

[Voiceover] Welcome to The Pathologists Cut podcast. This RCPA podcast highlights the critical work of pathologists and the integral part pathology plays in medicine and health care.

[Dr Michael Dray] I'd like to introduce Professor Richard Scolyer. He is a senior staff specialist at the Department of Tissue Pathology and Diagnostic Oncology at the Royal Prince Alfred Hospital, Sydney, Australia. He is both a consultant, pathologist and co medical director for the Melanoma Institute of Australia and a clinical professor for the University of Sydney.

Professor Scolyer provides a clinical consultation service for the diagnosis of difficult pigmented lesions. He receives more than 2000 cases for opinion from Australasia and beyond annually. That is a huge number. Hi, Richard. Thank you very much for joining us today.

You've got so many accolades. It's been embarrassing reading them all out just to see how busy you've been.

[Prof Richard Scolyer] Great to talk to you. And yeah, you know, we have to go way back from from when you were one of our trainees at Prince Alfred Hospital. Yeah, many, many moons ago and went back to New Zealand.

We don't get a chance to catch up too often these days. But, thrilled when I heard that you were going to become the RCPA president and you're doing a great job.

[Dr Michael Dray] Thanks, Richard. Well starting with our first question. So so Australia and New Zealand has one of the highest rates of melanoma in the world. Can you explain what is the problem with melanoma. What is melanoma and why we have these highest rates?

[Prof Richard Scolyer] Michael, you mentioned that Australia and New Zealand have one of the highest incidences of melanoma in the world. In fact, we have the dubious honor of having the highest incidences of melanoma. I think there's actually a battle at one stage.

Australia had that title for many years and New Zealand overtook Australia. But I think the latest data is Australia is back on top. So anyway, and it isn't a good honour to have, but unfortunately, that's what it is.

And it's really a consequence of the fact that the predominant population of people who are living in our countries have origins from Celtic origin. So they have very pale skin. And our skin is not really built to live in the beautiful climate that we that we live in.

And and we enjoy an outdoor lifestyle in Australia and New Zealand. And we expose our bodies, skin to the sun and ultraviolet radiation from the sun is what causes the vast majority of of melanomas. So what what is melanoma?

Melanoma is a cancer of the cells that produce pigment, which is called melanin. And these cells are located in the bottom part of the surface layer of the skin. So they're they do have a normal function, and that's to produce pigment and the pigment acts as a barrier to ultraviolet radiation.

So the pigment absorbs ultraviolet radiation. So that's its normal function. And people have pale skin that I make as much pigment. So the radiation gets in and that can cause damage to cells. In fact, that's damage to the DNA of the cells, these melanocytes that cause them to undergo changes which make those cells proliferate uncontrollably and then acquire the ability to infiltrate into underlying tissues. And then ultimately they get access to blood vessels and lymphatic channels which allow them to spread elsewhere around the body. And and unfortunately for people who that happens to, it can be can be fatal.

[Dr Michael Dray] If I recall not that long ago, a report of a metastatic melanoma was certainly bad news for the patient. There were limited treatment options and quite a poor outcome. But things have changed recently. Researchers really making a difference.

Can you explain more about your work?

[Prof Richard Scolyer] Well, it is absolutely incredible, I guess, to start off with. If you detect melanoma early and when it's on the skin surface, make the correct diagnosis so that all melanomas basically that can be suspected by clinicians, but ultimately they're diagnosed by a pathologist.

If it's detected early, diagnose accurately, then the patients treated the vast majority of patients, more than 90 per cent will be cured by simple surgery, so simple excision of the lesion. But up until a decade ago, if the melanoma spread beyond the skin surface, all bets were off.

And if it had spread around the body a decade ago, 50 per cent of people would be would be dead within a year. And in fact, if it had spread to the brain, most people would be dead within six weeks.

And the problem was we didn't have any effective drug therapies for people with with advanced melanoma. So melanoma that spread around the body. And really all we could do is give surgery. There's a few few toxic therapies like Interferon and some chemotherapies were tried to canvassing, but basically they didn't work.

And then through research that there was this incredible breakthrough, it was discovered, you know, through multi collaborative research, multidisciplinary collaborative research that about half of melanomas or a bit less were driven by a mutation in a particular gene called BRAF.

And that was the the driver that that was causing the melanoma cells to proliferate and grow. One of the genes that was affected. Some drugs were developed that initially in fact, drugs were developed that were thought to be targeting BRAF, but and they didn't really have much clinical effect.

And then people thought, oh, gee, this great discovery isn't amounting to anything. And then a few years later, some more selective BRAF inhibitors were developed. And we were fortunate at Melanoma Institute, Australia to be part of the initial trials of these drugs.

And patients were coming in on death's door. And Rick Kefford was leading these clinical trials and he was saying, this is incredible. I've never seen anything like it in a short period of time within a week. The tumors are melting away.

The incredibly hot PET scans were gone, completely cold. Patient's symptoms, it all go away. They felt great. They'd gone back to work. And, you know, this is amazing. I've never seen anything like it. So this is an incredible breakthrough for people with BRAF mutant melanomas.

