to regulation under several existing instruments. For example, the genome editing of crops will fall under the ambit of the *Gene Technology Act 2000* (Cth) and the relevant procedures it dictates, including licensing. In humans, somatic (non-inheritable) gene therapy is likely to require approval from a Human Research Ethics Committee.

If a clinical trial, the *Therapeutic Goods Act 1989* (Cth) and clinical trial regulations will also apply; as may the *Gene Technology Act*; although the definition of a 'genetically modified organism' (GMO) under the *Gene Technology Act* specifically excludes a human who is only modified due to having undergone somatic cell gene therapy (s10).

The permissibility of genome editing research in human embryos will be dictated by the *Research on Human Embryos Act 2002*, as amended (Cth) and the *Prohibition of Cloning for Reproduction Act 2002*, as amended (Cth) (as well as mirroring legislation in states and territories). These laws permit certain types of embryo research, subject to licence. However until a licence is applied for we cannot predict how the legislation will be interpreted; especially because genome editing did not exist at the time these laws were written.

A search of the NHMRC licensing database indicates that at the time of writing, no licences involving the use of genome editing in human embryos in Australia have been granted nor applied for.

Even within the boundaries of legitimate scientific enterprise, **there are concerns about 'directed evolution'.**

causing harm. This is a debate that has long been considered and which often underpins the difference between somatic and germ-line genetic modifications.

Somatic-cell modifications allow for the therapeutic use of gene modification to help treat identifiable genetic disorders in a particular person. The crucial element is that these are non-heritable changes. Germ-line interventions, however, make changes that are heritable. While this has the advantage that unwanted genetic conditions may be permanently removed if the germ-line is altered safely and as intended, any errors or unwanted consequences from altering the germ-line will also be passed on.

Genome editing is interesting in this regard because the accuracy of the technique minimises (although by no means eliminates) the risk of error and allows a much more nuanced genetic modifications to be made. However, even if changes to the genome turn out to be 'safe' there are implications arising from the scope and scale of the techniques.

If a technique can be used widely and efficiently, without careful guidance of its use, a certain 'tipping point' can be reached that changes the status of the technology. Widespread use can change expectations to the point where genome editing would become a norm in many areas of life. Moreover, such massive increases in scope and scale may mean that current scientific governance may no longer be sufficient to deal with the wider implications surrounding such issues as access, resources and social impact of its use.

The crossover between ethics and adequate governance in science seems

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particularly acute in the case of genome editing. The creation of such a cheap and effective means of modifying genes can lead to a need to limit the potential for these techniques to be misapplied in other areas; what is known as the 'dual use' problem. These might include the genetic manipulation of viruses, gene transfer as a weapon, or commercial exploitation in crops and animals to produce specific traits. Even within the boundaries of legitimate scientific enterprise, there are concerns about 'directed evolution', whereby the boundaries of the scope of genome editing need to be established and decisions made about who should select the genetic properties of any organism to edit. This will require global agreements as to exactly how gene editing is to be managed.

Although genome editing techniques present a relatively low cost means of achieving genetic modification, wider issues of social justice remain that attach to the equity in distributing its benefits. First amongst these would be whether equitable access to technology is both warranted and available. This may be a particular problem for low and middle income countries due to the likelihood that research interests will focus significantly on problems linked to 'Western' medicine and disease.

Commercialisation may further extend many potential inequalities if patents or other means of restricting access to resources developed through genome editing techniques take hold (and patents over CRISPR-Cas9 are already being granted and fought over). Imagine the situation where genome editing leads to the development of highly drought-resistant, disease-resistant, high-yield crops, destroying commercial opportunities for those who are unable to pay the high price demanded for the genetically altered product. Competitive advantage may be even further affected due to the disruptive nature of genome editing, as it may supplant alternative gene-modification technologies.

