Notes and transcript for Storyville *The Gene Revolution: Changing Human Nature (2020)*

Introductory Sequence: Professor Robert Sinsheimer addresses the California Institute of Technology in October 1966.

SINSHEIMER: *Dr Bonner, fellow prophets and, er...* [*LAUGHTER] ..ladies and gentlemen. This summer, I travelled through northern Arizona and southern Utah. In this land, the rivers have carved great gorges. And on the sheer cliffs of these gorges, one can read a billion years of the history of the Earth. On that immense scale of what represents the passage of perhaps 100,000 years, all of man's recorded history took place as an inch was deposited, all of organized science, a millimetre, all we know genetics, a few tens of microns.*

[Title sequence: THE GENE REVOLUTION Changing Human Nature]

SINSHEIMER: *The dramatic advances of the past few decades have led to the discovery of DNA, and to the decipherment of the universal hereditary code, the age-old language of the living cell. And with this understanding will come the control of processes that have known only the mindless discipline of natural selection for two billion years.*

SINSHEIMER: *And now the impact of science will strike straight home, for the biological world includes us. We will surely come to the time when men will have the power to alter, specifically and consciously, his very genes. This will be a new event in the universe. The prospect is, to me, awesome in its potential for deliverance, or equally for disaster.*

Chapter 1: Needle in a haystack (starts at 02:30)

DAVID SANCHEZ (Sickle cell patient): *Here we go, that's better.*

NURSE: *You want to squeeze my hand? Relax your shoulders. Relax your toes.*

SANCHEZ: *Being in the hospital isn't scary to me. Having a certain NEW problem isn't scary to me any more, because it's happened so many times.*

SANCHEZ: *I don't know, my blood just does not like me very much, I guess. Your red cells are supposed to be round and have oxygen in them. Mine are half—moon shaped, sickle shaped, which is why it's called sickle cell. So I don't get the same amount of oxygen.*

DOCTOR: *I always say, like oil change, you know, you drain the dirty out,*
and put clean in. Yeah, so he just needs a tune up every four to six weeks, yeah. Uh-huh, yeah. OK? OK. Put this on.
Take a deep breath and hold.
OK.
You OK, David? Uh-huh.

DOLORES SANCHEZ *(David's Grandmother): He used to tell me, "Don't cry, Nana. "Why are you crying?" I said, "You know, I love you, baby." He goes, "Don't worry about it." He says, "If I lose my life," he goes, "You'll see me again." And I thought, "This child has more strength and faith than I do."*

MATT PORTEUS (Sickle cell research, Stanford University): *It's often called the first molecular disease. It's caused by a single change in the DNA sequence.*
It's the letter A changed to a letter T.

INTERVIEWER: *That's it?*

PORTEUS: *That's it.*

TSHAKA CUNNINGHAM (Minority Coalition for Precision Medicine): *That mutation causes a kink in the protein that prevents it from folding properly. If your folding structure of a protein is disrupted, now that protein can't function. It causes the red blood cell to really collapse.*

PORTEUS: *It becomes very stiff and it can't squeeze through. And you're not able to get red blood cells to the tissues where they can deliver oxygen. And if you block the ability of oxygen to get to those tissues, those tissues won't work well and they'll get damaged.*

PORTEUS: *In Africa, the life expectancy for somebody with sickle cell disease is on the order of five to eight years of age. In the US, it's the early to mid 40s.*

INTERVIEWER: *What do you say to a kid that their life is going to be?*

PORTEUS: We avoid it. We avoid that conver...

INTERVIEWER: *Really?*

PORTEUS: *It's not a conversation we're good at having.*

DOLORES SANCHEZ: *Makes me very nervous. David can go from crazy teenager – joking, , jumping around – to a foetal position on his knees.*

DAVID SANCHEZ: *It's like pulsing. This hurts! "You're having a sickle-cell crisis!" Like, I can have, like, a little pain crisis where it really doesn't count. and then I ran have something really bad. But I'm not just going to not play basketball. You can't just not play basketball.*

DOCTOR: *This is David's old red blood cells, we're going to save for research.*

NURSE: *How do you sing it?*

GIRL: *OK.*
 # Rain, rain, go away
 # Come again another... #

CUNNINGHAM: *It's a genetic disorder. So in order to cure a genetic disorder, you literally have to go in and fix the gene.*

PORTEUS: *We just didn't have the tools to make that single letter change in a precise fashion.*

INTERVIEWER: *Even one letter?*

PORTEUS: *Especially one letter.*

ARCHIVE TELEVISION PROGRAMME: *Deoxyribonucleic acid – or DNA for short – is the material that's the basis of life. Each living thing has its unique DNA that determines what that living thing will be – plant or animal, man or muskrat.*

PAUL BERG (Biochemist, Nobel Laureate, [Old interview, 1975?]): *If we understood the structure of genes, the structure of chromosomes and how genes work, then we might better be able to understand and treat genetic diseases which occur in humans.*

ALTO CHARO (Bioethicist, University of Wisconsin-Madision): *The work that Paul Berg did, that was probably the beginning. This dream of gene therapy was born out of those 1970s*

experiments, and we were still very far away from it, but you'll see people talking about that hope right away.

ARCHIVE DOCUMENTARY [1986]: *The hope is that the isolation of the gene will lead to treatment of people with muscular dystrophy.*

ARCHIVE DOCUMENTARY [1999]: *Scientists are working on genetic cures for diseases such as Alzheimer's and Parkinson's.*

A-T-A-G. ..

HANK GREELY (Bioethicist, Stanford University): *The idea behind gene therapy is really simple. Add in a copy of the gene that works, then they'll make the protein that works and then they won't be sick any more. But the devil, as is often the case, is in the details.*

WAYNE MILLER [Archive footage]: *Right now we have the ability to identify the gene, to isolate it, but the ability to put it where we want it is still a long ways away.*

BERNARD DAVIS (Harvard Medical School) [Archive footage]: *If you put a gene into a cell, you cannot tell exactly where that gene is going to enter the cell's chromosome.*

FYODOR URNOV (Innovative Genomics Institute): *Conventional gene therapy is an essentially random process. So imagine taking this century—long narrative, which is human DNA, which is a very, very long text, and taking one paragraph and just sticking it somewhere random. The change you are creating is not a controlled one.*

[2000 Footage, in French, of clinical trial conducted in Paris by Dr Alain Fischer Subtitles: "Professor Alain Fischer's team is the first in the world to cure a human being using gene therapy. This method has been one of medicine's best hopes for the past fifteen years.]

