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BUILD YOUR OWN BABY?

It's a moral imperative, argues JULIAN SAVULESCU.

HOMO SAPIENS EVOLVED on the African savannahs, resigned to short, difficult lives. In just a few hundred years – a blink of evolutionary time – we've transformed our environment, as well as our odds of survival.

IN TODAY'S INDUSTRIALISED, globalised world, we live to extreme old age. But this extended life span comes with a trade-off: our DNA is now out of sync with our environment. We can live for eight, nine, even ten decades, while the use-by date on our DNA is closer to 40–50 years. That means people spend their later years living with the diseases of ageing: dementia, cancer, heart disease, arthritis and osteoporosis. If our DNA is letting us down, why shouldn't we alter it to suit our environment?

We've had the technology to manipulate genes since the 1970s – legions of plants and animals have been genetically modified. But the technique was deemed too crude to apply to human embryos. Now, an extremely precise new technique known as CRISPR Cas-9 has blasted through that barrier. It is so much more precise that it's known as genetic editing rather than genetic engineering. First introduced in 2012, it allows a cell's genome to be sliced and genes to be removed or added.

CRISPR Cas-9 has transformed the art of genetic modification. It has also shifted what was for decades an unmoveable ethical line in the sand. Since April 2015, Chinese scientists have twice carried out genetic editing on human embryos. While the researchers purposely used embryos incapable of maturing, they nevertheless opened the door to the possibilities. Once the technique is perfected, many wonder, will genetic editing of viable human embryos be inevitable?

In some countries, including Australia, the UK, and many European nations, ethical concerns have prompted restrictions or an outright ban on the use of CRISPR-Cas9. But others, such as China, have taken a more permissive approach to the technology.

The US has become a major battleground in the ethical debate over CRISPR-Cas9. In March 2015 a number of US researchers, including those employed by private companies who are testing gene editing as a treatment for diseases such as HIV, haemophilia, sickle-cell anaemia and cancer, called for a moratorium on the genetic editing of human embryos. A month later, Francis Collins, Director of the US National Institutes of Health, proclaimed the agency would not fund research that is viewed "almost universally as a line that should not be crossed".

At the end of that year, an international summit was held in Washington, co-hosted by the US National Academy of Sciences and US National Academy of Medicine, the UK Royal Society and the Chinese Academy of Sciences. The participants came to a different view. While they held that "it would be irresponsible to proceed with any clinical use of germline editing," they did not push for a moratorium on research. Instead, they concluded that "as scientific knowledge advances and societal views evolve, the clinical use of germline editing should be revisited on a regular basis."

The moral line in the sand, it seems, is now indistinct.

This debate may soon come to a neighbourhood near you. Ultimately it's not the scientists, but members of the public and their political representatives who determine what laws and regulations are needed. In Australia, the question is: should we allow the research to happen here? And does this new tool send us down a slippery slope to a world where all babies are engineered? Another consideration: genetically edited embryos would pass on their edited DNA to future generations. Do we have the right to consign all future generations to our current idea of what an ideal DNA code is?

Precision genetic editing has catapulted us to the threshold of a GATTACA-like world. Now we have to decide whether to take the next step.

By any measure, it will be a fraught decision. The perils of genetically engineering babies have been well-articulated. They range from the potential for creating a genetic elite to unpredictability of the long-term effects of altering the DNA of our species. That's why genetic editing of embryos has been seen as a moral no-go zone for four decades. But some ethicists are now changing their minds.

Oxford-based, Australian-born bioethicist Julian Savulescu is at the forefront of those who believe we should allow human embryo editing. An advocate of "procreative beneficence," which holds that parents should select the best child they could have based on the best available information, he believes the technique is an ethical imperative. Here, in his own words, Savulescu makes his case.

WHY PERMITTING HUMAN GENOME EDITING IS AN ETHICAL OBLIGATION —

The human animal is not some finely balanced masterpiece of divine creation. It is the result of natural selection under particular environmental pressures. Humans exhibit some 250 genetic disorders; only 20–25% of embryos are fit enough to develop into a baby; and 6% of newborns exhibit a major birth defect.

