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John F. W. Rogers: Hello, everyone. I'm John F. W. Rogers and welcome to this session of Talks at GS. It's a great honor, and it's certainly a personal pleasure to have Walter Isaacson with us once again. And I know everyone joins me in looking forward to hearing about his latest work. Walter, welcome to Goldman Sachs.

Walter Isaacson: Great to be back with you.

John F. W. Rogers: Walter, the book that you just finished, *The Code Breaker*, is about the history of gene editing and the journey of many people that were involved. But of course the central figure of your story is Jennifer Doudna. So tell us about her.

Walter Isaacson: You know, she was born in Hawaii and felt like a bit of an outsider, like many of my characters, from Henry Kissinger to Einstein to Leonardo da Vinci, to Steve Jobs, when she was growing up because she was a lanky, tall, blonde girl from the mainland in a tiny town in Hawaii where everybody else was of Polynesian descent.

And I think that outsider quality caused her and all the people I've written about that question of: How do I fit in? A certain curiosity hits them. And that's true of Jennifer Doudna. She was somewhat reclusive, and in sixth grade her dad left on her bed *The Double Helix*, the book by James Watson on the discovery of the structure of DNA. And she loved it. She realized it was a detective story about the secrets of life.

And she noticed that there was a character in there, Rosalind Franklin, who had been treated somewhat condescendingly by Watson, but it made her think, oh, girls can become scientists. Hewer school guidance counselor said, no, no, girls don't do science. But she did. She persisted, and she goes to Pomona, eventually to Harvard. And there she looks at the structure of RNA.

All the other guys in biology were tracing the double helix, the structure of DNA. But Jennifer Doudna realized that RNA was actually the more useful molecule. It does work. It comes out of the cell and to the outer region of the cell and builds

proteins. Or it serves as a guide for enzymes to cut up DNA. And so she was able to develop this gene editing tool, which she and her partner, Emmanuelle Charpentier, won the Nobel Prize for last October. And of course that ability to use RNA as a messenger is at the core of the Pfizer and the Moderna vaccines that we're now getting.

John F. W. Rogers: There's a lot of serious competition and scientific research. Fierce competition, it seems to me. I remember that Henry Kissinger built out the sort of view in his speech at Ashland University back in the '90s in which he said the intensity of academic politics and the bitterness of it is in inverse proportion to the importance of the subject.

But in this case, you know, the stakes are high. The competition is high because the stakes are high. Watson and Crick versus Linus Pauling and DNA. Doudna and Charpentier and CRISPR. But also versus Zhang in that work. And it seems to be a system that gives rewards to what I'll call "first past the post." Is that a healthy one? Is that really collaboration?

Walter Isaacson: I do think competition really does spur the human race forward, whether it's at Goldman Sachs or in journalism or by that matter in Washington where you used to work. So when people tell me, well, Jennifer Doudna is very competitive, I say, yeah, you know, that's a great thing about her. So is Eric Lander, the person who ran the Broad, which was the competing institution at MIT and Harvard that competed against Jennifer Doudna and Emmanuelle Charpentier in this race.

But I also think that you're right. There's a little bit of distortion in science that happened over the past 20 or 30 years that came because there was always a race for prizes, for patents, for publication, for being the first past the post, as you said. And sometimes I think that this competition for patents and prizes has distorted the nature of science a little bit from being as collegial or as collaborative as it would naturally be.

But one of the interesting things that happens about two thirds of the way through my book is the coronavirus pandemic strikes. And Jennifer Doudna not only rushes to pick up her 17-year-old kid from a camp that he was at, but also says, "I'm going to gather the scientists in the Bay Area, and we're going to turn our attention to using the tools we've developed in order to fight coronavirus."

And to simplify it a bit, CRISPR is simply something bacteria have been using for a billion years to fight viruses, so we might as well repurpose it to fight our own viral enemies. Also, in Cambridge, in the Eric Lander, Feng Zhang orbit, they turned their attention. But instead of being so competitive in the past year, each side was publishing papers in real time, you know, on Internet service without claiming intellectual property rights and saying people can use this to help fight the coronavirus.

So in some ways, this past year has been a bit of a restorative process to remind us, as we sometimes need reminding when we're in intense competitive races, that we also are all aiming for a higher purpose -- in this case, a really high purpose if you're a research scientist -- which is to help the human species. And so it restored a bit of that balance between cooperation and competition.

John F. W. Rogers: Well, scientific research, it seems to be dynastic. The theories of great men -- and just in a few cases, women -- they dominate and then abruptly transition. Ptolemy to Copernicus, Newton to Einstein. You know, you've heard the sayings before that theoretical physics, it moves forward one death at a time. Does medical research have the same tendency?

Walter Isaacson: Yeah, I mean, I think if you look at the modern history of medical research, you can begin with Darwin and Mendel, you know, in the 1850s, discovering, you know, through the beaks of the finches that Darwin looked at or the properties of the peas that Mendel grew, this notion of a unit of heredity known as the gene. And then nothing happens for quite a while. But eventually, 100 years later, Watson and Crick, racing against Linus Pauling and, for that matter, Maurice Wilkins and Rosalind Franklin, discover the structure of DNA. And so that pushes us forward.

Fifty years later, you get to the year 2000, Eric Lander, Francis Collins, Craig Venter, they sequence the entire human genome. And now where Jennifer Doudna and Emmanuelle Charpentier have led the way to is that allowed us to read the human genome, the Human Genome Project did. We sequenced our DNA. But it wasn't all that useful because you could just read it and say, "Oh, I can see what the problem is." What CRISPR allows you to do is edit that problem, to cut it. Just like bacteria cut the genetic material when they're attacking a virus, we can reprogram RNA, which is the guide, so it cuts our genes at a spot we want. And so that's the big leap that

happens in 2012.

