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DIY Genetics

The Ethics of CRISPR

Written by Leah Treidler
Illustrated by Della Copes-Finke

In April 2015, Chinese scientists became the first to ever successfully alter the human embryo, marking the fast-approaching possibility of human modification. After the publication of their research, news outlets across the world latched onto the discovery, proclaiming the approach of the science-fiction-inspired “Designer Baby.” But does this new research mean an upcoming batch of genetically engineered children? The answer: No — at least, not for a while. First, the word “successful” is used lightly here. Though scientists were able to edit the human genome in human embryos, out of 54 embryos, they were only able to correctly modify the DNA of four, and of those four, all had vast, off-target mutations. Additionally, since all of these embryos were terminated within 14 days of inception, it remains unknown how a fetus with edited genes would continue to develop, much less a child. However, while this experiment exposed the danger of human genetic engineering, it is a clear marker of the acceleration towards genetic understanding catalyzed by the new genetic technology, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR).

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Though scientists have been editing DNA for decades now, CRISPR has rapidly advanced the field in a matter of years, making

genome editing easier, faster, and, perhaps most importantly, cheaper. CRISPR consists of two parts: an enzyme called Cas9 and a guide RNA (gRNA). The gRNA is designed to target a specific sequence of DNA. Once the target sequence is found, the gRNA signals the Cas9 to cut across the strand of DNA. This damage causes the cell to panic and call its repair processes. By disrupting these processes, scientists are able to introduce new genes into the DNA, essentially hijacking the natural processes of the cell. CRISPR was originally discovered by studying the immune system responses of bacteria, which work in a similar way to defend against viruses. Because the gRNA is so specific relative to previous techniques and because it requires scientists to edit only a few base pairs of the gRNA (around 20), CRISPR is far simpler and faster than any previous technology. For comparison, CRISPR brought the cost of this process from thousands of dollars to only a few hundred and compressed the timeline for gene editing from weeks to days. This new technique has enormous and wide-reaching consequences that are propelling the field of microbiology quickly into the future, opening up possibilities from curing diseases like HIV to engineering food to editing the human genome itself. However, CRISPR is far from perfect; the gRNA often binds at the wrong point on the DNA, mis-recognizing a sequence with up to five incorrect letters as its target, leading to vast and hard to pinpoint side effects. Nonetheless, its discovery signals a new age in microbiology and opens up a complicated ethical discussion of wide-reaching genetic modification that was once merely hypothetical.

CRISPR is already being used in labs around the world. In addition to editing human genomes in China, it's being used for research on topics concerning every facet of life. Scientists at the University of Pennsylvania have been approved for a clinical trial beginning this year

to take out the immune cells of 18 cancer patients, modify the cells to be more effective at destroying cancer cells, and place the edited cells back into the patients. Martin Kampmann, a cell biologist at the Institute for Neurodegenerative Diseases at the University of California, San Francisco, is spearheading research using CRISPR to identify genes that cause Alzheimer's and Parkinson's. These projects are just a few of the many CRISPR-based studies across the world which have the potential to destroy viruses such as HIV, herpes, hepatitis, and HPV; engineer food more effectively; and understand why some species are going extinct. Most exciting, however, may be the possibility of a better understanding of the human genome itself. "We are getting to a point where we can investigate different combinations of genes, controlling when, where, and how much they are expressed, and investigate the roles of individual bases of DNA," says Nicola Patron, a biologist at the Earlham Institute in the UK.

While CRISPR is an incredibly exciting scientific development that is already spreading across the globe, it puts a spotlight on countless new ethical issues. "For decades, we've been able to say it's not there yet, so we're not going to [edit human genes]. It was an easy way to stop the conversation," says Debra Mathews, a bioethicist at Johns Hopkins University. "We're now at a point where it is precise enough that we do actually just have to have the conversation."