And I might just highlight at this stage that pathologists played a critical role in not only the research that identified the BRAF gene being critical in melanoma, but in fact to identify the patients who might respond to this therapy.

Pathologists, the ones who identify the presence of the mutated BRAF gene. But anyway, so the incredible breakthrough, great responses. But then after a while, most people after about a year, they tend to. Not to respond to the targeted therapy with BRAF inhibitor, nowadays, we combine it with another drug, what's called a mek inhibitor, which targets the next protein downstream in the in the signalling pathway that the mutant BRAF protein activates. So we combine these two drugs together anyway. Patients usually develop resistance within within 12 months. And unfortunately, resistance can be can be difficult to treat.

So that was the first big breakthrough. And, you know, the first superhero that we developed in this fight against advanced melanoma. But then more recently, probably around five years ago, immunotherapy came about. And that really has been a game changer so that it's effective in up to 60 per cent of people with advanced melanoma.

It's very effective in getting rid of the melanoma and the people who respond to it. In

fact, we think many patient patients are being cured by these therapies and how how immunotherapy works. Is it basically tumor cells are smart. They they develop mechanisms that can shield them from the body's own immune system, which its normal job is to recognize things like tumors and to try and kill them off, much the same as when you get an infection or you cut yourself. Your body's immune system responds to that and fixes up the damage done. Cancer is also a foreign population of cells and the immune system mounts a response against it. But tumors can that can block off the immune system.

These immunotherapies, what they do is to is to block that shield, if you like. So to allow the body's own immune system to now recognize their tumor cells and to fight and attack the the tumor cells. So that's how they work. And as I say incredible responses, we think some patients are being cured of their melanoma, who a decade ago would have been. Yeah, that would have been dead.

[Dr Michael Dray] That's a that's a great triumph, isn't it? Just such a short period of time. And two quite separate management protocols, two quite separate treatments. So tell me about the zero deaths go from melanoma.

[Prof Richard Scolyer] Well, I'm at Melanoma Institute, Australia. That's what our goal is, to make sure no person dies of melanoma. That's what we what we want to do. And we've got a multi pronged strategy to deliver on this goal. We've organised ourselves so that melanoma institutes really a well in some respects is a virtual collaboration of clinicians, clinician researchers, scientists, health professionals, researchers who come together to try and fight the disease. And we're affiliated with public teaching hospitals in Sydney and various universities, including the University of Sydney. And we get together every Friday morning at the at the Post Center in North Sydney to have our multidisciplinary team meeting where we discuss the most challenging melanoma patients and try and come up with a plan about how they should be managed anyway. This is the institute. This is the the best minds in melanoma that I know anyway.

And we have three principal pillars of our activity. One is clinical care of melanoma patients. The other is education of both health care professionals and and the community. And our last pillar is around research. So we recognize that not all patient melanoma patients can come and be treated at the Melanoma Institute, but we want to try and enable all patients to get the best possible care.

So one of the ways that we're going to deliver on this goal is through research. And we've got a multi pronged research program that's organised around five themes which basically follow the patient journey. The first theme is organized around prevention and management of patients at high risk of getting melanoma.

The second themes around early stage, melanoma diagnosis and treatment of that, the

third themes around advanced melanoma. So melanoma that's spread around the body and our fourth and fifth themes cut across all of those themes. The fourth one is supportive care and survivorship. And this is becoming an increasing problem in melanoma, where patients who previously would have died of their disease are now living for for a long time. And that in itself presents an additional set of problems that we're tackling.

And our last theme is around health economics, because we want to prove what we're doing is cost effective for the community. I must say, you know, we're talking about melanoma and but I did allude to our first theme, and I think it's really important for for all of us, particularly in Australia and New Zealand, is to heed the prevention message. So really important that we talk about sun smart behavior, try to avoid the sun in the middle of the day when you're outside, wear protective clothing, a broad brimmed hat, long sleeve shirt, put on sunscreen to any exposed skin sites, put on sunglasses and seek the shade whenever you're outside.

[Dr Michael Dray] It's a great public health message, isn't it? Now, we've had COVID in the last year, and that's been an interesting experience, to say the least. How is that? Has that created any unique problems in your clinical practice or in the world of melanoma?

[Prof Richard Scolyer] Yeah, well, it's been a challenge for all of us. I guess the first thing to say is the whole community, including health care and researchers have been focused on COVID and rightly so. But, you know, melanoma doesn't stop in a pandemic. Still had patients still getting melanoma. And we need to manage patients effectively. When we had the first lockdown period, we had some, you know, anecdotal evidence afterwards that perhaps some patients were developing more presenting with more advanced disease than what we would have liked to have seen.

But we don't really have hard data to show that there was any major systemic adverse consequences. But it has thrown its challenges to us at the Melanoma Institute, as I'm sure it has to you, in delivering health care.

