

Marci Krivonen ([00:00](#)):

This podcast episode is supported by Prudential. If you're at home thinking about your financial plan. So where we Prudential helps one in seven Americans with their financial needs, that's over 25 million people. With over 90 years of investment experience, our thousands of financial professionals can help with secure video chat or on the phone. We make it easy for you with online tools e-signatures and no medical exam life insurance plan for better days, go to prudential.com or talk to an advisor.

Tricia Johnson ([00:45](#)):

This is Aspen ideas to go from the Aspen Institute. I'm Trisha Johnson, Jennifer Doudna, and Emmanuel Shavante just won the 20, 20 Nobel prize in chemistry for their work on the revolutionary gene editing tool. CRISPR described as genetic scissors. CRISPR gives scientists a tool to precisely cut DNA and revise the code of life

Tricia Johnson ([01:05](#)):

And being able to make a single change.

Tricia Johnson ([01:07](#)):

What's single letter in the

Jennifer Doudna ([01:09](#)):

3 billion base pairs of the DNA of a human cell. That's now the kind of accuracy that we have with this technology

Tricia Johnson ([01:18](#)):

Aspen ideas to go brings you compelling conversations from the Aspen Institute today, we're featuring an Encore discussion from the 2017 Aspen ideas festival. CRISPR is the cheapest, simplest and most effective way of manipulating DNA ever. It has the power to give us the cure to HIV genetic diseases and some cancers. It could even help address the world hunger crisis, but it may result in unforeseen consequences. The technology could lead to intentionally mutating embryos to create quote better humans in 2015, Doudna called for a worldwide moratorium on CRISPR. The technology she helped create in this Encore episode recorded in 2017. She sits down with former Aspen Institute, president Walter Isaacson to discuss the ethical and societal repercussions of manipulating the code of life. Here's Isaacson,

Walter Isaacson ([02:08](#)):

Dr. James Watson, who's first the structure with Kratos crack of the double helix of DNA and among the great things he did is like Jennifer. He wrote a book about how we got there. And I think when you were 12 years old, your dad put that book by your bedside. So let's start there.

Jennifer Doudna ([02:28](#)):

Yeah, that story really was for me. I think the beginning of my interest in molecular science, my dad was a professor at the university of Hawaii, not in science. In fact, nobody in my family was a scientist. My father was a, somebody who liked to troll around in old used bookstores and things like that. He found this kind of dogeared copy of the double helix, threw it on my bed. And when I read it, I realized that this was a story. It was kind of a detective novel in a way, but it was actually real life. It was real science. It

was how you could figure out the structure of a molecule by doing investigative experiments. And from that moment on, I really thought that was the kind of thing I wanted to do in the future.

Walter Isaacson ([03:11](#)):

And there's a wonderful scene in there where Francis crack wings into the Eagle pub, I think is the way they describe it and say, I have discovered the secret of life, explain what he discovered. Yeah.

Jennifer Doudna ([03:23](#)):

So he discovered the structure of the DNA, double helix. So DNA is the code of life. It's the molecule that holds all the information in cells that teaches how to grow and divide and become an organism or tissue or whatever. And they had discovered that it looks like literally two ribbons wrapped around each other sort of a double helix structure. Why was that important? Well, it really mattered because it explained a lot of things about inheritance. It explained the way that information can be stored chemically in the cell and copied faithfully from generation to generation because each strand of this double helix in codes includes a set of letters of the DNA code that each pair with another letter on the other strand. And so it was a very beautiful way to explain a lot of questions that scientists had up until that point. It also, in many ways, I would say ushered in the modern era of biology because it opened the door to many of the kinds of technologies that we're now using, including CRISPR.

Walter Isaacson ([04:27](#)):

So are you a PhD at Harvard, went on to teach at Yale. You're now at Berkeley where you run, what you're famous for before CRISPR was understanding the structure of RNA, which is, I guess the way DNA expresses itself in the human or any organism, explain your RNA research because that's, before you even came to the notion of CRISPR, right?

Jennifer Doudna ([04:54](#)):

Right. Well, I like to call RNA DNAs, chemical cousin, and many people think that it actually came before DNA. If we looked back far enough in evolution, it's a molecule that unlike DNA tends to exist in a single stranded form, not a double helix, although it can form very complex, three dimensional shapes. And that was the question that I set out to address when I was a younger scientist, was what are those shapes look like in RNA? And again, why did we care? Well, it was an important question because again, many people think that RNA was the early primordial molecule that could both store genetic information and replicate it. And my research as a younger scientist was to understand how that RNA replication might've actually been catalyzed by RNA RNA molecules that could both store genetic information and replicate it and pass it on to new generations.

Walter Isaacson ([05:54](#)):

What is the function of RNA that we know now?

Jennifer Doudna ([05:58](#)):

Well, lots of things. So one of the fascinating things that's happened over the last two decades or so in biology is that we've appreciated that RNA is not a, you know, when I was learning biology originally, we sort of thought RNA was kind of a boring molecule. It was kind of the intermediary between DNA, which held the secret of life in a way and protein molecules that conduct all the activities in cells. And we now understand that RNA molecules do lots and lots of things to control the way that genetic information is

deployed and cells. And that's really what I've been interested in studying over my career is how that kind of regulation works by RNA. And in fact, that was how we got into working on CRISPR.

Walter Isaacson ([06:42](#)):

But when you say DNA is expressed in cells, which means express in who we are, to what extent, what sort of things are determined by our DNA and what sort of things are sort of just sort of guided by our DNA, but aren't completely determined by

Jennifer Doudna ([06:59](#)):

That's the \$64,000 question.

Walter Isaacson ([07:02](#)):

Yeah. And we're not paying you that much, but you can attempt it

Jennifer Doudna ([07:08](#)):

Well. So, you know, DNA, uh, you know, people have been trying to understand, uh, the code and what what's in the DNA, what are all the genes that make up a human being for example, and one of the great, I think it's great. You know, things that's come out of that is that it's complicated, right? It's really complicated. It's not just a list of genes, but in fact, there are many layers to the way that that information is actually used. And I think this is what you're alluding to is something that we call epigenetics, which sounds complicated. It really just means, uh, making chemical changes to DNA that don't alter the genes themselves, but change the way the information is actually used.

