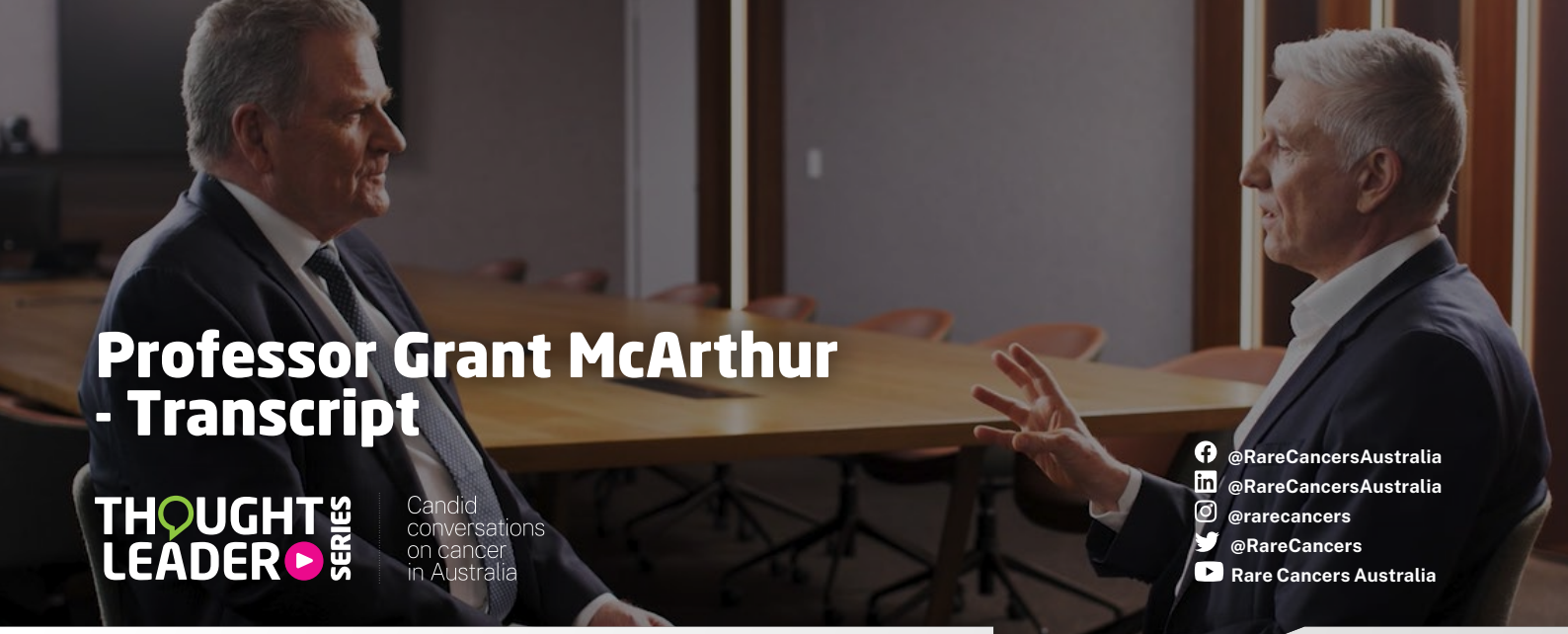

Professor Grant McArthur - Transcript

THOUGHT LEADER SERIES

Candid conversations on cancer in Australia

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Richard: So welcome, Grant.

Grant: Great to be with you, Richard.

Richard: I was thinking about how, how we met and our first conversation and it was in Adelaide and you said to me so I think rare cancers. Australia was about two years old and you said, so you're going to try and take over the world, are you? Because ultimately all cancers are rare. And I wondered how that in the intervening eight or nine years has evolved in your thinking?

Grant: Yeah, it's a really interesting conversation. We had, Richard, you know, back then. So that was just at the time when we really were picking apart the pieces of the cancer genome with genetic sequencing and really started to understand that every cancer is different, every patient's cancer is different and is unique. And so one of the challenges we have is dealing with that in the setting of wanting to build evidence and grouping cancers together that behave in a similar manner because it's easier to come up with the right treatments when you can do that. So yeah, still to this day, I think that remains a challenge for us. How do we really personalise and individualize cancer treatment, given the variations that one patient's cancer has to another?

