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Legal and Ethical Concerns Regarding Gene Editing

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ABSTRACT: The field of genetics has given rise to technology that will revolutionize the biological sciences: the powerful gene-editing tool known as CRISPR-Cas9. Between medical progress, ultimate new age cure for diseases and the risk of altering human DNA in an irreversible way, the legal challenges of applying CRISPR in the health context, along with the regulatory and ethical issues that might arise must be approached with increased responsibility. A main goal or a variety of purposes? Enhancement or gene editing to improve normal human traits, changes from edited genomes that might be inherited - repercussions of the new gene-editing technology could result in altering human DNA. Current international legislation and interpretation, global consensus worth pursuing on this subject and future regulations required.

KEYWORDS: CRISPR technology, designer babies, gene editing, moral vs. medical benefits, ethical vs. law

Introduction

The lack of public understanding of science, the different approaches of ethical and social matters, technical safety criteria make germline gene editing a topic on whom opinions remain divided and reaching a consensus on whether this technology should be used or prohibited highly difficult.

Deliberately making permanent, heritable changes to the genes of a human embryo and implanting it with the intent to establish a pregnancy has long represented a moral boundary. Techniques to alter the genetic material of living cells have been around since the 1970s, and scientists have long expected they could one day be used for this purpose - but human applications have remained limited due to concerns about safety and efficacy, even as modification of bacteria, plants and animals has become routine.

Independent experts of the UNESCO's International Bioethics Committee (IBC) published a report "*Updating its Reflection on the Human Genome and Human Rights,*" in which they argue that "gene therapy could be a watershed in the history of medicine and genome editing is unquestionably one of the most promising undertakings of science for the sake of all humankind (IBC 2015)"

Around 2012 a system known as CRISPR (which stands for Clustered Regularly Interspaced Short Palindromic Repeats) has been discovered. CRISPR utilizes a natural function of bacteria, which is faster, cheaper and easier to use than earlier techniques to target and change DNA.

In early 2013, Google searches for "CRISPR" began to skyrocket - a trend that has continued unabated. Within a year, investigators had reported the use of CRISPR-based genome editing in many organisms - including yeast, nematodes, fruit flies, zebrafish, mice, and monkeys. Scientific and commercial interest in potential applications in human therapeutics and commercial agriculture began to heat up - as did social concerns about the prospect that the technology could be used to produce designer babies. The early pioneers of CRISPR continued to push the frontiers, but they were no longer alone. Scientists around the world poured in a new cadre of heroes who further elucidated the biology of CRISPR, improved and extended the technology for genome editing, and applied it to a vast range of biological problems (Lander 2016, 26).

A new genome "editing" technique called CRISPR-Cas9 makes it possible for scientists to insert, remove and correct DNA simply and efficiently. It holds out the prospect of treating or even curing certain illnesses, such as cystic fibrosis and some cancers. But germline editing can also make changes to DNA, such as determining a baby's eye color, easier for scientists working with human embryos, eggs and sperm.

Scientists from the Oregon Health & Science University (OHSU) announced in August 2017 that they successfully programmed CRISPR to correct a genetic mutation linked to heart failure in human embryos. This news reignited fears of "designer babies" and "playing God" that opponents of stem cell research in the mid-1990s commonly cited. The news also brought the question of CRISPR regulation to the forefront of national debate, as questions surrounding use of human embryos in research are particularly controversial (Tomlinson 2018, 442).

Two of the scientists on the original CRISPR discovery team, Jennifer Doudna and Emmanuelle Charpentier, published a review paper in *Science,* in 2014*,* in which they concluded that the era of straightforward genome editing raises ethical questions that will need to be addressed by scientists and society at large. How can we use this powerful tool in such a way as to ensure maximum benefit while minimizing risks? It will be imperative that nonscientists understand the basics of this technology sufficiently well to facilitate rational public discourse. Regulatory agencies will also need to consider how best to foster responsible use of CRISPR-Cas9 technology without inhibiting appropriate research and development (Doudna and Charpentier 2014, 1258096-7)

The ethical issues and the rapidity with which the field is expanding requires particular precautions and raises serious concerns. A study examining global legislation and practices concerning genetic modification, published by Hokkaido University in Japan in 2014, showed that 29 of the 39 countries reviewed had a ban on editing the human germ line. In 25 countries, the ban was legally binding. The other four had guidelines, while rules in the remaining ten were described as ambiguous (Amelan, UNESCO).

A scientific breakthrough

CRISPR, an improved and relatively new gene editing tool, is one of the biggest science stories of the decade. It holds tremendous potential for biological and therapeutic applications. Being able to manipulate the human genome in unprecedented ways, with unprecedented precision, better than ever before, made this discovery a matter that could and should concern us all. A substantial debate has developed amongst scholars from a wide range of disciplines, national academies, ethics bodies, members of the public, learned societies and patients. This debate concerns the ethical acceptability of its human applications, among others, and the mechanisms of governance that would be needed to regulate these applications (Cavaliere 2019.)

In November 2018 it was reported that CRISPR was used to alter the DNA of embryos subsequently transferred to a woman, leading to a successful pregnancy and birth. Chinese scientist He Jiankui edited the genome of twin embryos, intending to make them resistant to human immunodeficiency virus (HIV) by disabling the gene CCR5. This experimental intervention has been widely condemned. Concerns have focused on the lack of safety assessments; the lack of a thorough ethical review process; the adequacy of the informed consent document signed by the prospective parents; and the exposure of the twins to the risk of genome editing without a proportionate harm/benefit ratio (Cavaliere 2019).