Walter Isaacson ([07:50](#)):

So give me an example of one of our traits. That's more epigenetic, meaning it's controlled partly by the environment and who, what we do and what is like purely genetic and encoded.

Jennifer Doudna ([08:02](#)):

Well, it's hard to give you a specific answer, but many people think that traits like things to do, even with our personalities, how we interact with our environment, things that are more, you know, it's very hard to put our finger on a particular gene. That's responsible for intelligence, for example, that a lot of that is really a consequence, not just of the genes in our DNA, but the way those genes are actually used, which is epigenetic,

Walter Isaacson ([08:28](#)):

But things like particular diseases, or maybe even childhood obesity is more genetically determined. That's what people think. Yeah. So you're doing RNA and you've got the structure of it. The atomic structure is pretty cool. And if I remember from the book correctly, another great woman, bio chemist gives you a phone call out of the blue, even though she's a colleague of yours, you don't know her. And she says to you, we're doing, and we need to know how it relates to RNA. You want to be part of it.

Jennifer Doudna ([09:01](#)):

Yeah. So that was actually Jill Banfield. So Jill is a colleague at Berkeley. She's a geo biologist. So she's not a biochemist. She works on our, on, on bacteria and where they grow in the environment and how they behave and interact with viruses and things like that. Her research had uncovered a lot of examples of

what we call CRISPR, which is an acronym that stands for a series of repeated sequences in DNA. So very easy to pick out if you're reading the letters in the DNA code, you could see this repetitive sequence very kind of unusual. And what was quite interesting about this pattern of sequences was that it included a series of unique sequences that were derived from viruses. And the question that Jill Banfield had that she was not equipped to answer in her own laboratory was whether those virally derived sequences stored within these CRISPR elements, might in fact be copied into RNA molecules in bacteria and then use to protect the cells from viral infection.

Walter Isaacson ([10:04](#)):

They first discovered some of that, I think in Spain, right? Yeah. Actually I was like in yogurt or something.

Jennifer Doudna ([10:10](#)):

Well, yeah, there several, several microbiology labs that had very important early roles in it. So Francisco Mojica was in Spain. He was one of the people that coined the acronym CRISPR. And then there was a, a group at a yogurt company in, in Denmark actually originally that was working on how to protect their yogurt cultures from viral infection and had uncovered crispers and started harnessing them for the use in food prep.

Walter Isaacson ([10:39](#)):

Now, just so the audience can not feel any less smart than you when you first heard it, you thought it was spelled crisper as in with a C R I S P E R. I think you looked it up and you realize, okay, there's no final E CNET and you decide, okay, I'm going to take on this question of CRISPR. Right.

Jennifer Doudna ([10:59](#)):

Well, it was just one of those things that sounded so crazy that to me, that it seemed really interesting to try to pursue this. And I, you know, I've always been, you know, I think there's two kinds of scientists, right? Sort of broadly speaking are those that dive extremely deeply into one area of biology and, and become the, you know, the world's experts in it. And there are those who are more sort of at a smorgasbord and they're a, they're picking things and looking at things and trying things. And I've always been more in the second category. And so when I heard about this, I just thought, well, that's so fascinating that I feel like I, I'd love to test a decent experiments and see whether it's really true.

Walter Isaacson ([11:36](#)):

How did you then get to the most amazing discovery of our time, which is CRISPR can edit our genetic code, our genomes.

Jennifer Doudna ([11:47](#)):

This is a great example of, of frankly of small science and curiosity driven as well as an international collaboration, all are things that have really characterized my career over the last 25 years. So I got together with a colleague Emmanuelle Charpentier. We met at a conference, neither of us knew each other beforehand. She was running a lab in Sweden at the time. And she was working in seemingly a very different area of science than me. She's a microbiologist, um, medical microbiologist, studying bacteria that infect people. And one of those bacteria turned out to have a very interesting type of CRISPR system in which a single gene, a gene known as CAS nine seemed to be required for those cells

to protect themselves from viruses using the CRISPR sequences. And the question was, how does this protein that's encoded by the CAS nine gene? How does it work?

Jennifer Doudna ([12:41](#)):

And she was not a biochemist. I was, we realized that we could get together and do some experiments to figure out the answer to this question. And the result of that collaboration was this publication in 2012, in which we described the fact that CAS nine is an amazing protein that can literally be programmed with little pieces of RNA that a scientist in the laboratory could easily change in sequence. And what it does is to use that piece of RNA, that it holds onto to find a matching sequence of letters in a DNA molecule, for example, the DNA of a cell, a chromosome. And when it finds that matching sequence that holds onto the DNA and makes a precise, a double stranded break in the day.

Walter Isaacson ([13:27](#)):

No, I did almost it added to it as you would.

Jennifer Doudna ([13:30](#)):

It's like cutting and pasting. I like to use the analogy of word processing because it's very analogous to that. You think of the DNA code, like the text of a document. This is the scissors that allows you to cut out texts, change it. Um, the cell takes over after this, after the DNA is broken and makes a precise change at the site of the repair.

Walter Isaacson ([13:51](#)):

Yeah. About make a little detour here because the three major characters in this narrative so far, Jill, yourself and Emmanuel Emmanuelle are all women. And I think back to the double helix when they kind of ignored Rosalind Franklin, the only woman involved, is this a change in science that, um, um, I mean, I don't think we've seen a major breakthroughs like this led this way or is this just coincidence?

Jennifer Doudna ([14:20](#)):

I think it's interesting. Serendipity. I think, uh, women are certainly making more forays into the scientific world as well as obviously in biotechnology and business. It's still harder, I would say for women in my own experience. Um, but I think that this is a great example where, you know, none of us planned it that way, but it just so happens that all of us were running research laboratories that were doing highly complimentary kinds of work that were made it very easy for us to work together harder for women's dope.