URNOV: *There was a clinical trial that was done in France. This was for really sick children. I want to be clear, this was for children who would have died otherwise.*

[Journal headline from 3rd October 2002 "'Miracle' gene therapy trial halted]

URNOV: *Four of these children developed cancer. One of them died. The gene went into the wrong place. Because it's a random process, and by chance it went into the wrong place, and that random event caused cancer.*

DAVID BALTIMORE (Microbiologist, Nobel Laureate): *You know, you always think that what you know is going to get a little better, a little better, a little better and soon be there. And what we knew how to do wasn't getting a whole lot better, it was getting a little bit better. The technology was just too clumsy to actually use it with human beings.*

URNOV: *It became very, very clear to us that we are at the foot of a very tall mountain, and we may not even have the right mountaineering gear.*

URNOV: *I worked at this company called Sangamo Biosciences. We decided to figure out a way to change human genes in a precise fashion. You know, this would be like word processors for your DNA.*

URNOV: *This will get technical, but good technical. DNA breaks all the time. You go get a dental X-ray, a technician points this thing at your face and the X-rays actually hit your DNA and they physically create a break, so that the familiar double helix of DNA physically goes... HE MAKES POPPING NOISE… The good news is the cell has its own machine to fixing breaks.*

URNOV: *Inside ourselves, there are two identical DNA molecules lying side-by-side, literally side-by-side. If one is broken, it can say to its sister – and that, in fact, is the technical term, the sister – "Hey sis, I'm sorry, I've had a break. I'm wondering if I can copy the missing genetic information?" And the sister goes, "Yeah."*

[Animation of homology-directed repair]

URNOV: *Done.*
Chromosome broken,
awaits sounds of strands pairing,
preserving life's thread.
This really... There's really a haiku about homology-directed repair.
OFF-CAMERA LAUGHTER

URNOV: *Why is that useful? So it's useful because if you can cut a gene inside a cell, so if you can create a break at a place of interest, then you can change that gene. You fool the cell. Give it a separate piece of DNA that you have made. A piece of DNA which is identical to the chromosome that you're cutting, Except for the change that you wish to make. And Mother Nature will not know she's being fooled. She will repair the break using this piece of DNA you provided as a template. And so whatever change you've brought in will then go into the chromosome.*

FENG ZHANG (Bioengineer, The Broad Institute): You can think of it like a cursor in Microsoft Word. In Word, if you have a document, where you edit first, you have to place the cursor there. In DNA, wherever you make a cut is the equivalent of a cursor in this word processor of the genome. That's where you can type in a new word.

JENNIFER DOUDNA (Biochemist, UC Berkeley): *So if you wanted to use that capability to engineer the genome, the challenge was to introduce breaks in the DNA at places where you wanted to alter the code.*

URNOV: *How are we going to do that? We need something that cuts only one gene out of the, you know, 25,000 that we have.*

BALTIMORE: *There were just such serious blocks in the way, so it looked like it was going to be along road. And that's what changed, and that came sort of overnight.*

DOLORES SANCHEZ: *David's doctor told me, "Just hold on. There's something coming."*

ANTONIO REGALADO (Reporter, MIT Technology Review): *When I first heard about it, I was at a conference in New York, and it was a very strange conference of futurists. It was put on by a Russian guy whose ambition is to download his brain and become an android who lives forever.*

ARCHIVE FOOTAGE: In this future, people will be young, beautiful. They will have multiple bodies, not only just one.

REGALADO: But they had a lot of good people there, including an important geneticist from Harvard, George Church. And I remember him saying, "Remember this word, CRISPR." C-R-I-S-P-R

GEORGE CHURCH (Archive footage): It's like, you know, in the Graduate, plastics — remember the word, CRISPR. This is going to allow human genome engineering on an unprecedented scale.

[Montage of Tweets about CRISPR]

INTERVIEWER: *How old is CRISPR?*

JILL BANFIELD (Microbiologist, UC Berkeley): *Oh, in terms of millions of years?*

INTERVIEWER: *Yeah.*

BANFIELD: *Ah, I mean, probably...billions.*

Chapter 2: CRISPR (starts at 15:00)

FRANCISCO MOJICA (Microbiologist, University of Alicante): *When you are a student, you think everything is known. But there are places where no one else looked. Well, I'll tell you the story that I know.*

MOJICA: *The organism I was working with is called Haloferax mediterranei. This microorganism's very peculiar. They only live in environments where the salinity is about tenfold that of the seawater. These tiny organisms are… how you say?... so clever. Clever because of the evolution, of course.*

BANFIELD: *Well I'll tell you the story that I know. Microbial genome sequencing started sometime in the 1990s.*

INTERVIEWER: *What does that mean?*

BANFIELD: *See, OK, so unravelling the DNA code of organisms of life is a relatively recent part of biology. And in the late 1990s, people started to turn their attention to the sequencing of microbial genomes.*

BANFIELD: *They're amazingly highly—evolved entities that just chose a different way of surviving in the world than the cells that became us.*

[Footage of Mojica reading ("base calling") an old-fashioned sequencing gel ladder of DNA]

MOJICA: *We saw a very peculiar pattern. These very short fragments of DNA. They repeated many times. And they were regularly interspaced. Eventually we realised these peculiar sequences, they were present in many different microorganisms. But they didn't have really any name. CRISPR came to my mind just thinking about the main features: Clustered regularly interspaced short palindromic repeats.*

URNOV: *There really wasn't much precedent for anything like this in the DNA of living things. And when you see something unusual, you automatically assume that it's interesting, that's just how science works.*

BANFIELD: *CRISPR is actually clustered regularly interspaced palindromic repeats, and so it's actually named for the repeats. But what was really interesting were these sequences in between, that were completely enigmatic.*

UNIDENTIFIED MALE, OFF-CAMERA: *Spacers.*

BANFIELD: *And each spacer was different. Never seen anything like this before.*

MOJICA: Where the hell come these sequences from?

REGALADO: I've my own way of kind of telling this story in short form, is I show this article from 2007, right? Five years before anybody was talking about CRISPR. And it's this headline from a

yoghurt company saying, "Holy Grail is discovered." And what was this yoghurt company's Holy Grail? It was CRISPR. It was CRISPR.

INTERVIEWER: *When did you get your CRISPR license plate?*

RODOLPHE BARRANGOU (Former Director of Genomics, Danisco): *First one I got back in the days in Wisconsin. And when I first moved to North Carolina, one of the first things I did was make sure I still had my CRISPR rights with my CRISPRmobile.*

BARRANGOU: People were, like, "Have you heard about this CRISPR thing?" And I'm, like, "Dude, I've heard about this CRISPR thing for ten years, "like, what the hell are you talking about?"

BANFIELD: *Danisco is a company that sells microbes to people who want to make food. A lot of foods are produced using bacteria. Yoghurt, for example. Rodolphe was trying to work out how to deal with the problem of his bacterial cultures suddenly dying because of viral infections.*

URNOV: *Most people don't wake up in the morning and think about how bacteria defend themselves against viruses. It's just not on the, sort of, front and centre in people's agenda, but it should be.*

BARRANGOU (?): Viruses are very simple, lean machines. They have one job to do – look for a host, take the host over and multiply. That's it.

