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Emerging Biotechnology Case Study: Genome Editing & the Ethics of CRISPR-Cas9*

In April 2015, scientists in China published a paper in an online journal, *Proteins & Cells*, about experiments editing the genomes of non-viable human embryos (Liang et al. 2015). The research team, led by Junjiu Huang, used an engineered enzyme complex, called CRISPR-Cas9, to target and edit the HBB gene that codes for human β-globin protein. Defects in that gene can lead to β-thalassaemia, a heritable blood disorder that can be fatal.

In 2012, scientists Jennifer Doudna and Emmanelle Charpentier developed the CRISPR-Cas9 bioengineered complex that was used by the researchers in China. The technology has been used in previous research on animal and adult human cells. The technology allows researchers to target a specific gene by binding and splicing the DNA at specific locations, and replacing or repairing the segment by inserting other molecules (Cyranoski & Reardon 2015).

In their research, Huang and his team used non-viable, single-cell human embryos, which they obtained from a fertility clinic. The embryos possessed an extra set of chromosomes because they had been fertilized by two sperm and thus could not develop beyond the first stages of development. Huang and colleagues' aim was to test whether the technology could reliably target defective genes and replace these genes with repaired sequences. Their results showed that only a small fraction of the 86 embryos used in the study had the replaced genetic material at the targeted gene. The researchers also found that there were many "off-target" mutations that might have been introduced in the genome as a by-product of the technological intervention (Cyranoski & Reardon 2015). These results led the researchers to conclude that clinical applications of the technology to human embryos were still premature.

The authors of the paper also claimed that the prestigious journals, *Science* and *Nature*, rejected their paper because of ethical objections to their research on human embryos, and specifically, because of ethical objections to any kind of germ line genetic modification. The editors at the journal, *Proteins & Cells*, justified publishing the paper by claiming that they verified the researchers' institutional approval and the consent forms from the embryo donors, and confirmed that the study was compliant with Chinese laws and the Declaration of Helsinki's set of ethical principles on human experimentation (Cressey & Cyranoski 2015).

Were the editors at *Science* and *Nature* right to decline to publish the research paper? Should the editors at *Protein & Cells* have refrained from publishing the paper? Should the individual scientists have conducted and reported their research at all? Did they violate any moral duties or obligations? Given the paper is now published, what should members of the scientific community do?

Discussion Questions:

1. Leading scientists called for a moratorium on research on human embryos using genome-editing technologies, such as CRISPR. What sorts of ethical concerns does a moratorium address? What are some goals that could be achieved? What do you think are the likely outcomes or consequences of a moratorium and of the technology?
2. Why did the editors at *Science* and *Nature* decided not to publish the paper? Were the editors at *Protein & Cells* too hasty in publishing the research on embryos? How should academic journals deal with potentially controversial research? What are their moral and social responsibilities?

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3. Should non-scientist members of the public be included in the decision-making process about whether or not, and to what extent, research with genome-editing technologies should be restricted? What kinds of concerns might be overlooked if the decision-making process included only scientists? What sorts of insights may non-scientist members of the public bring to the discussion?
4. What should be the social and ethical responsibilities of the individual scientists involved in research with genome-editing technology? How can they best fulfill those responsibilities?

Content Commentary

The publication of Huang and colleagues' research caused a stir in the scientific community and generated many editorials and opinion pieces in scientific publications warning about the ethical issues that must be addressed before this research is pursued any further.

Scientists were quick to call for a moratorium on all genome editing of human embryos, and invoked similarities to the technological innovation that led to recombinant DNA in the 1970s and the meeting at Asilomar in 1975, where molecular biologists met to discuss and set guidelines to ensure that genetic research would develop in a safe and ethical manner (Vogel 2015).

However, many are critical of the comparisons with the Asilomar meeting and the attempt to use that conference as a model on which to build bioethical guidelines for future research with genome editing technologies (Jasanoff et al. 2015). Critics claim that the 1975 Asilomar conference was not an inclusive meeting because many of the stakeholders were not invited, such as ethicists, politicians, religious groups, and representatives of human-rights organizations or patient-interest groups (Reardon 2015b). Because of the lack of representation from non-scientists in the discussions, critics claim that Asilomar was merely an effort by scientists to resist government restrictions and promote public trust in the idea that scientists are able to regulate themselves (Reardon 2015b).

In response to calls for a moratorium, the US National Academy of Sciences (NAS) and the National Academy of Medicine (NAM) have launched an initiative to develop new guidelines to address the use of technology which makes germ line genetic modification possible, and called for members of the scientific community to attend an international summit on the topic set in December 2015 (Reardon 2015b).

The International Summit on Human Gene Editing held in Washington, D.C., in December 2015, was hosted by the National Academy of Sciences, the National Academy of Medicine, the Chinese Academy of Sciences, and the U.K.'s Royal Society. Members of the Summit's organizing committee submitted a public statement shortly after the meeting, outlining four recommendations. First, basic and preclinical research on gene-editing technologies is needed and should proceed. Second, clinical use of the technologies on somatic cells should be explored. Third, it is irresponsible to pursue clinical applications of gene-editing technologies on germline cells at this time. And, fourth, there is a need for ongoing discussions regarding the clinical use of germline gene editing, so the national academies should create a forum to allow for discussions which are inclusive and which engage with a variety of perspectives and expertise.

Some science policy experts have argued that the complexity of the issues surrounding germ line genetic modification cannot be adequately addressed from a scientific perspective. For example, Daniel Sarewitz, co-director of Arizona State University's Consortium for Science, Policy, and Outcomes, argues:

> The idea that the risks, benefits and ethical challenges of these emerging technologies are something to be decided by experts is wrong-headed, futile and self-defeating. It misunderstands the role of science in public discussions about technological risk. It seriously underestimates the democratic sources of science's vitality and the capacities of democratic deliberation. And it will further delegitimize and politicize science in modern societies (Sarewitz 2015).

Sarewitz's comment signifies the importance of a democratic deliberative process when identifying and addressing ethical issues about emerging technologies, as well as developing guidelines that will help to decide how these technologies will be further developed and used. In this particular case, there is worry

that germ line genetic modification on human embryos to replace defective genes may lead to a slippery slope to eugenics, or attempts to create perfect designer babies.

Lastly, the decision by *Science* and *Nature* to decline to publish the research paper because of undisclosed ethical objections raised further ethical issues about the dissemination of scientific research within a global context. The managing editor of *Protein & Cells*, Xiaoxue Zhang, has claimed that their editorial board was not blind to the potential ethical objections to the research, but decided to publish the article as a way to "sound an alarm" to begin discussions about the future direction of genome editing technologies (Cressey & Cyranoski 2015). Whether these discussions should come before or after the scientific research is conducted or published raises important questions about how best to regulate innovative scientific research with uncertain outcomes or potential dual-use applications.

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Links

Embryo-Editing: The Ethics of CRISPR on Flipboard: https://flipboard.com/@naturenewsteam/embryo-editing%3A-the-ethics-of-crispr-27j1164kz

The National Academies of Sciences, Engineering, and Medicine – *On Human Gene Editing: International Summit Statement*: http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a