James Valentine's Interview on ABC Sydney with Professor Ian Alexander on Thursday, July 11.

Transcript:

James Valentine

I had the pleasure the other night of going to the Children's Medical Research Institute dinner their Jeans for Genes dinner, I think this is a dinner that many of you will be aware of perhaps you've been or do you see, here's the get a lot, a lot of publicity was quite a feature on the social calendar kind of thing got a lot of media attention. They use the whole genes as in denim jeans themes, a way of attracting attention to what the Children's Medical Research Institute was up to. And at this, of course, I then got the chance to go to the Institute to see some of the things they're doing, but also made extraordinary people doing work that just blows your mind. One of them is Professor Ian Alexander. He established the Gene Therapy Research Unit at the Children's Medical Institute in 1995 as a joint venture with Sydney Children's Hospitals, network and so I thought look, is there a chance can we get to him to have a bit of a chat and he's here today welcome Professor Ian Alexander. Hello. Nice, nice to have you along. It feels as though genetic research around the world and at your institution, is at a point almost where all the other technology the world is catching up to the available knowledge to the sort of things you can do.

Professor Alexander

That's exactly right. What's really driven the genetics and genomics field recently is the ability to decipher the human genetic code first on that was done just once took 10 years and $3 billion. We now have machines that sit on benches around cities like Sydney that can do 18,000 individuals in a year. In a week, he ran for under $1000. So, everyone's got my own genetic code. And now it takes a week and I could be if you wanted it done what that's mean, it's we've got this tremendous capacity to understand genetic disease and to diagnose it and where we're still lagging is their ability to treat. And there's a bit of a paradox really, and particularly as a paediatrician working in a Children's Hospital, you're often in the situation where you'll have an infant or a child with some undiagnosed condition. Modern genetic sequencing technology can be used to look at their genetic blueprint, the DNA can tell you exactly what to find the exact spelling error that's causing the problem. You can go back to the parents and say we know what the problem is. Question two from the parents is, what can you do about it? Yeah. And this this is where the field's at, we need to work on closing that gap between what we can actually diagnose and what we can meaningfully intervene in and treat and this is where the field is suddenly exploding.

Valentine

I suppose there's worse problems to have in the medical field. Isn't that like it's worse the other way, isn't it when you can figure out what it is? You've got to know what it is before you can treat it.

Alexander

It's a great step and that alone is a big advantage to children and their families or adults for that matter tonight to know what the cause is, and sometimes that immediately cues, the physicians and healthcare professionals into best medicine on the planet for that particular condition. Yeah, but very often, there isn't an answer out there. And that's where the area that I'm particularly interested in is starting to play a major.

Valentine

We'll come back to that. That explosion of treatment possibilities that you told me we've been talking there. But let's just go back now. We're now talking 20 years ago, you're sitting there when it's still, you know, $3 billion to look at somebody's someone's code. And your part of people saying, we're going to turn this whole place into a genetic research laboratory. That's what we're going to do here. What did what did you see then?

Alexander

Well, I don't think people foresaw the incredible diagnostic pair or not as immediately that the technologies that came along that have allowed us to do that so fast and on population scale. probably weren't anticipated, certainly not as quickly as it happened by people like myself, but that is perhaps one of the most transformative things in terms of this ability to just and understand not only individual, genetic makeup and population, genetic makeup and do understand genetics, at a population level, this almost inconceivable the power that sets.

Valentine

But you must have saying that like, this is the way to go. Because it was a big thing in the day, it wasn't a design, they say we won't be researching all sorts of things all sorts of treatment we're going to specialise in genetic research here.

Alexander

Correct. One, I guess part of it is that the destination is conceptually simple. But the path to get there is inordinately complex. So many of us could see where we wanted to go. But the challenge of getting there was, was the real issue. Yes, it has, it has quite a long journey. And we often think in terms of breakthroughs. But this has been a series of small difficult steps that over time have added up to something profound.