DNA manipulation allows us to correct genetic aberrations and enhance the human genome. It allows us to liberate ourselves from the biological constraints of evolution and move toward a state of self-designed evolution.

There are six ethical principles that obligate us to embrace human genome editing:

1. REDUCE HUMAN SUFFERING

Whether it's a single gene disorder like cystic fibrosis or a multi-gene disorder like schizophrenia, inherited diseases cause great suffering. Gene editing could theoretically repair these faulty genes. In April 2015, Junjiu Huang and colleagues at Sun Yat-sen University in Guangzhou, China, attempted to use CRISPR-Cas9 on embryos carrying the blood-clotting disorder beta thalassemia.

If the technique is safe, there is a moral imperative to use it, in the same way there's an ethical obligation to help alleviate the suffering of a person born with haemophilia. Those with the disease receive regular infusions of a clotting factor their entire lives. There is no morally relevant difference between treating a haemophiliac with drugs and restoring the function of that gene while the person is still an embryo.

We should treat gene editing as we would any other medical intervention.

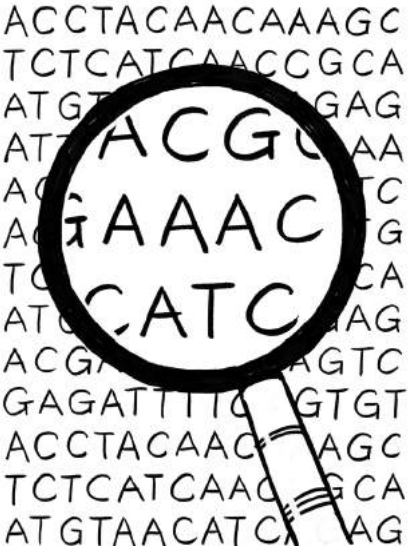
Some people argue that gene editing of human embryos is unnecessary since parents can already use in vitro fertilization (IVF) to select embryos that do not carry genetic disorders. But that argument fails for three reasons.

First, selecting embryos requires that parents are able to produce a sufficient number of embryos to select only the healthy ones. But 16% of couples produce only one embryo. A genetically-impaired embryo may be their only choice.

Second, when it comes to multi-gene disorders such as schizophrenia, there are never going to be enough embryos to select those with the healthiest combination of genes. For instance, in a disorder that involves the dysfunction of 15 genes, it's estimated it would take thousands of embryos to find those few that have a healthy combination of gene variants. Genetic editing with CRISPR-Cas9 has the potential to correct multiple genes in a single embryo. Moreover, genetic selection is not a cure for disease. It merely stops a person who would have had a disease from coming into existence and allows a different, disease-free person to be born.

Another argument is that gene editing of embryos is unnecessary because gene therapy can be carried out on people born with a disease. The genes of particular organs or tissues are treated – say the lungs of a person with cystic fibrosis.

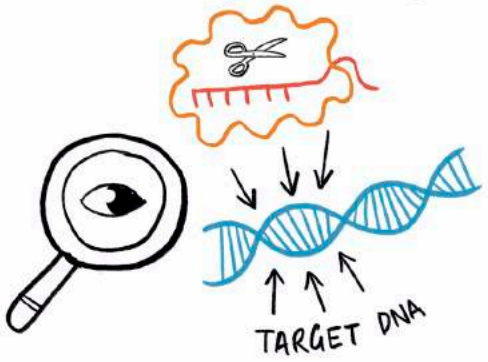
GENE EDITING COULD THEORETICALLY REPAIR FAULTY GENES.



