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Transcript

Peter Doherty: It's incredible, but some scientists seem terrified of the possibility they might discover something that puts them in odds with accepted wisdom. I mean, the greatest thing in the world is to overturn it, quite frankly!

Andrew Pollard: Hello, my name is Andrew Pollard. I'm director of the Oxford Vaccine Group at the University of Oxford.

Welcome to our podcast series, The Oxford Colloquy: Trust in Science, bringing you the stories, facts, and people behind the science. On this episode, I'm speaking with Professor Peter Doherty, who won a Nobel Prize for discovering how a type of white blood cell, the T cell, recognises things in our bodies that shouldn't be there, like cancer and viruses when we have an infection.

I'm really looking forward to this discussion with Peter Doherty.

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Andrew Pollard: Professor Peter Doherty, it's great to welcome you to the Oxford Colloquy podcast.

Peter Doherty: Thank you.

Andrew Pollard: So we're going to speak to you today as a Nobel laureate, as an immunologist, and a fellow of the Royal Society but partly also in your interest in connecting about communicating around science and trust in science, which I think is going to be an interesting part of the conversation that we have.

You have a long list of accolades from being the National Treasure in Australia which must be very special; I'm not quite sure what that exactly means... But also the Albert Lasker Award for basic medical research. You're a companion of the order Australia and

have a Nobel prize in medicine jointly with Rolf Zinkernagel, which was awarded in 1996.

So Peter, perhaps we could start off just by you telling us a little bit about how your career started - because I'm obviously disappointed to learn that you started as a vet. So tell me more about that.

Peter Doherty: Yes well, as an Australian of that vintage, I was educated in the British type of educational model, where you went straight from secondary school into professional school, if you're going in that direction.

I decided not to do medicine. I was very naive - I was 16 years old, and I decided not to do medicine because I didn't want to be around sick people listening to the complaints all the time. I didn't realise that animals have owners, but actually I went into the veterinary science area.

I was growing up in Brisbane the capital of the big state of Queensland, which is a very big agricultural state, especially then. And so I thought I'd go into the animal industries. But I'd also been very much influenced by kind of social constants by being brought up in Methodism. And so I decided I was going to save the world by improving food production, by doing research on domestic animals, which is what I did for 10 years, working in Australia and in Edinburgh.

And then decided I need to learn a bit more about immunology, especially the new science as it was then of T-cell immunology. So I went to the Australian National University, the John Curtin School of Medical Research to spend a couple of years before I intended to join the CSRIO, the big Australian government research institution that did a lot of animal health research and was well funded.

But while there, Rolf Zinkernagel and I happened to get together. We made a big and very unexpected discovery. So I never got back into the veterinary world and I switched from being a veterinary researcher to a basic medical researcher. As my friend Cedric Mims would have said, I became an MD, a Mouse Doctor.

Andrew Pollard: Peter, so going back to the mid 1970s, where you were doing your work on T cells and viruses - what was the observation that eventually led, I guess, 20 years after that, to the Nobel Prize?

Peter Doherty: We were using what was then a new technology and discoveries frequently come from application of new technology. And also, it often helps if you haven't been in the field too long, because you don't get trapped by thinking in the field.

And I hadn't been doing basic immunology. And Rolf Zinkernagel came from Zurich. He'd taken a course in immunology. He told me he'd been trained to be a surgeon, and

at some point, both he and the head of the surgery program agreed he might find something better to do. And so I've never questioned about what that was...

And so we weren't really immunologists and in the immunology world. And we were looking at lymphocytic choriomeningitis infection in mice. It's a fascinating...

Andrew Pollard: So this is a virus that causes a brain infection in mice?

Peter Doherty: Well, it causes a persistent infection that's passed on in utero. Mice are normally infected for life and without symptoms, but if you take that virus and you inject it into the brains of adult mice who've never been exposed, they develop a severe encephalitis and die.

And that's what we were studying. I was very interested in inflammation in the brain, so we were looking at T cells localising to the brain. That's what I was doing when Rolf came. We just happened to be in the same small lab and started working together, and we found there were very, very potent killer T cells.

Andrew Pollard: So those are a type of white blood cell that - was it known at that time that they interacted with virally infected cells?

Peter Doherty: There had been some work showing that T-cell transfer - done by a guy called Robert Blandon who was at the John Curtin School. You took inbred mice and you infected one with a virus, and then you transferred immune cells from another mouse into that mouse, and he'd shown that the T cell component seemed to be clearing the virus. And there was also evidence from a bacterial infection called listeriosis.