LUCIANO MARRAFFINI (Early CRISPR researcher): *The virus will attach to the surface and then it will inject its genetic material. It hijacks the cell and uses the cell just as a factory of new viruses. And then it's over. It's over for the cell.*

BARRANGOU: *This is when people call companies like Danisco and say, "You sold us a culture that's not working. "We want our money back."*

BARRANGOU: But there's a small subset of the population that survives the viral attack. We don't know why they make it, but they make it. They become resistant.

BARRANGOU: At that time, we still don't know what CRISPR is or what it does. So there's no assumption that CRISPR is involved. Then what we do is we take the survivor that made it and then we check its DNA. The DNA sequence had changed.

MOJICA: *There are new spacers, that were not present before, and those spacers are identical to sequences from the virus that infected the bacteria.*

BANFIELD (?): *And now, it's immune.*

URNOV: *So now scientists have a clue. And at this point, of course, you've sort of put your Sherlock Holmes hat on, you take your virtual pipe and you go, "What are these clues telling us?"*

BARRANGOU: *We do the experiment five different times. And consistently the bacteria acquired a spacer that contains a sequence from that virus, and became resistant. So what if I take it away? You lose the resistance.*

BANFIELD: *Without that little piece of DNA, the microbial cell, the bacterial cell, will die. And if it had it, it would survive.*

BARRANGOU: *That was like. . . That was like, "We've got it." CRISPR is an immune system.*

BANFIELD: *What an idea, a piece of the genome of your predator now stuck in your genome so you can recognise it in the future.*

MOJICA: *Bacteria have memory. They are able to remember invaders, recognise them and kill them. That was really fantastic.*

BARRANGOU: *At the time, you know, it's useful in manufacturing cultures that are resistant to viruses. It's extremely valuable to Danisco, you know, but… but we don't know what the future holds. We have no idea how useful or not this technology is going to be, or pan out in the end.*

DOUDNA: *I think I first heard about it when I had coffee with Jill Banfield, my colleague here at Berkeley, at the Free Speech Movement Cafe, classic Berkeley cafe.*

BANFIELD: *The one thing they'll write on my tombstone was, "Told Jennifer Doudna about CRISPR-Cas." Like, that will be the sum of my life!*

DOUDNA: *I love things that not a lot of people are paying attention to. Which certainly CRISPR was in its early days, not any more. But, you know, in the early days it was like that. But then you always ask yourself, "Huh, is everybody else just a lot smarter than me and they'd figured out that this is a, you know, a dead path."*

STUDENT (Incidental conversation, to Doudna): *So we've got antibody to link to Cas9, it's finding the T cells specific antigen…*

DOUDNA: *We're biochemists in a lab. We study the way molecules work. We try to isolate them from all of the other pieces and parts of the cell. We love to ask what are the essential parts of this little machine?*

DOUDNA: *In nature, what CRISPR systems are doing is they're giving bacteria immunity to viruses, so they're protecting them from viruses.*

URNOV: *When an invader shows up, the bacterium has a way to store a small bit of the invader's DNA in its own DNA. When the invader comes back, the bacterium makes a copy, like a little most wanted poster, of that spacer, and gives it to the marvellous machine at the heart of CRISPR. This extraordinary protein that we call Cas9.*

URNOV: *Cas9 is truly wondrous. When Cas9 polices the intracellular neighbourhood for invasions, it literally carries a copy of that most wanted poster with it, asking everyone that comes in, "Excuse me, do you contain an exact match to this little most wanted poster that I'm carrying?" "Yes? Then I'll cut you."*

DOUDNA: *The thing about Cas9 that struck me at the time was that, you know, fundamentally this thing was a programmable protein, that finds and cuts DNA. As a tool, right, you could immediately see a lot of uses for something like that.*

URNOV: *I will never forget reading the last paragraph of Jennifer Doudna's and Emmanuelle Charpentier's deservedly – immortal is a strong word, so I'm going to use it carefully – immortal Science paper in which they describe that Cas9 can be directed.*

URNOV: *Cas9 cuts DNA based on an instruction that it carries, and that instruction is a molecule of RNA that matches perfectly the DNA of the invader.*

DOUDNA: *RNA, I think about it as DNA's chemical cousin. Like DNA, it has four letters, and they can form pairs with matching letters in DNA. The letters in the RNA allow Cas9 to find a unique DNA sequence. Bacteria are programming this thing all the time with different viral sequences and then using it to find and cut and destroy those viruses.*

DOUDNA: *But because it's using these little RNA molecules, those can easily be exchanged. RNA molecules are trivial to make in a molecular biology lab or order from a company. And I can cut any DNA I want just by changing this little piece of RNA. It was clearly a useful tool. And initially I was thinking about it that way, right? Because, again, I'm a biochemist, I was thinking about it as a tool. I was thinking about all the cool experiments you could now do with this tool, right, I was thinking about that. I wasn't thinking about, "Oh, my gosh," I mean, this is a tool that, you know, it fundamentally allows us to change our relationship with nature. It actually allows us to change human evolution if we want to. Right? It's that profound.*

Chapter 3: The gene machine (starts at 29:20)

UNNAMED MALE RESEARCHER: *In my left hand here I have purified Cas9 nuclease. And in my right hand here, I have a guide RNA. And so CRISPR essentially is the combination of these two ingredients. It's actually millions of Cas9 molecules and this is millions of RNA molecules.*

GEORGE DALEY (Dean, Harvard Medical School): *I have to say, it didn't immediately hit me until I started seeing the data that this could be an extraordinary transformation. You know, it was real.*

BARRANGOU: *You can actually use CRISPR in humans to change DNA. OK, should we do it?*

URNOV: *Here's a copy of a human gene. We give it to Cas9 and put it inside human cells. It runs away, finds that DNA, and cuts it.*

PORTEUS: *Before CRISPR, we were getting 1 to 2% correction. We're now up to 50 to 80% of the cells. This could really work. This could really cure a patient.*

DAVID SANCHEZ: *I think it's going to help a lot of people. Not just people with sickle cell, because I know they're working on it for other things. And I know so many other people that have things like this. Like, my friend, he had leukaemia. He didn't actually, he didn't make it out of the hospital. If he had it just a little bit later, of course, he probably could have been cured of that, cos that's what they're working on.*

EMMANUELLE CHARPENTIER (Biochemist, Max Plank Institute): *CRISPR has really the ability to recognise and to target any piece of DNA in any type of cell and organism. It's really a universal tool. It's often described as a kind of Swiss Army knife.*

MICHAEL DABROWSKI (Co-founder, Synthego): *We have thousands of customers who are working with CRISPR in a wide variety of organisms, pretty much any organism you can think of, from butterflies, to dogs, to horses, to wheat, to corn.*

MICHAEL DABROWSKI: *We have a design tool online. Specify a gene that you're looking to knock out. You can specify the types of edit that you're looking to do. You swipe your credit card and a few days later, a couple of tubes of all the materials that you need show up at your door.*

PAUL DABROWSKI (Co-founder, Synthego): *Obviously we like to validate the researcher's authenticity and credibility with regard to their institution.*

INTERVIEWER: *Meaning, you're not just shipping it out?*

PAUL DABROWSKI: *Correct, we don't ship to just anyone. That's correct.*

GREELY: *The analogy I like is automobiles. There were cars before there were model Ts, but they were expensive and they broke down all the time. Ford comes out with a Model T and suddenly it's cheap and it's reliable. Pretty soon everybody's got a car.*

GREELY: *CRISPR gives us the chance to make precise, targeted changes in the DNA of any living organism. It's the power to change the biosphere. THAT'S what makes CRISPR revolutionary.*

INTERVIEWER: *Can you just sort of describe where we are right now?*

LUHAN WANG (Co-founder, eGenesis): Oh, here?