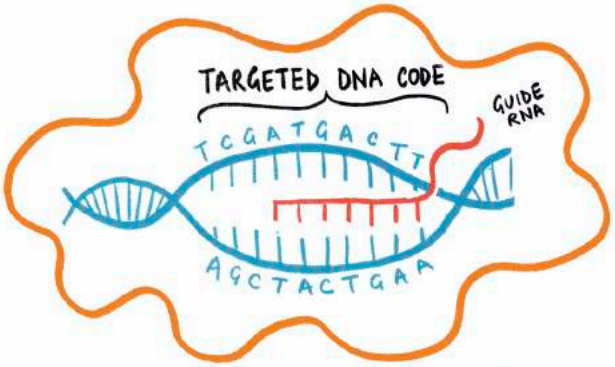
HOW GENOME EDITING WORKS

1 GUIDE MOLECULE AND ENZYME TOOL JOIN FORCES TO FIND TARGET DNA

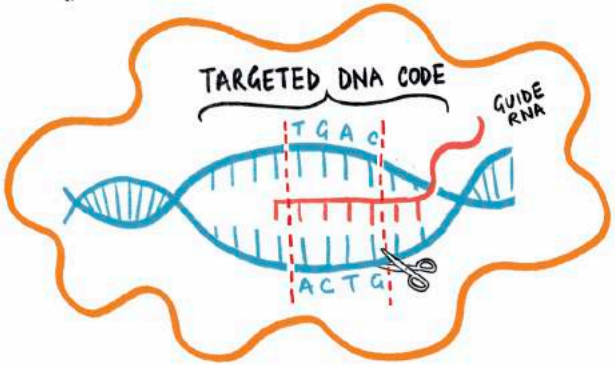
2 TARGET DNA IS FOUND



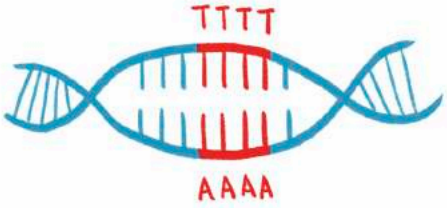
3 THE ENZYME OPENS THE DNA AND THE GUIDE RNA LINES UP WITH THE TARGET



4 THE ENZYME TOOL CUTS THE DNA



5 THE DNA CAN THEN BE EDITED



USES FOR GENE EDITING

FOOD & LIVESTOCK MODIFICATION

GENE THERAPY TREATMENT

DESIGNER BABIES

But so far, the successes of gene therapy have been extremely limited. No such treatment for cystic fibrosis exists, despite decades of attempts. Gene editing has the potential to cure every cell of a disease permanently.

2. A FAIRER WAY TO SPEND MEDICAL RESOURCES

In some cases we can effectively treat genetic diseases with existing methods. But those treatments are extremely costly. In a world of limited resources, excessive spending on one disease means there is less to spend on other diseases. Fairness requires we choose the most cost-effective option.

Take Gaucher's disease, for example, which affects babies born lacking an enzyme needed to break down fatty substances called sphingolipids. As a result, they build up in the liver, spleen, nervous system and bone marrow, interfering with the normal function of these organs. It is possible to treat the disease, which is especially common in Ashkenazi Jews, by giving a modified form of the missing enzyme via intravenous infusion every two weeks. But it is very expensive. In the UK the annual cost is around £18,000,000 ($31,339,659).

Such treatments are lifelong. Correcting the fault in the embryo through gene editing would cure this disease in a single hit and would be far less expensive. I estimate the cost would be in the range A$8,757–$17,515 in total per person, compared with A$876,834 for 50 years of treatment.

Carriers of a genetic disease like Gaucher's, which affects one in 500 Ashkenazi Jews (one in 14 are carriers) would likely know their status and opt to have IVF to test the genetic health of their embryos. But if all people are to have the opportunity to produce the healthiest embryos, then the entire population would need to have babies using IVF to enable genetic testing and editing.

So wouldn't this raise the costs to an unsustainable level?

Not in the long-term. I predict that within 20 years, as the effectiveness of IVF vastly surpasses natural reproduction and the cost of reading an entire genome plummets, the majority of births in developed countries will occur through IVF. Embryos will have their genome read, the best embryos will be selected, and increasingly they will be edited.

3. EDIT OUR DNA TO MATCHOUR LIFESPAN

The global population is greying. In 1950 one in 20 were over the age of 65; by 2050 that figure is projected to be one in six. People are also living to a very advanced old age. In developed countries the lifespan is over 80 years, and those in the less developed world are catching up. So far, graphs show no slow-down: lifespan increases by about 2.5 years each decade.

