Alison Kodjak: Thanks everybody. It's so great to see such a full room here. Um, this is gonna be a really interesting conversation. I think it was in 2003 16 years ago that it was announced that the heat human genome had first been successfully mapped. There's huge fanfare and promise. Everyone thought new ways of curing disease were just around the corner. There have been certainly some advances, particularly in cancer care, but the potential gains are still largely theoretical. In the past few years, there've been major technological advances with gene sequencing and editing and with those advances come huge promise again and also major ethical questions and that's what we'll be talking about with our distinguished guests today. To my immediate left, we have Francis de Souza. He's the CEO of Illumina, which is what, which is the biggest gene sequencing company in the world. Before joining alumina, Francis was a bit of a serial entrepreneur.

Alison Kodjak: He started two tech companies, flash communications, which was an early instant messaging company and that was eventually bought by Microsoft. And then in logic, which was sold to Symantec, he joined Illumina in 2016 which was clearly a major shift from communications to biotech. Illumina has streamlined technology that can identify individual genetic variations and that collection of genetic data allows people to learn more about their own genetic material makeup and is a treasure for researchers seeking to seek cures and illnesses in the roots of our genes. To his left Vinod Jaskula-Ranga, he's a molecular biologist who trained at Johns Hopkins under the Nobel Prize winning researcher, Carol Greider. He's the founder and CEO of Hunterian Medicine, which is focused on the gene editing technique known as CRISPR, which has shown a huge amount of promise in recent years. And he's also studying virus based gene editing. And it's almost embarrassing to try to do an interview and introduction of the man to my far left, Walter Isaacson, but I'll offer some highlights. He's a legend. Two journalists like me, he was the chairman and CEO of CNN, the managing editor of Time magazine. He's written biographies of small figures in history like Leonardo Da Vinci, Steve Jobs, and Benjamin Franklin for five years. He was the president and CEO here at the Aspen Institute. He's a native of New Orleans and he's back home now as a professor at Tulane University and he's working on a book about gene editing. Each of the speakers here is going to make a short presentation and then we'll go to questions, so please welcome first Francis DeSouza

Speaker 2: [inaudible]

Francis deSouza: good afternoon. Genomics is a study o f the DNA of an organism, the instructions for cells to develop, survive and reproduce the instructions of life.

Francis deSouza: 16 years after the first human genome was sequenced, we stand at a transition from an era where groundbreaking genomic discoveries promised or evolution in health care to enter an era where we can harness the power of genomics to improve our health today, but there are some big obstacles. I'd like to share two

stories that highlight both the promise and the urgency of this transition. This is Ellis. When Ellis was 16 months old, she got an infection that she just couldn't shake and she kept getting weaker. At 19 months. Her parents took her to a neurologist. He said the symptoms would probably clear up on their own, but they didn't at 20 months. Another neurologist misdiagnosis here with Ghillean Baris Syndrome leading to months of ineffective treatment. Then when Ellis was 25 months old, her mother saw a girl on good morning America who had the same symptoms as Ellis.

Francis deSouza: That girl had been diagnosed using genomic sequencing. Ellis's mom went to her doctors and demanded the test. Sequencing provided an answer. Alice had riboflavin transporter deficiency type two the good news is that a treatment is available high dose vitamin B too, but it's not a cure and couldn't reverse the damage already done. This is Ellis at 27 months. If Ellis had been diagnosed at 19 months when she first saw the neurologist instead of a 25 months, she might not have lost the ability to walk or her hearing. She might not have lost the use of her arms and hands. If Ellis had been diagnosed at 19 months, she might not have difficulty swallowing and need to be fed via tube. The right information at the right time. Can make all the difference.