INTERVIEWER: *Yeah, yeah, yeah.*

WANG: *Oh, so here is the eGenesis garage. This is our lab space. This is literally the basement. I feel it's a humble start for us.We're embarking on a very exciting journey.*

JORGE PIEDRAHITA (Translational Medicine, NC state): *The field is called xenotransplantation – transplantation of an organ from one species to the next. These things have actually been tried a lot and some are pretty weird, like people in the early 1800s, that kind of stuff, they were trying to transplant monkey testicles to men to make them more virile. So, conceptually, people have been trying this for a long time. But scientifically, this field is probably about 20 years old. Whether we like to believe or not, we are very similar to the pig.*

NEWS REPORTER: *This pig, this pig, this pig, all the organs in these pigs have been modified very, very slightly. ..*

CHURCH: *They tried it 20 years ago, Novartis had a billion dollar investment in it, sort of gracefully retreated. They just didn't have the technology.*

PIEDRAHITA: *Without the CRISPRs, can't do it.*

CHURCH: *Luhan Yang and her team, they started as a rag-tag team of scientists in my academic lab and then they went to a rag-tag team in the basement of a start- up incubator.*

YINAN: *Nice to meet you! Hey, happy Halloween! You're not dressed up, are you?*

WANG: *Can you see anything?*

YINAN: *Kind of. Something, not everything.*

WANG: So this is Yinan. Yinan is quite creative. Probably more creative than me.

YINAN: *When I first heard the story, I thought it is sci-fi. You know? We're going to make a pig that doesn't speak human language, but that can donate organs for the patient and save the world from organ shortage. I mean, it really takes a lot.*

WANG: *As you can imagine, if you put the organ from the pig into the human, there's a rejection. We can really exercise the power of CRISPR to engineer immunocompatibility by knocking out genes and knocking in genes.*

YINAN: If you compare the pig genome to an encyclopedia, this thick [gestures with hands], so what CRISPR does, it can find a specific word in the encyclopedia and delete that word. But instead of deleting a few words we have to change paragraphs after paragraphs.

WANG: *Right now, the convention of practice is doing one or two genes. And the record before us is five. We did sixty-two genes in a single step.*

CHURCH: *We have a revolution going on. We've never had a revolution like this. The closest we've come is maybe the internet and computer revolution. And that took us kind of unaware.*
INTERVIEWER: *How are the pigs coming along?*

WANG: *They are coming. We are expecting some pigs in a few weeks. We're so excited we even named the pig. The first one is Laika. It's the name of the Soviet dog which orbited the earth first. We want to symbolise it as an animal which can lead us to a new era of science.*

Chapter 4: Brave New World (starts at 38:45)

UNNAMED FEMALE*: I would like to give the floor to the distinguished President of the Russian Federation, Vladimir Vladimirovich Putin.*

[CAPTION: World Festival of Youth, Sochi, Russia, October 21st, 2017]
APPLAUSE

VLADIMIR PUTIN: *Genetic engineering will open up incredible opportunities in pharmacology, new medicine, altering the human genome if a person suffers from genetic diseases. All right that is good. But there is another part of this process. It means we can already imagine it – to create a person with the desired features. This may be mathematical genius. This may be an outstanding musician. But this can also be a soldier, an individual who can fight without fear or pain. You are aware that humankind will probably enter a very complicated period of its existence and development. And what I have just said may be more terrifying than a nuclear bomb.*

NARRATOR (Archive footage): *This is Aldous Huxley, a man haunted by a vision of Hell on Earth. Mr Huxley, 27 years ago, wrote Brave New World. Today, Mr Huxley says that his fictional world of horror is probably just around the corner for all of us.*

DALEY: *I first read Brave New World in a literature class in high school and, yeah, it was startling and, yeah, it was provocative. But I reread it recently and I was startled by how a book written in 1932 could have the foresight to predict in vitro fertilisation.*

DALEY: *Now, of course, it went beyond it. It told a story where human beings were literally manufactured to play specific roles in society. It was so sobering to me because CRISPR makes that original worry about engineering human heredity actually feasible.*

ALDOUS HUXLEY: *We mustn't be surprised by our own advancing technology. This has happened again and again in history, where technology has advanced and this changes social conditions, and suddenly people found themselves in a situation which they didn't foresee and doing all sorts of things they didn't really want to do.*

URNOV: *There is no question in my mind that as this field advances, people will be able to order a change of their genetic make up to create an outcome of interest to them, in their metabolism, in their appearance, in principle, potentially, in who they are as people, personality changes. Then again, we have to be delicate to not cross into science-fiction territory.*

DALEY: *We know that we could engineer a single gene, myostatin, in a way that could potentially make us all more muscular, but should we make that universally available?*

URNOV: *They discovered that there are people who can go by on four hours of sleep. What would I give for that mutation?! One gene, one change, four hours of sleep. No problem.* So*, should this be, I don't know, a job requirement for air traffic controllers? Do I want the world to go there?*

URNOV: *There are people who feel no pain. This was discovered by studying a 14-year-old boy in Pakistan who felt no pain, and guess what he did. He performed street theatre. He died before his 14th birthday. He jumped for money off a house roof. He knew it would be painless. The study of his DNA revealed he has a mutation in one gene, it makes a protein that transmits the pain signal from the periphery, your finger or your skin, through the spine to your brain. You get rid of that gene, you cannot transmit the signal, you feel no pain. Why? Well, I'll give you a legitimate reason. Pain due to cancer is terrible. Especially if it's terminal cancer and we know a person has months to live. Why not get rid of that gene? And I'm sure this will be, I am sure this will be. We will have gene editing of that gene to treat cancer pain. Now, do I want a scenario where there are parts of the world where special forces soldiers are made immune to torture?*

REGALADO: *I don't think my job is that different than what scientists do. There's a lot of kind of hunting around, hunting and pecking, you know, looking under things. Turning over stones. And then eventually, you know, you kind of get on the scent of something and then that's when the fun starts. Before science gets published, it circulates among scientists. Papers go out for a review, someone passes it to somebody else, like, they have a certain circulation, and so I'd gotten on to the trail of these papers coming out of China. This was the first case where someone had said about, you know, I'm going to use CRISPR and I'm going to modify a human embryo. They had knocked out CCR5. This is a receptor that if you don't have it, you can't get infected with HIV. But think about what they were proposing. They said, "We're going to make someone who's immune to HIV." Once I started digging into it, I found more examples of people that were thinking along these lines. John Zhang runs the third or fourth biggest fertility clinic in the country and then he started a company called Darwin Life. He said that he was enthusiastic about the whole idea of designer babies. He basically said that, of course, that's the whole point! There was a company called OvaScience. I discovered a tape recording that they'd put on their own website of an investor meeting.*

