

A peer-reviewed electronic journal published by the <u>Institute</u> <u>for Ethics and</u> <u>Emerging Technologies</u>

ISSN 1541-0099

27(1) - July 2017

Editing the Genome of Human Beings: CRISPR-Cas9 and the Ethics of Genetic Enhancement

Marcelo de Araujo

Universidade do Estado do Rio de Janeiro Universidade Federal do Rio de Janeiro

marcelo.araujo@pq.cnpq.br

Journal of Evolution and Technology - Vol. 27 Issue 1 - June 2017 - pgs 24-42

Abstract

In 2015 a team of scientists used a new gene-editing technique called CRISPR-Cas9 to edit the genome of 86 non-viable human embryos. The experiment sparked a global debate on the ethics of geneediting. In this paper, I first review the key ethical issues that have been addressed in this debate. Although there is an emerging consensus now that research on the editing of human somatic cells for therapeutic purpose should be pursued further, the prospect of using gene-editing techniques for the purpose of human enhancement has been met with strong criticism. The main thesis that I defend in this paper is that some of the most vocal objections recently raised against the prospect of genetic human enhancement are not justified. I put forward two arguments for the morality of genetic human enhancement. The first argument shows how the moral and legal framework within which we currently claim our procreative rights, especially in the context of IVF procedures, could be deployed in the assessment of the morality and legality of genetic human enhancement. The second argument calls into question the assumption that the average level of human cognitive performance should have a normative character.

Introduction

Recent developments in biotechnology have sparked a new debate on the ethics of scientific research. A ground-breaking gene-editing tool called CRISPR-Cas9 (Clustered Regularly-Interspaced Short Palindromic Repeats) has proved to be much cheaper, easier to use, quicker, and more accurate than other tools for genome editing. CRISPR-Cas9 promises a wide range of applications, and perhaps even a new era for research in

biology.¹But the limits for a morally acceptable use of CRISPR-Cas9 are still quite controversial.

Thus far, CRISPR-Cas9 has been used, for instance, in research for the creation of seeds of rice, soybeans, and potatoes that are more resistant to pests, or of grass that needs less mowing (Specter 2015; Ainsworth 2015; Ledford 2016). The legal status of these seeds is still uncertain in some jurisdictions. They do not count as "transgenic" because they are not produced by inserting the genes of one species into the genome of another species. For this reason they may escape the strict regulations that apply for transgenic food (Waltz 2016; Nature(Editorial) 2017a). CRISPR-Cas9 has also been used to edit the genome of the mosquitoes that carry the malaria parasite, rendering them unable to transmit the disease (Ledford and Callaway 2015). In 2015 CRISPR-Cas9 was used in the creation of smaller pigs, which can be sold as pets in a variety of coat colors and patterns (Cyranoski 2015b). GM pigs could also be engineered to grow organs for transplantation into human beings without the risk of rejection or the fear that they would trigger diseases (Reardon 2015b;Wu et al. 2017).²This would certainly reduce the number of deaths resulting from a shortage of human organs for transplantation. Because these pigs carry both pig cells and human cells they are called "chimeras." There has also been speculation on the use of CRISPR-Cas9 to "de-extinct" some species. It is not clear, however, whether it would be desirable or ethical to reintroduce into their original environment plants or animals that have been extinct for centuries (Charo and Greely 2015, 12).

Some philosophers, policy makers, environmentalists and animal rights activists have already expressed deep concern over the widespread use of CRISPR-Cas9. Some worry, for instance, that GM mosquitoes, once released in the wild, could behave in very unpredictable ways. They might disrupt an entire ecosystem (Ledford 2015a, 2015b). Supporters of animal rights argue that it is morally wrong to create GM pigs to give human beings new kinds of pets or spare human organs. The moral status of chimeras is also unclear. In August 2016 the NIH (National Institutes of Health), in the USA, issued a request for public comment on "Certain Human-Animal Chimera Research."³The fear that CRISPR-Cas9 might one day be used in the development of bioweapons has also been vented among intelligence officials in the USA. They suggest that bioweapons carrying GM pathogens would be easier and cheaper to produce, and far harder to control, than nuclear weapons (Dando 2016).

But no other field of application of CRISPR-Cas9 has generated more concern thus far than the prospect of editing the genome of human beings. It is now possible to identify three main questions in the current debate on the ethics of gene editing. I have listed these questions in what I see as an increasing order of moral concern. This means that Question 3 has generated more concern than Question 2, and Question 2 has generated more concern than Question 1.

Question 1. Would it be morally acceptable to use CRISPR-Cas9 in order to modify human *somatic cells* in the attempt to find a cure for diseases such as sickle cell anemia, Huntington's disease, AIDS, and different types of cancer?

Question 2. Would it be morally acceptable to use CRISPR-Cas9 in order to modify human *germ cells* (sperm, eggs, or early embryos) in order to prevent the occurrence of some genetic disorder in a child, and in the children descending from that child?

Question 3. Would it be morally acceptable to edit human cells (whether somatic or germ cells) in order to engineer a child with enhanced human capacities such as increased strength, higher intelligence, or improved resistance to diseases?

Question 1 concerns the use of CRISPR-Cas9 for genetic modifications that will not be inherited by the next generation. If this procedure proves to be safe in the future, a GM human embryo will develop into a fetus that does not carry genetic disorders; and people whose cells have been genetically modified later in life will be able to fight diseases such as AIDS or cancer. But the genetic modification will not be passed on to their offspring. Question 2, on the other hand, concerns the use of CRISPR-Cas9 to change DNA sequences in the human germline. In this case, the genetic modification will be inherited by subsequent generations. But while the first two focus on the use of CRISPR-Cas9 for the treatment of illnesses, Question 3 focuses on the prospect of editing the human genome for the purpose of human enhancement. It is the proposal expressed in Question 3 that has been most criticized thus far.

The prospect of genetically enhancing human beings has been received with more suspicion, and sometimes with hostility, than the goals expressed in Questions 1 and 2 (Blendon et al. 2016; Funk et al. 2016). One obvious reason for this is that we are still far from being able to engineer a human embryo with a specific set of desirable traits such as increased chances of living a long and healthy life, improved resistance to diseases, or augmented intelligence. But the main reason for the widespread hostility toward Question 3 is the eugenic implications it has. The prospect of living in a society of "designer babies" reminds us of the eugenic policies pursued early in the twentiethcentury in the USA, and the plans for the creation of a "master race" in Germany during the years leading up to World War II. But is the current hostility to genetic human enhancement justified?

