# Long Read Review: Redesigning Life: How Genome Editing Will Transform the World by John Parrington

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*In* **Redesigning Life: How Genome Editing Will Transform the World***,* **John Parrington** *traces a history of genetic engineering, focusing particularly on recent, rapid developments in the capacity to manipulate genomes. This painstakingly researched book acts as an engaging, comprehensive and urgent introduction to the debate over the wider societal impact of these emerging technologies, finds* **Thomas Christie Williams***.*

***Redesigning Life: How Genome Editing Will Transform the World*. John Parrington. Oxford University Press. 2016.**

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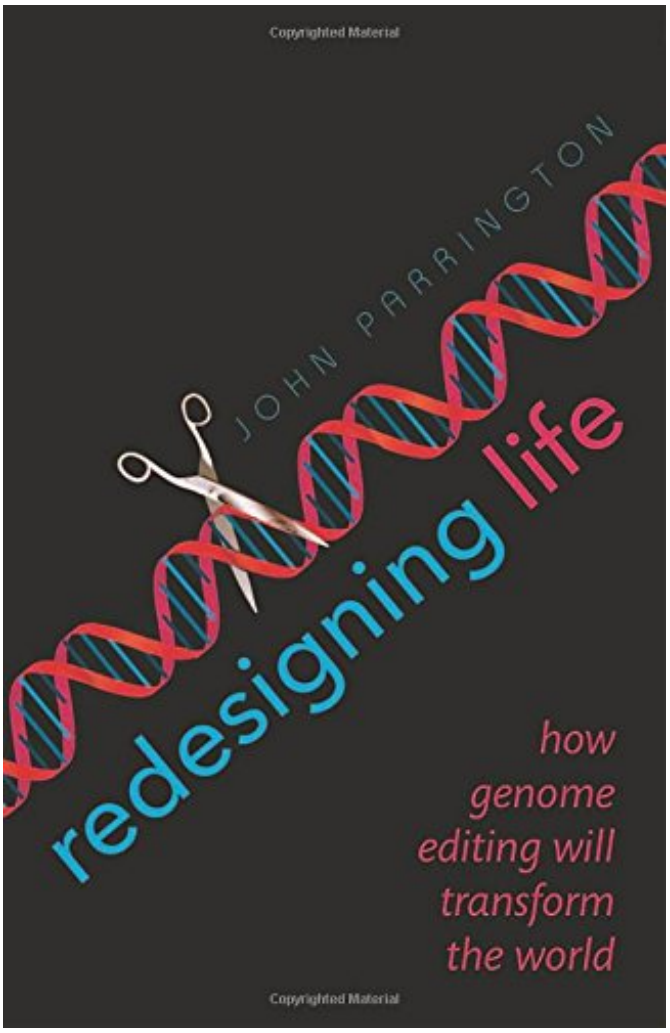
**Playing God**




'Scientists don't ask what we *should* do. Instead we think: what *can* we do?' This was the response of a cell biologist when I asked him what he thought of CRISPR/CAS9, the gene editing technique than in just four years has transformed laboratory science. As John Parrington stresses throughout his new book *Redesigning Life: How Genome Editing Will Transform the World*, scientists have never been scared to push the limits of social acceptability in pursuit of their interests.

Parrington describes Antonie van Leuwenhook, a Dutch pioneer of the use of the microscope, who in 1672 wrote to Lord Somer, President of the Royal Society, describing for the first time a living sperm cell. Having used his own semen for the studies, he hastened to add that 'what I investigate is only what, without sinfully defiling myself, remains as a residue after conjugal coitus'. In a sinister twist on this theme three and half centuries later, we subsequently learn about the Korean scientist Woo-Suk Hwang, who in 2009 was found to have coerced junior female scientists to donate eggs for the cloning necessary to produce embryonic stem cells. As the technology available to cell biologists, biochemists and geneticists develops rapidly, the high stakes of modern science are arguably fuelling a situation where startling, and sometimes unsettling, results are pre-empting our ability to regulate, police and understand them. *Redesigning Life* is pitched as a primer (no pun intended) for an audience who may not be acquainted with these rapidly evolving technologies, but who, Parrington believes, should be involved in a public debate about the issues they raise.