If we want to keep our patients in our health care professional, stay safe. So we've had to reorganise how we do our work. And so we've done a lot of things to do. A lot of patients are seen, wherever possible, through Zoom telehealth consultations, our clinical trials, teams broken up into two teams to try and avoid crossovers. If someone does pick up COVID-19, we're not going to infect the whole team. And yeah, and also we're reliant on philanthropic money at the Melanoma Institute to keep going and our major fundraiser at community based fundraisers. And obviously you can't do things like that in a in a pandemic. So that caused a big hit. And we had to, you know, make sure we had challenging decisions to make about how we could resource what we needed to do to to keep things afloat.

So, yes, it has been challenging. But, you know, I'm very proud of what we've done. In fact, our research output for the last 12 months has been a record year. We've had more than 200 publications and including some in in, you know, very, very high impact journals.

[Dr Michael Dray] Writing papers and lockdown has been the theme. Yeah. Now, that that brings me up to the fact that you've recently received the Cancer Institute of New South Wales Premier's Award as outstanding cancer researcher of the year. Now, that's that's kudos.

That's a huge achievement. And I'm also told that you're the first pathologist to ever receive this honor. So so what does that mean to you and what does that mean to the wider profession?

[Prof Richard Scolyer] Well, I think, first of all, you know, I'm very fortunate that I work in an incredible environment, both in the pathology department at Prince Alfred Hospital and at the Melanoma Institute, where, you know, we really strive for excellence. It's a it's a great team of people. And any any success that I've had is really a consequence of the opportunities that have come my way from being in such an environment. You and I were both mentored by Stan McCarthy, one of the world's greatest pathologists. So, you know, those sorts of things rub off on you and provide opportunities. The other person who really made a difference for me and my outlook, particularly in research, was John Thompson, who's a professor of surgery, used to be the head of the Melanoma Institute before Georgina Long and I took over.

Georgina is a medical oncologist, and she's someone also who I greatly admire and have worked very closely with a long time. But yeah, there's a great team of people. And me winning this award is more a reflection on the work that the team has done than than me as an individual.

I'm really, really proud that that pathology has been recognised in in this way, because I think it highlights the fact that as pathologists, we really have the unique place that we bridge the gap between the patients, so, say, clinical care of patients and basic science.

It's because, you know, we see bits of of patients in the biopsies as histopathologists, so we might unique observations, but we also have clinical knowledge. And and, you know, I know the team that I work with incredibly appreciative of their skills and insights that that I and the other pathologists that I work with can bring to the table. So I think it does highlight that that the opportunities for pathologists in research and to be honest, I think we've it's not just an opportunity. I think we've got a responsibility to to really, you know, make a difference.

Like when we make a diagnosis, when we see with one patient, we're reporting on a sample. And that's very important for that individual patient. How they get managed, to a

large extent, gets determined by how we interpret a pathology specimen.

But I think doing research, it gives you an opportunity to make a difference to many thousands of patients. So I think as pathologists, we should embrace that because it is important that we we try and make a difference to to as many people as we can.

[Dr Michael Dray] I really respect your modesty, Richard, but I know having worked with you. I hold you up in similar esteem as to Stan McCarthy. We're getting near the end of our conversation, I think what advice would you give to someone considering a role and pathology? You have told the virtues of the histopathology, but is there anything more specific or more general advice you would give?

[Prof Richard Scolyer] Well, the first thing that I'd say is it's incredibly interesting field of medicine to get into every day is different. I think of it with tissue. Detectives we're trying to figure out what a disease is and work out the best management for a patient in concert with the patient's clinical team.

It's a very diverse profession and very diverse working life that you get to experience. So when I started to be honest, I wasn't sure that this was a career that I wanted to dedicate my life to. It enjoyed seeing patients, but I thought I enjoyed that medical school, thought I'll give it.

I met some pathologists and one guy in particular, a called Bastian de Boer was he's a pathologist in Perth. He was singing the virtues of it. So I thought I'll give it a go. And I really enjoyed it.

And I think most pathologists that you speak to will tell you the same thing. They're really happy with their career choice. So my advice to anyone considering it, I think particularly to medical students who really going to make choices about what career they want to get, get into, and many great choices in medicine, speak to a pathologist, go visit their pathology laboratory and get an understanding of what the work involves and see if you think it's a good fit for you. And that'll give you a bit better understanding of what's involved. But from my perspective, it's a very enjoyable profession and couldn't couldn't speak highly enough of working in this vocation.

[Dr Michael Dray] We had a huge pathology curriculum when I was at med school, and more to my embarrassment is that actually I didn't realise you could have a career in pathology I just thought it was something you had to learn to pass the test to pass your exams. It wasn't till 10 years later, after some time in general practice, I realised oh, those guys are on to something and I'm came back onto path.

[Prof Richard Scolyer] As pathologists, we need to get out there and get involved in the teaching of medical students and junior doctors whenever we get an opportunity.

[Dr Michael Dray] OK, well, thank you very much for talking with me this afternoon, Richard. It's good to catch up and look forward to meeting face to face at some stage.

[Prof Richard Scolyer] Yeah. Great to talk to you as always, too, Michael. And yeah, and stay well and healthy. And congratulations on the great job you're doing as RCPA president.

[Voiceover] You have been listening to The Pathologist Cut podcast with the RCPA president, Dr Michael Dray. For the latest RCPA updates, make sure you're following us on Facebook and Twitter.