So we applied it into the system, and we took the killer T cells out of the brain, and we used virus infected cells and tried to kill them. And they killed like crazy. We discovered actually the nature of what we call immunological surveillance and we suggested after a number of experiments that what was happening is the virus was in some way modifying these transplant molecules so they looked like foreign to our own T lymphocytes and then our own T lymphocytes cleaned the cells out.

And what you have to do in a virus infection is get rid of the virus infected cells, because viruses can only grow in living cells. So the cell is a factory that's making new virus particles that are then infecting other cells. So unless you stop that, the disease will go ahead.

So we made an initial discovery. It was big. We developed a theory around it. And then a lot of people worked on it. We were quite controversial. We went from being totally unknown to being kind of famous or notorious, depending on your point of view. And 10 years later, it all came together in several different laboratories, two in the United States, particularly, and, one in England.

And of course the thing about winning a Nobel prize is make the initial discovery. A lot of other people will work on it. Then you get the prize.

Andrew Pollard: Fantastic. And so really, it's the ability of T cells, these white blood cells to recognise cells which are infected with a virus, which is critical for clearance because the virus is packaged inside cells. And if you don't remove those infected cells, you can't get better from a virus.

Peter Doherty: It was fairly soon found that some of the same rules apply to rejecting cancer cells. We now know that many cancers can be under T cell control for quite a long time, especially the virus induced ones like Epstein Barr virus, and now this is being exploited in totally new therapies, which use that T cell response.

Now, we can't claim responsibility for that. That's been another Nobel Prize to Jim Allison, and now I'm blocking out his name, old age, but a Japanese colleague [Tasuku Honjo]. And so that's revolutionised particularly melanoma therapy and now therapy against a number of other cancers.

Andrew Pollard: Well, I went to Guy's Hospital in about 10 years after that, 1986, to do a BSc in immunology. And it felt like such an exciting time in immunology when the T cell receptor had only just been discovered in 1982.

Peter Doherty: Well, that was 10 years after us, they discovered the T cell receptor. At the stage we were working on it was always described as the “enigmatic T cell receptor”, which means that nobody knew what the hell it was.

And then some people got it quite wrong. They claimed they'd found it and they got it totally wrong. And then the whole thing broke open. And again, It was very much driven by advances in technology that, gene sequencing advances; a lot of people who made great machines, engineers who made the machines, people who developed the ideas and so forth.

So, you know, science is a very collaborative endeavor between people with different skills and different disciplines. And we were lucky. We just at the pointy end of this particular one. And not all Nobel Prizes are like that, but majority of them actually, often come from quite a chance discovery.

You can't decide to discover something.

Andrew Pollard: So Peter, so you didn't set out to win a Nobel Prize, but given that we've got an opportunity to speak to young scientists today, and obviously I'm asking you this for a friend, what do you need to do to win a Nobel Prize?

Peter Doherty: Well, you know, obviously I didn't set out to win a Nobel Prize, I'm the first person ever with a veterinary qualification to win a Nobel Prize, so you wouldn't study to be a vet for a start.

I think it's about how do you do good science. If you're doing as I was, I had the privilege of being able to do curiosity driven science, follow the questions that interested me and follow the main chance. I tell young scientists you know, be very aware. Be aware of what's published and what's in the literature and stuff. But don't be trapped by it. I tell them - I'm an experimentalist - I tell them, love your data. Live with your data. Look at your data. So many young scientists will generate a mass of data and never really look at it properly.

And not only that, I tell them, as you're looking at that data and you're living with it, try to work out what it means. Don't be afraid if it seems to be telling you something that's not accepted in the field. It's incredible, but some scientists seem terrified of the possibility they might discover something that puts them in odds with the accepted wisdom. I mean, the greatest thing in the world is to overturn it, quite frankly.

And the other thing though, Andy, is they should write. Start to write early and write often, because I've found that enlightenment generally comes as you try to write what you've done or what you've found, that's when you really think your way through it properly.

Andrew Pollard: So the work you did that led to the Nobel Prize was almost 50 years ago. What have you done since? Does that sort of then define you for the rest of your life?

Peter Doherty: Well, the rest of my career was spent working on these killer T cells. I was trying to understand immunological memory, T cell memory, T cell effector function. I stayed with it.

What I actually found through the years is that many times I would come to a certain level of conclusion. And then basically because the technology improved, and the big change in technology was the discovery of what we call the tetramers, and its uses in flow cytometry and so forth. The technology would change, and suddenly you could do experiments you couldn't do before.

Then another big transformation was when we started to be able to do single cell PCR from cells. And that was a transformation in understanding what was happening.

Where I sort of decided enough for me was when we got into the area of how epigenetic control of T cell affect function and memory, which was something I very much wanted to see done, but I very much wanted to see it done by someone else.