The main body of *Redesigning Life* is an engaging stroll through the history of genetic engineering from the

domestication of the dog circa 33,000 years ago onwards. As well as gene editing, Parrington covers the growing fields of optogenetics, stem cell technologies, synthetic biology and the interplay between them. Given this ambitious remit, the book is heavy on science and painstakingly researched (as evidenced by its 725 endnotes). This emphasis on experimental case studies, the level of detail and the breadth of topics covered might prove somewhat overwhelming for the non-scientific reader. However, the examples themselves are clear, concise and often arresting. Whilst in the final chapter Parrington explores the novel possibilities opened up by these new technologies, the book's main goal is to provide a comprehensive snapshot of the modified and novel life forms emerging in laboratories worldwide.

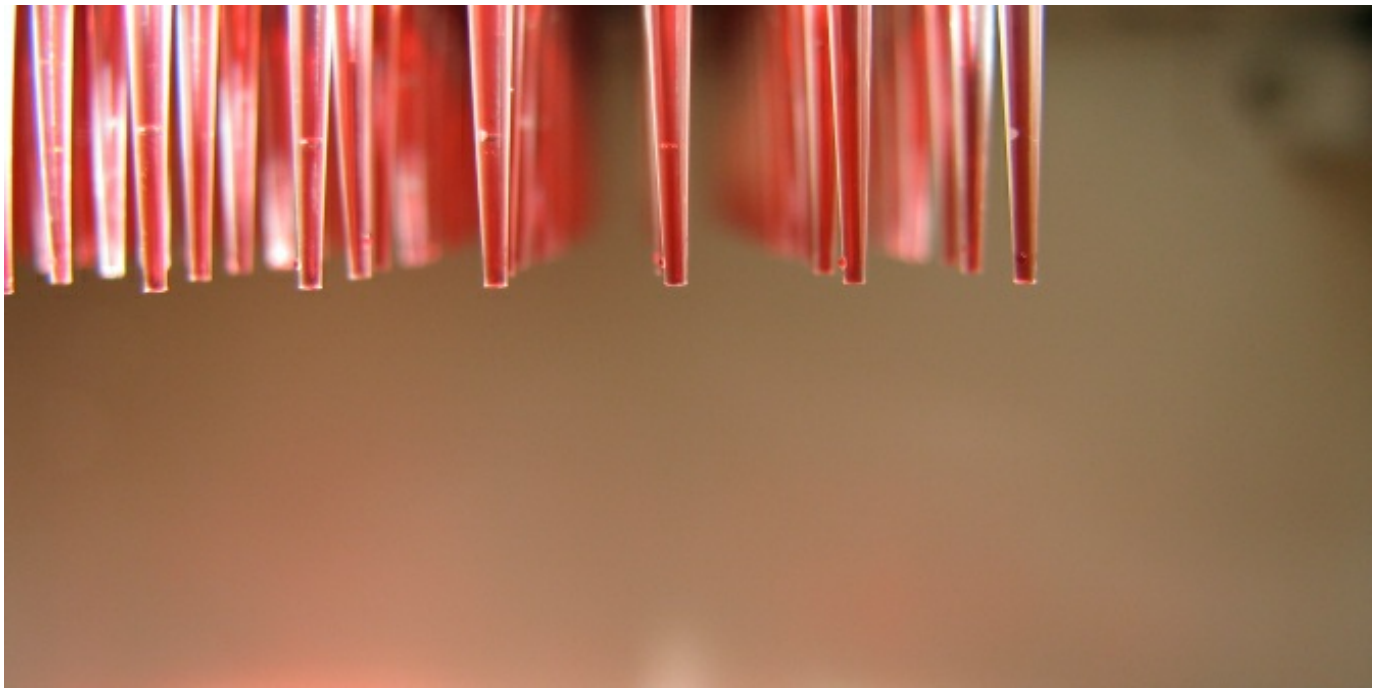


**Image Credit: 2010 DNA Distribution (igemhq CC BY 2.0)**

First discovered in the bacterium *E.coli*, the purpose of the CRISPR/CAS9 protein complex in nature is for bacteria to detect and destroy viruses that infect them. These viruses are essentially packages of genetic information – DNA – that insert themselves into bacterial cells to reproduce; there is huge benefit to the bacteria in having a system which can recognise and destroy these unwanted intruders. The first part of CRISPR/CAS9 stands for 'clustered regularly interspersed palindromic repeats'. This recognises whereabouts in DNA a cut should be made. CAS9 is the bacterial enzyme that acts as the molecular scissors to cut DNA, once the right location has been identified.

