Medicine's Big Breakthrough: Editing Your Genes (Panorama)
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Fergus Walsh (off camera): Tonight on Panorama - the scientific breakthrough that could change the lives of everyone and everything on the planet. It's an advance in gene editing, which holds out the promise of cures and personalised treatments for some of our most deadly diseases.

Jennifer Doudna (unnamed): Imagine a tool that allows scientists to change the letter code in the DNA of a cell, so precisely that we could change a single base pair in the three billion base pairs of the human cell.

Walsh: It sounds complex but gene editing has just been made simple and is revolutionising research into life's big killers and the diseases of ageing.

Fyodor Urnov (unnamed): Gene editing has created a fundamentally new kind of medicine, this means we can now treat genetic disease, infectious disease and cancer in ways that ten years ago would have seemed like science fiction.

Walsh: It crosses the animal and plant kingdoms and kick starts a new era of genetically-modified organisms. We can now control evolution so precisely that insects which spread disease could be eradicated.

But medicine's big breakthrough is not without risk.

Walsh (on camera): I've set out to discover how gene editing could change our world. It's just four years since researchers discovered a new technique to edit DNA, called CRISPR, which is so fast, cheap and accurate, it's swept through nearly every field of scientific research.

I've come to the coast of the west coast of the United States, to San Francisco, to meet a pioneer in this fast-moving field of science, one of the co-discoverers of CRISPR.

The University of California, Berkeley.

Jennifer Doudna (Professor of Molecular Biology, University of California, Berkley): The pace of science has just increased incredibly.

Walsh: Jennifer Doudna is a biochemist and now one of the world's most influential scientists. She is tipped to share a Nobel Prize for discovering a new form of gene editing.

Doudna: CRISPR's an acronym and it stands for Clusters of Regularly Interspaced Short Palindromic Repeats - big mouthful, easier to say CRISPR.

Walsh: Don't let the terminology put you off. Put simply, the CRISPR system acts as chemical cleaver, which allows scientists to alter any form of life.

Doudna: This is the thing that's so exciting. Laboratories around the world have adopted this technology for applications in animals, plants, humans, fungi, other bacteria, essentially any kind of organism that labs are studying.

Walsh: In Boston, a world-leading geneticist believes CRISPR heralds a breakthrough for transplant patients, growing their organs in animals - a revolution in science.

George Church (Professor of Genetics, Harvard Medical School): The power that we have now is almost limitless. CRISPR is one of the few technologies that works first time. There's almost no field of medicine, agriculture and ecosystems that will be unaffected.

Walsh: So what is gene editing? This is the Francis Crick Institute in London. When it opens in a few months, it will be the biggest biomedical laboratory in Europe and will be a centre for gene editing.

Inside each cell in our body is our genome - billions of pieces of genetic code. It's the blueprint or instruction manual for life. A single error or spelling mistake in that DNA can trigger disease. There are thousands of genetic disorders and many more conditions that develop as we age.

CRISPR gene editing enables scientists to scan the entire genome and then, using molecular scissors to cut both strands of DNA and delete, insert or repair the code.

One of the first targets is type 1 diabetes - a condition that affects ten-year-old Jack, who's from Minnesota in the Midwest United States. His pancreas doesn't produce the hormone insulin, which controls blood sugar levels, so his dad Chris has to keep a careful watch.

Chris Burlak (Schulze Diabetes Institute, University of Minnesota): This is one of the challenges you have when you take care of a type I diabetic is that you end up checking blood glucose Io to I2 times a day, to manage a healthy blood sugars. So we take turns at night checking at either 2.30am or 5.30am to make sure that his blood glucose doesn't go low at night.

Walsh: So you or your wife has to get up at 2.30am or 5.30am every morning, 365 days a year?

Burlak: That's exactly right, yeah.

Walsh: And Jack never wakes up?

Jack: Not at all.

Walsh: What can happen to you if you don't take action?

Jack: Well first of all, I could faint. Then that's why I bring a buddy with me, when I'm at school, and I feel low, so I don't faint and then no-one knows.

Walsh: Chris Burlak hopes gene editing might cure his son. He's an immunologist at the University of Minnesota.

Chris: Come on, Jack. Nice job, Jack.

Walsh: In type 1 diabetes, insulin-producing cells in the pancreas, called islets, gradually die. Islet transplants are possible but limited, because of a worldwide shortage of donor organs.

Walsh: Chris and his team believe the answer could come from pigs.

Burlak: We sequence genes. We sequence our PCR reactions, and...

Walsh: They're aiming to delete some key genetic markers that identify the pig cells as foreign, so that the human immune system won't reject the transplant.

Burlak: So what we're looking at here are pig cells that we've cloned and then gene edited using the CRISPR technology.