Even the invention of CRISPR has been a heated topic, leading to a patent dispute between University of California, Berkeley and the Broad Institute of MIT and Harvard (which was ultimately decided in favor of the Broad Institute). The dispute brings up questions of ownership, commercialization, and legalization: Could CRISPR put too much power in the hands of biotechnology companies? How will it be regulated? How will the FDA deal with expanded use of genetic modification?

In addition to legal issues, many challenge the use of CRISPR from a religious-ethical standpoint, positing that CRISPR puts too much power in the hands of people, likening genetic modification to the work of god. Kevin Esvelt, an assistant professor of bioengineering at MIT, however, disagrees: "The idea that nature is the essence of goodness, is purity and truth, is so foreign to my perception of the world that I can't even conceive of how people can think that way," he said. "There is such a fantastic degree of suffering out there." However, where should the line be drawn? CRISPR opens up the possibility of fundamentally changing the genetics of an entire species, which could have vast positive effects or huge, unpredictable consequences. As Esvelt puts, "Just one engineered mosquito, or fly, or any other animal or seed, [could] eventually change the fundamental genetics of an entire species." Is it unethical to edit ticks so that they cannot carry Lyme disease, or mosquitoes so that they cannot carry malaria, or do the benefits for humans outweigh the risks for the insects and ecosystem? And, most controversially, is it morally wrong to edit the human genome?

Right now, CRISPR is far too unpredictable for testing in humans. However, it's possible that CRISPR's mutation rate will be equivalent to the random mutation rate in humans in the near future. At that point, will moral qualms be an excuse to avoid human genetic modification when the benefits could improve lives? And should scientists be allowed to modify inheritable genes thus spreading certain traits down the genetic line? In response to questions like these, in December 2015, scientists held the International Summit on Human Gene Editing, reaching a general consensus that scientists should proceed with basic and clinical research, but that any inheritable changes are irresponsible. While this response may hold for now, it might not be a defensible regulation in the future. Furthermore, there are no specific laws regarding human gene editing, only a general consensus throughout the scientific community. For the past few decades, since the first in-vitro fertilization in 1978,

scientists have deferred to the 14-day rule, a rule that any edited human genome must be terminated after 14 days.

Fourteen days was chosen because it is the number of days in which a band of cells forms an embryo and can no longer divide into twins. While it made sense in 1978, when scientists were unable to cultivate human cells for close to 14 days, this regulation seems outdated today. The rule assumes that development is linear, but scientists are now able to redirect cells' development to skip phases generally defined as human development, using strategies such as creating specific organoids (essentially, mini versions of human organs).

Assuming that some form of modification is okay and that it will not lead to a dystopian future, how do we decide when it's too much?

While scientists can legally bypass the 14-day rule, it is a prerequisite for publishing in any scientific journal and membership to the International Society for Stem Cell Research. Updating the 14-day rule, such as by increasing it to 28 days, however, begs the question: What separates human cells and humans? "Now we're getting into experiments that call into question some of our deepest beliefs philosophically about what it means to be human and what it means to deserve moral respect," says Insoo Hyun, a bioethicist at Case Western Reserve University. Is it morally justified to edit humans as fetuses so that they will not develop Alzheimer's or muscular dystrophy? What about diminishing the likelihood of addiction? What about learning disabilities? Or intelligence? Or athleticism? This discussion can easily fall into the trap of the slippery slope — that allowing for any genetic modification will ultimately lead us into a science fiction world where all people are edited for "perfect" intelligence, strength, and looks. Assuming that some form of modification is okay and that it will not lead to a dystopian future, how do we decide when it's too much?

We can no longer put this discussion off. Under-regulation could have huge consequences; consider, for example, thalidomide, a drug meant to prevent morning sickness that also led to debilitating birth defects. The answer will not be easy or permanent, but it must be clear, universally determined, and flexible. Regulations must not cave to the wishy-washy language of moral ambiguity, but create strict lines. The answer must take into account the individual as well as society and address questions of rights. For example, should parents be able to genetically modify their child when the child is under the legal age of consent? This question may never have a clear answer, but the scientific community has a responsibility to address it now so that we can reap the real, life-saving benefits of CRISPR. ●