In what follows, my intention is first to review the reasons for the recent interest in the ethics of editing the human genome. Then, I would like to address Question 3. The main thesis that I defend in this paper is that some of the most vocal objections recently raised against the prospect of genetic human enhancement are not justified. I put forward two arguments for the morality of genetic human enhancement. The first argument shows how the moral and legal framework within which we claim our procreative rights could be used to assess the legality and morality of genetic human enhancement. The second argument calls into question the assumption that the average level of human cognitive performance should have a normative character.

Editing human embryos

In April 2015 a team of Chinese scientists published a paper about the use of CRISPR-Cas9 in an experiment involving 86 human embryos. Their aim was to find a cure for a hereditary blood disorder called beta-thalassemia. The embryos used in the experiment were non-viable – they could not develop into human fetuses (Liang et al. 2015). However, news that scientists had tried to edit the human genome sparked a cascade of different reactions both within the scientific community and in society at large. Some scientists and bioethicists argued that the experiment was morally unacceptable. They went as far as to call for an international moratorium on any research involving the editing of human genes (Lanphieret al. 2015; Darnovsky 2015; Pollack 2015; Cyranoski

2015a, Cyranoski and Reardon 2015; Ledford 2015a). But other people welcomed the experiment and declared that it represented the beginning of a new era for research that could one day lead to the treatment and cure of several diseases, including AIDS and many forms of cancer (Savulescu et al. 2015; Miller 2015; Pinker 2015; Harris 2015; Baltimore et al. 2015; Bosley et al. 2015; Doudna 2015; Reardon 2015a; Cyranoski 2015a; *The Economist* 2015a).

Following the uproar caused by the publication of the Chinese paper, a global forum was set up to address the ethical and the legal issues surrounding the use of CRISPR-Cas9 on human cells. The forum was called the "International Summit on Human Gene Editing." The first meeting took place in December 2015 in Washington DC, at the National Academy of Sciences. Two further meetings were held in Washington, and one in Paris.⁴The summit brought together leading scientists, policy makers, philosophers, and representatives of religious groups. Early in 2017,the National Academy of Sciences published a book-length report with recommendations for an ethical use of CRISPR-Cas9 on human cells. The editing of the human germline is still considered a very controversial topic. Most participants in the summit agreed that this procedure might represent a great risk for the health of future generations. But there seems to be now a broad consensus that the benefits resulting from research involving the editing of human somatic cells are not negligible and that research in this area should be pursued further (National Academy of Sciences 2017).

In April 2016, one year after the publication of the paper that sparked the global debate on the ethics of human gene-editing, another team of Chinese scientists published a new paper on the use of CRISPR-Cas9 on 213 human zygotes. Their aim was to induce a mutation that makes some people immune to the HIV virus (Kang et al. 2016; Callaway 2016a). However, this time the experiment was hardly reported in the press. Early in 2016 a team of British scientists from the Francis Crick Institute received formal permission to use CRISPR-Cas9 on human embryos (Francis Crick Institute 2016). But these embryos may not be used to start a pregnancy. Swedish researchers from the Karolinska Institute obtained similar permission in June 2016 (Callaway 2016b). And it was also in June 2016 that the NIH approved the use of CRISPR-Cas9 for the engineering of human immune cells that should be able to fight off some types of cancer (Kaiser 2016). A few months later, in October 2016, a team of Chinese researcherstook a step further: they used CRISPR-Cas9 to edit human cells *outside* of the human body. The cells were then injected into a patient with lung cancer (Cyranoski 2016). The use of CRISPR-Cas9 to edit human cells within the human body is expected to occur soon (Le Page 2017). The key question now, therefore, is not so much whether it is ethical to modify the DNA sequence of human cells for therapeutic reasons, but whether it is safe. Or to put it more precisely: the main ethical issue now concerns the safety of the geneediting procedure for the health of human beings.

Safety issues are especially pressing in the case of human germline modification. If anything goes wrong in the editing process, and an off-target mutation occurs, the next generations will be affected too. It is also possible that some of the mutations resulting from the unsuccessful editing of human genes could not be detected before childbirth, or perhaps only later in life. At the present stage of scientific research, the tools available for editing the human genome are still far from being sufficiently reliable to ensure that only the targeted genes will be affected. Moreover, our knowledge of the human genome is inchoate. Scientists are still struggling to understand how certain genes, or group of genes, express such and such diseases, or such and such human traits. Thus, for the time being, there are good reasons to ban the editing of human genes in embryos that will develop into human fetuses, especially fetuses that will carry germline modification. Many years of research maybe necessary before CRISPR-Cas9, or some other gene-editing technique,⁵ will be considered sufficiently safe, and legally acceptable, to be applied in embryos intended to start a pregnancy. For the time being, though, the risks for future generations are simply too high, so an ethical line must be drawn, and legal restrictions must be imposed.

However, the current debate on the ethics of editing the human genome has also prompted some scientists and bioethicists to criticize the morality of such experiments not only because editing the human genome represents a risk for the health of human beings. Some people argue that editing the human germline is morally wrong even if, in the future, the procedure would prove safe and efficacious for the treatment of a wide variety of diseases. For them, safety issues are not all that matters in the debate on the ethics of editing the human genome. Two main objections, unrelated to safety issues, have been raised against the prospect of editing the human germline. Both are related, rather, to the fear of human enhancementand eugenics.

The first objection is that editing the human germline for therapeutic purpose would be acceptable in itself, but it would also inevitably pave the way for non-therapeutic applications. This would enable the emergence of "designer babies" and the dystopian scenarios that films such as *Gattaca* (1997) and novels such as *Brave New World* (1932), by Aldous Huxley, have depicted in the past. Edward Lanphier and colleagues, for instance, made the following statement in the journal *Nature* shortly before the appearance of thefirst paper on the use of CRISPR-Cas9 on human embryos: "Many oppose germline modification on the grounds that permitting even unambiguously therapeutic interventions could start us down a path towards non-therapeutic genetic enhancement. We share these concerns" (Lanphier et al. 2015, 411).For the first objection, therefore, editing the human germline should be stopped because it would also lead us to pursue genetic human enhancement, and human enhancement itself is morally wrong.