*E.coli* recognise viruses that have infected them in the past by integrating the viral DNA sequence into their own genetic information. When a virus that has previously infected *E.coli* re-enters the cell, these CRISPR elements mean that the bacteria rapidly recognise this viral DNA sequence, activate CAS9 to cut this DNA and thus destroy the virus. Science journalist Carl Zimmer has described the system as a 'molecular most-wanted gallery'.

As Parrington points out, perhaps even more ingenious than this biological system was the realisation by Jennifer Doudna and Emmanuelle Charpentier that it could be re-engineered to recognise new DNA sequences and cut them at pre-specified locations within a genome. If you wanted to inactivate a particular gene, all that has to be done is to create a novel CRISPR sequence that will bind to a DNA sequence of choice, and attach it to the CAS9. The CRISPR sequence will guide the CAS9 to this part of the genome and cut the DNA, rendering it useless. This is how you create a 'knockout' of a gene.

Furthermore, if CRISPR/CAS9 is introduced with a new segment of DNA, this can be introduced into the cell's

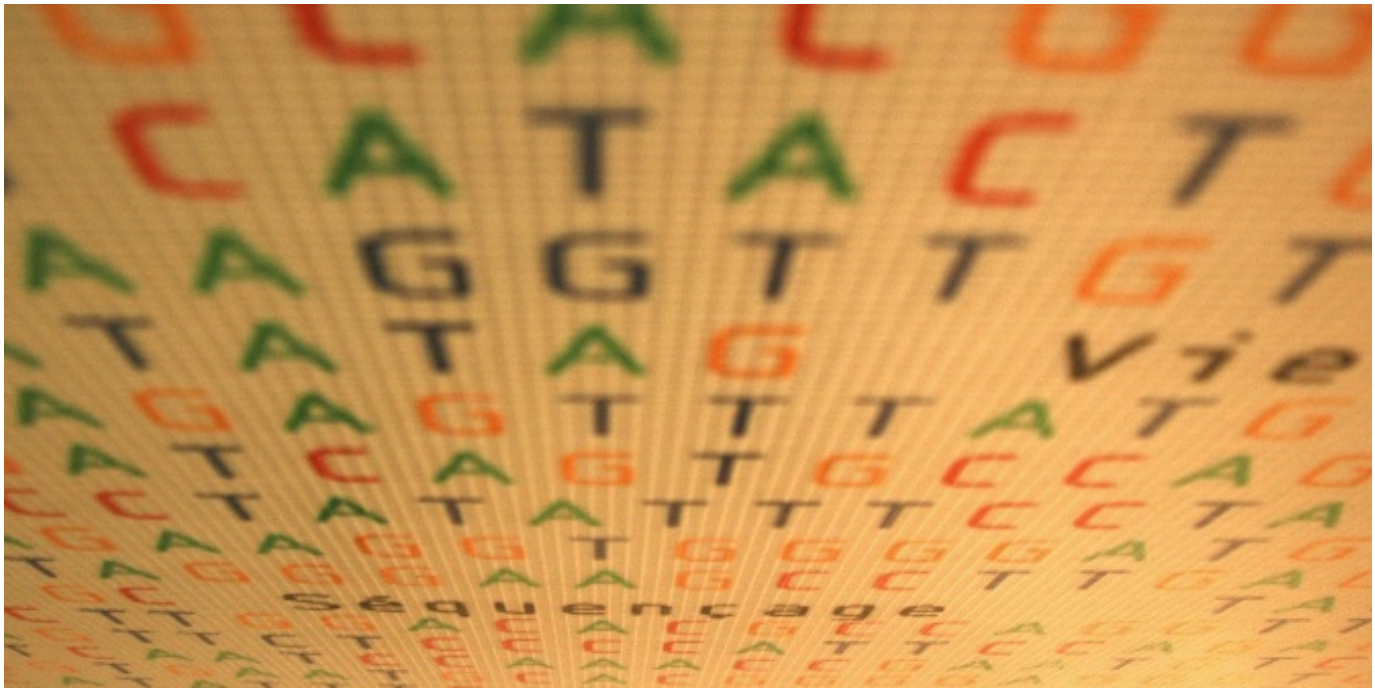
genome at the site cut by the CAS9: a ‘knock-in’. You can ‘knock-in’ a new gene or a modified version of an existing gene.  Essentially, this means that it is now possible to modify genomes to single nucleotide resolution. In humans, any one of our three billion nucleotides: the possibilities are dizzying. Parrington gives us some examples: one could knock out all 22,000 genes in a human cell in turn to look at their individual effects, an experiment which has already been carried out at MIT. Or create a pig with human lungs for medical experimentation, a project in development by a company called Synthetic Genomics.