Francis deSouza: Around the same time, Ellis was searching for a diagnosis. A three year old girl arrived at the pediatric intensive care unit in San Francisco with sudden heart failure, kidney failure, and muscle problems. Her doctors suspected a mitochondrial disorder, which meant that there was nothing they could do. They told the family to prepare for the end, but the medical team had one last idea. Genomic sequencing. Now medical doesn't cover whole genome sequencing, so her doctor reached out to Illumina's philanthropic sequencing program. The sequencing results revealed that the girl had a kidney disease caused by a genetic mutation. She was only the seventh person in the world to be diagnosed with that disease. When the disease was known, the medical team was able to stabilize her and send her home within a couple of weeks. With a kidney transplant, you'll be able to live a normal healthy life. It's a miracle, but the miraculous part of this story isn't that whole genome sequencing was able to diagnose her.

Francis deSouza: Sequencing does that for about 50% of kids with undiagnosed genetic diseases that do the test. The miraculous part of this story was that the doctor knew about genomic testing and had the connections to get her the testing she needed. Access to care shouldn't be a miracle. Applying genomics in medical practice will change the diagnosis and treatment of almost all diseases, cancer, infectious disease, cardiovascular disease, mental illness. Genetic testing can be life changing, but it's just not getting to the people who need it. Approximately 350 million people have undiagnosed genetic diseases. Half are children like the girls I described. 30% of those children will not reach their fifth birthday today in the u s children with undiagnosed genetic disease go on a five to seven year diagnostic odyssey. On average. During that time they will be misdiagnosed two

to three times imposing a huge pain on the child, the family and the healthcare system.

Francis deSouza: Almost 10% of the families will go bankrupt, yet less than 1% of undiagnosed disease. Patients today received genomic testing. Cancer is the second leading cause of death globally today. Responsible for 9 million deaths in 2018 genomics can improve cancer risk, prediction detection, diagnosis, therapy development, therapy selection, and monitoring, helping Ben that cancer mortality curve and finally allowing us to cure some cancers. Yet less than 10% of cancer patients have their tumor sequenced. More than 95% of Americans have genetic variations that mean that they won't benefit or could suffer adverse effects from common medications. Adverse drug reactions caused more than a hundred thousand deaths in the U S and cost the healthcare system. $30 billion each year. A third are caused by gene drug interactions. Having your pharmacogenomic profiles mean that you could avoid taking a blood thinner that won't stop clots after a stent and anesthesia that could put you into sudden cardiac arrest or a staton that causes muscle toxicity.

Francis deSouza: Yet few health systems do pharmacogenomic profiles on their patients. Genomics has the potential to impact so many aspects of healthcare, but too few people are reaping the benefits. Bringing genomics to patients who need it will require action across the healthcare ecosystem. The genomics industry must innovate to make generic analysis faster, cheaper, and simpler. In the last two decades, sequencing a genome went from costing over $3 billion and taking 15 years to a thousand dollars in a single day and we're working on a $100 genome. Healthcare providers must be equipped to take advantage of genomics. A recent Blue Cross Blue Shield Association study found that even where there's coverage, genomic tests are often vastly underutilized in the u s around 250,000 children with undiagnosed diseases are covered for genomic testing. You only 1000 were prescribed in the last year. Physician education is a major issue. Many physicians went to medical school well before the first human genome was sequenced.

Francis deSouza: We also need clinical decision support systems that help doctors know when to order a genetic test and what to do with the information they get pairs. Ms Accelerate how they evaluate the impact genomics will have on patient outcomes and policymakers must ensure that individuals feel confident that accessing their genome will not harm them or their families. We need robust protection around privacy, consent and antidiscrimination and philanthropists should incorporate genomics into their global health agendas. We need a global genomes initiative. Like the Global Alliance for vaccines to make sure that genomics improves healthcare for all, not just the 1% this is Ellis today. She's a fighter. She can walk short distances and has a cochlear implant to help her here. She starts kindergarten in the fall, but even with vitamin B too, she's at risk for devastating setbacks and her family has started a cure. RTD Foundation to fund research into a cure.

Francis deSouza: I want each of you to leave here today thinking of Ellis thinking of where she and other children like her would be if sequencing was a standard of care for children with undiagnosed genetic diseases out. Each of you leave here today, curious about the impact genomics can have. Understand your genome and be ready to advocate for yourselves and your families. I want each of you to leave here today knowing that genomics is not part of some distant far out. Future genomics is here today. Genomics is changing lives today and it's up to all of us to make sure that everyone can benefit. Thank you.