Jennifer Doudna ([14:53](#)):

Well, I think there's still biases. A lot of it is unintended bias, I would say, but you know, just a ways that women are excluded. Um, I think women, you know, if you've read the famous Sheryl Sandberg book, I think a lot of the things that she talks about in lean in resonate with me and with my colleagues, I think women are a little more reluctant to step forward and volunteer for things. And they get volunteered for things that take them away from focusing on, uh, you know, leadership roles and things like that. So I think it's, it's a lot of subtle things.

Speaker 4 ([15:36](#)):

[inaudible],

Jennifer Doudna ([15:37](#)):

You're listening to Aspen ideas to go on the show today, crack and creation, featuring biochemist, Jennifer Doudna and Walter Isaacson. Find Aspen ideas to go on Apple podcasts, NPR, one Google play and Sirius XM insight channel that's channel one 21. Our episodes cover need to know issues and introduce you to new ideas and different perspectives. Subscribe today on Apple podcasts. Now back to the show here's Walter Isaacson,

Walter Isaacson ([16:16](#)):

When you got to the notion of editing a genetic sequence, or, um, what is it you're editing exactly. I know it's a strand of DNA, but what would you call that length of strand that you add it?

Jennifer Doudna ([16:31](#)):

Uh, I would call it a length of strand. Yeah.

Walter Isaacson ([16:34](#)):

But to some extent it would have a gene function, right.

Jennifer Doudna ([16:40](#)):

The gene, or it might have a piece of sequence that controls a gene, right. So it could be either a gene itself or the part of the DNA that controls the gene. Um, but yeah, I mean, you can, you know, you can make changes that are very precise down to, I mean, imagine this imagine being able to make a single change to a single letter in the 3 billion base pairs of the DNA of a human cell, that's now the kind of accuracy that we have with this technology.

Walter Isaacson ([17:06](#)):

So explain to me the scientific, and maybe we'll get to the moral difference of doing that in a human being. And it's sell, leave aside animals, which are perhaps easier and doing it in a germ line, what would it mean to do it in the germline?

Jennifer Doudna ([17:24](#)):

Right. So, you know, if we talk about doing it in a, an adult, anything adult person, a plant animal, we're talking about making changes to cells in ways where those DNA changes are not heritable by future generations, but in the germline, that's a different scenario where now changes that are made to the DNA become part of the entire organism. If it's, if those germ cells are allowed to develop into a, into an animal, a full organism, and those changes can be passed on to future generations. So it becomes a permanent alteration. And if you really think about it, it's really changing the evolution of that species at that point,

Walter Isaacson ([18:03](#)):

But our evolution has always changed, right? So what's the difference here,

Jennifer Doudna ([18:08](#)):

Here? I would say the difference is that we're doing it in a targeted fashion. We're making decisions consciously about, you know, we're going to change this one gene or even a set of genes to do something that we think is desirable

Walter Isaacson ([18:21](#)):

And the timescale is different and the timescales varies. It would take millions of years. We can now do in about 20 minutes or so. Yeah.

Jennifer Doudna ([18:29](#)):

Well, proverbially, yeah.

Walter Isaacson ([18:35](#)):

Start me with the animals. Give me a couple of examples like baby pigs or whatever that you've all or that science has already been able to use this to do.

Jennifer Doudna ([18:49](#)):

Well, there's a lot of examples. So mice, you know, that mice are used very commonly as models of human disease. So it's been possible to make mice that have changes to their DNA that make them more human, like in certain ways and make it easier to study the effects of, of therapeutics drugs, for example, on genes, uh, similarly in, um, well you mentioned pigs, you know, so pigs, uh, the, one of the attractive things with pigs right now is the idea of engineering them. So they're better donors, organ donors for humans. And this is already being actively worked on both in research labs, but also in a startup company.

Walter Isaacson ([19:28](#)):

So you basically create pigs that become farms for Oregon's real humans. That's the idea that's right. And so what do you need, what happens to the pigs? What do you do? How do you change the genetic?

Jennifer Doudna ([19:40](#)):

You can literally program the DNA so that their, their, uh, organs or certain molecular properties that they have, their immune system, for example, looks more human. Like, so you put actually transplanting genes or just altering making more subtle alterations to their DNA so that the they're, uh, you know, at a molecular level, they behave in a more humanlike way.

Walter Isaacson ([20:04](#)):

And, uh, what about like mosquitoes that carry Zika or something? What could you do to help fix that?

Jennifer Doudna ([20:10](#)):

Right. So this is another fascinating use of a gene editing technology, the idea of gene drive. So that basically just means if you have a way to alter DNA, that's very efficient. You can use it, you can set it up in a way that it will drive a genetic trait very quickly through a population, for example, a population of insects. And if one does this in mosquitoes, and this is already being worked on in principle, one could create strains of mosquitoes that are resistant to viruses and therefore, thereby can't transmit Zika virus, dengue virus,

Walter Isaacson ([20:43](#)):

But you can also create them just as easily mosquitoes that reproduce the same way that say, uh, you cut back a population of the state does. And is that being done in response to the Zika virus? Are you, are you using CRISPR technology yet to take on mosquitoes?

Jennifer Doudna ([21:02](#)):

Well, I'm not doing it, but, but groups are doing it. Uh, so, so this is a very active area of research because I think many people imagine that this could be an effective way to control insects that would otherwise be, uh, you know, spreading disease.

Walter Isaacson ([21:17](#)):

And that passes along to mosquitoes from here on out. Right. Is that just a specific mosquito it's part of the germline of the mosquito species or whatever. That's right. That's right. You know, but let's start a little on the moral thing there. When I was young, I read Rachel Carson and we were able to get rid of mosquitoes. We did it with DDT and a generation later, there were no pelicans in my home state of Louisiana almost. We didn't know the consequences of doing that. How do we know the consequences of what science is now doing to the mosquito bomb?

Jennifer Doudna ([21:49](#)):

I would argue we don't, you know, and I think that's where we have to be proceeding with, with real caution in something like that. You know, there's a, I just, I was at a talk recently and somebody was talking about gene drive from mosquitoes and they showed a slide of, you know, building a very large structure and sort of maybe the size of this tent that is designed to contain these modified mosquitoes and really try to do experiments in a controlled environment to see what happens when you have a gene drive.

