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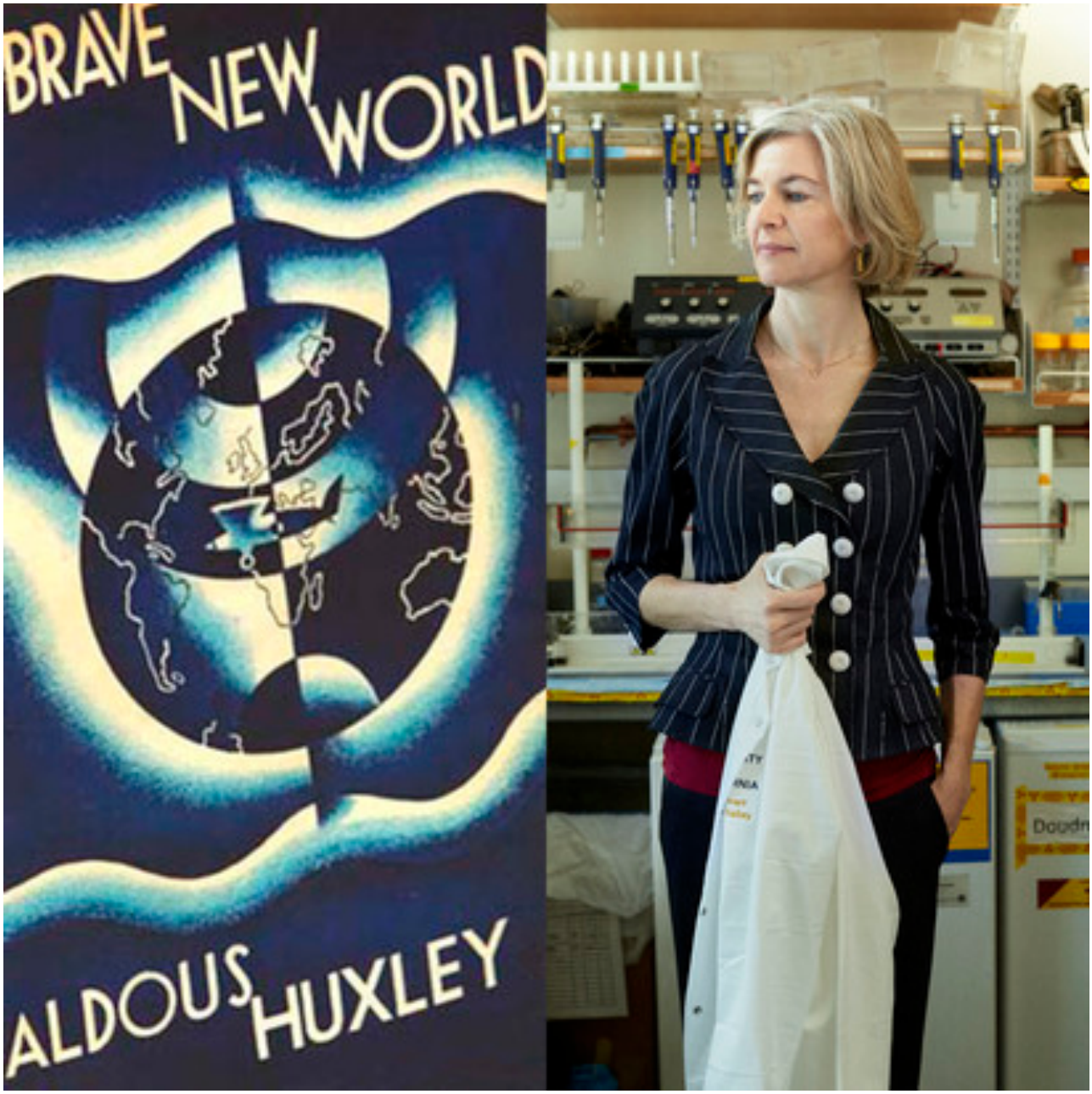

From left: the original edition of *Brave New World,* from Chatto & Windus, London, 1932; brave new Jennifer Doudna, pioneer in CRISPR technology, in her lab, in Berkeley, California.

SCIENCE

Should the Rich Be Allowed to Buy the Best Genes?

A letter from Quebec City and parts west ...

BY WALTER ISAACSON

QUEBEC CITY

Biology is the new tech. I'm at a conference in Quebec City on CRISPR, the molecular tool designed to edit genes, and it has the same vibe as the meetings of the Homebrew Computer Club and the West Coast Computer Faire did in the 1970s, except that the hip young innovators are programming with genetic code rather than computer code. Now that schools are finally realizing that every kid should learn how to code, they are going to have to switch from teaching 0101 to A.G.C.T., the four bases of our DNA.

Many of the star pioneers are here, including Berkeley's Jennifer Doudna, who in 2012 co-discovered how to combine two snippets of RNA with an enzyme to make a programmable scissors that could cut DNA at a precise location, and Feng Zhang of the Broad Institute, who raced her to show how the tool could edit genes in humans and is now in a battle with her for patents to the technology.