Gene editing has been available for decades, but Parrington argues that CRISPR/CAS9 is truly different. He likens the difference between the old and new technologies to that between movable type and the first word processors. CRISPR/CAS9 is relatively straightforward to use, and it is cheap by any standards. Parrington estimates there to be over seventy ‘biohacker’ groups around the world: amateur biotechnologists, often with minimal scientific training, having a go at genetic engineering. CRISPR/CAS9 kits are now being made available to the public for only $120, so that if you have an interest in it, you can go ahead and engineer, for example, the yeast for your own craft beer.

Whilst the technology is cheap, the potential rewards of harnessing it are huge. In *Redesigning Life*, we are informed that venture capitalists promised a total of $68 million for two companies set up by Charpentier and Doudna (now estranged and acting independently of one another). Subsequent to the writing of the book, and within just a few months of floating on the stock market, Editas, one of these companies, now has a market value of $695 million. Lumacaftor-ivacaftor, a targeted medication for patients with cystic fibrosis with the F508del mutation, costs £104,000 for a year of treatment.

Add to these potential rewards the pressures being put on academic scientists to publish novel research and you enter a Wild West of hard-to-regulate experimentation and publication. A recent report revealed that Chinese universities already pay bonuses for publishing in high impact journals – a paper in *Nature* or *Science* might earn an academic $30,000. In addition to these financial rewards, throughout the scientific world the pressure to publish frequently in any indexed journal is strong.

Given these incentives and pressures as well as the technical feasibility, it is not surprising to read that in 2015 the Chinese scientist Junjiu Huang published a paper showing the first use of CRISPR/CAS9 in a human embryo. Although the editing – targeting the beta-globin gene that causes thalassaemia – was in embryos that had been created by the fusion of two sperm with one egg and would therefore not be viable, it caused uproar amongst the scientific community.

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*Redesigning Life* shows us that CRISPR/CAS9, and other associated technologies, have many potential beneficial applications. These include improving crop yields and disease resistance; disseminating genetic changes through mosquito populations to make them sterile; and treating human disease with an underlying genetic component, such as cystic fibrosis. All of these applications carry theoretical risks. With genetically modified crops, one might also spread resistance genes into other species. The loss of mosquitoes might lead to unpredictable ecological consequences, and the genetic changes might spread to other insect species such as bees, whose populations are already in decline. The therapies for genetic conditions might have unintended off-target effects, such as unexpected consequences in other cells that depend on the activities of the genes being modified.