Social justice concerns have also been raised by specific interest groups that see genome editing as potentially directly affecting them. Should genome editing involving germ-line modifications go ahead, it has the potential to permanently eradicate certain genetic disorders. Although this may seem at first glance like a universally good thing, some argue that the attempt to eradicate certain conditions permanently implies a lack of respect for people who have those genetic diseases by viewing not only the conditions themselves as something undesirable but also the existence in society of such people with those conditions.

Concerns about social justice need not all be negative, however. Although only a small number of people are likely to benefit initially, the economic advantages of genome editing may readily lead to a rapid expansion of application of the technique. This, in turn, has the potential to benefit populations that are often disadvantaged under current conditions of scientific research and innovation, such as those who live with rare diseases that would otherwise not be viable areas of research.

The development of research and testing of genome editing techniques on human populations in the first instance will, however, still be a major challenge. The nature of such trials, on whom, and how risks are assessed for research subjects and society in general will all have to be addressed.

Is Genome Editing Legal?

There is currently little specific governance of genome editing technology anywhere and it is an open question as to whether specific regulation is required. But at a minimum, it does seem appropriate to query how genome editing will be governed in Australia (see Regulation and Oversight breakout, p 6)

One broad consideration is to query what role governance could or should play in the development of any new technology. What aspects of genome editing should be regulated, and how? While it is perhaps too early to answer this question, considerations of the approach to governance and the need for regulation of

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When the recombinant DNA revolution occurred in the early 1970's, **scientists mutually agreed to a moratorium until more was known.**

genome editing should not be forgotten as the field continues to develop.

In recent years, academics and policy-makers who research emerging biotechnologies have been engaging in a dialogue over how to govern rapidly emerging biotechnologies. The problem is that legislation can be problematic: it is slow to make and difficult to change. Using regulations instead of statute laws is one way around this; as the recent regulations governing mitochondrial donation in the United Kingdom (UK) have shown.

In the UK and Europe, responsible research and innovation (RRI) has recently gained traction. While there is not yet a single definition or approach to RRI, there are three common features: (i) democratic governance over the appropriate rationale and end-points for research and innovation; (ii) broadly framed responsiveness to current and future innovations and their impacts to both science and society; and (iii) framing 'responsibility' within a climate of all stakeholders working under uncertainty.[9] RRI is also hallmarked by ongoing interaction between researchers and regulators. Yet RRI is also complex, requiring a significant commitment of time and resources to 'get right'. RRI does not yet seem to have entered the policy landscape in Australia; and it would be interesting to consider how such an approach might work here.

Do We Need A Moratorium?

One way to prevent problems arising from a new technology is not to do it at all. When the recombinant DNA revolution occurred in the early 1970's, scientists mutually agreed to a moratorium until more was known. Something similar might be considered for genome editing; in particular its applications that could alter the human germ-line. In 2015, concerns about the implications of genome editing in humans and their descendants led to calls for a moratorium on the use of this technology where it might impact the human germ-line.[10,11] Others have taken a position that encourages prudence and transparency, but stop short of a moratorium.[12]

In our view, while moratoriums have been successfully used in the past, it's not clear that one is indicated here. Most countries already have laws or guidelines in place that robustly regulate modifications of the human germ line. Further, a moratorium will prevent the exact research that we need to undertake to look carefully at is implications, such as safety and efficacy; which in turn will assist with weighing up the potential benefits, risks and harms. Thus instead of a blanket ban, we should instead encourage all nations to enforce restrictions on some applications of genome editing, until the ethics can be worked out. This should then be done with wide consultation and debate.

Where To Next?

Many of the ethical issues in genome editing also arise elsewhere. It does, however, create something of a new context arising from the implications of the scope of the techniques. Potentially infinitely editable genomes using an accurate and relatively inexpensive technique presents the potential for changing many more aspects of the genome in humans, animals, plants and other organisms, and on a significantly greater scale, than has previously been considered.

CRISPR-Cas9 is an exciting technology, with possible applications across almost all living species. The ethical issues arising from this should be considered openly by a variety of stakeholders. Genome editing also offers new opportunities to assess how we regulate and govern emerging technologies; including limitations to current legal approaches and opportunities to assess novel governance frameworks. AQ

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