Speaker 2: All right,

Jaskula-Ranga: so this, uh, this CRISPR thing is everywhere, right? Um, you know, got covers. Have a time and you know, the economist and it's TV, it's, it's in movies. It's, uh, you know, it's on documentaries. Uh, it's even been in court. It might end up on Supreme Court. Um, it, it's, it's everywhere. Um, it's, it's one of these things that is obviously, you know, it's on my mind a lot. Uh, I remember the time when I, you know, I wa I was hungry and I walked into my kitchen out my fridge and I was on the drawer inside my fridge. It's as CRISPR and, and, and, and years later, I still do not know what it is doing there. Um, so there is one exception. There's one critical exception, right? It's not in the clinic. So I'm going to tell you about Christmas. Biggest problem. Crisper's biggest problem is delivery. So the cells in our body contained about 3 billion, not about 3 billion base pairs of DNA. Uh, to put that in context, that would be 6 million pages of text. Uh, just a little bit longer than one of our panelists is average length biography.

Speaker 5: Um,

Jaskula-Ranga: now a single letter change in that 6 million pages. Right? Can cause a variety of genetic disorders. We know this right where they're at. They're called mutations. So right now we know about six to 7,000 of these, uh, uh, genetic diseases. And over 95% of these have no FDA approved treatments, uh, therapies and certainly, uh, no cures, right? We're talking about als and Huntington's and cystic fibrosis, muscular dystrophy, uh, types of Alzheimer's and Parkinson's. Um, so, so this is the, this is, uh, um, the, the universe, right? This is what we're hoping for. The promise of CRISPR. So for the last 50 years, uh, scientists have been working on ways to edit the genome. Um, all of these prior technologies were proteins that recognized a sequence and they were just not very good. Um, it would be like if you were trying to edit, uh, the genome with a hacksaw, um, or if we go back to, uh, you know, the, the biography and you know, one way to think about this, that biography is your biography, right? So now if we go back and we think about this, if there is a Typo in that biography in your biography, you don't want to rip out 500 pages to remove that Typo.

Jaskula-Ranga: So what happens is CRISPR comes along and CRISPR is a radically different CRISPR. The main conceptual difference between CRISPR and everything else is

that there's two components as a protein and an RNA. The protein you can think of a scissors and the RNA tells it where to go. Now, RNA is a very easy thing to change and so it is, it's one, it's easy, it is cheap. And this is one of the significant contribution contribution factors to why this technology has spread across the world. Um, the other being the crispers incredibly good. Um, [inaudible]. Now if we go back to our analogy, if we're trying to edit the genome, uh, you know, CRISPR is like a scalpel or you know, if we're looking at this bar, this of ours, and there's a single typo somewhere in the 6 million pages, imagine moving the cursor right next to that mutation that that's what CRISPR can do.

Jaskula-Ranga: Um, now w w with all of that, um, again, you know the context and I told you about the promise. We have all of these diseases. We have this technology. The question everybody should be asking is why aren't there widespread? There are purpuric developments for this technology. Um, and the answer is actually quite simple. It's delivery. Uh, but unfortunately the problem is quite hard, right? We need to get these two components into the cell and, and a protein and an RNA are very different, uh, biological entities. It is hard to get even one of those things by themselves into a cell.

Jaskula-Ranga: So then let me, let's ask a different question. Uh, why is it everywhere, right? It came out and said it's everywhere. Well, um, as it turns out, you know, if you want to do editing in cells in a dish, it's very easy to do, right? There's ways that you can get CRISPR into that cell, right? There's ways that we can form little pores in the membrane. We could zap it with the electricity. There's a whole, you know, a catalog of things that we can do to get this into the cell. Um, and the same goes for animals. The big problem is that we cannot do, we cannot zap a person, right? We cannot get, you know, get the stuff in there, right. Um, you know, putting them, strapping them into the chair or something. So, um, you know, based off of what I've told you, you'll have some, you probably already have some insight into what are the clinical applications, right?