Walsh: So you're trying to make them more human-like?

Burlak: That's correct. So being like stealth islets means that they won't get recognised by the human immune system during transplantation.

Walsh: So for some people with type 1 diabetes, could this potentially be a life saver?

Burlak: This could be a life saver for sure. People who have suffered from type I diabetes, who have secondary complications that damage their nerves, impair their vision, cause kidney failure or cardiovascular disease.

Walsh: Human trials are some way off but if it works, then patients like Jack could have a tissue-matched treatment from gene-edited pig cells.

Walsh: And Jack, how cool would it be if it was your dad that found a cure?

Jack: It would be so amazing. It'd be five million times amazing, because he's my dad.

Burlak: That's sweet.

Walsh: Gene editing has revitalised the whole concept of cross-species transplantation. Although pig organs are of a similar size to ours, the human immune system would instantly reject them. And there have been fears that such transplants could allow diseases to jump across the species barrier.

Walsh: Now, gene editing offers the hope of solving both problems. Scientists envisage organ farms of the future providing an endless supply of hearts, lungs, livers and kidneys for transplant.

Walsh: What you are seeing here is the mixing of two species - pig and human. This pig embryo is being injected with human stem cells, by a team at UC Davis in California.

Walsh: So these are the human cells going down the tube into the pig embryo?

Pablo Ross (University of California, Davis): Those exactly.

Walsh: Into the pig embryo?

Ross: Exactly.

Ross: The idea is that these cells will integrate into this embryo, and then we'll transfer this embryo to a recipient, a female, and allow it to develop past this stage.

Walsh: The pig embryo was gene edited using CRISPR to delete the DNA instructions to create a pancreas. The ambition is the human cells will fill the void and grow a human pancreas inside the pig.

Ross: Our hope is that this pig embryo will develop normally, but the pancreas will be made out almost exclusively out of human cells. So that then that pancreas could be compatible with a patient for transplantation.

Ross: So this is the farm where we keep the animals after we've done the embryo transfer.

Walsh: Just like the earlier diabetes research we saw, this is an attempt to produce pancreatic tissue in pigs that the human immune system won't reject.

Walsh: The embryos carried by these sows are known as chimeras. In Greek mythology, chimeras were monsters made from a mixture of animals. Regulators are concerned where the human cells might end up in the embryo - perhaps even altering the pig brain.

Ross: We want to prevent that. We think that potential is very low, in part because of the whole architecture, size and composition of the pig brain, we don't expect human brain growing, but that's something that we want to support with scientific information.

Walsh: This research raises profound ethical concerns - crucially, just how human are the piglets developing inside these sows? It's such a sensitive area that the chimeric embryos will not be allowed to go to term, but be removed after 28 days' gestation for tissue analysis, when they're still about half an inch long.

Walsh: And a team in Boston has addressed another huge obstacle to cross-species transplants - that pig diseases might infect humans. They used CRISPR to delete dozens of copies of an animal virus embedded in the pig's DNA.

Church: It opens up the possibility of not just transplantation for pigs to humans but the whole idea that a pig organ is perfectible.

Walsh: Do you envisage that we will have pig organ farms that will yield a limitless supply of tissue for human transplantation?

Church: Absolutely. We have a huge shortage now, which is getting worse, and so this could be very clean and on demand so that they're very healthy when the surgeon gets them.

Walsh: But this is also a story in the here and now. Patient trials are already under way involving an older form of gene editing. Scientists are focussing on blood and immune disorders, because faulty cells can be removed from the body, corrected, and then put back. It provides a proof of principle that gene editing can treat disease.

Walsh: San Francisco, a centre of gay culture in the United States. In the early '80s, it one of the first places to identify AIDS. The Castro district was particularly badly hit. Thousands of mostly gay men were infected with HIV, a virus for which there was no treatment. Ever since, it's been a focal point for the fight against HIV AIDS.

Jacob Lalezari (Quest Clinical Research): It was a holocaust of young, delightful, gay men dying miserable, painful deaths of AIDS. We had two to three patients dying a week in this office, and it's been a sea change, where 27 years later, HIV is basically a stable, chronic, manageable illness.

Walsh: Jacob Lalezari is a veteran of the fight against AIDS. He's been running clinical trials here at the Quest clinic since the late '80s.

Matt Chappell (HIV trial patient): Hey, there

Lalezari: How are you doing?

Chappell: I'm good - yourself?

Lalezari: Good to see you. I was just looking at your chart and I like what I'm seeing. Your T cell count is still around 500.

Walsh: Matt is one of around 80 HIV patients who've been on the world's first gene-editing trails. This personalised treatment involved taking immune cells from their blood. Doctors deleted a gene to replicate a rare genetic trait carried by a few people, which makes them resistant to HIV infection.

