

Beyond the Science: Where Are the Safeguards in Gene Editing?

Walter Isaacson: This is going to be pretty awesome because these three people are all deeply involved. Uh, in China, the National Academy of Medicine, the United States in the World Health Organization and deciding what's going to be done with germline, uh, genetic editing. By germline we mean a genetic added that done in the early stages of an embryo. So it affects not only the person being edited but all the reproductive genes and therefore it goes down and there's inherited either the changes or any mutations may made a, the other type of editing is called somatic. We're just done in a, uh, an adult or a born humans. Uh, and that only affects usually, uh, the person whom the edit is made, uh, for ethical and moral discussions. I think it's pretty obvious why the germ line question is the most difficult one. If we kind of screw it up in the human being, that's really bad for that human being, but it doesn't destroy both the planet and society.

Walter Isaacson: So we're going to mainly focus on germline editing. The first germ line edit of a human embryo was in 2015 but they were non viable embryos embryos that could not be implanted and be born after that. Um, our panel, our panelists, um, you are the person that writes, I'll, I'll do you for as Victor Zhao who's an old friend is I'm president of the National Academy of Medicine. And so they created the panel to try to figure it out. Um, and then, uh, dawn getting pay, is that the way to say it? Served by lunging k or some blogs zoo and he's on the Gwangju Academy of Medicine, but there's also involved with the Chinese Academy of Medicine and how to handle germline editing in the future. And all of us know Peggy Hamburg, the FDA commissioner for the Obama administration, old friend of the Aspen Institute, old friend of ours. And fortunately for us, she's been tasked to be the Cochair, I think of the World Health Organization that's opposed to try to develop policies of whether or not countries can do this. So let me start immediately with the [inaudible] because you as well as victim. We're at this amazing meeting and last November in Hong Kong when one of your fellow countrymen Jakey Hey. Dot. Hey, announced as soon to your surprise, but you can tell us that he had, uh, edited human embryos and that twins had been given birth with edited Germline, uh, of germline edits. Tell me about being in Hong Kong, hearing about that and as a Chinese official, what was your pride

Walter Isaacson: or Hora?

Duanqing Pei: So, uh, thank you. Wonderful having us here. Um, so, so victor initially inviting me to be part of the international summit back in 2015. And so that was all of the report. They were a crispy inject into a two per embryo with a long wire embryo. Waters have said. And then, uh, I think you're very courageously, I think Victor and also the National Academy of Sciences, also the Chinese Academy of Sciences and organize the summit and try to sort of organize and

then, uh, uh, set of the path forward how this particular technology should be deployed.

Walter Isaacson: You're talking, they'll not have to Dr. Hayes announcement,

Duanqing Pei: what does that thing, so that's sort of background I need to be to give you that background. But see in China as you know, this a law prohibiting Wa regulation prohibiting any modification of the embryo or chemists. And if you do, that's a gains. It's like a against very severe punishment. So back in 2015, everybody asking me what this ever happened in China may answer is absolutely no, there'll be in no way it is what we have in in China because they're very clear law prohibiting this happening because all the IVF clinic is, are licensed by the government, they're all operated by university, uh, credible hospitals. And if you ever do anything illegal like that and they will revoke your license, they will most likely put you in jail. Right? So that was my answer to the panelist back in 2015. So obviously when this come, hi, I thought this is unreal.

Walter Isaacson: First reaction. So you learn, you learn Hong Kong, Hey makes you dance with your day or you're horrified. Yeah,

Duanqing Pei: he's a, even to this day I would say, why would somebody do something like that? Could you against a vague, clear stipulation.

Walter Isaacson: So you said you would be arrested if you did it. Was he arrested? Is he under arrest now?

Duanqing Pei: I think he is on the investigation in in Chinese terms is I think the sit and restriction is because they have to investigate that by

Victor Dzau: law that they have to answer why you did this. So the Sciton it'll be under house arrest. I don't know. But Victor, I was going to describe what happened. We invited a doctor her not because we knew that he was doing this, but because he's done some nice work on primates and the night before. But that's the question over though. But not about just clarify. So this is very unusual because when, when we invite

Duanqing Pei: people to come to our meeting at typically based on their scientific publication he sent you a publication would be a set of results gone through peer review, ethical review, well done and then does some sort of everything we accepted. And then we invite people to come and, and I think he just call somebody. And then I had this and the committee debate and where did you have him speak or not speak actually,

Victor Dzau: but not to do with those. What do he announce? So the day before the meeting there was a public announcement that he did it. Yeah. And so you can imagine how we all scramble and decided whether he should be on the program or not. And four of us met with him at dinner to go over this data is willing to share the

data and look reasonably credible. This is in the hotel in Hong Kong. Exactly. With Robin level bed. Exactly right. No doubt. And I had flown over but the sea had heard. Exactly. So, um, then he said he checked on hotel to say, you know, there's a lot of threat that he caught threats through email, et cetera. And that he just simply went into silence. The second day of meeting he showed up. And so we actually presented this data. You remember this, there were about 250 press there and you know the press is about to storm the stage.