Objections to genetic human enhancement are not new. In a paper published in 2003, Leon Kass, for instance, argues that: "Gene therapy for cystic fibrosis or Prozac for psychotic depression is fine; insertion of genes to enhance intelligence or steroids for Olympic athletes is not" (Kass 2003, 13). Francis Fukuyama made a similar point in 2002: "The original purpose of medicine is, after all, to heal the sick, not to turn healthy people into gods" (Fukuyama 2002, 209). Objections to genetic human enhancement have also been raised by philosophers such as Michael Sandel(2007) and Jürgen Habermas(2002). For them, genetic human enhancement is morally wrong because it represents a threat to our shared human nature.Many authors, though, have already addressed these objections over the last years (Agar 2004; Glover 2006; Bostrom and Ord 2006; Harris 2007; Blackford 2007, 2014). I intend to develop a further argument later on, as I address Sandel's "ethic of giftedness." For now, I would like to turn to the second objection against genetic human enhancement.

The second objection also states that editing the human genome should be stopped because it paves the way for genetic human enhancement. But the argument goes on that, even though genetic human enhancement is not morally wrong in itself, it would be the cause of major societal problems and social injustice: people who do not want to enhance themselves, or cannot afford the costs of genetic enhancement, are likely to face discrimination and stigmatization in the future. In October 2015 a committee of scientists, philosophers, lawyers and government representatives, working for UNESCO, issued a document entitled "Report of the IBC [International Bioethics Committee] on updating its reflection on the human genome and human rights." Their intention was to address some of the ethical issues raised by the Chinese experiment of 2015. In the document, the committee suggests that genetic human enhancement is a threat to "human dignity." Consider, for instance, the following passage:

The goal of enhancing individuals and the human species by engineering the genes related to some characteristics and traits is not to be confused with the barbarous projects of eugenics that planned the simple elimination of human beings considered as "imperfect" on an ideological basis. However, it impinges upon the principle of respect for human dignity in several ways. It weakens the idea that the differences among human beings, regardless of the measure of their endowment, are exactly what the recognition of their equality presupposes and therefore protects. It introduces the risk of new forms of discrimination and stigmatization for those who cannot afford such enhancement or simply do not want to resort to it.(UNESCO 2015, p. 27, §111;see also §9 and §122)

It is not clear, however, why the prospect of using gene-editing technology to enhance human beings represents a threat to the "principle of respect for human dignity." It is certainly not morally wrong, for instance, to try to improve one's cognitive capacities (or one's children's cognitive capacities) by means of a well-balanced diet, good education, and regular sleeping. These goods may have long-lasting or even permanent effects on people's lives as much as direct intervention in their genome. It is indeed true that human enhancement has the potential to create "new forms of inequality, discrimination and societal conflict" (Darnovsky 2015). But a healthy diet, good education, and a comfortable sleeping room may turn out to be even more expensive, and hardly affordable to many people, than genetic human enhancement.

If an extremely expensive new drug proved successful as a cure and prevention for cancer, most countries would soon be divided between two conflicting groups: the group of individuals who are going to die within the next few months, or live with the fear of developing cancer one day because they cannot afford the new drug; and the group of the lucky ones, rich enough to buy the new drug. This would certainly be the cause of a major "societal conflict." However, it would also prompt us to think of new social arrangements and public policies in order to make sure that the new drug would be available to every fellowcitizen. The attempt to ban research on expensive cancer treatment in the first place would be an irrational strategy. And although we cannot "redistribute" genes or talents in the same way we can redistribute basic goods such as housing and education, there is no reason to assume that genetic human enhancement is essentially incompatible with the pursuit of social justice. Before the emergence of CRISPR-Cas9,Allen Buchanan et al. had already made the point that:"[...] some of the most prominent and well-thought-out theories of distributive justice might be taken to imply that intervention in the natural lottery may sometimes be required" (Buchanan et al. 2000, 320. See also Glover 2006, 79). They particularly hadin mind interventions for the purpose of genetic enhancement.

Why not enhancement?

I would now like to propose two arguments that justify the use of gene-editing tools in the enhancement of human cognitive capacities. The first argument calls attention to our procreative rights, while the second criticizes the mistaken assumption that the current, average level of human cognitive performance has a normative character.

First argument for genetic enhancement: procreative rights

Let us suppose that the technology for editing the human genome becomes effective and safe in the future: so effective and safe that hereditary illnesses such as Huntington's disease, cystic fibrosis, Tay-Sachs disease, and other genetic disorders, could be eradicated. In this hypothetical scenario, would it be morally wrong to use this technology not only as a means of treatment, but also to promote the enhancement of healthy individuals? Some people might welcome the editing of the human genome as a means of treatment, but reject the morality of human enhancement. Human enhancement, for them, is a form of eugenics. And the practice of eugenics, by reason of our recent history, is always perceived now to be morally wrong. However, this objection, in my view, is not justified, or at any rate is not consistent with other practices that do not elicit such strong moral rejection in modern societies, and which are already regulated by law.

Many couples, including women who prefer to get pregnant without having to have sexual intercourse with a man, routinely resort to fertility clinics and sperm banks in order to have a baby. It was reported in 2015, for instance, that the importation of human semen for IVF (In Vitro Fertilization) had increased by more than 500 per cent in Brazil over a period of one year (UOL Notícias 2015). The demand for imported semen in Brazil became so high that the American company Fairfax Cryobank, which sells human semen in the USA, opened an office in the city of São Paulo. Brazilian legislation does not prohibit the importation of human semen for private use, but prohibits its commercialization within its territory. American sperm banks, on the other hand, provide a detailed account of the genetic profile of the donors, except for their identity. The profile may include information relative to their eye color, hair color, ethnic group, weight, blood type, height, and the medical records of the donor and his relatives. Some information on the educational achievements of the donor may also be provided as a means of assessment of his intelligence. Of course, there is no guarantee that the IVF procedure will actually result in the birth of a child with the traits attributed to the donor of the sperm. But neither Brazilian nor American law denies adult citizens "procreative rights," that is their right to choose a partner, or a sample of sperm, that is most likely to generate a child with a specific set of featuresthey consider preferable (Robertson 1994). Now, if we do not stop people from making these choices when the probability that their children will actually have the desired traits is only slightly increased, why should we deny them the right to make these choices when the probability, thanks to advances in biotechnology, will become much higher? Procreative rights have already enabled men and women to "design" their babies on legally and morally acceptable grounds.

In countries such as Canada, Australia, China, and Great Britain the demand for human semen for IVF has also soared over the last years. Sperm banks in these countries have recently reported that they have not been able to meet the current demand, which has been boosted mainly by an increasing number of women who decide to delay pregnancy; and by same-sex couples who, thanks to changes in societal attitudes toward homosexuality, feel now encouraged to have their own children (*Daily Mail Online* 2014; Elgot 2015; *Global Times* 2016; Woudstra 2016). In 2016, the London Sperm Bank launched an app that now allows prospective parents to receive an automatic notification on their mobile phones whenever a new sample arrives. The information about donors includes items such as "occupation" and "highest qualification," which work as predictors of intellectual capacity (Sklar 2016). An increasing number of people are finding new ways to make use of their procreative rights. But procreative rights, of course, are not absolute rights(Robertson 1994, 17 and 93; Agar 2004, 15; Glover 2006, 77).