Walter Isaacson ([22:17](#)):

What happens if you have a tent like this, it's supposed to contain mosquitoes. We have nutrient Louisiana. We had places that was supposed to contain them too.

Jennifer Doudna ([22:26](#)):

Yeah, it's, it's a, it's a big challenge.

Walter Isaacson ([22:29](#)):

So who's in charge of saying stop.

Jennifer Doudna ([22:34](#)):

Um, well, right now there are various obviously government regulatory agencies that are, you know, in charge of controlling the environmental release of organisms that are modified this way. But right. I would say that right now that it's, we're at an interesting time because you know, this thing about this technology is that it's moving incredibly fast. So just to give you a sense, so this technology is really just barely five years old right now. Right. And, and already, and we didn't talk about this yet, but it's already in clinical trials for cancer treatments in, in China. And, you know, it's, it's a, it's sort of mind boggling how the pace of just scientific research has picked up with, with this tool. I mean, I'm seeing now they're, you know, literally probably, you know, a dozen at least, or maybe more papers a week in the

scientific literature using the CRISPR technology. So, you know, one of the big challenges is how do you keep government regulatory groups up to speed with this? How do you make sure they are aware of how fast things are moving? And the pace of government is, is, you know, not that fast,

Walter Isaacson ([23:38](#)):

I will give you an example of it from yesterday, which will either be reassuring or not. Um, I guess you could say this Tom Price, the secretary of health and human services, as you know, is here on the stage. Uh, and he's worried about the affordable care act, but he's also, this is in his wheelhouse something we should be thinking about and he saw your book in my office and he started to asking about it. I said, you know, actually this will be even more important, 50 years, a hundred years from now, what you do on this, then what you do on the affordable care act, it'll affect the world more. And he said, well, maybe I ought to read the book. So I gave him a copy

Jennifer Doudna ([24:24](#)):

[inaudible]

Walter Isaacson ([24:24](#)):

You can send them a signed copy without. Um, so, uh, let's start talking about humans. If we may tell me, you know, um, you know, you've made long, I'll tell you, I'm looking at the pictures, longer hair on sheep, you know, uh, uh, virus resistant, pigs, hypoallergenic EDS, but then it gets to the part where you can actually start changing the human genome. Um, where will we start on that? What will we do first? I mean, a little blood diseases, cancers, what?

Jennifer Doudna ([25:01](#)):

Yeah. So I think, you know, the, the things that kinds of treatments that really are the focus right now of research are not first of all, not in the germline, right? So really talking about what we call somatic cell changes, changes to adults or kids, but not that, not those that would become a heritable. And it's like you said, you know, it's, I think the it's very attractive to think of being able to cure diseases that have a known single mutation that's causative. So for example, sickle cell disease is one, that's talked about a lot, it's attractive for a treatment like this because it's in the blood. So it's possible to take blood STEM cells from a patient, do the editing outside the body and then replace the correctly edited cells. So they repopulate the blood supply. And, um, and you know, the sickle cell you Titian has been known for a long time. It's a severe disease that we have no treatments for it right now. And there's a fairly large group of people that are affected. So it's, you know, I think that'll likely be one of the early targets of genetic.

Walter Isaacson ([26:03](#)):

And as we do our little moral, a spectrum, that's pretty solidly in the, yeah, let's do that. It won't affect the germline and won't affect children, but it will save people from a bad disease in Gwangju because China's now ahead of us on this, we'll get to the fact that we're not spending enough on research in this country. So China gets to take the lead. They're now using it for what

Jennifer Doudna ([26:29](#)):

Well they're, uh, I think you might be referring to using it to in embryos, right? Yeah. And, uh, you know, they're actually in China have been working on asking the question, does this technology work in

developing human embryos? Could we actually imagine someday using it to, you know, maybe we want to correct the sickle cell mutation, but we want to do it, not in someone who already has this disease as an adult, but we want to do it at the stage of embryogenesis. And so the first paper, and now there's several actually published. That was about this topic was, was published in the spring of 2015 using non-viable human embryos. And it really sparked, you know, attracted a huge amount of attention because I think it really brought to the forefront. The idea that, you know, this technology is really on our doorstep and we have to make a decision as a society. Are we going to proceed with this kind of, of heritable

Walter Isaacson ([27:29](#)):

Say the embryos? It meant that it would be all future generations would have this,

Jennifer Doudna ([27:35](#)):

If, if those embryos were be implanted, if they were viable and implanted, uh, then in principle. Yes.

Walter Isaacson ([27:42](#)):

And the fact that they were non-viable was just a small choice. You could, they could have chosen to use viable one. Correct? Yeah. So this is ready to go. Well, I mean, in the next five to 10 years,

Jennifer Doudna ([27:56](#)):

I certainly think in that period of time. Yes.

Walter Isaacson ([27:59](#)):

Yeah, yeah. So, um, what type of things could, if you were thinking of doing it, what would be the things that you would say, I want to apply it to this in, in embryos. Yeah.

Jennifer Doudna ([28:15](#)):

I personally am not ready to go there yet. I have to say, I think that, you know, first of all, I think that there needs to be a broad, what we call sort of a broad societal consensus about whether that type of use of gene editing should proceed. And there obviously hasn't been the opportunity.

Walter Isaacson ([28:33](#)):

We knew that somebody genetically an embryo was going to get a fatal blood disease. You would not fix it.

Jennifer Doudna ([28:41](#)):

I would advise, um, other approaches, I think today, I think, I think the use of it in somatic, in a somatic cell kind of application should happen first and, um, you know, partly for safety reasons, but really frankly, also to, to, you know, give us us all of us, time to grapple with this, this issue. Are we going to start editing the germline? Because honestly once that begins, I think it will be very hard to stop it. It'll be very hard to say I'm going to do this thing, but not that thing because everybody's feelings about this, I think will be, be different. And who decides, who pays for it? You know, there's a lot of,

Walter Isaacson ([29:17](#)):

Can you say we, should we, the responsible people should pause, put a moratorium, not do it until we grapple, um, your coauthor, uh, Sam Sternberg, right? I think with a graduate student of yours. And so a woman, I assume it's a woman by the pseudonym named Christina. Who's a, I assume an entrepreneur type. This is very, comes to him and says, let's do it. And she's not, she's trying to commercialize this. And she would, I assume, make all of our children taller and smarter. And it's pretty easy to do. Um, let's take a specific example that you could do with the gene, which I think is have stronger bones. That's a pretty simple genetic thing, right? Or bigger muscles, bigger muscles, two things that people might want to say. I want all my kids in kids, kids to have stronger bones and bigger muscles. And that's scientifically conceivable because those are truly things you can find on the genome that you could change right. When they drive the science. Right. So Christina goes to your partner and says, let's market this

Jennifer Doudna ([30:32](#)):

That's a true. And by the way, that's a true story that blew my mind. Oh, do you want her last name? We'll talk later.