But with ageing comes Alzheimers' disease, heart disease, cancer, osteoporosis. The world's medical systems are buckling under the weight of this burden.

The diseases of ageing could possibly be delayed or arrested by gene-editing. Genes associated with cancer, dementia, heart disease and bone density are known. Mice have already been genetically engineered to be resistant to cancer and delay ageing.

4. GENETIC SHORT STRAWS

Nature is a biological lottery. Some are born healthy; others are dealt painful, abbreviated lives.

The prospect of genetic inequality are at the heart of public concern about genetic editing.

While we may legitimately worry about the creation of a genetic masterclass, we should also be concerned about those who draw the short genetic straw. The US Department of Education has estimated that nearly 50% of the US population lack the literacy to enjoy the rights and responsibilities of citizenship. This is largely social but also partly genetic.

THE PROSPECT OF GENETIC INEQUALITY IS AT THE HEART OF PUBLIC CONCERN ABOUT GENETIC EDITING.

We already accept that as a society we need to intervene to help those short-changed by their biology. We do so with remedial education, diet and social support. Why not use gene editing to even the playing field?

If gene editing were targeted at natural genetic inequality it would reduce rather than increase inequality.

5. DISCOVER CURES

People worry that gene editing will be used to benefit the richest, not the neediest. But gene-editing of human embryos could benefit all of us — by giving us a greater understanding of human development and disease.

AT PRESENT GENE EDITING SHOULD ONLY BE USED IN RESEARCH TO REFINE THE TECHNIQUE.

To that end, last February, the UK Human Fertilisation and Embryology Authority licensed a research team at London's Francis Crick Institute to carry out gene editing on embryos. The experiment aims to discover how a particular gene called OCT4 influences an embryo's development. The research may reveal why IVF so often fails — and ultimately improve IVF success rates. This would reduce, not increase inequality.

6. HUMAN ENHANCEMENT

In April 2016, a second Chinese group led by Yong Fan at Guangzhou Medical University attempted to engineer HIV resistance in human embryos. Their goal was to replicate a naturally-occurring human genetic variation in a gene called CCR5. People with two copies of this genetic variation are completely resistant to HIV infection. This experiment showcases how gene editing could be used to protect populations that are highly at risk of contracting HIV, such as those in Sub-Saharan Africa.

Extending our imagination a little further, if there is a mass bioweapon attack, or catastrophic climate change, natural evolution will be too slow to reconstitute a resistant human population. Like the dinosaurs, we would likely become extinct. The ability to genetically enhance embryos is the insurance policy for human survival.

We also need to consider our moral fitness. We live in a world populated by 70,000,000 psychopaths – 1% of the population. If a small percentage are technologically savvy or have access to wealth and power, they could inflict great harm on society. Genes that control antisocial behaviour are well-known. For instance the so-called "warrior" gene, first identified in a Dutch family whose violent members often wound up in prison, is a mutation in a gene called MAO-A, which controls the levels of neurotransmitters in the brain.

But we don't have to look to deviant behaviours for examples of the potential benefits of human gene editing. When it comes to ordinary populations, altruism and concern for others is in short supply. Reseacher Wojciech Kopczuk and colleagues report that Americans value the life of a non-American at just 0.5% of their compatriots. In the US and Europe, anti-immigration parties and policies are bringing our xenophobic tendencies into high relief. Our DNA is partly responsible: we evolved to be tribal rather than global citizens.

If these xenophobic genes could be identified, it may be possible to do away with the trait. As I have argued in my book "Unfit for the Future" (with co-author Ingmar Persson) we have a moral obligation to bring about radical enhancement of the ethical aspects of our own human nature.