Rules concerning the anonymity of donors, or the medical requirements that they have to fulfill, or the human traits that would-be parents are allowed to request for the IVF procedure, may vary from country to country. The sperm of a specific donor, for instance, may be legally used to fertilize only a limited number of eggs. This reduces the risks of consanguinity. Sperm banks must also take every measure to unsure that the sperm sample chosen by a specific client will be the same sample eventually used in the IVF procedure. And precedents resulting from legal disputes involving misconduct by sperm banks – for instance the case *Cramblett v. Midwest Sperm Bank, LLC* (initiated in 2014) in the USA – might be adopted later as a legal framework for the regulation of genetic human enhancement (Mcknight 2014).

IVF has its downsides too. Retrieving or "harvesting" the eggs from the ovaries is a difficult and expensive process. It is also very uncomfortable for the woman. Daily injections of hormones are necessary in order to stimulate the ovaries to release more eggs than usual. Hormones shots occasionally lead to the overstimulation of the ovaries, putting the health of the woman at risk. It is reasonable to assume, however, that these disadvantages will eventually, within the next few decades, give rise to new (and cheaper) methods of fertility treatment. Henry Greely, for instance, argues that, in the future, instead of harvesting the eggs from the ovaries, clinicians will be able to use skin cells to create iPSCs (induced Pluripotent Stem Cells), which can be turned into virtually any human cells, including eggs. Alternatively, iPSCs could also be used to produce male reproductive cells. This would allow two men to have a child of their own without having to resort to donated eggs, although a gestational surrogate mother would still be necessary. According to Greely, the use of iPSCs for the creation of human reproductive cells would enable clinicians to fertilize simultaneously hundreds of eggs stemming from the same woman. And as genome sequencing technology becamefaster and cheaper, it would be possible, then, to screen hundreds of embryos for genetic diseases and for traits that current IVF methods can predict only with far less accuracy. Greely calls this procedure "Easy PGD." He argues that children generated through Easy PGD should not be called "designer babies," for they are "selected" from a wide range of embryos rather than "designed" by means of geneediting (Greely 2016).

Second argument for genetic enhancement: the myth of giftedness

Children who are above the average, as far as cognitive performance is concerned, are sometimes called "gifted," as though nature itself had given them a sort of gift. Gifted children are usually encouraged to cultivate their intelligence to the utmost degree. This can be achieved by means of special classes or supplementary education. Many countries have their own GATE (Gifted and Talented Education) programs. Decisionmaking in GATE programs usually occurs at the state or municipal level, rather than federal level.⁶But governments, at a federal level, have the moral duty to enforce legislation that provides every gifted child with equal access to GATE programs, without bias to gender, religion, or ethnicity (Grissom et al. 2016). The academic performance of children who go through GATE programs is likely to be superior to that of "normal" children. But this kind of inequality is not usually perceived as a form of injustice. The very existence of GATE programs relies upon the assumption that gifted children should be encouraged to cultivate their cognitive capacities to their full extent. No one would reasonably propose an education policy that promotes equality in public schools by making sure that gifted children will not fare better than other children.

Yet, the use of the word "gift" is misleading. There is no such a thing as a "gift," bestowed on us by nature. For this reason one might prefer to speak here of a "talent" instead of a "gift." But the word "talent," too, has a metaphysical connotation. It originally evoked the idea of a monetary gift, as the word occurs, for instance, in the Bible, in "The parable of the talents" (Matthew 25:14-30) (Lühe 1998). The document issued by the UNESCO, quoted above, deploys a similar vocabulary: it speaks of an "endowment," which human beings have received in different measures. The idea here is that people cannot tamper with "the measure of their endowment" without violating a sort of natural law - without impinging "upon the principle of respect for human dignity." But an "endowment" or a "gift" implies the existence of an entity that gives us these things. This entity, however, does not exist, or if it exists it is hard to make sense of it in a debate in which theological or metaphysical assumptions should not be mandatory for people who do not share these ideas.Still, many people, in the public sphere, speak of "talents," "gifts," or "endowments" while implicitly assuming that there is an entity that we ought to respect, an entity toward whom we should have a sense of gratefulness.

Sandel, for instance, argues that we should "acknowledge the giftedness of life" (Sandel 2007, 27). This means that prospective parents should refrain from the temptation to design their babies by means of genetic engineering and remain open to "the unbidden" (Sandel 2007, 45–46). Sandel is willing to recognize that his argument resonates with "religious sensibility," but he actually does not present a better argument, devoid of disguised theological assumptions (Sandel 2007, 27). The current reaction against the prospect of editing the human genome for the purpose of human enhancement, when it is not motivated by safety reasons, seems to be a remnant of the same kind of "religious sensibility" that pervades Sandel's argument and also lurks behind the use of words such as natural "gifts,""endowments," and "talents."

Why, after all, should we have a positive attitude toward people's talents, and urge gifted children to cultivate their cognitive capacities, but have a negative attitude when a superior level of intelligence does not emerge at random, but arises as the product of our deliberate attempt to change our natural genetic makeup? Criticism of genetic human enhancement involves the assumption that the "normal" or average level of human intelligence should be preferred simply by virtue of its being the current state of the human condition (Bostrom and Ord 2006). But this assumption is mistaken on both normative and descriptive grounds. It is mistaken on normative grounds because, as we have just seen, unless one embraces a teleological conception of nature, or a religious worldview, there is really no reason to assume that we ought not to depart from the

status quo line. And it is mistaken on descriptive grounds too, for the average level of human cognitive capacities is not stationary. The IQ of the world population has steadily increased over the twentieth century, though not at the same pace in every part of the world. This phenomenon has been known as the "Flynn effect."

The explanation for the Flynn effect has been the object of much debate, but the phenomenon itself is well-documented (Flynn 2007, 2012, 2013; Steen 2009; Feyrer et al. 2013;Clark et al. 2016). It is believed that massive gains in IQ throughout the twentieth century are attributable to the interplay of different factors such as better nutrition, compulsory education for all children in most countries, and the emergence of more cognitively demanding jobs. Other factors are less apparent but equally important for the IQ increase. It is well-known, for instance, that iodine deficiency is associated with mental retardation. Iodine deficiency during pregnancy can also lead to irreversible brain damage. Some studies suggest that the average IQs of iodine-deficient populations are 10 to 15 points lower than the average IQ in iodine-sufficient populations (Steen 2009, 83–84; Feyrer et al. 2013, 8). A document issued by the UNICEF in 2007 warns that iodine deficiency is still a "major public health problem in Europe" (UNICEF/World Health Orgization 2007, vii). This problem is associated with "subtle degrees of mental impairment" that account for lower academic performance in school children (UNICEF/World Health Organization 2007, vii. See also Aburto et al. 2014, 10). The fight against iodinedeficiency in large populations is usually pursued through salt-iodization, which is a quite inexpensive procedure (Steen 2009, 83).