Jaskula-Ranga: So if you can do editing in, in a dish, in a petri dish, right, like it's going on across the world, um, then from the clinical standpoint, you can imagine if you could take cells out of the body and do that editing and then put it back, then that would work. And that's exactly what we see, right? If you take bone marrow cells out of the body, you can do the editing and you can put that back, um, now and, and you know, the types of diseases that you know, that can address are things like sickle cell or Beta thalassemia. Um, uh, obviously car t and those kinds of things. A, uh, if for cancer, um, the, the, uh, the, the other thing that I would put in that category, right, is embryos. Um, now, uh, the one thing I would stress is that doing that, uh, type of editing in an embryo is not technically difficult.

Jaskula-Ranga: It is difficult to do it correctly. And we've seen that now. So the, the vast majority of diseases we are going to have to treat, we're going to have to get crisper into the cells in the body, right? We call this in Vivo, right? It's, it's in the

person. Now. Uh, there is a gold standard way of getting things into the body. Um, it's, it happens to be a, uh, a virus known as a Ab. It's a nonpathogenic virus. It has a long history of, uh, over 200 trials. It's been approved in Europe. It's been improved, uh, here by the FDA. And, um, you know, the, the, the drug that, uh, um, uh, the person who introduces was talking about is, is, is an, is an ab drug. Um, now there is one problem. There's one thing that's been known for a long time about V and Avi happens to be very small.

Jaskula-Ranga: So if you take these CRISPR components and you try to fit it into a v, you will find that the protein component ended of itself will occupy 85% of that payload. So you have one another little components, but you can't just stick that into the cell, right? You can't just put a gene into the cell. You need to also provide the instructions. We call these promoters, right? This is the thing that, uh, the cell recognizes and says, okay, I will make this gene. And if you take all of these components, all of these things that are necessary to reconstitute the CRISPR system within your cell, you will quickly find that you are above this packaging capacity. It's fundamentally a math problem.

Speaker 6: So, um,

Jaskula-Ranga: this is where I'm a, the company that I work with comes in. Uh, we work on a tiny little, uh, genetic control element, uh, for the scientists out there in the crowd. It is a, a bi-directional promoter. And what this allows us to do is to shrink the instructions component of, of what I was just describing to you. Um, now there's two remarkable features of this little, uh, genetic element. This, first of all, this genetic element exists in all of us. It's conserved throughout all the mammals. Um, and what it does inside of all of us is it makes a protein on one side and it makes an RNA on the other side. And now if you think about, if you work on CRISPR, you have a protein component and you give an RNA component and you know the sizes of all of those, and you added up and you find that it'll fit inside of a v.

Speaker 6: So, um,

Jaskula-Ranga: where does that put us? Well, um, now that we can get this in, this is basically a way to marry, uh, the CRISPR technology with a delivery vehicle, a something that can get to specific cells of your body and to do so, uh, both safely and effectively. Um, uh, and you know, and you know, we start off talking about, uh, you know, there's the six to 7,000 genetic disorders. Um, and you in sequencing technology has, uh, you know, catalog to hundreds of thousands of mutations that correspond those diseases.

Jaskula-Ranga: This is the universe of potential that we see

Speaker 2: [inaudible] which is

Walter Isaacson: combining pure curiosity ideas for their own sake. Can they talk, has a wonderful talk on the beauty of curiosity for curiosity's sake, along with how do we translate then into from ideas into actions that will benefit a mankind. And finally, how do we make that intersect with our deep values? CRISPR was first really studied by a graduate student named Francesco Mo Hiko, who was from a small town on the Mediterranean coast of Spain. And he kept looking at microbes that survived and really strange environments like high salt water ponds or high heat. And what he noticed in them was when he started sequencing the DNA, which was a lot harder to do back then because we didn't have the Lumino technology, he found that they will repeat in the DNA back and forth, repeat over and over again. And because he wasn't using Illumina technology, he assumed he had screwed up and he would never get his phd.