Victor Dzau: We have to hand control this and importantly, uh, we live that they were 1.8 million viewers. It's a big issue. So I think what really came out is his rationalization of doing this in a non life threatening disease, arguing that in fact he's following some of the guidance from various reports. Let me real quickly put you on the spot on that because it gets to the guidance that you were trying to get. For those who don't know, Dr had tried to do it with a gene that would allow a worth sapped or not to be as susceptible to HIV. In fact, Jen, leave aside the complexities of whether that would work, that was his rationale after 2015 when it was decided, hey, we have to go slow on this, and y'all were on the panel. You can put a whole lot of recommendations out there.

Walter Isaacson: There were a whole lot of tests, but you then say, let's have a moratorium until this guy ran through a, did you make a mistake in that calling for a moratorium? No, I don't think so. I mean I think that it's important to understand that what was said was it really shouldn't be done now because we're not ready. So if you wanted to find where not moratorium means, but we just say you need to meet all these conditions and you have to have a compelling medical reason. You can argue with HIV, which is treatable is a compelling medical reason. So I think that I'll report in 2017 we're still correct but maybe travel a little bit

Victor Dzau: of high level. The principals, which was left for interpretation and now I think where we need to do is to make sure that we get this nice, probably not gonna get to grab one more question, which is even if he had made it really strict and you said we have to have a moto bar toy me, he didn't have all these treatable disease. Do you think doctor hey would have just gone ahead and done it anyway? Probably there was a lot,

Margaret H: again speaking in China. No, no, no, no, no.

Duanqing Pei: Gonna actually the Chinese law is very clear. Yeah. So I, I used to give it a knowledge is here, you know, there's a lot could you to say you shouldn't kill anybody, right? Yeah. And uh, you see so many murders around anyway, so that's sort of the uh, the, the analogy I gave you, it is woe is somebody like the uni in the case of IVF, they're all very clearly regulated. So the, so the, I don't think he did it, you know, real license, IVF clinic.

Walter Isaacson: Let me get to begging. We giggered out on the Hong Kong announcement, but now your in charge or leave cochaired drug of the world trying to figure this out. The walls held by our mandate. Tell us what your mandate is.

Margaret H: We were asked by the, um, director general of the World Health Organization in response to these events and the recognition that there was this incredibly important technology that was evolving, that had huge positive implications for treating, curing, preventing disease, but also could be misapplied in serious ways, including as you noted in your introduction, changing the germline and, um, heritable conditions in permanent ways into the future. So he put together a group that's very diverse in terms of background, so scientists as well as regulatory experts, legal experts, um, and ethicists, um, from all around the world, um, to, uh, help, who think about how can we create a framework for global governance and oversight of this, um, sort of set of technologies. Because CRISPR Cas9, which we're talking about here isn't the only way of doing gene editing. It is sort of the most recent, um, and it will continue to evolve, um, probably with greater specificity and, um, and capability.

Margaret H: And we need to be able to think about, and not just in the more advanced scientifically, uh, countries like the U.S. and Europe and China. Um, but in terms of what it means for countries all around the world, so that the task to us was really to think about first what kinds of research and development, um, in this area is relevant that WHO needs to be thinking about. What kinds of standards and practices for responsible stewardship, biological science should we be drawing on in this instance? And then what are the, um, the attributes of effective governance frameworks and how can the different elements, um, be applied at an institutional level, an individual practice level, and then at a national and regional and global level, recognizing that there is no one answer to how we provide oversight of this kind of technology.

Walter Isaacson: Different countries will do it differently. Just like different countries have different feelings about GM genetically.

Margaret H: Absolutely. And different countries have different regulatory standards. You know, I think how countries approached the oversight of this kind of science and the regulatory, um, context in which it occurs reflects a lot the history of the country, the social values of the country, and also the scientific capabilities of the country. Um, but every, every country, every person on the earth has a stake in what happens in this realm of science. So I think who has a sense of real responsibility about playing a role, not in isolation but working with the broader science. Yep.

Walter Isaacson: Let me, is an example of the type of specificity that you hope to come out with to recommend to countries such as you should be able to do germline editing for clear a genetic disease but not for boom.