Richard: Yeah, and we were talking about that a few weeks ago when I when you sent me a paper on the six hallmarks of cancer, which have now become the eight or ten hallmarks of cancer. And it's always fascinated me that we think we've got our targeted therapy and it and it attacks what we think is the cause of cancer. But six months down the track, cancer's outsmarted that and it progresses down its inevitable path or its seemingly inevitable path. And that's all about the rarity of cancer, I suspect.

Grant: Yeah. Well, I think what's fascinating about the hallmarks of cancer. So Weinberg and Hanna and Bob Weinberg, Doug Hanrahan, you know, articles that have been so well cited in the scientific literature always point young students, you know, to those articles to understand cancer, just how it's evolved in my career. You know, it started off with limited number of hallmarks and they just keep growing because our knowledge of cancer is improving all the time. And probably what we're recognizing, particularly in the last 10 to 15 years, is it's not just what's within the cancer cell. It's the environment that the cancer cell sets in, the immune system, the blood vessels, other factors that dictate how the cancer behaves that now are very important. And we're starting to think about how one can leverage that knowledge to come up with new treatments.

Richard: And when you talk about the time in your career, I mean, you you've done incredibly well and built an enormous history of success. But what attracted you to medicine in the first place?

Grant: Well, actually, first of all, Richard, I have to say that I don't think about, you know, personal success as well. It's all about what the field is doing and what it's been delivered for patients. So I'll get to your question about what drives me personally.

But, you know, what I love is the fact that, you know, the cancer survival, five-year survival, which is the benchmark we usually like to use. When I started training, 50% of people with a cancer diagnosis would survive for five years. It's 70% now. That's a phenomenal improvement. So that is the success and that's multifaceted. And I can tell you what gets me out of bed in the morning is to see the next wave, the science that the discovery scientists are working on today, how that's going to continue to enable us to improve that percentage even more. And that's what's very exciting.

So I guess I better answer your question around, you know, so look, I was a as a as a young kid, I was lucky enough to go through primary school when the Americans put astronauts on the moon. I mean, that was just phenomenally exciting for a curious kid to see something like that happen. You know, the greatest engineering feat perhaps in the history of humankind. Yeah. And that enabled me to develop a love affair with science. I loved astronomy. I love the human body I found very interesting and. As a young teenager. Then I started to think, well, you know, I really want to help people and I want to see the world a better place for people. And medicine is just such a remarkable way of combining a career that involves science and involves caring and helping people. And so that's what attracted me to medicine.

And then the other question is why cancer? Yeah, so and cancer to me as I was a medical student was just full of mystery. And it was an area of a lot of scientific development. It was pretty rudimentary back when I was a medical student in the 1980s. It was still pretty rudimentary back then and it's really accelerated since then. But gee, I made the right choice for sure because cancer oncology, so I'm an oncologist. So cancer as an area of research is just full of some fascinating science that now we can turn into better outcomes for patients.

So I feel privileged that I had the intuition to be attracted to it. And actually when I lecture, I give lectures about career development to young scientists, young clinicians. You know, I say trust your intuition. My intuition was cancer is a fascinating problem that we can do something about. And we have as a field. And that's what to me has been remarkable way to earn a living. But it's more than earning a living, of course. It's about seeing improvements in individual patients and then in the statistics across the many patients. And now increasingly, we want to look across the world. We want to deal with the problems of inequity in cancer outcomes. So much work to be done, but I feel so lucky and privileged to be living at a time where one could be so stimulated in your work.

Richard: So we've discussed why medicine and then why cancer. But the obvious next step is why melanoma?

Grant: Oh, that's a very interesting question for me, because I had not done melanoma research or clinical work before I got recruited to the Peter Mac. And so there was a bit of serendipity here because my predecessor that was leading the melanoma work at Peter Mac had been recruited and moved away. And so it was offered to me. Would you like to do Melanoma Grant? And so I stopped and I said to myself, Well, no drug treatments work. That's a really good place to be in for a research clinician, scientist, clinician to move into where you don't have effective drugs. Furthermore, melanoma was a disease where you relatively could get access to tissue a bit easier to study what was happening in the cancer. And so I put all that together and I thought, yep, I'll do that. I'm interested in research LED improvements in clinical care, no drugs,

work, what an opportunity. And where is that? Now is another interesting question. So I love seeing young people that are putting their hand up to work in brain cancer because I think brain cancers where melanoma was when I moved into it.

Richard: Yeah, fantastic. And if you're going to have an impact on Australian society, melanoma would also be a good place to start I should imagine, because we, we do well in melanoma or skin cancers don't we, because of our geographic location.

