

## ***WHAT GENE EDITING CAN DO FOR HUMANKIND***

*By Walter Isaacson*

Wall Street Journal

Feb. 19, 2021 10:58 am ET

In the spring of 2014, Jennifer Doudna had a nightmare. The Berkeley biochemist had helped to invent a powerful new technology that made it possible to edit the human genome—an achievement that made her the recipient of a Nobel Prize in 2020. The innovation was based on a trick that bacteria have used for more than a billion years to fight off viruses, a talent very relevant to us humans these days. In their DNA, bacteria develop clustered, repeated sequences (what scientists call CRISPRs) that can recognize and then chop up viruses that attack them. Dr. Doudna and others adapted the system to create a tool that can edit DNA—opening up the potential for curing genetic diseases, creating healthier babies, inventing new vaccines, and helping humans to fight their own wars against viruses.

But Dr. Doudna’s nightmare didn’t concern these happy prospects. In it, she was asked to meet someone who wanted to learn about CRISPR. When she entered the room for the meeting, she recoiled: Sitting in front of her was Adolf Hitler with the face of a pig. “I want to understand the uses and implications of this amazing technology you’ve developed,” he said.



Chinese geneticist He Jiankui, seen speaking during a November 2018 conference on human genome editing at the University of Hong Kong, helped create the world's first gene-edited babies.

PHOTO: S.C. LEUNG/SOPA IMAGES/ZUMA PRESS

Four years later, He Jiankui, a young Chinese scientist who had attended some of Dr. Doudna’s conferences, used CRISPR to create the world’s first designer babies: twin

girls whose DNA had been edited when they were embryos to remove a gene that produces a receptor for the virus that causes AIDS. There was an immediate outburst of awe, and then shock. Arms flailed, committees convened. After more than three billion years of the evolution of life on this planet, one species (us) had developed the talent and the temerity to seize control of its own genetic future. We seemed to have crossed the threshold into a whole new age, perhaps a brave new world, summoning up images of Adam and Eve biting into the apple or Prometheus snatching fire from the gods.

Our newfound ability to edit our own genes raises fascinating—and troubling—questions. Should we alter our species to make humanity less susceptible to deadly viruses? That seems like a wonderful boon, especially amid the pandemic. And what about trying to get rid of deafness or blindness? Or being short? Or depressed? And if such remedies are possible and safe, why not go farther and allow parents to enhance their children, giving them higher IQs, stronger muscles, greater height, and a preferred hue of skin and hair?

That slippery slope should prompt us to consider both the wonderful benefits as well as the potential moral issues posed by the astonishing new technology. What might CRISPR do to the diversity of our species? If we are no longer subject to a natural lottery of endowments, will it weaken our feelings of empathy and acceptance? If the marvelous enhancements offered at the genetic supermarket aren't free (and they won't be), will that greatly increase inequality—and even encode it permanently in the human race?



Dr. Haydar Frangoul (left) of Sarah Cannon Research Institute has a follow-up visit with Victoria Gray, the first participant in a gene-editing sickle-cell disease clinical trial, Nashville, June 2020.

PHOTO: AMANDA STULTS, RN, SARAH CANNON RESEARCH INSTITUTE/THE CHILDREN'S HOSPITAL AT TRISTAR CENTENNIAL

Let's start by considering the least controversial cases: fixing dreadful maladies caused by simple mutations, such as sickle-cell disease. Victoria Gray, a Mississippi woman, was effectively cured last year by removing some of her stem cells and editing them with CRISPR. That spurred no controversy because the gene editing was done in an adult's cells and wouldn't be inherited. But such treatments cost more than \$1 million. A far more efficient approach would be to fix the mutation causing sickle-cell in early stage embryos, so that the resulting children and all their descendants would never have it. So why not make inheritable edits and eliminate the disease from our species?

One reason for caution is the risk of unintended consequences. For example, people who get a copy of the flawed sickle-cell gene from only one parent don't develop the disease, but they do develop immunity to most forms of malaria. But suppose researchers show that editing out the sickle-cell mutation can be done safely. Would there then be any reason to prohibit it?

Maybe. Consider a delightful young man named David Sanchez. He is a plucky, charming, reflective Black teenager in California who loves to play basketball—except when his sickle-cell disease makes him double over in pain. Mr. Sanchez is one of the stars of “Human Nature,” a powerful 2019 documentary about CRISPR (now on [Netflix](#)). “My blood just does not like me very much, I guess,” he says. Matthew Porteus, a pediatrician and gene-editing pioneer at Stanford University, has been helping to treat Mr. Sanchez. “Maybe one day with CRISPR,” Dr. Porteus told him, “they could go in and change the gene in the embryo so that the kid, when it's born, doesn't have sickle-cell.”