Policy makers seem to agreethat preventable low IQ levels are a matter of public health concern. Policy makers, then, have the moral duty to ensure that school children will not suffer from lower IQ levels as a result of iodine deficiency. But once this problem has been addressed, why should policy makers stop at salt-iodization? What ifsome new gene-editing tool could enable us to increase safely the IQ levels of children even further, and at the same cost as salt-iodization?

One might argue here that the implementation of public policies that involve the use gene-editing tools for the purpose of enhancing the IQ levels of children would not be acceptable, for this would conflict with parents' procreative rights. Public policies for the purpose of geneticcognitive enhancement, it might be argued, seem to depart from the less controversial form of "liberal eugenics" that I have defended in the previous section of this paper. However, there is some evidence now suggesting that the number of years that children spend in education is correlated with several genetic markers that have been recently discovered (Hayden 2016. See also Sniekers et al. 2017; Nature (Editorial) 2017b).For sure, there are many other markers that are also relevant for cognitive performance, but that have not been discoveredas yet. And it is also far from clear whether gene-editing technologies might be deployed one day to change these markers without the risk of off-target mutations or unintended impairmentof other human capacities. Yet asour knowledge in this area increases, we will have to face the question whether we do not have a duty to improve the academic performance of children who lag behind through no fault of their own, or because the educational systems of their communities are defective, but simply because the natural lottery did not favor them.

Oxford philosopher Anthony Kenny has summarized the moral problem posed by new technologies aptly: "As technology increases our knowledge of evils and our power to

remove them, it increases our responsibility for not removing them" (Kenny 2006, 124). This means that policy makers are morally responsible for inappropriate use of new technologies as much as for failing to deploy new technologies altogether. If geneediting tools are used forthe treatment of children with poor academic performance in the future, then the status quo line for cognitive performance will move upwards in the same way that the use of salt-iodization has contributed to an increase of IQ levels in our recent past.

The assumption that the average level of human intelligence should work as a normative threshold for the improvement of human cognitive performance is misleading. Several longitudinal studies show that there is not a stable, permanent status quo line for human cognitive performance. Now, whether or not massive IQ gains throughout the twentiethcentury really amount to "cognitive enhancement" is an interesting question. Cameron Clark and colleagues, for instance, argue that the Flynn effect should not be interpreted as a sort of "*real* cognitive enhancement of our species":

The central thesis of this paper is that although it would be convenient to conclude that the rises in measured IQ scores throughout the 20th century signify a sort of straightforward or *real* cognitive enhancement of our species, these rises are more appropriately viewed as real increases in test performance due to enhanced cognitive environments conferred upon our species by the social and cultural environments of the 20th century and likely before; that is, the Flynn effect does not represent genuine increases in general intelligence but rather increasing test performance due to an increasing aptitude for the types of modern thinking that modern life requires and that IQ tests measure. (Clark et al. 2016, 41)

What Clark and colleagues have in mind here is that modern life presents us with an array of cognitively demanding tasks. An increasing number of people have to process a flood of information, and deal with a variety of symbols, tables, graphs, and statistics in their everyday lives. We have also grown accustomed to expressing our own ideas by means of abstractions and hypothetical reasoning. The language of science pervades the public sphere in a way that would have been comprehensible to only a limited number of educated people before the twentieth century (Flynn 2007, 146). Clark and colleagues, therefore, are right in suggesting that our great-grandparents were not generally less "intelligent" than we are now, although our great-grandparents would have shown signs of mental retardation if, in the past, they had been submitted to the standard IQ tests that are applied today(Clark et al. 2016, 40-41. See also Flynn 2007, 9-10). Our great-grandparents simply did not have to face the same kinds, and a similar amount, of cognitive tasks and intellectual puzzles that we do. IQ tests are supposed to assess our ability to deal with the typical conundrums of modern life, not our capacity to deal with the pre-industrial tasks that most people had to face on a daily basis in the past.

However, what is at stake in the current debate on "cognitive enhancement" is not so much whether or not we can obtain "genuine increases in general intelligence," even though genuine increases, too, would count as cognitive enhancement. Cognitive enhancement concerns, rather, the use ofdrugs or techniques that have the potential to help us in dealing with the challenges, and explore the possibilities, of modern life.⁷If CRISPR-Cas9–or some other gene-editing technique–ever becomes reliable and safe for

therapeutic purpose, there are no good reasonsto assume that CRISPR-Cas9 should not ever be used to help us live in cognitive environments that, in the future, are likely to be even more demanding than the cognitive environments in which we live today.

Conclusion

Genetic cognitive enhancement may turn out to become necessary in the future in the same way that antibiotics and mass vaccination have become indispensable in the attempt to make us fit to meet pathogens that we had not encountered before, or were only poorly equipped to fight with our natural, unenhanced immune system. In the future, policy makers may even come to consider genetic cognitive enhancement as a matter of public policy for the same sort of reasons that measures such as salt-iodization, mass immunization, and GATE programshave been implemented in our recent past.

The final report of the National Academy of Sciences on the ethics of human genome editing concludes its chapter on genetic human enhancement with the following recommendation: "Government bodies should encourage public discussion and policy debate regarding governance of somatic human genome editing for purposes other than treatment or prevention of disease or disability" (National Academies of Sciences 2017, 123). The present paper is, indeed, an attempt to contribute to this debate.

Acknowledgments

This research benefited from financial support granted by CNPq (The National Council for Scientific and Technological Development, Brazil) and the bilateral cooperation agreement between FAPERJ (Rio de Janeiro State Funding Agency) and the University of Birmingham (2014–2016).

Notes

1. For an account of the emergence of CRISPR technology, see Ledford 2016; Lander 2016; Specter 2016; Doudna and Sternberg 2017.

2. See for instance the website of the company eGenesis (eGenesis 2017).

3. See NIH, Notice Number: NOT-OD-16-128, entitled "Request for Public Comment on the Proposed Changes to the NIH Guidelines for Human Stem Cell Research and the Proposed Scope of an NIH Steering Committee's Consideration of Certain Human-Animal Chimera Research" (National Institutes of Health 2016).