Grant: Yeah. Sadly we lead the world in melanoma and skin cancers based on our geography and the amount of UV radiation we have in our environment and the fact that we're of European ancestry, so many people in Australia. So it's a worrisome combination. The statistic that always blows me away is 10% of the world's melanoma cases are in Australia. And you think about what a small population we have relative to the rest of the globe. That's a phenomenal statistic

Richard: Extraordinary. Yeah. Thank you. I was going to ask you, too, I've always been a little bit confused and it's slightly different subject, but about what's the difference between the Triple C and Peter Mach and how do they work together and what your role in that in that as executive director of that composite organisation?

Grant: It's yeah, we had now it's going back over 15 years. We had a vision for a comprehensive cancer centre in in Melbourne modelled on the US Comprehensive Cancer Centre model, where you have treatment, research, public health, science and research, education, everything rolled into one physical location and at the time it was recognised that well we really want to invest. And when I say we, that's federal and state governments, a lot of philanthropy. It was a very successful philanthropic project to fundraise to build this building that we're in today. But what really division was to get maximum benefit for all patients, no matter where they enter the health system, they need to benefit from the investment of having a cancer centre. And so for me to have the privilege of leading the VCCC Alliance ten organisations coming together in Victoria, we may have additional members and organisations involved in the future, but we want all patients, no matter where a patient enters the cancer system, to get the very best care research led care because that's what's made a difference to outcomes for people with cancer.

Richard: Yeah. And it's I've heard the expression before that particularly for a rare cancer, which we can assume now embraces a lot, that the new standard of care is clinical trials for rare cancer patients. And I know that that here I think within this building, there's something like 200 clinical trials going on at any one point in time. It's an amazing exercise to run at. I said to Christine, my colleague, this morning, that you could not walk into this building as a cancer patient and you would have to believe that a lot of people care about your health. Just it's an extraordinary building. And you must have gone through the transition from the old Peter Mac to this. It must have been quite an exciting time, I should imagine.

Grant: Yeah. So the old Peter Mac and Peter Mac was in a remarkable growth phase in a cancer center, the model of care, of embedding research into a clinical treatment facility as well as established. It's been associated with much better patient outcomes across the globe. And Peter Mac was just growing and completely outgrew the space that was previously in East Melbourne, about three kilometres from here. So Peter Mac needed to expand and has continued to expand into this into this new building. But one of the exciting things was to bring Peter Mac into a vibrant academic environment where you've got the Walter and Eliza Hall Institute, the we have the University of Melbourne, Melbourne Health, Royal Women's Royal Children's, and it goes on now just down the road here. Now, you know, the Monash Institute of Pharmaceutical Sciences, Science number one ranked Pharmaceutical Science University in the world right here, you know, down the road walking distance from where we're sitting now. So, you know, it's a remarkable precinct here. But what is more important than the precinct is the community. It has to serve the community and take that research, lead clinical care out. And that's why I'm very passionate about my role now as executive director of the VCCC Alliance.

Richard: Yeah. And on that decision to move into that role, then there must be some reduction in the amount of clinical activity. And that must be a hard decision for someone as passionate about patients who committed your life to it. But there's an opportunity there to build a better system or to create something as powerful as this is. Was that a difficult decision to go down that path?

Grant: Well, yes, I think you've hit a nail on the head. Not easy. And that's why I still do one clinic a week. Yeah, because I you know, I love clinical work. It's very satisfying. Also enables me to keep my finger on the pulse of changes and the way care has been delivered by experiencing it. I'm a person that, you know, I understand things better if I've experienced it rather than hearing and reading about it. So I've kept that going. But really the reason for moving from a full time research and clinical role then into a leadership position for me was to benefit more patients. Yeah. And that's what we can achieve.

Richard: One thing that you have experienced and you've being quite open about it is cancer yourself. And that that must have been quite a...it must have been always a shock and a trauma, but it must have been a unique experience for a clinician to experience themselves as a patient.

