‘Hacking the Code of Life’: How gene editing will lead to disease cures and nutritionally enhanced food

Across the US, more than 100,000 people are awaiting organ transplants. But there simply aren’t enough hearts, lungs, livers, and kidneys to meet demand, and 20 people die every day without the organs they need. For decades, scientists have dreamed of using animals to help fill the gap. They’ve been particularly interested in harvesting organs from pigs, whose physiology is similar to our own. Unfortunately, pigs also present some big biological challenges, including the fact that their genomes are chock full of genes that code for what are known as retroviruses, which could pose a serious threat to patients who receive porcine organs.

hack

BOOK REVIEW — “Hacking the Code of Life,” by Nessa Carey (Icon Books, 176 pages).

In 2015, George Church, a geneticist at Harvard University, announced a stunning breakthrough: Working with pig cells, he and his colleagues had managed to disable 62 copies of a retrovirus gene in one fell swoop. “This would have been virtually impossible and a logistical nightmare with older forms of genetic modification,” writes Nessa Carey in her new book, “Hacking the Code of Life: How Gene Editing Will Rewrite Our Futures.” But by using the new gene editing technology known as Crispr, the task was a relative cinch.

It’s just one example of how gene editing is giving us the power to alter the genome with unprecedented speed and precision. Carey, a biologist with a background in the biotech and pharmaceutical industry, offers a brisk, accessible primer on the fast-moving field, a clear-eyed look at a technology that is already driving major scientific advances — and raising complex ethical questions

“It’s giving every biologist in the world the tools to answer in a few months questions that some scientists have spent half their careers trying to address,” Carey writes. “It’s fueling new ways to tackle problems in fields as diverse as agriculture and cancer treatments. It’s a story that began with curiosity, accelerated with ambition, will make some individuals and institutions extraordinarily wealthy, and will touch all our lives.”

Though there are several different approaches to gene editing, the most prominent — and the one that really supercharged the field — is Crispr. The technique, based on an anti-viral defense system that’s naturally present in bacteria, requires two pieces of biological material: an enzyme that acts as a pair of minuscule scissors, slicing strands of DNA in two; and a guide molecule that tells the enzyme where to cut.

In bacteria, these guide molecules direct the enzyme to chop up the genomes of invading viruses, preventing them from replicating.

But in 2012 and 2013, two teams of scientists reported that it was possible to hack this system to slice into any strand of DNA, at any complementary location they chose. Researchers could, for instance, create a guide molecule that steered the enzyme to one specific gene in the mouse genome and insert the editing machinery into a mouse cell; the enzyme would then make its cut at that exact spot.

The cell would repair the severed DNA, but it would do so imperfectly, disabling the gene in question. In the years that followed, scientists refined the technique, learning to use it not only to inactivate genes but also to insert new genetic material at specific locations along the genome.

The approach is cheaper, easier, and faster than older methods of genetic engineering, which were first developed in the 1970s. In addition, as Carey explains, “it can be used to create smaller modifications to the genome, and leaves fewer extraneous genetic elements. In its most technically exquisite form, gene editing leaves no molecular trace at all. It may just change, in a precisely controlled manner, one letter of the genetic alphabet.”

The applications are almost endless. Gene editing has immense potential for basic research; scientists can learn a lot about what genes do by selectively disabling them. In addition, researchers have used the technology to create a wide variety of organisms that could become valuable agricultural commodities, including mushrooms that don’t brown; wheat that produces fewer gluten proteins; drought tolerant, high-yield rice and corn; disease-resistant pigs; and super muscular goats.

How these products will do on the market — if they ever reach it — remains uncertain. Globally, gene-edited organisms are regulated by a patchwork of conflicting rules. For instance, in 2018, the U.S. Department of Agriculture announced that it would not regulate gene-edited crops that “could otherwise have been developed through traditional breeding techniques.” A few months later, however, the European Union said that it would subject gene-edited plants to stringent restrictions.

genes

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Image: Chuck Nigash ,Stephen Sedam / Los Angeles Times

Beyond agriculture, gene editing has enormous potential for medicine. It might, for instance, become a much-needed treatment for sickle cell disease. That painful, debilitating disease results from a genetic mutation that causes patients to produce a deformed version of hemoglobin, a protein that helps red blood cells transport oxygen. In a clinical trial currently underway, scientists are removing stem cells from the bone marrow of sickle cell patients, using Crispr to edit them, and then infusing the edited cells back into patients.

Even if this trial succeeds, however, gene editing will not be a cure-all. It doesn't always work perfectly and can be challenging to administer directly to living humans (which is why some scientists are instead editing patients' cells outside the body). Moreover, many diseases are caused by complex interactions between multiple genes, or genes and the environment. "In fact, many of the most common and debilitating conditions aren't likely to be good candidates for gene editing any time soon," Carey writes.

And, of course, the ethics of human gene editing can be enormously fraught. That's especially true when scientists modify sperm cells, egg cells, or early embryos, making tweaks that could be passed down to subsequent generations. This kind of gene editing could theoretically cure some absolutely devastating genetic conditions, but we still have a lot to learn about its safety and effectiveness. It also raises a host of difficult questions about consent (an embryo obviously cannot give it), inequality (who will have access to the technology?), and discrimination (what will the ability to edit a gene related to deafness mean for deaf people, deaf culture, and the disability rights movement more broadly?).

Even in the face of these questions, at least one scientist has already forged ahead. In November 2018,

He Jiankui, a researcher then at the Southern University of Science and Technology in China, shocked the world by announcing that the world's first gene-edited babies — twin girls, who He called Nana and Lulu — had already been born. Months earlier, when Nana and Lulu were just embryos, He had edited their CCR5 genes, which code for a protein that allows HIV to infect human cells. By disabling the gene, He hoped to engineer humans who would be protected from HIV infection.

The outcry was swift and harsh. Scientists alleged that He's science was sloppy and unethical, putting two human beings at unnecessary risk. After all, there are already plenty of ways to prevent HIV transmission, and the CCR5 protein is known to have some benefits, including protecting against the flu. And He had raced ahead of the experts who were still trying to work out careful ethical guidelines for editing human embryos. "He Jiankui has shot this measured approach to pieces with his announcement, and now the rest of the scientific community is on the back foot, trying to reassure the public and to create consensus rapidly," Carey writes.

"Hacking the Code of Life" doesn't break much new ground, and for readers who have been paying attention to Crispr over the past few years, little in the book will come as a surprise. But it does provide a broad, even-handed overview of how much has already happened in a field that is less than 10 years old.

Carey swats down the most dystopian dreams about Crispr, like the prospect that criminals might edit their own DNA to evade justice. She's similarly skeptical that we'll end up using the technology to create "super-beings with enhanced genomes that will make them taller, faster, more attractive."

"We actually understand very little about the genetic basis of these traits and what we do know suggests that it will be very difficult to enhance humans in this way," she writes.

But she also acknowledges real risks, including the possibility that the technique could be used to create dangerous bioweapons, that gene-edited organisms could destabilize natural ecosystems, and that our new, hardy crops could prompt us to convert even more of the Earth's undeveloped places into farmland.

None of this means that the technology should be abandoned; it has immense potential to improve our lives, as the book makes clear. But it does mean we need to proceed with caution. As Carey writes, "Ideally, ethics should not be dragged along in the wake of scientific advances; the two should progress together, informing one another."

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