Valentine

We're talking to Professor Ian Alexander from the Children's Medical Research Institute, the Gene Therapy Research Institute, in particular, and talking about gene therapy, what's available now? One of the kind of things, you know, as he says, the sort of techniques that are exploding at the moment, so what, what are you saying, what's the excitement, you know, like, this is what I was getting at when I was out there and at the dinner, this is, I think, all of you, I feel like all of you are sitting on something, it's almost like, we can't quite tell you yet. But it's amazing.

Alexander

Well, I think we're wanting to tell, but many of us are more excited now than we've ever been. And we've hit this point where we have the possibility of, of treating genetic disease by actually going into the genetic code, and either repairing or replacing parts of the genetic code, and we call this gene therapy. And it's probably worth just give me a little bit of background. And, you know, the human genetic blueprint is 3000 million, 270 Sydney telephone books worth of letters, and getting a single letter wrong can cause a devastating disease. So, the idea of being able to go in and repair a particular spelling error, replace the little bit of text that, that the spelling error's located in, is mind blowing. The other thing that's worth appreciating is that we can do this for particular organs. So, it's every cell of our body has the full genetic code. But the challenge isn't that we need to go into every cell, if you've got a sick liver, then we may just want to go into the liver cells. If you've got a particular congenital blindness, you might want to go into the back of the eye the retina, right?

Valentine

Because the cells are always being replaced, the defect keeps being replaced?

Alexander

It depends which tissue so the cells in your brain, the nerve cells pretty much last your lifetime and they're not being replaced. In other locations, like the lining of your gut or your blood cells, a lot of them turn over. So, it's very dependent on exactly which condition you're trying to treat, which tissue and organ it involves understanding the biology and tissue.

Valentine

So, it's not going to help everyone?

Alexander

It’s not going to help everyone. That's it's not a panacea. But it's tremendously powerful in certain contexts. And the other, you know, we often think about, oh, I can fix the genetic code in this condition or that. So, are you just talking about genetic disease? And the answer here is now we're not just talking about genetic disease, there's extremely exciting things happening in in the cancer field. And we can talk a little bit more about that. There's even things happening in the infectious diseases field where you can use various tricks to render people's bone marrow resistant to certain viruses. So, we're only limited by our imaginations. It's, it's a profoundly exciting space.

Valentine

I suppose that's what I mean, we're seeing a world and you know, medicines, an example of and as many others, but we're seeing a world where it's really computing power, a lot of ways that technology has reached our imaginations, you know, there is, you know, you could crunch enough data, all of that genetic data and all the information and all of my individual information to get a potential treatment.

Alexander

That’s right. The challenge is a combination of the ability to number crunching all that data, and then design and develop the technologies that can go in and make the genetic corrections or deliver the corrective piece of DNA. And we've recently been thinking about how we can the technologies at the point where we can actually edit the genome. So, you know, we all know about word processes and editing documents, there's the biggest thing that's happening at the moment is editing technology.

So, we're looking at a future where, for some, say conditions, genetic conditions in the liver, rather than a child, needing a liver transplant, we could go in and edit the spelling error in the particular gene that's faulty in the liver, and the child would be cured and be able to keep their own liver.

Yeah, that's where it's going. But you need the technology to do that. And if you want it to work on a broad population basis, often you've got to feed in all of that number crunching and genetic information that you've just mentioned.

Valentine

We’re talking to Professor Ian Alexander from the Gene Therapy Research Unit, the Children's Medical Research Institute. Now, some hearing this will start to think, hang on, we're talking about genetically modifying babies, are we talking about what happened in China a year or so ago with a, you know, a, GM baby.

Alexander

This is a very, very good and important question, because it goes straight to the heart of the ethics and morality, what we're doing. So, when I mentioned before specific organs, the point here is that we can go into cells and tissues in the body, that are causing a particular condition in a person but have nothing to do with a future generation. So, if you stay away from the tissues in our bodies, like the testes and the ovaries, whether the cells that lead to sperm and eggs that give us the future generations, you're treating an individual, you're not changing the genetic blueprint. In future generations, what they did in

China was exactly that. They went into a, basically a fertilised egg genetically modified it so the person that arrives arises from that every single cell in the body is genetically modified.