4. A summary of the four meetings is available at National Academies 2017.See also National Academy of Sciences 2015 and Reardon 2015c, 2015d.

5. A new technique called CRISPR-Cpf1 has recently been reported to be even more effective and precise than CRISPR-Cas9. See Zetsche 2015; *The Economist* 2015b.

6. See for instance the websites of the National Association for Gifted Children (n.d.) in the USA; the Australian Association for the Education of the Education of the Gifted and Talented (n.d.); and Potential Plus UK (2017).

7. For the current debate on the ethics of cognitive enhancement, see Jotterand and Dubljevic 2016.

References

Aburto, Nancy, Minawaer Abudou, Vanessa Candeias, and Tiaxiang Wu. 2014. *Effect* and safety of salt iodization to prevent iodine deficiency disorders: A systematic review with meta-analyses. Geneva: World Health Organization.

Agar, Nicholas. 2004. Liberal eugenics: In defence of human enhancement. Oxford: Blackwell.

Ainsworth, Claire. 2015. Genome editing allows much smaller changes to be made to DNA compared with conventional genetic engineering. *Nature* 528 (December 3): S15–S16.

Australian Association for the Gifted and Talented. n.d. Website. <u>http://www.aaegt.net.au/</u> (accessed June 26, 2017).

Baltimore, David, Paul Berg, Michael Botchan, Dana Carroll, R. Alta Charo, George Church, Jacob E. Corn, George Q. Daley, Jennifer A. Doudna, Marsha Fenner, Henry T. Greely, Martin Jinek, G. Steven Martin, Edward Penhoet, Jennifer Puck, Samuel H. Sternberg, Jonathan S. Weissman, and Keith R. Yamamoto. 2015. A prudent path forward for genomic engineering and germline gene modification. *Science*, April 3. DOI: 10.1126/science.aab1028.

Blackford, Russell. 2007. Review of *The case against perfection: Ethics in the age of genetic engineering* by Michael J. Sandel. *Monash Bioethics Review* 26(3): 60–64.

Blackford, Russell. 2014. *Humanity enhanced: Genetic choice and the challenge for liberal democracies*. Cambridge, MA: MIT Press.

Blendon, Robert J., Mary T. Gorski, and John M. Benson. 2016. The public and the gene-editing revolution. *New England Journal of Medicine* 374: 1406–1411.

Bosley, Katrine S., Michael Botchan, Annelien L. Bredenoord, Dana Carroll, R. Alta Charo, Emmanuelle Charpentier, Ron Cohen, Jacob Corn, Jennifer Doudna, Guoping Feng, Henry T. Greely, Rosario Isasi, Weihzi Ji, Jin-Soo Kim, Bartha Knoppers, Edward Lanphier, Jinsong Li, Robin Lovell-Badge, G. Steven Martin, Jonathan Moreno, Luigi Naldini, Martin Pera, Anthony C.F. Perry, J. Craig Venter, Feng Zhang, and Qi Zhou. 2015. CRISPR germline engineering – the community speaks. *Nature Biotechnology* 33: 478–86.

Bostrom, Nick, and Toby Ord. 2006. The reversal test: Eliminating status quo bias in applied ethics. *Ethics* 116: 656–79.

Buchanan, Allen, Dan W. Brock, Norman Daniels, and Daniel Wikler. 2000. From chance to choice: Genetics and justice. Cambridge: Cambridge University Press.

Callaway, Ewen. 2016a. Second Chinese team reports gene editing in human embryos. Study used CRISPR technology to introduce HIV-resistance mutation into embryos.*Nature*, April 8.DOI:10.1038/nature.2016.19718.

Callaway, Ewen. 2016b. Embryo-editing research gathers momentum. *Nature* 532 (April 21): 289–90.

Charo, R. Alta, and Henry Greely. 2015. CRISPR critters and CRISPR cracks. *American Journal of Bioethics* 15(12): 11–17.

Clark, Cameron M., Linette Lawlor-Savage, and Vina M. Goghari. 2016. The Flynn effect: A quantitative commentary on modernity and human intelligence. *Measurement: Interdisciplinary Research And Perspectives* 14(2): 39–53.

Cyranoski, David. 2015a. Scientists sound alarm over DNA editing of human embryos. *Nature* (March 12).DOI:10.1038/nature.2015.17110.

Cyranoski, David. 2015b. Gene-edited pigs to be sold as pets. *Nature* 526 (October 1):18.

Cyranoski, David, andSara Reardon. 2015. Embryo editing sparks epic debate. *Nature* 520 (April 29): 593–94.

Cyranoski, David. 2016. CRISPR gene editing tested in a person. Trial could spark biomedical duel between China and US. *Nature* 539 (November 24): 479.

Daily Mail Online. 2014. Australia facing "serious shortage in donor sperm" as demand from single women and same-sex couples triples in just four years. November 11. <u>http://www.dailymail.co.uk/news/article-2829418/Australia-facing-shortage-donor-sperm-supply-not-meeting-single-women-sex-couples-rise-demand.html</u> (accessed June 25, 2017).

Dando, Malcolm. 2016. Find the time to discuss new bioweapons. *Nature* 535 (July 7): 9.

Darnovsky, Marcy. 2015. Public interest group calls for strengthening global policies against human germline modification. Center for Genetics and Society press statement. 22 April.

https://www.geneticsandsociety.org/press-statement/public-interest-group-callsstrengthening-global-policies-against-human-germline (accessed June 25, 2017).

Doudna, Jennifer, and SamuelSternberg. 2017. A crack in creation: Gene editing and the unthinkable power to control evolution. Boston: Houghton Mifflin Harcourt.

Doudna, Jennifer. 2015. Embryo editing needs scrutiny. Nature 528 (December 3): S6.

The Economist. 2015a. Editing humanity. A new technique for manipulating genes holds great promise – but rules are needed to govern its use. August 22. <u>https://www.economist.com/news/leaders/21661651-new-technique-manipulating-genes-holds-great-promisebut-rules-are-needed-govern-its</u>(accessed June 25, 2017). *The Economist.* 2015b. Even CRISPR. A new way to edit DNA may speed the advance of genetic engineering. October 3.

http://www.economist.com/news/science-and-technology/21668031-scientists-havefound-yet-another-way-edit-genomes-suggesting-such-technology-will (accessed June 25, 2017).

eGenesis. 2017. Website. egenesisbio.com (accessed June 26, 2017).