Grant: So it's eight years now, almost eight years since I had my cancer treatment for stage three prostate cancer. And it was interesting. I did an interview actually with Neil Mitchell on the radio here in Melbourne not that long after returning to work after I had my prostate cancer treatment. And I said, Neil asked me the same question. I said, Oh yeah, things haven't changed much. But now with the years going by, I do recognise that I've learnt probably two key things. You know, I do have an even greater sense of empathy with what patients are going through and I've recognised, you know, a change there. The other thing is I recognised that I didn't communicate very well with my family and I've had heightened recognition of the importance of people that are close to a patient family and their or other loved ones that are close to the patient in dealing with cancer most effectively is very important and at least for me, an unusual situation, I guess, being a cancer clinician and cancer researcher. But I didn't communicate very well with my family. And so I spend a little bit of time when I see a risk now for poor communication between patient and their family or their loved ones. Their supporters just, you know, give some lessons about how to do it because it's so important that you can't deal with cancer on your own. You need support.

Richard: Yeah, it is. And I remember we had a young father who had a had a cancer that was he was not going to get better. But it took us, I think, about six months of working with him to work out how to tell his nine-year-old son. Yes. And it was it those sorts of elements of cancer are so, so troubling and so perplexing, but they don't fit within the clinical framework as such.

We've talked a bit about before, I know you've had some high profile patients that are where you've, they've inevitably been treated by things that are not funded on the PBS. And that's inevitable as I think we were talking on the phone the other day and you said, you know, unless you've got a way of funding medicines 2 minutes after they're approved by the FDA in the US, then there's always going to be this, this, this gap. But sometimes people have suggested that to prescribe something that is not PBS funded is in some way not evidence based, which I, I thought it would be interesting talking to asking you that question, given that I know that you've done it and you're about the most evidence focused person that you could possibly imagine. And so how do you make that decision and where do you make that judgment?

Grant: And and yeah, I think it's very important to be on top of the details of the evidence, because when something gets listed on the PBS, it's because, firstly, the medicine is safe and it's effective. So there's an evidence base around safety and an evidence base around it being effective. But on top of that, the PBS listed because it's passed the hurdle of cost effectiveness.

Richard: Yes.

Grant: So if the question for an individual patient is, can this medicine improve my survival or improve my quality of life and without causing untoward side effects that are unacceptable? Well, that evidence comes in well before a PBS listing. So we have the Therapeutic Goods Administration in Australia which assesses safety and efficacy and will list medications. There's usually a gap between listing on the approval by the Therapeutic Goods Administration and then listing on the Pharmaceutical Benefits Scheme. So there's a gap there. There's also a gap in time between the evidence being presented and or published in peer reviewed scientific journal before there's a Therapeutic Goods Administration listing. So there are these these inconsistencies, if you like, between when the evidence becomes available and when there's access. Either one can write a prescription, which you can do after Therapeutic Goods Administration listing or reimbursement on the PBS.

So to get to your question as to how does one communicate that well. A study from quite some time ago, actually led by one of my mentors, John Swartzberg, actually went and asked patients, do you want to know about information that's about medicines that are not yet listed on the PBS that your doctor thinks you might not be able to afford because they're very expensive? And the answer is the vast majority of patients want to know. And to put it simply, and we say this to my junior clinicians, well, you don't know that that patient doesn't have a wealthy uncle that in this situation will fund the medicine. So you've got to give the patient your best opinion based on the evidence, but in a supportive way and an understanding way, because it is difficult if there is a new medicine that has significant efficacy and it's not yet on the PBS.

Richard: Yeah, yeah, absolutely. We see it every day in with very rare cancers. There's not much listed on the PBS. So it's always that conversation. And I think that one of the other points around getting things listed on the PBS is it's normally largely based on clinical trial data. But I know that you have done a lot of work and a lot of thought around real world data and and how we might use that in this.

Grant: Yeah. No, it's I think I think it's vital. So it's about gets back to the how do you gain evidence and evidence can be obtained from clinical trials. That's the usual way of getting evidence together. You have to be eligible. A patient has to be eligible on certain criteria to get on the clinical trial. Sometimes in the real world situation, not all patients with a diagnosis will necessarily fit the eligibility for the clinical trial. So you want to get additional evidence in the real world setting.

But what we really need is to change the way we're thinking that instead of having to have a large clinical trial, large numbers of patients, irrefutable evidence, we go through a more staged approach where you might get an earlier listing and approval and then you continue to collect real world data after listing to firm up the evidence. And that is one potential way of getting medicines accessible sooner. But it has to be a rigorous process to enable that evidence to be collected. You don't want to make mistakes and less medicines that that have that really are not very effective and expensive. You know, I understand that the funders don't want to do that very much understand that. But we do need to speed things up because at the moment it's just too slow for patients with life threatening illnesses of getting listings on PBS.