Valentine

Did they do it? As it a hoax?

Alexander

I don't think the West really knows fully what's going on, the scientist involved has been censored but what we're talking about is the fundamentally different, it's just that you have some cells in your liver that are not working properly. We can fix them for you. It has and then it has not. Let me give you an example. Imagine you had haemophilia. We don't want to get too technical with the genetics, but it's X links. So, when you have daughters, they'll all be carriers. If I treat you by Gene therapy by correcting your liver, and then you have your daughters afterwards, your daughter still gets the X chromosome with a faulty gene on it and they're still at risk of having.

So, you've only treated the individual. There's no implications for future generations. So, it's a totally different approach, really, because even though it's important to understand because people do get concerned about

Valentine

Yeah, because even though in the examples that you're saying we might think to ourselves, but to be good to get rid of haemophilia from the population, wouldn't it? You're saying ethically that's wrong, we should continue to only deal with individual cases?

Alexander

Well, I think that's personally I think, ethically, that's wrong. But I think this is something that would excite tremendous debate and diversity of views. And I would argue, there's no real need to do it. Because we're going to have the technology when people come along with those conditions, there'll be a direct treatment for that individual, that doesn't pose any greater risk to the society. If we were to start trying to intervene in a way that meant that people were being born where every cell in their body had been corrected, including what we call the germ cells, the ones that are going to give rise to the next generation. What if we didn't get it quite right. And, and there was we did things to the human genetic blueprint that are unintended. So, it's a very important area. And, and I think, fortunately, we don't have to go there. Because we can just look after the particular cells and tissues in the body, you have a problem with the CNS, the nervous system, then you can just go in and fix the nerve cells and no implications for the next generation at all.

Valentine

So what sort of successes have you had so far? What kind of things in there right now.

Alexander

Let me give you a really profound example. And obviously, I'm a paediatrician, so I'm interested in in peadiatric disease. So quite a bit going into children, adults, but also some amazing things in children, but the one most recently, and we've been participating in an international clinical trial in this space.

And this is a condition called spinal muscular atrophy. So, this is a genetic condition, that you have infants born that are healthy at birth, that very quickly, the nerve supply and their muscles, what we call motor neurons just die off. And in many of these children with the severe form of the disease, pass away by the time they're 15 to 20 months old. Gene therapies have come along, and we have a strategies and technologies we can we can deliver a healthy copy of that gene to the nervous system by a peripheral injection into a vein. And so, we've been, this is technology that's coming from North America, or at least the treatment of that disease, we've participated in some of the development of the underlying technology, but that there's children walking and talking, yeah, that would have lost their lives. And so, this is fundamentally transformative. And this is very early days, and that, that product, it's still being travelled around the world, but it just got licensed in the US the other day.

Valentine

Okay, so this is the kind of thing gives you hope for our conditions.

Alexander

Well what we do this one, it was about six different conditions where there's no licensed product, there's, there's another one for a rare form of blindness, where you just inject these gene transfer formulations at the back of the eye, and you can recover genetic function in the retina. That's the bit of your eye that's detecting the light coming in through the front of your eye, and, and help these people retain vision. And this is just the beginning. Yeah, it doesn't, it's an absolute New World Order.

Valentine

Does it give an increase of hope to a lot of those conditions that are rare, where, like a drug treatment will often be very difficult to get if it's rare, because you can't afford the trials and, and all that sort of stuff. But this sort of thing, I'm getting a sense of a technology that's somewhat more transferable. And you might be able to sort of say, Oh, actually, we can take that and treat, a dozen different things .