Margaret H: Well, I wouldn't be getting way out in front of our committee if I did that, but what I would say is that, um, we feel that it is, it is very, very important that our work be done. Uh, recognizing number one that there is going to be, dare I say, a Chinese menu of, um, of options that we will not, you know, say this is the absolute, um, framework and normative.

Walter Isaacson: Does he have any sanctions you could use on the country that says to heck with it. We're just going to allow this willy nilly and have a great tourist industry of people want to [inaudible]

Margaret H: I think one of the great questions is exactly that and you know, there it is very hard in many realms of science to absolutely enforce um, you know, the practice and standards. But there are different overlays of normative standards, the culture of science, the expectations of funders of science, the expectations of, of publishers of science that all help how fine tests are trained, how science is, is communicated in um, research conferences and within institutions. All of those things have to align to help support the best. Most.

Walter Isaacson: Well I know victor you want to get in but I have, Peggy was Bedo galesh I have one more quick thing for you. Yeah. Which is when you tried to, cause you've been in many administrations when you try to do that with nuclear weapons, you could have a start treaty and inf treaty and I'm non proliferation and you pretty much can assure that people aren't going to just make atom bombs and surprise you. Although it's happened in Pakistan and other places. Is this technology something that's even controllable?

Margaret H: Well, this isn't first of all unique in the life sciences in terms of complex science that can be used to do enormous good, but can also be misused and abused. And those of us that have spent part of our careers working on biological terrorism and biological weapons understand that very well. Um,

Walter Isaacson: do you know where most of the funding in the United States now it comes with CRISPR cas nine I don't Darpa the Defense Department close to weaponize it and defend against weapons.

Margaret H: Yeah, but so I think that we have to recognize that this is not like nuclear weapons where you can have guns and guards and padlocks to have a security regimen. This really involves the scientific community stepping up to the plate and taking responsibility as well as a set of governmental standards and enforcement mechanisms. And it's, I think one of the great challenges of our time. Right?

Victor Dzau: Well first I was going to ass Peggy. We Chinese restaurant

Victor Dzau: go to the column and the Column v Anymore. We have food desert. Right?

Victor Dzau: But no, I think the issue is getting to basics. So earlier we chatted when this area started, uh, the well meaning scientific community and metal community says how can we self regulate? But we know that in 1974 was a famous Sylmar conference that says recombinant DNA, how do we regulate and that have caused, allow us to move forward with all the great advances with a good governance structure. So this is how we got involved and we back involve again because we put out this 2017 report and I think that Peggy's got a big job ahead

of her because trying to get all the countries to agree, but I'll intention is to go back to the basics and asked about the scientific basis, that medical basis, the medical ethics, the uh, the, um, the, uh, regulatory environment framework and specific conditions. And how do you know when it's ready?

Walter Isaacson: Yeah. And to make it clear, what you're talking about is that you and Dr peg are on a separate group. That's the national academy of Medicine, United States and one in Britain, the one in China. You all were involved in your own separate yes. Task Force to figure out German. Well, genetic editing, should we do it? And you're more digging down into the science of it as a good kind of say something goes up. We have 27 academies, right? And organizations signed up, so there'll be one report is the international commission. That advisory committee is moving forward, but why you all have not be why I was up in Quebec. I told you all this right before for the Creswick conference last week and boom, Jennifer Doudna who helped co invent CRISPR cas nine to fung John who helped go invent the ways to put it in human cells.

Walter Isaacson: They bow all criticized you all by saying the Wia Joe is off doing his own thing on policy and all the national academies of medicine or doing something totally different. They should merge effort because the last time around we got two or three different reports and so nobody knew what to do. Why are you all, why don't you all merge right now and make it the aspen consented? We both work in the same place, but I'll put it this way, this time. There'll be one report from the scientific medical community that's important. There were several to be sure. And then we are coordinated with who have you listened to mandate. She's got a lot of work to do to how they get the countries involved. So I think I'll report can be quite fun durational to that deliberation because it's a big job

Margaret H: and that's the point is that, you know, there is no one group of a dozen people, two dozen people that can sit in a room and decide for all the world what needs to be done. This needs to be looked at in a multifaceted way and they're different parts of the puzzle that need to be put together into a coherent hole. They're digging much more deeply into the science than we are. We're thinking about it in the context of a need to provide some normative guidance and, and uh, oversight recommendations for countries that look very, very different and have different requirements. So we're gonna, we're working closely with them. We're going to build on what they do. We are timing actually our work so that we will finish after they do so that we can be fully informed. We need what they're doing to inform what we're doing. But if we tried to have one committee that took on all the aspects of this complicated task, we would just be so bogged down, we'd make no progress whatsoever. So it's going to be iterative. What the work we do is going to have to be further developed.