Walter Isaacson ([30:42](#)):

Just tell the camera. I actually think, well, I'm not going to go there, but this is something that ought to be talked about more. If there are Silicon Valley entrepreneurs trying to hire you and your graduate students to market this, to make people's kids have stronger bones or bigger muscles, there probably should be more publicity.

Jennifer Doudna ([31:03](#)):

My knowledge that isn't happening today. But, but, but that doesn't mean it won't in the future. I certainly am aware of the whole better Sam. Right? Well, this person really came to, to my student. Yes. And, and, and said that she wanted, she said she herself wanted to have the first CRISPR baby and that she wanted to commercialize the technology, create a company that would offer this service to parents and allow them a, you know, kind of a menu of options. And wow. We were really pretty shocked at the time. Uh, Sam and I, uh, not, not so much now given all that's gone on, but you know, I think it really does illustrate a couple of important points. I think you're bringing up this idea that, you know, there's a whole commercial aspect to all of this. That is, um, something that I think people are, you know, we're all sort of grappling with. And secondly, uh, you know, it really does get to the moral and ethical challenges around this technology. She, Christina could not do that today in the United States. Right. It would not be possible for her to do that, but could she do it in certain other parts of the world, potentially. Yes.

Walter Isaacson ([32:06](#)):

You suspect that Christina or some Christina like that is nail in Gwangju, China, trying to make that.

Jennifer Doudna ([32:13](#)):

Let's just say I wouldn't be surprised if I were told that were true.

Walter Isaacson ([32:16](#)):

So people in the United States who are wealthy enough and have the feeling they could go this far on the moral spectrum could in theory, go to a company in the foreseeable future, say five to 10 years and say, here's the menu I want on my baby. I think it could happen. This episode is

Jennifer Doudna ([32:40](#)):

Supported by Prudential. If you're at home thinking about your financial plan. So we're, we Prudential helps one in seven Americans with their financial needs. That's over 25 million people with over 90 years of investment experience, thousands of financial professionals can help with secure video chat or on the phone. We make it easy for you with online tools e-signatures and no medical exam life insurance plan for better days, go to prudential.com or talk to an advisor.

Walter Isaacson ([33:13](#)):

Let's start thinking now through the moral things, suppose in the genetic lines of family, they've got a blood disease, whatever it may be. Um, would that be okay to say, let's turn that one off.

Jennifer Doudna ([33:32](#)):

Are you asking me my personal? Yeah,

Walter Isaacson ([33:34](#)):

Yeah, yeah. We could ask. Yeah. Yeah.

Jennifer Doudna ([33:36](#)):

Well, you know, again, I think it comes down to, you know, is it safe to me, you know, I think with any technology you first and foremost, have to ask sort of risk versus benefit. So if it were me, I'd want to know, you know, first of all, does this even work right? Is this company that I have any credentials that they have, any evidence, you know, what's the, what's the safety of this, does it work? Um, and then you have to decide, you know, is the risk because there's always risk, you know, is the risk worth the benefit? Are there alternatives that would be better or just as good that I should consider? I think we have to do that with any,

Walter Isaacson ([34:09](#)):

I suppose, uh, the benefit is better than the risk.

Jennifer Doudna ([34:13](#)):

Well, then I think, I think at some point it might be something we have to, we have to consider. I mean, I, we had an interesting meeting in early January of 2015. I think we talk about it in the book where a group of scientists was kind of a smaller group, about 20 people, including Paul Berg and David Baltimore who had been involved in the early discussions in the 1970s around the ethics of molecular cloning.

Walter Isaacson ([34:35](#)):

Yeah. Why would you let's pause there because there's something famous called the bird letter on cloning where they say moratorium on cloning. Right, right. That's kind of held right.

Jennifer Doudna ([34:46](#)):

Well, it's a, we're talking about two different things. So, you know, molecular cloning means making copies of little pieces of DNA in bacteria and that has been shown to be quite safe to do so. Um, so that's done widely now and across the world in, in biology labs.

Walter Isaacson ([35:03](#)):

Um, so flash forward to today, could you all have a moratorium cause all of you scientists get together or is that wishful thinking?

Jennifer Doudna ([35:12](#)):

Oh, I think you could. I mean, I think, you know, that was the idea of that early meeting was to ask, you know, would it be possible to build a consensus globally among the scientific and clinical communities about the way to proceed with this very powerful technology. And that's really what many people are now working to do. But the, the point I wanted to make about that meeting was I thought it was very interesting that even in that small group of scientists who one could argue are some ways, you know, all cut from the same cloth in a way, right. But we were having this conversation and it was quite a, quite a, quite a heated conversation. And at one point, somebody leaned across the table and said, you know, at some point we may decide it's not ethical to not use this in the germline for certain things. And it kind of made everybody sit back and, you know, think about it a little bit differently. So I think, you know, there's still a lot of work to be done to develop the technology to the point where it would be in principle, even safe enough to do that.

Walter Isaacson ([36:07](#)):

My opinion. Yeah. But I mean that's five years from now or so. So we might as well start the moral thought now. So the question is, as I asked you earlier, but you asked at that meeting, wouldn't that be a moral to say to a family, your kid has this genetic easily marked trait. That's going to a blood disorder not to fix it, right.

Jennifer Doudna ([36:31](#)):

If there was no other treatment and the treatment

Walter Isaacson ([36:34](#)):

Let's go down the spectrum, suppose the kid is going to be born deaf, would you fix that?