And one of my postdocs really drove it forward. But at that stage, I was already in my early sixties. And I thought, this is their stuff, not mine. And I started to back off and the last 10 years of my active research career were really spent building other people's careers. And some of them are highly successful and dominating the field. So I'm very pleased with that.

I've also written seven books on science and the scientific life. And my latest book is the first one I've ever written that's different. It's actually partly a family story, but it's the definitive work on empire, war, and tennis. Nobody has ever written that book and nobody will ever be stupid enough to do it again... But it was a lot of fun to write it!

Andrew Pollard: So Peter, I think certainly over many years now, you've been very much engaging with the media and discussing science. Have you, looking from an Australian context, seen a change in the trust in science from the public in those interactions, the way the journalists ask you the questions?

Peter Doherty: Well, you know, I came into it totally as an amateur. I hadn't been involved in that area really at all. And I'm not a teacher. I've never been a teacher, I've always been a researcher. So teaching is at the level of, you know, in the lab, I've had professorships - that's been in research operations, basically.

So, after, the Nobel Prize was announced, I was working at a place called St. Jude Children's Research Hospital in Memphis, Tennessee. And, that's where we were living, but I got a call from Australia. The Nobel Prizes are announced in October, and I got a call from Australia around Christmas Eve, I think, telling me I'd been made the Australian of the Year, and I said, “what the hell is that?” Because I've been in Memphis for eight years at that stage, and, they explained it and said, you have to come out to Australia for this.

So I took it on, and we went out there four times through the coming year, and I was actually found myself speaking at all the national capitals and speaking in town halls and to very, very broad audiences, being interviewed by the local journalists who mostly wrote about football as far as I could see. And I suddenly realised there was a tremendous void in people talking about science to a broad audience. There been some people who'd really tried very hard, like Sir Gustav Nossal, who was a great leader at that time.

And so I started to get into that. Then I found I was getting more broadly interested in the other big scientific challenges we face, like climate change. And I started putting a lot of time into talking to those people, finding out about it. I even wrote a book called A Light History of Hot Air - and then I just kept up with that theme.

Now, has it gotten worse? It's gotten better in some senses because you can disseminate things very, very quickly by the internet and by social media, and it's all great. But there's just so much information out there and of course, bad information gets disseminated just as readily.

And not only that, groups like people who are embittered or angry, anti-vaccination people, for instance, they've all found each other. So there are now national sort of networks. And so it's an enormously challenging time.

I think, we're all struggling with this. What does it mean for our future, firstly, and the nature of communication? And then basically the way our children are growing up, in front of an iPad or a screen for much of the time, what are they absorbing? What direction are they going? Book sales have certainly fallen off a lot. I think books are enormously important. I think long form writing is enormously important. I think not everything can be said in 200 words or in a very short treatment.

But I hope it takes us to good places. It does in some senses, but it also takes us to very bad places at times.

Andrew Pollard: Do you think the public understanding of science has improved over the course of your career? And in other words, I suppose science education in schools and the general knowledge that there is about science publicly.

Peter Doherty: I think that the problem with us is that we live in this universe where, small universe where people operate by evidence and reason and reasoned debate and we go backwards and forwards, we criticise each other. We're used to pretty robust critique. Quite frankly, if you publish scientific papers, you get it absolutely slammed by anonymous reviewers. And even in the public sphere, we can get into some very heated discussion. We're used to all that.

Public isn't. The public - there's a substantial part of the public, if they want to hear anything, they want a dogmatic statement. So I spent a lot of my time pointing out, we're not a priesthood, we're not telling you what it is. The best thing any scientists can say is "our best understanding is that". Now, of course, that's not what a lot of people want to hear. It's not what politicians want to hear. They want a dogmatic statement, but if you make dogmatic statements in science, you're going to be wrong some of the time and maybe much of the time.

But I think, we need professionals in this and we need to have a much better understanding of how information gets across, how it gets through. What I try to tell all the young scientists I know is: don't get obsessed by this. But you have the skills that I often lack with things like social media, YouTube, and so forth. Spend a little bit of time on that. Do it thoughtfully. If you've got good visual material, put it up on a YouTube or something like that. And just try to learn to interact at the right level.

I think a lot of them get it, actually. I think, for instance, I used to get invited all the time to speak at schools. I'm exactly the wrong person to speak at a school. You need your young postdoc or student, someone who's got good communication skills, and some of them are absolutely wonderful at talking to school kids. You need people they can relate to. People can't relate to me. I'm a grandfather figure, if that...

Andrew Pollard: Peter, when you look at where science is in your field at the moment, what excites you about the future and particularly the understanding of T cells and surveillance using cytotoxic T cells, the killer T cells?