Mr. Sanchez's eyes lighted up. “I guess that's kind of cool,” he said. Then he paused. “But I think that should be up to the kid later.” Asked why, he reflected for a moment

and continued slowly. “There’s a lot of things that I learned having sickle-cell. I learned patience with everyone. I learned how just to be positive.” But would he like to have been born without sickle-cell disease? Again, he pauses. “No, I don’t wish that I’d never had it,” he says. “I don’t think that I would be me if I didn’t have sickle-cell.” Then he bursts into a large, lovely smile.



David Sanchez, 15, at home in Menlo Park, Calif., with his grandmother Delores Sanchez, October 2018. He was born with sickle-cell disease, an inherited disorder caused by a mutation in one gene among the roughly 20,000 in our DNA.

PHOTO: TIMOTHY ARCHIBALD

It is a brave and admirable view, but it is hard for me to imagine a young person being willing to endure sickle-cell disease when they could not have it. It is even more difficult to imagine parents, especially ones who have endured a life with sickle-cell disease, deciding that they want their children to have it. So I tracked down Mr. Sanchez last year to discuss these issues. His thinking is different now. Would you like to find a way, I ask, to make sure your children are born without sickle-cell disease? “Yes,” he replies. “If that’s an option, then of course.”

What about the empathy that he learned by having sickle-cell disease? “Empathy is something that’s really important,” he responds. “That is something I would really want to convey to my kids if they could be born without sickle-cell. But I wouldn’t want my kids or others to go through what I went through.”

**‘I wouldn’t want my kids or others to go through what I went through.’**

— David Sanchez

As Mr. Sanchez recognizes, so-called disabilities often build character, teach acceptance and instill resilience. They may even be correlated to creativity. Take Miles Davis, who was driven to drugs and drink by the pain of sickle-cell disease. It may have even led to his death. It also, however, may have driven him to be the pioneering musician who could produce “Kind of Blue” and “Bitches Brew,” among the greatest jazz albums ever made. Would Miles Davis have been Miles Davis without sickle-cell?

An even more challenging question will arise if, a few decades from now, we find safe ways to edit the genes that produce a disposition to schizophrenia, bipolar disorder and depression. Eliminating these psychological disorders would alleviate enormous suffering, but it might also lead to fewer geniuses such as Vincent Van Gogh and Ernest Hemingway, whose art was profoundly shaped by battling these conditions. Would you cure your own child of schizophrenia if you knew that it would help to make her a transformative artist? Should that decision be up to you or the government? Most of us, I think, wouldn’t want the government to forbid us from protecting our children from such diseases, even if it makes our culture less rich.

What about crossing the blurry line between treatments for diseases and enhancements designed to create traits that are better than average? Consider muscle mass. A gene curtails the growth of muscles when they reach a normal level, and suppressing that gene takes off the brakes. Researchers have already done this to produce “mighty mice” and cattle with “double muscling.” Athletic directors are going to be interested in these types of gene edits, and pushy parents who want champion children are sure to follow.

So what do we say to parents who want to use gene editing to produce bigger, stronger children? Ones who can run marathons, break tackles and bend steel with their bare hands? That would change our concept of athletics. Instead of admiring the diligence of athletes, we would admire the wizardry of their genetic engineers. It is easy to put an asterisk next to the home-run tallies of Jose Canseco or Mark McGwire when they admit that they were on steroids. But what do we do if athletes’

extra muscles come from genes they were born with? And why does it matter if those genes were paid for by their parents rather than bestowed by a natural lottery?

We will reach an even more controversial frontier if and when gene editing is able to improve cognitive skills such as memory, focus, information processing and perhaps even the vaguely defined concept of intelligence. Scientists have already improved memory in mice, including by enhancing the genes for receptors in nerve cells.

The consensus these days among bioethicists is that inheritable gene edits shouldn't be made unless they are medically necessary. But as genetic editing becomes safer, not everyone will agree that it is morally wrong to use it to make enhancements. In fact, some might view the creation of healthier babies as morally good, and perhaps even morally imperative.

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— George Church, Harvard geneticist

Why shouldn't we leave these decisions about gene editing to individuals and parents, just as we do with other reproductive choices? "I don't see why eliminating a disability or giving a kid blue eyes or adding 15 IQ points is truly a threat to public health or to morality," says the Harvard gene-editing pioneer George Church.