AUDIO RECORDING OF OVASCIENCE MEETING: *We will be able to correct mutations before we generate your child. It may not be 50 years, actually. It may only be ten, the way things are going.*

DOUDNA: *I ended up having several dreams that were very intense for me at the time, where I walked into a room and a colleague said, "I want to introduce you to someone and I want you tell them... They want to know about CRISPR." And I walked into this room and there was a silhouette of a chair with someone sitting with their back to me and as they turned around, I realised with a horror that it was Adolf Hitler. You know? And he leaned over and he said..."So, tell me all about how Cas9 works." I remember waking up from that dream and I was shaking. I thought, "Oh, my gosh!" I mean, "What have I done?!"*

PORTEUS: *Five and a half years ago, it was recognised that we could take the CRISPR system out of bacteria and move it first into a test tube and then into mammalian cells and use it as a tool for genome editing. The Cas9 protein is going to make the cut in the DNA. We are correcting the sickle mutation in blood cells. So if it's a woman, their eggs are not corrected, if it's a man, the sperm is not corrected. That change will not get passed along to future generations. So they will be cured, but their children might get the disease as well.*

PORTEUS: *Now, we need to give the cell another piece of DNA, except instead of having the T, it has an A. So why not just do it, so that the diseased gene never gets passed along to future generations? And there's some people out there who think that's what we should do. But we may be creating things that we can't put back into the bottle.*

DALEY: *When we engineer gene changes into my blood or into my skin, those gene changes die with me. But the germ cells, sperm, eggs, embryos – those cells are very different. They're part of what we call the germ line. If we engineer gene changes into my sperm, they're passed to my son. They're passed to his son and forever.*

URNOV: *My colleagues and I wrote a fairly strongly worded piece in Nature with the fairly unequivocal title, quote, "Do not edit the human germ line", end quote. We proposed that there be an unconditional moratorium. Don't edit human embryos, don't use edited sperm and eggs to make human embryos, just nothing. We must understand that when we authorise research on human embryo editing, we're enabling ultimately human embryo editing for human enhancement. That's what we're doing. We're putting the recipe out into the world.*

REGALADO: *The debate that's being had is whether society should go in this direction. Should you be allowed to make a genetic change into the next generation that will then go on to other generations? The gene pool, like nature itself, is kind of a common good.* I *used to have a T-shirt and it had a little...a guy that was kind of a DNA spiral, right? But he was a lifeguard and he's blowing a whistle and he says, "Hey, you, get out of the gene pool!" I loved that shirt.*

NEWSREEL (1972): *Baby shopping. Imagine being able to program the IQ of a baby.*

NEWSREEL (1983): *Will we be sitting at computer terminals like this one, punching up the traits we would like in our children? Like the shape of their faces or the colour of their eyes?*

CHARO: *Well, you know, the fear that everybody focuses on most is this whole designer baby business.*

UNNAMED WOMAN (Archive): *We're turning reproduction into production. We're turning children into consumer products.*

CHARO: *Every time there's a new technology, we hear the same concerns.*

NEWSREEL (1997): *If there's a market for cloning, there is no force on Earth that will keep buyer and seller apart.*

PATRICK DIXON (Unnamed, Archive footage): *Perhaps Saddam Hussein would like to give birth to himself.*

CHARO: *With CRISPR, even reputable magazines could not resist the temptation. A little thing that says "high IQ", as if we know what intelligence is, let alone how to measure it, let alone how to design it. Why do we keep ignoring the fact that we've seen the same argument every decade for the last five decades? And these nightmares – they haven't come to pass.*

CHARO: *We are capable of really evil things, but we don't need technology to commit evil acts. If the goal is genocide, if the goal is eugenics, if the goal is discrimination, there will be another way to do it and it will be found. I kind of divide the world into the bio-optimists and the bio-pessimists.*

[STAR TREK: Space, the final frontier.]

CHARO: *I grew up with the original Star Trek... and have been a devoted follower of all of the Star Treks since then. I've read pretty much every Star Trek novel. Don't get me started. It is a vision of progress and the potential of science to make life better. There are other people who have read the cautionary tales.*

[BLADE RUNNER: A Blade Runner's job is to hunt down replicants, manufactured humans you can't tell from the real thing.]

CHARO: *But I don't think the technologies are inherently good or evil. The technologies, or tools, they are power. What you do with the power determines if the result is something that we applaud, or something that we deplore, but it's not the tool that determines the end point, it's the user.*

Chapter 5: Good genes (starts at 52:10)

ARCHIVE: *Now, here are 23, representing mother's chromosomes, 23 for father's. Now... we put them together.*

BALTIMORE: *Our way of determining the inheritance of the next generation is a lottery. And it's a perfectly good argument to say, "I would rather determine it, than take a lottery."*

STEPHEN SHU (Co-founder, Genomic Prediction): *Well, I think the right way to say it is that sex is for recreation and science is for procreation. 50 years from now, people may say, like, 'I can't believe it was barbaric, people in the early 21st century, they were having kids this crazy, old-fashioned way. "They were just, like, rolling the dice with their kids' lives."*

SHU: *You've gone through in vitro fertilisation. You've harvested the eggs. It's not uncommon to produce multiple viable embryos. Which one do you choose? One possibility is, "Yeah, we'll just roll the dice, "we'll just... I'll just point at one." Another option would be I run some fancy genetic tests.*

GREELY: *Pre-implantation Genetic Diagnosis is the process of doing genetic tests on an embryo. When I talk to most people about it, they think it's science fiction, but it was first used clinically in 1990. With today's technology, you've been limited to looking at only a handful of traits... but soon genome sequencing will become cheap enough, easy enough and accurate enough, that you'll be able to learn everything genetics can tell you.*

SHU: *In the future, let's imagine the CRISPR gets really, really good. Maybe you don't need to produce lots of embryos. Maybe you just produce one, but you can make whatever edits you want to it.*

KELSEY McCLELLAND (Genetic Counsellor) : *So the carrier screening I was talking about earlier tends to focus on disorders that show up early.*

McCLELLAND*: Everyone wants to have a healthy, perfect baby. I think that's a universal truth. You know, how can I make sure that my child will be healthy? How can I make sure that, you know, they're going to have some of these positive traits, that they're going to do well, they're going to learn well?*

[McCLELLAND (Incidental): *And looking at this family history, certainly...]*

McCLELLAND: *The opinion is that information is good and almost everyone that talks to me wants more information and even wants more, like, we'll give them a whole bunch of information and they even want more.*