Walsh: So, Matt, how did that go?

Chappell: It was really interesting. My lab values look really good, my viral load is pretty good, pretty, well controlled. I mean that's the kind of point of the study, to see how well you can naturally control HIV after you get the treatment.

Walsh: And how long have you been off your meds?

Chappell: I've been off my meds for two years.

Walsh: That's pretty amazing.

Chappell: It is pretty amazing.

Walsh: You are, and have been, at the forefront of HIV trials now since then. How, in general terms, have those studies gone?

Lalazari: It's too early to say for sure whether gene therapy is going to be the key component of HIV cure or whether it might be a component in combination with other therapies, that specifically address the viral reservoir.

Walsh: and what would it mean for you if we got a cure?

Lalazari: I'm planning my retirement around an HIV cure. After 27 years, I've had a bellyful and I can't wait to hang it up.

Walsh: Cafe Flore, in the Castro district. Matt's been coming here since the late 80s and met up with two fellow survivors from the AIDS epidemic.

Chappell: When I sit here, I can name I0, I5, 20 people that I used to talk with, the very thing we're talking about now - how do we get a cure? They're all dead.

Matt Sharp: We're sitting in a restaurant where people used to come dump ashes of their loved ones. So we're sitting in, essentially, a graveyard.

Walsh: You guys have known each other over 20 years, what is it like to be very much at the heart of the search for a cure?

Sharp: It's definitely personal, being here in the city in the centre of where a lot of the research is happening, where a lot of friends, and family and lovers have passed away.

Jeff Sheehy: I have a friend who's 23, recently infected with HIV. When I talk to him, I tell him, take your medications, take care of yourself because you will be cured.

Walsh: The next gene editing trial will be in patients with the serious blood clotting disorder haemophilia. The treatments were designed here by the biotech firm Sangamo, which also did the HIV studies.

Fyodor Urnov (Sangamo BioSciences): The joy of editing is DNA becomes a drug target. We can approach the human genome and change it, essentially, at will. There is good hope that, in your and my lifetime, genetic diseases of the bloodstream will be very significantly diminished, that we will have essentially cured.

Walsh: Many people carry genetic traits that make them less susceptible to certain diseases. It might be possible to develop these into a genetic vaccine, so that everyone could benefit.

Urnov: We know what the disease-protective signatures are in human DNA that cause people to be resistant to cardiovascular disease, and neurodegenerative disease. And as technology develops, I see no fundamental obstacle to - if you wish - a vaccine. I think gene editing as a vaccination against cardiovascular or neurodegenerative disease is not futuristic.

Walsh: Gene editing also raises the extraordinary possibility of eradicating diseases like malaria, Dengue fever and the Zika virus, by targeting the mosquitoes which carry them with what are known as gene drives.

Walsh: Scientists do this by inserting an artificial gene into the DNA of mosquito embryos that will make an increasing proportion of female offspring sterile. The gene drive is embedded in the DNA to ensure the changes are inherited - unlike natural evolution, where chance is involved. Within a few years, an entire species of mosquito could be eradicated.

Walsh: The research is not taking place in Africa, but in London, in a sealed basement laboratory at Imperial College - just yards from the Science Museum.

Walsh: Rather than using insecticides - which kill multiple organisms - gene drives could pursue any one of the thousands of species of mosquito down the generations to extinction.

Tony Nolan (Imperial College): This can be a very powerful technology because the mosquitoes do the work. We're making sure that we build the gene drive to work as efficiently as we possibly can.

Walsh: But a genetic destruct button would raise concerns about possible unintended consequences on the ecosystem.

Nolan: People are right to have concerns with any new technology. We need to make sure there are no ecosystem consequences.

Walsh: Given that there are hundreds of thousands of people, mostly children in Africa, who die from malaria infection every year why not go ahead and introduce this and see if it can save lives now?

Nolan: Well, I mean the temptation is to use it as soon as you've got it. But I think it would not be ethical to throw something in there that's not tested as much as you possibly can, which is what we're doing here.

Walsh: Gene editing is already allowing scientists to take ownership of natural selection and make radical changes to farm animals. Let me show you a powerful example of gene editing. Many breeds of cattle have horns, like these Herefords here. But scientists took the genetic variation for hornless cattle from the Black Angus you can see there, to produce these - hornless cattle. Currently, millions of dairy cattle have their horns physically removed each year.

Alison Van Eenennaam (University of California, Davis): It's a fairly painful procedure where typically the horn buds are treated with lidocaine and then burnt off. And it's not pleasant for the animals or the farmers. The advantages are you can basically go into a single animal and make a number of changes in genes that you know are superior, rather than having to cross it in from different animals. So it basically accelerates the rate that you can make genetic improvement.