Elgot, Jessica. 2015. UK sperm bank has just nine registered donors, boss reveals. *The Guardian*. August 31.

https://www.theguardian.com/science/2015/aug/31/britains-national-sperm-bank-wantsmen-to-prove-their-manhood(accessed June 25, 2017).

Flynn, James R. 2007. *What is intelligence? Beyond the Flynn effect*. Cambridge: Cambridge University Press.

Flynn, James R. 2012. Are we getting smarter? Rising IQ in the twenty-first century. Cambridge: Cambridge University Press.

Flynn, James R. 2013. *Intelligence and human progress. The story of what was hidden in our genes.* Amsterdam: Elsevier.

Feyrer, James, Dimitra Politi, and David N. Weil. 2013. The cognitive effects of micronutrient deficiency: Evidence from salt iodization in the United States. National Bureau of Economic Research Working Paper No. 19233. http://www.nber.org/papers/w19233 (accessed June 25, 2017).

Francis Crick Institute. 2016. HFEA approval for new "gene editing" techniques. *Francis Crick Institute News*. February 1. <u>https://www.crick.ac.uk/news/science-news/2016/02/01/hfea-decision/</u> (accessed June 25, 2017).

Fukuyama, Francis. 2002. *Our posthuman future: Consequences of the biotechnology revolution.* New York: Farrar, Straus and Giroux.

Funk, Cary, Brian Kennedy, and Elizabeth Sciupac. 2016. U.S. public wary of biomedical technologies to "enhance" human abilities. Pew Research Center. July 26. http://www.pewinternet.org/2016/07/26/u-s-public-wary-of-biomedical-technologies-to-enhance-human-abilities/ (accessed June 25, 2017).

Global Times. 2016. China's sperm banks facing dire shortage of quality donations. May 10.

http://www.globaltimes.cn/content/982324.shtml (accessed June 25, 2017).

Glover, Jonathan. 2006. Choosing children: Genes, disability, and design. Oxford: Clarendon.

Greely, Henry. 2016. *The end of sex and the future of human reproduction*. Cambridge, MA: Harvard University Press.

Grissom, Jason, and Christopher Redding. 2016. Discretion and disproportionality: Explaining the underrepresentation of high-achieving students of color in gifted programs. *AERA Open* 2(1): 1–25.

Habermas, Jürgen. 2002. DieZukunft der menschlichen Natur: Auf dem Weg zu einer liberalen Eugenik? Frankfurt: Suhrkamp.

Harris, John. 2007. *Enhancing evolution: The ethical case for making better people*. Princeton: Princeton University Press.

Harris, John. 2015. Germline manipulation and our future worlds. *American Journal of Bioethics* 15(12): 30–34.

Hayden, Erika Check. 2016. Gene variants linked to education prove divisive. Study uncovers 74 genetic markers that influence the number of years spent in education. *Nature* 533 (May 12):154–55.

Jotterand, Fabrice, and Veljko Dubljevic (ed.). 2016. *Cognitive enhancement: Ethical and policy implications in international perspectives*. Oxford: Oxford University Press.

Kaiser, Jocelyn. 2016. First proposed human test of CRISPR passes initial safety review. *Science* June 21. DOI: 10.1126/science.aaf5796.

Kang, Xiangjin, Wenyin He, Yuling Huang, Qian Yu, Yaoyong Chen, Xingcheng Gao, Xiaofang Sun, and Yong Fan. 2016. Introducing precise genetic modifications into human 3PN embryos by CRISPR/Cas-mediated genome editing. *Journal of Assisted Reproduction and Genetics* 33(5): 581–88.

Kass, Leon R. Ageless bodies, happy souls: Biotechnology and the pursuit of perfection. *The New Atlantis* 2003 (Spring): 9–28.

Kenny, Anthony. 2006. What I Believe. London: A&C Black.

Lander, Eric S. 2016. The heroes of CRISPR. Cell 164: 18-28.

Lanphier, Edward, Fyodor Urnov, Sarah Ehlen Haecker, Michael Werner, and Joanna Smolenski. 2015. Don't edit the human germ line. *Nature* 519 (March 26): 410–411.

Ledford, Heidi. 2015a. CRISPR, the disruptor. *Nature* 522 (June 1): 20–24.

Ledford, Heidi. 2015b. Caution urged over DNA editing in wild. *Nature* 524(August 6): 16.

Ledford, Heidi, and Ewen Callaway. 2015. "Gene drive" mosquitoes engineered to fight malaria. *Nature* (November 23). DOI: 10.1038/nature.2015.18858.

Ledford, Heidi. 2016. The unsung heroes of CRISPR. Nature 535 (July 21): 342-44.

Le Page, Michael. 2017. Boom in human gene editing as 20 CRISPR trials gear up. A pioneering CRISPR trial in China will be the first to try editing the genomes of cells inside the body, in an effort to eliminate cancer-causing HPV virus. *New Scientist*. May 30.

https://www.newscientist.com/article/2133095-boom-in-human-gene-editing-as-20crispr-trials-gear-up/ (accessed June 25, 2017).

Liang, Puping, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv, Xiaowei Xie, Yuxi Chen, Yujing Li, Ying Sun, Yaofu Bai, Zhou Songyang, Wenbin Ma, Canquan Zhou, and Junjiu Huang. 2015. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. *Protein &Cell* (6): 363–72.

Lühe, A. 1998. Talent. In *Historisches Wörterbuch der Philosophie* Vol. 10, ed. Joachim Ritter and Karlfried Gründer, 886–890. Basel: Schwabe.

Mcknight, Matthew. 2014. The Ohio sperm-bank controversy. *New Yorker*. October 14. <u>http://www.newyorker.com/news/news-desk/ohio-sperm-bank-controversy-new-case-reparations</u> (accessed June 25, 2017).

Miller, Henry. 2015. Germline gene therapy: We're ready. Science 348(June 19): 1325.

National Academy of Sciences. 2015. *International Summit on Human Gene Editing: A global discussion*. Washington: National Academies Press.

National Academies. 2017. Human gene-editing initative. National Academies of Sciences, Engineering, and Medicine.

http://nationalacademies.org/gene-editing/consensus-study/meetings/index.htm (accessed June 26, 2017).

National Academy of Sciences. 2017. *Human genome editing. Science, ethics, and governance.* Washington: National Academies Press.

National Institutes of Health. 2016. NIH notice: Request for Public Comment on the Proposed Changes to the NIH Guidelines for Human Stem Cell Research and the Proposed Scope of an NIH Steering Committee's Consideration of Certain Human-Animal Chimera Research.

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-128.html (accessed June 26, 2017).