Walter Isaacson: But as he did it over and over again, he realized that these were peated sequences with spacers that seem to have DNA of other organisms kept reappearing. And eventually as he compared those spacer parts of the DNA between the repeated sequences, he noticed something amazing. It was the DNA from viruses that in the past had attacked those bacteria. They are, we know about all the great struggles on this planet, but the greatest of all struggles and all of the millennia of the planet earth has been that between bacteria and viruses, viruses try to get into the bacteria, take over the DNA and replicate themselves. That's what viruses do for a living and bacteria come up with incredibly beautiful and clever ways to stop it. And that's what CRISPR is, which was an acquired immune system to fight off viruses. Now, that was just something out of pure curiosity until a couple of people who worked for Dennis go realize that if they could save the bacteria, that was the culture for Cheeses and yogurt.

Walter Isaacson: That was a $3 billion prize. If they could pull it off. And so they started figuring out how does CRISPR work. This is fairly poor vass and rode off barren go uh, in France and in Wisconsin. They were collaborating at Dennis go food research facilities and they discovered eventually that the way CRISPR works is that it does as was described, combine a guide RNA with an enzyme, a piece of protein to just chop up the DNA of an invading virus. Now that was totally beautiful. It was a great advance for DNS go in the science and by doing that at the very end of their paper they do something that's a clever little line. It says it has not escaped our notice that that might be good at editing genes. I will confess something which some of you may be a little appalled out if you know of him, is that I spent a part of this afternoon talking to James Watson, the 90 something year old discover of the double helix.

Walter Isaacson: He, as you may recall, was in the big tent with us awhile back and he's been in trouble a whole lot these days because he keeps talking about things he probably shouldn't and doesn't know much about and shouldn't go onto including racial and other issues. But he's still very sharp when it comes to the double helix structure of DNA and the promise of CRISPR technology. And he

said that CRISPR technology is the most important advance for us since the discovery of the double helix nature of DNA. I don't know whether that was a arrogant or a humble statement on his art, but, uh, what we now have to face as he put it to me as Jennifer Doudna and others. I've just come from the CRISPR conference at, uh, in Quebec is now, besides figuring out the delivery mechanisms and figuring out the technology and off target, which may take us five, 10, 15 years figuring out the morals and ethics.

Walter Isaacson: So real quickly I'll just pose the ethical question. They mainly deal with germline editing, meaning editing in a a embryo so that whatever edits to the DNA you make go from generation to generation rather than what's called somatic editing, where you do it just in a person you can cure and do a lot just with doing it in a person as somatic at it. But if you're really want to take on something, it probably has to be in the germline. There are things that almost every one of you in this room would approve of even in the Germline, which they've called for a moratorium on because it's a mass, it's controversial. We're not ready yet, but if you could just take out that single mutation that causes Huntington's or tastes ax or a sickle cell or other things, you'd probably say, yes, we should do that.

Walter Isaacson: We should take that out. And if somebody were going to be incredibly small, you might say, okay, let's fix it. So there'll a normal height and then you start getting into the gray areas of people who are like me, slightly short and why don't I add five or six feet or another 20 IQ points. This is way down the road, but it's still something we have to start wrestling with that now many people say we should use CRISPR to cure diseases but not doing enhancements. Nice thing to say. First of all though, there's that blurry line between what's an enhancement versus what is killing something, whether it be obesity or shortness or for that matter, low IQ. Somebody could argue it one way or the other. The more difficult question is why not enhancement? Why not make a whole species smarter? Make it more a whole species, more resistant to any problems they may have.

Walter Isaacson: And I guess one of the big questions there is, the problem with enhancement is that like everything else in healthcare, it won't be equally done. So I'll end with the brave new world problem. It's what Huxley wrote about in that book, which is if you have genetic editing, the greatest fear would be creating two types of people. On this planet, those in the top 1% or 10% who are in jet, genetically and hands and those who aren't. So like every other topic you're discussing here at Aspen ideas, health is a question, not just of the more reality but the equity of it. Thank you all.