Imagine a world in which genetic engineering is determined mainly by individual free choice, with few government regulations and no pesky bioethics panels to set limits. You would go into a fertility clinic and be given, as if you were at a genetic supermarket, a list of traits that you can buy for your children. Would you eliminate serious genetic diseases? Of course. I personally would also ensure that my children wouldn't have genes leading to blindness or deafness. How about avoiding below-average height, above-average weight or low IQ? Many of us would probably select those options too. I might even pick a premium-priced option for extra height and

IQ. Some people might even rationalize choosing their child's sex and sexual orientation.

At that point, gene editing really does start to look more like a genuinely slippery slope. Without gates or flags, we might all go barreling down at uncontrollable speed, taking society's diversity with us. Permitting parents to buy the best genes for their children would also exacerbate inequality. The social bond that arises from the American creed that all people "are created equal" would be severed if we turn financial inequalities into genetic inequalities.



Jennifer Doudna photographed with a 3-D model of a CRISPR molecule at the University of California, Berkeley, February 2016.

PHOTO: DREW KELLY FOR THE WALL STREET JOURNAL

When it became clear that the CRISPR tool that she had co-invented could be used to edit human genes, Jennifer Doudna had a "visceral, knee-jerk reaction." The idea of changing a child's genes, she says, felt unnatural. "In the early days, I was instinctively against it."

But then she began to hear stories from people who had been affected by genetic diseases. "The ones about kids were especially touching to me as a mother," she says. We should be cautious, she came to feel, about imposing a moratorium or hard-and-fast restrictions. As one participant said at a conference that Dr. Doudna organized, "Someday we may consider it unethical not to use inheritable gene editing to alleviate human suffering."

My own opinions about gene editing have also evolved. When I first began reporting on the topic, I sat on the balcony of my home in the French Quarter of New Orleans and tried to process my thoughts.

The French Quarter was hopping that weekend. There was a naked bicycle race intended (oddly enough) to promote traffic safety. There were parades to celebrate the life of the Creole chef and civil rights pioneer Leah Chase. There was the annual Gay Pride Parade and related block parties. And coexisting quite happily with all this was the French Market Creole Tomato Festival, featuring truck farmers and cooks showing off the many varieties of succulent, non-genetically-modified local tomatoes.

From my balcony, I marveled at the human diversity passing below: short and tall, gay and straight and trans, fat and skinny, light and dark. A cluster of young people wandered by wearing Gallaudet University T-shirts and speaking in sign language.

The supposed promise of CRISPR is that we may someday pick which of these traits we want in our children and all our descendants. But the sight of the bustling French Quarter, with all of its exuberant variety, suggested to me that CRISPR's promise might also be its peril. It took nature millions of years to weave together three billion base pairs of DNA into a complex—and often imperfect—way to permit all the wondrous diversity within our species. Are we right to think that we should now edit that genome to eliminate what we see as imperfections? Will we lose our diversity? Our humility and empathy? Will we become less flavorful, like our tomatoes?

I still worry about that. But the advances in CRISPR technology, combined with the havoc wrought by the Covid-19 pandemic, have pushed me to be more open to gene editing. I now see the promise of CRISPR more clearly than the peril. If we are wise in how we use it, biotechnology can make us more able to fend off lethal viruses and overcome serious genetic defects.



After millions of centuries during which evolution happened “naturally,” humans now can hack the code of life and engineer our own genetic futures. Or, for those who decry gene editing as “playing God,” let’s put it this way: Nature and nature’s God, in their wisdom, have evolved a species that can modify its own genome.

Like any evolutionary trait, this new ability may help our species to thrive—and perhaps even produce successor species. Or it may not. It could be one of those evolutionary traits that leads a species down a path that endangers its survival. Evolution is fickle that way.

This is why it is useful for all of us to try to understand this new room that we are about to enter, one that seems mysterious but can also fill us with hope. Not everything needs to be decided right away. We can begin by asking what type of world we want to leave for our children. Then we can feel our way forward together, step by step, and preferably hand in hand.

*—Mr. Isaacson’s books include biographies of Albert Einstein, Leonardo da Vinci, Benjamin Franklin and Steve Jobs. This essay is adapted from his new book “The Code Breaker: Jennifer Doudna, Gene Editing and the Future of the Human Race,” which will be published by Simon & Schuster on March 9.*