National Association of Gifted Children. n.d. Website. https://www.nagc.org (accessed June 26, 2017).

Nature (Editorial). 2017a. Legal limbo. Europe is dragging its feet on gene-editing rules and scientists should push the issue. *Nature* 542 (February 23): 392.

Nature (Editorial). 2017b. Intelligence test. Modern genetics can rescue the study of intelligence from a history marred by racism. *Nature* 545 (May 25): 385–86.

Pinker, Steven. 2015. The moral imperative for bioethics. *Boston Globe*. August 1. <u>https://www.bostonglobe.com/opinion/2015/07/31/the-moral-imperative-for-bioethics/JmEkoyzlTAu9oQV76JrK9N/story.html</u>(accessed June 25, 2017).

Pollack, Robert. 2015. Eugenics lurk in the shadow of CRISPR. *Science* 348(May 22): 871.

Potential Plus UK. 2017. Website. https://www.potentialplusuk.org/ (accessed June 26, 2017).

Reardon, Sara. 2015a. Ethics of embryo editing paper divides scientists. Research community also split over how close the method is to being an option for preventing disease. *Nature*, April 24. DOI:10.1038/nature.2015.17410.

Reardon, Sara. 2015b. New life for pig-to-human transplants. *Nature* 527 (November 12): 152–54.

Reardon, Sara. 2015c. Gene-editing summit supports some research in human embryos. *Nature*, December 3. DOI:10.1038/nature.2015.18947.

Reardon, Sara. 2015d. Global summit reveals divergent views on human gene editing. *Nature* 528 (December 10): 173.

Robertson, John. 1994. *Children of choice: Freedom and the new reproductive technologies*. Princeton: Princeton University Press.

Sandel, Michael J. 2007. *The case against perfection: Ethics in the age of genetic engineering*. Cambridge, MA: Harvard University Press.

Savulescu, Julian, Jonathan Pugh, Thomas Douglas, and Christopher Gyngell. 2015. The moral imperative to continue gene editing research on human embryos. *Protein* &*Cell* 6(7): 476–79.

Sklar, Julia. 2016. The U.K.'s largest sperm bank is now an app. *MIT Technology Review*. September 28. https://www.technologyreview.com/s/602505/the-uks-largest-sperm-bank-is-now-an-

<u>app/</u> (accessed June 25, 2017).

Sniekers Suzanne, Sven Stringer, Kyoko Watanabe, Philip R. Jansen, Jonathan R.I. Coleman, Eva Krapohl, Erdogan Taskesen, Anke R. Hammerschlag, Aysu Okbay, Delilah Zabaneh, Najaf Amin, Gerome Breen, David Cesarini, Christopher F. Chabris, William G. Iacono, M. Arfan Ikram, Magnus Johannesson, Philipp Koellinger, James J. Lee, Patrik K.E. Magnusson, Matt McGue, Mike B. Miller, William E.R. Ollier, Antony Payton, Neil Pendleton, Robert Plomin, Cornelius A. Rietveld, Henning Tiemeier, Cornelia M. van Duijn, and Danielle Posthuma. 2017. Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. *Nature Genetics*49: 1107–1112. DOI:10.1038/ng.3869.

Specter, Michael. 2015. The gene hackers: A powerful new technology enables us to manipulate our DNA more easily than ever before. *New Yorker*. November 16. <u>http://www.newyorker.com/magazine/2015/11/16/the-gene-hackers</u> (accessed June 26, 2017).

Standaert, Michael. 2017. China genomics giant drops plans for gene-edited pets. *MIT Technology Review*. July 3. https://www.technologyreview.com/s/608207/china-genomics-giant-drops-plans-for-

https://www.technologyreview.com/s/608207/china-genomics-giant-drops-plans-forgene-edited-pets/(accessed July 3, 2017).

Steen, R. Grant. 2009. *Human intelligence and medical illness: Assessing the Flynn effect.* New York: Springer.

UNESCO. 2015. Report of the IBC [International Bioethics Committee] on updating its reflection on the human genome and human rights. October 2. http://unesdoc.unesco.org/images/0023/002332/233258e.pdf (accessed June 25, 2017).

UNICEF/World Health Organization. 2007. *Iodine deficiency in Europe: A continuing public health problem.* New York: UNICEF.

UOL Notícias. 2015. Importação de sêmen estrangeiro aumenta 500% no Brasil em um ano. June 17. https://noticias.uol.com.br/saude/ultimas-noticias/redacao/2015/06/17/importacao-desemen-de-estrangeiros-aumenta-500-no-brasil-em-um-ano.htm (accessed June 25, 2017).

Waltz, Emily. 2016. Gene-edited CRISPR mushroom escapes US regulation. *Nature* 532 (April 21): 293.

Woudstra, Kristy. 2016. Sperm donor Canada: Banks are almost empty of homegrown supply. *Huffington Post Canada*. July 3. <u>http://www.huffingtonpost.ca/2016/03/07/sperm-donor-canada_n_8638488.html</u> (accessed June 25, 2017).

Wu, Jun, Aida Platero-Luengo, Masahiro Sakurai, Atsushi Sugawara, MariaAntonia Gil, Takayoshi Yamauchi, Keiichiro Suzuki, Yanina Soledad Bogliotti, Cristina Cuello, Mariana Morales Valencia, Daiji Okumura, Jingping Luo, Marcela Vilariño, InmaculadaParrilla, Delia Alba Soto, Cristina A. Martinez, Tomoaki Hishida, Sonia Sánchez-Bautista, M. Llanos Martinez-Martinez, Huili Wang, Alicia Nohalez, Emi Aizawa, Paloma Martinez-Redondo, Alejandro Ocampo, Pradeep Reddy, Jordi Roca, Elizabeth A. Maga, Concepcion Rodriguez Esteban, W. Travis Berggren, Estrella Nuñez Delicado, Jeronimo Lajara, Isabel Guillen, Pedro Guillen, Josep M. Campistol, Emilio A. Martinez, Pablo Juan Ross, and Juan Carlos Izpisua Belmonte. 2017. Interspecies chimerism with mammalian pluripotent stem cells. *Cell* 168: 473–86.

Zetsche, Bernd, Jonathan S. Gootenberg, Omar O. Abudayyeh, Ian M. Slaymaker, Kira S. Makarova, Patrick Essletzbichler, Sara E. Volz, Julia Joung, John van der Oost, Aviv Regev, Eugene V. Koonin, and Feng Zhang. 2015. Cpf1 is a single RNA-guided endonuclease of a class 2 CRISPR-Cas System. *Cell* 163: 759–71.