But as the furore around the publication of Huang's paper demonstrates, the most controversial issue is that of germline editing: making changes to the DNA of the cells that will go on to form a new human being. The fear is that the antenatal modification of embryos will become widespread, leading to the creation of designer babies. In November 2015, 150 biologists met at a summit in Washington to discuss genome editing, and their conclusion was clear: a recommendation for a worldwide ban on the genetic editing of embryos.

Why is fear about germline editing so prevalent, and why is it such a sensitive issue? Part of this may be an ongoing legacy of the eugenics movement. The movement, which in the pre-war years had acquired a degree of acceptability in the UK and the US, was subsequently discredited as the horrors of Nazi Germany emerged after World War II. A letter from Adolf Hitler, dated to 1939, asked that 'certain physicians be personally authorised so that incurable patients can, after most careful evaluation of their condition, be granted a mercy death'. In practice, this meant that all newborns and infants with severe congenital diseases were to be reported to the regional health offices, after which they were transferred to 'Special Children's Departments' and administered sedatives until they died.

However shocking this seems, arguably the public (in Europe, at least) remain ambivalent in their view regarding the value of life in those born with severe disability.  In Germany, doubts about the value of lives of infants born with disabilities continued until at least the 1970s, suggesting the lack of a clean break with the eugenics movement. In the UK, when in 1980 the paediatrician Leonard Arthur instructed the nursing team to withdraw food and provide opiates to a child with Down syndrome and other severe congenital abnormalities, public opinion was split between those who supported and condemned him. In court he was found not guilty of attempted murder.

Currently, it is fairly routine and uncontroversial to screen embryos antenatally for mutations in IVF pregnancies if one or both parents are known to carry a deleterious mutation such as that for cystic fibrosis. Later in pregnancies, most of those without strong religious beliefs are supportive of the selective termination of foetuses found to have life-threatening or life-shortening conditions. In the UK, 90% of women who received an antenatal diagnosis of Down syndrome between 2011-12 decided to terminate the pregnancy.

So why this generalised unease about 'playing God', despite the fact that we are already doing so to a certain extent? The biologists at the Washington summit stated that germline editing would 'irrevocably alter the human species', and expressed concerns that there might be long-term, as-yet-unrecognised complications in individuals who had been genetically modified. But these concerns do not hold back the widespread adoption of IVF, and clinics (admittedly more commonly private ones) still routinely implant more than one embryo, despite the recognised higher risks of twins and triplets to both mothers and infants.

There seems to be something about creating new life with such a degree of *precision* that is so unsettling, creating a potent taboo around the topic. Strong underlying religious feeling is likely to be a substantial factor, or at least the remnants of this in the moral and ethical codes that structure our ostensibly secular public sphere. Thinking about the precision involved does carry strong echoes of Genesis. Clearly, people have been making decisions about what offspring they would like to engineer for centuries, by choosing particular partners for animals, plants, or, of course, humans. But in these cases, the ongoing element of chance in how the offspring will develop perhaps makes it seem more of a 'natural' process than precisely determining them.

Realistically, the main question regarding germline editing is more likely to be *if* than *when*. The combination of technological development, scientists' enthusiasm for experimentation, the pressures being put on them and the lucrative potential rewards will mean that the technology will continue to race ahead of our ability as a society to make sense of it. Government agencies are already having to make difficult choices about whether to regulate and monitor the more controversial aspects of genetic engineering, or watch this work move to countries where there are fewer restrictions on experimentation.

Thus the sense of urgency conveyed by Parrington in his conclusion. Whether or not as a society we will actually have much control over the new technologies as they race ahead remains a moot point. However, if one is optimistic enough to believe that a wide-ranging discussion might impact on how they are implemented, *Redesigning Life* will act as an engaging and comprehensive introduction prior to entering the debate.

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*Note: This review gives the views of the author, and not the position of the LSE Review of Books blog, or of the London School of Economics.*