Peter Doherty: Look, I think, as you know, the medical advances are often incremental and they don't necessarily answer the question scientifically. I mean, we know, for instance, treating with anti TNF can have a great benefit in cases of rheumatoid arthritis. But talking to a friend who's really an expert in that inflammation area, he says we really don't know how it works.

Andrew Pollard: Yes.

Peter Doherty: I mean, a lot of the time, we make a good medical advance, but we're really not too sure on how it works. I'm very excited by, I think, the work that my colleague Katherine Kedzierska, who sort of followed me and is heading the group in Melbourne, and my other colleague Paul Thomas, who took over, really, my Memphis effort. They're both doing fantastic work now on human immunology.

It used to be really pretty difficult to do definitive studies in humans, but I think what's changed that is something I talked about earlier, the capacity to work with very small numbers of cells and interrogate what's happening in single cells.

And now we can, for instance, do pretty good science with babies and old people where you can't get much material, all you can get is a bit from blood. Of course, the whole human thing is always a bit limited by what you can sample compared with a mouse, but then we have to study humans because in immunology, because they live a long time. We need to understand what's happening in aging. As we know with COVID, majority of people who are dying were old people. What's wrong with their immune systems? What's happening here? We don't really understand it very well, but we're getting a much better understand much faster.

So I'm excited about that area, the capacity to have great collaborations with clinicians. And we found them pretty easy to set up and to really push ahead with trying to understand human disease much better.

Andrew Pollard: And I think certainly when you look at the immune system in the elderly, that's an area which has had very little attention, until recently.

Peter Doherty: It's very odd, and when you think about it, when I came in to do biomedical research, there were two communities that were particularly interested in immunology. One, for obvious reasons, were the rheumatologists. The other was the neurologists, who were interested in multiple sclerosis. So those were the two communities.

There was never, surprisingly, that much interest from paediatricians, and gerontologists only really became prominent fairly late in the day, I think. And most general physicians, cancer researchers were appalled by immunology. I think what's happening in cancer research and with immunology coming so much into play and having such an effect - I think it's really exciting and great because you know, as a scientist, in the end we want to find solutions. That's what we're about.

Andrew Pollard: Peter, there was one great story about you in the pandemic, when you were looking up on Google, about Dan Murphy's opening hours and people won't know that Dan Murphy's is an off license...

Peter Doherty: Ha! What was happening is my publishers had got me on Twitter and I had a following of maybe 20 or 30,000 people on Twitter.

I used it a bit, but not much. And when the pandemic came, well, I thought, I'll use this as much as I can to to try and get messages across to people. And it was actually extremely good through the pandemic until it became X and a lot of the controls were taken away and a lot of good people went off it.

But basically, I had Google open, I had my email open, and I had Twitter open. And I meant to find out Dan Murphy's opening hours on Google, but I put it into Twitter and tweeted it. So that probably gained me about 100,000 followers, because suddenly - my Twitter handle is @ProfPCDoherty - and suddenly it's like, this guy's an idiot! He's human!

Andrew Pollard: So Peter, what's next for you? Are you currently writing or what's the next project?

Peter Doherty: I retired the middle of last year. I formally retired at age 82 and I'd been working part time, but through COVID. I was spending six days a week doing science communication. I was extremely busy, I got quite exhausted. I wrote 120 weekly blog articles. I published two books, but the one was a book on tennis, which I just about finished before COVID hit. So I was totally taken up that, but I was Zooming and talking to people across the planet and in Australia. It was fascinating and flattering, but I really did get very tired.

And so we've been spending a year getting all our things like getting a financial advisor, getting wills sorted out properly, doing all those sorts of things. Just put a lift in our little two story house so we don't fall down the stairs and break our neck...

But I'm contemplating a book, a kind of a rapid wrap-up book on COVID, for my own satisfaction. I haven't been reading the literature closely. I need to go back in again, talk to a lot of people. I'm thinking of a book on the long and the short of COVID-19 or something like that. I really think I've got to try and pull this together in my own mind.

This is the most documented pandemic in history and we've had great science applied to it. So hopefully we're going to find out some really significant things from it.

But so anyway, that might be my final scientific type of book. But I am thinking of writing another book on fragility, which would be somewhat different.

Andrew Pollard: Well, let's hope you keep thinking and writing about science, Peter. It's been a great pleasure speaking with you today, and thank you for joining us.

Peter Doherty: Thank you. It's been fun, and I wish I could have been in Oxford for this discussion because it's always so nice to be in Oxford.

Andrew Pollard: Maybe next time.

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Andrew Pollard: That was the Oxford Colloquy, Trust in Science, bringing you the stories, people, and facts behind the science. So you might be wondering, what is a colloquy? A colloquy is a discourse or conversation, and I hope you'll agree that that's what we've been having.