McCLELLAND*: I actually first heard about genetic counselling from my mother. Haemophilia A is the condition that runs in my family. It's a genetic bleeding disorder. There is a gene on the X chromosome. It encodes for a protein called Factor 8.When Factor 8 isn't working... you can have a bleed that will lead to death. If I decide to have children naturally without reproductive technology, I am putting that child at 25% risk to have a really severe disorder. That responsibility feels like it's on me. It takes it from the universe's decision to my decision.*

McCLELLAND: *Today, I'm unusual because I know that I'm a carrier of a genetic condition, but soon everyone will know genetic information about themselves.*

INTERVIEWER: *What about the cost of it?*

SHU: *In the short term, there's a disturbing possibility that people with means will be availing themselves of this technology, and people who don't have those means will not. So I kind of hope for a future where government makes it free for everybody. You would have a generally healthier population, maybe longer-lived population on average, um, maybe slightly smarter population on average.*

SHU: *So, if you have a smaller fraction of your population with Down's syndrome, the average intelligence is a little bit higher, and, you know, society might run a little bit more efficiently if people are a little bit smarter.*

JULIAN HUXLEY: *What is the bearing of the laws of heredity upon human affairs? Eugenics provides the answer, so far as this is known. Eugenics seeks to apply the known laws of heredity so as to prevent the degeneration of the race and improve its inborn qualities.*

SHU: *Well, the concept of eugenics, if you go way back, it really just means good genes. The idea is that the human race could improve itself.*

[NAZI PROPOGANDA FILM, 1937): *Children are not brought into the world just for their own sake – rather they should be healthy, worthwhile people. And that's why it's important that we make sure that our bodies are physically and genetically healthy. And that we investigate whether the genetics of our ancestors are fit to pass on.]*

SHU: *It was, of course, hijacked, and when people today talk about eugenics, they think specifically of the Nazis, of Nazi Germany, of compulsory sterilisation where, by force, people were compelled to be sterilised or killed because the state didn't like their genes.*

[ARCHIVE NEWSREEL: *There was shock last month over the revelation that the state of Virginia sterilised thousands of persons between 1922 and 1972 in a programme aimed at ridding the state of so-called misfits.]*

SHU: *What we're talking about here, where we are being paid to do these genetic tests by loving parents who want to have a healthy child, to equate that with Nazism is, I think, not just stupid, but actually insane.*

[GATTACA, 1997 (Clip):
FERTILITY DOCTOR*: I've taken the liberty of eradicating any potentially prejudicial conditions, alcoholism and addictive susceptibility, propensity for violence, obesity.*
PROSPECTIVE MOTHER: *We didn't want... I mean, diseases, yes, but...*
PROSPECTIVE FATHER: *Right, we were just wondering if...if it's good to just leave a few things to chance.*
DOCTOR: *You want to give your child the best possible start. And keep in mind this child is still you, simply the best of you.]*

PALMER WEISS: *My greatest fear in life, honestly, my two greatest fears going back to me wanting to be a mom at the age of five, my first greatest fear is that I wouldn't be able to have a child and my second greatest fear is that something would be wrong with my child.*

*[*ETHAN WEISS *(Incidental): Oh, careful, sweetie.]*

PALMER WEISS: *With Ruthie I started seeing that she kind of wasn't tracking. When I would feed her, her eyes would slide back and forth. And then one day I went to my friend's house and her baby looked me right in the eyes, and I came home to Ethan and I said, "There's something wrong."*

ETHAN WEISS: *We did genetic testing. She inherited one mutated copy of this OCA2 gene from me and one from Palmer. I don't think I even really understood that people with albinism had such impairment of their vision.*

PALMER WEISS: *It's kind of like wrapping Saran Wrap over your eyes with Vaseline. Very, very hard for her to see. You know, I just wanted to protect her, like, "This isn't true, "this isn't happening." It was horrible. It was bad.*

[PALMER WEISS (Incidental): *One, two, three, four. OK, Ruthie, Ruthie! Whoa!... Hi!]*

ETHAN WEISS: *She was really easy and happy. And early on, I think we wondered if she was sort of... I don't know, protected by the fact that she couldn't see a lot. The world wasn't as noisy to her.*

[INCIDENTAL: Look! Like this.]

ETHAN WEISS: *She was smart and talkative. Super curious.*

PALMER WEISS: *You don't know what you don't know, you don't know that even though it's going to be different than what you thought, you don't know, you know maybe how much better that's going to be.*

RUTH WEISS: *I want to be a professional basketball player but I don't think that's going to be.*

[INCIDENTAL: CHATTERING, then RUTH WEISS: "The mission is simply one..."]

ETHAN WEISS: *I've known about CRISPR from the perspective of being a doctor, probably since the first publications, whatever it was, 2012. It really didn't intersect with our own world with Ruthie until probably about a year and a half ago when I read something on Twitter.*

[Tweet by Daniel MacArthur (@dgmacarthur) from 30th November 2015]

ETHAN WEISS*: A scientist who I respect a lot said he thought that in one or two generations that all children would be born with all of these genetic abnormalities edited out.*

PALMER WEISS: *I know people who have children who have really debilitating diseases that make their children suffer, make their family suffer a lot, so I totally understand a desire to change that. Um... But the rest of it scares me to death.*

PALMER WEISS: *I don't know where you draw the line between not having albinism and deciding your kid needs to be an extra foot taller so they can be a good oarsman and go to Yale. You know, where...where is that line? Who is going to draw that?*

McCLELLAND: *We're maybe a society who is afraid of things that are different, or afraid of people who are different, afraid of people who have needs.*

PALMER WEISS(?): *I worry that when we're manipulating future generations, those opinions are going to be passed on.*

DALEY: *You know, we as a society may think that doing better on the SATs is better than doing worse. Being taller, being handsomer, being more creative, being more courageous – those are traits that we would want to potentially select for. Should we go there? Is there an inevitability to going there?*

SHU: *You know, sometimes I'm invited to give a talk on, like, a kind of futuristic science things. And I've had tall, blonde, trophy wives come up to me after the talk and say, "Wow, that was incredible, that was an incredibly interesting talk, "but don't you think there's a problem with all this? "Won't every parent just select their kids to he tell and blonde?" The geeks all come up to me and say, "Isn't this dangerous" because all the parents are going to select for the smartest kid*

they can possibly get?" Because that's what the geeks think is cool. You know, probably if you're talking to some NFL coaches, they'd say, "What? Everyone's going to select their kid to be six-five "and run a 4.2 40, you know." So, um... there will be a wide range of what people think is the right thing to select for, or engineer for and, actually, there's nothing wrong with that, right? Let a million flowers bloom.