Alexander

Absolutely, if you've mastered, imagine you've mastered delivery of gene transfer the technology to the back of the eye, then there's a whole host of diseases, or genetic conditions at the back of the eye that you could go after. Yeah, so it's a heavily. It's a therapeutic approach that's heavily founded in the underlying technology. And you're quite right, the ability to its transferability. So, you're using the same technology, say, to get into the back of the eye, but the bit of DNA, or genetic material that you packed inside your little gene transfer formulation is dependent on the condition you're trying to treat. So yeah, it is more transferrable. And I think the other thing we're seeing, we've been involved in generating this underlying technology. And we did some work in 2014. It was in the clinic treating adults with Haemophilia a by 2017, so three years from the lab to the clinic, right, that's amazingly fast, much faster than we've seen in the history of say, drug development. Yeah. And then the other thing that's nice about the genetic therapies is, depending on your approach, it might be a one-off treatment and cure for life. It may not be it depends on the condition and the approach. But that's in a perfect scenario. That's what you'd be shooting at. Yeah, you come in, you get a single treatment. And that's it. Fixed.

Valentine

Are you envisioning envisaging a world where genetic treatment of the kind of thing you're describing is as common as drug treatment?

Alexander

I don't think as common as drug treatment. But I think, and I'd like to, I'd say, I may sound like an over-enthusiastic individual in this space, I'm so close to it. Yeah, that may be true. But, you know, this is not a panacea. But the reach of this technology is way beyond where it is at the moment. And it's not going to, you know, it's important listeners understand that this is not the panacea for everything. Yeah, there are lots of reasons that there are some conditions that won't be able to go after. But it's, it's going to be a very widespread paradigm, if you like, probably, it's not like you'll have a gene transfer formulation in your bathroom cupboard, but it'll be something that, you know, most of the big public hospitals and private hospitals, there'll be a therapeutic strategies for a whole range of things. As I said, not just genetic conditions, various forms of cancer, or some forms of infectious disease, and even problems, potentially wound healing or things that you might not think of as remediable with genetic intervention. The bottom line is genes are the software that runs cells in your body. And so most functions of your body physiological functions, there's the potential to modify those working with genes. And it's not always about repairing a defect, in the context of the biggest thing that's hitting the cancer field at the moment. You know, there's a bit of jargon, but it's called car T cell therapy. So, this is where T cells which are white cells that are capable of attacking and killing cancer cells. And conditions and scientists around the world are discovered, you can take these cells out of the body, you can genetically engineer with a new function. So, this is not repairing a fault they had, this is putting in a function. So, when they go back in now specifically recognise features on the cancer cells. And, and then so you grow them up in the tissue culture disc the genetically modifying them, you put them back in, and I specifically go and target the tumor cells. And this, this form of gene therapy has absolutely exploded globally. And is, you know, becoming very widespread. It doesn't. It's an immune immunological approach, because the, the cells have to recognise the cells for immune recognitions. So again, it's not going to it's not the answer to cancer, if you like, but it's, it's, it's a big step forward. And it's, and it's gene therapy.

Valentine

Say it's like it, it strikes me a lot like, you know, we're walking around now with a small device in our pocket, that's a giant computer, which was a science fiction idea. Generation ago, this is the same thing we were This is a science fiction idea that they'll be the sort of interventions at this level that we can, we can do and fixed off. It's amazing.

Alexander

I mean, we're not quite at the device in your pocket. But I mean, you've made me think about there's one company in the UK that's building a little device that’s no bigger than your mobile phone that sequences DNA. So, you know, you could have one takeaway on weekends, recreational sequencing while you're on a picnic somewhere, you can actually you know, take a little blood spot, prick your finger, a little drop on a microfluidic device into the machine, sequence the DNA, upload it to the cloud, right? And then get report when you get home.

Valentine

Oh, this will tell me if there's something wrong.

Alexander

They're talking about the democratisation is not therapeutic. But, you know, the technologies pushed in this incredibly powerful direction, where, where they'll be more and more accessible.

Valentine

In Alexander fascinating. I feel like we get back tomorrow and do a whole different half hour.

Alexander

I’d always be happy to come and chat about it.

Valentine

That’s Professor Ian Alexander from the Gene Therapy Research Unit, Children's Medical Research Institute, one of the one of the great things of Australia, really, the Children's Medical Research Unit. Yeah, it's fantastic unit, doing extraordinary work at the highest level. So, thank you so much for coming in and telling us what's up.

Alexander

Thanks for having me and thanks to the listeners for listening.