Alison Kodjak: Okay, well Walter, get the Mike De, um, I'm gonna build on that issue of ethics and actually go to a, a sort of lower level question. We're going to talk about the sequencing when people you know, are very concerned about what happens when you start editing genes. And, and Walter laid out those, those questions

very clearly. But what happens when you tell people their genetic makeup but there's nothing you can do about it. Can you talk a little bit about the ethics there because that's more real right now.

Francis deSouza: Yeah. And you can imagine we spent a lot of time thinking about, uh, what to do in that case. And there are a number of questions. One is, you know, it's really important, uh, that, you know, people understand what they're getting. Um, and so some of our customers are in the direct to consumer space where they will do consumer genomics and they'll publish reports back to consumers. Um, and they now do work with the FDA to make sure that every report they give back is understandable in terms of what it means that you have an elevated risk of x. It doesn't mean you're going to get x. Um, and I personally spent time talking to people saying, well, what, what do you, you know, what happens when you do this test? And, and I also spend time talking to parents who checked the health of their babies to say, look, what do you do when you find that you have that?

Francis deSouza: In a lot of cases, you, people will say things like, one, at least it's the end of a diagnostic odyssey in some cases. So if you talk about the kids that are on that five to seven year diagnostic odyssey, they'll say, look at this. I know what it is and I'm not going to look anymore and I'm not going to do all these other tests. In some cases it allows parents to be better prepared, you know, saying, okay, we can anticipate what's going to happen to our child because we can understand the trajectory of this disease. Um, in some cases that allows them to qualify for benefits to say they now have a diagnosis and so they can get special needs, you know, funding, they can get qualification in their school. And so you know that that comes into play as well. There's still some people who will worry and some people who will say, look, I just don't want to know because what's the point of me knowing that I'm going to have early onset Alzheimer's, for example, if there's nothing I can do. And I think that's a valid choice too. I think if that's how people feel they shouldn't go get that test. So while the read journal is Tra trade and information we sort of live by, the more knowledge is better than people can work it out in the marketplace of ideas. What are your thoughts about the idea of information about your own genetic makeup that you can't do anything about?

Walter Isaacson: Well, I'd say it was a very good answer because you can always do something about it, including resign yourself to what's going to happen and prepare yourself for it. But also there's, so, I mean that is a smaller case than, than the number of cases in which there will be some treatment or some amelioration that can occur if as a you said, you know, it's a kidney problem or you know, it, some other problem. Um, so I'm perfectly willing for people to say, don't test me. I don't want to know what the cause of this is or don't sequence my genome because I'm afraid you might tell me that I will be susceptible to a type of cancer or I will be susceptible to Alzheimer's. And I just don't want to know that. But the good thing about, you know, our society is we allow people to

make that decision of whether to keep themselves in the dark about certain things or to know it.

Walter Isaacson: And the bigger problem, and we talked about it this afternoon, is people who don't understand how important it would be to do large scale genetic sequencing. And Derek Lander has really been pushing this idea of not only doing it but being part of something called calc me. Yeah. So that if you've got a bad problem and maybe even an unfixable, you do your sequencing and you put it into a database and you sign away some of your HIPAA privacy things and you'd say, count me in. I want my genomic sequencing to be just like, I want to be an organ donor. Just like I want to be a blood donor. I want to be a genome donor so that other people can better understand how to do things. Okay.

Alison Kodjak: Did He, when we talk about CRISPR, it's sort of an elegant

Alison Kodjak: solution or hopefully will become an elegant solution to genetic diseases where we can identify a single gene that's problem. But there are a lot of diseases out there where there are a variety of genes that are contributing and maybe we are not fully certain. Um, what exactly those are. Can you talk about the complexity of dealing with those kinds of issues? Yes.

Jaskula-Ranga: So, I mean, I think a, you know, as you highlight it, things where there are multi genes involved in, in, in complex mutations are going to be, uh, difficult to, um, now, you know, some of those things are going to be figured out by sequencing that and it's just a matter of time and getting enough people and, and, and we will figure out what those are. But to fix it, it is complicated, right? I mean, it, you have to do multiple things. If you don't, I tend to focus in on the six to 7,000 that we know of because, you know, from planning, right? Yeah. It's plenty in. And I also think a lot of, um, you know, some of the disorders that you might historical think of that are, you know, poly genic, maybe diabetes or hypertension or whatever, right. Are the ones where, where traditional biopharmaceutical companies have focused in on.