Walter Isaacson: Let, let me, let me get Doug to pay and then because I want to know what China is doing on the tongue. So [inaudible]

Duanqing Pei: sorry, just back to the 2017 report I was in Marvin, I think that's a very important document. The consensus report, uh, you laid out I think seven principles and the 10 different guidelines on how this should be proceed. So a win the Hong Kong and me came out, uh, I bought I think 100 copies with me. So this is this an eco nine. You guys don't ask me. I read this report. Uh, you know, we hand out, uh, those who report, I think it well received in Hong Kong. I bother a hundred copies. You translate translator. So now I have a chance to read that document into Chinese and just being published by the Chinese science report, a science Chinese science press with ambition from the National Academy of Sciences. So the, the dissemination of this analysis is critical. I think the, despite the criticism you heard from Quebec, but the once strong positive messages, you have a one single document, it pretty much heavy everything you need to set up a policy.

Walter Isaacson: Lovely. Then let's move on to the policy because we've talked, uh, uh, what the, what the athletes should be, do you to pay. Believe that germline editing of a human genome should be done for, let's start with trying to fix, assuming it's practical, simple, single edit, uh, maladies like Huntington's sickle cell, Tay Sachs.

Duanqing Pei: So, uh, I maybe, you know, my president of you wouldn't count two months by you, one of our conferences. I can tell you just like a conference like this in China organ that I asked the people, you know, uh, if there's a Saturday, this one, uh, would you, uh, sort of, uh, allow this to happen? And the consistency is actually pretty positive. They say, you know, this, if this is such a great technology, it can benefit our human health. Although without knowing too much, how, how much would that be? And actually the response probably about 60 or 70%. That's, that's sad. That's sad. But then still that's just, it's sort of like raise your hand that's very, uh, that can shift anywhere. Right? But that's just an initial reaction. But I don't know what they will say after they read the report,

Walter Isaacson: but I'm only interested in the women would say, because you're are one of the world decks barge.

Duanqing Pei: So I would say, I think in the future may be a hundred years from now. Uh, we understood and everybody agree in this room. This is a wonder, this is a technology. We should deploy it with caution. And it may happen a hundred years from now. When I see, I think we need, sorry with Victor, I just, you know, you know, ever since that report came out I think has been very positive and receiving in China and I think every graduate students not as reading that because this is sort of a, uh, a prototypic, you know, ethical, advanced technology, how that impacted,

Walter Isaacson: let me make clear, we all understand what you meant by a hundred years. It will be far, far sooner. We'll be able to do things like single gene mutations such as Huntington State Sachs, sickle cell, right in your mind.

Duanqing Pei: So you, my mind, so I give you one reference point. So gene therapy, the idea of gene therapy has been around for how many years? As far as I know, only recently FDA gave the okay or green for gene therapy to deploy it. So that I think with Crispr, maybe in next generation of Crispr I think may take a little longer than we think.

Walter Isaacson: But if in you were in charge in China, at least in Gwangju, would you allow CRISPR cas nine editing of Huntington's, it tastes act and others as soon as it was effective.

Duanqing Pei: Um, so as a scientist, yes, I would like very much and actives to be sort of, uh, go to the clinic as soon as we can, but then in China will have a very strict recommendation how this can be done. And without changing law, I don't think anybody, Andy Credible institution would be able to put their resources into that, uh, practice.

Victor Dzau: Well, I'm the physician. And yet when you see the sufferings are people with the lethal genetic diseases, very moving, I think that signs you to be put into the right way to enable, to enabled cures and saving lives. So my feeling is there's nothing intrinsically wrong, both technologies, how we use it. So I would hope that this will see the light of day soon as Susan, meaning five to 10 years. Well, I think this is what we need. Okay. We need to know how safe it is. And you know you do a single um, twins and you have no idea what long term effect is right. We need to be able to say, ah, is it ethically is supported by the society. But I think importantly as I said earlier, if you imagined that you have a new cell therapy or drug FDA, usually regulatory did you say, I'd know it's saving long term because you've got to do these things first. Toxicology, animal study. None of this existed at this point. I think once we get that to that stage and we convinced the safe and useful absolutely

Walter Isaacson: to see that it happen. Okay, let's try to keep this on the ethical issues as opposed to the regulatory and practical things because we know it takes five 10 failures, you know better than anybody. But I just want to press you, you have absolutely no hesitation that you could use it to fix diseases and you should,

Margaret H: I mean I think the science has to evolve still. We are not at the point where I think any of us would think it would be responsible to ever know. We understand that. But it's, and so I think we need to continue to advance the science and advanced the science in the context of a clear understanding of how do you ask and answer the questions of, of safety, efficacy, clinical utility, and the appropriate regulatory oversight and, and societal context for its implementation in youth. So we're not there yet,

Walter Isaacson: not on the safety and efficiency because that will come as it comes. But would you feel personally that we should edit the germline of human genomes to fix diseases once the efficiency and safety is decided?