Richard: Yeah. And do you think that when we talk about the hallmarks of cancer and we talk about the multifactorial causes that that we will have to be looking down the track at sort of multi factorial solutions. It won't just be one therapy, it will be multiple therapies used in use in tandem. And that in itself, again, I suspect, will cause challenges for the for the funders and the and the reimbursers. It's going to be a big problem.

Grant: So only one working day ago I was sitting down one of my PhD students who's just done a genetic screen with a new drug and found a potential new target where you might combine two drugs together to turn on, you know, really important protein in cancer. And I said to her, you know, this is great. You know, we're going to have to work out if this really looks as promising as this initial screen suggests. So there's still more science to do. But I said to her, one of the things I need to do, though, is to think about, well, you're talking about putting two drugs together, neither of which is currently approved. And that is a challenge.

So, as you say, cancer is complex. We have to put different approaches together to get the best effect. And sometimes that will be putting one or two drugs together or maybe even more that are not yet listed. And to get the evidence for that is challenging. And we need to be clever about the way we develop drugs so that we can get those very effective combination treatments, which for rare cancers is going to be very important through as quickly as we can.

So, yes, so this is the clinician and the PhD science. A student, I'm thinking big. We've got to think big because it's about patients. I want to encourage her to think about what she can do for patients. But I also need to think about, well, how would we speed up putting these two unapproved drugs together? And so, yeah, we have a lot of a lot of challenges in our system, I think, to the need for reform.

Richard: Yeah. And it does seem to me that sometimes the way that we the way that the, if you like, mass media communicates cancer oversimplifies it. And I always think when it's going out to the public, it's also going out to our politicians. And we have to be we have to be a bit more astute about educating people in Canberra and Spring Street and Macquarie Street and every other street around the country, that this is not a this is not a one cancer. It's not a one trick pony. It's a very complex beast.

My last question is, we'll be hopefully sitting here in ten years' time and cancer knowledge and treatment will have moved on. What how do you where do you think will be with it in in ten years' time? And you strike me that you would be optimistic. But just how good how close will we be to chronic disease or cures?

Grant: Well, I think the first thing is there'll be things we're doing in ten years that are not apparent today. And that's why it's so important to have a research led clinical system so that you can adapt new evidence, new discoveries, new ways of thinking quite quickly into benefits for patients. So I'm very confident we'll have continued improvement in cancer outcomes.

And that's, you know, it's not just the discovery, science and new drugs, even though in my field of melanoma research, we've now seen a 50% reduction in age adjusted mortality since the introduction of the new drugs for melanoma. It's a phenomenal, phenomenal outcome. So drugs are contributing substantially in blood cancers, breast cancer and others. That's contributed a lot as well. So we'll also, though, continue to improve our early detection. So lung cancer screening is right on the agenda now. So that's going to help a lot because lung cancer is our biggest killer, unfortunately, of all the cancer types. So detecting lung cancer early with a screening program and of course, continuing to prevent cancer wherever we can.

We need to get people's body mass index down, you know, deal with the obesity problem. Exercise, you know, is useful in in other means as well in directly to affect to effect cancer. But not only that, you know, UV radiation from the sun, looking carefully at our diet, increasing fruit and vegetables in our diet, increasing fibre, you know, in our diets, because colorectal cancer remains, you know, a huge problem.

You know, the most common cancer in our community. And, you know, we will see across those multifaceted approaches improvement. I do think that the relative impact of discovery, science and drugs, they will grow. So getting access to those new treatments is going to be very important.

And, you know, what really excites me is new ideas that we're not using today that will start to come through. You know, one thing, for example, we're very interested in and many others at the moment is how a cancer cell can change. It gets exposed to a drug, and there's a process called plasticity where it changes its properties, allowing it to survive and not die the cancer treatment. So understanding the fundamental mechanisms of that switch, that plasticity that. Pizza cells can utilize to stay alive rather than die is is, I think, a really interesting area. So maybe we'll have some treatments that fundamentally target that process could be a game changer. That's one idea. I might be wrong. That may never deliver the goods.

But what we do know is that prevention, early detection, better treatments have delivered the goods 50%, five year survival up to 70%, five year survival in my career. And I think that's going to continue.

Richard: Yeah, fantastic. that's a great note to end on. So thank you, Grant.

Grant: Thank you, Richard. It's been very enjoyable chatting with you today.