ARCHIVE NEWSREEL: *On this estate, 30 miles north of San Diego, is housed a sperm bank said to be made up exclusively of donations by Nobel Prize winning scientists. The bank's founder will consider for fertilisation only women of high intelligence.*

CHARO: *You don't know about the Nobel Sperm Bank? Oh!*

ARCHIVE NEWSREEL: *Businessman inventor Robert Graham adds liquid nitrogen once a week to a lead-shielded sperm repository in an underground concrete bunker in his back yard.*
ROBERT GRAHAM: *The more good genes in the human gene pool, the more good individuals will come out of it. We aren't even thinking in terms of a super race...*

CHARO: *The so-called genius sperm bank, a sperm bank to provide women for free with donor semen from men that they viewed as geniuses.*

ROBERT GRAHAM: *We utilise sources such as this… Who's Who of Emerging Leaders.*

CHARO: *Very few women actually went ahead and took advantage of this offer to be given superior sperm for free. I did a tour of sperm banks for the US Congress. I think I'm the only person who's ever gone on a congressionally financed tour of California sperm banks. Despite the fact that the donors are described taller, skinnier, you know, better looking or not... people tended to pick somebody who looked like their partner, no matter how imperfect, because the emotional importance of the connection outweighed any notion of improvability or perfectibility.*

CHARO: *If I were trying to have a child and my partner was light-skinned, short with eczema, I would have had a child with a guy who was light skinned, short and prone to eczema.*

INTERVIEWER: *But what if you could take that guy's sperm and edit those specific things out?*

CHARO: *Could I change his sperm so it's still him, but a better him?*

INTERVIEWER: *Exactly. Right? Yeah.*

CHARO: *Maybe, but every change does come with risks that you'll make changes you didn't intend. So, I think it'll be a long, long time before you would take that risk for anything other than something that was pretty significant.*

CHARO: *But I might want to take advantage of editing something out that would give my kid a very strong chance of developing a severe cancer, even if it's 40 years in the future. Yeah. So maybe that will happen.*

NATIONAL ACADEMY OF SCIENCES (Archive footage):
CHARO: *This committee is going to be looking at both somatic and germ line applications of gene editing.*

CHARO: *The committee that I co-chaired for the National Academy of Sciences, we were asked to look deeply at whether or not there was something intrinsically unethical about manipulating genes in a way that makes them heritable.*

NATIONAL ACADEMY OF SCIENCES (Archive footage):
HILLE HAKER: *This should be the goal of society – to promote a better life for all and to ensure that everybody can live a life in dignity and freedom. Can this be achieved by germ line gene editing? My view is no.*

REGALADO: *The American Medical Association, a bunch of European countries, you know, any number of organisations all had positions, like, meddling in the germ line would be wrong, it would be unethical. But they all said those things at a time when it couldn't be done, so it was easy to say, it was a gimme, right? And then as soon as it comes that you can do it... then the positions change.*

UNNAMED FEMALE (NAS meeting, Archive): *Huntington's lurks in our DNA like a time bomb. It would really eliminate this scourge in the world, so I would go for it.*

REGALADO: *At the big National Academy Meeting there was not a good representation of patients, but the few who did speak were definitely in favour.*

UNNAMED FEMALE: *I say yes, it is worth pursuing in a safe and rational manner. Definitely, let's go.*

UNNAMED MALE: *Anything that will stop my child from suffering... I'm for.*

REGALADO: *You know, draw this ethical line whenever you want, but don't draw it in front of my disease.*

UNNAMED FEMALE: *He was six days old...*

REGALADO: *I remember one woman told the story about a child she had, and died of an inheritable disease.*

UNNAMED FEMALE: *...he had seizures every day. We donated his body for research. If you have... SHE CRIES ...the skills and the knowledge... SHE CRIES ...to fix these diseases, then fricking do it.*

CHARO: *The statement of task demanded that we try to follow the evidence and follow the logic, not that we follow the politics. We said, "We conclude it is not intrinsically evil." It is what we called "ethically defensible". But we understood that this was now a break from the past in the thinking on this topic. Yes.*

UNNAMED CHURCH MINISTER: *In Genesis chapter one, we discovered the concept of the Imago Dei, being in the image and likeness of God.*

CONGREGATION: *Mmm.*

UNNAMED CHURCH MINISTER: *What does that mean for this science where we have the capacity to edit in some things perhaps that we think are important? Are we playing God?*

Chapter 6: Playing God (starts at 69:20)

RACHEL CARSON (Author, Silent Spring): *The balance of nature is built of a series of inter-relationships between living things and between living things and their environment. Now, to these people, apparently the balance of nature was something that was, um, repealed as soon as man came on the scene.*

WANG [looking at photo of genetically-engineered pigs]: *This is Laika, this is Nova, and this is Joy. Our pig is the most advanced genome-modified animal roaming on the Earth.*

CHURCH: *The babies that came out of that are now adults and the adults are having their own babies, so it seems like making that many edits is completely compatible with a happy, healthy pig.*

CHURCH: *I tell people to be visually underwhelmed by my lab. It's just a bunch of small rooms with usually very few people in them. But in terms of what I see, it's very exciting.*

[HEADLINE: "George Church Playing God with our genes"]

CHURCH: *I've never really felt the mad scientist was realistic for anybody that I knew, including myself. My lab has been accused of taking science fiction and turning it into science fact. I consider that very high praise. But turning science fiction into science fact is not mad. It actually can be quite useful.*

[HEADLINE: "George Church: The maverick geneticist who wants to reverse ageing"]

CHURCH: *Ageing reversal is the term that I prefer. I'm 63 years old, I feel like Ijust barely got trained to do my job last year, and so now you're going to pull the plug and recycle me. This doesn't make sense. We need to be cautious in that, you know, there's this whole population problem, so we could do that if we have a place to put all those people.*

[HEADLINE: "Engineering the perfect astronaut"

CHURCH: *Almost everything we do, people just think, "This is goofy, this is "not feasible, it's science fiction." But I think originally people thought that sequencing human genomes inexpensively was a pipe dream.*

INTERVIEWER: *I can't not ask you about mammoths because there's a bunch of them behind you.*

CHURCH: *Yeah, that should be up at the top of the list of things that seem, er... quixotic or, er, misguided. So, in the mammoth project, we read the ancient DNA... decide which genes we're going to resurrect... put those into the Asian elephant cells and then we're developing technologies, it's not yet working, er... to take those embryos all the way to term, and we scale it up to make a herd of these things, maybe 80,000 of them to repopulate the tundra.*

JURASSIC PARK (1993, clip):
JEFF GOLDBLUM: *Don't you see the danger, John, inherent in what you're doing here? Genetic power is the most awesome force the planet's ever seen, but you wield it like a kid that's found his dad's gun.*
RICHARD ATTENBOROUGH: *I don't think you're giving this our due credit. Our scientists have done things which nobody has ever done before.*
JEFF GOLDBLUM: *Yeah, but your scientists were so preoccupied with whether or not they could, they didn't stop to think if they should.*

RYAN PHELAN (Co-founder, Revive & Restore): *Well, I... I often try to avoid talking about Jurassic Park, but I'll give you this.*
You know, Jurassic Park was about hubris.