Jennifer Doudna ([36:41](#)):

That gets into a very interesting realm because I've had a number of conversations with people in that community. Many of them actually feel that, uh, there, that deafness for them is not a defect that they would fix.

Walter Isaacson ([36:54](#)):

So suppose you had two parents, both deaf and from genetic reasons and they felt it was not a defect. And they were about to have a child that was not deaf. Could they ask to fix it? So their child would be death. Whoa, by the way, Michael sat down and asked that question, his class, I didn't

Jennifer Doudna ([37:20](#)):

Well, right. I mean, this gets into the realm of who decides, right? Who, who decides should the parents decide, should they be told they can't do that? If they want to do it, should they be told they can do it, but only if they want to pay for it. It's I think these are tricky. Yeah.

Walter Isaacson ([37:34](#)):

But if it's going to go down, the germ line is not there to see just their decision and their child doesn't have a voice, but one has to think of the interest of the child too. Right? Yeah. So, uh, as you go through the spectrum of things you could do, um, certainly as we said, bone mass muscle, perhaps even height, to some extent, uh, other trades, where, where is there some moral line or is this, this some big old slippery slope?

Jennifer Doudna ([38:06](#)):

I think that's, that's the question right. Is really that we're all grappling with where is there a line? And if there is, where is it? I think it's hard, honestly, to, you know, you look at what's happened in, in vitro fertilization over, over the last, you know, couple of decades. I mean, I'm old enough to remember before and after. Right. And you know, there was a lot of controversy when in vitro fertilization first became available. Right? A lot of people said, well, that seems, that seems wrong. Somehow I remember my own parents saying, you know, this, that seems wrong. You know, test two babies that seems really wrong. And then, you know, as there was obviously demand for it from infertile couples and it was shown over time to be apparently, uh, safe to do, um, you know, it's become accepted at least largely. And now, you know, if you go to different in vitro fertilization clinics in different States, they offer different things. So some will offer the possibility for parents to select the sex of their child, some don't right. So some doing something, it's a very funny thing, you know, some, you know, and there's the regulation around, this is a bit nebulous. So will that happen also with gene editing? It could, I don't know.

Walter Isaacson ([39:14](#)):

You say, you're trying to pull together a consensus audit. Did you bring in the Chinese researchers from the gung gel lab and what did they say?

Jennifer Doudna ([39:23](#)):

Oh, they were very interesting. They, they, they, you know, they acknowledge the, the controversy around the work they were doing, but they frankly, they were very Frank, very honest. They said, look in our society in our culture. There's a very different view about human life and about early embryos then sort of the Western, um, Christian Judeo tradition. So it's just a, you know, it's a different culture. And I think that's just something that we, we have to grapple with.

Walter Isaacson ([39:49](#)):

I'm going to quote a sentence from your book. The argument that germline editing is somehow unnatural. Doesn't carry much weight with me anymore. What happened?

Jennifer Doudna ([40:02](#)):

Well, I, I really, I describe this in the book. I really found this and this was a surprise to me actually, but I found my own attitudes about editing the germline changing over time. Um, because you know, for, for many reasons, I guess I started thinking about the fact that, uh, you know, after all we, you know, we pick our, our partners and we have kids. So that some level where, you know, we're, we're affecting our kids just by our choice of partner. Um, actually these days you can believe it or not. You can buy eggs, right? You can buy eggs, you can go to a sperm bank. I mean, you can look in a catalog and decide who do I want the father of my child to be in a, you know, from a sperm bank, if you want to, um, that's already being done. And, uh, and then, you know, there are countries like, like Israel that actually pay, you know, they pay for a couples to have up to two kids by, in vitro fertilization if they want to. And they

pay for preimplantation genetic diagnosis to remove embryos that have, uh, devastating genetic diseases associated with them. So, you know, there's already a lot of, you know, engineering in a way that's going on, right?

Walter Isaacson ([41:07](#)):

Yeah. Germany did that in the 1930s.

Jennifer Doudna ([41:12](#)):

Exactly. So it's not a, it's not a it's, it's not a straight forward, it's not a straightforward thing at all, you know, but, but the fact is that it does go on. And I think that, you know, and I also, the other thing that happened was that, you know, here I am a biochemist and I do a lot of just, you know, I've always done very fundamental research on molecules. I don't do anything with embryos or, or even animals in my

Speaker 1 ([41:34](#)):

Laboratory. And yet I was getting contacted. And this happens now routinely by patients, families of parents who reach out and say, I have this disease in my family. A lot of them send pictures of their children, very beautiful children, and they're facing a devastating disease. And you know, that, that hits you very, very deeply. And you start to ask, well, if this technology were available in a way that prevented that kind of suffering, why would we not want to use it? Today's speakers are Jennifer Doudna and Walter Isaacson their conversation at crack and creation, gene editing, and the unthinkable power to control evolution was held onstage at the Aspen ideas festival. If you liked today's show, check out the episode, should we design our babies? It features center for genetics and society, director, Marcy Karnofsky and Duke law, professor Nita Farahani, the two explore the major ethical concerns and lack of regulation and oversight with genetic modifying technology. Find a link to this recommended companion episode in our show notes, or by searching the Aspen ideas to go archive on Apple podcasts. Now back to our featured conversation, here's Walter Isaacson,

Walter Isaacson ([43:09](#)):

The draw, not a sharp line, but try to put a line in the sand between fixing things that are diseases very harmful to people versus creating enhancements, like making children taller, muscled, smarter blonder people say, okay, I want to change race. I want my children to be different race. That's not a disease. That's something. Can we draw a line between that type of thing and saying, I've got a genetic disorder that's going to destroy my blood or is there no line to be drawn?

Speaker 1 ([43:46](#)):

I think it's hard. And the reason is this, like, let's say that. I say that, let's say that. I told you we can make a change to an embryo that will remove a single gene that, um, if left in place will make a person susceptible to cardiovascular disease when they get older. And, um, and there's no deleterious effect of removing this gene. So, um, you know, it's a good idea to do it.

Walter Isaacson ([44:12](#)):

You could do a bad cholesterol already, right? I mean, you could do CRISPR to take out, not Mike, but somebody has bad cholesterol in the whole germline. That's the idea. And that's right. As you're saying, that's right on the borderline of a disease in the hands, or would you call preventing disease?