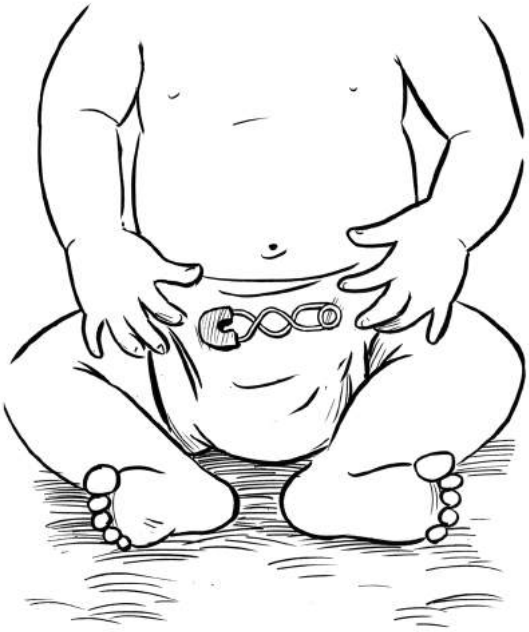
OTHER OBJECTIONS —

There are, of course, grave and well-founded concerns about safety. As the two Chinese experiments showed, gene editing is not ready for clinical use. The percentage of embryos that received any editing at all was only 15% — and of these, many incurred errors. Edits were placed in the wrong part of the DNA and the embryo did not receive uniform editing of the DNA in all its cells. That means not all tissues would receive the benefits — a major problem if the embryo is being edited for HIV resistance.

Given these issues, at present, gene editing should only be used in research to refine the technique. One law that mandates this is the UK's Human Fertilisation and Embryology Act. It only allows embryos to develop until 14 days.

If gene editing were to be used to cure a disease in an embryo, it should first be attempted in a disease that is lethal in early life and where there is no treatment, such as the severe form of OTC deficiency, a rare genetic disorder in which ammonia accumulates in the blood. The accuracy of gene editing could be tested in the embryo prior to implantation and tested again during early pregnancy.

Another objection from some ethicists is that



gene editing goes against freewill since it involves one person designing another. There is also the problem that the embryo cannot consent to such life changing interventions.

But if it's impossible to get consent, consent is irrelevant. The embryo can neither ask to be edited or to be left alone. As moral agents, we must make the most ethical choice.

As far as freedom, genetic illness drastically reduces it. Take cystic fibrosis. Those who suffer from the disease spend most of their lives in hospitals. If we had a drug that would cure cystic fibrosis on day one of life, we would administer it. Gene editing merely involves curing disease at day zero. It increases freedom.

THE EVILS OF EUGENICS

Isn't this just what the Nazis would have dreamt about?

Eugenics, per se, is not an evil thing. The objectionable part of Nazi eugenics was that it was coercive, designed to achieve a racist society, and was based on bad science. Modern, ethical eugenics involves free choice by parents, is aimed at achieving health and well-being for the child, and is based on good science.

The Nazis also used sterilisation to achieve their goals. But we haven't banned sterilisation – we use it in a regulated, ethical way.

EMBRYO EDITING IS PASSED ON TO THE NEXT GENERATION

A final major concern about editing the DNA of embryos is that these changes will be passed on to future generations. Many have argued that we cannot predict the long-term consequences. In some cases, we won't know the consequences for the individual who harbours the modification for their entire life. We also don't know the consequences for the human population. For example, what if a gene that appeared to cause some harm to an individual actually protected them from an epidemic? For instance, people who carry a single copy of the sickle cell anemia gene are more resistant to malaria.

It comes down to a case-by-case basis. In the case of curing a fatal genetic disease like cystic fibrosis, where the affected embryo carries two copies of the flawed gene, the consequences for that person are clearly positive. For cases where the merits are less clear, we need to wait for the rapidly developing science of genomics to reveal the consequences of genetic editing.

Of course there are risks with anything in life. We are constantly modifying our genome unintentionally, by smoking, drinking, plane travel, sun exposure, exposure to viruses, even delayed parenting.

If it is OK to damage the genome, why isn't it OK to repair it? And if it is OK to repair it, why isn't it OK to enhance it?

CONCLUSION —

Many will disagree with me about the great potential of genetic editing to prevent disease, and the ethics of using it on embryos to achieve this goal. Drawing a distinction between the editing of embryos for research purposes and for reproductive purposes will allow us to debate such issues without impeding research in the meantime.

All things considered, manipulation of human DNA is an ethical imperative.

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ILLUSTRATIONS
Jeffery Phillips