John F. W. Rogers: Well, Walter, let me turn to what's a central theme that you get to in particularly towards the end of the book, which is the moral dilemma. You know, in the second half of the 19th century, social Darwinism had spread throughout Europe. The nations looked like species. They were fighting for this idea of survival, survival of the fittest. What nation would be the one that is the purest in this regard?

And in Germany, under national socialism, the notion of racial hygiene unleashed a horror of unspeakable proportions. But this medicalization of racism was advanced by scientists and doctors. You describe in your book Jennifer's nightmare of -- her recalling the nightmare of the meeting of Hitler and the implication of what would happen with CRISPR technology? Would it be used to in fact enhance a future of Aryans or be misused in terms of it?

And I don't have to go back to the '40s because just a couple years ago the Chinese biophysicist He, he stunned the world with the first gene-edited baby twins. And you address those moral questions. You bring this up, that conference in Hong Kong that took place in the book. But you describe the step-by-step process. And I think we all understand that we could be on slippery slopes with these things, but what is it about a step-by-step process that can give us more confidence that we're just not going to have a whole bunch of these sort of independent rogue things happening to enhance our muscle tone or height or all of these other conditions?

Walter Isaacson: Let me start with the Nazi eugenics, state-sponsored eugenics that you talked about because I don't think we have a big worry right now about state-sponsored eugenics. The Nazi experiments and then, you know, the horrors of the Nazis but also even before that when it was happening in Cold Spring Harbor in the United States. That's not going to happen.

But what we may face is what I would call a free-market eugenics, where it's all left to individual choice, what type of edits you would make in your family. And so people would say, if they went to the genetic supermarket at a fertility clinic, they'll say, yes, I'll check off being taller. I'll check off not having Tay-Sachs disease. I'll check off having blue eyes. I'll check off maybe, you know, even though I'm going to be kind of quiet about it, sexual orientation. I want to make sure the sexual -- or maybe the gender of the child, skin colors, all

that.

And if you allow a free-market, personal choice system, you could march down a path where you edit out some of the diversity of our society, and you're not quite creating a master race the way a state-sponsored eugenics was, but you're getting to an ethically tricky situation where the diversity that makes our society so rich -- when I sit on that balcony behind me and look at Royal Street in New Orleans and people tall and short and fat and skinny and gay and straight and trans and Black and white and whatever, you don't want to get into a society where we decide here's the perfect child and we all try to edit our children to meet that. And that gets your slippery slope argument.

As you know, all slopes are slippery, so the question is how do you get a toe hold without barreling down? And I think in my book I try to do it case by case where I say something like if it's a serious medical disease that will be debilitating such as sickle cell or Tay-Sachs or Huntington's or cystic fibrosis, and we can edit it out then do so. If it's an enhancement like making our children or us have more mental capacity or memory or more oxygen in our blood so that we have greater endurance, all right, that's getting a little bit trickier if we're starting to make enhancements with those who can afford it.

And you get all the way go to editing personality, editing the disposition to be schizophrenic or manic depressive. And I don't think there's a right answer in these. And that's why I think it's good to do it by the case study method where we can each form our opinion of what would we do in such a case.

John F. W. Rogers: Let me ask you another provocative question here because when I look back after I read the book, I went back and looked at the Nobel Prize in Chemistry. And it seems to be that it was given almost the majority of the time to three people in each year. So why didn't Zhang get the Nobel along with Doudna and Charpentier?

Walter Isaacson: Yeah, well, last October, when it was announced, it was 4:00 a.m. here in New Orleans, but I set my alarm clock because I thought, you know, it's not likely to be given for CRISPR. It's only an 8-year-old technology. The previous day they had given it to Roger Penrose for black hole theories that he had developed 50 years earlier. So usually they wait a couple of decades, but I wanted to be up just in case.

I'm watching the streaming. They say this will bring science into a whole new epoch. It's the scissors that rewrites the code of life. So I go, wow, it's going to be CRISPR. Then they announce Emmanuelle. And then they announced Jennifer Doudna. And that's it. And I thought they would have announced Feng Zhang as well. I think the reason not was it was a prize in chemistry, and the basic chemistry of the system was the discovery made by Emmanuelle Charpentier and Jennifer Doudna.

What Feng Zhang did was apply that into human cells. And so I suspect, and I hope since I like Feng Zhang a lot even though he and Jennifer are competitors, that someday the Nobel Prize in Medicine will be awarded to Feng Zhang and to George Church, who is the Harvard professor, older, who also applied it to human cells. And to a brilliant young guy at Harvard named David Liu, who has created base editing and prime editing, which takes the CRISPR movement forward. And so I think he deserves probably the prize in medicine. But my guess is they'll wait a couple of years, especially now that these medical technologies using CRISPR have become successful.

John F. W. Rogers: Walter, I just want to thank you for spending the time with us. We could go on and on. There's so many questions that I have, that I could ask and that my colleagues could ask.

Walter Isaacson: Oh, I'll come back. Thank you for being so well prepared, too.

John F. W. Rogers: I'm delighted. Delighted to be with you. And to all of our guests that are joining us, this is an incredible book. Highly recommend it. Go out, buy it, read it.

Walter Isaacson: Leave it on the bed of your niece or nephew.

John F. W. Rogers: And thanks, Walter, and thanks to all of my colleagues for joining us today.