Walsh: But animal welfare groups warn gene editing could create unforeseen problems, and is only needed where you have intensive farming.

Van Eenennaam: I look at the benefits of this technology and, to me, that that outweighs any potential risks which, in this case, I think are very minimal. We've actually brought in the variant from a different cow breed and so we've been eating that variant for hundreds of years. So I don't see food safety risks, I just see an animal welfare benefit.

Walsh: And you don't need a science degree to do gene editing. Manipulating DNA is now so simple that many people are trying DIY gene editing at home and buying their kits, from here.

Walsh: Hi, Josiah, good to see you.

Josiah Zayner (Biohacker, The Odin): Nice to meet you.

Walsh: This is your CRISPR gene editing lab?

Zayner: Welcome to my lab.

Walsh: How difficult is it? Would you be able to show me how to do it?

Zayner: Yes, I can definitely show you how to do it. It's something you could learn almost as simply as driving a car. Everything somebody would need.

Walsh: He showed me the CRISPR kits he sells - starting at around $140.

Zayner: We have DNA that that you'll need to do the experiments. There's a lot of things people can do. We like to promote a lot of things related to food and brewing. A lot of people use yeast to bake, to brew, completely safe and it's actually a genetic engineering tool that a lot of scientists use. Or engineer a yoghurt, right? To have different flavours.

Walsh: It feels like I'm in an episode of MasterChef.

Zayner: All right, you ready to do an experiment?

Walsh: OK, I'm ready.

Zayner: All right. So, first you need to put on one of these.

Walsh: OK. Why do I need to wear that?

Zayner: Just to make you look silly. So these are the tubes we're going to put the chemicals we need to do the experiments. Now you can see the bacteria on there, they are white. Move your loop over and fill up with some bacteria. And now we're going to break up any of the clumps. Looks good.

Walsh: Yeah.

Zayner: Now we're ready to add some DNA. We need this tube, which has part of the CRISPR system. Once they get the DNA inside their cells, the whole genetic engineering process will take place.

Walsh: So this really is democratising science.

Zayner: Yes, it's really that simple. So this media wouldn't let the bacteria grow, but now, after editing its genome, you can see the little bacterial colonies, the white dots there.

Walsh: Wow.

Zayner: 30 years ago people were taking computers, starting companies with computers and just completely changing the world. And the fact that this is going on with synthetic biology and genetic engineering is amazing, right? The next amazing company could come out of a two-car garage in the San Francisco Bay area, or anywhere, anywhere in the world.

Walsh: But it is gene editing in human embryos which raises the biggest ethical concerns. This might cure inherited disease or add in genetic enhancements - paving the way for designer babies. A team here, at the Francis Crick Institute in London, has been given permission to do gene editing in one-day-old human embryos - but purely for medical research.

Walsh: Kathy Niakan, named by Time magazine as one of the world's 100 most influential people, will use CRISPR to edit out key genes from the embryo to try to identify the genetic faults which lead many women to repeatedly miscarry.

Kathy Niakan (Francis Crick Institute): What I'm hoping is that it provides us with really crucial insights into early human development.

Walsh: The UK is the first country to formally approve gene editing in human embryos, which will be allowed to develop for just a few days.

Niakan: I think it could help in identifying ways in which we could improve IVF to identify those embryos that are likely to continue to develop and thrive, and give rise to healthy babies. And, in terms of miscarriage, it could help us identify some of the underlying molecular basis of why certain embryos do not go on to develop successfully.

Walsh: But this research rings ethical alarm bells for a San Francisco-based society which monitors biotechnology and genetics.

Mary Darnovsky (Center for Genetics and Society): Once we produce genetically modified human embryos in labs around the world it's really not that big of a jump to try to initiate a pregnancy with one of those.

Walsh: And for critics, it raises the spectre of a brave new world of genetic discrimination.

Darnovsky: You could find wealthy parents buying the latest offspring upgrades for their children, genetic changes that either did or even that were thought to make their children superior in some way. And there we could start seeing the emergence of genetic haves and have nots. Some people have called them genetic castes, people have thought about this. They've called them the "gen-rich" and the "naturals". And we could be seeing much greater forms of inequality even than the already horrendous levels of inequality we live with.

Walsh: Now that the gene genie is out of bottle, society will have to decide what limits should be placed on this emerging technology, which has the potential to alter so much about the world around us and to transform our health.

Doudna: Just thinking about the opportunity to cure a genetic disease - not treat it, but really provide a cure in the future is so exciting that I think, you know, we want to embrace that and we want to enable clinicians and scientists to work together to bring that to reality.

Walsh: And do you think diseases will be cured?

Doudna: I feel they will. You know, people say that this is going to be the century of biology and I think there's a lot of truth to that.