Jennifer Doudna ([44:32](#)):

I don't know. It's a little of both.

Walter Isaacson ([44:34](#)):

And is there any way anybody's going to decide that or is it going to be a global free for all

Jennifer Doudna ([44:39](#)):

Boy? That's, that's a, that's a great question. I think in the end it may end up being regulated differently in different jurisdictions. Probably I suspect just because people's opinions and values are going to be different and it's hard to change

Walter Isaacson ([44:54](#)):

When we get to the borderline that one of the things that amuse me is you can get rid of armpit odor easily CRISPR. Is that something we should do here?

Jennifer Doudna ([45:04](#)):

That'd be very useful.

Walter Isaacson ([45:07](#)):

One of the things, uh, in a broader sense is that I'm talking to secretary price, but also others people question the value of basic science. They want to get rid of NIH and, you know, national science foundation. And yet it seems to me that everything from the sequencing of the human genome, to the ability to add transistors on a piece of semi-conducting material, all comes out of pure, basic research labs like yours. What would happen to a lab like yours, which is really a, just a wonderful group of people, graduate students, people doing experiments. If the government quit funding, basic research,

Jennifer Doudna ([45:54](#)):

Oh, that'd be a disaster. I mean, you know, we would probably just mostly fold up our operation and go do something else. I mean, this is the thing I think, you know, we've been facing this in the, in the U S for the last decade, at least this push towards initially it was really this push towards true what's called translational research. In other words, people saying, why are we working on fruit flies and, you know, fungi when really what we want to be doing is curing cancer and curing Alzheimer's. Well, I don't think anybody would argue that. Of course we want to deal with cancer and Alzheimer's and other diseases. But the question is, how do you get there? And, you know, what's, what's happened if you look back over sort of the history of modern medical science, a lot of the fundamental discoveries and the technologies that enable those discoveries have come about through curiosity driven research projects that are not aimed in any particular direction.

Jennifer Doudna ([46:47](#)):

They're just a group of smart people. Often, often a small group of smart people that are just, you know, asking gee, I wonder how this works and they do experiments. And that was very true with this whole CRISPR project for us, that, um, that lead in a very unexpected direction. I think that, you know, that there has to be a balance. It's not to say that we don't want to have people working in targeted ways on diseases. We need that too, but we need both. And, um, and the danger right now, I think is that, and you alluded to this earlier, right? Is this, is that if the United States really cuts back on funding for that

kind of fundamental curiosity driven research, a lot of it done in small, you know, laboratories. I think we're going find ourselves falling behind other countries and already we're on the cusp of that happening because countries like China are investing huge amounts of money.

Walter Isaacson ([47:40](#)):

China, once red is investing 20 times more than the U S in basic research in genetic technology. Does that sound

Jennifer Doudna ([47:47](#)):

Sounds about right. You know, my own colleagues, I mean, we struggle here in the United States to get, you know, we're, and I'm at Berkeley, I'm at a, you know, I'm at one of the top research universities, but we struggle to get enough money to put together money, to buy equipment like electron microscopes and other field. That's gone through this huge, you know, explosion over the last few years in, in the, the advances of the technology. And meanwhile, we see our colleagues in China, uh, buying up, you know, 20 at a time. And, uh, you know, it's really astounding

Walter Isaacson ([48:17](#)):

And you needed that microscope to figure out the molecular and atomic structure of RNA. That's absolutely right. So I could do the thought experiment, which is suppose we had done this 70 years ago and stopped as Beneva Bush pushed basic research. We had not done it if Eisenhower had knocked on it and we hadn't invented, the transistor had not invented. The microchip had not invented. The laser had not invented the internet and not been able to do circuits and GPS that sort of like, that's what would have happened if we hadn't done the basic research on subbing, conducting materials, various things, and someplace like Russia or China had actually invented everything from the microchip to the internet, to the personal computer, to GPS. And you could imagine Russia being the dominant economy in the world. Right. So can you imagine China being the dominant economy in the world if we cut back basically.

Jennifer Doudna ([49:18](#)):

Yeah. I think we all, we all wonder about it, uh, in the scientific community, for sure. We joke about, you know, someday we'll all be working in, uh, somewhere in China. You don't have running a lab there if we're lucky, but it's a very real question. I think for many of us is, you know, what is the future of scientific research in this country? Are we going to maintain our predominance in that area? Or are we going to let it slip away

Walter Isaacson ([49:45](#)):

Of research in this field is very collaborative. And then it's also competitive, almost like any other, whether it's, you know, Amazon and Google or whatever, there's competition in collaboration, but in science, there are certain things that tend to, it seems to me, but I want you to push back if I'm wrong, promote a little bit more competition than they do collaboration. For example, in your field, there's been some controversy where you have George Church and others at Harvard, who've done things in their lab. Um, Eric Lander at the Brode, and I can't remember it from John is that he's done a lot on CRISPR. You all have been even battling over patents that deal with it. Uh, Eric wrote a piece called the heroes of CRISPR that got a lot of criticism because it minimized your role. And he was hit both for being ungenerous, scientifically, and also perhaps sexist. I think he got hit for it too. But part of this competition seems to me to be driven by two things, one, a patent office that needs to find something

that is hard to find in science these days, like who gets the credit for this amazing thing. And secondly, a Nobel prize committee that can only award it to three people. Does this bother you? Is this a problem in science now?

Jennifer Doudna ([51:07](#)):

I think it is a problem. Definitely. I don't know how one solves this problem. I think that, you know, science always has included elements of both collaboration and competition and you need both in a way, you know, competition can be very good, obviously spurs people on to do,

Walter Isaacson ([51:22](#)):

We'll read the double helix. It was, you know, Linus, Pauling, Wilkins,

Jennifer Doudna ([51:26](#)):

Yeah. Kind of a race. And, you know, um, and, uh, and the challenge is how to get that balance. Right. And I think one of the things that I think about a lot is, is, uh, how to attract younger scientists into our field. I think we really want to draw in, because they're the ones, honestly, that are driving the work right now. Am I in my lab? Uh, actually pipetting, no, I'm sitting here talking to you, right. So, uh, but, but people in my lab are, they're doing it. And, um, and they're the ones that are really driving the next, uh, results that will be coming out. And so how do we ensure that they continue to be attracted to our field and drawn into it? And I think that, you know, one runs, uh, if there's a danger of, you know, especially certain types of people feeling excluded, um, if there is, if there's a feeling of unfairness somehow that that can be very detrimental to attracting younger scientists and same thing with prizes.