The atmosphere is charged with the catalytic combination of competition and cooperation reminiscent of when Bill Gates and Steve Jobs frequented the early personal-computer shows. The big news involves transposons, known as "jumping genes," which in nature can hop from one place to another on chromosomes. Sam Sternberg, a whip-smart young biochemist who studied under Doudna, has just published his first breakthrough paper, which describes how to create a CRISPR-like system that inserts a tailored jumping gene into a desired DNA location. But to Sternberg's surprise, Feng Zhang was able to get a similar paper of his own into a journal a few days earlier. "Is there any field that is more cutthroat and competitive than biological research?" Sternberg asks me.

The Jumping Gene

Well, yes, I think actually almost every field can be, from business to journalism to

Little League baseball. What actually distinguishes biological research is the collaboration that is woven in. The comradery of being rival warriors in a common quest suffuses the conference. The desire to win prizes and patents tends to create competition—which spurs the pace of discoveries—but equally motivating, I think, is the passion to uncover what Leonardo da Vinci called the "infinite works of nature," especially when it comes to something so breathtakingly beautiful as the inner workings of a living cell. "The jumping-gene discoveries show just how fun biology is," Doudna says.

"Is there any field that is more cutthroat and competitive than biological research?"

Some of us go to dinner at an inventive restaurant named Chez Boulay, which features crispy seal meatloaf, huge raw scallops, Arctic char, seared bison, and Quebec-made gin and wine. The talk turns from science to the ethical issues hovering over CRISPR. Feng Zhang and another of the early pioneers, Erik Sontheimer, talk about the need for a moratorium on making edits that can be inherited. But already the genes may be out of the bottle. In November, a Chinese doctor made the explosive announcement that he had edited two embryos to try to make them immune to H.I.V., and a Russian doctor is touting his own plans to edit embryos to try to fix congenital deafness.

There is general agreement among the scientists at dinner that, when it's safe and

practical, heritable edits ought to be used to fix bad single-gene mutations, such as Huntington's disease and sickle-cell anemia. But they recoil at the idea of using gene editing for human enhancements, such as trying to give our kids more muscle mass, or height, or perhaps someday higher I.Q.'s and cognitive skills. The problem is that the distinction is difficult to define—is preventing obesity a cure or enhancement?—and even more difficult to enforce. "Look at what parents are willing to do to get kids in college," Feng Zhang says. "Some people will surely pay for genetic enhancement."

Genetic Inequality

"A big problem with enhancement is equal access," Sontheimer adds. "Should rich people be allowed to buy the best genes they can afford?" That could lead to the dystopia described in Aldous Huxley's 1932 novel *Brave New World*, in which the modification of embryos produces a caste system ranging from intelligence-enhanced leaders to stunted menial laborers. Our world is already suffering from widening gaps in wealth and opportunity, and a free market for genetic enhancements could produce a quantum leap in these inequalities and also, literally, encode them permanently. "In a world in which there are people who don't get access to eyeglasses," Feng Zhang says, "it's hard to imagine how we will find a way to have equal access to gene enhancements. Think of what that will do to our species."

ASPEN

Speaking of wealth inequality, I travel from Quebec City to Aspen, Colorado, to interview some of the world's top policymakers who are wrestling with the challenge of regulating the use of CRISPR: Duanqing Pei, a charming and thoughtful Chinese cell biologist who runs the Guangzhou Institute of Biomedicine; Victor Dzau, a Chinese refugee who is president of the U.S. National Academy of Medicine; and my friend Peggy Hamburg, chair of the American Association for the Advancement of Science and former commissioner of the Food and Drug Administration, who has been named the co-chair of the World Health Organization's advisory committee on gene editing.

Pei and Dzau were in Hong Kong last November when the Chinese scientist Jiankui He made his shocking revelation that he had edited the DNA of two newborn twin

girls when they were early-stage embryos. Pei learned of the impending announcement from Jennifer Doudna when he arrived in the lobby of the Hong Kong hotel. "I had trouble believing it," he says. "We all stood there in the lobby and tried to figure out what it would mean." He was horrified, he said, because there was a restriction in China against such experiments, and he had assured global researchers it would not happen. So, like Hamburg and Dzau, he now realizes it will be almost impossible for the W.H.O., or anyone, to come up with a global policy that will be enforced everywhere.

"Should rich people be allowed to buy the best genes they can afford?"

"There is no one framework that will fit all countries," Hamburg says. "They have different attitudes and regulatory standards, like they do on genetically modified foods." The W.H.O. will therefore likely come up with a menu of options for countries to consider. That could, unfortunately, lead to genetic tourism. Privileged people who want enhancements will travel to the countries that offer them. "It's very hard to enforce practices and standards," Hamburg says. "This is not like nuclear weapons, where you can have guards and padlocks to enforce a security regimen."