Margaret H: I think that if we can treat and cure devastating diseases in a way that is safe and effective and is appropriately regulated, um, then we should, but we're not there yet. And we don't know what the future's gonna look like, but I think we have a responsibility to, to really deepen our understanding of what the science is, what the opportunities are, and how we can responsibly steward that scientific advance forward and ultimately what it will take to implement.

Walter Isaacson: But Victor, let us assume as I said, that we, the efficacy, safety, regulatory issues, Assad morally, my own opinion, your own opinion.

Victor Dzau: I think for lethal genetic

Victor Dzau: diseases that you can fix it. You can do in any other way. Yeah, I'd like to see that happen. Would you do it

Walter Isaacson: for other, how, how, how far would you push it? Would you do it for uh, somebody being born as dwarfism or deafness?

Victor Dzau: Yeah. So let me finish my point about diseases first. So you mentioned sickle cell, correct? There's another way to cure sickle cell. You can do bone marrow transplant and gene edit the stem cells. Right now there are ways to do inducible pluripotent stem cells. So all that, you don't have to go into the embryo, right? So once you get an embryo, you are going to change that make up forever. That's the important ethical issue.

Walter Isaacson: So you would draw a line that, that if there's any other possible way of doing it, including bone marrow transplant and plea preimplantation of embryos, you would not allow gene editing if there's any other possible way to do it.

Victor Dzau: I would say at this point, yes, yes. But I would argue at some point in the future, this technique used to be so effective and safe that we should think about really treating for generations. And yes.

Duanqing Pei: Good. Thanks. That was the principal when they are in the a consensus study. So you had to be absolutely no tentative. Therefore this may be permitted with brought us out a consent. That was a very accurate statement we made in that, in that, uh, contents of report. So, uh, I was talking to many of the leading Chinese colleagues back home. They say you're crazy. We never should edit that out with, you know, that's actually a very pervading thought too. Those are the wellness. Well, uh, respect your signed is the very, very, let's just say this is something we shouldn't read a touch. Okay.

Victor Dzau: Is there, that's the one actually gauge Boral that doctor pay has put his finger on that we shouldn't play God. Oh, absolutely. I think we as again, there's a physician, we're trying to save lives not to play God. So you kind of led us into this whole issue of enhancement. Right? And then would you edit to make your children brighter with a high Iq with greater, I think right now the prevailing

feeling is no, we can do that aside from the fact that we don't really know the science behind it because the genes, but luckily the sides this, so I think that is very clear from our report and almost ever waters as a integral part of that because you know, the genome has been evolved for so many years to be as perfect as it is.

Duanqing Pei: Amy, artificial temporary with a, you know, there are many, many consequences. We don't even know a well, we only need a, the do you know how many years ago and we're still studying the genome the way surprises us every day. So if you think you can, you know, do this something magical to happen as a biologist, I think I, I'm not that confident at this point.

Margaret H: You know, I think that there's also another really important ethical question here, which is part of what the, who committee really wants to take on, which is

Margaret H: that

Margaret H: there will be, you touched on it, uh, huge, um, attraction in certain countries and by certain people to exploit this evolving technology and what people believe about it, whether it's even true and the what, you know, medical tourism and a new term I learned recently ethical dumping, which means that in countries that have less stringent, um, legal regulatory frameworks that, you know, clinics will start to emerge where people are offering, um, blue on interventions that they actually can't deliver on, but there are be happy to um, uh, collect money for it. Maybe they actually will start to do some of this, that technology, you know, I think one of the challenges is very, it's increasingly accessible. It doesn't require, you know, really advanced training to be able, um, to do it. The materials you can get, you know, over the internet or in, you know, standard by online labs. Right. Um, so, you know, I think that one of the things that the who committee is going to try to look at not, you know, answering the question of how much will we play God, but how can we, um, reduce potential harm? How can we try to create enough transparency, understanding and systems so that, um, we can at least reduce the exploitation and the inappropriate, irresponsible science that can and likely will occur.