Jennifer Doudna ([52:17](#)):

You know, I think the problem with prizes is that, um, you know, they, it's very difficult and I now sit on various prize committees, as you can imagine. And so just thinking about when you want to give a prize in a certain area, you want to recognize scientists that have done the work, but you appreciate that, you know, at some level everybody's work is built on other peoples and involves the work of a lot of younger scientists in the laboratories who aren't being sort of named in particular by these prizes. So how do you deal with that? It's very,

Walter Isaacson ([52:43](#)):

So how much would you say you had to depend on, even though you're competing against sort of the George Church or the Brode Institute and others, and, um, what, what, what, how would that be made better? Cause you know, in your book, you don't talk about them in his article. He doesn't talk about you. And it feels to me that, uh, if I may, I could tell a story about what this hat did, technology with the microchip we're about Texas instruments, uh, with Jack Kilby and Bob Noyce at Intel co invent in Brown the same time. And it's a 20 year patent battle and a Nobel prize battle or whatever, but finally, um, Noyce calls, Kelby and says, look, let's just share the patent. And they do. And when Kilby gets the Nobel prize, because no, he said died. He said, if Noyce were alive, he'd be standing with me here. Is there, would you like to make a phone call and sort of bring all these people together at some point?

Jennifer Doudna ([53:41](#)):

Um, well it sounds lovely when you put it that way. Of course life is, life is always more complicated. Um, you know, first of all, I don't, I don't own any patents and, you know, they're all owned by my

university. And so it's my university. That's making decisions about what to do with intellectual property. They are the ones hiring lawyers and, you know, deciding how to pursue things. And the same is true. I would imagine at the Brode and MIT. So, you know, unfortunately I think if, if it were up to the scientists, it might be better, but, or maybe not

Walter Isaacson ([54:15](#)):

Some lawyers in the room, so you don't have to keep criticizing and blaming them. But, uh, well thank you. Let me open it up if I'm a way in the back firsthand to be seen.

Jennifer Doudna ([54:27](#)):

Yeah. I'm a recent high school graduate in 2017 from Berkeley high, actually. Um, and, um, so to give context for the question one, um, as a context in what you were talking about with, you want to young scientists to be like interested and excited about this, but there might be concerns about fairness and things like that. That really resonated with me. Secondly, um, I'm part of a community that has been historically oppressed through the idea of genetic inferiority and still to this day, there's many systematic, um, discriminations that we face. And so my question is how do we make sure, and is there any way that you can encourage us to allow our compassionate evolution and our evolution of our moral conscience to evolve at the same rate as our technology?

Walter Isaacson ([55:18](#)):

I know in your book, you talk about making it equitable, making it fair, making it so that it's non-discriminatory so why don't you end with that? Yeah,

Jennifer Doudna ([55:26](#)):

Well, I guess, I guess, you know, it's, it is a great question and it's something I think about a lot and I've actually been working with a group at Harvard medical school run by a wonderful professor, Tang, Wu, and, and it's called personal genetics education, PG ed. I encourage anyone. Who's interested to look it up [pga.org](#) and it's a nonprofit. And what they do is they actually outreach to groups that have been traditionally excluded from genetics, you know, understanding what is genetics all about? How does it affect me personally? Um, and I think what she's doing is very important because her really her mission is to be inclusive. I think the only way we can proceed is really to have an open community of people where we invite everyone to get involved. It can't be just the elites doing something and everybody else, you know, sort of trying to figure it out and figure out how it's affecting them. I think it really has to be

Speaker 1 ([56:24](#)):

A societal and global effort. And I think PGN is doing a great job, uh, of, of trying to do that outreach

Walter Isaacson ([56:30](#)):

In the history of science. There's been almost no examples of advances in technology and science outrunning, our moral processing power to deal with them could argue maybe the atom bomb, that few examples. This to me is one of the closest calls we're going to have in our lifetime. And I'm really glad that you're part of the discussion. Thank you. [inaudible]

Speaker 1 ([57:06](#)):

This transcript was exported on Oct 14, 2020 - view latest version [here](#).

Jennifer Doudna winner of the 2020 Nobel prize in chemistry with Emmanuel Chapin TA spoke with former Aspen Institute, president Walter Isaacson about the technological developments in gene editing and the unthinkable power to control evolution. Doudna is the Lee Kachin chancellor's chair in biomedical and health sciences at UC Berkeley. Her 2012 research on RNA molecules led to extraordinary insights in gene editing, CRISPR technology. She wrote a crack in creation, which Chronicles the story of her discovery and the responsibility that comes with rewriting genetic code. Walter Isaacson is a professor of history at Tulane. He's written biographies of Leonardo DaVinci, Steve jobs, and Albert Einstein. He's the author of the forthcoming book, the code breaker, Jennifer Doudna, gene editing, and the future of the human race. Their conversation was held in 2017 as part of the Aspen ideas festival. Make sure to subscribe to Aspen ideas, to go wherever you listen to podcasts, follow us on social media at Aspen ideas. Listen on our website, Aspen ideas.org, and sign up for our newsletter. This Encore show was produced by Marcy [inaudible] and Eliza Kostas with help from Shauna Lewis. Our music is by Wanderly I'm Trisha Johnson. Thanks for listening.

Speaker 1 ([58:36](#)):

This podcast episode is supported by Prudential. If you're at home thinking about your financial plan. So our we Prudential helps one in seven Americans with their financial needs. That's over 25 million people with over 90 years of investment experience, our thousands of financial professionals can help with secure video chat or on the phone. We make it easy for you with online tools e-signatures and no medical exam life insurance plan for better days, go to prudential.com or talk to an advisor.