JURASSIC PARK (clip):
SAM NEILL: *What species is this?*
TECHNICIAN (Disinterested): *Er, it's a velociraptor.*

PHELAN: *It's just the opposite of what scientists like George Church and others that we work with are thinking about. When people say, "Aren't you playing God?" my real reaction is um, nobody is playing in this field, nobody is toying with it, um, just to see if it can happen.*
PHELAN: *You know, in order to even fathom bringing back an extinct species, there is no end of engineering that has to happen. And it is all novel, important, new science that can be used to protect any species, endangered as well as extinct.*

PHELAN: *Once you realise the magnitude of humans' impact on the environment, you know, it's hard for me to say that we can't try to correct it.*

[HEADLINE: "How gene editing could save coral reefs"]

PHELAN: *We can't have our head in the sand. We have a responsibility to use our human ingenuity and our human skills and our wherewithal. Sometimes it's leaving nature alone and sometimes it might be intervening.*

[HEADLINE: "CRISPR: can gene-editing help nature cope with climate change?]

UNNAMED SYNGENTA SCIENTIST: *So the gene we've edited controls how the pores on the underside of the leaves open and close. In the non-edited plant, these stomata, or pores, will stay open during the hot, dry conditions. Water is lost, and then these leaves lose water, they wilt and they roll. In the edited plant, those stomata pores close sooner under dry conditions, and the water is retained inside the plant.*

GREELY: *We have been messing with nature ever since we came out of the trees. Most of the life forms we eat are things we've made. Corn used to be a grass. Tomatoes used to be tiny little berries that were bitter. Geneticists changed that. Now, we didn't call them geneticists. We called them farmers.*

[CAPTION: ÇATALHÖYÜK, TURKEY Early Human Settlement, 7000 BC]

INTERVIEWER: *Do you think among these people, there was anyone that it would be fair to call a scientist?*

IAN HODDER (Archaeologist, Stanford University): *Well, that's a really interesting question. I think there's lots of different types of science that were involved. The first people who invented pottery were really chemists, in a way. And certainly, the people who were... inventing agriculture, and controlling plants and animals, they were biologists, you know, botanists and biologists, in our sense.*

HODDER: *You can see people trying things out. What is the best way to grind grain? And how do you make bread? You know, that was invented here. To work that out... you know, is really not... is not straightforward.*

HODDER: *In this period of time, something more modern-like, in terms of our relationship with nature, was beginning to emerge.*

HODDER: *As far as we understand it, hunter-gatherers had a relationship of equality with nature, and had to look after nature. And if you hunted an animal, you would have to give a gift to nature, to... to thank it for the animal that you've been given. And then, as people started domesticating plants and animals, they started having a new relationship where they were dominating and controlling the natural world. That made it something that you could transform.*

HODDER: *We definitely see great advantages in genetic engineering... as agriculture, you know, was a great advance. Certainly, it's the building block of civilisation as we understand it. But it definitely comes with its negatives. You could say that the long—term consequences were*

pollution and environmental degradation, and so on and so forth. But you'd have had to be very far seeing, you know, 9,000 years ago to realise that that was what was going to happen.

CHARO: *These things creep in slowly. It's not like everybody was hunting and gathering, and then next year somebody said, "Oh, let's farm," right? It happened slowly. And so it IS disruptive, but it creeps up on people. You don't realise it's disruptive until you look backward. Often, you don't realise that you're in the middle of a revolution until after the revolution has occurred. Right, so I don't know where we are right now. It'll be interesting to see. I hope I live long enough to see it.*

INTERVIEWER: *Do you think you want to have kids?*

DAVID SANCHEZ: *I have too many siblings for that. The answer's probably going to change, but for now, probably not, no. I'm not crazy.*

INTERVIEWER: *They're saying maybe one day, with CRISPR, they could go in and change the gene in the embryo, so that the kid, when it's born, doesn't have sickle cell.*

SANCHEZ: *Hmm. I guess that's kind of cool, that they're thinking that it can do that in the future, but I think that would be up to the kid, later.*

INTERVIEWER: *What do you mean?*

SANCHEZ: *There's a lot of things that I learned, having sickle cell. Just because I had it, I learned patience with everyone. I learned... just to be positive.*

INTERVIEWER: *So you don't wish that you never had it?*

SANCHEZ: *I don't wish I never had it, no. I don't think I'd be me if I didn't have sickle cell.*

GREELY: *Sickle cell's a really interesting, unusual genetic disease. If you've got two copies of the sickle gene, you're really sick and without modern medicine, you die young. If you've got two copies of the normal gene, you don't get sickle cell at all. It turns out, though, that if you've got one sickle gene and one non-sickle gene, you make cells that are somewhat sickle. You're not sick, but the organism that causes malaria doesn't like those red blood cells.*

PORTEUS: *Having a sickle gene is protective against getting severe malaria. So in the environment where there's lots of malaria, it's better to be sickle cell trait than not to be sickle cell trait.*

GREELY: *And that's why you see sickle cell anaemia in Sub-Saharan Africa, but you also see it in the Mediterranean, in Greece and in Sardinia. That's because they have mosquitoes and malaria.*

PORTEUS: *The relationship between our genes and our environment is incredibly complex.*

[INCIDENTAL FOOTAGE: "Thanks, little brother, said the dog..."]

PORTEUS: *And we don't understand that.*

[BIRDS NOISE]

ASIAN MALE SCIENTIST: I think we have to have humility. Nature is one of the greatest inventors of all time. What we can do is a very, very insignificant fraction of what nature has already done. Nature invented CRISPR.

PORTEUS: *So now we're mixing the cells with the CRISPR. That's really cool. Once it's into the cell, that starts the editing process. We can't see that, we just know it happens.*

SANCHEZ: *I don't know how, out of all the genes that you have, that it targets the one that's doing sickle cell and not the thing that's making you grow hair.*
[Looking down microscope] Oh!
But it does, apparently. Like, that's cool!

DOUDNA: *You have to appreciate that this is a technology that's only about five years old, but it's been deployed incredibly rapidly… We've never had the ability to change the fundamental chemical nature of who we are in this way, right? And now we do. And what do we do with that?... It does make us really think deeply about what it means to be human. What do we value about human society?*

URNOV: *The things that make us most human are some of the most genetically complex, which is kind of a relief. Creativity... emotionality… love. Now, I want to be clear. They all have a biological basis. They are all written in our DNA. But we are a very, very, very long way away from being able to edit the person.*

INTERVIEWER: *Do you think that day will come?*

URNOV: *I do. But I'm hopeful that we will mature as a species before we get this incredible technology to play with for our own detriment. I am hopeful for that, yes. Is that hope based in fact? We'll see.*

SINSHEIMER: *How might we like to change our genes? Perhaps we would like to alter the uneasy balance of our emotions. Could we be less warlike, more self-confident, more serene? Perhaps. Ours is, whether we like it or not, an age of transition. After two billion years, this is, in a sense, the end of the beginning.*

[ON-SCREEN ADDENDUM: In November 2018, reports surfaced that CRISPR was used to alter the DNA of twin girls born in China. It marked the first time in history that humans edited the genetic code of a future generation. This controversial experiment has intensified the global debate about where we, as a species, should draw the line.]