Victor Dzau: Yeah, I was just going to say he's already happened because, uh, many of you may know about mitochondrial disease. And so that my code conduit, a replacement savvy is what they call it, the three parent, uh, the approach. So the mother carries the mutation and about 200, there's some DNA in there. And so that's passed from generations onwards and now have caused, it's possible to take the nucleus of the mother and then implanted into an egg of, you know, a donor and then have the father virtualized a and therefore through IVF. And so we actually did a study on this to say

Margaret H: FDA commissioner and asked you to try that. Thank you. And we say, we're not ready.

Victor Dzau: Guess what? One of the, one of the famous person, virtual fertilizers, it's because you went to Mexico and Peru fondant. Sure.

Margaret H: But to show how bad that's what medical tourism, yeah. But, but to all countries are different. The UK went through a responsible process and decided that science was safe and, and it is legal in the UK too.

Victor Dzau: That's why I think you've got such a tough job trying to create a good global governance. Each country's so different. Before I open it up, I want to ask the very high level question, which has nothing to do with, is there other ways to do it or is it possible that he's a, but I'm gonna ask the question of if it could be done, what is wrong with enhancement? In other words, not just fixing a disease, but having a clinic to say, you want your kids to have blue eyes. Boom. They'll have blue eyes. You want them to have higher muscle mass. Boom. It'll happen. Why is that morally offensive?

Walter Isaacson: Dr. Beck?

Duanqing Pei: Uh Huh.

Walter Isaacson: Those of us who hire sat tutors, right?

Duanqing Pei: Yeah.

Duanqing Pei: Uh, wow. You know, this is very oppressive though, right? I mean everyone who can ask yourself, you know, uh, would you want to do that?

Walter Isaacson: Okay, let's do it. If you knew that your children or grandchildren could be edited to have certain personal enhancing trade safely, be taller, blue eyed, whatever, who would do it?

Victor Dzau: Hi Miss Realm. Surprising. Okay. That's about the same I told you about the Pew. The Pew Research Center did a big survey, American survey, 2018 and that's about it. 16% somewhere around there says yes. About 70 some percent says disease cure disease.

Walter Isaacson: Yeah. And about

Duanqing Pei: 40% of them are lying. Yeah. I wish to or rephrase the question. What has this ask? I think part of having offspring is to carry out the genes to the next generation. If you would alter that, the university you're not passing on your own teens, uh, on top of the line.

Walter Isaacson: Do you want me to do that? Interesting. Thank you. Do you have a answer there?

Margaret H: All I can say is that when I first heard the idea about sat tutors, I thought this is insane. Why would people do that? And then I realized that everybody else was doing.

Duanqing Pei: Yeah. And this is different though. Yeah, no, I mean

Margaret H: I just think that these are questions that us three are not particularly equipped to provide. You know, the most relevant insights. I think these are, are, you know, questions that as individuals and as a society we are going to have to grapple with. There's no doubt about it, but it's, you know, it's hard to be Glib about,

Victor Dzau: I think you'd need a bunch of Esther's synced up here. But I will answer this way. You know, when people ask for more Toria man, I've talked to Eric Lander, others quite a bit on this and they write in the sense that at this point of time, many genes are cleared traffic. That is, they can perform many different functions. You change one, you don't know what the consequence of the others. So that's true, right? Yeah. But that trip got it. Secondly is that, you know, we are, I mean through generations, you know, millions of years we've evolved naturally. It's the genetic pool that we have to now maintain. Yeah. And when we start manipulating this and forever change it because it will be passed on to generations. We have really upsetting and evolutionary system is a good or bad you can decipher. You send that to a doctor.

Walter Isaacson: Kay said too, which is Willie. I they got Doctor Carl and Francis Collins and Eric and said is that evolution has been doing this for 3.2 billion years. Why do we think five years after we've gotten the gun gene sequence we should change and you don't know the consequences of doing it and I'll give a quick answer of my own even though I'm not a problem and then open it up, which is the other problem I have both with sat sat tutors but wet a thousand fold with genetic engineering is that it probably is almost impossible to have it be totally equitable. Where a family in a village and you know India and the family and it was back of Stan and somebody from Scarsdale. We'll all have the equal ability to enhance the genes of their children and the brave new world problem. Everybody should go back and read.

Walter Isaacson: Huxley's brought is about creating a two tiered society of the genetically enhance the top one to five to 10% that could have taller children with more muscle mass. When I say taller and more muscle mass, that's not too far down the road. Cause we do that in animals. Now we're able to increase with a generic. Likewise, blue eyes is not the hardest thing and Iq is much, much harder. But you can imagine that we would create a society where all the advantages that the privilege now have, which I call the sh t tutor advantages would be not only multiplied by a thousand but literally encoded into our DNA. And so to me that's the big ethical problem set that we can do. Let me open it up. Yes sir. Walter, how are you editing regularity with the light right behind me. And can you expand a little bit famous, I'll, I'll repeat it, expand a little bit on

what you think the implications of Darpa funding all this CRISPR cas nine research. Oh yeah, I'd been, uh, I'd, I'd defer to the experts, but I do know a lot about what Darpa is doing. Please.