Jaskula-Ranga: Right? So, so there's, there's been, you know, treatments and, and there's drugs or something, uh, or at least efforts, um, probably because of, you know, the, the size of, uh, the patient population. Um, so, you know, I tend to think of this, uh, technology as, uh, [inaudible] a lot of people in the field uses term. It's, it's incredibly democratizing. Um, you know, for people who are part of a very small, uh, population, um, and you know, if, if there is a site, if there's a way that CRISPR can do it, it's largely random. Um, and uh, and you know, that's, that's what I think drives the, um, you know, the choice of disease. It's a technical,

Alison Kodjak: okay. I'd like to bring in, uh, our audience to the discussion. So if you have a question, please raise your hand and wait for a microphone. The microphone is far away right now for this gentleman right here in the front who asking does he

see this as a rule? We have [inaudible] call on the person furthest away from the microphone, but we have somebody running on those. We'll get at your size. If you could, uh, if you could, uh, right here.

Speaker 2: Thank you.

Speaker 10: First of all, thank you all for your time. My name is [inaudible]. I work out of Harvard's innovation labs. I run a sperm freezing company called legacy. Part of the reason we do this is because as men get older, the quality of the sperm declines in part due to the introduction of genetic mutations in their sperm. One of the topics we talk a lot about is the decoupling of sex and reproduction

Walter Isaacson: as couples increasingly turn towards IVF. And I'm curious to hear your thoughts on the introduction of CRISPR, uh, into the future of reproduction. You know, one interesting topic is when you do things like find a problem, especially Huntington's, which if you look up, it's just a horrible disease and you don't know you really have it until you're 35 or 40 and may have already had children and it's a math. The question is there other ways to do it? Then editing, you can even have donor sperm, donor egg, etc. And a lot of the ethicists, I was just reading a book by Francois Balers says, and that's bad because our society unfairly and without real rationality, people prefer to have children that are genetically related to them than children that aren't genetically related to them. And I think that's not a, um, is that a statement that I think is sustainable because ever since the first virus took over, the first, uh, is cell of a bacteria.

Walter Isaacson: The whole point of all evolution has been to evolve, is been to have your genetic material survived. So I think it's very hard to take that out of us. I know that doesn't address the whole question you answered, but it gives me an opportunity to say, we used to think IVF was achy. We used to worry about, uh, Louise Brown. We put the first, um, you know, baby, uh, clown, uh, uh, Dolly the sheep. But I think we become more accepting of these things, but I do not think we'll become more accepting of we want our children to have somebody else's DNA instead of ours. And I say that with all respect to people have foster children and adopted children, everything else, it's still a human drive that I think will be difficult not to have in the future. Yeah. That's why you call the company legacy.

Speaker 8: We have a question way in the back. I didn't mean that. Sorry. It's all probably up. No, no, no. That's good.

Speaker 11: Hi. Uh, Illumina has a kind of like B2B app marketplaces and then you spun out helix a few years ago, which is uh, analogous to the iPhone and I guess more like B to c type of kind of an app, a model. Where do you see that going? Kind of what do you see as the trigger to get that hockey puck growth when it comes to enabling and unlocking all this kind of third party kind of software innovation on top of this data?

Francis deSouza: Yeah, sure. You know, one of the things about genomics is it is, it's a foundational technology that has applications in literally hundreds of domains. So from, from cancer, reproductive health, you know, mental health all the way to forensics, like CSI to data storage to, to, to if we have a company that's using our tools in oil and gas exploration for example. And so it became very clear to us that we weren't going to be able to create all those hundreds of applications. And so we actively have a number of things we do to catalyze these different industries. But not create the applications ourselves. We spin out some technologies like grail for cancer screening, like for forensics. We spent out Virgin Helix for consumer. Uh, we also have an accelerator program where we bring in entrepreneurs every six months, teams of five, and we give them free sequencing to launch genomics companies. We have Illumina ventures a to $230 million fund to fund startups. So we want to be very active in catalyzing any application that uses sequencing and make sure that if the natural VC ecosystem isn't funding it, because we're closer to it, we may see it closer than the people. And so we want to make sure that those still happen

Speaker 2: right here.