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This technology has the potential to permanently eliminate hereditary diseases from the human genome in its entirety. But, in the wrong hands, CRISPR could negatively impact the course of human evolution or be used to create biological weaponry.

There are several reasons in favor of conducting basic research with genome editing on human embryos, such as improving the efficacy and precision of genome editing technologies themselves, but also a better understanding of the differences between human and non-human animal developmental biology and improving the understanding of genetic diseases by creating models for in vitro drug testing. The hope is that this would have therapeutic implications such as addressing causes of early miscarriages and improving clinical uses of In Vitro Fertilization (IVF).

Lastly, genome editing's potential to reduce the occurrence of genetic diseases, thereby improving the health of many worldwide, is considered a compelling reason in favor of conducting basic research with this technology.

Therefore, within the debate many ethicists argue that continuing genome editing research in human embryos should be considered a 'moral imperative'.

Germline genome editing research with human embryos involves the destruction of the embryos employed in research. Often ethical distinctions are based on the source of the embryos. For instance, research with human supernumerary embryos (i.e. embryos created during IVF to establish a pregnancy that will no longer be used for this purpose) is often considered more ethically acceptable than research with human embryos created specifically for research purposes. This distinction is reflected in the various legislative approaches to governing embryo research. While some countries allow the creation of embryos for research purposes, others only allow research on supernumerary embryos.

Genome editing is likely to require embryos at the single-cell stage, which will present a governance dilemma for some legislators: the embryos will need to be created specifically for this purpose (i.e. they will not be supernumerary embryos originally created to establish a pregnancy), but many jurisdictions forbid this.

Legal concerns on a global scale

In addition to potentially challenging existing regulatory and ethical frameworks on how to obtain embryos for research purposes, the use of genome editing for basic research raises questions regarding existing limits to conduct research on human embryos.

Amongst the concerns are that, allowing basic research in human embryos with genome editing, may lead to future clinical research regarded as ethically troubling. Second, that allowing basic and clinical research with genome editing on human somatic cells may pave the way to eventually allowing basic and clinical research on the germline. Another set of concerns refers to the risk of moving from "therapeutic" to "enhancing" uses of genome editing.

Given the cross-border effects CRISPR research could have, it calls for an international regime to govern the use of CRISPR. Current and proposed international agreements are aimed at global cooperation. International ban on the matter would risk depriving us of valuable knowledge about human development, and may deprive future generations of novel disease treatments. In international law, the most widely accepted agreement is the United Nations Convention on Biological Diversity.

The European Union's position on human embryo research is set forth in the European Convention on Human Rights and Biomedicine, which bans the creation of human embryos for research purposes. Several countries within the European Union, notably Belgium and the United Kingdom, declined to sign the Convention because they found the terms too restrictive.

The researchers argue that a separate framework is necessary for CRISPR technologies, as opposed to other forms of biotechnology, because of its unprecedented promise and peril, divided

into 5 phases: before preclinical research, during preclinical research, prior to clinical development, during clinical development, and distribution.

It would be an unwise strategy to leave the gene-editing market to regulate itself. To date, the scientific community has done a laudable job of regulating the use of gene-editing technology despite the global absence of law mandating that they do so. For example, following the International Summit on Gene Editing in 2015, the organizing committee released a statement supporting a ban on any CRISPR research that would permanently alter the human germline until there has been further proof of the safety and efficacy of such procedures.

Although many countries or states have strict regulations regarding the creation of human embryos for research, there are still many countries which are ambiguous about the legal status of the modification.

In order to push the conversation forward, media coverage on the topic should be largely involved and the political climate should favor the creation of proper legislation for health purposes best use, so regulatory proposals will be critical for increasing efficiency and ensuring appropriate expertise worldwide.

Also, countries such as China, India, Ireland, and Japan forbid it based on guidelines that are less enforceable than laws, and are subject to amendment. The regulatory landscape suggests that human germline gene modification is not totally prohibited worldwide although there is room for further investigation regarding the "ambiguous" countries. USA currently does not ban, but has imposed a temporary moratorium on the germline gene modification under the Food and Drug Administration vigilance and the National Institutes of Health guidelines. When the safety of genome editing-mediated germline gene correction is enhanced, international community might permit it. In addition, Israel, which explicitly bans germlie gene modification, but has possible exemptions in the relevant law may permit it upon the recommendation of an advisory committee (Motoko and Tetsuya 2014).

Conclusions

In the pursuit to pushing moral boundaries in the quest for greater good, before CRISPR can be largely accepted and used, an increased level of safety that permits clinical applications in the immediate future is entirely required. There are several critical challenges and future prospects of CRISPR-based systems for human research but also the legislation worldwide must keep up with medical progress, regulate and protect all human rights. Each and every country must construct mechanisms of governance for overseeing research with genome editing in humans and will need to consider whether it should be permitted with respect to socioethical implications as well as safety and efficacy. Also, preventive measures against abuses must be taken into consideration, as well as a global cooperation and consensus, since the domino effect might involve the entire humankind.

Taking into consideration the significant potential promise, but also the theoretical potential for misuse, it is reasonable for the global community to take regulations, if not revising older agreements to reflect changes in genomic engineering technologies. Although it's unlikely to eliminate all risks, it is arguably one of the few options available to reasonably control and/or minimize them.

Undoubtedly, it is extremely important to deal with ethical issues raised by rapid changes in medicine, life sciences and technology. Human genome is part of the heritage of humanity. It therefore outlines rules that need to be observed to respect human dignity, human rights and fundamental freedoms.

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