Margaret H: Well I'll, I'll start. I mean Darfur number one is very interested in cutting edge technologies and has supported a lot of work in a range of areas, but there also is a clear implication for enhancing the capabilities and safety of war fighters. You know, whether it's making them stronger and, and tougher. Um, yeah, making them resistant to certain infectious problems, um, or other toxic exposures, um, making them able to be alert longer. There, there are a lot of ideas about how you could use these technologies, um, to actually strengthen, um, you know, military capacity.

Victor Dzau: They just don't have to do an embryo law to Togo somatic so you can actually put in your muscle and right now for example, in Mu Duchenne's muscular dystrophy, pure able to do gene editing in the muscles and now moving into human therapy, all you need is about 15, 20% of those cells have been edited. You see significant improvement in function.

Walter Isaacson: So would a victor just said is actually important cause I've stressed during this panel germline editing, which everybody keeps pushing back and saying it's five, 10, 50 a hundred years on the and stuff. But we already have a genetic editing that's actually being done today. What do we effectively on Duchenne's muscular dystrophy who is from Columbus, Ohio at the children's hospital. And so earlier a great guy there who has just done it and I met the child that he saved. But um, oh yeah, there you are. Thank uh, the other taking on Darpa real quickly is, um, you could create genetically modified mosquitoes with a gene drive that would take the entire mosquito population and could wipe out whatever you wanted to in a village in North Korea if you decide to do it with mosquitoes rather than with a missile. Now to defend Darpa, wipe out malaria, but right.

Walter Isaacson: And you could wipe out malaria if you want it. And that is what the gene drive they're doing from the, from the broad institute is trying to gene drive mosquitoes to knock out malaria and to knock out, um, Zika, the Zika virus. All of which sounds good to me, but I remember reading Rachel Carson silent spring when they were knocking out problems like mosquito issues with DDT and all of a sudden the Pelicans in my home state disappeared. So I'd take, give you release genetically modified mosquitoes, either the knockout Zika or to attack somebody that's almost is frightening to me as a enhancing the muscle mass of a human

Audience Member: height. So you post a question, a lot of would you to be on the single gene, horrific diseases. Uh, but it wasn't clear to me at all as to when you would do that rather than just select the embryo that doesn't have the single gene mutation. It didn't come across clearly as to why you do that. Yeah. Secondly, how much do we, do we, how verified is it that the, that the gene edited twins

really exist? Uh, how, how far has that gone? What's happening to you at the moment? And we'll quickly

Walter Isaacson: you're explaining, but it's got that carb preimplantation genetic counseling and other days where you have a whole lot of embryos and you pick the one that doesn't have sickle cell or planted a couple of answers to that. One is in very few cases in that probably shouldn't drivers that can't be like with Huntington's or both parents have et cetera. The other question is what if it just becomes easier to do it through genetic editing? Then they have people produce a whole lot of embryos and it which is ec year, uh, which is playing God worse. I don't know. Do you have a no, I think this is exactly why the committees being formed to debate those issues. So I want to want to give you my own personal opinion. I think that's what a commission supposedly love come on now. But I think people who have argued that, yeah, you know, you can use PGD to in vitro fertilization, pick the embryo that doesn't carry the gene and do it. You know, that could be one of the conditions for, uh, for, uh, you know, gene editing, right? That you failed the whole process. [inaudible] alternatives. I don't know what that's going to be. Recommendations that debated the twins exist. So they were even

Duanqing Pei: three and a summit enough, uh, towels. When did that really happen? I think we even putting a statement, I need to be a independent verify. I think the information is not there yet. I think once the investigation by the authority, I think they're going to release that is a, is a duty for, for us to know. Definitely. We'll have to know.

Walter Isaacson: I feel like the good old days when I first came Nash or the Stephens hand was always the first one up by the way, talked to pay at that. A doctor. That meeting most of the set is a second pregnancy that's ongoing. And by the way, whether or not they exist, which I, I think it's probably likely they do. I mean it's a little hard to affect this old thing. The Russian doctor now says he's gonna do it. So I think we have to face the issues even if mean it's starting to happen one way or the other.

Walter Isaacson: Okay.