Speaker 8: So I'll set the question in the context. Is it morally incorrect to not vaccinate children? Um, so we're asking is it morally correct to use some of these tools, but could you see a future state, maybe 10, 20 years down the road where it might be looked at as backwards for a couple to naturally procreate when they would put that child at risk of having disease versus creating designer children that would be at lower risk? I really hope not. Um, you know, I want to make sure that, you know, couples have the options and that if they want to go down or their an IVF path or an adoption path, they should absolutely be able to do it. But I hope that as far as the, I can see, you know, people can still have children the normal way too. And so that's my personal wish.

Walter Isaacson: Let me give you a Michael Sandel thought experiment, which is a couple that is congenitally deaf. Something that is basically a, um, hereditary disease that can, you know, be cured. Uh, Hal is about to have a child and the child is going to be born deaf and they decide to do some genetic engineering, uh, you know, they agree so that they would have a hearing enabled child. We would all think, okay, that makes sense. And it's a good application of the genetic editing technology. Now put your mind around a uh, couple that is deaf that really believes that that's part of the essence of who they are and that signing as part of a society and that we shouldn't lose that. And they're told that they're about to have a child that's going to be hearing enabled and they asked the doctor to edit it to make sure that it born genetically def the way they are. Should the doctor do that? By the way, I'm not going to answer that question, but it's a thought experiment that goes down the road that you've asked.

Speaker 8: Nobody's going to answer that question. I mean, only they have time for maybe two more. I had two questions. I'm just wondering, are those your DNA socks? No, but kind of more serious doubts. I was recently Helsinki and

Speaker 12: meeting with Mark Daley, who is a researcher on part of the Fin Gen project. So this is a national project where they have a network of biobanks across the country and they've collected I think 200 over 200,000 samples with a goal of 500,000 with the idea of how are they going to, as a population improve health. And they're very specifically focused on the rare disease community. But I'm curious from the standpoint of where you are in thinking about this on the, the ethics, the morality of it as it becomes a population initiative. What are your thoughts about that?

Francis deSouza: Well, I think Walter sort of touched on a really important point that you know, the success, our success in the future is going to depend on us. You know, sequencing very, very large cohorts that we've got sort of the easy understanding of the monogenic diseases where, you know, one gene, one disease, but most complex diseases, you know, require the interplay, as you said, of many, many, many genes. And the only way we're going to get to understand that is if we sequence huge cohorts like in the millions and tens of millions. And then if we sequence in a single cell level, tens of millions of cells to understand the difference in the cells in our own body. And you get there through these population initiatives in the UK really pioneered this in 2012 2013 with the genomics England project, the first ever population sequencing project of 100,000 genomes. And now we're tracking over 50 population sequencing initiatives around the world.

Francis deSouza: Uh, and some are in developed countries like the u s has all of us, the UK is doing, one, France is doing on Australia is doing one, but some are in developing countries like Bangladesh for example. And I think that's hugely exciting from a discovery perspective. And the interesting thing too is that most of these now are driven out of the healthcare system. So the next phase of Gel in the UK is driven out of the NHS. And so what they're doing is they're actually diagnosing kids with genetic diseases, changing therapy for people who have cancer. And along the way they get the research for free because you're getting these giant databases, as Walter said, that people want to contribute because they actually want treatments for their conditions. So I think population sequencing is something that we're going to see over the next few years and it's going to be essential to has understanding genomics.

Alison Kodjak: Okay. Well we are actually out of time, so that works pretty well. I want to thank

Alison Kodjak: our three speakers today, this event was

Alison Kodjak: fantastic. Walter Isaacson, Vinod Jaskula-Ranga, France DeSouza. Thanks so much for being here.