COLD SPRING HARBOR

From Aspen I head to Cold Spring Harbor Laboratory, on the North Shore of Long Island, where Nobel laureate James Watson, aged 91, lives with his wife in splendid and tortured exile in a stately pale mansion overlooking Oyster Bay and the seminar buildings to which he is no longer invited. Watson helped launch the march of molecular biology toward gene editing when he and his colleague Francis Crick discovered in 1953, partly based on X-ray diffraction images produced by Rosalind Franklin and Maurice Wilkins, the double-helix structure and four-base coding scheme of DNA.

A decade ago, Watson spoke to a British newspaper reporter he knew, in his blunt and unfiltered manner, about his belief that there are differences in the average I.Q. of various ethnic groups, with that of Africans being lower, and that these differences are largely genetic. He soon apologized, saying, "There is no scientific basis for such a belief," and was forced to retire from being chancellor of Cold Spring Harbor Laboratory, which he had helped to lead for 40 years. But a year ago, when interviewed for an *American Masters* television documentary, he reconfirmed his opinions. The Cold Spring Harbor board issued a statement calling his views "unsubstantiated … reckless … reprehensible, unsupported by science," and it stripped him of his honorary titles.

The Jefferson Conundrum

Watson thus presents historians with what could be called the Jefferson Conundrum: to what extent can you respect a person for great achievements ("we hold these truths") when they are accompanied by reprehensible failings ("are created equal")? One question raised by the Jefferson Conundrum relates, at least metaphorically, to gene editing. Cutting out a gene for an unwanted trait (sickle-cell anemia or H.I.V. receptivity) might affect some existing desirable trait (resistance to malaria or the West Nile virus).

For what it's worth, I personally think it's both true and moral and useful to believe that people's flaws cannot be excused by saying they are interwoven with their greatness. But I nevertheless believe we can learn from people who have made great achievements even as we recoil from their flaws.

Feng Zhang, who wants a moratorium on pregnancies from edited embryos, in his Broad Institute lab, in Cambridge, Massachusetts.

So I ask Watson what he thinks about CRISPR. "What Jennifer did is the biggest advance in science since the discovery of the double helix," he says. "But it's important to use it so that it's equitable. If it's only used to solve the problems and desires of the top 10 percent, that will be horrible. We have evolved more and more in the past few decades into an inequitable society, and this would make it much worse."

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few decades into an inequitable society, and this would make it much worse."

One step that might help a little, he suggests, is to not allow or enforce patents for genetic-engineering techniques. There would still likely be a lot of funding for finding safe ways to fix maladies that are clearly devastating, such as Huntington's and sickle-cell anemia. But if there were no patents, there might be less payoff for racing to be the first to devise methods of enhancements, and the enhancements that did eventually get invented might be cheaper and more widely available if anyone could copy them. "I would accept some slowdown in the science in return for making it more equitable," he says. "Even if we didn't give patents for these products, some researchers would still be eager to pursue the science and make discoveries. That's what researchers are motivated to do in life."

NEW ORLEANS

Back home in New Orleans, I attend the funeral of the beloved grande dame of the city, Leah Chase, who died at 96 after almost seven decades of running a restaurant in the Tremé neighborhood. With her wooden spoon, she would stir the roux for her shrimp-and sausage gumbo (one cup of peanut oil and eight tablespoons of flour) until it was the color of café au lait and could bind together the many diverse ingredients. Chase was a Creole of color, and her restaurant and her life likewise bound together many flavors of New Orleans life, black and white and Creole. Uptown gentry met political leaders and civil-rights activists in her dining room in the late 1960s to try to keep the city together.

People like Leah Chase remind me of ligases, which are enzymes that can bind and stitch together strands of DNA. Today the cells of our society have too few ligases and far too many people who act as nucleases, the enzymes that cut and cleave and divide our DNA.

The French Quarter, where we live, is hopping that weekend. There is a naked bicycle race that is intended (oddly enough) to promote traffic safety. There is one of many parades and second lines to celebrate the life of Mac Rebennack Jr., the funk musician known as Dr. John. There is also the gay-pride parade and related block

parties. And coexisting quite happily is 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 marvel at the diversity of the passing humanity. There are people short and tall, gay and straight and trans, fat and skinny, light and dark, and even a few wearing Gallaudet University T-shirts excitedly using sign language. The supposed promise of CRISPR is that we may someday be able to pick which of these traits we want in our children and in all of our descendants. We could choose for them to be tall and muscular and blond and blue-eyed and not deaf and not … well, pick your preferences.

As I survey the delightful pageant with all of its natural variety, I ponder how this promise of CRISPR might also be its peril, up there with the encoding of unequal opportunities. It took the laws of nature and of nature's God more than 3.2 billion years to weave together three billion bases of DNA in a complex and occasionally imperfect way to permit all of the wondrous diversity within our species. Are we right to think we can now come along and, within a few decades, edit that genome to eliminate what we see as imperfections? Will we lose our diversity? Will we become less flavorful, like our tomatoes? Will that be good for our species?

Walter Isaacson is a professor of history at Tulane and the author of biographies of Benjamin Franklin, Albert Einstein, Steve Jobs, and Leonardo da Vinci.

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Times/Redux (Zhang); Graeme Mitchell/Redux (Doudna); Paulo Tre/A3/Contrasto/Redux (Isaacson)

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