Audience Member: I have very simple question. Everybody seems to know how to do it. I don't know. What are the technical, what are the mechanics of identifying? Gene is little object because it's out of sand on it. This gene is the blue eyed and want as other, you know this gene is for blackheads. Ah. How do you actually identify? I went to view as best or that Victor Victor was on the human genome project or I would say it goes

Victor Dzau: like this. We now know enough about the sequences in the genome and the disease genes. This technique that a Downer and others develop, use what they call it, guide our ne just a piece of RNA that is fitting into that piece of the genetic disease that you have there. The mutations. Once you get the gardener

into work and find the sequence, it's like a missile finding a place. There's a set of enzymes quite into the nucleus. I would cut off precisely that sequence. And that's how you do it. And the gene is just brain while it goes into the nucleus and it was physically bind the DNA, that particular sequence it's guided to towards, and then with that you use an endonuclease to cut it and enzyme. It's quite amazing,

Walter Isaacson: uh, the nod who is doing delivery mechanisms in his own company. So,

Audience Member: so my question, Mike, my question relates to the two babies. Lulu Nana I believe are the gaps. There was some question about whether they exist. I mean, I think if we assume they exist, what is gonna happen to me?

Walter Isaacson: What is going to happen Dilullo and Nona if they exist.

Duanqing Pei: Oh, so, uh, so I think the, the proper authority has to, to decide, you know, what you, how to deal with them. And I think the summer committee made some recommendations already. Yeah. In terms of identity and how, you know, should Dav identified should not be in IB at five. I think part of a condition of

Victor Dzau: going forward, which is to be considered, I'll commission to say you have to know what happens to longterm fall of all these babies. Right? Cause when they grow up 50 years later, are there any surprise or whatever that has been part of a condition to move forward.

Walter Isaacson: But what about the privacy of that individual nature? I don't want my name out there. I'll say that hasn't been to do. Okay, but that raises an interesting question because of privacy of individuals and visuals not doesn't exist. It's the parents who's going to say yes. Walter, I'm just curious about why you picked this topic for your next book and I will after this panel and and, and when is the book going to be released? I don't know. It'll be a couple of years from now. I'm in no rush, but I picked it because I believe that the first half of the 20th century was totally defined. Perhaps in 1905 you get today with Einstein, three grade papers in a century of physics, I brought as everything from the atom bomb to space travel, the gps to microchips, the uh, quantum theory, second half of the 20th century with the invention of the computer, the microchip, and the network. Was it information technology centric? What we will grapple with for the first half of the 20th century is the life sciences technology. Many people, not people in this room that many by that just have no clue as to what it's all about. And so I'm doing a book because a, I want to have a clue of what it's about, but also perhaps allow other people to understand the issues we're discussing here.

Audience Member: Yes sir. There's one area that you haven't touched at all and I'm pleased to have more complicated than what you all have been talking about. That's the morality way. Look, you know, part of this country, especially those people were

still in the truck. The virality becomes the most important thing. They talked about how we deal with that issue where maybe it's not

Walter Isaacson: the morals of editing a gene. Why did we tried to deal with it? Um,

Margaret H: I mean if you want to, we don't want to go into politics, I know, but you know, the whole issue of how do you achieve the right balance between what is the responsible stewardship of science based on the scientific community and the public and politicians all trying to align. And I think we unfortunately have seen how sometimes politics and, uh, purely legislative approaches can lead to actually a chilling of the environment for science, a limiting of opportunity for important science to go forward. And I think that's something I'm very worried about at the present time. This, I think is, is an issue that is especially complicated cause it's, it's actually dealing with the very meaning of what it is to be human in many ways. And so I think this is one, you know, and I applaud you for wanting to take it on because this is one where the public really needs to be educated and we need to be able to have, you know, thoughtful, um, in depth conversations in communities and as a nation and around the world.

Victor Dzau: It's only the beginning, right? I, you know, that as you said, does the, the tech Keto, central of life sciences, all the things that we can do. So it's really important that we actually stay ahead and start thinking about the issues of ethics, governance, equity that you emphasize. I think there's a very big issue for society. I have to pay. Is that a word?

Duanqing Pei: It's a unique opportunity for all of us to work together because we all share one single genome. They all in all of us. I think this is a, a, a unified maybe. Uh, uh, can you light it us somehow?

Walter Isaacson: And as we talk about the ethics of doing this, it's easy about to talk about the ethics of why you would stop something. But we also have to keep in mind is Peggy reminded us that it may be unethical for us not to try to pursue the science if it makes us all healthier and better in the long run. I really want to thank you all. This was really good. Yeah.

Margaret H: [inaudible].